C O N T E N T S

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VIEWPOINT

JIACM 2008; 9(1): 13-4

Sad Demise of the Doctors' White Coat

*BM Hegde**

"You medical people will have more lives to answer for in the other world than even we Generals."

– Napoleon Bonaparte.

The white coat with full sleeves is the hallmark of every doctor in the hospital. I still remember the day when I wore my first white coat with all the pride in my medical school days. That could only be surpassed by the stethoscope around one's neck the day one enters the clinical wards for the first time after passing that formidable examination, the first MB,BS examination! Over the years, the white coat has come to be recognised as a sign of a doctor's authority on patients and society at large. Moreover, not for bad reasons: a recent survey of elderly patients in British hospitals showed that patients did like that attire of their doctors.

Sadly, the days are not far off when this very symbol of authority is going to be banned in British hospitals as a recent survey showed that the white coats, as worn today, are one of the biggest sources of the deadly "super bugs" in hospitals, posing a serious threat to sick patients with compromised immune systems due mainly to their original disease. These germs seem to wreck havoc with the lives of many such patients in hospitals with hospital acquired (nosocomial) infections that have killed a significant number of patients in the intensive care units and elsewhere in the wards! The white coats rank next only to doctors' and nurses' hands in passing these dangerous bugs from patient-to-patient.

Hand washing between patients has become mandatory now; but sadly, the compliance, mainly by the senior staff, is appallingly low! This should remind us of the fate of Semmelweis who showed two hundred years ago that washing hands with carbolic soap after dissecting the dead bodies before delivering babies in the wards would save lives in the maternity wards. He was declared mad and was to be admitted to the mental hospital! This world is weird indeed. Every new invention is viewed with great suspicion.

The year was 1846. The scene was the Viennese General Hospital – the largest of its kind in the world. Here, Semmelweis got a job as obstetrical assistant.

"Semmelweis noticed that three times as many women were dying at the hands of the medical students than at the hands of the midwifery students from puerperal fever, commonly known at the time as, the black death of the childbed. In the medical school division the mortality from puerperal fever was so terrifying that this division became notorious." Semmelweis described, "There were heart rendering scenes when (pregnant) patients knelt down, wringing their hands, to beg for a transfer (to the midwifery division)...."

"Why this difference? The food and ventilation were the same in both. The surgical skill was better in the medical school and overcrowding less. The idea at the time was that the excess mortality was due to the emotional strain of being examined by male students, since the midwives were all female. Therefore, the elders of the Medical School met in council and proceeded to exclude the foreign students from the hospital on the ground that they were, "rougher in their examination than the Viennese." Death rates didn't change," wrote Semmelweis.

Before Lister, before Pasteur, Semmelweis made the connection between the autopsies the medical students were doing and the, "examining finger which introduced the cadaveric particles." In May, 1847, he asked every medical student to wash his hands with a chlorine solution before making an examination, and the death rate plummeted. For the first time in the history of the Vienna Hospital, the mortality rate at the medical school fell below that of the school of midwives. That much for history.

Hospital deaths due to hospital-acquired infections are going up everywhere. The culprits, apart from doctors' and nurses' hands, are the following in that order of importance. The white coat, the stethoscope, the necktie, cell phones,

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and other gadgets used by doctors repeatedly like the blood pressure (BP) apparatus! There is a change now even in the clinical examinations in the west. I saw in a recent MRCP examination that the candidate would ask for time to wash hands in-between examining even short cases and if she did not wash, it showed lack of clinical skills. British obstetricians have been advised not to wear a necktie; instead, they are advised to wear a bow tie that does not need to be hanging and touching the thigh of the patient while they do the pelvic examinations. The tie tips were shown to contain some of the deadliest germs.

What worries managers and doctors are the drug-resistant germs like the simple staphylococci, which have become deadly by getting immunity against methicillin – the MRSA. Worse still are the Vancomycin-resistant variety – VRSA. In-between there are the ones resistant to both those drugs. Thanks to the drug companies trying to push antibiotics in their campaign with doctors, antibiotic misuse and abuse has reached epidemic proportions.

Some people in the west are happy that the white coat is slowly dying. White coat today has lost its stature. Every one from the butcher to the hairdresser – not to speak of all and sundry in the medically related fields – are using them. The National Health Service (NHS) in the UK is thinking of a new uniform for doctors. These are large sleeveless covers going down to the knee and below. For female doctors they have large internal pouches to keep their essentials, usually kept in the handbags. The latter have also become dangerous for patients. Many lady doctors there have liked the prototypes of the new attire. There are voices of dissent as usual. People claim that if hospitals could supply a freshly washed white coat to every doctor every day the problem could be solved but they do not realise the enormous cost of doing that. The NHS is already in the red. Any more drain on its budget will make it get broke sooner than later.

In the midst of all this, we are missing the essential part of infections. In the reductionist science of medicine, germ versus antibiotic is the major battle. However, unfortunately in the human body the immune system is the one that could defeat the germs in normal situations and could even do that under disease conditions provided we doctors look at the human system as a whole. Germs are our friends. We kill them needlessly and make the immune system weak – to be invaded by even simple innocent germs, the saprophytes! Altering the gut environment by keeping the gut empty in sick patients and giving them oral powerful antibiotics will destroy the gut endothelium environment which is the most important defense in the immune shield against infections. The medical science has to change to the non-linear science of CHAOS and holism to have permanent solution to the problem of doctor and hospital induced deaths. One can only hope that wisdom prevails. Until then Napoleon Bonaparte would be right in his conviction.

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 2008** so as to reach Dr. A. K. Gupta, 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-2007.
- 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 2007 at Amritsar, Punjab.

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

Dr. (Prof.) A. K. Gupta, *Hony. Gen. Secretary, Indian Association of Clinical Medicine,*
Professor of Medicine, Postgraduate Department of Medicine, S.N. Medical College, Agra-282 002, U.P.

ORIGINAL ARTICLE

JIACM 2008; 9(1): 15-9

Glucose Tolerance in Non-Diabetic Patients with Acute Myocardial Infarction – A Short Term Follow-up Study

MS Gupta, RK Yadav**, H Singh****

Abstract

Background: *In patients of acute myocardial infarction, glycometabolic state is an important risk marker for long-term morbidity and mortality. The aim of the study was to detect the prevalence of impaired glucose metabolism in non-diabetic patients of acute myocardial infarction.*

Methodology: *We studied 50 patients admitted with acute myocardial infarction with no previous diabetes mellitus and a blood glucose level less than 180 mg% at admission. Glucose levels were estimated during hospital stay and a standardised oral glucose tolerance test with 75 gm of glucose was done at discharge and again at 3 months. Glycosylated haemoglobin was estimated at admission and at 3 months. At 3 months all patients were subjected to a treadmill test (TMT), and cardiac functions were evaluated by echocardiography.*

Results: *Based on the blood glucose levels at the end of 3 months of AMI, patients in the study were divided into two groups, i.e., group A (those patients with normal glucose tolerance) and group B (those patients with abnormal glucose tolerance). Of the 50 patients, group A had 30 and group B had 20 patients respectively. Further, in group B, of the 20 patients, 17 had impaired glucose tolerance test while 3 had positive glucose tolerance test. Mean glycosylated haemoglobin was 5.51 ± 0.64% in group A and 5.95 ± 0.86% in group B (p value > 0.05) at second day of admission while it was 5.52 ± 0.46% in group A and 6.27 ± 0.70% in group B (p value < 0.001) at 3 months. The lipid profile in the two groups was comparable (p value > 0.05). During follow-up, group B patients had developed more adverse cardiovascular events (p value < 0.05) as compared to group A. Six patients (20%) of group A and nine patients of group B (45%) had positive treadmill test (p value < 0.05). Echocardiography revealed left ventricular ejection fraction to be 62.2 ± 4.8% in group A and 56.7 ± 7.28% in group B (p value < 0.05).*

Conclusion: *Impaired glucose tolerance and diabetes mellitus are common in patients after acute myocardial infarction. Patients with abnormal glucose tolerance develop more adverse events, have higher TMT positivitiy rate (an index of provocable ischaemia) and decreased left ventricular systolic function. So, it is recommended that all patients of AMI should be followed-up closely using oral glucose tolerance (OGTT), so as to detect it early for initiating appropriate preventive measures so as to decrease cardiac event.*

Keywords: *Myocardial infarction, Ischaemic heart disease, Diabetes mellitus, Glucose tolerance.*

Introduction

Cardiovascular disease (CVD) is major cause of death in diabetic patients[1]. All manifestations of CVD, including myocardial infarction (MI), angina pectoris, and sudden death, are at least twice as common in diabetic than in non-diabetic patients[2]. More than half of the patients with diabetes die from CVD. The prognosis after MI has improved markedly, in particular as a result of reperfusion therapy. Despite these advantages in treatment modalities, patients with diabetes mellitus (DM) still have a relatively poor prognosis after MI[3].

On the other hand, hyperglycaemia and impaired glucose tolerance (IGT) are common during acute MI (AMI)[4, 5]. This hyperglycaemia may result from stress or pre-existing undiagnosed DM or IGT[6]. Hyperglycaemia after AMI is associated with an increased risk of in-hospital mortality and congestive heart failure (CHF), cardiogenic shock, arrhythmia are increased[7]. DM is strong risk factor for development of atherosclerosis; and in patients with DM, MI is major cause of death. On the other hand, after AMI, DM and IGT are common. Whether coronary artery disease (CAD) is secondary to a fundamental metabolic defect in DM or a primary disease in which diabetes is a secondary manifestation, is still not clear. But intensive secondary preventive measures and intensive insulin treatment improve the outcome of AMI in patients with IGT and DM[8]. Therefore, the study was planned to assess the incidence of impaired glucose metabolism in patients of AMI, without DM, thereby permitting early initiation of

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appropriate preventive measures.

Material and methods

The present study comprised of 50 patients (less than 80 years of age) who had evidence of acute MI diagnosed by presence of typical chest pain of > 30 minutes duration unresponsive to nitrate therapy and having ST-segment elevation of > 0.1 mV in more than one limb lead or ST segment elevation of > 0.2 mV in more than two successive precordial leads.

All patients included in this study had a blood glucose concentration less than 180 mg at admission. All patients older than 80 years of age or those having serum creatinine more than 2 mg% or who were diabetic, were excluded from the study.

All patients were briefed about the research protocol, and a written consent of participation was taken thereafter.

Fasting blood glucose was measured daily morning till discharge and concentrations of HbA_{1c} was measured on the first morning after admission. Various fractions of lipids were also measured on the first morning after admission. A standardised oral glucose tolerance test with 75 g of glucose (dissolved in 200 ml of water) was performed at discharge in all.

At 3 months, again oral glucose tolerance test was done alongwith repeat estimation of HbA_{1c}. All patients underwent a treadmill test alongwith echocardiography to assess left ventricular function.

Positive GTT and IGT was defined according to American Diabetes Association (ADA) criteria.

The observations were expressed as mean ± SD. The significance of observations were evaluated by using student's t-test.

Results

At end of the study, (i.e., 3 months), patient had either normal glucose tolerance or abnormal glucose tolerance. Based on glucose tolerance, the patients were divided into two groups – A and B.

Group A – This group comprised of 30 patients with normal glucose tolerance.

Group B – This group comprised of 20 patients with impaired glucose tolerance.

