Letter from the Editor

Dr. D. G. Jain

As a new decade dawns and I assume charge as editor of India's widely read premier medical journal for practicing clinicians/internists, post-graduate students, medical teachers and researchers – the *Journal, Indian Academy of Clinical Medicine (JIACM)* – I feel humbled and honoured to have been entrusted with this daunting yet academically enriching task of encapsulating in each issue the nectar of distilled scientific knowledge from all spheres of clinical medicine which is currently relevant to the needs of all those involved in patient care. To have been associated with the editing of this journal ever since its revamp by Dr. (Prof.) A.K. Agarwal over a decade ago, I must admit that it has been a unique and immensely satisfying experience in more ways than one.

My immediate predecessor Dr. B.B. Rewari deserves enormous appreciation and thanks for his focussed efforts in bringing out the *JIACM* to the present standards. I wish to place on record Dr. Rewari's skills as an able editor and publisher who managed all the affairs of the *Journal* with dexterity and swiftness. I have enjoyed a very memorable bonhomie with him as editor of the *JIACM* during the last six years.

Dr. Alladi Mohan

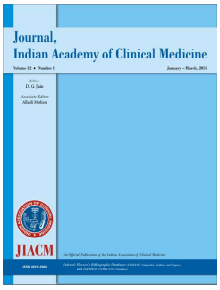
The *Journal, Indian Academy of Clinical Medicine* would never have seen the light of day had it not been for the mammoth efforts of Dr. (Prof.) A.K. Agarwal, our former editor. I must confess that both Dr. Rewari and myself have had the constant, gentle, and sometimes stern (!) guidance of Dr. Agarwal from time-to-time. All of us at the *JIACM* cherish his candid views and suggestions. He is a constant source of inspiration and we have benefitted from his help and wisdom at all times. However, I am glad that I will not miss Dr. Agarwal's or Dr. Rewari's unflinching support and guidance as they continue to be passionate about seeing a world class medical journal in the *JIACM*. Members of the Governing Body of the *Indian Association of Clinical Medicine* have always been very encouraging and generous in all matters related to the *JIACM* and their help and support is greatly appreciated. While carrying the torch forward, I look forward to seeing the *JIACM* indexed in PubMed in the near future.

It is with great pleasure that I welcome on board Dr. Alladi Mohan from the holy city of Tirupati (Andhra Pradesh) as associate editor, and Dr. M.P.S. Chawla from New Delhi as editorial secretary. I am sure that their infective enthusiasm and dynamism will bear delicious fruit and help in the growth and outreach of the *JIACM* as an outstanding journal in the field of clinical and applied medicine.

Dr. M.P.S. Chawla

Producing the *JIACM* has always been fine-tuned teamwork and I have deep appreciation for all our team members who continue to work incognito backstage. My sincere thanks go to Dr. Pushpa Yadav – who has been painstakingly assisting in editorial work since the last many years – and Dr. S. Anuradha and Dr. Alladi Mohan who served as editorial secretaries in succession. I am indebted to our production team – Mr. Sanjeev Choudhary of Initials (typesetting and designing), Mr. Yogesh of Tan Prints (printing), Mr. Vijay (binding), Mr. Yashpal Satmukhi (office management), and Mr. P.R. Mishra (computer and logistics) – who continue to coordinate all the technical work of the *Journal*.

As you are already aware, without financial support no scientific publication can survive, and the *JIACM* is no exception. As such, the commitment and contribution of the Indian pharmaceutical industry towards the cause of continuing medical education in the form of advertisements in this journal is positively appreciated. I hope we shall continue to receive this much needed support for furthering the cause of clinical medicine and research by way of regular advertisements in future issues of the *Journal* also.



Finally, the *JIACM* looks forward to the stimulating indulgence of its readers who have always been a source of inspiration and encouragement with their constructive criticism, and authors who contribute by way of Lead Articles, Original Articles, Review Articles, Case Reports, PG Clinics, Images in Clinical Medicine, Viewpoint, Letters to the Editor, etcetera. I am grateful to our distinguished prime reviewers/ referees (whose names appear elsewhere in this issue) for graciously giving their invaluable time in the form of expert advice, guidance, and suggestions which have helped the *Journal* in achieving and maintaining high academic standards.

May the *Journal, Indian Academy of Clinical Medicine* continue to be a catalyst in raising the bar for the teaching and practice of clinical medicine in India and help in sharpening and augmenting our clinical acumen and professional skills.

I wish you all insightful reading and a very happy new decade!

– Dr. D. G. JAIN

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Journal, Indian Academy of Clinical Medicine

JOURNAL, INDIAN ACADEMY OF CLINICAL MEDICINE

is edited by

DG Jain

for the

Indian Association of Clinical Medicine

Headquarters :

Postgraduate Department of Medicine, SN Medical College, Agra – 282 002 (U.P.)

Editorial/Mailing Address

Barnala House, 867, Guru Gobind Singh Marg, New Delhi – 110 005.
Tel.: (011) 23671305 E-mail: sanjeev.initials@gmail.com, iacmjournal@gmail.com

Typesetting by: Initials, Tel.: 2354 7929 E-mail: sanjeev.initials@gmail.com

ISSN 0972-3560

RNI Regn. No. : DELENG/2000/1686

Indexed in Elsevier's Bibliographic Databases

Indexed in IndMED (http://indmed.nic.in)

"Bibliographic details of the journal available in ICMR-NIC's database – IndMED (http://indmed.nic.in). Full-text of articles (from 2000 onwards) available on medIND database (http://medind.nic.in)."

Indexed Internationally on Elsevier's Bibliographic Databases (a leading indexing service) from January 2005. These databases include EMBASE, Compendex, Geobase and Scopus (Science Direct Navigator).

Printed and published by Dr. D. G. Jain
for and on behalf of the Indian Association of Clinical Medicine
and printed at Tan Prints, A-47, Mangolpuri Industrial Area, Phase II, Delhi,
and published from Barnala House, 867, Guru Gobind Singh Marg, New Delhi – 110 005. Editor: Dr. D. G. Jain

Indian Association of Clinical Medicine

Headquarters:
Postgraduate Department of Medicine, S.N. Medical College, Agra – 282 002 (U.P.)

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VIEWPOINT

JIACM 2011; 12(1): 13-4

Orphan Diseases – Industry Exploitation

*BM Hegde**

"All good is hard. All evil is easy. Dying, losing, cheating, and mediocrity is easy. Stay away from easy."

– Scott Alexande.

Foundation of modern medical science, if there is one, is very shaky. The 'gold standard' of medical science is only statistical – randomised controlled trials (RCTs) – used to test drugs and instruments. In short, if there is a science (I have shown elsewhere that there is no science of man) it is just statistical science and does not meet the strict standards of either science or technology, as defined by NASA-TRL or MSE, i.e., National Aeronautical and Space Administration's Technology Readiness Levels or Modern Systems Engineering. I have extensively written about the unscientific base of the RCTs both in my books and articles over the last four decades.

Even the President of NICE, which is the highest body to oversee drug research in the UK, Sir Michael Rawlins, in his Harveian oration at the Royal College, had this to say about RCTs: "*that randomised controlled trials (RCTs), long regarded as the 'gold standard' of evidence, have been put on an undeserved pedestal*". Sir Michael outlines their limitations in several key areas, arguing that a diversity of approaches should be used to analyse the whole of the evidence base[1]. This is bad news for the conventional thinkers, coming as it does from the highest level in their own backyard.

Using this kind of science, the industry tries to exploit the public to make money with all kinds of chemicals passed off as effective drugs! History tells us that Nujol, the useless byproduct of petroleum extraction, was the first anti-cancer drug and chlorpromazine (largactil) used extensively in psychiatry, is a by-product of rocket fuel extraction! Many of the present expensive anticancer chemicals have not even gone through the inadequate RCT test! Now my friends who hate me for writing that routine check of healthy individuals is dangerous will understand why I wrote what I wrote. Check-up means labelling, which is followed by drugging or intervening by other means. Most modalities of medical treatment, both using drugs and surgery, have no scientific base, although many of them seem to work through the very powerful placebo effect. Corrective surgery is an exception.

Most body parameters do change as there is a need for them to do so for reasons unbeknownst to us at the moment. Sugar, cholesterol, and blood pressures belong to that category. The surest way to get them back to *what we think* should be the normal is to change our unhealthy lifestyle. Interventions with drugs have a dubious reputation in this field. Lifestyle change is something that is universally useful. Instead of going for a check-up when one is *healthy*, it is safer to change one's lifestyle and try to live as close to nature as is possible, keeping one's mind filled with universal love, devoid of hatred, greed, jealousy, and anger. Heavy smokers and alcoholics need regular check-up as their body warning signals of diseases get blunted, anyway. Rest of us could make do with seeing doctors only at the first symptom of any change in our body. Symptoms denote the failure of our inbuilt repair mechanism, the immune guard. This also is due to wrong lifestyle these days.

The pharma industry could go to any extent to fool even the governments to sell their wares. A recent revelation in *The Guardian*, London, exposed one such heinous act that could have endangered and/or extinguished many lives already[2]. The European Union has defined some diseases as "Orphan Diseases" where the drug companies are not interested in finding a cure since the financial return might not be attractive. Companies finding out

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newer treatments for "orphan diseases" would get special incentives from the governments. Please note that the industry is very keen only on imaginary diseases (so called silent killers) that need lifelong drug therapy; the latter are their cash cows. Hypertension, diabetes, and dyslipidaemia are the three biggest milch cows.

It is now discovered that some drug companies have repackaged some of the old drugs in a new format and called them new drugs for "orphan diseases" and have milked the National Health Service of millions of pounds! *The Guardian* article gives graphic descriptions of the fraud going on. These so called *new drugs* could easily pass the RCT test to qualify them to have evidence-base. The tall talk about evidence-based medicine is as hollow as many of our claims to superiority to all other modalities of treatment like Ayurveda, homoeopathy, etc. In fact, most of them have better scientific base than our modern medicine. While US medical schools teach six months out of their four year MD course, the basis of other complementary systems, in India the cradle of the best medical wisdom – Ayurveda – we seem to be averse to teaching anything other than the unscientific modern medicine.

The result is that most of our graduates become good technicians mastering a couple of interventions to make money. Rest of them become researchers, doing RCTs for western drug companies, making tons of money in the bargain through the new Contract Research Organisations (CROs). One has only to see one of the modern prescriptions which reads like a laundry list with one beta-blocker, one ACE-inhibitor, one blood thinner, one sugar lowering drug, of course, one cholesterol lowering drug and many other drugs for every patient. There is NO science base for this kind of poly-pharmacy, not even the imperfect RCT to back such practices. Recent studies have shown that patient compliance in such poly-pharmacy is less than 23%. 77% of the recipients are, therefore, safe as they forget to take those tablets! God only can save mankind from human greed. The latter has invaded every sphere of human activity ranging from Spectrum 2G to patient care! "Do not make money in the sick room," wrote Hippocrates. We take our oath in his name when we graduate only to become hypocrites in later life!

"It is double pleasure to deceive the deceiver."

–Niccolo Machiavelli.

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1 Rawlins M. The Harveian Oration of 2008, De Testimonio. On the evidence for decisions about the use of therapeutic interventions. Royal College of Physicians, 2008.

2 http://www.guardian.co.uk/society/2010/nov/17/drugs-companies-exorbitant-profits-nhs.

ACKNOWLEDGEMENT

LIST OF *JIACM* REVIEWERS (2010)

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- Alladi Mohan (Tirupati)
- Annil Mahajan (Jammu)
- Anita Sharma (Dehradun)
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ORIGINAL ARTICLE

JIACM 2011; 12(1) : 15-20

Correlation of Intima Media Thickness (as a Marker of Atherosclerosis) with Activity and Duration of Rheumatoid Arthritis using Carotid Ultrasound

H Singh*, Mukesh Goyal**, J Sen***, Harish Kumar****, Rahul Handa*****, Susheel Garg******

Abstract

Background: Inflammation has a strong association with increased atherosclerosis in RA. Indirect evidence of accelerated atherosclerosis in RA comes from studies measuring carotid artery intima media thickness (CIMT).

Aims of the study: To study the correlation, if any, between inflammation (severity and duration) to intima media thickness (a marker of atherosclerosis).

Methodology: Carotid intima media thickness (CIMT) was measured in 90 patients of RA divided into three groups of thirty each based on duration of disease (less than two years, two to five years, and more than five years). Both common carotid intima media thickness (CCIMT) and total carotid intima media thickness (TCIMT, i.e., mean of values of CCA, ICA, and ECA). The values were compared to DAS-28 activity score. Ninety healthy subjects (age and sex matched) were taken as controls.

Results: The RA subjects had a CCIMT and TCIMT 0.80 ± 0.15 mm and 0.80 ± 0.15 mm respectively when compared to controls, i.e., 0.59 ± 0.11 mm and 0.58 ± 0.11 mm (p value < 0.001). Both CCIMT and TCIMT increased significantly with duration of disease but did not differ when compared to disease activity.

Conclusion: In view of relation to duration of disease, the physicians should regularly screen the established RA patients, so as to identify the evidence of atherosclerosis and manage it earlier.

Keywords: Rheumatoid arthritis, atherosclerosis, carotid intima media thickness (CIMT).

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder involving the joints (nonsuppurative proliferative synovitis) along with other organ involvement including blood vessels and heart[1]. RA is associated with disability, shortened life expectancy, and increased mortality as compared to the general population[2].

Cardiovascular cause is the leading cause of mortality in RA[3]. This increased cardiovascular risk in RA patients has been attributed to accelerated atherosclerosis which has been found to be independent of the traditional risk factors[4]. Inflammation[5], increased levels of homocysteine[6], homoeostatic imbalance[7,8], decreased mobility[9], low levels of antioxidants[10], side-effects of medication[11,12], and dyslipidaemia[13-16] have been attributed to cause accelerated atherosclerosis in RA. Amongst the above causes, inflammation has the strongest association with increased atherosclerosis in RA[17,18].

Indirect evidence of accelerated atherosclerosis in RA comes from studies using carotid artery intima media thickness (CIMT) as a marker of atherosclerotic burden and cardiovascular risk[19,20]. CIMT measurement is a non-invasive and economical test which is quite reliable and sensitive for assessment of atherosclerosis[21]. Increased atherosclerosis in carotid arteries holds true for atherosclerosis for multiple vascular beds including coronaries, and so measurement of carotid IMT is an important surrogate marker of increased cardiovascular risk including acute coronary syndrome[22].

There are only a few studies available which have studied the relationship of disease activity and duration of disease in RA patients with carotid artery intima media thickness (a marker of atherosclerosis). So a cross-sectional study was planned to study the correlation, if any, between inflammation (activity and duration) to intima media thickness (a marker of atherosclerosis).

Material and methods

This study was performed in rheumatoid arthritis patients

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(as per American Rheumatism Association revised criteria) reporting to our institute's Rheumatology Clinic. The patients included as subjects (after getting informed consent) were divided into three groups (of thirty subjects each) based on duration of disease. These were:

Group I – those subjects who had RA of less than two years

Group II – those subjects who had RA between two to five years

Group III – those subjects who had RA more than five years

Another 90 healthy subjects (age and sex matched) were taken into group IV as controls.

All subjects included were not known cases of IHD, did not suffer cerebrovascular events in the past, and did not have evidence of renal/liver/lung failure.

All subjects included in the study were evaluated for their disease activity using DAS 28 (disease activity score).

$DAS\ 28 = 0.56\sqrt{TJC} + 0.28\sqrt{SJC} + 0.70\ (\log ESR) + 0.014\ GH$

where,

- TJC is tender joint count
- SJC is swollen joint count
- GH is general health status as assessed by patient on visual analogue scale (VAS).

All subjects (including controls) underwent carotid sonography. The common carotid arteries (CCA) were examined bilaterally upto the bifurcation (including proximal part of internal carotid artery (ICA) and external carotid artery (ECA). The intima media thickness (IMT), plaque characterisation (including echotexture, calcification, and cavitation) were assessed – initially by gray scale USG and then followed by colour flow imaging. All measurements were taken in diastole, measured in the phase when the lumen diameter is at its smallest and IMT at its largest.

The results so obtained were subjected to student's t-test and chi-square test for statistical analysis.

Results

The study comprised of three groups (based on duration of disease). The following were the observations:

1. Demographic profile

a. Age

The mean age of each group was comparable (p value > 0.05) (Table I).

b. Gender

In the study group, there were 27 males and 63 females, i.e., male:female ratio was 1:2.4. The control group also had a similar male:female distribution (Table I).

2. Biochemical parameters

The groups were compared for various atherogenic biochemical risk indices. All groups were comparable – including the mean values of blood sugar and lipid profile (Table II). Despite normal mean values of lipids in the groups, 12 patients had evidence of dyslipidaemia (10 had hypercholesterolaemia, 6 had hypertriglyceridaemia, and 5 had elevated LDL levels).

3. Disease duration and activity

The disease activity, as per DAS 28, was comparable in all three groups (p value > 0.05) (Table III).

Although the mean values of DAS 28 were comparable across all the groups but on further subdivision, i.e., Group A – mild disease (DAS 28 = 2.6 – 3.2); group B – moderate disease (DAS 28 > 3.2 – 5.1) and group C – severe (DAS 28 > 5.1). These groups were not comparable in number (Table III).

4. Carotid intima media thickness (CIMT): Case vs. control

The mean value of common carotid intima media thickness (CCIMT) and total carotid intima media thickness (i.e., mean of total CIMT of CCA, ICA, and ECA) were significantly higher in the study group when compared to control group (p value < 0.001) (Table IV).

5. Relationship of intima media thickness with disease duration

a. Common carotid IMT (CCIMT)

The CCIMT ranged from minimum of 0.56 mm to maximum of 1.4 mm, the mean value of group I was 0.703 ± 0.09mm; of group II was 0.791 ± 0.146 mm and of group III was 0.91 ± 0.136 mm, the increase in CCIMT with duration was significant (Table V and VI) (p value <0.001).

Table I: Showing mean age and gender distribution.

Group	Age (in years)		Gender (number)	
	Range	Mean	Males	Females
Group I	18 – 65	44.8 ± 14.28	9 (30%)	21 (70%)
Group II	25 – 67	44.60 ± 11.63	10 (33%)	20 (67%)
Group III	30 – 75	46.4 ± 10.27	8 (26%)	22 (73%)
Group IV (Control)	24 – 75	45.29 ± 13.29	27	63

Table II: Showing atherogenic biochemical profiles (mean value).

Biochemical parameters	Group I	Group II	Group III
Blood sugar (mg%)	95.83 ± 17.45	91.33 ± 26.29	78.93 ± 15.60
Triglycerides (mg%)	150.6 ± 32.28	155.43 ± 84.24	141.43 ± 36.48
Cholesterol (mg%)	141.23 ± 29.95	164.86 ± 45.83	164.93 ± 24.46
HDL (mg%)	48.63 ± 9.3	40.86 ± 4.67	39.23 ± 4.21
LDL (mg%)	90.36 ± 17.77	81.00 ± 19.95	82.86 ± 22.12
VLDL (mg%)	29.93 ± 10.7	36.26 ± 14.92	41.53 ± 20.49

Table III: Showing disease activity.

Group	Mean duration of disease (in years)	DAS 28 score		DAS Activity (number of patients)		
		Mean	Range	2.6 – 3.2	> 3.2 – 5.1	> 5.1
Group I	1.04 ± 0.41	4.48 ± 0.98	2.54 – 6.83	6	16	8
Group II	3.31 ± 1.0	4.61 ± 1.32	2.34 – 6.89	4	16	10
Group III	11.26 ± 4.14	4.79 ± 1.22	2.45 – 6.77	4	16	12

Table IV: Showing CIMT.

Site	Study group	Control group (n = 90)	p
CCIMT (in mm)	0.80 ± 0.15	0.59 ± 0.11	< 0.001
Total CIMT (in mm)	0.80 ± 0.15	0.58 ± 0.10	< 0.001

Table V: Showing values of CCIMT and TCIMT.

	CCIMT		Total CIMT	
Duration wise	Range	Mean	Range	Mean
Group I	0.56–0.92	0.703±0.09	0.57–0.89	0.68±0.84
Group II	0.68–1.4	0.791±0.146	0.60–1.10	0.74±0.114
Group III	0.78–1.35	0.91±0.136	0.75–1.27	0.850±0.106

6 Relationship of intima media thickness with activity of RA

Based on DAS 28 i.e., disease activity score, each group was further studied as group A (2.6 – 3.1); group B (> 3.2 to 5.1) and group C (> 5.1). In these sub-groups the relationship of activity of RA with intima media thickness of carotids was studied (Table VII).

On comparison of various sub-groups A, B, and C to each other, the CCIMT and TCIMT were found to be statistically non-significant (p value > 0.05 in each).

Table VI: Showing carotid IMT.

Groups compared	p value	
	CCIMT	TCIMT
Group I and II	< 0.05	< 0.05
Group I and III	< 0.001	< 0.001
Group II and III	< 0.001	< 0.001

traditional risk factors for accelerated atherosclerosis. Studies by Chung *et al*[26] and Mahajan *et al*[20] did not find significantly correlated dyslipidaemia with accelerated atherosclerosis in RA patients, although Jonsson *et al*[27] and Roman *et al*[28] did show correlation of dyslipidaemia. Moradet *et al* showed decreased levels of HDL in women with RA[29].

Table VII: Showing intima media thickness relationship to severity of disease.

Severity of RA	No. of subjects	CCIMT		Total CIMT	
		Range	Mean	Range	Mean
Group A	14	0.57–1.00	0.78±0.14	0.59–0.97	0.75±0.12
Group B	46	0.56–1.40	0.81±0.18	0.57–1.27	0.76–0.11
Group C	30	0.61–1.06	0.81±0.11	0.60–0.91	0.76–0.10

7. Comparison of plaque positive with plaque negative group

Of the ninety subjects, there was evidence of plaque in fourteen subjects. The CCIMT was 0.95 ± 0.12 in plaque-positive group and 0.7 ± 0.14 in plaque-negative group (p value < 0.001) whereas TCIMT was 0.80 ± 0.11 in plaque-positive patient and 0.69 ± 0.17 in plaque-negative group (p value < 0.001).

Discussion

Atherosclerosis is an inflammatory disease and so there are striking parallels between the inflammatory and immunological mechanism operating in atherosclerotic plaque and in rheumatoid synovitis. The common pathogenic features in the affected tissues include an abundance of activated macrophages which release or induce inflammatory mediators, including cytokines (e.g., interleukin 1 and TNF), growth factors, adhesion molecules with matrix metalloproteinases, and an infiltrate of T-cells. RA and atherosclerosis are associated with elevated levels of acute phase reactants – C-reactive protein (CRP), serum amyloid A, erythrocyte sedimentation rate (ESR), fibrinogen, and secondary phospholipase 2[25].

The accelerated atherosclerosis has been reported in RA to be independent of traditional risk factors. In the present study, diabetes mellitus, hypertension, and smoking were exclusion criteria while the mean values of triglyceride, cholesterol, HDL, LDL, and VLDL were within normal range (Table II), thus our study was free of the effects of these

CIMT is a reliable marker for coronary atherosclerosis and peripheral vascular disease[30]. According to Homa *et al*, the intima media thickness of common carotid artery (measured at areas devoid of plaque) increases linearly with age from 0.48 mm at 40 years of age to 1.02 mm at 100 years of age (following a formula 0.009 x age + 0.116 mm)[24]. The mean age of the present study (including control group) was 45 years. So expected common carotid thickness was approximately 0.521 mm. In the present study, common carotid intima media thickness (CCIMT) in the control group was 0.591 ± 0.113 mm (almost nearing the homa equation, i.e., 0.521 mm) whereas the common carotid intima media thickness in RA was higher, i.e., 0.808 ± 0.154 mm (Table IV) p value < 0.001.

The mean total carotid intima media thickness (TCIMT) was calculated by taking the mean of all three dimensions of carotid, i.e., common, internal, and external on both sides[24]. The mean of total carotid intima media thickness in RA study group was 0.803 ± 0.154 mm when compared to the control group, i.e., 0.586 ± 0.104 mm (p value < 0.001) (Table IV). A similar observation has also been shown by Gonzalez *et al*[31] and Alkabbi *et al*[32] in their respective studies. In a recent Indian study, Mahajan *et al* have similar observations[20]. All the studies (including the present study) show a significantly higher value of CIMT in RA subjects than the normal population (i.e., non-invasive evidence of accelerated atherosclerosis).

The mean common carotid IMT was significantly higher in group III (disease > 10 years) when compared to group

I and II (p value < 0.001) (Table V, VII), thus suggesting that increasing carotid IMT increased with duration of disease. Gonzales *et al* in their study had found disease duration as one of the best predictor for the development of severe morphologic expression of atherosclerotic disease[31]. DelRincon *et al*[33] and Mahajan *et al*[20] also had similar observations. This may be due to more years of exposure to increased inflammation[5,10,13-16], and other factors like increased arterial stiffness[33] and prothrombotic markers in RA patients[35]. Role of inflammation as a basic pathogenic mechanism in atherosclerosis is well known[33]. Liuzzo *et al* found increased levels of unusual subsets of T-cells – CD4+, CD28 in 65% of patients with unstable angina, but not in patients with stable angina. These lymphocyte subpopulations were originally described in patients with RA and have been associated with presence of extraarticular especially vasculitis[36]. Shared immunological disease mechanisms in systemic autoimmune disorders and coronary vascular disease such as clonally expanded CD4+ and CD28 T-cells[36], systemic endothelial activation[37] and circulating immune complex[38], may be involved in the development of cardiovascular comorbidities in RA patients[4]. The presence of decreased insulin sensitivity and increased ceruloplasmin levels (antioxidant factor) have been attributed to atherosclerosis in RA[39].

The mean values of common carotid IMT for mild, moderate and severe activity sub-groups were 0.78 ± 0.14; 0.80 ± 0.18 and 0.81 ± 0.10 mm respectively; these values when compared with each other were found to be statistically non-significant (p value > 0.05) (Table VII), suggesting no correlation between disease activity at a particular time and carotid intima media thickness. Similar observations were presented by Jonsson[27] and Roman *et al*[28].

In the present study, when patients with plaque and those without plaque were compared for variables like demographic data, disease activity, and traditional risk factors, carotid IMT (common and total) were found to have significant association with plaque development (p value < 0.001). Various studies have also shown increased incidence of plaque, especially to age and carotid intima media thickness[20,27,31,33].

So, rheumatoid arthritis which is a chronic inflammatory disease mainly involving joints has been found to have accelerated atherosclerosis when compared to age and sex-matched controls. This effect of accelerated atherosclerosis in RA was found to be independent of traditional risk factors like diabetes mellitus, hypertension, smoking and dyslipidaemia. The study also shows a significant, i.e., directly proportional relation between carotid intima media thickness to longer duration of disease. But this study did not show significant relationship between activity of disease and carotid intima media thickness (maybe because it was a cross-sectional study). However, in view of the relation to duration of disease, the physicians should regularly screen the established RA patients so as to identify the evidence of atherosclerosis and manage it earlier.

Thus, prevention of cardiovascular disease in RA requires a combined approach incorporating cardiovascular risk factors screening and management, effective and sustained control of RA disease activity, a high index of suspicion and prompt investigation of suspected cardiac disease. The treatment of the underlying disease process, i.e., atherosclerosis, and preventing its acute complications present an enormous challenge and opportunity simultaneously.