The difference in mean fasting blood glucose levels in the two groups was statistically significant ($p < 0.05$) during hospital stay after the 2nd day of admission (Table II). At discharge and at 3 month follow-up, the difference in mean fasting and post-prandial blood glucose between the two groups was statistically significant ($p < 0.001$) (Table II). The difference in mean HbA_{1c} levels in the two groups was statistically insignificant on the 2nd day of admission ($p > 0.05$) but significant at the 3 month follow-up ($p < 0.001$) (Table II).

IGT was present in 13 (26%) patients at discharge and 17 (34%) patients at 3 months, while positive GTT was present in 2 (4%) at discharge, and 3 (6%) patients at 3 months.

There was no statistically significant difference in the mean value of various fractions of lipids ($p > 0.05$) between the two groups (Table I).

All patients were assessed for any adverse cardiovascular events during hospitalisation and follow-up. In group A, 4 (13.33%) patients developed adverse cardiovascular events – 2 patients developed congestive heart failure, 1 developed angina, and 1 patient developed arrhythmia; while 11 (55%) patients in group B developed adverse cardiovascular events – 2 patients developed cardiogenic shock, 5 developed congestive heart failure, 3 developed angina, and 1 reinfarction during the three month follow-up ($p < 0.05$) (Table III).

The treadmill test was positive in 6 (20%) patients in group A, and 9 (45%) patients in group B. The difference was statistically significant between the two groups ($p < 0.05$) (Table III).

On two dimensional echocardiography, group B patients had poor cardiac functions. The difference in mean left ventricular ejection fraction was statistically significant between the two groups ($p < 0.05$), although the mean ejection fraction was within normal range in both the groups (Table III).

Table I: Showing demographic and lipid profile data.

Parameter	Group A	Group B	P value
Mean age (in years)	48.23 ± 11.88	50.15 ± 11.37	> 0.05
Male : Female ratio	9:1	9:1	> 0.05
Lipid profile (in mg%)			
Cholesterol	174.1 ± 27.8	168.85 ± 35.5	NS
LDL	95.1 ± 24.7	107.65 ± 32.4	NS
VLDL	34.16 ± 31.5	22.95 ± 8.58	NS
HDL	39.2 ± 6.1	39.8 ± 9.1	NS
Triglyceride	104.3 ± 51.4	98.35 ± 35.91	NS

Table II: Showing blood glucose and glycosylated haemoglobin values.

Blood glucose (in mg%)	Group A	Group B	P value
2nd day	76.16 ± 11.7	87.8 ± 25.0	> 0.05
3rd day	75.3 ± 7.79	88.1 ± 19.6	< 0.05
4th day	72.3 ± 7.5	80.6 ± 17.2	< 0.05
5th day	73.8 ± 8.15	82.35 ± 15.5	< 0.05
At discharge			
Fasting	73.86 ± 8.15	88.35 ± 22.9	< 0.05
Post-prandial	102.46 ± 9.25	136.35 ± 39.3	< 0.001
At 3 months			
Fasting	77.9 ± 4.46	91.7 ± 14.2	< 0.001
Post-prandial	146.2 ± 30.2	168.26 ± 4.8	< 0.001
Glycosylated haemoglobin (%)			
2nd day	5.57 ± 0.64	5.95 ± 0.86	> 0.05
3 months	5.52 ± 0.46	6.27 ± 0.70	< 0.001

Table III: Showing comparison of data of cardiac events/function at 3 months.

Parameter	Number of patients (%)		
	Group A	Group B	P value
Adverse cardiac events	4 (13.33%)	11 (55%)	< 0.05
Treadmill positivity	6 (20%)	9 (45%)	< 0.05
Left ventricular ejection fraction	62.2 ± 4.8%	56.7 ± 7.28%	< 0.05

Discussion

The hyperglycaemia and IGT are common during AMI. This hyperglycaemia may result from stress or may be due to pre-existing undiagnosed DM or IGT. The hyperglycaemia after AMI is associated with an increased risk of in-hospital mortality in patients with or without diabetes, the risk of CHF, cardiogenic shock, arrhythmia are also increased[7].

But intensive secondary preventive measures and intensive insulin treatment improve the outcome of AMI in patients with IGT and diabetes mellitus[8]. Consequently, it is important to identify patients with hyperglycaemia at admission for AMI.

Our results indicate a high prevalence of abnormal glucose metabolism (40%) in patients with AMI at three months.

Thirteen (26%) and two (4%) had IGT and positive GTT at discharge respectively. Whereas at 3 months, seventeen (34%) had IGT and 3 (6%) had positive GTT respectively.

This prevalence of glucose abnormalities was evident despite the exclusion of patients with previously diagnosed diabetes mellitus or with blood glucose concentration > 180 mg% at admission. The results of our study correlate well with the results of other studies. Anna *et al* found that IGT was present in 35% at discharge and 40% after 3 months, while newly detected DM (i.e., positive GTT) was present in 10% at discharge and 13% after 3 month in patients of AMI[9]. Similarly, Gupta *et al* found abnormal glucose tolerance in 32% patients after an AMI[10].

These abnormal blood glucose levels could be due to abnormalities of insulin secretion due to reduction in pancreatic blood flow as a consequence of splanchnic vasoconstriction secondary to disturbed left ventricular function. Additionally, increased activity of sympathetic nervous system with augmented circulating catecholamines inhibit insulin secretion and augment glycogenolysis, which contribute to the elevation of blood sugar[11]. Relative insulin resistance has also been suggested by Elliot *et al*[12].

Soler *et al* suggested that determination of HbA_{1c} concentration could be used to separate hyperglycaemia in patients of AMI from stress or pre-existing undiagnosed DM or IGT[13]. In group B patients, mean HbA_{1c} was within normal range on the 2nd day of admission, but higher at 3 months ($p < 0.001$) (Table II). This suggested that hyperglycaemia in group B patients developed after an attack of MI. Our results showed that hyperglycaemia was stress-induced because of AMI and not due to pre-existing undiagnosed DM or IGT as HbA_{1c} was within normal range at admission in group B patients but increased at three months follow-up. Lakhdar *et al* also suggested that hyperglycaemia in patients with AMI is a stress-induced phenomenon, since only one out of 21 hyperglycaemic patients had elevated HbA_{1c}[4].

On echocardiography, in group B patients (i.e., those with impaired glucose tolerence), various cardiac functions were more deranged than group A patients as also reported by Jorik *et al*[14]. Group B patients had a higher positivity on treadmill test, indicating more extensive coronary artery disease/residual provocable ischaemia (Table III).

Adverse cardiovascular events, i.e., arrhythmia, CHF, recurrent angina or cardiogenic shock were more common in group B patients than group A patients ($p < 0.05$). Our findings matched with other studies. Capes *et al* showed that patients of AMI with hyperglycaemia are at increased risk of in-hospital mortality, CHF, and cardiogenic shock[7]. They explained that hyperglycaemia is a reflection of relative insulin deficiency which is associated with increased lipolysis and excess circulating free fatty acids (FFA), this exaggerated in cases of acute stress such as MI. Further, free fatty acids, normally a substrate of choice for healthy myocardium, are toxic to the ischaemic myocardium and may lead to damaged cardiac cell membranes, calcium over-load and arrhythmias. Moreover, in animal studies, high concentrations of free fatty acids during myocardial ischaemia increase myocardial oxygen demand and reduce myocardial contractility. Furthermore, acute hyperglycaemia may precipitate osmotic diuresis. The resulting volume depletion may interfere with the Frank-Starling mechanism[15].

There are many evidences that improvement of metabolic control through infusion of fluids containing glucose, insulin, and potassium (GIK) may reduce mortality rates in AMI[16]. The beneficial effect of GIK is thought to be the result of a shift in primary energy substrate from free fatty acids to glucose during ischaemia.

Oswald *et al* showed that in-hospital mortality increased significantly in patients of AMI with increasing plasma glucose concentration[17]. Jorik R *et al* divided the patients of acute myocardial infarction on the basis of admission glucose level, group 1 (7.8 mmol/l), group 2 (7.8 – 11.0 mmol/l) and group 3 (> 11.1 mmol/l)[18]. Group 3 patients had marked reduction in left ventricular function and high mortality rate than group 2 patients, whereas group 1 patients had the lowest mortality rate and better left ventricular function than other groups.

The findings in the present study revealed an unexpectedly high prevalence of abnormal glucose tolerance in patients with AMI after an oral glucose tolerance test was performed. Therefore, it is recommended that in all patients with AMI, random blood glucose and HbA_{1c} should be measured at admission, and

fasting blood glucose at discharge. Further, needless to say, recommendation to perform an oral glucose tolerance test in all patients with AMI, presuppose that intensive pharmacological or lifestyle intervention in the group with newly detected abnormal glucose tolerance improves the prognosis as these patients developed more adverse cardiovascular events than in patients with normal glucose tolerance.

Conclusion

IGT and DM are common after an attack of AMI. These patients developed more adverse cardiovascular events, i.e., CHF, angina, as compared to patients with normal glucose tolerance. Therefore, in all patients of AMI, a glucose tolerance test should be performed at least at discharge from hospital and again at 3-month follow-up to detect glucose abnormalities as early as possible to prevent future adverse cardiovascular events.

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ORIGINAL ARTICLE

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Relationship Between Skin Diseases and CD4 Cell Counts in a Hospital-based Cohort of HIV-infected Adults in North India

V Satya Suresh Attili, VP Singh*, Shyam Sundar*, AK Gulati*, DV Varma*, M Rai**

Abstract

***Background:** Dermatological manifestations are seen at every stage of HIV/AIDS, and are often the presenting features. These manifestations not only act as markers but also reflect the underlying immune status.*

***Objectives:** To examine the relationship between various skin diseases and CD4 cell counts in a hospital-based cohort of HIV-infected adults in and around Varanasi, North India.*

***Patients and methods:** All HIV patients attending the SS (Sir Sunderlal) hospital, Varanasi, between January, 2001 and December, 2003 were studied. The relationship between CD4 counts and various skin diseases was analysed.*

***Results:** Rate of cutaneous diseases was 223 episodes per 1,000 PYO. CD4 counts were significantly lower in individuals with some skin diseases (warts, psoriasis, etc.) as compared to healthy HIV persons and some other skin disorders (dermatophyte skin infections, scabies, etc.). In HIV patients, there is a significant fall in the CD4 levels from baseline, when the patient develops a skin disease and recovery of CD4 is also prompt as soon as the patient recovers from the skin disease.*

***Conclusion:** There is a strong negative association between CD4 counts and the incidence and severity of skin disease in the HIV/AIDS patients. Fluctuations in CD4 levels observed during skin disease require further studies to establish the underlying pathophysiology. It may not be advisable to rely on CD4 levels in HIV patients having active skin disease, as transient but reversible fall in CD4 counts are known during the period of active skin disease.*

***Key words:** HIV, Common skin diseases, Epidemiology, CD4.*

Introduction

HIV already has more than 60 million victims globally, and in India, it figures around 2.6 – 3.1 million. NACO (National AIDS Control Organisation) had reported more than 1,24,995 full-blown AIDS cases by the end of 2006[1]. HIV is characterised by a few rare diseases occurring more commonly (like Kaposi's sarcoma, CNS lymphoma, etc.) and the common diseases with their rare manifestations (disseminated tuberculosis, systemic helminthic infections etc.). Among the various systems involved, skin has some special features in that:

a. Kaposi's sarcoma (KS) was one among the first recognised diseases that brought HIV into light.

b. Skin is involved in more than 90% of the HIV patients during their lifetime.

c. Skin involvement is the first presenting manifestation in a large proportion of patients (ranging from 32.5 – 95% according to the stage of the disease)[1-4].