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ACKNOWLEDGEMENT

LIST OF *JIACM* PRIME REVIEWERS (2010)

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ORIGINAL ARTICLE

JIACM 2011; 12(1): 21-5

Profile of Medical and Psychological Disorders in the Elderly Persons attending a Tertiary Care Hospital in Delhi

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Abstract

Background: *The elderly population is increasing rapidly globally, and presently, India has the second largest number of elderly persons. The population of the elderly has shown an increase from just 5.6 per cent in 1961 to 7.7 per cent in 2001. This has resulted in an increase in the burden of disease in the elderly due to various physical and mental ailments.*

Aims of the study: *To study the profile of medical and psychological disorders in the elderly persons attending the medical out-patient department in a tertiary care hospital.*

Methodology: *The study was conducted in the medical out-patient department of Guru Teg Bahadur (GTB) Hospital, Delhi, and a total of 200 consecutive patients, aged 60 years and above were enrolled. The data from these patients was collected by detailed history and physical examination as per the pre-designed proforma. The relevant investigations were done, wherever needed. The prevalence of depressive features was assessed by Beck's Depression Inventory (BDI).*

Results: *The mean age of our patients was 64.5 years and 61% were males. The prevalence of various medical disorders in this population was: chronic obstructive pulmonary disease - 41.5%, hypertension - 39.5%, coronary artery disease - 25.5%, diabetes mellitus - 17%, stroke - 6.5%, chronic kidney disease - 4.5%, pulmonary tuberculosis - 4%, chest infection (non-tubercular) - 4%, congestive heart failure - 3%, bronchial asthma - 3%, various types of cancers - 3% and cirrhosis of liver - 2.5%. Assessment of mental function revealed a mean BDI score of 15.4, and 31.2% patients had BDI score < 10, suggestive of depressive disorder.*

Conclusion: *The study shows high prevalence of chronic obstructive pulmonary disease, hypertension, coronary artery disease, and depressive disorders in the elderly persons attending a large tertiary care hospital in East Delhi.*

Key words: *Old age, disease pattern, psychiatric disorder, depression.*

Introduction

All over the world, the elderly population is growing continuously and it is projected that by the year 2025, majority of the elderly people worldwide will be residing in developing countries[1]. India is amidst a demographic transition with a trend towards an ageing population[2]. In India, the ageing population above 60 years has been estimated to almost double-up from 7.7% in 2001 to 12.30% in 2025 and the number of elderly people will be nearly 150 million[3,4].

With improving living standards come better health and easy access to medical services, leading to a decline in mortality rates and higher life expectancy. According to UN estimates, during the period 1995 - 2000 in India, the life expectancy of males stood at 62.3 years while that of females was 62.9 years. For the period 2020 - 25, the projected figures are 68.8 years for males and 72.1 years for females and for the period 2045 - 50 the estimates are 73 years for males and 76.9 years for females[1]. In the Indian scenario, like in many developing countries, health problems and medical care are the major concern among a large majority of the elderly. The elderly are more vulnerable to disease because of impaired physiological reserves and defense mechanisms. A nationwide survey from our country conducted by the National Sample Survey Organisation, reported that 45% of the elderly suffered from chronic illnesses[5]. The health problems in the elderly living in a rural area in West Bengal were studied by Chakraborthy, in which he found that 72.6% of the elderly (> 60 years) were suffering from chronic illnesses[6].

Hence, elderly population shall constitute a major chunk of the total population at any given time and would need a bigger share of the health care facilities. Hence it is important for any country to know the prevalence and the peculiarities of the common diseases among the

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elderly in their population. Hence, the present study was undertaken to know the pattern of various common diseases for which elderly patients seek medical attention in a medical out-patient department in the setting of a tertiary care hospital in East Delhi.

Materials and methods

The study was conducted in the medical out-patient department of Guru Teg Bahadur Hospital located in East Delhi. A total of 200 consecutive patients aged 60 years and above from either sex were enrolled and data from these patients was collected in the form of a detailed history and physical examination as per the pre-designed proforma. The relevant investigations were undertaken in all the patients, wherever needed. The diagnosis of various diseases was made as per the standard disease definitions corroborated with the relevant investigations. Hypertension was diagnosed according to JNC VII guidelines. Coronary artery disease was diagnosed by history, electrocardiogram, stress testing, or from coronary angiography reports already available with the patients. Patients were labelled diabetic if they fulfilled the ADA criteria on blood sugar levels. Chronic kidney disease was diagnosed as per National Kidney Foundation - K/DOQI guidelines when patients had evidence of structural renal disease on ultrasonography and/or abnormalities on urinalysis or deranged kidney function tests. Cirrhosis of liver was diagnosed as per ultrasonography and liver function tests. Pulmonary tuberculosis and other chest infections were diagnosed on chest skiagram findings corroborated with sputum examination. Stroke was confirmed by CNS imaging (CT scan/MRI). The prevalence of depressive features was assessed by Beck's depression inventory (BDI). The BDI score < 10 was taken as suggestive of depressive disorder. The data collected was analysed and the results were obtained as the percentage of total elderly patients for various diseases.

Results

The age of the patients ranged from 60 to 88 years with the mean age being 64.5 years. There were 122 (61%) males and 78 (39%) females. The prevalence of various medical disorders in this population was: chronic obstructive pulmonary disease (COPD) - 41.5% (n = 83), hypertension - 39.5% (n = 79), coronary artery disease - 25.5% (n = 51), diabetes mellitus - 17% (n = 34), stroke 6.5% (n = 13), chronic kidney disease - 4.5% (n = 8), pulmonary tuberculosis - 4% (n = 8), chest infection (non-tubercular) - 4% (n = 8), congestive heart failure - 3% (n = 6), bronchial asthma - 3% (n = 6), various types of cancers - 3% (n = 6) and cirrhosis of liver - 2.5% (n = 5). Assessment of mental function revealed a mean BDI score of 15.4 and 31.2% patients had BDI score < 10 suggestive of depressive disorder.

Discussion

Ageing process in itself rarely results in illness or death; however, morbidity and the rate of illness rise sharply with each decade, becoming very high after 70 years of age[7]. About 85 per cent persons have chronic problems of one kind or another and require frequent visits to doctors and hospital stays, but still about 80 per cent are able to move about on their own legs[7]. Common problems affecting the elderly include chronic bronchitis, arthritis, cataract, degenerative diseases of heart, diabetes mellitus, nutritional problems, etc. Besides this, the mental health needs of the elderly are substantial[7]. Emotional and mental illnesses escalate over the course of life. Depression and hypochondriasis commonly accompany many physical ailments of old age. Organic brain disorders also show increased incidence in old age[7]. In our study, chronic obstructive pulmonary disease, hypertension, coronary artery disease, and depressive disorders were the most common diseases for which the elderly urban population in East Delhi attended the medicine OPD.

Chronic obstructive pulmonary disease affected 41.5%, and bronchial asthma 3% of all the elderly patients presenting to the medicine OPD. COPD is particularly important as this is a major cause of hospitalisation and mortality among the elderly and has significant financial implications for the society. The association of ageing and COPD is a result of the cumulative effects of smoking and environmental exposure in susceptible individuals. For this reason, a greater proportion of elderly patients with COPD are likely to have more severe disease than the younger age groups. COPD is the only major disease with increasing mortality, and by the year 2020, it will be the third most important cause of death worldwide[8]. Death in patients

with COPD is typically due to acute respiratory failure, pneumonia, lung cancer, cardiac disease, or pulmonary embolism.

In various studies, the prevalence of COPD in subjects aged over 65 years is 6 – 15% in women and 7 – 34% in men, and the prevalence of asthma is respectively 7% and 3%[9]. The variability in these figures, especially in relation to COPD, is probably due to the under- or misdiagnosis of respiratory diseases and limited use of spirometry in this category of patients. It is commonly believed, even amongst geriatricians, that elderly patients cannot perform spirometry properly. In addition, elderly patients often have concomitant diseases with similar clinical symptoms that may confuse the diagnosis[9,10]. COPD in the elderly has been shown to adversely affect the quality of life. In a study to investigate the factors influencing quality of life (QoL) and functional status in elderly COPD sufferers, it was shown that a decrease in FEV_1 is the factor most strictly related to the deterioration of QoL in COPD patients[11].

Hypertension was the primary diagnosis in 39.5% of the elderly patients attending the medicine OPD. Studies from India about the prevalence of hypertension showed a linear increase in blood pressure as the age advances, with casual blood pressure being high in 15% of all surveyed; 34.5% in those over 55 years, 38.5% in those over 65 years, and 44% in those over 70 years[12]. Hypertension is a powerful, independent, and modifiable risk factor for the development of all the major clinical manifestations of atherosclerotic cardiovascular disease that commonly afflicts the elderly, including coronary artery disease, stroke, peripheral artery disease, heart failure, renal failure, and dementia[13]. Blood pressure reduction has been shown to be effective in preventing major vascular events including stroke and heart failure in hypertensive individuals[14]. However, it has remained unclear whether treatment of hypertension in the very elderly is beneficial[15,16]. The main differences between the treatment of older as opposed to younger individuals are careful monitoring of elderly patients towards postural and postprandial hypotension before initiation of treatment. Elderly patients may have sluggish baroreceptors and sympathetic nervous responsiveness as well as impaired cerebral autoregulation. Thus the reduction of blood pressure should be gradual to minimise the risk, and these patients may require lower initial doses of medication. Existing data, specifically the Hypertension in the very elderly trial (HYVET) trial results, indicates an overall benefit of hypertension treatment in the very elderly[17]. Treatment of hypertension is likely to prevent heart failure, reduce stroke and prolong life. The target blood pressure in the very elderly needs to be further established, but based on the HYVET, a blood pressure target of less than 150/80 mmHg seems both effective and safe[17].

Coronary artery disease was the primary diagnosis in 25.5% and congestive heart failure was present in 3% of the individuals. Coronary artery disease is extremely common among elderly people and accounts for half of all deaths in those who are above 65 years[18]. There are some special features of coronary artery disease in the elderly such as the atherosclerosis is more severe and is also more diffuse[19]. The manifestations of cardiovascular disease also differ in elderly patients over 75 years of age when compared with a younger patient population[20]. Although chest pain is the most common manifestation of myocardial ischaemia, angina may have atypical features in the elderly population and ischaemia may manifest predominantly as fatigue or dyspnoea, occasionally occurring at rest.

The treatment of coronary artery disease in elderly subjects can be difficult because the anticipated benefits and risks of the various treatment options are often altered by the presence of co-morbid conditions. Unfortunately, the data available to guide therapy and predict outcomes in the elderly population are relatively limited, given that advanced age has been an exclusion criterion in most large randomised cardiovascular trials. The elderly patients benefit as much as the younger ones, if not more, in reducing the incidence of death or nonfatal myocardial infarction. Patients with stable symptoms and low-risk stress test results (cardiac mortality rate ≤ 1%) should be maintained on medical therapy, given the higher risk of revascularisation in elderly patients.

Diabetes mellitus was the reason for consulting a physician in 17% of the elderly attending the medicine OPD. Globally, diabetes mellitus affects 10 – 20% of the

elderly in the age group 65 – 74 years and about 40% of elderly over the age of 80 years[21]. In India, the prevalence of diabetes in the elderly has been variably reported from 27.1% in a study conducted in Chandigarh in North India[22] to 12.1% in a study conducted in South India[23]. As the average life expectancy has increased in India, many older diabetic patients can be expected to live a decade or more after diagnosis, so clinicians must carefully weigh the potential risks and benefits of available interventions on reducing the excess morbidity and mortality associated with diabetes.

The management of older adults with type 2 diabetes requires careful consideration of the effects that advancing age and changes in health status can have on the competing risks and benefits of therapeutic interventions. Although tight glycaemic control is not always an appropriate treatment goal, many older people with diabetes are undertreated and could benefit from improved glycaemic control and more aggressive management of risk factors for macrovascular disease. Older patients may be more predisposed to hypoglycaemia because of poor or erratic nutritional intake, changes in mental status that impair the perception or response to hypoglycaemia, increased polypharmacy, and noncompliance with medications, dependence or isolation that limits access to early treatment for hypoglycaemia and impaired renal or hepatic metabolism[24]. Also, presence of co-morbid conditions can mask or lead to misdiagnosis of hypoglycaemic symptoms (dementia, delirium, depression, sleep abnormalities, seizures, myocardial infarction, and cerebrovascular accident). Chronic complications in elderly patients with diabetes include cardiovascular disease with twice the mortality rate of age-matched controls without diabetes. According to an estimate, the life expectancy of patients who develop diabetes after the age of 65 is shortened by at least 4 years[25].

In our study, 31.2% of the patients attending the medical OPD had concomitant depression, thus significantly affecting the functional status in ill elderly patients. Depression in old age is reported to occur in 2 – 5%, and depressive symptoms occur in as much as 50% of persons aged 65 and above in the community[26]. Patients with chronic medical illnesses are known to have a high prevalence of co-morbid depression as the concurrent physical illnesses increase the vulnerability to mental health illnesses[27]. The rates of depressive disorders amongst hospitalised elderly have been reported to be 10 times greater[28]. Also, the depressive disorders are inadequately diagnosed, more so in the elderly with medical problems[29]. In a study among all the geriatric clinic attendees, 23% of patients had depressive symptoms, and 18% had a definitive depressive disorder; but surprisingly, none of the geriatric physicians even from tertiary clinic setting had made a diagnosis of depression in them[30]. In addition, advancing age is often accompanied by loss of key social support systems due to the death of the spouse or siblings, retirement, and/or relocation of residence. Because of their change in circumstances and the fact that they are expected to slow down, doctors and family may miss the diagnosis of depression in elderly people, delaying effective treatment. Epidemiological and clinical studies consistently indicate that depression adversely affects the lives of older adults[27]. The confounding relationship between atypical phenomenology of depression in the elderly and the co-occurrence of physical illnesses influences both diagnosis and treatment, presenting a unique clinical and therapeutic challenge[30]. So, looking for the associated depression and treating it may substantially improve quality of life in the elderly patients.

Stroke (6.5%), chronic kidney disease (4.5%), pulmonary tuberculosis (4%), chest infection (non-tubercular) (4%), and cirrhosis of liver of all aetiologies (2.5%) constituted other reasons for elderly patients to attend the medicine OPD. The management of these illnesses should be done as per the standard guidelines with special focus on adjusting drug doses, to be vigilant for the side-effects and drug toxicities and to watch for the associated co-morbid conditions.

Conclusion

This study shows a high prevalence of chronic obstructive pulmonary disease, hypertension, coronary artery disease, and depressive disorders in the elderly persons attending the medical out-patient department in a tertiary care hospital in East Delhi. However, larger studies are required

to elucidate the exact magnitude of the problem. Further, the management protocols for these diseases in the elderly would be required, taking into consideration the physiological changes that occur with ageing per se and other co-morbidities in the elderly population.

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ANNOUNCEMENT

Best Paper Awardees of IACMCON-2010 held at Kolkata

Mrs. Uma Bansal - Prof. B.C. Bansal Best Paper Award

First Prize:	Dr. Rajesh Singh Laishram, Imphal
Second Prize:	Dr. S.C. Chaudhary, New Delhi
Third Prize:	Dr. Geeta A. Khwaja, New Delhi

Dr. N.L. Patney Best Paper Award (Free Paper)

First Prize:	Dr. Swarup Kar, Dibrugarh
Second Prize:	Dr. Deeptarka Roy, Kolkata
Third Prize:	Dr. H.K. Agarwal, Rohtak

Dr. G. Narsimulu Best Paper Award (Poster Session)

First Prize:	Dr. R. Jhamb, New Delhi
Second Prize:	Dr. A. Gupta, Agra
Third Prize:	Dr. Deep Jyoti, Dibrugarh

ORIGINAL ARTICLE

JIACM 2011; 12(1): 26-7

Medical Negligence

*Shibani Mehra**

Abstract

A study to analyse the level of awareness regarding medical negligence among doctors who are providers of medical services and among patients who are consumers of those services keeping in mind the judgement of the Honourable Supreme Court of India wherein the medical services provided by the doctors have been included in the pursuit of Consumer Protection Act. A glance at the emerging scenario provides no reason for the common people to indulge in euphoria or the medical professionals to sink in deep depression.

Intorduction

The classical concept of a doctor-patient relationship born in the golden days of family physicians has undergone a drastic change due to dramatic advancement in medical technology, availability of sophisticated imaging systems, high tech electronics, and preponderance of new diseases. With the immense strides in technology, health care has emerged as a profitable sector attracting investors from varied backgrounds. Like other professionals, the medical men are liable to pay damages for their negligence under the *law of torts*. However, the accountability of the doctors under the law of professional negligence has emerged as a debatable issue among the medical fraternity all over the country after the enactment of the Consumer Protection Act 1986, which has not only changed the law of medical negligence, but created an inexpensive and speedy remedy against medical malpractice. The judgement of the Honourable Supreme Court of India in Indian Medical Association vs VP Shantha AIR 1996 SC for the first time held that medical services ought to be brought under the purview of Consumer Protection Act since the patient is like a consumer and the discharge of duty of the doctor is a service. This has given a new dimension to the law of medical negligence and compensation by transforming the law from 'a sealed book to a living letter' and by making the law as 'inheritance of the poor from patrimony of rich'. The dictum of the Apex Court has been greeted with mixed feelings by common people on one side and the medical profession on the other.

Materials and methods

A sample group of eighty was selected which was divided into two equal groups. Group one consisted of doctors and group two consisted of patients. The doctors selected for the sample belonged to those who were gainfully employed/practicing in the private sector and owe a much greater responsibility towards their patients than those doctors who were rendering free services to their patients and draw their salary from the government.

The patients selected for the sample belonged to that economic strata of society which could afford the services of private doctors. It was ensured that those who were given the proforma for filling were literate and could understand the contents after little explanation. Lawyers were eliminated assuming they would have knowledge of the subject.

In order to study the awareness regarding medical negligence and its consequences among doctors and patients, a questionnaire was prepared consisting of two parts. Part I contained personal information and part II contained questions which covered various aspects of medical negligence, including case studies based on reported judgements of the Hon'ble Supreme Court of India. While soliciting personal information, the level of education of the sample was sought, so as to analyse whether education played a role in the level of awareness of the rights and duties of the sample. The other aspect which was covered was whether the individual was gainfully employed to see if he or she could afford the cost of care by oneself or had to be dependent on the

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family. The proforma highlighted various aspects of the Consumer Protection Act (CPA), namely, what negligence is, the amount of care, the relationship between the doctor and the patient, the type of consent and the level of knowledge the doctor should possess before he can actually be allowed to practice. This also included some case studies where the evaluator was allowed to judge whether the act or procedure performed was right or wrong. The questionnaire was duly filled by the participants (both doctors and patients). Data was analysed using Kappa and Chi Square test which are non-parametric tests because of the skewed distribution of the data. The descriptive data indicating the qualification and the type of employment was not taken into consideration while studying the data as most of them belonged to the educated and the gainfully employed category.

Results

A very large number of doctors are aware of the fact that medical negligence or misconduct on their part can attract compensation to the injured as well as a penal action wherein negligence will depend upon the facts and circumstances of each case. They believe that they are expected to take only reasonable care and possess reasonable knowledge of their field which any prudent person in his place would have possessed. On the other hand, the consumer is aware of the fact that any medical unjust done to him can be lawfully questioned; also the expectation level of the services provided by the doctors is high. The fact that the doctor-patient relationship is of contract was not very clearly opined and was greeted with mixed feelings of human and friendly nature both by doctors as well as patients. Doctors feel that the informed consent which the patient and the attendant has to sign should highlight both the pros and cons of the procedure. However, sometimes there is a remote possibility of risk if everything is disclosed to the patient, and which could lead to a high degree of mental stress and trauma to the patient, then the doctor can be judgemental and may opt to reveal such risks only to the attendant.

Discussion

Doctors and patients are two extreme points of the same pole and there is no meeting of their minds. However, it is pertinent to mention that there is one common characteristic present in the two extremes, i.e., most of them are unaware of the correct position of the problems they face day in and day out in regard of the law of torts and criminal justice system. While the patients want the best of care and attention from the doctor on one hand, the doctor expects that all his mistakes should be overlooked as human judgemental errors on the other hand. It is therefore important for both doctors and patients to realise and become aware of their own rights and duties, i.e., the rights which they exercise over the other set, and the duties which they are obliged to perform.

Recommendations

To minimise risk of litigation, preventive steps could be taken at three different levels:-

1. Primary prevention would protect against a complaint being filed. This can be managed by educating the public about the limitations of medical science and the inherent risks involved in surgical and medical treatment of any person on one hand and making continued medical education programmes necessary for the doctors to attend to keep them at par with the latest trends in the medical profession.
2. Secondary prevention would protect against the defendant from being held negligent by doing proper documentation, preservation, and supply of medical records and obtaining a legally valid consent from the patient.
3. Tertiary prevention would protect against direct financial consequence in case compensation is awarded. A professional indemnity insurance should be made mandatory for all practicing consultants to meet the claims of compensation which may be awarded against a doctor for medical negligence which is called deficiency in service under the Consumer Protection Act 1986.

REVIEW ARTICLE

JIACM 2011; 12(1) : 28-31

Brugada Syndrome Revisited

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Abstract

Brugada syndrome is a distinct syndrome consisting of 'rsr' pattern, persistent ST-segment elevation on ECG, and sudden cardiac death. It is an autosomal dominant sodium ion channelopathy and associated with mutation(s) in the gene named SCN5a, located on the short arm of the third chromosome (3p21) that encodes for the sodium ion channel in the cell membranes of the muscle cells of the heart (the myocytes). Both ECG and clinical features are important to establish the diagnosis of Brugada syndrome. Pharmacologic (antiarrhythmic) therapy has been tried, only an implantable cardioverter-defibrillator (ICD) has proven efficacy.

Key words: Sudden cardiac death, 'rsr' pattern, implantable cardioverter-defibrillator.

Introduction

In 1992[1], Brugada and Brugada described a distinct syndrome of *rsr* pattern, persistent ST-segment elevation, and sudden cardiac death. Pathophysiologically, it is believed to be a sodium channelopathy. It is now recognised as an important cause of sudden cardiac death. Sudden cardiac death (SCD) is defined as unexpected natural death from a cardiac cause occurring within a short time (generally within 1 hour of onset of symptoms) in a person without prior conditions that would appear fatal. Important genetic causes of SCD are: long QT syndrome, Brugada syndrome, hypertrophic obstructive cardiomyopathy, arrythmogenic right ventricular dysplasia, catecholinergic polymorphic ventricular tachycardia, and WPW syndrome. Brugada syndrome constitutes 4 - 12% of all SCD and 20% of SCD in structurally normal hearts[2]. Studies in heterogeneous populations suggest that the majority of affected individuals are Asian[4]. This syndrome is characterised by a coved-type ST-segment elevation in the right precordial leads of the electrocardiogram (ECG)[2]. The Brugada syndrome has a genetic basis that has been linked to mutations in SCN5A, the gene that encodes the β-subunit of the sodium channel. The average age at the time of initial diagnosis or sudden death is 40 ± 22 years[2].

Genetics and pathophysiology

Approximately 20% of the cases of Brugada syndrome have been shown to be associated with mutation(s) in the gene that encodes for the sodium ion channel in the cell membranes of the muscle cells of the heart (the myocytes). The gene, named SCN5A[6], is located on the short arm of the third chromosome (3p21). Loss-of-function mutations in this gene lead to a loss of the action potential dome of some epicardial areas of the right ventricle[7]. This results in transmural and epicardial dispersion of repolarisation[8,9]. The transmural dispersion underlies ST-segment elevation, and the epicardial dispersion of repolarisation facilitates the development of phase 2 re-entry, to precipitate ventricular tachycardia and/or fibrillation that often results in sudden cardiac death[8,9]. This condition is inherited in an autosomal dominant pattern and is more common in males. Genetic testing for Brugada syndrome is clinically available and may help confirm a diagnosis in patients suspected of having Brugada syndrome, as well as to differentiate between relatives who are at-risk for the disease from those who are not at risk.

Clinical manifestations

History

Syncope and cardiac arrest[2,3] are the most common clinical manifestations leading to the diagnosis of Brugada syndrome. Nightmares or thrashing at night may occur. However, sometimes no symptoms have been recognised and the diagnosis of Brugada syndrome is based on a routine ECG showing ST-segment elevation in leads V_1 through V_3. A family history of sudden cardiac death is common, though not essential for the diagnosis as the syndrome can occur sporadically. The context of the

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cardiac event is important. In many cases, cardiac arrest occurs during sleep or rest. Cases occurring during physical activity are rare. In addition, fever is often reported to trigger or exacerbate the clinical manifestations of Brugada syndrome.

Physical examination

The physical examination is usually normal in patients with the Brugada syndrome. Nevertheless, physical examination is required to rule-out other possible cardiac causes that may be associated with syncope or cardiac arrest in an otherwise healthy patient, e.g., heart murmurs from hypertrophic cardiomyopathy or from a valvular disease or septal defect.

Diagnostic criteria

Brugada syndrome is not yet well defined and establishing the diagnosis is often difficult. Both ECG and clinical features are important[10, 11] to establish the diagnosis of Brugada syndrome. The morphology of the Brugada syndrome electrocardiogram is classified into three types:

Type 1: In a consensus report from the study group on the molecular basis of arrhythmias of the European Society of Cardiology, it was proposed that type 1 Brugada syndrome should be strongly considered in patients who meet the following criteria[10]:-

- Appearance of type 1 ST-segment elevation (coved type in type 1, the ST-segment gradually descends to an inverted T wave) in more than one right precordial lead (V1 – V3) in the presence or absence of a sodium channel blocker plus at least one of the following (Fig. 1).
  - a Documented ventricular fibrillation
  - b Self-terminating polymorphic ventricular tachycardia (VT)
  - c Family history of sudden cardiac death at < 45 years
  - d Type 1 ST-segment elevation in family members
  - e Electrophysiologic inducibility of VT
  - f Unexplained syncope suggestive of a tachyarrhythmia
  - g Nocturnal agonal respiration

Type 2 and type 3: In type 2, the T wave is positive or biphasic and the terminal portion of the ST-segment is elevated ≥ 1 mm. In type 3, the T wave is positive, and the terminal portion of the ST-segment is elevated < 1 mm.

- Appearance of type 2 or type 3 ST-segment elevation (saddle-back type) in more than one right precordial lead under baseline conditions, with conversion to type 1 following challenge with a sodium channel blocker (Fig. 1).
- Plus one of the features (a-g) described above.

Drug challenge: Among patients with the Brugada type 2 or type 3 ECG pattern, the Brugada type 1 ECG pattern can occasionally be unmasked by sodium channel blockers (e.g., flecainide, procainamide, ajmaline, pilsicainide)[12-14]. The reported sensitivity of pharmacologic challenge with these drugs has been variable ranging from 100 per cent[13] to as low as 15[15] per cent .

The recommended doses by the second consensus conference on Brugada syndrome were:

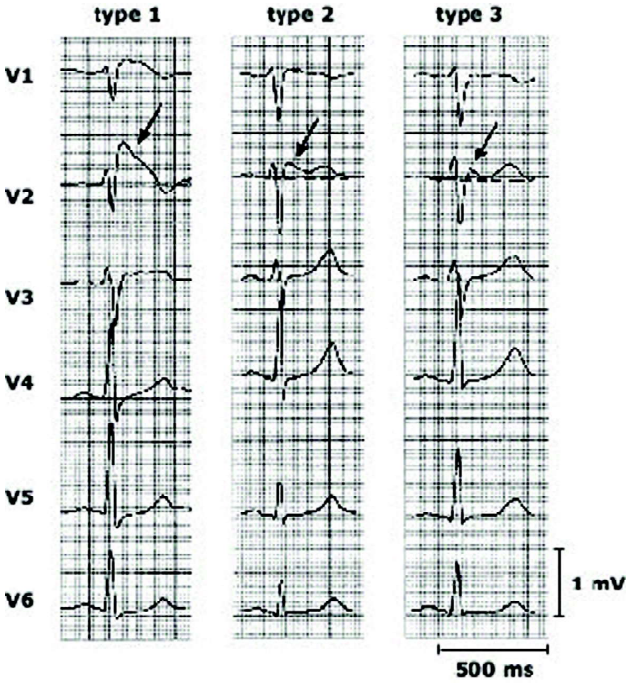

Fig. 1: *Patterns of ST-segment elevation in Brugada syndrome. Three distinct types of ST-segment elevation have been described. In type 1, the ST-segment gradually descends to an inverted T wave. In type 2, the T wave is positive or biphasic, and the terminal portion of the ST-segment is elevated 1 mm. In type 3, the T wave is positive, and the terminal portion of the ST-segment is elevated < 1 mm.*

- Flecainide – 2 mg/kg over 10 minutes intravenously or 400 mg PO.
- Procainamide – 10 mg/kg over 10 minutes intravenously.
- Ajmaline – 1 mg/kg over five minutes intravenously.
- Pilsicainide – 1 mg/kg over 10 minutes intravenously.

The test should be performed under continuous ECG monitoring. Indications for termination are development of a diagnostic type 1 Brugada ECG, a ≥ 2 mm increase in ST segment elevation in patients with a type 2 Brugada ECG, the development of ventricular premature beats or other arrhythmias, widening of QRS 30% above baseline.

Treatment

Although pharmacologic therapy has been tried, only an implantable cardioverter-defibrillator (ICD) has proven efficacy.

Pharmacologic therapy: As ICD use is too expensive in most Indian patients, relatively high doses of quinidine (1,200 to 1,500 mg/day) may be beneficial. Antiarrhythmic drugs may have a role in patients with an ICD who continue to have frequent discharges. Amiodarone is usually the drug of choice, but quinidine or hydroquinidine may be an alternative in patients with BS[16-18].

The 2006 ACC/AHA/ESC guidelines include the following recommendations regarding treatment of the electrical storm in Brugada syndrome[19]. Electrical storm is generally perceived as the rapid or incessant succession of recurrent poorly tolerated ventricular arrhythmias, generally requiring repeated cardioversions, occurring during a short period of time.

- Isoproterenol is reasonable for treatment of electrical storm in Brugada syndrome.
- Quinidine might be reasonable treatment of electrical storm in Brugada syndrome.

ICD therapy: The 2008 American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) guidelines for device-based therapy of cardiac rhythm abnormalities included the following statements regarding ICD therapy in Brugada syndrome[20]:

- There is evidence and/or general agreement supporting ICD implantation in all Brugada syndrome patients with a prior cardiac arrest. (Class 1, level of evidence-C).
- The weight of evidence/opinion supports ICD implantation in Brugada syndrome patients who have had a history of syncope. (Class 2a, level of evidence-C).
- The weight of evidence/opinion supports ICD implantation in Brugada syndrome patients with a history of VT that did not result in cardiac arrest. (Class 2a, level of evidence-C).

This approach can be implemented in clinical practice with one caveat regarding syncope: other causes of syncope, such as typical vasovagal events, bradycardia, or neurologic causes, must be excluded before proceeding to ICD implantation.

Investigative approaches: These have been evaluated in patients with Brugada syndrome who are at risk for SCD. They include:

- Focal radiofrequency ablation to prevent the ventricular premature beats that trigger VT/VF[21]
- The administration of cilostazol, which is a phosphodiesterase inhibitor that impairs platelet aggregation and is approved for the treatment of intermittent claudication. Its efficacy in Brugada syndrome may be related to the suppression of I_{to} (calcium-independent transicen outward potassium current) secondary of the increase in heart rate and/or to an increase in calcium current (I_{Ca}) due to an elevation of intracellular cyclic AMP concentration via inhibition of phosphodiesterase activity[22].

Conclusions

Because the syndrome has been identified only recently, it is difficult to ascertain its incidence and distribution in the world. Presently, no Indian data is available for this lesser known entity. However, sporadic cases are reported in clinical practice. Recent data from France and Japan show a prevalence of 1 per 1,000 electrocardiograms compatible with the syndrome in the normal adult

population. This disease is genetically determined. The incidence of sudden death in this syndrome is very high and, at present, can only be prevented by implanting a cardioverter-defibrillator. This syndrome has already been recognised in virtually all parts of the world. The lack of cases in some countries probably is due more to the lack of recognition than to the absence of the disease. Cumbersome drug challenge may be one of the important cause for the under-reporting especially in type 2 and 3 Brugada syndromes. In the future we can expect a sizeable increase in the number of identified cases as the recognition of the disease grows.

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REVIEW ARTICLE

JIACM 2011; 12(1): 32-7

Understanding Aphasia in a Simplified Manner

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Abstract

Speech disorders including aphasia and dysarthria are common neurological disorders. Aphasias are commonly seen with stroke. This part of neurological examination frightens many physicians probably because of the great volume and complexity of literature on this topic. Therefore we present here a simplified and easy approach towards the understanding and examination of these disorders.

Key words: Aphasia, language, speech disorders.

Definitions

Speech is a highly evolved function of the cerebral cortex. Speech is the human faculty by which thought processes are symbolically expressed. Speech is the vocal form of human communication. It is based upon the syntactic combination of lexicals and names that are drawn from very large vocabularies (usually > 10,000 different words). Each spoken word is created out of the phonetic combination of a limited set of vowels and consonant speech sound units.

Components of speech

Speech is the mechanical function of one's ability to communicate in oral language. It includes language production, phonation, and articulation.

Language

Language is the symbolisation of ideas. It is the ability to convert thoughts into comprehensive words. It consists of five parameters i.e., speaking, hearing, repeating, reading, and writing.

Speech and hemispherical dominance

Speech is the function of the cerebral hemisphere. It is undertaken by the dominant hemisphere. 9 out of 10 humans have right handedness. 90% of humans also have left hemispherical dominance. The other 10% have left handedness. 7% out of these 10% have left hemispherical dominance. 3% out of the 10% have right hemispherical dominance. Thus 97% of humans have left hemispherical dominance. Only 3% have right hemispherical dominance.

Pathological symptoms related to language functions:

Language related symptom	Explanation
Literal (phonematic) paraphasia	Words with false or left-out sounds
Verbal (semantic) paraphasias	Wrong or inadequate words
Neologisms	Non-existent words
Anomia	Word retrieval difficulties
Agrammatism	Syntactically incomplete sentences, telegram style
Stereotypes	Repetitive set phrases
Dysarthria	Disturbance of articulation
Dysprosody	Disturbance of speech melody or rhythm
Alexia	Disturbance of reading
Agraphia	Disturbance of writing

Wernicke's area

The auditory comprehension of spoken speech takes place in the posterior end of the superior temporal gyrus. Karl Wernicke, a German neurologist, identified it and described the pathway connection to Broca's area via the arcuate fasciculus. This area is neuroanatomically described as the Brodmann area 22.

Broca's area

The motor area for spoken speech is situated in the posterior part of the left inferior frontal gyrus. Paul Broca, a French Surgeon, described it in 1865 in two patients who lost speech and showed a lesion in the lateral frontal lobe at autopsy. This area is neuroanatomically described as the Brodmann area 44 and 45.

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Conduction area

A deep, white matter tract, connecting the Wernicke's area to the Broca's area, also called arcuate fasciculus, derived from a Latin word meaning curved bundle neural tract, is important in dominant hemisphere lesions. Damage to the arcuate fasciculus leads to conduction aphasia: repetition deficits arise following damage to the arcuate fasciculus of the dominant hemisphere.

Exner's area

It is an area of the brain just above Broca's area and anterior to the primary motor control area. It is the area for writing, close to the area for hand movement. Damage to it results in agraphia. This area is neuroanatomically described as the Brodmann area 6.

Reading area

It is an area of the brain just medial to the left occipital lobe and in the splenium of the corpus callosum. It is the centre for reading. It recieves impulses from the eye and transmits them to the association area for analysis by red matter, then passes it on to the arcuate fasciculus. A lesion here causes pure word blindness. This area is neuroanatomically described as Brodmann area 17.

Speech disorders are of 4 types

1. Aphasia/dysphasia
2. Anarthria/dysarthria
3. Aphonia/dysphonia
4. Mutism

Definitions

Aphasia: Loss of language due to dysfunction in the central mechanism of the brain is called aphasia. Minor disorders of the same is called dysphasia, e.g., right hemiplegia producing dysphasia.

Dysarthria: Dysfunction of the peripheral mechanism of speech leading to defective articulation is termed dysarthria, e.g., lower motor neuron type of facial palsy, pseudobulbar palsy.

Dysphonia: Loss of voice due to dysfunction of the voice producing mechanism is called dysphonia, e.g., vocal cord palsy, acute laryngitis.

Alexia: Loss of ability to read is alexia.

Agraphia: Loss of ability to write is agraphia.

Approach to diagnosing aphasia/dysphasia

What is Aphasia?

- disturbance of comprehension and formulation of language (i.e., higher neuropsychologic functions)
- affection of language related functions: reading and writing
- produced by damage of cortical regions related to language functions
- reasons of damage: stroke, head injury, or cerebral tumours
- different major aphasia syndromes

Analysis of aphasia

1. Sensory component: comprehension
2. Motor component: articulation, fluency, repetition, naming, writing

Testing spontaneous speech

Fluency: See whether speech is fluent without hesitations, uninterrupted by searching for a forgotten word

Effort taken for speech: See whether the patient has effortless/effortful speech

Vocabulary: See whether there is any word-finding difficulty. Whether patient stammers and stumbles. Look for ability to speak in full sentences, or whether the patient is able to talk only in phrases

Grammer: See whether the grammer is correct or not

Testing comprehension

Whether patient can hear and understand speech?

Tested by asking the patient to obey a command. Ask the patient to show the tongue, close the eyes, lift a limb.

Whether fluency is preserved or not? Speech whether fluent, i.e., without hesitations? Is it incessant, rapid, and uninterrupted?

Use of paraphasias, a descriptive phrase instead of a forgotten word. Use of neologisms, invented words and nonsense words. Jargon speech, an extreme example of the above speech, devoid of meanings.

Testing repetition

Patient is asked to repeat a simple sentence. It has to be clearly stated by the examiner, e.g., today is Wednesday, August the 17th, 2009. See whether the patient is able to repeat what you say. Remember never to shout at an aphasic patient, as hearing is usually normal in these patients. A patient with a left frontal lesion can repeat simple words and phrases. A patient with posterior lesions in the angular gyrus, cannot repeat what the examiner says. This is the characteristic feature of conduction aphasia. This function is preserved in transcortical aphasia.

Testing for naming

The patient is shown an object and asked to name it. A commonly used object should be shown, e.g., a pen or match box. See whether the patient is able to name the object. Patient may be handed over the object, or asked to demonstrate the use of the object. In anomic aphasia or nominal aphasia, the patient is unable to name it however but can use it. Auditory comprehension, repetition, reading and writing are usually preserved in such a patient. Memory testing otherwise will be normal.

This function is preserved in transcortical aphasia.

Other tests to be done

Ask the patient to read from a command. See whether he answers a written question. See whether he obeys commands which are written down. Ask the patient to read aloud, to write name and address, to draw a picture or clock, or do small calculations, e.g., 4 + 4.

Aphasia syndromes

1. Broca's aphasia

Non-fluent telegraphic speech

Reduced verbal content and phrase length – generally less then four-word agrammatical sentences (or with frequent errors). Mostly content words are used (nouns and verbs). There is absence of functional words (prepositions and conjunctions). The matter is conveyed anyway. Functional comprehension is present, but the patient has trouble following complex grammatical statements. Reading aloud is not possible.

Cause: Middle cerebral artery (MCA) territory stroke involving the left frontal lobe

2. Wernicke's aphasia

Jargon speech

Fluency increased, increased verbal content, paragrammatism – speech running, phrase length – generally greater than five words. Grammatical sentences (or close to normal). Paraphasic errors (literal or verbal). Literal – sound substitution with errors (winging, ringing), semantic – word substitution (sister for mother). Neologisms (made-up words). Logorrhoea – inability to stop speaking, severely impared auditory comprehension. Cause: Middle cerebral artery territory stroke involving the left superior temporal lobe.

3. Conduction aphasia

Repetition defect

It is relatively uncommon. Spontaneous speech is fluent, and there is considerable word finding difficulty. Preserved auditory comprehension. Significant difficulty with repetition. Literal paraphasia, self correction, numerous pauses, filled pauses – Aaaaa Aaaaa, reading deficit – variable, writing deficit – variable.

Lesion: left superior temporal area, supramarginal gyrus.

4. Nominal aphasia

Primary deficit – word finding and naming

Speech output is fluent with numerous pauses, pauses may be filled with circumlocutions, describing the function of an object; but the name cannot be retrieved. Auditory comprehension is intact. Reading and writing are also intact. There is focal damage to the left temporal and parietal area. Usually residual or good recovery as compared to other aphasias. Also indicates good prognosis if seen in the acute stage.

5. Global aphasia

Severe impairment in all modalities

Speaking, listening, reading, and writing severely impaired. Auditory comprehension – very limited. Speech output – only few understandable utterances. Some areas of spared speech function are utilised in communication.

Brain damage resulting in a massive fronto-temporo-parietal lesion, complete occlusion of MCA. Rarely, without hemiplegia.

6. Transcortical motor aphasia

Similar to motor aphasia but with intact repetition

Lesion in the border zone superior or anterior to Broca's area. Non-fluent, limited speech output. Auditory comprehension is good. Reading comprehension is good. Syntax not as bad as in Broca's aphasia. Lesion: occlusion of anterior cerebral artery.

7. Transcortical sensory aphasia

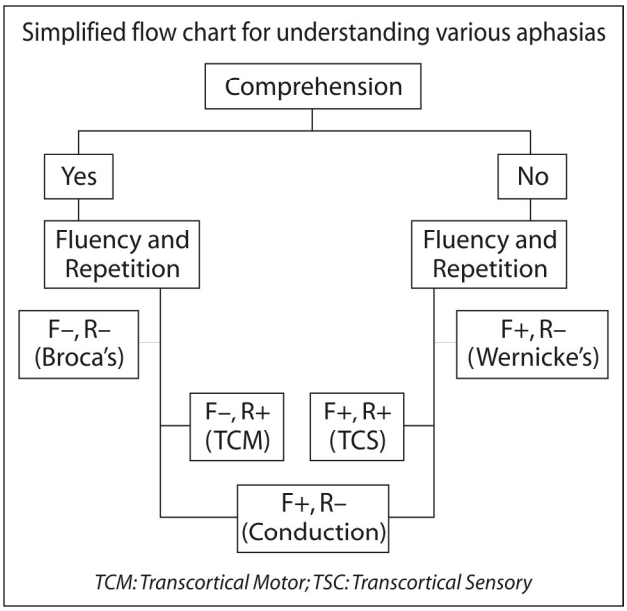
Similar to sensory aphasia, but with intact repetition

Deficits in all language modalities, fluent aphasia. Echolalia – they can repeat, but cannot understand. Much difficulty in communicating. Syntax not as bad as in Broca's aphasia. Lesion in the border zone posterior and inferior to Wernickes' area – occlusion of anterior cerebral artery.

Aphasias - comparison

Diagnoses of aphasia in the database

Diagnosis	N	%
Wernicke's	47	17.74
Broca's	42	15.85
Global	33	12.45
Anomic	24	9.06
Conduction	19	7.17
Undecided	51	19.25
Transcortical	6	2.26
Residual	24	9.06
No aphasia	19	7.17
Total	265	100



TCM: Transcortical Motor; TSC: Transcortical Sensory

Speech disorder: dysarthria

Definition

Any combination of disorders of respiration, phonation, articulation, resonance, and prosody, that may result from a neuromuscular disorder.

Types of dysarthria

1. Flaccid dysarthria (Bulbar)

Lesion: lower motor neuron level.

Features: breathy phonation.

Hypernasality: other features of bulbar palsy particularly, dysphagia to solids, and nasal regurgitation of liquids.

2. Spastic dysarthria

Lesion: upper motor neuron level.

Communication: individual syllables are slurred and precision of consonant pronunciation is lost. British constitution becomes Brizh conshishushon. Exaggerated jaw jerk. Dysphagia particularly to liquids. Emotional incontinence is seen.

3. Ataxic dysarthria

Lesion: cerebellum level.

Communication: scanning or staccato speech. Irregular articulatory breakdown. Rhinoceros becomes Rhi-noc-er-os.

4. Dyskinetic dysarthria

Lesion: basal ganglia level. Hypokinetic type (Parkinsonism): monotonous speech.

* Rapid rate

* Short rushes of speech with final decay.

5. Myasthenic dysarthria

Voice may be normal at the beginning of each sentence, but abnormalities develop as the sentence progresses. Testing by asking the patient to count up to 30.

6. Mixed dysarthria

May be the most common.

Examples:

* Motor neuron disease – Flaccid + spastic.

* Multiple sclerosis – Ataxic + spastic.

* Wilson's disease – Ataxic + spastic + hypokinetic.

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A N N O U N C E M E N T

Suggestions are invited from Fellows/Members for the following **Orations for the year 2011** so as to reach Dr. Ashok Shiromany, Honorary General Secretary, Indian Association of Clinical Medicine, on the official address given below:

1. **Prof. B. C. Bansal - Mrs. Uma Bansal Oration**
2. **Dr. G. S. Sainani - Dr. Mrs. Pushpa G. Sainani Oration**
3. **Dr. G. B. Jain Oration**
4. **Founder -President Prof. M. C. Gupta Oration**

- The suggestions are to be made for above Orations to be awarded during IACMCON-2011.
- The suggestions are to be made only by Fellows/Members of the Association, and must be accompanied with reasons for recommending the particular person showing the value of his/her research and accompanied with eight copies of three of his/her best publications. All the relevant papers in connection with suggestions such as Bio-data, List of Publications etc., should be submitted in **EIGHT SETS** by the proposer.
- The recipient of the above awards should deliver a lecture pertaining to his/her work at the Annual Conference of the Association in 2011 at Patna, Bihar.

Members of the Governing Body of the Association are not eligible to receive the orations.

Eligibility Criteria:

1 The Nominee should have minimum 3 years standing in the Association as a Fellow/Member (kindly mention the Fellowship number and date of award).

i. The member should have a standing of minimum three years in the Association.

ii. The member should have participated in the annual conferences, scientific programmes, contributed to the *Journal* and actively engaged in the organisation of the annual conference of IACM.

iii. For Founder-President Dr. M. C. Gupta's Oration, the subject of Oration should be related to cardiology.

Dr. Ashok Shiromany, *Hony. Gen. Secretary, Indian Association of Clinical Medicine*,
Postgraduate Department of Medicine, S.N. Medical College, Agra-282 002, U.P.

REVIEW ARTICLE

JIACM 2011; 12(1) : 38-43

Strengthening Human Resource Practices in Healthcare in India: The Road Ahead

Aashima Agarwal, Shalini Garg*, Udai Pareek**

Preamble

India has a historical background of absorbing managerial ideas and practices from around the world. The roots of management principles and prevalence of human resource practices can be traced to the world's first management book, titled 'Arthãshastra', written three millennia before Christ, which highlighted many aspects of human resource practices in ancient India. The socio-cultural roots of Indian heritage are diverse and have been drawn from multiple sources including ideas brought from other parts of the old world.

Arthãshastra written by the celebrated Indian scholar-practitioner Chanakya had three key tenets: 1) public policy; 2) administration and utilisation of people; and 3) taxation and accounting principles.

India has been in the forefront of various international movements in the health and population sectors. Overall, the Indian healthcare industry is going through a transition and the future is likely to see significant changes in the nature of provision of healthcare and the roles of various players in the industry. The healthcare service scenario in India is expected to evolve into a more developed stage. With this transition, management of human resources in health is a major challenge to health systems development in India. This includes planning for, production, recruitment, and utilisation of health personnel. Although a number of measures have been instituted to meet this challenge, considerable gaps still remain.

What is health services management?

Health services management research is a relatively new area of research[1]. The importance of human resources management (HRM) to the success or failure of health system performance has, until recently, been generally overlooked. To put simply, HRM is a planned approach to manage people effectively for performance by providing a more open, flexible, and caring management style so that the staff will be motivated, developed, and managed in a way that they can give their best to support departments. HRM in hospitals has to function in a sector with some unique characteristics. The workforce is relatively large, diverse, and includes separate occupations.

In an organisational context, HRD may be defined as the process in which the employees of an organisation are helped and supported in a continuous and planned manner to acquire and sharpen capabilities and skills required for performing various functions associated with their present and expected future roles. They are further helped to develop and enhance their undeveloped potential for their own and organisational developmental process. Developing an organisational climate contributes to professional well-being, motivation, and pride of the employees which is considered as the third dimension of the process[1]. The organisational goal of HRD normally is to have competent, motivated, dedicated, and disciplined employees to ensure higher levels of productivity, profitability and growth of the organisation.

The human resource development is the process of helping people acquire competencies and capabilities for their present and expected future roles. It not only develops their individual capabilities but also unveils and taps their hidden potential, further developing them as well as their organisations. As a continuum, it provides an organisation culture of trust; cooperation and healthy supervisor-subordinate relationships among subunits, resulting in professional well being and motivation of the employees. The competencies people needed include knowledge, attitude, skill, and values. Organisations need to build on the existing

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competencies of the employees so that they continue to provide high quality services in the face of ever-changing needs and newer challenges, be it in the private or public sector. The ultimate role of human resource development in any country is to improve the quality of life of its people[5].

Good HRM practices are instrumental in helping achieve departmental objectives and enhance productivity. Medical and health services managers – also referred to as healthcare executives or healthcare administrators – plan, direct, coordinate, and supervise the delivery of healthcare. These workers are either specialists in charge of a specific clinical department, or generalists who manage an entire facility or system.

The need for human resource management in healthcare in India

It has been increasingly recognised that getting HR policy and HR management right has to be the focus of any sustainable solution to health system performance. A well-motivated and appropriately skilled and deployed workforce is crucial to the success of health system delivery. The actual methods used to manage human resources in healthcare are in themselves a major constraint or facilitator in achieving the objectives of any health organisation.

How is HRM in healthcare more challenging as compared to the other sectors?

The management of healthcare is very challenging when compared to management in other sectors. Worldwide, many ideas have been introduced in an attempt to address the problems of inefficiency.

First, healthcare outcomes are highly complex. Healthcare organisations face continuous pressure to become productive, innovative, and provide quality healthcare[2]. Second, frequently uncertain and difficult to assess[3]. Third, healthcare outcomes are public organisations, hospitals cannot, in most cases, be judged on the basis of profitability. Finally, healthcare organisations are particularly complex due to their dual lines of accountability: professional and administrative.

Healthcare delivery is highly labour-intensive and health sector performance is critically dependent on employee motivation[4]. Also, as the demand for quality services rendered by the government health set-ups gets stronger day-by-day, continuous human resource development becomes crucial both for service improvement and client satisfaction.

Organisational HRD efforts are usually directed towards commitment and competency development among the employees since, without competent employees, it is difficult to harvest good productivity irrespective of the sophistication in technological or infrastructural resource base. Organisations use many mechanisms to achieve HRD goals. These HRD issues or mechanisms include manpower planning, recruitment selection, and other forms of job assignments, induction programme, training, performance appraisal, rewards, punishments, etc. Although it is widely recognised that improved management of human resources is the key to provide a more effective, efficient, and quality health service, only a few developing countries have made significant progress in this area.

Hospitals, unlike any other industry, are a different entity. The role of this department and its head has a role cut-out and exclusive. Unlike any other industry, the advent of technology, modernisation, computerisation, newer diagnostic and intervention techniques, has not reduced the need of human labour in hospitals, which is now an industry. On the contrary, there is a quantum growth in the need to appoint specialised manpower at various levels of patient care, which has originated from the thought process of those professionals and promoters, who are enlightened with the need to induce quality control in patient care.

In a study by Rondeau and Wagner[6], the impact of HRM practices and the contingency theory on 283 Canadian nursing homes was assessed. They had reported that the "best performing" nursing homes (as measured by indicators of client and staff satisfaction, operating efficiency, and revenue) were found to be more likely to have implemented "progressive/high performance" HRM practices and to have a workplace climate that strongly values employee participation.

As also stated by (Franco *et al*, 2002)[7], the health sector,

resource availability and employee competence are essential but are not enough to guarantee desired employee performance. Although employee motivation is a critical element of health systems performance, it is largely understudied.

The most precious resource for any organisation is its human resource because of its related potentials. The potential can be used only by creating a climate that can continuously identify, bring to surface, the nature and use the capabilities of people.

To obtain performance on quality, cost, and patient satisfaction dimensions, health organisations will also have to satisfy their physicians and employees[8]. Because physicians play a crucial role in the use and distribution of health system resources as well in the total work of healthcare organisations, it is important that managers examine how motivation theories may apply to them[9].

The technical aspects of the performance management processes have been significantly covered in the literature[10]. Despite the importance of the behavioural factors on the performance management process, the research in this area has been underexposed in the literature. Specifically, fewer studies have concentrated on physician motivation[11].

Today, hospitals are in the forefront of health services delivery and their main concern is providing quality health services to the clients. A hospital is an integral part of a social and medical organisation, the function of which is to provide for the population complete healthcare, both curative and preventive and whose outpatient services reaches out to family and its home environment.

The irony is that whilst HR is under-researched in health, partly because of its unique context, the main "business" of health – clinical interventions – is the subject of continuous and detailed research-based scrutiny.

The challenge for researchers attempting to build the evidence base on HRM in the health sector is that they have to draw on these non-clinical research methods to assess the HRM "inputs" whilst attempting to identify appropriate and sector-specific measures of processes, output, or outcome.

Key human resource issues limiting the health system

The large public health infrastructure follows a more or less similar pattern across the states. This system faces several managerial problems which are well-recognised and which limit its effectiveness:

Inadequate assessment of soft skills and other competencies at the time of recruitment

The procedure adopted for recruitment should use procedures which are clearly understood by candidates and which are open to public scrutiny apart from being fair, giving candidates who meet the stipulated minimum requirements equal opportunity for selection. The primary criterion for selection of candidates should be merit and ability. Apart from the eligibility criteria requirements, the system is deficient in assessing the soft skills of candidates like their ability to withstand stress, communication skills, psychological testing, values, attitude, and personality of an individual, etc.

Inadequate training at various levels

Training is the basis for human resource development. Several problems have emerged in the area of training over the past few years. Basic medical education has a heavy focus on urban curative care and is provided in tertiary care settings. This does not prepare doctors for their roles in the rural primary health care system. There is hardly any system of induction training for medical officers of the primary health centres when they join the government health system. Furthermore the medical officers do not have any public health or management training even though they are supposed to manage the staff under them. There is no training for health education, interpersonal communication, doctor-patient and doctor-staff interactions, and counselling. The technically oriented training does not help to bridge the gap between the doctor – who is regarded as supreme – and the clients who are usually poor and illiterate.

At the lower level, the auxilliary nurse-midewife's training is also mostly technical with a very limited component of social aspects of health, community involvement, mobilisation, health education, etc.

The Independent Commission on Health in India observed that the standard of teaching in training schools for auxilliary nurse-midwives was very low and that "the main reasons for substandard patient and community care are: substandard training, especially in the staff-nurse, midwife, and auxilliary nurse-midwife training courses, the lack of a proper system of training; and absence of regular reorientation courses." (VHAI, 1997).

A recent review of training programmes under the World Bank-assisted population, health, and nutrition projects in India from 1972 to 1997 indicated that in a total of 22 projects costing 3.2 billion dollars, only 7.6% of the project budget was spent on training. Even in projects specifically aimed at strengthening of training, only 13% of the funds were used for training. The review found that, "knowledge and skills related to some specific areas of service delivery were poor among the health workers and that there was a need to enhance training skills of most trainers at the state and district level." (Ramaiah, 1998). In summary, it is clear that training has been a neglected area in the health sector.

Centralised planning and target-oriented performance appraisal

Central level planning has, over the years, killed many initiatives at the state level to adapt or augment health and family planning programmes to local needs. States lack public health expertise to develop new health programmes and are not allowed to take direct assistance from foreign donors or to collaborate with foreign partners in the health area without clearance from the central government. It has been seen that during the process of performance appraisal, the process of writing ACRs was routine (subjective and generalised) rather than reflective of the individual's capability (objective and customised) in absence of any output indicators. While reporting, the officer tended to tread a middle path so as to avoid controversy and unnecessary explanations. Moreover, the reviewing officer was not intimately associated with the working of the officer being reported upon to make any realistic opinion.

Rewards not linked to performance

In the health system, there are no concrete rewards except promotions and salary increments. All promotions and increments are linked to seniority in the system and vacancy available. For many posts, promotions are few anyway. The current system of annual confidential reports does not reflect performance as these reports are written as a routine procedure, indicating satisfactory performance except in very extreme cases. Postings and transfers are also not based on performance but on "government's wish", for which there is a lot of scope for political and administrative contacts to be used. The staff who stay at their place of posting and provide 24-hour service get the same salary as the staff who are absent or are available for only three to four hours a day. In such a system, many settle for the minimum acceptable level of performance. Further training is of little help as staff do not see any personal benefit of the training.