Till date, many retrospective and prospective studies have been carried out to study the incidence of skin disorders and identify those occurring with disease progression[2, 5-14]. The global variation in the incidence of various skin disorders is attributed to the variations in the climatic conditions, lifestyles, local variations in pathogens, and socio-economic strata. So far there is no study reported on ethnic north Indian HIV-patients, who constitute a distinct group among the populations from the Indian subcontinent, correlating CD4 levels and skin diseases (MEDLAR). So we conducted this prospective study to examine the relationship, if any, between various skin diseases and CD4 cell counts in a hospital-based cohort of HIV-infected adults in and around Varanasi, North India.

Patients and methods

All the patients attending the ID clinic at SS hospital, Varanasi between January, 2001 and December, 2003 were enrolled for the study. Detailed history was taken from each patient and thorough physical examination

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was performed at the first visit with emphasis on mucocutaneous manifestations. The clinical diagnosis was supplemented with laboratory procedures like microscopy (KOH preparations, Tzanck smear) wherever applicable.

CD4 cell estimation

CD4 counts were measured routinely during the first visit and the follow-up visits, done at 3-monthly intervals (as per the hospital protocol, for monitoring the response to treatment) if the patient is asymptomatic, and every time of the visit whenever the patient became symptomatic. For this study, each time a participant attended the clinic, their most recent CD4 count (that was done immediately after the patient developed any symptom, or at the scheduled 3-monthly visit), was used for the analysis. All patients in whom CD4 count was not available at all visits, were excluded from the analysis.

Statistics

Analyses were performed using Medcalc 7.5 for Windows software. The mean CD4 levels and the 95% confidence intervals were calculated for each disease. Retrospective analysis of the CD4 counts was performed and the patients with fluctuation of more than 20% of the baseline were taken as cases and the fall in CD4 count was taken as significant. Age and sex matched controls, who did not have skin disease, were chosen randomly from the same study population (who had other opportunistic infections other than CDC category C diseases – as these diseases were also known to cause a fall in CD4) and the odds of the patients with skin disease with fall in CD4 was calculated against the controls. Initially we calculated the odds of having a fall in CD4 levels during the skin infection for each disease separately (univariate analysis) and then compared with the total population in a multivariate model.

Results

A total of 470 HIV-infected individuals were followed for 830 person years of observation (PYO), and 385 skin diseases (in 185 patients) observed during this period. Rate of cutaneous diseases was 464 episodes per 1,000 PYO. In the present study, 185 (39.3%) patients had some skin infection during the course of illness. Various skin diseases and their relative frequency are shown in Table I.

It was observed that candidiasis was the commonest manifestation, followed by drug-induced cutaneous reactions (of various severities), dermatophyte infection, molluscum contagiosum, recurrent herpeszoster (a total of 12 patient had herpes zoster – three patients had single episode, 6 had 2 episodes, 2 had 3 episodes, and one patient had a total of 5 episodes and died of the disseminated infection) seborrhoeic dermatitis and scabies. Diseases like warts, psoriasis, and folliculitis were uncommon. There were few patients with skin disease who had CD4 levels of more than 500. The exact distribution of the patients with different skin diseases in three distinct immune categories is shown in Table II.

The cases and controls were matched for all the baseline parameters as shown in Table III.

The mean fall in the CD 4 counts with the development of each disease and the time required for its recovery is mentioned in Table IV.

An odd of the patients with skin disease with fall in CD4 was calculated against the controls and the results are shown in Table V.

Test for heterogeneity Q = 14.1794, DF = 9, P = 0.1161

The results indicate that except scabies, psoriasis, and folliculitis, rest of the skin diseases pose a significant risk of fall in CD4 levels.

Discussion

HIV infection produces a panorama of mucocutaneous manifestations, which may be the presenting features of the disease[7], varying from macular, roseola-like rash seen during the acute 'seroconversion' syndrome to extensive end-stage Kaposi's sarcoma[15]. Oral candidiasis and seborrhoeic dermatitis are seen with higher frequencies and increased severity[16]. These skin conditions have been well-delineated in the western literature and in studies from southern parts of the Indian subcontinent[2, 3, 5, 7, 14, 17, 18]. The present study gives an overview of the dermatological manifestations of the HIV infected population of a north Indian population.

Table I: Cutaneous manifestations of HIV in relation to CD4 levels.

Disease	No. of patients (%)	CD4		Range	95% CI	p
		Mean	SD			
Oral candidiasis	78 (42.2%)	237.2 (348.2)	141.2 (194.8)	3-610 (105-980)	206.3-268.5	<0.0001
Drug rashes	25 (13.6%)	201.8 (356.1)	113.7 (150.3)	15-501 (124-693)	154.2-248.1	<0.0001
Dermatophyte infection	22 (11.7%)	267.1 (391.8)	122.9 (168.2)	64-442 (134-723)	212.6-321.6	=0.0688
Seborrhoeic dermatitis	13 (7.0%)	165.7 (328.1)	139.9 (164.2)	12-456 (152-864)	81.1-250.2	=0.0021
Molluscum contagiosum	12 (6.5%)	195.3 (331.9)	171.9 (158.2)	18-569 (164-886)	86.1-304.5	=0.0316
Recurrent herpes zoster	12 (6.5%)	138.3 (395.8)	105.7 (128.2)	14-390 (237-496)	71.1-205.4	=0.0001
Scabies	10 (5.4%)	290.8 (374.9)	190.3 (137.8)	112-650 (208-778)	154.6-426.9	=0.6683
Warts	6 (3.3%)	127.5 (387.8)	77.4 (169.4)	36-240 (209-693)	4.3-250.6	=0.0162
Psoriasis	4 (2.2%)	180.8 (393.2)	66.5 (47.8)	11-154 (324-470)	74.9-286.7	=0.0261
Folliculitis	3 (1.6%)	127.3 (425.2)	15.9 (49.8)	114-145 (324-542)	87.8-166.7	=0.0023

** Figures in parenthesis indicate the values for controls.*

Table II: Skin diseases distribution in three distinct immune groups.

Disease	CD4 < 200/mm^3	CD4 200 - 500/mm^3	CD4 > 500/mm^3
Oral candidiasis	48	27	3
Drug rashes	15	9	1
Dermatophyte infection	7	15	0
Seborrhoeic dermatitis	10	3	0
Molluscum contagiosum	9	2	1
Recurrent herpes zoster	10	2	0
Psoriasis	4	0	0
Scabies	5	5	0
Warts	5	1	0
Folliculitis	3	0	0

Table III: Baseline parameters of cases and controls.

Baseline characters of the patients

Characters	Cases	Controls	P
Age	35.2± 12.6	38.9± 14.6	NS
Male: female ratio	3.8:1	3.7:1	NS
Total duration of symptoms (in months)	14.6± 1.8	15.7± 2.6	NS
Mean time of AIDS diagnosis (in months)	6.5 ± 0.74	7.3 ± 0.7	0.06
Mean CD4 levels	214.9	195.5	NS
Patients on HAART	89%	87%	NS
% with lower socio-economic status	68%	72%	NS

Table IV: The mean fall in the CD 4 counts with the development of the each disease and the time required for its recovery.

Disease	No. of patients (%)	Time for the recovery of CD4 to the pre treatment levels (median- in weeks)	Fall in CD 4 counts from baseline	
			Mean	SD
Oral Candidiasis	78 (42.2%)	10	42.9	28.9
Drug rashes	25 (13.6%)	8	71.8	15.7
Dermatophyte infection	22 (11.7%)	8	21.8	12.6
Seborrheic dermatitis	13 (7.0%)	11	33.9	14.7
Molluscum contagiosum	12 (6.5%)	10	49.6	17.2
Recurrent Herpes	12 (6.5%)	12	83.7	14.3
Scabies	10 (5.4%)	9	21.6	22.5
Warts	6 (3.3%)	7	38.6	13.6
Psoriasis	4 (2.2%)	12	32.9	14.6
Folliculitis	3 (1.6%)	6	26.8	14.9

Table V: Odds ratio of skin diseases vs other opportunistic infections which led to fall in CD4 levels of > 20%.

Disease	No. of patients	ODDS ratio	95% CI		P value
			Min	Max	
Oral Candidiasis	78	9.821	2.800	34.451	S
Drug rashes	25	84.333	12.839	553.940	S
Dermatophyte infection	22	5.714	1.051	31.073	S
Seborrhoeic dermatitis	13	27.000	2.561	284.708	S
Molluscum contagiosum	12	22.000	2.050	236.065	s
Recurrent herpes zoster	12	55.000	4.300	703.465	S
Scabies	10	1.000	0.148	6.772	NS
Warts	6	25.000	1.200	520.763	S
Psoriasis	4	21.000	0.639	690.031	NS
Folliculitis	3	4.200	0.116	151.980	NS
Total (fixed effects)	185	11.689	6.274	21.777	S
Total (random effects)		13.043	5.448	31.226	S

Out of the 470 patients of HIV, who presented during the three-year study period, 39.3% had mucocutaneous manifestations, similar to any other Indian study[7]. Admittedly, this figure is far less as compared to western literature (upto 90%)[15]. Short follow-up (only 3 years) could be one reason for this. Males dominated over females with male: female ratio of 3.69:1. Most of the patients were in an advanced stage of disease at presentation, therefore females and early HIV infection were under-represented in the present study.

Among the skin manifestations, the predominant ones were oral candidiasis, drug reactions, and dermatophyte infection of the skin. In the drug reactions, the most offending one was found to be co-trimoxazole followed by nevirapine, zidovudine, and anti-tubercular therapy (we could not assess the exact drug causing the reaction as we used the combination of drugs as a single tablet – WHO combination tablets) and phenytoin. Kaposi's sarcoma (KS) and *Penicillium marneffei* infection were not observed in our study, although these have been occasionally reported from

India[2,7]. The possible reason for the non-occurrence of the KS in our population may be the low prevalence of the HSV-8 and absence of the homosexual transmission of the HIV which is also an important risk factor for the KS[19]. Auto-immune infections like vitiligo, alopecia, etc. which are predominantly due to immune-deregulation seen in HIV, have been reported by some authors[20], but not observed in our study. Almost all skin manifestations, with marked exception of the dermatophyte infection and scabies, are good markers of declining immunity in this population[7]. Though the CD4 counts in the patients with oral candidiasis were more than 200, which are far less compared to the controls ($P < 0.001$).