Role of good HRM practices

In recent years, it has been increasingly recognised that getting HR policy and management "right" has to be at the core of any sustainable solution to health system performance. In comparison to the evidence base on healthcare reform-related issues of health system finance and appropriate purchaser/provider incentive structures, there is very limited information on the HRM dimension or its impact.

In many countries, access to health professional training and employment is controlled by standards and entry requirements determined by the professions, and aspects of their work are regulated. The health sector is a major recipient of public and/or private expenditure, and healthcare delivery is a politicised process.

Recent research[12] has also highlighted a so-called "prime building block" of HRM – the principle of "AMO". There must be sufficient employees with the necessary Ability (skills, knowledge, and experience) to do the job; there must be adequate Motivation for them to apply their abilities; and there must be the Opportunity for them to engage in "discretionary behaviour" – to make choices about how their job is done. The authors suggest that organisations wishing to maximise the contribution of their workforce need to have workable policies in these three broad areas.

Table I: Issues pertaining to key HRM practices in the Indian scenario.

No.	HRM practice	Key features
1	Job description	Percentage of employees with formally defined work roles is high in the public sector.
2	Recruitment	Direct recruitment from institutions of higher learning is very common amongst management, engineering, and similar professional cadres. Amongst other vehicles, placement agencies, internet, and print media are the most popular media for recruitment.
3	Compensation	Strong emphasis on security and lifetime employment in public sector including a range of facilities like healthcare.
4	Training and development	Poorly institutionalised in Indian organisations. Popularity of training programmes and their effect in skill and value development undeveloped.
5	Performance appraisal	A very low coverage of employees under formal performance appraisal and rewards or organisational goals.
6	Promotion and reward	Moderately variable across industries. Seniority systems still dominate the public sector enterprises. Use of merit and performance limited mostly to globally orientated industries.
7	Career planning	Limited in scope. The seniority based escalator system in the public sector provides stability and progression in career. Widespread use of voluntary retirement scheme in public sector by high performing staff. Cross-functional career paths uncommon.
8	Gender equity	Driven by proactive court rulings, ILO guidelines, and legislative provisions. Lack of strategic and inclusion vision spread.

Challenges ahead and the way forward

While there have been substantial policy changes in India in the area of public sector of healthcare, human resource management will have to be managed strategically and in an integrated manner. Here we present a model which is adopted from Pareek and Rao (1992) and takes an integrated look at training and other key functions.

Whilst many health systems have been attempting to decentralise to improve efficiency, they tend to be characterised by a broad range of active stakeholders, a high level of direct and indirect governmental and regulatory intervention, and recurrent "top-down" attempts at reform. Health is also very labour-intensive – the proportion of the total money spent on staff is much higher in health than in most manufacturing industries and in many service industries.

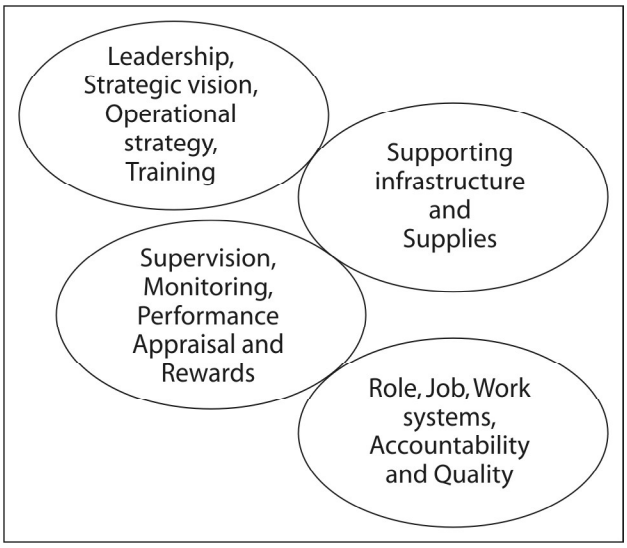

Fig. 1: *Integrated model of human resource management healthcare organisations/hospitals.*

Conclusions

The critical importance of HRD and its various issues can no longer be ignored. Various HRD issues/mechanisms in the government sector exist without the basic 'HRD-orientation'; often devoid of the spirit of HRD. This is evident from the opinions of the respondents in the present study. Rational recruitment procedures to meet the organisational goals, timeliness of the reward systems, transparent transfers policy, effective support systems, etc., are the felt needs of the times. The spectrum of probable reasons for the opinions expressed varies from the issues being dealt with by the respondents in a generic rather than a specific manner. The intensity of the appreciation and apprehensions expressed on many issues in the present study is probably an indication that these need to be handled in a more empathic and technically correct manner to foster an effective and efficient organisational work culture in any organisation.

Table II: Competencies of human resources management in the health services.

Competencies	Areas of competence and activities
Analysis of the human resources situation, identification of human resource and programming	Includes: a) Data collection, analysis, and determination of the overall human resources situation (availability, composition, structure, and distribution of human resources; the output of human resources by educational institutions); b) Comparison with a particular pattern or standard to identify gaps and needs (which can be determined using the best available methods, based on the characteristics of the health services system and the possibility of obtaining information); c) Identification of problems and qualitative and quantitative needs for human resources (in consultation with the authorities and relevant actors in the health services system); d) Preparation of a plan to procure the most appropriate human resources to meet the identified needs.
Staffing	Ensures that the health system obtains a sufficient supply of human resources (in all the necessary occupational categories) to meet its objectives, as budgetary resources permit. Includes personnel from the labour market, as well as personnel that is needed but not available in the labour market and who must be trained by educational institutions.
Performance management	Its objective is to optimise the productivity and quality of human resource performance in the health services. It includes interventions for performance management as such (ways of organising the work, technology management, formation of work teams, use of incentive systems) and ways to evaluate this performance.
Management of labour relations and personnel administration	Ensures proper management of work contracts, remuneration systems, conditions for the social protection of workers (which includes career appointments, incentive systems, relations between the employer and employees, collective working relationships – unions, collective bargaining), and the search for effective communication modalities between administration and personnel, as well as ways to enable staff participation in key decisions that affect their performance with the resulting benefit to the population.
Development and training of human resources	Ensures that all human resources in a health system are properly qualified and motivated. Includes interventions that range from the ongoing identification of educational needs, the definition of work competencies, curriculum development, instructional design, education, in the most effective and suitable modalities to meet the established objectives, and evaluation of the competencies acquired. It is a valuable strategy for improving performance and for changing the practices and attitudes of human resources.
Assurance of working conditions, safety, and the work environment	Ensures the proper environment, conditions, and modes of work organisation to counteract the potentially negative impact of the nature of health work on the health of the staff themselves. Most risks can be minimised with adequate precautions and preventive interventions that emphasise occupational safety and health promotion for the employer and employee alike.

Source: PAHO. Progress of Activities in Health Sector Reform. CD39/13. 39th Directing Council, Washington, D.C. September 1996.

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REVIEW ARTICLE

JIACM 2011; 12(1): 44-5

Angiogenic Factors in Pre-eclampsia and Pregnancy-induced Hypertension

Susmita Sharma, Parveen Mohan***

Pre-eclampsia (PE) is a hypertensive disorder of pregnancy which frequently develops after 20 weeks of gestation[1]. This is associated with high blood pressure and proteinuria and is reported to affect between 2 - 7% of pregnancies worldwide and is the major cause of maternal and foetal mortality[2, 3]. The basic aetiology of pre-eclampsia is not clear. The pathophysiological changes seen in pre-eclampsia include increased vasoconstriction and coagulation, vascular endothelial dysfunction, and reduced placental perfusion. Oxidative stress on the endothelium leading to endothelial dysfunction is also now thought to be the primary cause of pre-eclampsia. Pre-eclampsia occurs more commonly in first pregnancies and primarily affects maternal, renal, cerebral, hepatic, and clotting functions. Placental insufficiency arising from abnormal 'placentation', that is, failure in adequate trophoblast invasion of maternal vasculature, and possibly from abnormal autacoid production which is responsible for the ill effects on the foetus. Pre-eclampsia is due to widespread maternal endothelial cell damage from release of cytotoxic factors by the placenta. Pressor activity to infused angiotensin II (AII) is also increased despite reduced plasma concentrations of AII, renin, and aldosterone. There is decrease in prostacyclin production, and the thromboxane/prostacyclin balance favours vasoconstriction and platelet aggregation. There is a paradoxical elevation of plasma concentrations of atrial natriuretic in the face of plasma volume contraction. There is disturbance of volume homoeostasis with redistribution of intravascular volume to the interstitial fluid space due to increased capillary permeability and reduced plasma oncotic pressure. This redistribution is not always clinically apparent as peripheral oedema. Whether this change in volume is compensated for by venoconstriction and maintenance of adequate cardiac output, is undetermined. Improved understanding of the pathophysiology of pre-eclampsia is necessary to allow better clinical management of this serious disorder.

There are certain key angiogenic factors in pregnancy as an indicator for the early onset of pre-eclampsia in pregnancy. These are plasma levels of circulating soluble forms like tyrosine kinase-1, (sFlt-1) an anti-angiogenic factor, vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) – both pro-angiogenic factors which have been measured in patients of pregnancy-induced hypertension and pre-eclampsia. Maynard *et al*[4] compared the gene expression profile in placental tissue from women with and without pre-eclampsia and identified soluble Flt1 (sFlt1), a vascular endothelial growth factor receptor, as a molecule of particular pathophysiologic interest. It is now suspected that trophoblastic injury markedly enhances placental sFlt1 production, antagonising the endothelial protective role of vascular endothelial growth factor and/or placental growth factor and eventually leading to clinical pre-eclampsia[5, 6]. A recent study pointed out that, compared with women with a retrospective diagnosis of normal pregnancy (i.e., without hypertension), pre-eclamptic women had increased serum sFlt1 several weeks before the onset of clinical disease, suggesting that this protein might be used as a predictive marker for pre-eclampsia[7].

So the over-expression of Flt-1 and significantly lower levels of proangiogenic factors in early pregnancy can be used as a biomarkers for the onset of pre-eclempsia and PIH disease. Therapies and preventive strategies for pre-eclampsia must target the imbalance of these factors as it is evident 5 - 8 weeks prior to the onset of the disease[8].

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POSTGRADUATE CLINIC

JIACM 2011; 12(1): 46-8

Hirsutism and Abnormal Genitalia

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Key words: Hirsutism, virilisation, clitoromegaly.

Case history

A 26-year-old unmarried female, presented with complaints of excessive facial hair since her pubertal growth spurt. She also has excessive body hair and regularly uses hair-removing mechanical options. There was no significant family history. She had menarche at 13 years and is having regular periods since then. Systemic examination was unremarkable except for an abnormal genital finding (Fig. 1), which the patient revealed was present since early childhood and had increased gradually over the years including during puberty.

1. What is the pictorial diagnosis? Describe the abnormality evident in the photograph.
2. What are its causes?
3. What other clinical features should be sought for in such a patient?
4. How will you investigate such a case?
5. What are the possible therapeutic strategies/options?

1. **Clitoromegaly:** The picture shows the external genitalia of a female with an enlarged clitoris with a well-formed glans. The urethral opening is normally visualised (small arrow). Clitoromegaly is a rare condition. Some amount of enlargement of clitoris occurs during sexual arousal and is normal.

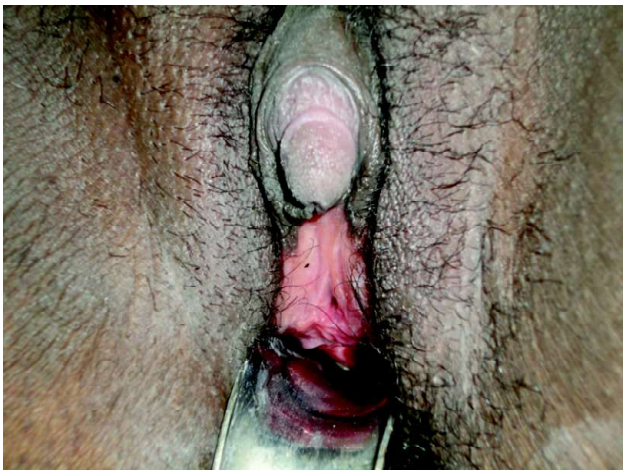

Fig. 1: Abnormal genital finding.

For academic purposes, measurement of the clitoris is precisely performed with plastic calipers with rounded edges (for ease of comfort), although a measuring tape or flat ruler can also be used. Glans width is assessed in its greatest transverse diameter, glans length from its tip to the back of the corona, and total clitoral length is measured as the distance from the tip of the glans to the point at the symphysis pubis at which the crura are thought to insert, thus including the clitoral body and glans[1]. A concept of clitoral index also exists which is the product of the glans width and the glans length. In one of the largest studies[1], the average total clitoral length was reported as 16 ± 4.3 mm, mean transverse diameter of glans as 3.4 ± 1 mm and mean longitudinal diameter of normal glans as 5.1 ± 1.4 mm. A clitoral index of > 35 mm^2 is considered abnormal (clitoromegaly).

2. Clitoromegaly may be present since birth wherein it could be a manifestation of congenital adrenal hyperplasia or Fraser syndrome. Fraser syndrome is an autosomal recessive congenital disorder characterised by cryptophthalmos and genital malformations. More often, it occurs later in life wherein it is a manifestation of hormonal imbalance or androgen excess in a female. This could be secondary to polycystic ovarian syndrome, pathological disorders of the ovaries and other endocrine organs. Ovarian virilising tumours like arrhenoblastoma or neurofibromas are important causes. Adrenal neoplasms can also be associated with hyperandrogenic states. Use or abuse of anabolic steroids can also contribute to clitoromegaly. In some cases there is no evident cause of clitoromegaly, and

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it is labelled as idiopathic[2], but presence of hirsutism in this case makes the diagnosis of idiopathic clitoromegaly unlikely. Less commonly, cysts and haemangiomas of the clitoris have been found to cause clitoromegaly[3,4].

3. Every patient who is noted to have an enlarged clitoris should be subjected to a detailed clinical examination. Associated clinical features that may be observed in such patients include hirsutism and signs of virilisation. Cutaneous manifestations like acne and male pattern balding may accompany hirsutism. Signs of virilisation should be specifically sought for in a patient who presents with clitoromegaly since it could be a pointer towards an underlying adrenal or ovarian neoplasm in adults. Virilisation refers to a condition in which androgen levels are sufficiently high to cause signs and symptoms such as deepening of the voice, breast atrophy, increased muscle bulk, clitoromegaly, and increased libido[5].

4. A thorough investigative work-up should be done in any case who presents with clitoromegaly, since it is a sign of virilisation[5,6]. Presence of signs of virilisation (as enumerated in point 3 above) indicate a state of androgen excess. To confirm this, serum testosterone levels and serum DHEAS (Dehydroepiandrostenedione sulphate) levels should be ascertained. Androgens are primarily excreted by the adrenals and the ovaries; both the organs contribute equal amounts. Markedly elevated androgen levels should always prompt investigation for ovarian or adrenal neoplasms. Serum total testosterone levels > 200 ng/dl are suggestive, while > 350 ng/dl usually indicates a virilising tumour; basal serum DHEAS > 700 mg/dl suggests an adrenal tumour. Serum free testosterone levels are also of value since the unbound fraction of the hormone is biologically available for conversion to the active form. Hyperinsulinism and/or androgen excess decrease hepatic production of sex-hormone binding globulin (SHBG), resulting in levels of serum total testosterone within the high normal range, whereas the unbound testosterone levels are much elevated. Normal range for morning serum total testosterone in females = 6 – 86 ng/dl; unbound testosterone levels = 20–301 pg/dl; normal DHEAS levels in premenopausal female = 12 – 535 mg/dl. DHEAS is considered to be a marker of predominant adrenal androgen excess, but modest elevations are also observed in female patients of polycystic ovarian syndrome. Polycystic ovarian syndrome is the commonest cause of ovarian hyperandrogenism, and the typical elevation in the ratio of luteinising hormone to follicle stimulating hormone (> 2:1) is seen only in less than 50% of such patients. Sonographic evidence of polycystic ovaries can be taken as corroborative evidence but *per se* it is a relatively insensitive and non-specific finding for the diagnosis of ovarian hyperandrogenism.

In cases of elevated serum testosterone and DHEAS levels, low dose dexamethasone suppression test can be employed (0.5 mg 6 hourly for 4 days) to ascertain the source of androgen excess – whether adrenal or ovarian. If there is suppression of the unbound testosterone to normal levels, then an adrenal androgen source is suspected. However, a partial or no suppression suggests an ovarian source.

ACTH stimulation test can be used to assess non-classic CAH (congenital adrenal hyperplasia). Measurement of 17-hydroxyprogesterone levels 60 minutes after bolus administration of 250 mg synthetic ACTH (cosyntropin) intravenously is required, wherein the levels are found to be elevated in cases of non-classic CAH. Alternatively, a normal morning 17-hydroxyprogesterone level (drawn in the follicular phase; normal range = 20 – 100 ng/dl) can be used reliably to exclude 21-hydroxylase deficiency (commonest cause of partial CAH).

Imaging studies of the abdomen are used to supplant hormonal studies. Sonography of the abdomen and pelvis may reveal polycystic ovaries and CT or MRI is helpful to image the adrenals and also the ovarian tumours.

A summarised algorithmic approach is outlined in Fig. 2.

In the present case, routine haematology and serum biochemistry including glucose tolerance test were normal; serum FSH was 5.27 U/L, LH 3.13 U/L, serum prolactin 15.4 ng/ml, testosterone 176 ng/dl (elevated), 17-hydroxyprogesterone level was 1,172 ng/dl (elevated) and DHEAS was 600 mg/dl (elevated).

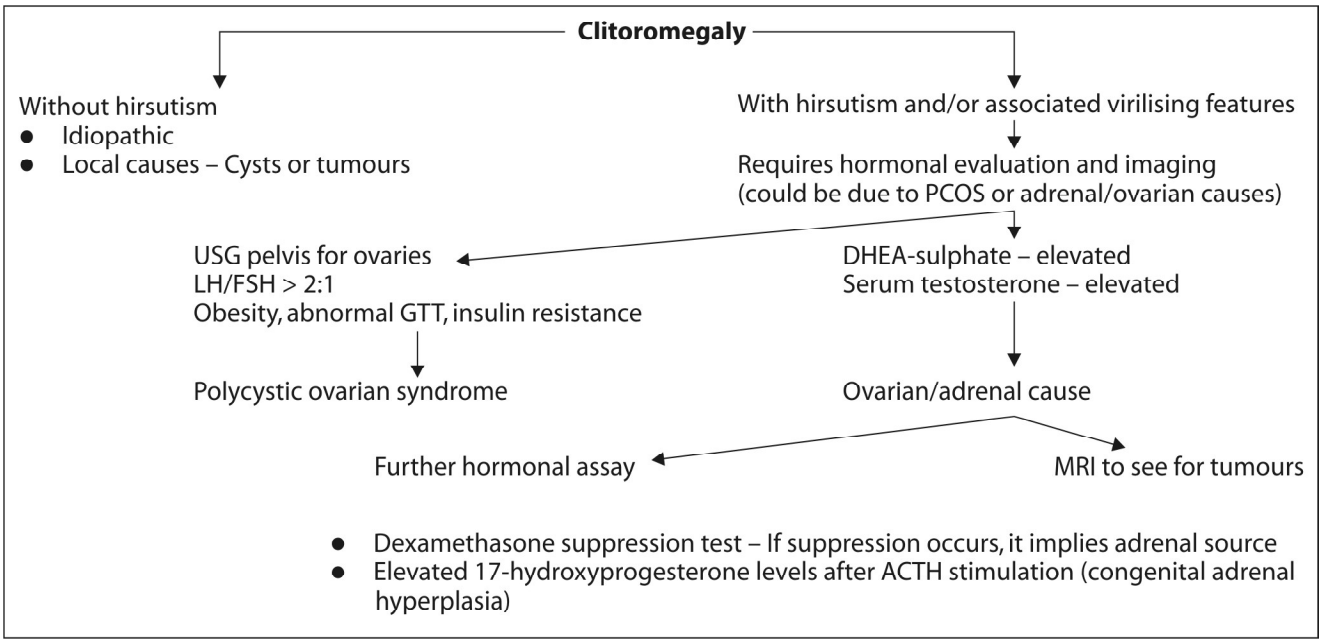

Fig. 2: *Algorithm showing approach to clitoromegaly.*

Sonography of the pelvis in this case was normal (normal uterus and adnexa). A diagnosis of congenital adrenal hyperplasia was made.

5 Management of clitoromegaly depends on the underlying aetiology which needs to be rectified. Ovarian virilising tumours and adrenal neoplasms need specific therapy, while polycystic ovarian syndrome may require hormonal therapy or insulin-sensitising drugs like metformin. Use of exogenous steroids needs to be curtailed in patients where it is the culprit. On the contrary, patients of CAH need small evening doses of steroids to curb ACTH release. Cysts and haemangiomas need surgical excision but require great expertise. Cosmetic correction can be done by clitoroplasty[7]. There are three different clitoroplasty procedures: clitorectomy, clitoral recession, and reduction clitoroplasty[8]. Reduction clitoroplasty with preservation of the neurovascular bundle is considered superior in terms of formation of the external genitals and sensation. However, the disadvantage is that detachment of the neurovascular bundle from the clitoral shaft is difficult and that there is a high possibility of sensory and blood flow disorders in the clitoris. Accompanying hirsutism can be addressed by pharmacological or mechanical means. However, a thorough patient and family counselling is required and the advantages and disadvantages of the surgery need to be explained. In the present case, the patient has been prescribed prednisolone 30 mg once daily; and once her hormonal profile returns to normal, surgery for clitoromegaly is being planned.

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CASE REPORT

JIACM 2011; 12(1) : 49-51

Extensive Deep Vein Thrombosis in a Case of Hyperhomocysteinaemia

SA Sangle, SS Karne**, SD Guthe***, RV Lohiya****

Abstract

Hyperhomocysteinaemia is a common condition predisposing to venous thrombosis. We are reporting a case of hyperhomocysteinaemia with extensive deep vein thrombosis. A 51-year-old female presented with progressive swelling and pain in her left lower limb. She had marked knuckle hyperpigmentation. Her left lower limb arterio-venous doppler was suggestive of thrombosis with absence of flow in the left iliac vein. Haematological investigations were suggestive of hyperhomocysteinaemia. The patient was treated with low molecular weight heparin and oral warfarin along with vitamin supplementation. She went on to make a full recovery, and follow-up arterio-venous doppler showed complete recanalisation with good venous flow.

Key words: Hyperhomocysteinaemia, hypercoagulable state.

Case report

Hyperhomocysteinaemia is a well-recognised risk factor for thrombotic and atherosclerotic vascular disease. It is one of the common causes of cerebral venous sinus thrombosis. However, there are very few cases of extensive deep vein thrombosis due to hyperhomocysteinaemia. This case report is of one such rare case of deep venous thrombosis in a case of hyperhomocysteinaemia.

History

A 51-year-old menopausal female, a staff nurse at a rural hospital, a non-vegetarian, presented with 2-month history of gradually progressive swelling and pain in her left lower limb. There was no h/o trauma to the limb, prolonged immobilisation, any surgery, and no h/o taking hormone replacement therapy. On examination, her vital signs were normal. General examination revealed knuckle hyper-pigmentation. Her left leg was oedematous up to the thigh with calf tenderness present. Systemic examination revealed no abnormality.

Investigations

Hb - 11.1 gm/dl, MCV - 99 fl, TLC - 6,700/mm^3, platelet count - 200,000/mm^3, PT - 16/16 and INR - 1.0. Metabolic lab - normal.

Her left leg arterio-venous doppler revealed a large thrombus extending from the tibioperoneal trunk vein and deep femoral vein onwards upto the left common iliac vein (Fig. 1 and 2) with absence of flow.

USG abdomen and pelvis was normal. ECG, chest X-ray and 2D echocardiography were normal. Antinuclear antibodies (ANA) - negative. Antiphospholipid antibodies were negative. Protein C, protein S, antithrombin-III levels - normal. Fasting plasma homocysteine levels > 50 µmol/l (markedly raised).

Treatment

The patient was treated with low molecular weight heparin, overlapped with warfarin. The patient was given

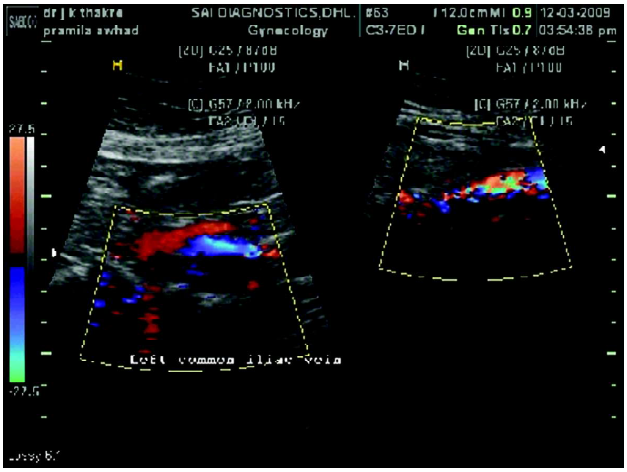

Fig. 1: *Arterio-venous doppler of left lower limb on admission showing thrombus in left common iliac vein with patchy flow.*

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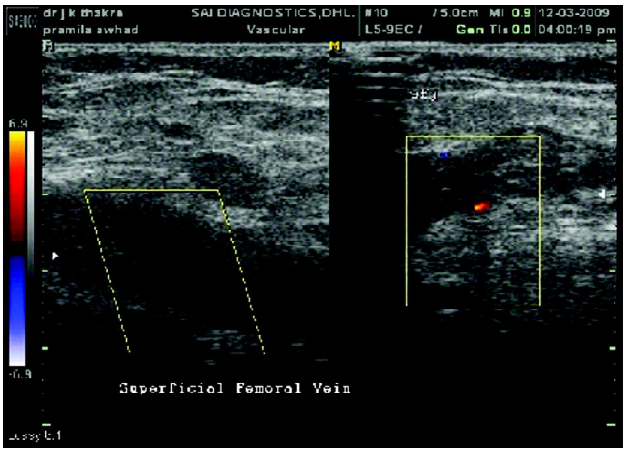

Fig. 2: *Arterio-venous doppler of left lower limb on admission showing thrombus in left superficial femoral vein with absence of flow.*

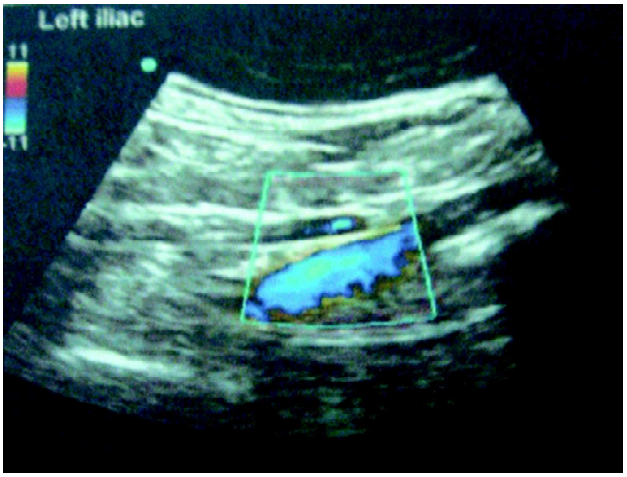

Fig. 3: *Arterio-venous doppler of left lower limb after anticoagulation showing recanalisation of left common iliac vein with good flow.*

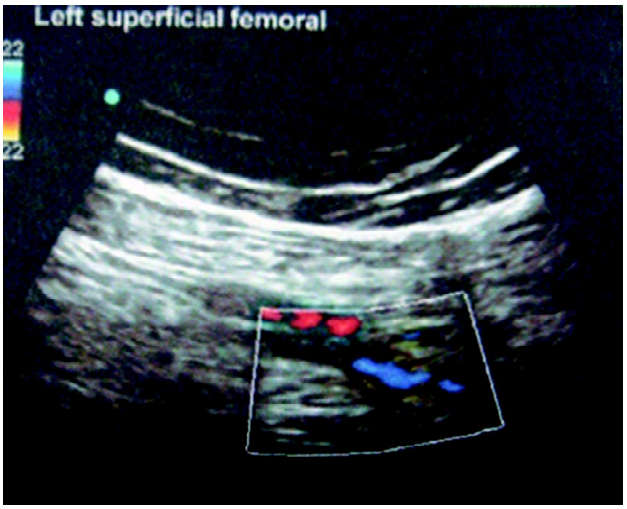

Fig. 4: *Arterio-venous doppler of left lower limb after anticoagulation showing recanalisation of left superficial femoral vein with good flow.*

cobalamin and folic acid injections daily for 1 week. She made good recovery, the leg swelling subsided, and pain decreased. Review doppler study after 10 days showed considerable resolution of thrombus, recanalisation of iliac vein and good flow (Fig. 3, 4). She was advised to continue warfarin with PT/INR monitoring every 21 days and oral cobalamin with folic acid.

Discussion

Homocysteine is an intermediary amino acid formed by the conversion of methionine to cysteine. Elevations in the plasma homocysteine concentration can occur due to genetic defects in the enzymes involved in homocysteine metabolism (e.g., thermolabile variant of methyltetrahydrofolate reductase), nutritional deficiencies of vitamins – folate, B_{12}, B_6, or due to other factors – including some chronic medical conditions and drugs[1]. Some drugs used in the treatment of hypercholesterolaemia, such as fibrates and nicotinic acid, can raise homocysteine levels by approximately 30 per cent; however, the clinical significance of this is uncertain. Cigarette smoking also may elevate homocysteine levels. Chronic kidney failure can increase homocysteine levels due to decreased renal removal and impaired metabolism.

There is increasing evidence that hyperhomocysteinaemia is a risk factor for venous thromboembolic disease (pulmonary embolism and deep vein thrombosis)[2-4]. Meta-analyses of case-control studies have found an odds ratio of 2.5 to 2.95 for venous thromboembolic disease in patients with homocysteine levels more than two standard deviations above the mean value of control groups[3,4].

Moderate hyperhomocysteinaemia (15 to 30 µmol/l) may also be a risk factor for recurrent venous thrombosis. This was illustrated in a multicentre study in which patients with a single episode of idiopathic venous thromboembolism were prospectively followed after discontinuation of oral anticoagulants[5]. Recurrent venous thromboembolism was significantly more likely in the 66 patients with hyperhomocysteinaemia than in the 198 with normal levels (18.2 per cent versus 8.1 per cent, respectively). Some studies have suggested that the risk of thrombosis increases 10- to 50-fold in patients who have both hyperhomocysteinaemia and an inherited

thrombophilia (e.g., factor V Leiden)[6].

Homocysteine has primary atherogenic and prothrombotic properties. Histopathologic hallmarks of homocysteine-induced vascular injury include intimal thickening, elastic lamina disruption, smooth muscle hypertrophy, marked platelet accumulation, and the formation of platelet-enriched occlusive thrombi.

The majority of hyperhomocysteinaemia is caused by low levels of folate and vitamin B_{12}. Correcting nutritional inadequacy in diet and vitamin supplementation with folic acid, vitamin B_{12}, and vitamin B_6 will lower homocysteine levels.

Conclusion

Hyperhomocysteinaemia is one of the important treatable causes of thrombophilia and can involve the deep venous system also. Supplementation with folate, vitamins B_6 and B_{12} can substantially lower homocysteine levels in patients with both genetic and nutritional causes of hyperhomocysteinaemia, and the role of dietary therapy in reducing thrombosis risk warrants further investigation.

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Aztor Ez

CASE REPORT

JIACM 2011; 12(1): 52-3

Statins in Surgical Patients: a Lesson for all Physicians

Krishnendu Mukherjee, Uddalak Majumdar**, Jayanta Das***

Abstract

Statins are very commonly used lipid lowering drugs, whose use is likely to increase in the future. A rare but serious adverse reaction is myositis which may lead to rhabdomyolysis. Surgical stress and several drug interactions increase the chance of myositis. Citing two case reports and reviewing the literature, we propose statins should be withheld for few days during the perioperative period of all elective and semi-urgent surgical operations.

Key words: Statins, myositis, rhabdomyolysis, operative complications, dyslipidaemias.

Introduction

Statins, one of the most widely prescribed drugs today, inhibit HMG-CoA reductase, a rate limiting enzyme in the biosynthesis of cholesterol *in vivo*. Atorvastatin and simvastatin are most commonly used; the newer and more expensive rosuvastatin and the older lovastatin are also prescribed. The beneficial effects of statins go beyond their LDL/triglyceride lowering (and HDL-elevating) actions and they are used not only for dyslipidaemic patients but also for secondary and primary prevention of coronary artery disease, peripheral vascular or cerebrovascular disease and in many patients with diabetes and hypertension. Though generally well tolerated, statins can rarely produce a reversible myositis with myopathy. This is a potentially lethal complication which may progress to rhabdomyolysis[1]. We report two patients undergoing surgical operations who developed this adverse reaction, one of them had a fatal outcome. Patients undergoing any form of surgery are more prone to develop myositis[2,7]; diagnostic confusion is also likely to occur in this setting.

Case 1

A 66-year-old male was referred to us for excision biopsy of a lymph node mass from the anterior triangle of the neck for full histopathological diagnosis of a lymphoma, discovered by FNAC. He was on 20 mg of atorvastatin daily for hyperlipidaemia and a non-fatal coronary event three years ago, along with beta-blockers and nitrates. He was prescribed azithromycin for three days by a physician for dry cough; this he had completed a day prior to surgery. His chest X-ray did not show a widened mediastinum or infective changes. He underwent the procedure under local anaesthesia with MAC (monitored anesthetic care) with intravenous midazolam and was discharged next day with ibuprofen and pantoprazole. Next day he reported pain in the neck and both shoulders; the significance of the latter was missed by the senior author. A standard combination of dextropropoxyphene and paracetamol was advised over telephone. Next morning he again reported a diffuse weakness and sense of breathing difficulty. Immediate review was advised. He was re-hospitalised but no abnormal signs were evident to explain the symptoms including a normal chest X-ray and arterial blood gases. All medications were continued. Twenty four hours later he was mildly febrile. He had reduced limb tones and a falling urine output. A raised serum urea and creatinine with hyperkalaemia was detected. Subsequent tests confirmed profound rhabdomyolysis with serum creatine kinase more than 7,000, with a normal CK-MB. LDH and total leucocyte count were grossly raised, with mild elevation of CRP and normal uric acid and procalcitonin. He developed full-blown multi-system organ failure (MSOF) and died three days later, despite full intensive care support. Tumour lysis syndrome or occult sepsis could not be substantiated and though there are rare reports of rhabdomyolysis from an advanced lymphoma[3], this patient did not have anatomically extensive disease. A bone marrow study performed during the work-up in intensive care did not show lymphoma infiltration. The posthumous biopsy report confirmed moderate grade non-Hodgkin lymphoma.

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Case 2

A 47-year-old male underwent a laparotomy for recurrent retroperitoneal liposarcoma; he had undergone the first resection 3 years ago under our care. Meanwhile he was diagnosed with diabetes and raised triglycerides, and was on 10 mg of atorvastatin a day with oral hypoglycaemics. The procedure was prolonged, and apart from several anaesthetic drugs, he received perioperative metronidazole. He complained of diffuse muscle pain on the first operative day; this was presumed to be related to succinylcholine. Pain and weakness progressed till next day with diffuse muscle tenderness. Myositis was confirmed with raised creatine kinase levels. Despite slight elevation of urea and creatinine, he responded promptly to fluids and mannitol and the myositis reversed spontaneously.

Discussion

Several drug interactions have been described with statins, including macrolide antibiotics[4] (case 1) and imidazloes[5, 7] (case 2) which increase the risk of myositis. Diabetes (in case 2) has also been reported to increase the incidence of statin induced rhabdomyolysis[6]. Operative stress can also be contributory[7]. In both of these patients, the pain of myositis may have been partially masked by post-operative analgesics. Statins are widely prescribed drugs today and their use is likely to increase in future. Numerous fixed ratio drug combinations are also available along with antihypertensives. Unscientific as they may be, they are aggressively marketed. However, the beneficial effects of statins (lipid lowering action and other effects on the endothelium) can only accrue following moderate to long-term use. Hence, no untoward effect can be expected from stopping them for a few days. With introduction of new molecules in medical practice almost on a daily basis, more drug interactions are likely to be discovered in future.

Physicians have already learnt to be careful with aspirin, clopidogrel and ticlopidine in surgical patients. We believe, we should be similarly careful with statins and fibrates (which too can cause severe myositis). These medications should be discontinued from a day prior to and the following 4-5 days following elective or semi-urgent surgical operations.

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CASE REPORT

JIACM 2011; 12(1): 54-5

Myocardial Injury in Celphos Poisoning

Neelima Singh, Ram Kumar Gupta*, Shubha Laxmi Margekar**

Abstract

Since celphos consumption is most commonly used for suicidal intent, awareness of myocardial toxicity is important for better management. This is done by serial ECGs, and enzyme measurement, thus paying rich dividends in the form of increased survival; hence this report.

Key words: Celphos, myocardial toxicity, enzyme measurement.

Introduction

Celphos (trade name for aluminium phosphide tablets) poisoning is very common in India. Phosphine gas (produced when aluminium phosphide comes in contact with water) is a protoplasmic poison which inhibits various enzymes and protein synthesis[1] at the cellular level leading to cell damage. A confirmed diagnosis is made by history, typical foul odour, and the silver nitrate impregnated paper test[2]. Myocardial damage is frequently observed, but infrequently reported. Celphos being one of the most commonly used poisonous substance and being a cause of myocardial damage, deserves reconsideration.

Case report

A 19-year-old male from a neighbouring district presented to us some twelve hours after accidental ingestion of an exposed celphos tablet. He had vomited several times and was drowsy with systolic BP of 70 mmHg at admission. His pupils were normal and so were the superficial and deep reflexes. After gastric lavage and administration of charcoal slurry, IV fluids and inotropic support was given to the patient. IV injection hydrocortisone hemisuccinate, IV sodium bicarbonate, proton pump inhibitors, and cefotaxime sodium were also added to the regimen.

ECG at arrival showed ST segment elevation in leads V1, V2, T inversion in lead III and ST segment depression in lead aVL at a heart rate of 104/min. Subsequent ECG done on the same day showed marked ST segment elevation in leads V1 to V3, aVL and ST segment depression in the inferior leads at the same heart rate. Atrial ectopics were also observed. On the second day, the patient developed widening of the QRS and RBBB with ectopics still persisting. This bundle branch block was transient, as it disappeared the next day but T inversion in leads V1, V2 persisted till the end. To confirm the ECG changes, CPK-MB was done which was raised. Other bio-chemical alterations were as shown in Fig. 2.

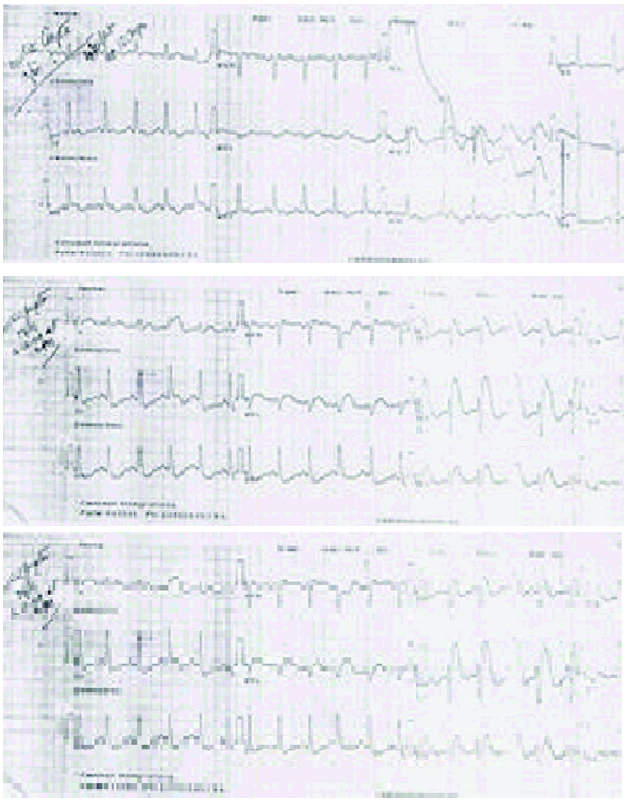

Fig. 1a:

** Assistant Professor, Department of Medicine, GR Medical College, Gwalior - 474 009, Madhya Pradesh.*

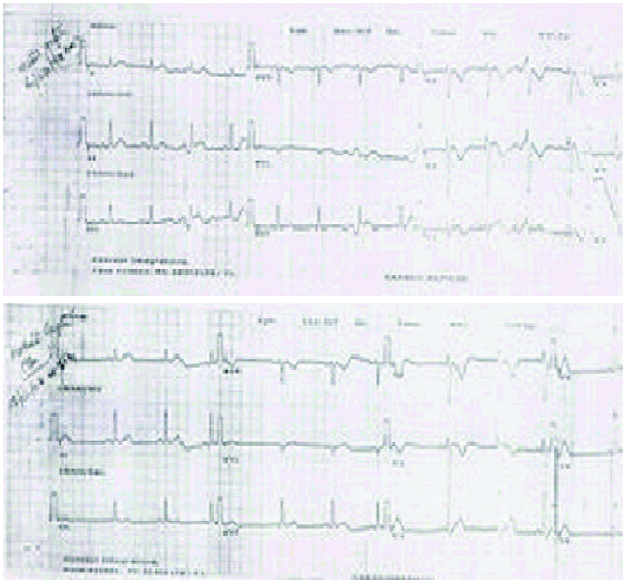

Fig. 1b:

Hospital course

The patient remained afebrile throughout and had no dyspnoea at any point in time. Drowsiness improved with the improvement in vitals. Inotropic support was gradually tapered. Enzyme levels continued to rise till day three followed by decline to normal levels on day five. The patient was discharged from the hospital on day seven.

Table I: Biochemical profile showing alterations.

Investigations	Day 1	Day 3	Day 5
Haemoglobin (g/dl)	10.28	_	14.0
Total leucocyte count/ (mm^3)	10,400	_	10,500
Blood sugar (mg/dl)	67	_	_
Serum bilirubin (mg/dl)	1.35	1.89	.72
SGOT (U/L)	76.12	307.34	53.17
SGPT (U/L)	55.87	460.9	90.1
SAP (U/L)	526.1	607.4	_
CPK-MB (U/L)	81.02	81	_
Urea (mg/dl)	17	69.2	35.6
Creatinine (mg/dl)	.83	1.62	.99

Discussion

Raised CPK-MB levels and serial changes in ECG confirm myocardial damage. Earlier reports of Lalchandani *et al*[3] predicted a poor prognosis in patients with elevated CPK-MB levels at admission. In our case, an old exposed tablet of celphos did induce myocardial damage although the outcome was favourable. Another report of subendocardial infarction in a young survivor showed clinical recovery much earlier as was in our case[4]. Subtle changes in ECG may go unnoticed or may appear as late as twelve hours after ingestion, as seen in this case.

Conclusion

Recording serial ECGs and CPK-MB for at least 24 hours should be made routine as the cardiovascular system is the major target organ for damage.

Repeat ECGs and serial enzyme levels may unfold more and more cases with myocardial involvement requiring prompt treatment of arrhythmias to prevent death. Serum alkaline phosphatase (SAP) and CPK-MB were the first to rise. Minimal alterations in bilirubin, urea, and creatinine were also observed, which eventually returned to normal on day five.

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CASE REPORT

JIACM 2011; 12(1): 56-8

Empyema following Diesel Siphonage – a Rare Complication

Nitya Nand, A Goyal**, R Kumar***

Abstract

Siphoning of diesel/petrol from fuel tanks is a common practice in India especially in semiurban/rural areas. Accidental aspiration of mineral oil during siphonage can cause consolidation, atelectasis and abscess formation. Empyema following mineral oil aspiration is a rare complication and is scarcely documented in literature. We hereby report a case of a young labourer who presented with chest pain, cough, and shortness of breath following accidental aspiration of diesel during siphoning. Diagnosis of mineral oil pneumonia with empyema was based on the findings on ultrasound (US), computed tomography (CT), and biochemical analysis of pleural aspirate.

Key words: Diesel siphonage, hydrocarbon pneumonitis, empyema.

Introduction

Mineral oil pneumonia due to hydrocarbon aspiration is an uncommon and often unrecognised clinical entity. Hamilton first described pneumonitis due to hydrocarbon aspiration in 1897[1]. Since then accidental poisoning has been reported with kerosene, dry-cleaning fluids, mineral seat oil and diesel. Mineral oil is commonly used as a vehicle fuel in our country. Aspiration of diesel/petrol may occur accidentally while siphoning from fuel tanks[2-6]. We herewith report a labourer who presented with aspiration of diesel-induced lung injury leading to development of pneumonitis, and more distinguishly, empyema.

Case report

A 32-year-old man presented to us with a history of accidental diesel aspiration while siphoning diesel from the fuel tank two days prior to admission. This was followed by progressively increasing breathlessness associated with pain on the left side of chest. He also developed cough with mild expectoration and haemoptysis. Expectoration was white coloured and non-foul smelling. There was no history of nausea, vomiting, dysphagia, hoarseness of voice, or CNS involvement.

On examination, the patient was febrile with a pulse rate of 120/min, regular, good volume with BP of 120/80 mmHg. The patient was dyspnoeic at rest with a respiratory rate of 26/min. There was no cyanosis or pedal oedema, and JVP was normal. Left hemithorax showed markedly decreased respiratory movements with dull percussion note. On auscultation, breath sounds were markedly diminished in the left hemithorax. Breath sounds were also decreased in the right infra-axillary and infra-scapular areas.

Complete haemogram showed TLC of 16,000 with 80% polymorphs. Blood gas analysis (BGA) showed a pH of 7.37, pCO_2 36.9, and pO_2 of 34.3 with 63.8% oxygen saturation.

Initial chest X-ray (PA view) (Fig. 1) showed an opaque left hemithorax with blunting of left-sided cardiophrenic (C-P) angle. Right C-P angle blunting was also present. US

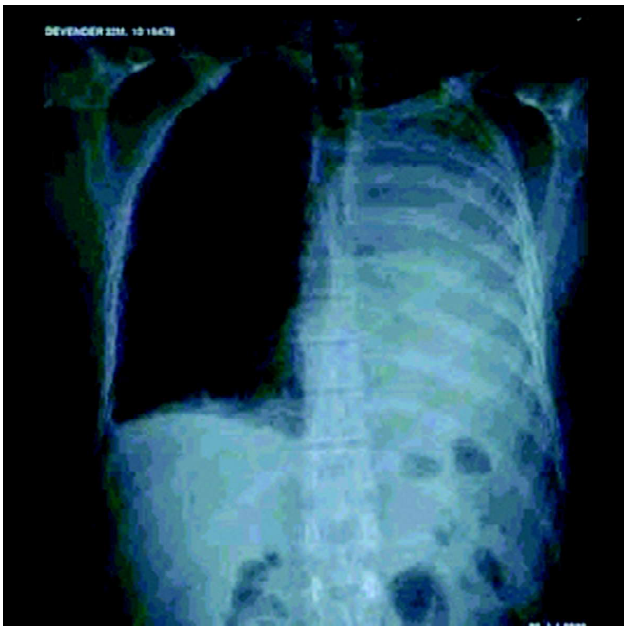

Fig. 1: *Chest X-ray shows opaque left hemithorax with blunting of left C-P angle. There is mediastinal shift to the left.*

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chest showed massive left-sided pleural effusion with septations with middle and lower zone consolidation. Right-sided pleural effusion was also present (a diagnostic tap was tried under US guidance, but nothing could be aspirated). Provisional diagnosis of diesel aspiration with left lower and middle zone pneumonitis with loculated effusion was made. The patient was treated with O_2 inhalation, analgesics and IV amoxycillin-clavulanic acid.

The patient improved symptomatically with the treatment. Five days later, the chest X-ray PA view showed partial resolution of left-sided pleural effusion with left middle and lower zone pneumonitis (Fig. 2). Blood gas analysis also showed improvement with pO_2 of 66.5, and O_2 saturation of 93.1%. CECT chest showed a collection in the left pleural cavity with thickened enhancing parietal and visceral pleura suggestive of empyema (Split pleura sign) with consolidation in the left lower lobe (Fig. 3). Another attempt at US guided pleural fluid aspiration showed a pus-like aspirate. Biochemistry of pleural fluid revealed protein of 4.7gm% and sugar < 20 gm%. Pleural fluid cell count was 4,000/mm^3 with 80% polymorphs. On Gram-staining, Gram-negative bacilli were seen. Culture showed growth of *E. coli*. Ziehl-Neelsen staining was negative.

Hence, a final diagnosis of diesel aspiration with left middle and lower zone pneumonitis with left-sided empyema with minimal right-sided pleural effusion was made.

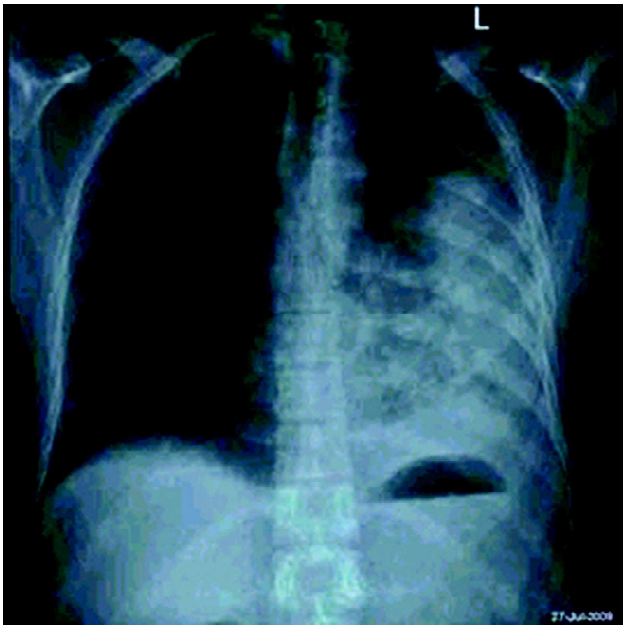

Fig. 2: *Chest X-ray done after five days shows consolidation in the left middle and lower zones with slight collapse. There is blunting of left C-P angle.*

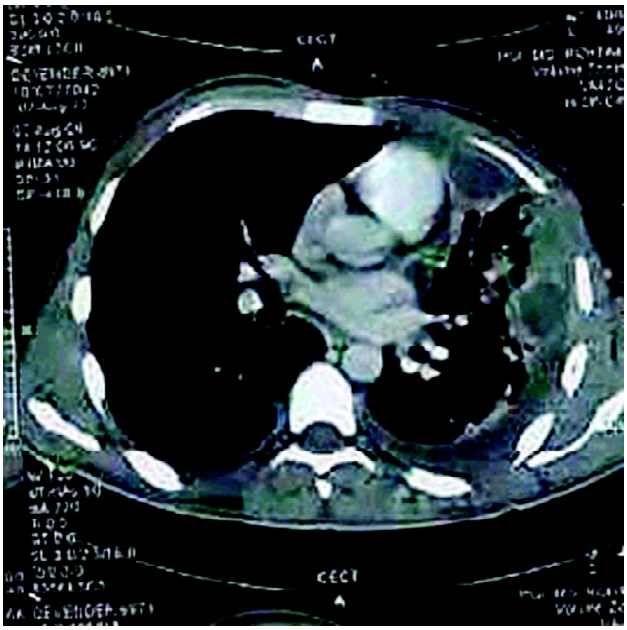

Fig. 3: *CECT chest showing loculated fluid collection in the left pleural cavity with thickened enhancing parietal and visceral pleura ("Split pleura sign") suggestive of empyema. Consolidation is also seen in the underlying left lower lobe.*

Discussion

Siphonage of fuel from a motor vehicle is a very common practice in our country. Accidental aspiration of diesel/other mineral oil during siphoning can occur as a result of direct inhalation or may follow ingestion[1-6].

Symptomatic involvement of the pulmonary system occurs in the form of consolidation, airway obstruction leading to atelectasis and abscess formation[2]. Clinically, aspiration may cause diffuse scarring in the lung, leading to pulmonary fibrosis.

Pathogenetically, the viscosity of oil is the most important property that directly determines the risk of pulmonary aspiration. Compounds with low viscosity and high volatility (e.g., gasoline, kerosene, and lighter fluids) can spread over mucosal surfaces easily and rapidly. The mechanism of oil aspiration is the failure of the mineral oil, and similar other substances, to evoke a cough reflex[2].

Mineral oil pneumonia has been defined as "the inflammatory granulomatous and fibrotic reaction of the lung to the aspiration of mineral oil". This is thought to

be an indolent and benign process resembling low grade bronchopulmonary infection with non-specific clinical findings. The characteristic histopathological picture of gasoline aspiration is the presence of lipoid cells or foamy cells in a fine state of subdivision[7].

The most common radiological appearance is that of a bilateral basal involvement due to aspiration into lower lobes without much of a cough response. Middle lobe involvement has been reported to be common in patients who have been reported to develop chemical pneumonia following siphonage related to petrol or diesel aspiration postulated to be related to the forward bending of the patient while siphoning the fuel[3-5]. Empyema following hydrocarbon aspiration has been reported previously as a rare complication due to kerosene aspiration[8]. In contrast, our patient developed empyema following diesel aspiration and so this is the first case report of its kind.

The clinical presentation of hydrocarbon pneumonitis is often non-specific and includes breathlessness, cough, chest pain, and haemoptysis. In all cases of hydrocarbon pneumonitis induced by siphonage of diesel/petrol that have been reported so far, a favourable clinical outcome has been observed[3-6]. The treatment is usually empirical, as there is insufficient data advocating the utility of corticosteroids and antibiotics[7]. Our patient showed clinical improvement with the symptomatic therapy.

When ingested, hydrocarbons produce toxic effects in several organs and organ systems including pulmonary, CNS, gastrointestinal, CVS, and the haematopoietic systems. Among these, the most serious damage occurs to the pulmonary system[7].

Our case highlights the fact that empyema, though very rare, can occur due to accidental diesel aspiration while siphoning, along with hydrocarbon pneumonitis. Physicians should be aware of such a possibility that can arise following siphonage of motor fuel.

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FORM IV (See Rule 8)

The following particulars regarding the ownership of the **"JOURNAL, INDIAN ACADEMY OF CLINICAL MEDICINE"** are published as called for by Rule 8 of the Registration of Newspaper (Central) 1956.

1 Place of Publication – Barrala House, 867, Guru Gobind Singh Marg, New Delhi – 110 005.

2 Periodicity of Publication – Quarterly

3 Printer's Name – Dr. D.G. Jain
Nationality – Indian
Address – Barrala House, 867, Guru Gobind Singh Marg, New Delhi – 110 005.

4 Publisher's Name – Dr. D.G. Jain
Nationality – Indian
Address – Barrala House, 867, Guru Gobind Singh Marg, New Delhi – 110 005.

5 Editor's Name – Dr. D.G. Jain
Nationality – Indian
Address – Barrala House, 867, Guru Gobind Singh Marg, New Delhi – 110 005.

6 Name and address of individuals who own the newspaper and partners or shareholders holding more than one per cent of the total capital.

– Indian Association of Clinical Medicine, Headquarters: Postgraduate Department of Medicine, S.N. Medical College, Agra – 282 002 (U.P.)

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CASE REPORT

JIACM 2011; 12(1) : 59-60

Tubercular Splenic Abscess

TP Singh*, AK Gupta*, Ashwini Nigam*

Abstract

Tubercular splenic abscess is an uncommon entity in immunocompetent patients. It has been reported in association with immunodeficiency states. A 35-year-old male, immunocompetent, was diagnosed as having a tubercular splenic abscess. The aim of reporting this case is to stress the fact that tuberculosis should be considered as a differential diagnosis in all cases of splenic abscess in areas where tuberculosis is endemic.

Introduction

Tubercular splenic abscess is still a rare entity, mostly seen in a immunocompromised host. In view of the rarity of the condition, especially in immunocompetent persons, we report such a case along with review of the literature.