During the study period we observed that there is a fall in the CD4 levels of the patients when they had skin infection despite the patient regularly taking the anti-retroviral drugs; and these started rising soon after he started recovering from the particular cutaneous syndrome. It is well known that few chronic infections will cause a transient fall in the CD 4 levels, but we did not come across such incidences occurring with skin infections. Therefore, we retrospectively analysed this particular group. During the analysis of the CD4 counts, fluctuation of more than 20% of the baseline was taken as significant. The results indicated that except for scabies, psoriasis, and folliculitis, rest of the diseases had a significant fall in the CD4 levels during the periods of their respective cutaneous syndromes (a significant fall in the CD4 levels was observed from the baseline as soon as the patient developed skin disease). Another interesting finding is that, despite being a patient on HAART therapy (this excludes drug resistance), the CD4 levels recovered as soon as the infection resolved. There is no significant difference between different diseases in causing the dip in the CD4 levels ($P = 0.116$) (all the diseases will cause a similar fall in CD4 levels – probably indicating a final common pathway). However, as the analysis is retrospective, it had an inherent drawback of bias and improper matching. So it will be premature to make any statement. There is no proven pathophysiological basis to support our finding as of now (MEDLAR).

Badri *et al* found that the onset of infections like tuberculosis in HIV-infected patients is associated with an increased risk of AIDS and death[21]. The authors had the view that prolonged immune activation induced by tuberculosis boosted HIV replication (secondary to stimulation of CD4 cells) and consequently accelerated disease progression (with fall in CD4 levels). The same phenomenon might play a role as in most of the cutaneous syndromes, as the immunity in these diseases is also mediated by CD4 cells.

Conclusion

1. There is a strong negative association between CD4 counts and the incidence and severity of skin diseases in the HIV/AIDS patients.
2. Cutaneous manifestations of HIV can be considered as good clinical indicators to predict and assess the underlying immune status in resource-poor countries.
3. There was a fall in the CD4 levels as soon as a patient developed any skin manifestation and the CD 4 levels return to pre-disease status as soon as the disease resolved.
4. Though this phenomenon (the fall in the CD4 levels during skin diseases and its recovery after the improvement of those diseases) was prominent for some diseases (all, except for scabies, psoriasis, and folliculitis in the present study), it needs further studies to establish the pathophysiology.
5. It is not advisable to take into account the CD4 levels, if the patient is having active dermatological infections as CD 4 levels may be falsely low.

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ORIGINAL ARTICLE

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Hypothalamo-Pituitary-Adrenal Axis in Tuberculosis

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Abstract

Aim: *To asses the integrity of Hypothalamo-Pituitary-Adrenal (HPA) axis in tuberculosis using low dose 1 µgm ACTH stimulation test. (LD-ACTH).*

Methods: *Twenty four patients (19 men, 5 women) of whom seventeen had active pulmonary tuberculosis and seven with active extra-pulmonary tuberculosis, alongwith ten healthy volunteers as control group (7 men, 3 women), were assessed using low dose 1 µg ACTH stimulation test (LD-ACTH).*

Results: *The mean basal cortisol was higher in the tuberculosis group (15.48 µgm/dl ± 8.22) compared to the control group (11.55 µgm/dl ± 2.733). Eleven patients (45.8%) comprising of eight with pulmonary tuberculosis and three with extra-pulmonary tuberculosis, had subnormal response, as defined by post-ACTH peak cortisol value of less than 18 µgm/dl.*

Conclusion: *The adreno-cortical reserve is significantly reduced in patients with active pulmonary and extra-pulmonary tuberculosis.*

Key words: *HPA axis, LD-ACTH, HD-ACTH, Adrenal insufficiency.*

Introduction

Tuberculosis per se is a well-known cause of adrenal insufficiency[1]. An autopsy study in 403 patients with Addison's disease between 1900 - 1929 reported tuberculosis of adrenal glands in 69.7% of them[2]. In the past, several studies have documented decreased adrenocortical reserve in 17 - 50% of patients with pulmonary tuberculosis in India[3-5].

Adrenal crisis is considered in a terminally ill patient with active pulmonary or extrapulmonary tuberculosis.

In all the Indian studies done so far, the standard high dose ACTH stimulation test was performed using 250 µg of ACTH (HD-ACTH). This supraphysiological or pharmacological dose may induce false-positive cortisol response in some patients and may result in under diagnosis of HPA axis insufficiency. A maximal adrenal response can be obtained with much smaller doses of ACTH which may reveal more subtle disturbances in the HPA axis[6]. This prompted us to do a pilot study using low dose 1 µgm ACTH stimulation test to assess the HPA axis in patients with active pulmonary and extra-pulmonary tuberculosis.

Materials and methods

24 patients, comprising of 19 men and 5 women in the age group of 17 - 60 years admitted in the hospital between 2001 - 2002 were studied after obtaining informed consent. 17 patients had active pulmonary tuberculosis (sputum positive) and 7 patients had extra-pulmonary tuberculosis. 10 healthy individuals 7 men and 3 women in the age group of 25 - 50 years were taken as controls.

Patients with pregnancy, chronic steroid therapy, chronic renal failure, hepatic failure and HIV seropositivity (Double ELISA positive) were excluded from the study.

On entering the study, all patients were subjected to detailed clinical evaluation with particular reference to signs and symptoms of adrenal insufficiency and investigations like X-ray chest, sputum for AFB, complete haematological, renal and liver function tests, X-ray thoracic spine, and ascitic fluid analysis (in cases of spinal and abdominal tuberculosis respectively) were performed as required. Basal venous blood samples for cortisol were drawn at 8 AM and ACTH stimulation was performed with 1 µg synacthen Ciba administered intravenously. One microgram of ACTH was obtained by dissolving 250 µgms of synacthen in 250 ml normal saline, then using 1 ml for testing. Post-ACTH venous blood samples for peak cortisol were drawn at 45 minutes after ACTH administration. Serum cortisol was estimated by radio-immuno assay using cortisol kits (Diasorin Inc. USA). The intra-assay and inter-assay coefficients of variation were

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4.0% and 6.5% respectively. Post-ACTH peak cortisol value of > 18 µg/dl was taken as criterion for normal response to low dose 1 µg ACTH test.

Results

None of the patients studied had clinical evidence of adrenocortical insufficiency. The renal and liver function tests were normal. All patients with pulmonary tuberculosis were sputum positive for acid-fast bacilli. The mean duration of illness was between six months to one year.

The basal and post-ACTH cortisol response in the two groups are shown in Table I.

Table I:

	Group	N	Mean serum cortisol in µgm/dl	Std deviation
Basal Cortisol	Control	10	11.5500	±2.7330
	Tuberculosis	24	15.4833	+8.2266
Post-ACTH Cortisol	Control	10	20.0000	+1.3333
	Tuberculosis	24	22.3958	+10.3829

The mean basal cortisol was higher in tuberculosis group (15.48 µgm/dl ± 8.22) compared to the control group (11.55 µgms/dl ± 2.733).

Eleven patients (45.8%), of whom eight had pulmonary tuberculosis and three had extrapulmonary tuberculosis showed subnormal response as defined by the internationally accepted criterion of post-ACTH peak cortisol value of < 18 µgm/dl which was significant according to Fisher's exact probability test (P = 0.014) (Table II).

Table II: Post-ACTH cortisol response.

Group	Serum cortisol level < 18 µg/dl	Serum cortisol level > 18 µg/dl	P value
Control	0 (0%)	10 (100%)	
Tuberculosis	11 (45.8%)	13 (54.2%)	*0.014
Total	11	23	

** Significant*

Post-ACTH stimulation (1 µgm) test response, peak value.

Discussion

In active tuberculosis, there is an increased rate of cortisol metabolism which imposes an increased demand on cortisol secretory reserve. Also, most of the anti-tubercular drugs, in particular rifampicin, induce the hepatic cytochrome P450 oxidative enzyme system which enhances the rate of cortisol metabolism.

In the present study, we demonstrated a high mean basal cortisol in the tuberculosis group, suggestive of HPA axis activation. The active disease per se increases cortisol secretion.

A post-ACTH peak cortisol value of < 18 µgm/dl was taken as sub-optimal response to low dose ACTH stimulation test and it was found that 45.8% of patients in the tuberculosis group had a sub-normal response, which can be further compromised during stressful situations precipitating a crisis.

Kelestimur *et al*, using the criterion of post-ACTH peak cortisol response value of < 550 nmol/lt at any time during the test as sub-normal response to high dose ACTH stimulation test in patients with active pulmonary tuberculosis, found no sub-normal response. In another study done by Kochupillai using the criterion of post-ACTH peak cortisol value of < 500 nmol/lt demonstrated sub-optimal response in 49.5% of patients to high dose ACTH stimulation test in patients with active pulmonary and extra-pulmonary tuberculosis. In both these studies, the mean basal cortisol was higher in the tuberculosis group, while the post-ACTH response to high dose ACTH stimulation test was different.

The reasons for the above disparity could be differing degrees of severity of illness, or more likely a varying criterion for defining sub-optimal response. When adrenal glands are stimulated to their maximum by endogenous ACTH seen in stressful conditions such as in tuberculosis, plasma cortisol levels will be high, and therefore exogenous ACTH may fail to further stimulate the adrenal glands to secrete cortisol[6]. It has also been reported that there is an inverse correlation between the basal cortisol level and the cortisol response to synacthen[7].

The climatically stressful environment of the tropics, the frequent occurrence of gastroenteritis and other acute infections and infestations, are all major stresses that greatly enhance the demands on the adrenocortical reserves of the individuals in our country. We have

observed a high incidence of compromised adrenocortical reserve in tuberculosis patients (45.8%). This highlights the need for considering the possibility of adrenal insufficiency in patients of tuberculosis presenting with shock.

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Flavedon

ORIGINAL ARTICLE

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Ascitic Fluid Examination for Diagnosis of Spontaneous Bacterial Peritonitis in Cirrhotic Ascites

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Abstract

Objectives: To study the prevalence of spontaneous bacterial peritonitis (SBP) in patients of cirrhosis, and also to identify differences, if any, in biochemical parameters of the ascitic fluid in patients with and without SBP.

Methods: 41 adult patients of cirrhotic ascites were studied. Apart from a detailed history, thorough physical examination and routine laboratory investigations were done. Ascitic fluid was subjected to conventional culture and culture in blood culture bottles, cytological and biochemical examination including protein, albumin, glucose, LDH and pH.

Results: Ascitic fluid culture was positive in 11 patients: in 5 by both conventional culture and culture in blood culture bottles, and in 6 by culture in blood culture bottles alone. 14 patients were diagnosed to have SBP or one of its variants – a prevalence of 34.14%. Fever, abdominal pain, altered mentation, and jaundice were more common in the SBP group. Ascitic fluid biochemical parameters were not significantly different in the two groups. However, patients with SBP had more severe liver disease as judged by Child Pugh class.

Conclusions: Ascitic fluid culture in blood culture bottles and cytological examination of ascitic fluid must be carried-out routinely in every case of cirrhotic ascites to detect SBP or one of its variants in view of the high prevalence of this complication in such patients, especially those with more advanced liver disease.

Key words: Cirrhosis, Cirrhotic ascites, Spontaneous bacterial peritonitis.

Introduction

Spontaneous bacterial peritonitis (SBP) and its variants are important causes of morbidity and mortality in patients of cirrhosis[1, 2]. Diagnosis of these conditions can be difficult as there are no typical signs and symptoms, and may be revealed only if the ascitic fluid is subjected to cytological examination and cultured in blood culture bottles. Low protein (< 1 g/dl) ascites is particularly prone to develop this complication[3]. Taking these facts into consideration, this study was carried-out to determine the prevalence of SBP in patients of cirrhotic ascites, validate the advantage of ascitic fluid culture in blood culture bottles over conventional culture, as well as identify differences, if any, in various biochemical parameters like protein, albumin, glucose, LDH and pH of the ascitic fluid in patients with and without SBP.