Case report

A 35-year-old immunocompetent male patient presented with history of low grade fever, and left-sided upper abdominal pain for the last 8 months. There was history of breathlessness, swelling over feet, decreased appetite, and weight loss for the last 2 months. The patient had received ATT for 2 months, 3 months prior to admission. There was history of occasional alcohol intake. There was no past history of hypertension, diabetes, haematemesis, melaena, and jaundice.

On physical examination, the patient was febrile with an average body build. His pulse rate was 92/minute and blood pressure was 140/80 mmHg. He had icterus and pedal oedema.

On examination, the chest and the CVS was normal.

Abdominal examination revealed a palpable liver (2 cm, soft, and non-tender with smooth surface), and spleen (5 cm, firm in consistency, with smooth surface and mild tenderness). There was no evidence of free fluid in the peritoneal cavity.

The routine blood tests revealed Hb - 11.6 gm/dl, TLC - 8,800 cells/cumm, blood sugar - 85 mg/dl, blood urea - 40 mg/dl, S. creatinine - 1.27 mg/dl, S. bilirubin - 1.2 mg/dl, SGPT - 45 U/L, SGOT - 74 U/L, and the urine examination was normal. Widal test for typhoid was negative, ELISA test for HIV was negative, marker for viral hepatitis was negative. Serum albumin was 3.86 g/dl, and stool examination did not reveal any parasite. Contrast-enhanced spiral CT examination of abdomen showed hepatosplenomegaly with a hyperechoic lesion in the splenic tissue likely to be splenic abscess. FNAC was done; it showed reactive lymphoid cells, few ill-formed epithelial cells, granulomas, and necrotic material. Stain for AFB was negative. This report is consistent with tuberculosis.

Discussion

In recent times, the incidence of splenic abscess has increased due to the increasing number of immunocompromised patients being diagnosed. The pathogenesis of splenic abscess includes haematogenous spread of a remote infection, haemoglobinopathy, chemotherapy, and other immunodeficiency states[1].

The classic presentation of fever with chills, left upper abdominal pain with marked leucocytosis as is seen in the majority of splenic abscesses, is usually not seen in a tubercular splenic abscess[2].

Diagnosis of tubercular splenic abscess has been made by ultrasound examination or computed tomography examination of the abdomen combined with the use of guided fine needle aspiration of the abscess[3].

This patient was prescribed a full course of the 4-drug anti-tubercular treatment and monitored by serial imaging. There was diminution in the size of the abscess on subsequent imaging[3].

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Splenectomy can be avoided if there is clinical improvement on anti-tubercular treatment. Splenectomy should be advised to patients who fail to respond to anti-tubercular treatment (ATT).

The probable mechanism of tubercular splenic abscess could be due to entrapment of slow growing mycobacteria in the red pulp of the spleen, which is relatively devoid of phagocytic activity, thus escaping entrapment by the reticulo-endothelial system of the spleen.

Tuberculosis should be considered as a differential diagnosis in all cases of splenic abscess in immuno-competent patients.

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CASE REPORT

JIACM 2011; 12(1): 61-5

Dual Neurotoxicity (Acute Encephalopathy followed by Delayed Myeloneuropathy) following Dichlorovos Poisoning

Geeta A Khwaja, Om Prakash**, Daniel Vinita**, Meena Gupta***, Debashish Chowdhury*, Makrand Hirve***

Abstract

Organophosphate compounds (OPCs) are used as pesticides, and suicidal ingestion is the most common mode of OPC poisoning in India. Several clinical syndromes, including acute muscarinic syndrome, acute encephalopathy, intermediate nicotinic syndrome, delayed neuropathy, and rarely Guillain Barre-like syndrome, extrapyramidal syndrome, dual neurotoxicity, chronic neuropsychiatric disorder, and war gas poisoning can be encountered, depending on the dose and the type of organophosphate exposure. Dual neurotoxicity is extremely rare and the clinical profile and electrophysiological features of one such case following suicidal ingestion of the organophosphate dichlorovos are described along with a brief review of the literature.

Introduction

Organophosphates are primarily used as pesticides, and suicidal ingestion, occupational exposure, or consumption of oil or food contaminated by organophosphates are well documented modes of poisoning. The severity of the poisoning depends on the dose and the type of organophosphate exposure. Several clinical syndromes can be encountered, but dual neurotoxicity is extremely rare. One such case, caused by exposure to dichlorovos, is being reported by us.

Case summary

A 14-year-old female, in an attempt to commit suicide, consumed around 20 ml of an organophosphate compound (dichlorovos) with the trade name of "Badal", 2 months prior to admission in our hospital. Immediately after ingestion of the insectide, she developed nausea and a tingling sensation in the mouth and all over the body, followed by loss of consciousness within 5 minutes. She was rushed to the emergency where she was subjected to gastric lavage and put on ventilatory support. She was also treated with injection atropine and pralidoxime (PAM) besides being catheterised and put on the Ryle's tube. She regained consciousness within 24 hours of initiating treatment; but remained restless, agitated and paranoid and also suffered from formed, vivid fearful hallucinations comprising of bloody and stabbing scenes for the next 12 hours or so. She however became fully conscious and oriented and was taken off ventilatory support by day three. The Ryle's tube and catheter were removed by day five, and by day seven she could sit up in bed and stand and walk with support. At the time of discharge on day nine, there was no motor or sensory deficit and she could walk unsupported.

She remained relatively asymptomatic for the next one week, but then started noticing calf pain and easy fatiguability on walking. Over the next 3 to 4 days she developed a painful, burning sensation accompanied by impaired touch, pain, and temperature sensation in the stocking and glove distribution. This was accompanied by a progressive motor weakness and wasting of the legs with bilateral foot drop, besides clawing and wasting of the small muscles of the hand. Within 2 weeks of the onset of the limb complaints, she also developed an increased urinary frequency along with urgency and hesitancy, and therefore had to be re-catheterised for retention of urine, for the next 12 days. All the symptoms progressed over a period of 4 weeks, and subsequently remained static over the next 2 weeks, when she reported to us. There was no history of sweating abnormalities, visual complaints, cranial nerve involvement, or any systemic disturbance.

On examination at the time of presentation, her vitals were stable, and systemic examination was normal. Skin, hair, and nail examination was also normal. On neurological examination, the higher mental functions were normal and cranial nerves were intact. On motor examination,

** Professor, ** Senior Resident, *** Director-Professor and Head, Department of Neurology, GB Pant Hospital, New Delhi - 110 002.*

tone was reduced distally and there was a marked wasting of the hand, forearm, and leg muscles with bilateral hand clawing and foot drop. Power was grade 5 at the shoulder and hip, and grade 4 plus at the elbows and knees. There was severe weakness of hand grip and small muscles of the hand, and grade 0 power at the toes and ankles. All deep tendon reflexes (DTRs) were brisk, but the ankle jerks were absent and the plantars were not elicitable. On sensory examination, touch, pain and temperature sensations were impaired by around 50% in the distal parts of the lower and upper limbs. Vibration and joint position sense was impaired in the toes.

On investigation, haemogram, blood sugar, LFT, KFT, serum electrolytes, ECG, and X-ray chest were normal. On nerve conduction studies, motor conduction was not recordable in the median, ulnar, common peroneal and post-tibial nerves bilaterally. Sensory nerve conduction was normal in the upper limbs but reduced amplitude (2.1 and 2.4 μv) and conduction velocity (35 and 37 m/s) was recorded in both the sural nerves. EMG revealed fibrillation potentials and reduced interference in the distal muscles, suggestive of denervation.

In view of a history of complete recovery from dichlorovos-induced acute encephalopathy followed by a delayed onset myeloneuropathy (2 weeks post-ingestion), a diagnosis of dual neurotoxicity was entertained. The diagnosis of myeloneuropathy was supported by a history of urinary retention during the acute phase of the illness accompanied by a distal symmetric motor-sensory deficit with generalised hyper-reflexia, but absent ankle jerks. She was treated with physiotherapy and pregabalin (150 mg/day) which resulted in complete relief of hypersthetic pain and at a subsequent one month follow-up, there was no further progression and a partial recovery in motor function.

Discussion

Organophosphate compounds (OPCs) are used as pesticides, petroleum additives, plastic modifiers, lubricants, antioxidants, and flame retardants[1]. They may be absorbed via the skin or respiratory and gastrointestinal tracts[1]. Suicidal ingestion is the most common mode of OPC poisoning in India[2]. Occupational exposure to organophosphates in agricultural workers or consumption of oil or food contaminated or adulterated by the toxin are other well documented modes of poisoning[2]. The severity of poisoning depends on the dose and the type organophosphate exposure[3]. Commonly implicated OPCs include diazinon, malathion, fenthion, sumithion, chlorpyrifos, chlorfenvinphos, paroxanmethyl, dimethoate, oxydementon, tri-orthocresyl phosphate (TOCP), dichlorovos, leptophos, mipafox, chlorphos, trichlorfox, metriphonate and metamidophos[1,2,4].

Early manifestations of organophosphates are caused by phosphorylation and inhibition of the enzyme acetyl-cholinesterase. This results in accumulation of acetylcholine (Ach) and a depolarisation block at the muscarinic, nicotinic, and central nervous system receptor sites[5]. Several clinical syndromes can be encountered in patients with organophosphate poisoning. These include an acute muscarinic syndrome (type I syndrome), acute encephalopathy or CNS syndrome (uncommon), intermediate nicotinic syndrome (type II syndrome), organophopsphate-induced delayed neuropathy (type III syndrome) and rarely organophosphate-induced Guillain Barre-like syndrome, extrapyramidal syndrome, dual neurotoxicity, chronic neuropsychiatric disorder, and war gas poisoning[1,4,5].

'Acute muscarinic syndrome' is due to the parasympathetic effects of acetylcholine on hollow organs, bronchi, salivary, lacrimal and sweat glands[6]. Acetylcholinesterase is easily inhibited at the muscarinic synapses and muscarinic effects appear early, within minutes to half-an-hour, and only rarely beyond 12 hours[5]. Muscarinic effects include salivation, nausea, vomiting, abdominal cramps, diarrhoea, urination, sweating, rhinorrhoea, bronchorrhoea, broncho-constriction, pulmonary oedema, headache, miosis, blurred vision, bradycardia, and hypotension[4-7]. Depending upon the severity of intoxication, the acute syndrome may last for a few days and responds to atropine[1].

'Acute encephalopathy or CNS manifestations' are uncommon in acute organophosphate poisoning but may appear in untreated, severe poisoning with agents that cross the blood brain barrier[4]. Anxiety, restlessness, apathy, confusion, tremors, headache, seizures,

drowsiness, and coma may be encountered[5]. Miosis, bilateral pyramidal and extrapyramidal signs, ataxia, slurred speech, and respiratory or circulatory failure may also occur. These features may accompany the acute muscarinic syndrome and also respond to atropine[5]. Our patient also presented with acute encephalopathy, as evidenced by the loss of consciousness within 5 minutes of ingesting dichlorovos. As to whether it was accompanied by acute muscarinic features, is not known, as details of the initial hospitalisation were not available. She however received and responded to atropine and pralidoxime (dose not known). Moreover, during recovery from acute encephalopathy, historically, she was paranoid and hallucinating, presumably due to atropine toxicity. Atropine crosses the blood brain barrier and toxic delirium characterised by garrulousness, tactile and visual hallucinations, failure to recognise persons, and restlessness can be attributed to atropine over-dosage and may last for up to 48 hours as was observed with our case[6]. It has been reported with a lowest cumulative dose of 5.4 mg and higher doses of up to 165 mg[6]. It is usually associated with tachycardia, dryness of mouth and hot flushed skin, and is an indication to discontinue atropine. The details of the associated clinical features are, however, not known in our case.

The 'nicotinic or intermediate syndrome' occurs in cases with severe poisoning only and follows the acute muscarinic phase in 20 to 50% cases[1]. It usually sets-in 24 to 96 hours after the initial exposure to the organophosphate and may last for 2 to 18 days[4,7]. Nicotinic effects are motor and sympathetic in nature and require a failure of at least 80% of the synaptic acetyl-cholinesterase at the nicotinic nerve terminals[4]. The cardinal features of this syndrome include fasciculations, muscle cramps, and weakness of the neck flexors, face, ocular (ptosis and ophthalmoplegia) and bulbar muscles besides weakness of the trunk and proximal limb muscles. Respiratory paralysis may occur and reflexes are depressed or absent[1,5]. Electrophysiologically, such weakness is usually associated with normal or very mildly slowed motor nerve conduction velocities[2]. The amplitude of the CMAP is, however, reduced and characteristically shows a repetitive response to a single stimulation[2]. The OPC-induced intermediate syndrome reflects transmission failure at the neuromuscular junction and the repetitive response which is the hallmark of organophosphate poisoning, occurs with supramaximal electrical stimulation of the motor nerve and recording over the muscle innervated by it[4]. In acute OPC poisoning it can be recorded over multiple muscles and characteristically occurs in a resting muscle and decreases or disappears after voluntary muscular exercise and repetitive nerve stimulation (RNS)[4]. The repetitive action of the excess acetylcholine at the motor endplate is responsible for this electro-diagnostic finding.

A decremental response to high rate (30 to 50 Hz) RNS is seen in the intermediate phase, due to a desensitisation type of neuromuscular block. The ratio of the amplitude of the ninth CMAP to the first (9:1 ratio) is arbitrarily taken as an objective marker of the severity of the decremental response[4]. In majority of the cases, a significant decremental response is seen more frequently at high stimulation rates of 30 Hz and less often at 10 or 3 Hz[5]. It may last for 4 to 11 days after the onset of paralysis[4]. EMG is usually normal and does not show any evidence of fibrillation or positive sharp waves[2]. The interference pattern may be mildly reduced, depending on the degree of muscle effort.

'Organophosphate-induced delayed neuropathy (OPIDN)' may occur 2 to 4 weeks after poisoning by a very limited number of OPCs including triorthocresyl phosphate (TOCP), mipafox, trichlorophenol, and methamediphos[2,4]. Poisoning with TOCP has been recognised as a cause of delayed distal motor-sensory neuropathy. It may follow ingestion of cooking oils (mustard, sesame), drinks, or flour adulterated or contaminated with TOCP, or may follow massage with contaminated oil[3,5]. The first major epidemic of TOCP poisoning occurred in the USA in 1930 and was labelled as Jake-leg paralysis or Jamaica-ginger paralysis[5]. TOCP continues to be seen in small epidemics in India, due to adulteration of cooking oil and has been reported from Bombay (1960), West Bengal (1962) and Assam, besides other countries like Sri Lanka and Morocco[(3,5)]. Exposure to massive, large amount of TOCP has been reported to cause an initial prodromal phase with nausea, vomiting, abdominal pain, and diarrhoea a few days before the onset of neuropathy in around 50% cases[5]. OPIDN is a predominantly motor, distal dying back axonapathy characterised by cramps in the calves, distal paraesthesias

and limb weakness with foot drop and intrinsic hand muscle wasting. Proximal lower limb muscles may be affected in up to 40% cases[5]. Ankle jerks are usually absent but knee and other deep tendon jerks are often exaggerated, pointing to a spinal cord involvement. Stocking and glove sensory impairment may be encountered in up to 46.5% cases, but joint position sense and vibration is usually preserved[5]. Evolution of the neuropathy is acute to subacute and recovery is slow[1]. The clinical manifestations of OPIDN are not caused by acetylcholine excess at the myo-neural nicotinic receptors. OPIDN is probably caused by phosphorylation and inhibition and subsequent ageing (dealkylation) of a protein enzyme called neuropathy target esterase (NTE) in the nerve cells[1,8]. This enzyme is present in the brain, spinal cord, and peripheral nerves as well as in non-neural tissues and cells such as spleen, muscle, and lymphocytes[1,8]. Electrodiagnostic studies of OPIDN demonstrate an axonal neuropathty with acute and chronic denervation in distal and occasionally proximal limb muscles[1]. Motor conduction studies are either normal or minimally slowed but the compound motor action potentials are low in amplitude[1]. Despite symptoms being predominantly motor, diminished sensory action potential amplitudes are a sensitive marker for OPIDN[1].

A 'Guillian Barré syndrome' like picture with flaccid, areflexic weakness, bilateral facial palsy, raised CSF proteins and a demyelinating neuropathy following organophosphate poisoning has also been reported by Fisher, but is rare, and the association remains speculative[1,5].

An 'OPC-induced extrapyramidal syndrome' has also been reported by some authors. It usually occurs after 1 to 3 weeks of exposure and is usually transient and reversible[1,4]. Tremor, rigidity, oculogyric manifestations and a neuroleptic malignant syndrome-like picture have been reported, and are believed to be caused by abnormalities of acetylcholine transmission in the substantia nigra and basal ganglia[1,4].

Chronic neurological effects have been reported to occur following either, one or more attacks of acute cholinergic episodes, or a long-term, low-level exposure to organophospate compounds, and have been labelled as 'chronic organophosphate-induced neuropsychiatric disorder' (COPIND)[8].

'Dual neurotoxicity' due to organophosphate poisoning is extremely rare[1,2,7,9,10]. It is characterised by recovery from acute CNS manifestations or encephalopathy, to be followed by a delayed neurotoxicity or neuropathy, 2 to 4 weeks post-exposure, as was the case with our patient[5]. The initial manifestations are due to inhibition of acetyl-cholinesterase and cholinergic excess while the delayed manifestations are presumably due to inhibition of the enzyme neuropathy target esterase in nerves and spinal cord[1]. Only a few cases of dual neurotoxicity are documented in literature and all reported cases from India have been caused by exposure to dichlorovos[9]. Dichlorovos or 2, 2-dichlorovinyl dimethyl phosphate (DDVP) is a highly volatile organophosphate, available as an aerosol and as a soluble concentrate. Wadia *et al*, in their experience with over 2,000 cases of suicidal organophosphate poisoning, came across only 3 cases of dual neurotoxicity, all following ingestion of dichlorovos[2]. These cases showed all the features of a delayed severe motor axonal degeneration neuropathy, similar to that seen with TOCP, 10 to 15 days after an initial episode of clinical organophosphate anticholinesterase poisoning[2]. EMG in these cases revealed fibrillation potentials and reduced interference in distal muscles. Motor nerve conduction studies showed normal velocities but low amplitude compound muscle action potentials suggestive of axonal degeneration[2]. Sensory conduction was normal. The authors also stressed that no case of delayed neurotoxicity was detected in patients exposed to diazinon, sumithion, fenthion, and malathion – the four most common organophosphate poisonings[2].

Vasconcellos *et al*, have also reported a case of dichlorovos-induced acute cholinergic crisis followed by delayed, subacute, predominantaly motor axonal peripheral neuropathy accompanied by evidence of pyramidal tract dysfunction similar to that seen with TOCP poisoning[1]. Delayed myeloneuritis following acute organophosphate (dichlorovos) intoxication has also been reported in two cases by Koc *et al*[7]. Our case also developed an acute encephalopathy followed by a delayed myeloneuropathy, 2 weeks post-dichlorovos ingestion. In our case however, unlike the reported cases in literature, motor conduction was not recordable, while

sensory conduction velocity and amplitude was reduced in the sural nerves suggestive of a severe, predominantly motor neuropathy with evidence of denervation on EMG.

Overall, delayed polyneuropathy, developing 1 to 26 weeks after exposure to organophosphate compounds, with or without preceding acute cholinergic toxicity, has been reported in around 22% cases with organophophorous poisoning in one recent study[7]. The neuropathy is predominantly motor, and pyramidal findings may accompany these symptoms as was the case with our patient[1].

Diagnosis is based on a history of pesticide ingestion, classical clinical signs or syndromes with characteristic electrophysiological findings and depression of erythrocyte cholinesterase level[5]. Neurologic weakness is usually associated with erythrocyte cholinesterase levels of less than 20% of normal[2]. In patients with acute organophosphate poisoning, the erythrocyte cholinesterase level is usually diminished by 50% or more, but the plasma cholinesterase shows a rising level in the first one month[3]. Both the plasma and erythrocyte cholinesterase levels however, return to normal after a period of 3 to 6 months[3]. Due to financial constraints, erythrocyte cholinesterase level was not estimated in our case.

Treatment of acute poisoning includes stomach wash and ventilatory support, if required. Atropine crosses the blood brain barrier and is the physiological antidote that combats the acetylcholine excess at the muscarinic receptors[5]. It is not effective in the intermediate syndrome[6]. The recommended dose is 2 mg IV every 10-30 minutes, till salivation and sweating are controlled. It may be continued for 4 to 7 days, depending on the severity of the poisoning[4,5]. Atropine glycopyrrolate does not cross the blood brain barrier and hence does not cause toxic delirium, but is not effective in reversing the central muscarinic signs of drowsiness and coma[5]. Pralidoxime (PAM) reactivates cholinesterase and can be given in a dose of 1 gm, every 4 to 6 hours, intravenously. It is effective only if given in the first 24 to 36 hours or at the most 72 hours[4,5]. Obidixime in a dose of 3 mg/kg body weight by intramuscular injection is an alternative to PAM[4,5]. There is however, no specific therapy for organophosphate-induced neuropathy or myeloneuropathy. Physiotherapy and symptomatic treatment for neuropathic pain and dysaesthesias may provide relief, as was observed in our case also. Cases of OPIDN with severe deficits may not recover completely and may be left with residual claw hand deformity, foot drop, persistent atrophy, spasticity, and ataxia[1]. In one series, nearly 50% of patients had some evidence of pyramidal tract dysfunction, although the signs were relatively mild and often delayed in appearance[1]. In our case, however, the pyramidal signs were early to manifest.

In conclusion, patients presenting with acute encephalopathy or CNS manifestations, following exposure to organophosphates, particularly dichlorovos, should be kept under observation for the occurrence of delayed neurotoxicity. Moreover, all patients presenting with neuropathy or myeloneuropathy should be screened for possible exposure to organophosphates or other toxins.

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CASE REPORT

JIACM 2011; 12(1): 66-70

Posterior Circulation Stroke as the Initial Manifestation of Cranio-vertebral Junction Anomaly with Atlanto-axial Dislocation

Geeta A Khwaja, Amit Batla**, M Gupta***, D Chowdhury*, R Ranjan**, A Kulkarni**

Abstract

Atlanto-axial dislocation (AAD) is the commonest skeletal cranio-vertebral junction (CVJ) anomaly in India, followed by occipitalisation of atlas and basilar invagination. They usually present with a progressive neurological deficit (70 - 94% cases) implicating the high cervical cord, lower brainstem, and cranial nerves. The association between skeletal CVJ anomalies and vertebro-basilar insufficiency (VBI) is recognised and angiographic abnormalities of the vertebro-basilar arteries and their branches have been reported, but posterior circulation stroke as the presentation of CVJ anomalies is extremely rare. We report one such case with the even more rare presentation of posterior circulation stroke as the initial presentation of the disorder.

Introduction

The clinical and radiological profile of skeletal cranio-vertebral junction (CVJ) anomalies is well-documented, and atlanto-axial dislocation (AAD) is the commonest type reported from India. Vertebro-basilar territory infarction however, is one of the rarer presentations of CVJ anomalies. We report one such case with the even more rare presentation of posterior circulation stroke as the initial presentation of the disorder.

Case history

An 18-year-old male student, presented to us with a 2-months history of a sudden onset vertigo lasting for a few hours, accompanied by bilateral visual impairment, forgetfulness, and apathy. He also had mild imbalance with a tendency to sway towards the left side while walking. There was no history of altered sensorium, headache, vomiting, diplopia, cranial nerve involvement, speech difficulty, motor weakness, sensory loss, limb incoordination, or any bladder disturbance. Within 3-to-4 days of onset, his vision and gait improved, but the impairment of memory, apathy, and social withdrawal persisted. This was associated with a difficulty in reading and writing, interfering with his studies. There was no history suggestive of hypertension, diabetes, rheumatic heart disease, or any neck pain, manipulation, or trauma.

On examination at the time of presentation, he was conscious and alert but withdrawn. On general examination, he had an abnormal neck posturing with tilting of the neck towards the left-side. There was no scoliosis or kyphosis of the spine but he had bilateral pes cavus with claw feet. His hair line and body: neck ratio (10:1) were however normal. Vitals were preserved and systemic examination was normal.

His mini mental score examination (MMSE) score was 23/30. On detailed cognitive examination, his attention was normal and comprehension and speech were intact. His memory evaluation revealed a severe loss of new learning ability (0/3 recall after 5 minutes) with preserved remote memory. He had difficulty in reading and writing with defective syntax and letter formation. His mathematical calculations ability was also impaired, but construction and copying were normal; and there was no apraxia, finger agnosia, or right-left disorientation. On cranial nerve examination, visual acuity, fundus examination and field of vision were normal. Other cranial nerves were intact. On motor examination, size, tone, power and reflexes were normal in all the four limbs and plantars were bilaterally flexor. There was no sensory loss. On cerebellar examination, he was found to have a mild intention tremor with finger nose incoordination, past-pointing, dysdiadochokinesia and impaired rebound check in the left upper limb. His heel-shin coordination was also impaired on the left-side.

In view of the history of a sudden onset vertigo accompanied by bilateral visual impairment, recent

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memory loss, apathy, and gait ataxia with subsequent partial recovery over the next few days, a possibility of a posterior circulation stroke affecting the left cerebellum, bilateral occipital and temporal lobes and thalamus was entertained. Moreover, in view of a young stroke without any obvious risk factors and the presence of abnormal neck posturing and pes cavus, a possibility of an associated cranio-vertebral junction (CVJ) anomaly was also entertained.

His investigations revealed a normal haemogram and ESR. Blood sugar, LFT, KFT, lipid profile, electrolytes, and homocysteine levels were within the normal range. Tests for HIV, rheumatoid (RA) factor, and ANA were negative. X-ray chest, ECG, echocardiography, carotid and vertebral doppler studies were normal. VEP testing was in the normal range (R – 97 ms; L – 99 ms). X-ray of cervical spine including the CV junction revealed an occipitalised atlas with C 2 – 3 block vertebra and atlanto-axial dislocation (Fig. 1). MRI of the brain and CV junction revealed recent onset small infarcts involving bilateral occipital and medial temporal lobes, left thalamus, and both cerebellar hemispheres (Fig. 2). Atlanto-axial dislocation with indentation over the cervico-medullary junction and reduction of the retro-odontoid spinal canal space (8 mm) was also observed (Fig. 3). On MR angiography of the brain and neck, there was a partial attenuation of both the posterior cerebral arteries along with non-visualisation of the left vertebral artery (Fig. 4).

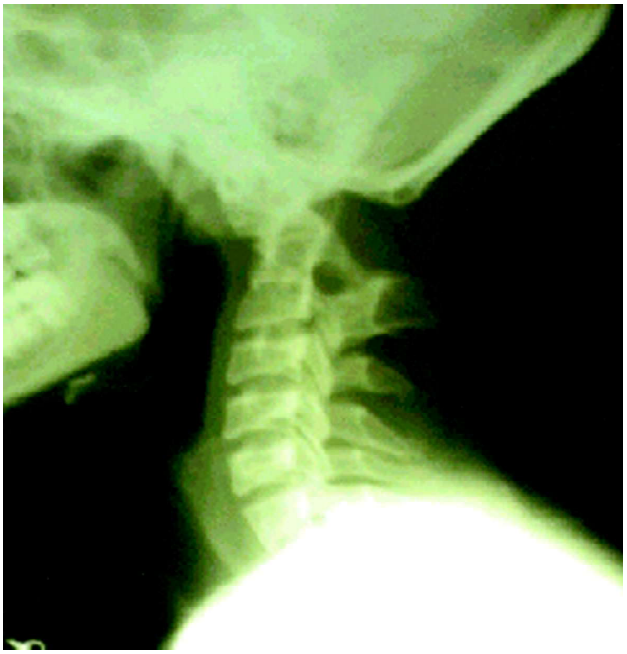

Fig. 1: *X-ray of CV junction showing occipitalised atlas, atlanto-axial dislocation, and C 2 – 3 block vertebra.*

Discussion

Congenital cranio-vertebral junction (CVJ) anomalies encompass the developmental defects of the occipital bone surrounding the foramen magnum, atlas and axis vertebrae. During foetal development, the mesodermal somites form 4 occipital and 2 cervical sclerotomes that form the CVJ. Defects occurring in the 3rd and 4th week of embryogenesis can cause CVJ anomalies which may implicate either the skeletal or neural structures or both[1,2]. The bony anomalies may implicate the occiput (basilar invagination and platybasia) or the atlas (occipitalisation of the atlas and atlanto-axial dislocation) or axis (odontoid malformations) and other vertebrae (Klippel-Feil anomaly)[1,2]. Neural or soft tissue anomalies include Chiari malformation, syrinx, and Dandy-Walker syndrome)[1,2].