Materials and methods

The study was carried out on 41 adult patients of cirrhotic ascites. Inclusion criteria were: a histopathological diagnosis of cirrhosis, no obvious surgically treatable abdominal pathology, and patient should not have been subjected to any of the following in the previous one week: a) antibiotic treatment; b) abdominal paracentesis; c) endoscopic or any other invasive abdominal procedure. A detailed history was taken from each patient and complete physical examination was performed. Routine investigations carried-out in every case at the time of admission included haemogram, ESR, urine (routine and microscopy), blood urea, blood sugar, X-ray chest, liver function tests including serum bilirubin, AST, ALT and serum alkaline phosphatase, serum proteins with A: G ratio, serum LDH and prothrombin time. On admission, 50 ml ascitic fluid was drawn under all aseptic precautions; 15 ml was inoculated in biphasic blood culture bottles (with a solid slope and liquid broth) at the bedside, 5 ml was sent to the laboratory for conventional culture, and the rest was sent for cytological and biochemical examinations. 10 ml of blood was drawn at the same time and inoculated into blood culture bottles. Diagnosis of SBP and its variants, monomicrobial non-neutrocytic bacterascites (MNB) and culture-negative neutrocytic ascites (CNNA) was made as per the following criteria: SBP – growth in ascitic fluid culture and ascitic fluid polymorphonuclear (PMN) count > 250

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cells/mm^3 without evidence of an intra-abdominal surgically treatable source of infection. MNB- pure growth in ascitic fluid culture with ascitic fluid PMN count < 250 cells/mm^3. CNNA – no growth in ascitic fluid culture, ascitic fluid PMN count at least 250 cells/mm^3, no recent use of antibiotics and no other explanation for the elevated PMN count such as hemorrhage into ascites, peritoneal carcinomatosis, etc.

Statistical Analysis: The conventional ascitic fluid culture method was compared to culture in blood culture bottles by McNemar test which is a form of chi-square test for matched pair data. Ascitic fluid parameters in patients with and without SBP or its variants were compared by student's 't' test. Chi-square test was used to compare clinical parameters in patients and healthy controls.

Results

The age of the patients ranged from 25 to 70 years with a mean of 46.56 ± 11.42 years. There were 31 males and 10 females. 4 patients belonged to Child Pugh class A, 19 to class B and 18 to class C. Blood culture was positive in 5 out of 41 patients (12.2%). The organisms isolated were *Staph. aureus* in 3, and *Escherichia coli* and *Enterococcus fecalis* in 1 each.

Ascitic fluid culture was positive in 11 out of 41 patients by conventional method/culture in blood culture bottles. The organisms isolated are shown in Table I. Ascitic fluid PMN count: 7 patients had a PMN count > 250 cells/mm^3. Out of them, 4 also had a positive ascitic fluid culture. The mean neutrophil count in these 7 patients was 492.85 ± 151.18. Thus, 4 patients had full-fledged SBP, 3 had CNNA and the rest 7 had MNB. Thus the prevalence of SBP (including its variants) was 34.14%.

Comparison of the culture techniques: 5 cases were diagnosed by both conventional and modified techniques and 6 by the modified technique alone. 3 were cases of CNNA. When compared by McNemar test, the difference was statistically significant ($p < 0.05$). Compared to the non-SBP group, a greater percentage of patients in the SBP group had fever, abdominal pain, altered mentation and jaundice. Signs of liver cell failure (spider naevi, asterixis, gynaecomastia, and palmar erythema), haematological parameters (haemoglobin, TLC, DLC, and ESR), serum biochemistry (blood glucose, blood urea, serum sodium and potassium, and serum LDH) including liver function tests (serum bilirubin, AST, ALT, serum alkaline phosphatase, serum proteins, serum albumin, and prothrombin time) were not statistically different between the two groups.

Table I: Showing the organisms isolated on culture of ascitic fluid.

S. No.	Organism	No. of patients (%) N = 11
1.	Gram negative bacilli *Escherichia coli*	 3 (27.27)
2.	Gram positive cocci – *Staphylococcus aureus* – *Enterococcus fecalis* – *Streptococcus milleri*	 3 (27.27) 2 (18.18) 1 (0.09)
3.	Miscellaneous – *Corynebacterium jeikeium* (JK Group) – *Serratia sp*	 1 (9.09) 1 (9.09)

Child Pugh class – 12 (85.71%) of the 14 patients in the SBP group belonged to Child Pugh class C and 2 (14.28%) to class B. Thus patients in the SBP group had moderate to severe liver disease as judged by Child Pugh class.

Ascitic fluid parameters (protein, albumin, sugar, pH and LDH) were not significantly different in the SBP and non-SBP groups (Table II). The mean ascitic fluid protein in the SBP group was 1.68 ± 0.8 gm/dl compared to 1.91 ± 0.68 gm/dl in the non-SBP group. 7 patients had an ascitic fluid protein < 1 gm/dl; 6 of them belonged to the SBP group. Serum ascites albumin gradient (SAAG) was 2.36 ± 0.65 gm/dl in the SBP group and 2.26 ± 0.61 gm/dl in the non-SBP group.

Table II: Showing ascitic fluid biochemical parameters in patients with and without SBP

S No.	Parameter	Total patients n=14 mean ± SD	SBP group n=14 mean ± SD	Non SBP group n=14 mean ± SD
1	Protein (g/dl)	1.76±0.72	1.68±0.80	1.91±0.68
2	Albumin (g/dl)	0.86±0.39	0.86±0.48	0.89±0.31
3	Glucose (mg/dl)	88.95±19.20	89.14±23.10	91.00±22.13
4	pH	7.50±0.08	7.51±0.07	7.48±0.09
5	LDH (IU/l)	96.44±67.99	126.28±83.00	85.29±50.35

Discussion

The prevalence of SBP, including its variants CNNA and MNB, was 34.14% in this study. In various studies, routine paracentesis has documented a prevalence of SBP of 10 - 27%[1,2,4]. Andreu *et al*[5] reported a prevalence of 28% while Amarapurkar *et al*, found it to be 22.5%[6]. In a study involving 169 cirrhotic patients, Jarcuska *et al* found evidence of SBP by first paracentesis in 27 (16.0%) and in another 13 (7.7%) by repeated paracentesis[7]. In contrast, Romney *et al*, in a study involving 67 cirrhotic patients found no case of SBP or CNNA and only 10 of MNB[8]. The reason for a higher prevalence in our study could be that there were comparatively more patients in Child Pugh class C (18 out of a total of 41 patients) who are more prone to develop ascitic fluid infection. Of the 14 cases with ascitic fluid infection, 4 (28.57%) had full fledged SBP, 3 (21.43%) had CNNA and 7 (50%) had MNB. Runyon *et al* had also reported a high percentage of MNB (31.9%) in their series[7] while Pinzello *et al* have reported a figure of 33.3%[10]. In our study ascitic fluid culture was done at admission when ascitic fluid infection might have been in the early stages without a reactive increase in the PMN count. It has been reported that 61.9% of episodes of MNB can resolve without neutrocytosis[9].

Culture technique: 35.7% cases of SBP (including its variants) were detected by the conventional culture compared to 78.5% by the modified technique of culturing ascitic fluid in blood culture bottles. Bobadilla *et al* have reported a culture positivity of 81% by the modified technique compared to 52% by the conventional technique[11] while Runyon *et al* have reported 93% positivity by the modified technique versus 57% by the conventional technique[12]. The modified technique has a greater probability of detecting microorganisms as it treats ascitic fluid as if it was blood, and hence, can detect a very low concentration of microorganisms.

Organisms in the ascitic fluid: *Escherichia coli* and *Staphylococcus aureus* were the most commonly detected organisms each in 3 cases (27.27%). In the study by Runyon *et al*[9], *E.coli* was responsible for 27.3% of cases of SBP and *Staphylococcus aureus* for 6.8%, while Wilcox *et al* demonstrated *Escherichia coli* as the culprit in 45% cases and *Staphylococcus aureus* in 12% cases[13]. The higher incidence of *Staphylococcus aureus* in our study group is slightly intriguing; in 2 of these 3 cases, the blood culture was also positive for the same organism, thus precluding the chances of some shortcoming in the culture technique. In our study one case each of SBP caused by *Streptococcus milleri* and *Corynebacterium jeikeium* (JK diphtheroid) was detected. The latter has been reported in 1% of cases in one series[13]. It has been reported to cause sepsis primarily in patients with predisposing factors like prolonged hospitalisation, immunocompromised status, etc[14]. It is known to cause peritonitis in chronic ambulatory peritoneal dialysis patients, but has not been frequently reported as a cause of SBP. *Streptococcus milleri* is a genetically heterogeneous microaerophilic haemolytic *Streptococcus* with a propensity for invasive pyogenic disease, exhibiting tiny colonies in 24 hour culture[14]. It has been extensively described in liver abscesses but has been isolated only rarely in the ascitic fluid of patients with SBP[15,16].

Child Pugh classification: 12 of the 14 (85.71%) patients with SBP belonged to class C while 2 (14.28%) were in class B. In their study, Amarapurkar *et al* had found that 6 of the 7 patients detected to have SBP belonged to class C[6]. This finding supports the view that SBP is more common in patients with advanced liver disease.

Ascitic fluid protein: Low protein (< 1 gm%) ascites has been reported to be prone to infection due to defects in opsonisation and neutrophil phagocytosis of bacteria in several studies[1-3]. In our study, the mean ascitic fluid protein in the SBP group was 1.68 ± 0.8 gm/dl compared to 1.91 ± 0.68 gm% in the non-SBP group. 7 patients had an ascitic fluid protein < 1 gm%; 6 of these belonged to the SBP group.

Serum ascites albumin gradient (SAAG): The SAAG was 2.36 ± 0.65 gm/dl in the SBP group and 2.26 ± 0.61 gm/dl in the non-SBP group. A SAAG of 1.1 gm/dl implies the presence of portal hypertension[1,2]. There was no significant difference in the SAAG between the two groups.

Conclusion

Our study thus shows that a high proportion of patients of cirrhotic ascites have ascitic fluid infection, meriting routine culture of the ascitic fluid in blood culture bottles in addition to cytological examination of the ascitic fluid. Moreover,

the risk of developing SBP increases with the severity of cirrhosis as judged by Child Pugh class.

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

MRCP EXAMINATION IN INDIA

Applications are invited from the prospective candidates for the following forthcoming Examinations:

MRCP Part I	:	**13th May, 2008**
MRCP Part II Written	:	**15th April, 2008**
MRCP Part II Clinical	:	**December, 2008**

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ORIGINAL ARTICLE

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Incidence of Methicillin Resistant *Stahylococcus aureus* (MRSA) in Pus Samples at a Tertiary Care Hospital, AIIMS, New Delhi

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Abstract

Between December, 2001 and March, 2002, patients with MRSA were treated at All India Institute of Medical Sciences, New Delhi, a tertiary care hospital with 1,200 beds. Methicillin resistant Staphylococcus aureus (MRSA) is an important cause of nosocomial infections worldwide. The prevalence of MRSA in surgical wound infections at AIIMS in 2001-02 was determined. The analysis of 2,080 pus samples was done. A high incidence of S. aureus was observed. The MRSA prevalence rate was 44% of all S. aureus isolates. All isolates were sensitive to vancomycin, rifampicin and teichoplanin. MRSA occurred sporadically in a wide distribution of surgical wards. The high incidence of MRSA in this hospital warrants the use of antibiotics and application of control measures to prevent the spread of such resistant strains.

Key words: Methicillin, MRSA, Staphylococcus aureus, Vancomycin, Teichoplanin, Surgical wards.

Introduction

MRSA emerged as a nosocomial pathogen in the early 1960s. Most occurrences were isolated in sporadic outbreaks but in the 1970s, an increasing number of large hospital outbreaks were reported in many countries including the USA, Europe, Japan, and Australia[1]. MRSA was first reported in a teaching hospital in Malaysia in 1972. *S. aureus* is the organism, predominates in surgical wound infections with prevalence rate ranging from 4.6% - 54.4% of all *S. aureus* isolates[2-5]. The choice of treatment for post-surgical wound infections requires an understanding of the usual flora, available antimicrobial agents, and susceptibility patterns. Routine surveillance for hospital acquired wound infections is thus recommended by both, the Centres for Disease Control and Prevention, and the Surgical Infection Society[2]. Thus the incidence of MRSA in both developed and developing countries prompted to carry out a retrospective study to determine the prevalence of MRSA in surgical wound infections at AIIMS hospital in north India, in order to utilise the information obtained from this study to apply appropriate control measures.

Material and methods

Specimens

The retrospective analysis included 2,080 pus samples obtained from patients with surgical wound infections admitted to All India Institute of Medical Sciences hospital during a three-month period from December 15, 2001 to March 15, 2002.

Collection and transport of specimens

Samples were obtained using cotton tipped swabs from all skin wounds, and direct aspiration of pus from deep-seated wounds. Swabs were transported to the laboratory in Thioglycolate broth (TGB) (Hi-media Limited, India). The samples were delivered to the microbiology laboratory within 30 minutes of collection.

Culture

If pus discharge/aspirate/any other infected fluid, is used for culture, then one loopful is used for inoculating blood agar (BA) and MacConkey agar (MA) plates, and one loopful in TGB medium and for direct smear. If catheter tip is sent, roll the tip all over with sterile forceps on BA and then MA. The tubes are then put into TGB. The samples cultured on blood agar (BA) and MacConkey agar (MA) plates are incubated aerobically at 37° C for 48 hrs. The isolates were identified using standard laboratory procedures[6].

Anti-microbial susceptibility

All staphylococcal strains were tested for susceptibility to amikacin, teichoplanin, ciprofloxacin, vancomycin

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amoxycillin, cefuroxime, and rifampicin by standard disc diffusion method recommended by the National Committee for Clinical Laboratory Standards (NCCLS)[7].

Detection of MRSA

As recommended by NCCLS, the isolates of staphylococci were tested for oxacillin susceptibility by agar screen method using 6 µg/ml oxacillin[8]. The four strains i.e., *S. aureus* (ATCC-25923), *S. epidermidis*, WHO-23, and WHO-2 were used as a control. Agar plates were incubated at 35° C and read after 24 hrs. of incubation. All bacterial growth on oxacillin screen agar was considered to be MRSA.

Table I: Distribution of resistant *S. aureus* isolates in relation to surgical speciality.

S. No.	Surgical speciality	No. of isolates (%)
1	Neurosurgery	30 (26%)
2	Orthopaedics	26 (24%)
3	Paediatric surgery	20 (17.8%)
4	Cardio-thoracic surgery	15 (14%)
5	General surgery	8 (7.1%)
6	Skin OPD	7 (6.25%)
7	Oncology	3 (2.6%)
8	Physical medicine and rehabilitation	2 (1.78%)
9	General ICU	1 (0.89%)

Table II: Antibiotic-sensitivity of MRSA isolates.

S. No.	Antibiotics	Sensitivity (%)
1.	Vancomycin	100%
2.	Rifampicin	62%
3.	Teicoplanin	56%
4.	Amikacin	31%
5.	Ciprofloxicin	16%
6.	Cefuroxime	11%
7.	Amoxycillin	6.25%

Results

Of the 2,080 specimens received, 800 (38%) were culture positive. *S. aureus* was the most common cause of surgical wound infections accounting for 260 (32%) of the total isolates; coagulase-negative staphylococcus was isolated in 60 (75%) samples. Methicillin resistance was documented in 112 (44%) of the *S. aureus* isolates. Of the 60 coagulase-negative staphylococci, 25 (42%) were methicillin resistant. The distribution of 112 MRSA isolates in relation to the surgical speciality from which they were taken, is as follows: neurosurgery (26%), orthopaedics (24%), paediatric-surgery (17.8%), cardio-thoracicsurgery (14%), general surgery (7.1%), skin OPD (6.25%), oncology (2.6%), physical medicine and rehabilitation (1.78%), general ICU (0.89%). All the 112 MRSA were sensitive to vancomycin, rifampicin and teichoplanin. The sensitivities of methicillin resistant staphylococci to various antibiotics were as follows: vancomycin (100%), rifampicin (62%), teichoplanin (56%), amikacin (31%), ciprofloxacin (16%), cefuroxime (11%), amoxycillin (6.25%). Out of 112 MRSA, the 66 were detected to be positive β-lactamase, and 46 were negative β-lactamase.

Discussion and conclusion

The previous inclination of MRSA is in high intensity in the surgical and intensive care services, where antibiotic usage is the greatest. According to this study, there is high occurrence of MRSA in surgical wound infection, especially in the neurosurgical and orthopaedics patients, due to overcrowding, workload, and understaffing of wards. The MRSA could be prevented by identifying and screening MRSA carriers inside high-risk wards as it is an important clinical problem at AIIMS. It should not be ignored as it can seriously disrupt the efficient delivery of healthcare services in the hospital. Preventing colonisation and infection remains the most effective way to control the spread of MRSA and simple measures such as patient isolation, cohorting doctors and nurses working with patients. Strict enforcement of hand washing and early discharge of infected patients will go a long way towards reducing the spread of this pathogen in this hospital[3,5]. All the isolates of MRSA were sensitive to vancomycin and teichoplanin, in contrast to recent reports of *S. aureus* isolates with reduced susceptibility to vancomycin by the Centres for Disease Control and Prevention (CDC, USA), and of three *S. aureus* isolates fully resistant to vancomycin by Japanese workers[9,10]. Thus, the results of the present study show a high endemicity of MRSA at AIIMS hospital, New Delhi. This poses a serious problem for drug therapy because the treatment options have been restricted to potentially toxic antimicrobials like vancomycin, leading to increased mortality and morbidity.

Therefore, preventing surgical infection with MRSA requires application of surgical first principles and immediate reinforcement of the appropriate use of antibiotics plus commitment of local resources.

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REVIEW ARTICLE

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Non-Alcoholic Fatty Liver Disease (NAFLD)

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Abstract

Non-alcoholic fatty liver disease (NAFLD) is a broad term encompassing a spectrum of abnormalities of the liver. The incidence of NAFLD is rapidly rising and so is the available knowledge and information regarding it. NAFLD is emerging as a common cause of liver dysfunction in non-alcoholics. It is found to be associated with multiple conditions like obesity, diabetes mellitus, hyperlipidaemia, etc. Basic pathogenesis includes fat deposition in hepatocytes with varying degree of inflammation and regeneration of the liver. Presentation of NAFLD varies from asymptomatic to florid liver cell failure in advanced cases of NASH (non-alcoholic steatohepatitis). The disease is mainly diagnosed by exclusion of other conditions with a high index of suspicion for NAFLD. There is no specific management available for NAFLD; early diagnosis and treatment of the underlying condition remains the mainstay of treatment. However, there is much scope for research to let us understand the disease and deal with it appropriately. Non-alcoholic fatty liver disease (NAFLD) is a common cause of chronic liver disease and its incidence is rising worldwide. Understanding its pathogenesis, biochemical parameters, histological grading and staging, and its management, are vital issues today in clinical practice.

Key words: Obesity, Insulin resistance, Hyperlipidaemia.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a common cause of chronic liver disease and its incidence is rising worldwide. Understanding its pathogenesis, biochemical parameters, histological grading and staging, and its management, are vital issues today in clinical practice.

The term NAFLD is used to describe a wide spectrum of fatty liver changes ranging from fatty liver and steatosis on one side, to non-alcoholic steatohepatitis (NASH) and cirrhosis on the other.

Before diagnostic tests for hepatitis C were available, cases of NAFLD were diagnosed wrongly as non-A, non-B hepatitis. Now after such tests for hepatitis C and E are available, NAFLD is more accurately defined. Initially it was thought to be a mild disease with little clinical significance, but at present NAFLD is recognised as a major cause of cryptogenic cirrhosis of liver.

Definition

As the term suggests, NAFLD is deposition of fat in the liver of a non-alcoholic subject, a condition which may progress to end-stage liver disease[1]. The spectrum of progression of NAFLD is similar to alcoholic liver disease, but is not caused by chronic alcohol consumption. The spectrum of pathological changes described in NAFLD consists of 4 types[2] (Table I). The clinical implications of NAFLD are of significance as it occurs in the general population and may progress to cirrhosis of liver and liver cell failure.

Table I: Pathological changes in NAFLD.

I.	Only fat deposition
II.	Fat deposition + inflammation
III.	Type II + advanced inflammation and ballooning degeneration
IV.	Type II + fibrosis and/or Mallory bodies and cirrhotic changes

Prevalence

NAFLD is an extremely common liver disease in the United States (USA) affecting approximately 20% of the adult population. In different countries, its prevalence is 10 – 24% of the general population. Amongst the obese persons, the prevalence rises to 57 – 74% and 25 – 75% amongst obese diabetics[1]. Accordingly, NASH can be considered as the 3rd commonest cause of liver disease after hepatitis C and alcohol abuse in the US[2].

Investigators in their studies found that once chronic alcohol ingestion, viral, drug-induced, autoimmune and metabolic

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causes such as Wilson's disease and haemochromatosis were ruled out, virtually all the remaining patients were proved to have NAFLD.

In India, data regarding NAFLD is lacking, but with increasing awareness and understanding about this disease, a gradually rising trend is seen.

NAFLD and associated conditions

NAFLD is associated with various conditions, which may be considered while diagnosing it. It is mainly associated with:

- Obesity (69 – 100%)
- Diabetes mellitus (36 – 75%)
- Hyperlipidaemia (20 – 81%)

These conditions are associated with insulin resistance and metabolic syndrome, which is frequently observed with NAFLD.

Obesity: More than 70% of patients with NASH are obese. Body weight ranging from 10 – 40% higher than ideal is associated with 4 – 6 fold higher incidence of NAFLD. There is direct correlation between the severity of obesity and severity of NAFLD[1].

Diabetes: Upto 75% patients with NASH have diabetes mellitus. Obese, middle-aged females with DM are more likely to have fatty liver changes on ultrasonography (upto 70%)[3].

Hyperlipidaemia: 20 – 80% of patients with NASH have hyperlipidaemia in the form of high blood cholesterol level and/or high triglyceride levels.