Presently, there is no epidemiological data available, and most of the information regarding skeletal CVJ anomalies is derived from retrospective reviews of hospital records. CVJ anomalies are more common in India as compared to the West[1]. Basilar invagination is more common in the West, whereas atlanto-axial dislocation (AAD) is the commonest in India, followed by occipitalisation of atlas, and basilar invagination. AAD, occipitalisation of atlas, and fusion of C2 and C3 vertebrae are the commonest anomalies occurring in combination in India[1]. The CVJ anomalies occur since birth, but the mean age of manifestation is around 25 years. Males are most commonly affected and a predisposing factor like trivial neck trauma may be identified in nearly 50% of the cases[2]. Our patient was also a male and first became symptomatic at 18 years of age but there was no history of preceding neck trauma or manipulation.

Skeletal CVJ anomalies commonly present with a progressive neurological deficit (70-94% cases) implicating the high cervical cord, lower brainstem, and cranial nerves[1]. The clinical features include spastic quadriparesis (100% in some series), but hemiparesis and Brown-Séquard syndrome can also occur[1]. Sensory loss is seen in around 33% cases, and loss of proprioception is

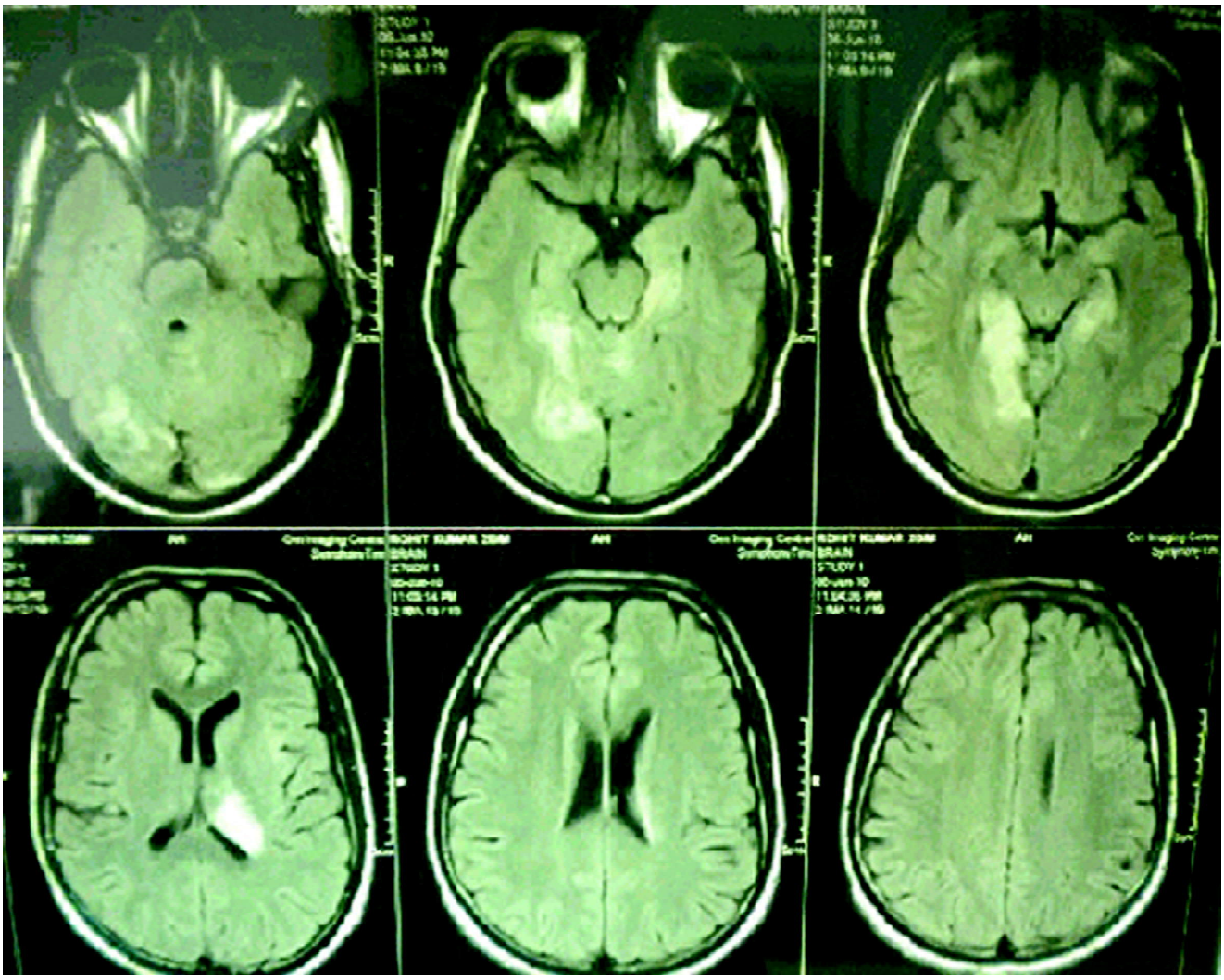

Fig. 2: *Flair MRI brain, axial sections, showing multiple infarcts in the posterior circulation.*

more prominent in fingers than toes[1, 2]. Lower cranial nerve involvement is seen in 12%, and cerebellar signs in 10% cases[1, 2]. Bilateral hand wasting is a common (25% cases) false localising sign[1, 2]. Urinary involvement is uncommon. Mirror movements and pseudoathetosis are infrequent but useful signs in the diagnosis of CVJ disorders. Transient deficits are seen in around 20% patients and may include motor weakness, sensory disturbances, visual loss, dysarthria or inability to speak, and urinary disturbances. These may last from a few minutes to hours and are possibly due to platelet microembolisation in the vertebro-basilar artery territory[1,2]. Our patient however presented as a case of young-onset posterior circulation stroke with apathy, visual, memory and cerebellar dysfunction of acute onset.

The association between vertebro-basilar insufficiency (VBI) and skeletal CVJ anomalies is well-recognised but may be under-estimated, as according to some studies only 30% of cases with VBI undergo X-rays of the cervical spine, and only 11% are evaluated using proper flexion and extension views of the CVJ *per se*[3,4]. However, posterior circulation stroke as the presentation of CV junction anomalies, as was observed in our case, is extremely rare[1]. In a study of 115 patients with CVJ abnormalities, Wadia *et al*[1] have reported symptoms of VBI with posterior circulation stroke in three, and angiographic narrowing of the vertebral arteries at the level of the atlanto-axial joint in one patient with symptoms of VBI only[1]. Another study of 40 patients with C V junction anomalies from India, has reported symptoms of VBI in three, but stroke

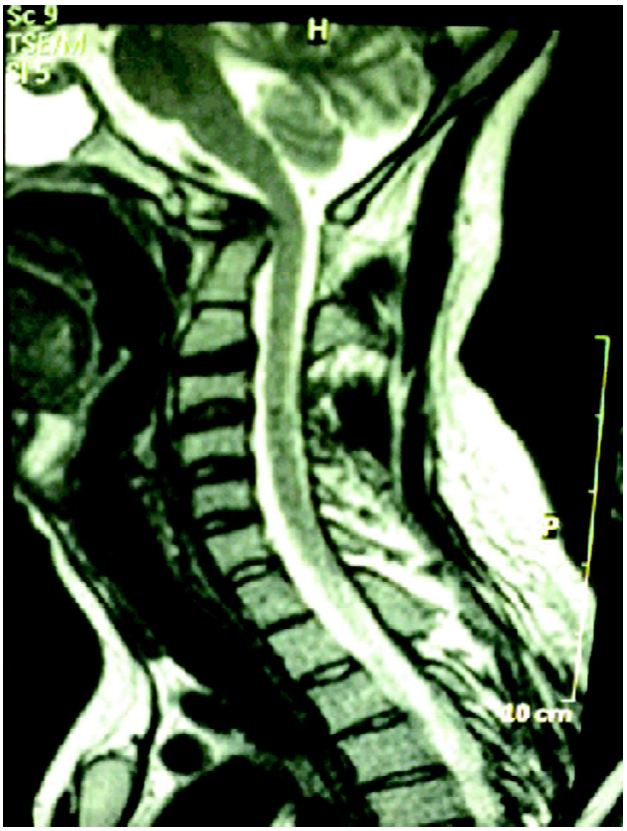

Fig. 3: *T2 weighted MRI cervical spine (saggital section) showing indentation of the cervico-medullary junction by the odontoid process.*

in none of the cases[5]. Satishchandra *et al*, in a series of 200 cases with CVJ anomalies, have reported acute stroke in the vertebro-basilar artery territory in eight cases *per se*[6]. The clinical rarity of posterior circulation infarcts in CVJ anomalies has been attributed to dual supply through the two vertebral arteries and the adequacy of the circulation from the circle of Willis[3].

Atlanto-axial dislocation[1,3,7-9], is the commonest CVJ anomaly implicated in causing stroke or VBI, followed by odontoid aplasia[10], basilar impression, occipitalisation of the atlas, Klippel-Feil anomaly[1], and anomalous osseous process of the occipital bone projecting to the posterior arch of the atlas[11]. Our patient also had atlanto-axial dislocation in conjunction with occipitalisation of the atlas and C 2 – 3 block vertebra with posterior circulation stroke. In most reports of CVJ anomalies with stroke, cerebellar infarction is common but multiple areas supplied by the vertebro-basilar system can be affected as was observed with our case.

Angiographically, vertebral arteries are most commonly

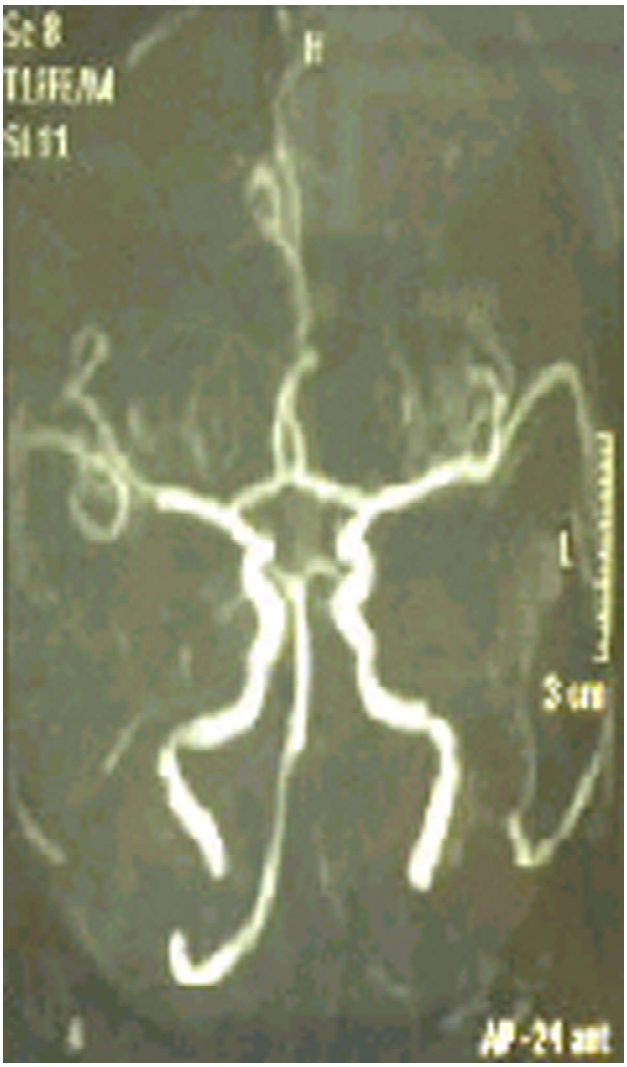

Fig. 4: *MR angiography showing non-visualisation of the left vertebral artery and partial attenuation of both the posterior cerebral arteries.*

affected[1, 7, 8] but branches of the vertebral, basilar, and the posterior cerebral arteries may be attenuated or poorly developed[7, 9-11] with thromboembolism being sometimes reported[9-11]. Vertebral artery dissection and posterior circulation stroke following neck manipulation has been reported in three cases with basilar invagination; during intubation in one case, following cervical traction in another case, and no obvious cause in one case[12-14]. In one study of 7 cases with AAD and VBI, DSA (digital subtraction angiography)/MRA (magnetic resonance angiography) revealed obstruction of the vertebral artery at the C1 through C2 level on one side and a "stretched loop sign" (shortened and straighter loop of the third segment of the VA) on the contralateral side[15]. In our case there was a partial attenuation of both the posterior

cerebral arteries along with non-visualisation of the left vertebral artery. The association of VBI with CVJ anomalies has also been studied using Technetium 99m ethylene cysteine dimer brain SPECT (single photon emission computed tomography). One such study assessed cerebellar perfusion in a cohort of 19 patients with congenital CVJ anomalies, with or without VBI[3]. The authors reported decreased perfusion in 75% of the symptomatic as compared to 14% of the asymptomatic cases prior to surgery. These findings were explained by the presence of intimal damage and thromboembolism of the vessels secondary to chronic low-grade micro-trauma due to repeated flexion and extension of the neck. The authors also assessed the operative outcome in 12 patients with symptoms of VBI (drop attacks, episodic vertigo, visual disturbances, and dysarthria) and 2 patients with cerebellar infarctions. One month post-surgery, improvement in cerebellar perfusion and the symptoms of VBI were observed in 8 patients (88.9% cases) in the symptomatic group and none of the patients in the asymptomatic group[3].

In conclusion, physicians should be aware of the uncommon or rare presentations of CVJ anomalies. All young patients presenting with features of VBI or posterior circulation stroke should be screened for CVJ anomalies. As to whether the outcome of corrective surgery in these patients is determined by the presence or absence of angiographic abnormalities of the vertebrobasilar arteries or a prior history of VBI or stroke remains speculative.

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CASE REPORT

JIACM 2011; 12(1):71-2

Parotid Gland Tuberculosis

SH Talib*, Manjiri R Naik**, Pritam Patil***, Prasad Nikam****, Sagar Redkar****

Abstract

Tuberculous infection of parotid gland is uncommon. We describe tuberculous abscess of parotid gland in a 35-year-old male patient. The diagnosis was confirmed by pus smear, and culture for Mycobacterium tuberculosis. This case is presently under treatment and is progressing satisfactorily.

Key words: Parotid, tuberculosis, abscess.

Introduction

Tuberculosis of the parotid gland is a rare entity. The diagnosis is entertained always with a high index of suspicion. Less than 200 cases are recorded in the literature upto 2002, since the first description of this entity in the year1894[1]. There is a paucity of reported cases of parotid tuberculosis in the Indian literature[2,3,4].

Case history

A 35-year-old male patient having chronic rheumatoid arthritis presented with swelling of his right cheek of 1½ months duration, with rapid increase in size over a period of two weeks. The swelling was painful and tender. The patient also had inability in opening his mouth properly since the past one month. He gave a history of consumption of gutkha masala (chewing tabacco) 10 - 15 sachets a day for nearly 15 years. There was no history of fever, cough, weight loss or any other systemic symptoms. He had no personal and family history of tuberculosis. The patient was receiving steroids and immunosuppressant drugs (methotrexate) regularly for the past 2 years for his rheumatoid disease. He denied history of hypertension and diabetes mellitus. The general physical examination was normal. Local examination revealed diffuse glandular tender swelling of the right parotid region, 15 x 10 cms, soft-to-firm in consistency with fluctuation at the centre. Haematological parameters were within normal limits. His X-ray chest was normal. Tuberculin test done with 5 tuberculin units was negative. Ultrasound evaluation showed right parotid gland as swollen and showed echogenic, thick, movable internal echoes suggestive of suppurative pathology. Insignificantly enlarged cervical lymph nodes were also seen. FNAC was done and it was inconclusive. The patient underwent incision and drainage, and 50 cc of frank purulent pus drained. Gram's staining of pus smear showed plenty of polymorphonuclear leucocytes but organisms were not appreciated. Ziehl-Nielsen (Z-N) staining was (++) positive for acid-fast bacilli (AFB). Culture of the specimen confirmed the growth of *Mycobacterium tuberculosis* at a later date. Anti-tubercular treatment (Category-III regimen) was started with marked recedence of inflammatory signs and size of the swelling. The patient is now on maintenance phase and presently asymptomatic on regular follow-up.

Discussion

Tuberculosis is rampant in South-East Asia and its incidence is on the rise due to co-infection with HIV and development of resistant strains. The salivary glands are rarely affected in tuberculosis, maybe due to the inhibitory effects of saliva on the mycobacterium[5]. Parotid gland tuberculosis may develop from the focus in oral cavity with spread of infection via parotid duct involvement, or spread to lymph nodes via lymphatic channels. The spread may involve the haematogenous or lymphatic route from a distant pulmonary focus[6]. The entity of parotid glandular tuberculosis becomes a real diagnostic problem when chest radiographic evidence of tuberculosis is lacking and the vital constitutional features are denied by the patient. Our patient did not have chest radiographic evidence of either current or old Koch's pathology. The outcome of the tuberculin test,

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when showing an accelerated reaction or strong positivity helps in diagnosis of the condition. In this case, the tuberculin test was negative which could be due to prolonged use of steroids and methotrexate for rheumatoid disease. The definitive diagnosis of tuberculosis depends on isolation and identification of mycobacteria from the diagnostic specimen. FNAC is advocated as a useful diagnostic tool for parotid gland tuberculosis[5,7,8]. The technique has a sensitivity of 81–100% and a specificity of 94 – 100%[9]. In the presence of necrotic tissue, the FNAC yield is often poor as seen in our case; however, the drained pus from the gland revealed (++) positivity for *Mycobacterium tuberculosis*. The necrotic pus culture report was positive for *Mycobacterium tuberculosis*. The imaging studies, i.e., USG and MRI examination, may not only help to rule-out other diseases, but may also help to identify the multiple sites of gland involved in the periparotid region. Our patient had no evidence of oral submucous fibrosis, although he had been consuming gutkha masala for over 15 years with poor oral hygiene. CT of temporo-mandibular joint was also normal. Because of underlying muscle spasm, he had developed partial lock jaw leading to poor oral hygiene. The systemic factors that favour development of oral infection in tuberculosis include lowered host resistance, increase virulence of the organism, local predisposing factors like poor oral hygiene, trauma, leucoplakia, and various other dental conditions[10]. Parotid gland tuberculosis has a varied presentation with a localised mass resulting from infection of intracapsular or pericapsular lymphnodes, or may present as diffuse glandular involvement. It may also present as a periauricular fistula or an abscess[11]. Our patient presented with a glandular abscess and needed incision and drainage (Fig. 1). This case was started on anti-tubercular therapy with category III regimen and responded well, without sinus formation.

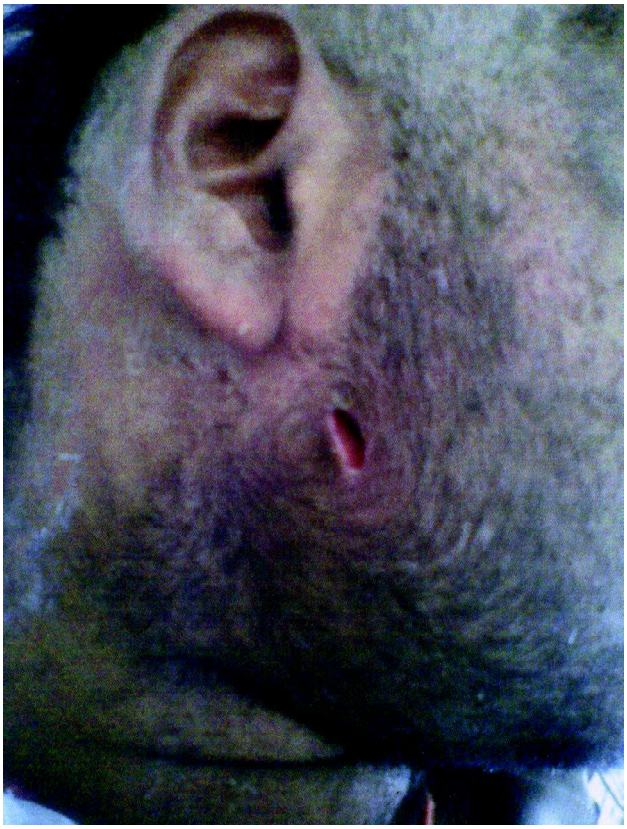

Fig. 1: *Right parotid swelling.*

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CASE REPORT

JIACM 2011; 12(1): 73-5

An Unusual Complication of Liver Abscess

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Abstract

A 26-year-old man of Indian origin presented with a progressively increasing cavity in the liver following a percutaneous liver abscess drainage procedure. Repeated aspirations revealed bile in the liver cavity. CECT abdomen revealed a very large cavity occupying almost the whole liver. Patient underwent exploratory laparotomy and had a rapid and complete recovery.

Key words: Biloma, liver abscess.

Introduction

Hepatic abscess remains an important clinical problem in developing countries with a significant mortality rate. Antiprotozoals and antibiotics with or without percutaneous or open surgical drainage are the treatment modality. Ultrasonography-guided percutaneous drainage procedure yields a better therapeutic response with low complication rate as compared to open surgical procedure[1]. Localised intra-abdominal bile collection or "biloma" is usually extra-hepatic. Intra-hepatic biloma in association with liver abscess is infrequently reported[2].

Case report

A 26-year-old man of Indian origin was brought to the emergency room with a history of high-grade fever, abdominal pain, and abdominal distension since five days. There was no history of diarrhoea, vomiting, constipation, obstipation, blood in stools, ingestion of toxic substances, or illicit drug or alcohol use. There was a history of percutaneous drainage of 200 ml of pus from the hepatic abscess seven days back. On examination, his temperature was 101 degree Fahrenheit and blood pressure was 126/80 mmHg. He was mildly dehydrated and icteric. Per-abdomen examination revealed tender hepatomegaly and a small scar of percutaneous drainage procedure in the anterior axillary line in the right sixth intercostal space. Examination of the chest and cardiovascular system was unremarkable.

His initial laboratory evaluation showed: Haemoglobin – 9.5 gm/dl, total leucocyte count – 12,500/cumm, blood urea – 36 mg/dl, and serum bilirubin – 4.5 mg/dl. Chest radiograph revealed an elevated right hemi-diaphragm and ultrasonography of abdomen revealed a 13 x 15 cm cavity occupying almost the whole liver with impending rupture. About 1,500 ml of green-coloured fluid was tapped percutaneously under USG guidance immediately (Fig. 1).

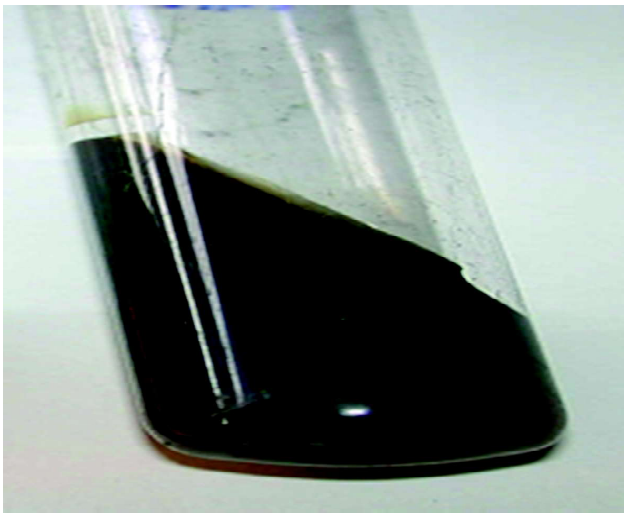

Fig. 1:

The patient showed marked clinical improvement as the pain and abdominal distension diminished. He was also given a third generation cephalosporin, metronidazole, and an aminoglyoside along with supportive therapy. Further investigations revealed markedly elevated serum alkaline phosphatase level of 1,880 IU/l. Hepatitis B surface antigen, anti-HCV and HIV were non-reactive. Within 36 hours of admission, the patient again developed severe abdominal pain and distension. A repeat USG abdomen revealed 15 x 17 cm sized cavity occupying almost the

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whole liver. Again, about 1,000 ml of green coloured fluid was tapped under USG guidance and was sent for biochemical analysis, which revealed presence of bile salts, bile pigments, and a bilirubin level of 46 mg% with lot of amorphous deposits. Gram-staining of the fluid was negative, and culture was sterile. CECT abdomen revealed a hypodense, homogeneous, 17 x 13 cm sized cavity in the liver with a thin margin of liver all around it without post-contrast enhancement (Fig. 2).

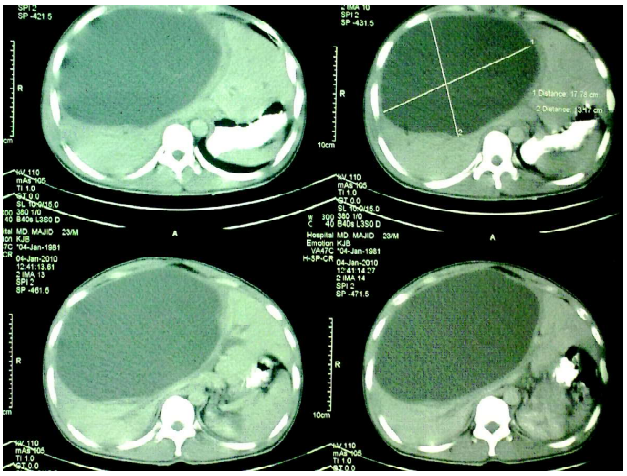

Fig. 2:

A diagnosis of intra-hepatic biloma complicating hepatic abscess was made. The patient, thereafter, underwent exploratory laparotomy which revealed a bile-containing cavity in the liver without any biliary fistula. A percutaneous drainage tube was kept in-situ for ten days. Magnetic resonance cholangiopancreatography (MRCP) revealed a normal biliary tree anatomy without any biliary ductal leak. The patient recovered completely and is now under close follow-up.

Discussion

Biloma or extra-biliary collections of bile are usually extra-hepatic, but a few cases of intra-hepatic biloma have been reported. Whipple first reported post-traumatic intra-hepatic biloma in 1898[3]. The term biloma was first introduced in 1979 to describe a loculated collection of bile outside the biliary tree[4].

Bilomas are caused by iatrogenic, traumatic, or spontaneous rupture of the biliary tree. Surgical procedures associated with biloma formation are cholecystectomy, common bile duct exploration, choledocho-enteric anastomosis, and partial hepatectomy[2, 4]. Nonsurgical iatrogenic causes of biloma are liver biopsy, biliary drainage procedure, and percutaneous transhepatic cholangiography. Spontaneous formation of biloma may occur proximal to, or at the site of an obstruction, or secondary to inflammatory drainage[4].

Biloma usually presents with right hypochondriac pain, flatulence, obstructive jaundice, or distension of abdomen. Fever is unusual unless biloma is secondarily infected. Symptoms occur as the biloma, which is formed by a leak in the biliary tree, slowly accumulates bile and grows. The intra-hepatic biloma may potentially become infected or may be associated with haemobilia. Intra-hepatic biloma may be asymptomatic and may be discovered fortuitously because of unrelated symptoms. Consequently, intra-hepatic biloma usually manifests at a variable delayed interval after the initial injury. The presentation varied from 11 days to 2½ years in the literature[3].

The size and location of bilomas depends in part on the cause of bile duct rupture, the site and rate of bile duct leakage, and the rate of bile reabsorption by the peritoneum. Needle aspiration is essential in confirming the diagnosis of biloma[5]. Typically, biloma contains clear, greenish bile, but may be discoloured by secondary infection, exudate, or blood[4].

The differential diagnosis of intra-abdominal biloma includes abscess, pseudocyst, liver cyst, haematoma, seroma, and lymphocoele. Helpful distinguishing features are history, the anatomy and location of the lesion, CT number, and character of the material obtained by aspiration[4, 5].