Other associated conditions:

- Total parenteral nutrition for prolonged periods.
- Severe insulin resistance.
- Significant and rapid weight loss in obese subjects.
- Familial lipid disorders, e.g., aβ-lipoproteinaemia, hypoβ-lipoproteinaemia.
- Limb lipodystrophy.
- Weber-Christian disease.
- Drugs[4]: corticosteroids, methotrexate, tamoxifen, diltiazem, nifedipine, tetracyclins, perhexilin, synthetic oestrogens, etc.
- Occupational exposure to toxins such as hydrocarbons.
- Surgical procedures: jejuno-ileal bypass, gastropexy, biliopancreatic bypass, extensive loss of small intestines during surgery[5], post liver transplantation.
- Human immunodeficiency virus (HIV) and NAFLD: NAFLD has been reported in acquired immuno-deficiency syndrome (AIDS) patients. HIV itself, or nucleoside analogues, (e.g., Nevirapine, Stavudine, etc.) used in its treatment, DM, obesity, etc., also contribute towards the initiation and progression of NAFLD[6].

Pathogenesis and natural history

Pathogenesis in NAFLD is characterised by fat deposition, inflammation, and fibrosis of liver.

Fat deposition: macrovesicular fat deposition occurs in the liver.

Inflammation: steatohepatitis results as a consequence of multiple factors – chiefly, insulin resistance leading to accumulation of free fatty acids; and other mechanisms like oxidative stress, lipid peroxidation, endotoxins, iron overload, etc. Various cytokines, like tumor necrosis factor (TNF) and interleukins (IL-6, IL-8) are responsible for inflammation. TNF affects mainly the triglyceride synthesis in the liver.

Fibrosis: steatohepatitis progresses to increasing fibrosis and later on cirrhosis may develop. About 12% of patients with NAFLD may progress to cirrhosis within 7 years. Cirrhosis secondary to NASH may progress to hepatocellular carcinoma.

Predictors of NASH and advanced fibrosis[7]:

HAIR score

1. Hypertension
2. Alanine transaminase (ALT) > 40 IU/l
3. Insulin resistance (IR) index > 5

Presence of 2 or all 3 factors predict NASH.

BAAT score

1. Body mass index (BMI) > 28 kg/m^2
2. Age > 50 yrs
3. ALT > 2-fold rise
4. TG > 1.7 mmol/l

Presence of none or only 1 factor rules out the possibility of fibrosis or cirrhosis.

Clinical features

Most patients of NAFLD (45 – 100%) have no symptoms or signs of liver disease at the time of diagnosis[1]. In these patients, abnormal liver function tests are often discovered incidentally.

When symptoms occur, they are non-specific – like persistent fatigue (50 – 73%), pruritus (0 – 6%), oedema (2 – 10%), malaise, and right upper quadrant discomfort or pain[8].

Other features like GI bleeding (0 – 3%), jaundice (0 – 5%), ascites (0 – 3%), pruritus, and oedema point towards severe liver disease. Ascites, hepatic encephalopathy, and variceal bleeding indicate cirrhosis of liver due to progressive NASH[2].

When the disease is not advanced, diffuse non-tender smooth hepatomegaly is present in 25 – 53% of patients. Such patients are usually obese and/or diabetic. Advanced disease may present with right hypochondrium tenderness, jaundice, palmar erythema, spider angioma, portal hypertension, ascites, varices, and splenomegaly.

Diagnosis

Diagnosis of NAFLD is one of exclusion of other causes of liver dysfunction. Thus one needs to ascertain the absence of alcohol abuse, viral, autoimmune, metabolic, hereditary or other known causes of liver pathology before keeping the diagnosis of NAFLD. Generally, absence of alcohol abuse or consumption of alcohol of < 20 g/day for prolonged periods, and negative serological tests for hepatitis B and C should raise the suspicion of NAFLD (Table II).

Table II:

Approach to diagnosis of NAFLD	
Identification of NASH	Rule out alcoholism
Raised ALT in high risk groups Fatty liver on USG or imaging	History from patient relatives Random blood alcohol level MCV for B_{12} and/or folic acid deficiency.
Exclude other causes like viral, autoimmune, metabolic, etc.	AST/ALT ratio, mitochondrial AST/ total AST ratio
Liver biopsy (required for diagnostic documentation and staging of the disease)	Desialated transferrin/total transferrin ratio, plasma pseudocholinesterase

Diagnosis by biochemical parameters: (Table III).

Table III: Biochemical parameters.

Lab parameter	**Abnormality**
ALT	4–5 fold increase
AST	4–5 fold increase
ALT/AST ratio	Usually <1 in cirrhosis, <2 in alcoholic liver disease
Alkaline phosphatase	2–3 fold increase
GGT	Usually normal, upto 2–3 fold rise in some cases
Bilirubin	Increases in late stages of NAFLD
Albumin	Decreases in late stages of NAFLD
Prothrombin time	Increases in late stages of NAFLD
S. iron chemistry	
S. ferritin	Raised in upto 50% cases
S. iron	Raised
Transferrin saturation	Decreases
ANA	Positive in 15–20% cases
Lipids	Raised in underlying hyperlipidemia
Viral markers	To exclude viral hepatitis

Diagnosis of NAFLD by imaging: Non-invasive radiological imaging studies[9] such as USG, CT scan of abdomen, and MRI may help in diagnosis of fatty infiltration of liver; but they do not distinguish between fatty liver, steatohepatitis and steatohepatitis with fibrosis – for which liver biopsy is required.

a. USG findings in NAFLD:

- Increased echogenecity of (hyperechogenic) liver.
- Increased liver contrast compared to kidney.
- Vascular blurring – mainly of hepatic veins.

- Attenuation of echogenic level in deep-seated areas.

USG examination is to be performed first as it is the least expensive and carries no risk of radiation. Its sensitivity is more, but it lacks specificity.

b. CT scan findings in NAFLD:

- Focal areas of fatty infiltration may be picked-up.
- Mean CT Hounsfield unit in liver less than that in spleen helps in diagnosis.

It is a costly technique, sensitivity is comparable to USG, but specificity is more than that of USG.

c. MRI findings in NAFLD:

- Fatty infiltration of liver correlates very well to phase contrast imaging giving very good quantitative assessment of disease status.
- Useful for excluding fatty infiltration.
- On T1-weighted images, there is loss of intensity in the focal areas of fat deposition. So, early stage of disease with small lesions are readily identified on MRI.

It is more sensitive and specific compared to USG or CT scan, but considerably more expensive.

d. Radionuclide scanning (scintigraphy) studies:

- With technetium-99m sulphur colloid scanning, focal areas of fat deposition are identified as filling defects.
- Radio-xenon has a very high affinity for fat and it remains bound to and retained in fat. This provides qualitative as well as quantitative assessment of fat deposition in liver.

e. Laparoscopy:

It provides a direct view of the liver for macroscopic pathological changes. It shows scattered yellow spots on the surface of liver, when > 30% of it is involved and there is no fibrosis. Diffuse yellow appearance is seen when similar fatty changes are present with fibrosis of the liver. This difference may be accentuated by use of a dye – indocyanine green.

Histological diagnosis by liver biopsy: After exclusion of other liver diseases, diagnosis of NAFLD can only be ascertained by a liver biopsy. It is the most sensitive and specific investigation, also necessary for staging, typing, and explaining prognosis of the disease.

On histological examination, the findings of NAFLD are very much similar to those of alcoholic liver disease. Determination of hepatic iron store is an important parameter in distinguishing NAFLD from haemochromatosis. Degree of rise in ferritin level is much high in haemochromatosis than in NAFLD.

The histopathological changes in NASH include hepatic steatosis, ballooning degeneration, acute, chronic or mixed inflammation, perisinusoidal fibrosis, and Mallory hyaline bodies[2].

Burnt *et al*[9] have described fibrotic changes in NASH in 4 stages (Table IV).

Table IV: Stages of NASH.

Stage	Changes
I	Zone III perisinusoidal or pericellular fibrosis, either focal or diffuse
II	Stage I + extensive periportal fibrosis
III	Stage II + focal or extensive bridging fibrosis
IV	Cirrhosis of liver

Table V compares the histological findings in NASH and alcoholic liver disease (ALD).

Table V: Comparison of NASH with alcoholic liver disease.

Comparative histology in NASH and alcoholic hepatitis		
	Alcoholic hepatitis (%)	**NASH (%)**
Severe steatosis	15	15
Lobular hepatitis	54	85
Periportal fibrosis	0	33
Mallory bodies	3	16
Fibrosis/cirrhosis	38	63
Nuclear vacuolation	76	7
Bile duct proliferation	53	96

Management options for NAFLD

No established treatment is available for NAFLD. Some empiric treatment strategies have been suggested.

General measures: Gradual weight loss is advised in obese and overweight subjects. It results in improvement in laboratory abnormalities and steatosis. More than 10% patients will show normalisation of elevated ALT levels and decrease in hepatomegaly. Rapid or abrupt weight loss (> 1.6 kg/wk) is not advocated as it may lead to progression of NAFLD[10]. Weight loss should not be complete either. Gastrojejunal bypass surgery for obesity and long-term parenteral nutrition therapy should be avoided as far as possible.

Dietary management: diet should have restriction in rapidly absorbed carbohydrates like monosaccharides and disaccharides. High protein diet with high protein-calorie is also helpful[2].

Management of associated conditions:

a. **Diabetes mellitus:** patients with DM should have proper control of blood sugar. Insulin resistance is associated so insulin sensitisers like metformin and pioglitazone may be added in therapy. Metformin also has anorexiant action and helps in weight loss. However, there is no definite study carried out for the use of these agents in NAFLD; the suggestion is logical.

b. **Hyperlipidaemia:** dietary fat restriction and lipid lowering drugs are helpful in this condition. Mainly drugs causing decrease in triglyceride levels are helpful. Drugs like gemfibrozil, clofibrate, and statin group of drugs are indicated. But it is to be kept in mind that fibrates may cause drug-induced hepatitis in some patients.

c. **Certain drugs:** are associated with development of NAFLD as described earlier. They should be discontinued and other proper alternatives should be substituted.

d. **Metronidazole:** in a dose of 750 – 2,000 mg per day for 3 months is shown to resolve steatohepatitis associated with jejunal bypass surgery[2]. This therapy needs evaluation for use in other types of NAFLD.

e. **Calorie-free amino acid infusions:** have reversed steatohepatitis associated with jejunoileal bypass, but this is not assessed in cases of NAFLD.

Drugs used in management of NAFLD: drugs used to reduce insulin resistance and triglyceride levels have already been described above. Certain drugs called 'hepatoprotective drugs'; like ursodiol (ursodeoxycholic acid) 13 – 15 mg/kg/d, vitamin E 400 – 1,200 mg/d, betaine 20 g/d, N-acetyl cysteine 1 g/d are also used. Lastly, role of antioxidants is also investigated extensively as accumulation of lipid peroxidation products in response to free radical injury leads to oxidative stress which is important in causing liver cell injury.

Hence, antioxidants like vitamin E, beta-carotene, vitamin C, lecithin, etc., may be tried. Vitamin E is shown to decrease liver enzymes significantly. Betaine and other methylated amino acids act as methyl group donors and decrease fat uptake and there by fat accumulation in liver cells. Betaine is a promising drug.