Most bilomas have a CT number less than 20 Hounsfield units, but may be higher when the bile is mixed with blood or exudate. Bilomas do not often show an identifiable capsule on imaging. An abscess or pseudocyst usually has a well-defined wall and is often located at sites atypical for bilomas[4].

Sonographic differential diagnosis in the post-traumatic patient includes haematoma and abscess. Differentiation from biloma is necessary from the therapeutic point of view. Usually, haematomas and abscesses tend to have more internal echoes and do not have a pronounced distal

sonic enhancement as bilomas. Biliary tree communication may occasionally not be demonstrated initially. A delayed radionuclide imaging/MRCP may demonstrate the communication with the biliary tree[3].

Although small bilomas may be watched safely, the appropriate treatment for most bilomas is drainage. Percutaneous drainage procedures with pigtail catheters are nearly invariably successful. Nevertheless, surgical drainage may be warranted in some patients. Whether drained percutaneously or surgically, most bilomas resolve without the need for localisation or repair of the bile leak[4].

Acknowledgement: We are thankful to Dr (Prof) NK Chaturvedi, Director, Postgraduate Institute of Medical Education and Research and Dr. Ram Manohar Lohia Hospital, New Delhi - 110 001, India, for granting permission to publish this article, and to the Council of Scientific and Industrial Research (CSIR), New Delhi, for assistance and advice during the preparation of this manuscript.

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Rozavel F

CASE REPORT

JIACM 2011; 12(1): 76-9

Gum Hypertrophy – A Manifestation

BK Kundu, AK Gadpayle***

The manifestations of some diseases are myriad to say the least. It would be very easy to mention the final diagnosis at the outset; however, the joy of navigating and reaching there, is something which we want the reader to experience.

Mrs. XX a 40-year-old female was referred to our Medical Unit for the purpose of a bone marrow aspiration for the clinical manifestation of hypertrophy of the gums, which she had been having for the past three weeks, with the provisional diagnosis of AML.

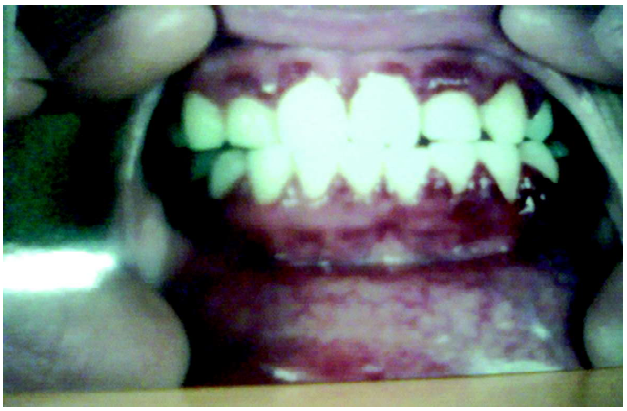

Fig. 1:

On reviewing the history, it was found that she also had:-

• Low grade fever	15 days
• Cough	15 days
• Chest pain	15 days
• Pain in left ear and mastoid region	11 days
• Swelling of gums with mild bleeding	11 days
• Discharge from ear	3 days

H/o present illness revealed the following:-

- All the symptoms were gradual in onset, additive, and progressive.
- Initially diagnosed as URTI, and given antibiotics.
- Subsequently had s/s of otitis media and therefore a change of antibiotics.
- Subsequent gum hypertrophy was seen and treated as drug reaction.
- Hypertrophy continued to increase even with treatment.

She did not give any history of haemoptysis/dysuria/breathlessness/arthritis/photosensitivity/oral ulcers/rash/erythema nodosum/dry eyes/dysphagia.

Past h/o dermographism was revealed for which the patient used to take fexofenadine.

Family history revealed that her father had been treated for pulmonary tuberculosis.

General physical examination of the patient revealed pallor, axillary and cervical lymphadenopathy, with normal vitals.

Systemic examination of the patient revealed the following:-

- CHEST: S/S of left-sided pleural effusion
- CVS: normal sounds; no murmurs/rub
- CNS: no focal deficit/neuropathy
- P/A: nothing significant

At this stage we kept our provisional diagnosis as:-

- Tuberculosis
- Maligancy

We started investigating the patient and the reports are summarised below:-

Hb	10.5 g/dl
TLC	13,900/cumm
ESR	127 mm at 1st hr
DC	N94/L6
Platelets	4,75,000/cumm
Urine R/M	20-30 RBCs/hpf, 5-10 pus cells/hpf, traces of protein, no casts

** Chief Medical Officer, Nursing Home, ** Consultant and In-charge, Nursing Home, Department of Medicine, PGIMER, Dr. Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi - 110 001.*

24 hr urinary protein	390 mg
Widal test	negative
USG	Left-sided pleural effusion
Pleural fluid exam	Total proteins – 3.8 g/dl Cells – 450/cumm – N70/L30 Adenosine deaminase level – normal No malignant cells
PCR for Koch's (pleural fluid)	Negative
ELISA for Koch's	Negative
Sputum AFB	Negative
Bone marrow	Hypercellular with reactive changes

Other investigations are outlined below:-

ENT examination	Ulcers in nasal septum, ASOM.
Gum Biopsy	Non-specific inflammatory changes
Serum protein electrophoresis	Raised alpha-1 and 2 globulins
Serum ACE levels	Normal
Coagulation profile	Normal
Anti-MPO, Anti-PR3	Negative
ANA	Negative

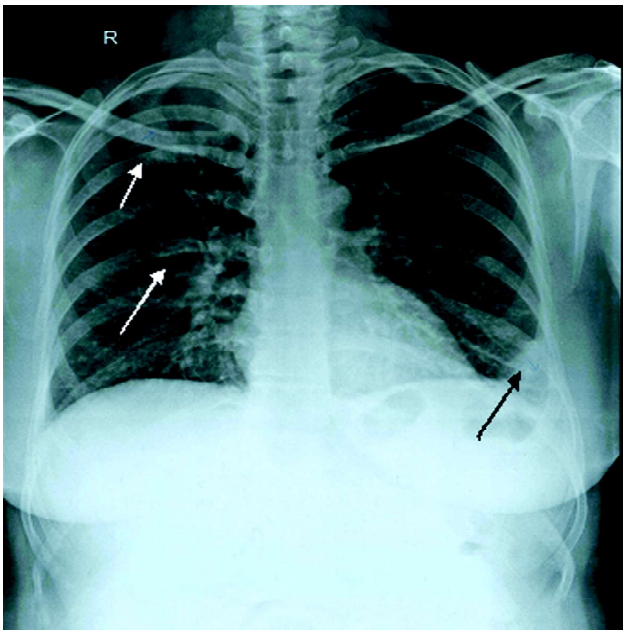

Fig. 2: *Chest X-ray showing nodular opacities (white arrows) and left pleural effusion (black arrow).*

CRP (qualitative)	Strongly positive
RF	negative

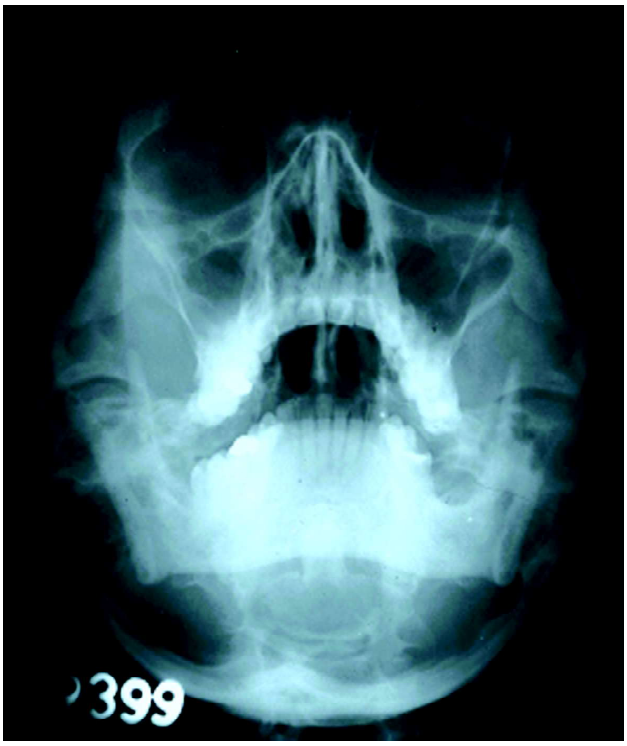

Fig. 3: *X-ray of para-nasal sinuses showing bilateral maxillary sinusitis.*

A contrast-enhanced computed tomographic scan (CECT) of the paranasal sinuses and the chest was done. The findings are shown below in Figures 4, 5, 6 and 7.

Keeping in view the presentation, nodular cavities in lungs Figure 2), presence of sinusitis (Figure 3), haematuria,

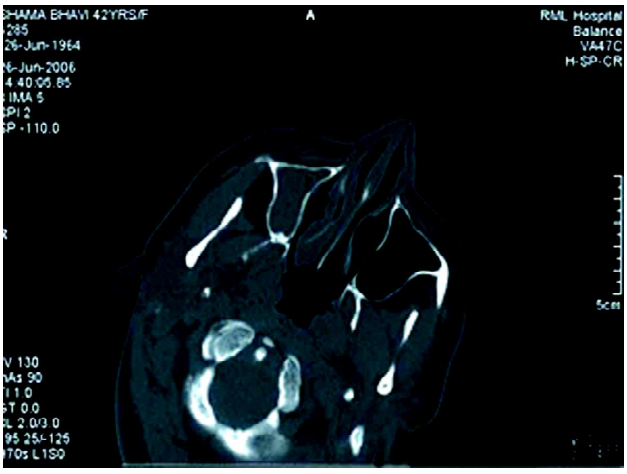

Fig. 4: *CECT PNS showing mucoperiosteal thickening of all sinuses, blockage of right osteomeatal unit, air-fluid level in right maxillary sinus, deviated nasal septum to the right and, mucosal thickening of the middle turbinate.*

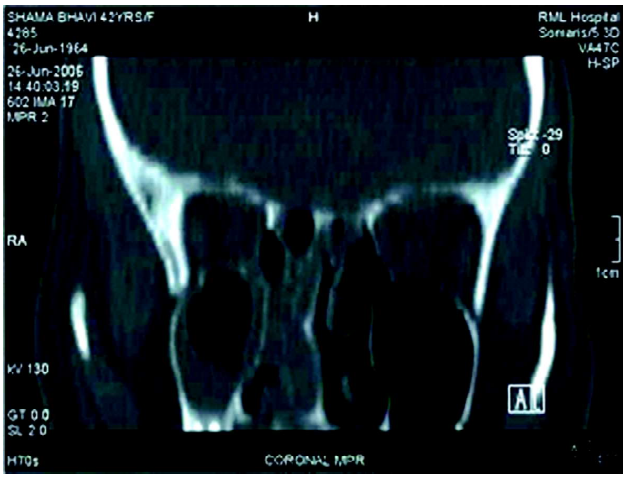

Fig. 5: *Coronal section of the PNS seen on CECT.*

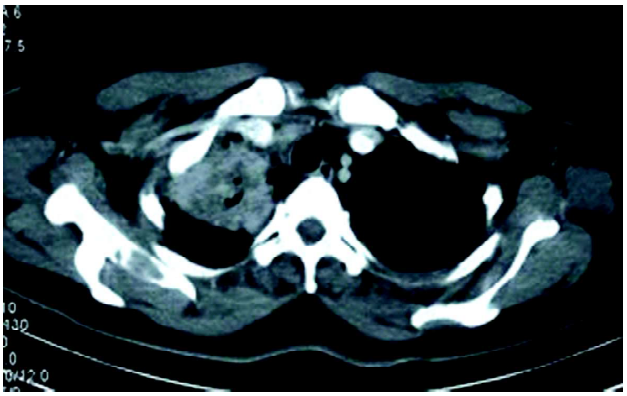

Fig. 6: *CECT chest showing apical cavitating nodule.*

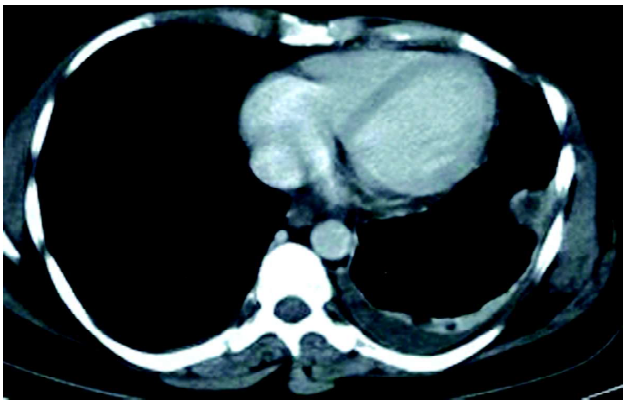

Fig. 7: *Sub-pleural nodule and pleural effusion seen on CECT chest.*

raised inflammatory parameters, and our strong suspicion of vasculitis, specifically Wegener's granulomatosis, we repeated the c- and p-ANCAs. Their levels were as follows:-

Anti-PR3	–	180.6 (<3.5)	(sensitivity 71%, specificity 80%)
Anti-MPO	–	0.9 (<9.0)	(sensitivity 67%, specificity 85%)

Thus the final diagnosis was Wegener's granulomatosis.

The patient was managed with pulse methylprednisolone followed by oral prednisolone along with oral cyclophosphamide; she remained in our follow-up for the next two years. During this period, her inflammatory parameters normalised, and the disease was relatively quiescent except for a brief flare at the end of six months, which was managed by increasing the dose of steroid, and one episode of leucopenia which was managed by stopping cyclophosphamide for a short period.

Discussion

Vasculitis is characterised by inflammation of blood vessels. They may be primary or secondary. They are not only heterogeneous, but also overlapping in their clinical features. They should be considered in any patient with unexplained systemic illness involving many organ systems. Wegener's granulomatosis is part of a larger group of vasculitic syndromes, all of which feature the presence of ANCAs (antineutrophil cytoplasmic antibodies) and affect small and medium-size blood vessels. This category also includes Chürg-Strauss syndrome and microscopic polyangiitis[1].

In the Chappel Hill system, it is classified as a small vessel vasculitis[8].

In 1936, Friedrich Wegener described cases of a peculiar small-vessel vasculitis with granulomatous inflammation. With the publication of a review of 22 cases and seven of their own by Godman and Chürg in 1954, the disorder became more widely known as Wegener's granulomatosis. Wegener faded into obscurity until the 1980s, when he began to receive more personal attention until his death in 1990[3].

Pseudoepitheliomatous hyperplasia, microabscesses, and multinucleate giant cells were recorded as present in almost all cases of gingival Wegener's granulomatosis. Necrosis, vasculitis, and granuloma formation were present in only a few cases[4].

Gum hypertropy with typical strawberry appearance and scattered petechial haemorrahges are seen in cases of Wegener's granulomatosis[5]. Only 3 cases have been so for reported[5]. Strawberry appearance of gums is considered

to be pathognomic of Wegener's granulomatosis[4, 5]. The diagnosis is confirmed by typical features of vasculitis, if found, but many times biopsy may be non-specific. Approximately 50% of biopsies provided little information for the diagnosis of Wegener's granulomatosis. Biopsy is needed to exclude other disorders[5]. Wegener's granulomatosis (WG) is classically associated with the presence of cytoplasmic antineutrophil cytoplasmic autoantibodies (c-ANCA) and proteinase 3 (PR3)[7]. Sometimes anti-MPO can be elevated in renal vasulitis and in patients of HIV[4]. c-ANCA is very good marker for the diagnosis of Wegener's granulomatosis[1]. Presence of cANCA/anti-PR3 in a patient presenting with gum hypertrophy, with or without tell-tale signs of other organ involvement establishes the diagnosis and reduces the need for further diagnostic procedures[5]. Early diagnosis and treatment will help the patient. In an otherwise normal individual, gum hypertropy should always arouse the suspicion of a systemic disease once, other causes including local causes, and drug reactions are ruled-out. An algorithm to demonstrate the different causes of gum hypertyrophy is presented below[9].

1. V – Vascular.
2. I – Inflammatory lesions include gingivitis, whether viral (aphthous stomatitis), fusospirochaetal ("trench mouth"), or monilial. Focal abscesses of the gums are common. Alveolar abscesses also cause focal swelling of the gums.
3. N – Neoplasms remind one of monocytic leukaemia and multiple myeloma, which are associated with diffuse hypertrophy and local tumours such as a sarcoma, papilloma, odontoma, and squamous cell carcinoma.
4. D – Deficiency diseases include scurvy and most vitamin deficiencies.
5. I – Intoxication suggests the common diffuse hyperplasia in patients with epilepsy taking diphenylhydantoin and related drugs, including barbiturates.
6. C – Congenital or acquired malformations remind one of the gingivitis secondary to malocclusion, poor-fitting crowns or orthodontal appliances, and periodontal cysts, secondary to chronic periapical granuloma.
7. A – Autoimmune and allergic diseases include the hypertrophy of thrombocytopenic purpura and the contact gingivitis from dentures, mouthwashes, and toothpastes.
8. T – Trauma to the gums may cause local hematomas and fractures.
9. E – Endocrine disorders suggest several conditions that may cause gum hypertrophy. Gingival hyperplasia in pregnancy, the giant cell granulomas of hyperparathyroidism, juvenile hypothyroidism, pituitary dysfunction, and diabetes mellitus are the most important.

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CASE REPORT

JIACM 2011; 12(1): 80-3

A Rare Case of Thyrotropin Secreting Tumour Managed Preoperatively with Octreotide

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Abstract

Thyrotropin (TSH) secreting pituitary adenomas are a rare cause of thyrotoxicosis. They typically present with signs and symptoms of hyperthyroidism, but can rarely be asymptomatic. We present a 28-year-old female who presented with goitre and occasional palpitations. Biochemical investigations revealed elevated T3, T4, and non-suppressed TSH levels (7.15 mIU/ml). T4 suppression test was negative and imaging revealed a sellar mass (10 x 10 x 18 mm). The patient was rendered euthyroid within 2 weeks with a combination of carbimazole and octreotide therapy. TSH levels were suppressed to 0.339 mIU/l with octreotide therapy. However, there was no change in the tumour size. Minimal signs and symptoms of thyrotoxicosis, a large pituitary lesion and partial selective response to octreotide therapy extend the cliniocpathologic spectrum of this exceedingly rare TSH secreting tumour.

Introduction

Functional Thyrotropin (TSH)-secreting pituitary adenomas are rare tumours accounting for less than 1% of all pituitary tumours. There has been some increase in the incidence of TSH secreting tumours in the recent past, possibly due to the development of high sensitivity TSH assays and greater use of immunohistochemistry. Most TSH secreting tumours present with symptoms that result either from tumour mass effect or hormonal overproduction, but some patients may have few, if any, symptoms. Due to the indolent nature of the tumour and delay in diagnosis, these tumours generally present as macroadenomas and are invasive in approximately 60% of cases. Here, we present a rare case of TSH secreting tumour in a 28-year-old female who presented to us with goitre and minimal symptoms of thyrotoxicosis.

Case report

A 28-year-old female presented with chief complaints of neck swelling for 2 years along with episodic palpitations and lethargy mainly on exertion. There was no history of weight loss or other common complaints associated with thyrotoxicosis. Her menstrual cycles had been regular. Thyroid profile was suggestive of thyrotoxicosis (FT3 = 11.0 pg/dl (normal range = 2.0 - 4.4), and FT4 = 8.81 ng/dl (normal range = 0.7 - 2.0) but with nonsuppressed TSH (7.15 mIU/l) (normal range = 0.5 - 5.0 mIU/l). Levels of other pituitary hormones including LH, FSH, prolactin, and cortisol were normal. We repeated her thyroid hormone profile twice over a period of one month and found similar results. We further investigated this patient with T4 suppression test and MRI of the brain. In T4 suppression test, we used 100 µg of thyroxine thrice a day for 2 weeks. TFT and Radio Active

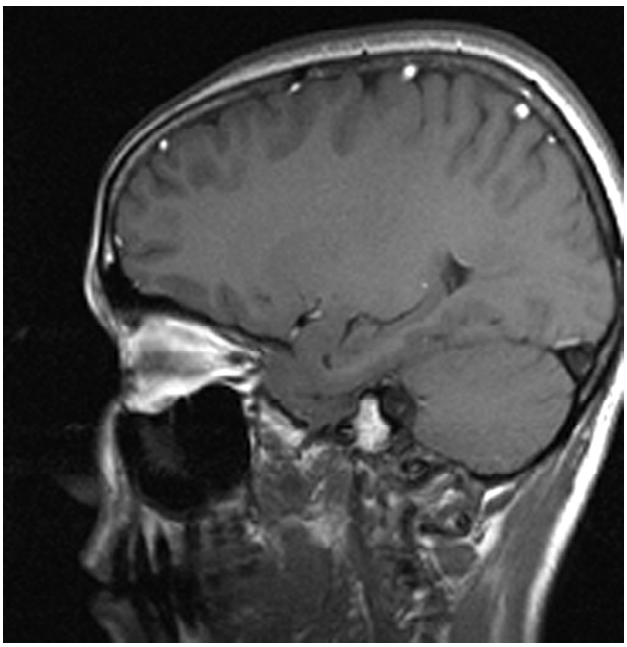

Fig. 1: *MRI of brain showing pituitary macroadenoma (10 x 10 x 18 mm mass) abutting the optic chiasma and encasing the right internal carotid artery.*

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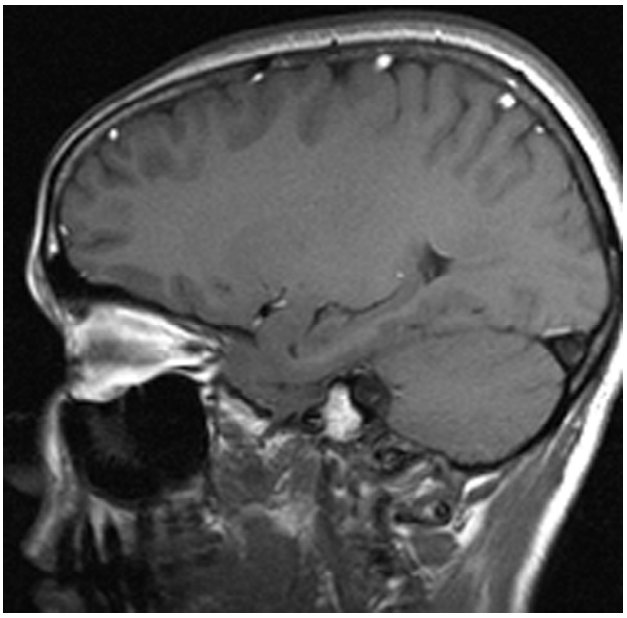

Fig. 2: *MRI of brain showing no change in the size and density of the tumour with medical management after two weeks.*

Iodine Uptake (RAIU) were performed before and after thyroxine administration. There was no suppression of TSH levels over a 2 week period (TSH = 7.89 mIU/l). Basal RAIU – 2 hr uptake was 13.6% and 24 hr uptake was 35.9%. Post-thyroxine, there was no suppression in the RAIU – (2 hr uptake was 16.4% and 24 hr uptake was 45.7%). MRI brain (Fig. 1) showed a large pituitary mass of 10 x 10 x 18 mm abutting the optic chiasma with right internal carotid artery encasement. Her visual field charting showed normal visual fields. A diagnosis of TSH-secreting pituitary tumour was made and surgical removal of the tumour planned. We prepared the patient for surgery by rendering her euthyroid with octreotide 100 µg 8 hrly and carbimazole 10 mg twice daily. The patient become clinically and biochemically euthyroid over a period of 2 weeks with suppression of TSH levels to 0.339/0.401 units along with normalisation of FT3 and FT4 levels (1.32 pg/ml, 3.78 ng/ml respectively). However, there was no reduction in the size of the tumour.

Discussion

TSH secreting pituitary tumours are rare functioning pituitary tumours constituting less than 1% of all pituitary masses and less than 1% cases of hyperthyroidism[1]. These tumours generally present after 35 years of age and have no sex predilection. They are usually large with 88% of TSH secreting tumours presenting as macroadenomas and only 12% as microadenomas[2, 3, 4]. More than 60% are locally invasive. TSH levels are frankly elevated in more than 50% of cases[2, 5], with the remaining having either mildly elevated or high normal range TSH values. Around 80% of patients present with goitre and increased RAIU, 40% present with visual field defects and around 30% present with menstrual disturbances and galactorrhoea[3, 6]. Signs of thyrotoxicosis are present in about 88% of cases ranging from moderate to severe symptoms. However, 10 to 12% of patients may be asymptomatic[3]. TSH-secreting pituitary tumours can also be associated with secretion of GH in 15% of cases and with excess prolactin secretion in around 10%[2, 7, 8].

The characteristic biochemical profile in TSH-secreting tumours includes nonsuppressed TSH levels inspite of raised FT4 and FT3 levels, a finding also seen with thyroid hormone resistance. Normal or increased TSH levels inspite of raised thyroid hormone levels indicate a loss of thyroid hormone feedback inhibition[2, 9]. It is often very challenging to distinguish between TSH-secreting pituitary adenomas and resistance to thyroid hormone (RTH) due to complex and expensive investigating procedures, and presence of pituitary incidentaloma in 5 – 10% of the normal population[10]. T3 or T4 suppression test can be used to differentiate these two conditions[10, 12]. While thyrotropinoma is less likely to show any suppression in RAIU or TSH levels, in RTH there is a decline in serum TSH levels in 90% of cases. Thyroid releasing hormone (TRH) stimulation test or response to octreotide can also be used to discriminate the two conditions. The ratio of α subunit to TSH is higher ranging from 1 to 5.7 in pituitary tumours, which is not so in RTH[11, 12].

Pituitary surgery is considered the first therapeutic approach in patients with TSH-secreting pituitary adenomas to restore euthyroidism and to ameliorate symptoms of mass effect. In a study by Beck-Peccoz *et al*[2], pituitary surgery led to normalisation of thyroid hormone levels and the disappearance of pituitary tumour in 44% of patients, normalised thyroid profile despite incomplete tumour removal in 25%, and was unsuccessful in 29%[2, 3, 13]. Radiation therapy is considered for patients not in

remission after surgery, however the results are not satisfactory[3]. In fact, surgical resection is difficult due to fibrous and hard consistency of these tumours, which may be linked to the secretion by the tumour of a basic fibroblast growth factor.

octreotide therapy and carbimazole therapy.

In conclusion, this was a rare case of TSH-secreting tumour, mildly symptomatic, managed preoperatively with octreotide therapy.

Table I: TSH levels both pre- and post-treatment with medical management.

	TSH normal range - (0.5 - 5.0 mIU/l)	Free T4 normal range - (0.7 - 2.0 ng/dl)	Free T3 normal range - (2.0 - 4.4 pg/dl)
Pre -octreotide therapy			
1st visit	8.56	3.2	12.1
2nd visit 2 weeks later	7.25	4.87	13.0
Post-octreotide therapy			
After 10 days	0.339	1.32	3.78
After 17 days	0.401	1.38	3.75

The presence of somatostatin receptor subtypes detected by both *in vitro* and *in vivo* techniques on TSH-secreting pituitary adenomas has allowed the use of somatostatin analogues in treating patients with TSH-dependent hyperthyroidism[15,16]. Somatostatin analogues are usually indicated for patients with persistent TSH-dependent hyperthyroidism or incomplete tumour removal of macroadenomas. In a study by Chanson *et al*, subcutaneous octreotide treatment suppressed TSH secretion in more than 90% of cases, with normalisation of thyroid hormone levels in 75% of cases and modest tumour reduction in half the patients within three months of treatment[17]. However, some authors have reported minimal change in tumour size or lack of sustained biochemical response with octreotide therapy.

Our patient was diagnosed as having a TSH-secreting tumour on the basis of biochemical profile and imaging. The presentation was unusual since the patient had minimal symptoms of thyroid hormone excess. An earlier case of thyrotropinoma from India was reported by Jha *et al* in a 63-year-old lady being investigated for syncopal attack who had no signs or symptoms of hyperthyroidism[18]. Another case of thyrotropinoma reported from India had a prompt response in terms of euthyroid status and reduction of tumour size with octreotide therapy[19]. Our patient was rendered euthyroid within a short span of 2 weeks with preoperative

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