Ursodeoxycholic acid (UDCA) in a dose of 13 – 15 mg/kg/d for one year has been found to improve ALT and steatosis in patients with NAFLD. It acts by its cytoprotective, immunomodulatory, chemoprotective, and antioxidant properties. UDCA is cytoprotective as it has high lipid altering property. It stabilises the hepatocyte membrane and prevents cell membrane injury. It also improves cell injury in liver. It helps in preservation of mitochondrial function which in turn reduces steatosis because of clearance of fat accumulation in liver[11]. Early treatment is the best option to prevent further progression of NAFLD and to reverse the changes to near normal.

Conclusion

NAFLD is an important common cause of chronic liver disease and cryptogenic cirrhosis of liver associated with insulin resistance. Its incidence is reportedly on the rise the world over. Realising its significance, there is now greater understanding of its aetiology, pathogenesis and management. Early diagnosis and early management is of vital importance. Early treatment with UDCA and antioxidants has been advocated. However, effective treatment options are still lacking for which future stepwise work is required by research workers.

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Triclazone

CLINICAL MEDICINE

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Understanding and Managing Tension Pneumothorax

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Definition

The term 'Pneumothorax' denotes air in the pleural space, i.e., the space between the chest wall and the lung (Fig. 1). This is a potential space and not an actual space, because the visceral and parietal layers of the pleura are held in contact by the surface tension of their moist surfaces[1].

In a tension pneumothorax, the intrapleural air pressure exceeds atmospheric pressure throughout expiration and often during inspiration as well. The mechanism by which a tension pneumothorax develops is probably related to some type of a one-way valve process in which the valve is open during inspiration and closed during expiration. During inspiration, owing to the action of the respiratory muscles, the pleural pressure becomes negative, and air moves from the alveoli into the pleural space. Then, during expiration, with the respiratory muscles relaxed, the pleural pressure becomes positive[2].

Predisposing factors

Interstitial and obstructive lung diseases.

Classification of pneumothorax

Pneumothorax is classified according to:

A. Aetiology.

B. Extent.

C. Mechanism.

D. Duration.

A. Classification by 'Aetiology':

i. **Spontaneous pneumothorax** – It is by far the commonest form of pneumothorax in clinical practice and is always secondary to pulmonary or pleural pathology[3]. There is no obvious cause or antecedent trauma. Patients are usually in the 20 – 40 years age group and present with sudden, sharp chest pain, and dyspnoea[3]. In patients of chronic bronchitis and emphysema who are over 40, there is progressive destruction of alveolar walls, and thus the high intrapulmonary pressures produced by coughing result in spontaneous pneumothorax[1].

a. Primary spontaneous pneumothorax

- Occurs in apparently healthy persons due to leak of air through a weak area of the pleura. It is initiated by marked variations in intra-thoracic pressure as in the following:
  - aeroplane ascent to sub-atmospheric pressure[1, 4].
  - too rapid decompression to atmospheric pressure of divers or caisson workers[1, 5].
  - pilots who eject at high altitudes.
- Is seen in smokers.

b. Secondary spontaneous pneumothorax

- Is seen in cases with any underlying lung conditions, e.g., COPD usually.
- Is more serious as it further reduces the sub-optimal pulmonary function of the underlying diseased lung.

ii. **Traumatic pneumothorax (non-iatrogenic)** – The usual cause is direct or indirect trauma to the chest, e.g., road accidents, stab injuries, war injuries.

iii. **Iatrogenic or artificial pneumothorax** – Occurs as a result of any diagnostic or therapeutic procedure.

B. Classification by 'Extent':

i. **Localised pneumothorax** – When the parietal and visceral pleura have developed adhesions.

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iii. **Generalised pneumothorax** – When the whole pleural cavity, i.e., hemithorax, has air.

C. **Classification by 'Mechanism':**

i. **Open pneumothorax** – When there is movement of air in and out of the pleural cavity without any hinderance. This is due to communication between the pleural space and the airways and may lead to development of a broncho-pleural fistula (BPF). But if the hole through which the air flows is small, then the intra-pleural pressure during respiration could fluctuate.

ii. **Closed pneumothorax** – When there is no movement of air, i.e., air is trapped in the pleural space because the hole through which air entered has been obliterated.

iii. **Valvular pneumothorax** – When air is able to enter during inspiration, but is unable to exit during expiration. This type of pneumothorax becomes a medical emergency because the air pressure keeps on increasing gradually, and the lung deflates more and more, leading to pressure effects on the mediastinum and great veins. As an effect, the mediastinum is dispaced and the great veins become kinked, leading to decreased venous return to the heart. This leads to increasing cardiac and respiratory embarrasment At this stage it is usually termed a 'tension pneumothorax' because of the rising pressure which builds up in the pleural cavity[1].

D. **Classification by 'Duration':**

i. **Acute**

ii. **Chronic**

Aetiological factors[6,1]

1. **Common**

- Iatrogenic, e.g., insertion of a central venous catheter while managing a patient in shock.
- Mediastinal emphysema
- Spontaneous (ruptured bulla)
- Trauma

2. **Rare**

- Broncho-pleural fistula from lung abscess or granuloma (tuberculosis)
- Fibrocystic disease of the pancreas
- Honeycomb lung
- Hyaline membrane disease
- Oxygen toxicity; Wilson-Mikity syndrome
- Perforation of the oesophagus
- Pneumonia
- Pneumoperitoneum with passage through diaphragm
- Primary or metastatic neoplasm
- Pulmonary infarction

Pathophysiology

With reference to the atmospheric pressure, the pleural space normally has negative pressure during the complete respiratory cycle. This negative pressure is created by the chest wall which tends to expand, and the lungs which tend to collapse. As such, the alveolar pressure is more than the pleural pressure. As a result, if a leak develops between an alveolus and the potential pleural space, air moves from the alveolus to the pleural space till the pressure equalises on both sides. As a consequence, the lung volume decreases, and the thoracic cavity volume increases.

A pneumothorax results in a decrease in the vital capacity as also a decrease in the PaO_2. A healthy person is likely to easily cope with this reduction in lung function. But in patients with underlying lung disease, the reduced vital capacity progresses to respiratory insufficiency with alveolar hypoventilation and respiratory acidosis as a result of reduced PaO_2 and an increase in alveolar-arterial oxygen difference ($AaDO_2$).

Clinical manifestations of tension pneumothorax

Symptoms of pneumothorax will depend on its type and extent. Usually, the patient experiences severe pain. Often, a small pneumothorax is asymptomatic. But when there is progressive dyspnoea with pain and tightness in the affected side of the chest, then the possibility of tension

pneumothorax has to be considered[7]. On examination, the following are present:

1. Deviation of the trachea and apex beat to the opposite side.
2. Hyper-resonance on percussion.
3. Diminished air entry.
4. "Anvil-clink" heard on tapping two coins on the chest.
5. Tinkling rales (crepitations).

All these findings are suggestive of the presence of positive intra-pleural pressure.

Many a times, it is a spontaneous pneumothorax which progresses to become a tension pneumothorax. In a hospital setting, it could occur in patients with the following:

1. Ventilatory support.
2. Cardio-pulmonary resuscitation.
3. Pneumothorax secondary to trauma or infection[2].

Striking clinical features

1. Anxious and distressed look, restlessness with rapid laboured breathing (respiratory distress).
2. Weak, rapid pulse; and cold, clammy skin of shock as a result of increasing intra-pleural pressure which progressively impairs the venous return to the heart[1].
3. Cyanosis – is unusual in the younger patients except when severe tension pneumothorax is present. But in older patients with chronic bronchitis and emphysema, cyanosis may occur even with a small pneumothorax[1].
4. Profuse diaphoresis.
5. Marked tachycardia[1].

Physical signs in the chest depend essentially on the degree of pulmonary collapse, and whether or not there is an associated pleural effusion[1]. Both chest pain and dyspnoea are present in about 64% patients with primary spontaneous pneumothorax. Chest pain is present in about 90% patients. It is acute in onset, and is localised to the side of the pneumothorax.

Surgical emphysema over the neck or chest wall commonly accompanies pneumothorax due to trauma or ruptured oesophagus[8].

N.B.: *Unless the condition, i.e., the tension pneumothorax is relieved swiftly, death will occur from a combination of respiratory and cardiac failure*[1].

Physical findings – are those of any large pneumothorax[4].

1. In primary spontaneous pneumothorax, there is moderate tachycardia, and the vital signs are usually normal.
2. In tension pneumothorax:
   - Pulse rate $\geq$ 140.
   - Hypotension.
   - Cyanosis.
   - The side of chest with pneumothorax is larger in comparison to the contralateral side.
   - Trachea is shifted to the contralateral side.
   - The intercostal spaces are widened and appear bulged-out on the affected side.
   - Movement — i.e., excursion of chest wall — is decreased on the side with pneumothorax.
   - Tactile fremitus is absent.
   - Breath sounds are absent or reduced due to diminished air entry.
   - Percussion note is hyper-resonant.
   - "Anvil clink" (produced by tapping two coins on the chest) is heard.
   - In left-sided pneumothorax, the metallic tinkle may be synchronous with cardiac contractions ('clicking' pneumothorax)[8].
   - With a right-sided pneumothorax, the lower edge of liver is shifted inferiorly.

All these signs are conclusive of the presence of positive intra-pleural pressure.

3. Surgical emphysema[9]: Some air escapes into the tissue planes of the chest wall after most wounds of the chest – surgical or traumatic – but it is generally slight in extent and is rapidly re-absorbed. It differs in no respect from mediastinal emphysema, and should it increase, it demands intrathoracic exploration, as a penetrating

wound of a bronchus or the trachea could be present.

ECG changes

In spontaneous left-sided pneumothorax:

- Rightward shift of frontal QRS axis.
- Diminution of precordial R voltage.
- Decrease in QRS amplitude.
- Precordial T-wave inversion.

These changes should not be mistaken for an acute sub-endocardial myocardial infarction.

Radiological appearances

On a roentgenogram of the chest, a pneumothorax is classically seen as an area of 'absent' lung markings between the bony thoracic cage and the edge of the lung.

1. A shallow pneumothorax could be missed on a cursory viewing of the chest film, but is well seen in a film taken in full expiration, or a lateral decubitus film with the affected side uppermost.

2. In a major collapse, the lung appears as a globular mass at the hilum, the density proportional to the degree of collapse, and there may be mediastinal shift to the opposite side. A tension pneumothorax usually displaces the mediastinum to the opposite side. A major degree of collapse of one lung usually results in increased blood flow and congestion in the other with appearances which may simulate lobular pneumonia[1].

3. Recognition of a tension pneumothorax is usually easy because of the marked compression of the lung. The lung tends to retain its shape in pneumothorax due to its elastic recoil[6, 10] and to traction by the pulmonary ligament[6, 11]. High pressure pneumothorax secondary to valve-like communication with the lung or through the chest wall often overcomes this tendency, squeezing the lung into a formless shadow along the spine, and often displacing it along the midline. The high pressure sometimes inverts the diaphragm[6].

4. A pleural effusion alongwith a pneumothorax on the same side is seen as an opacity with a horizontal upper edge; sometimes this may appear as just a blunting of the costo-phrenic angle[1].

5. Usually, presence of air in the thorax is clearly seen on the chest film, but it needs to be differenciated from a distended lung cyst in which reticulae are seen across the air shadow[7].

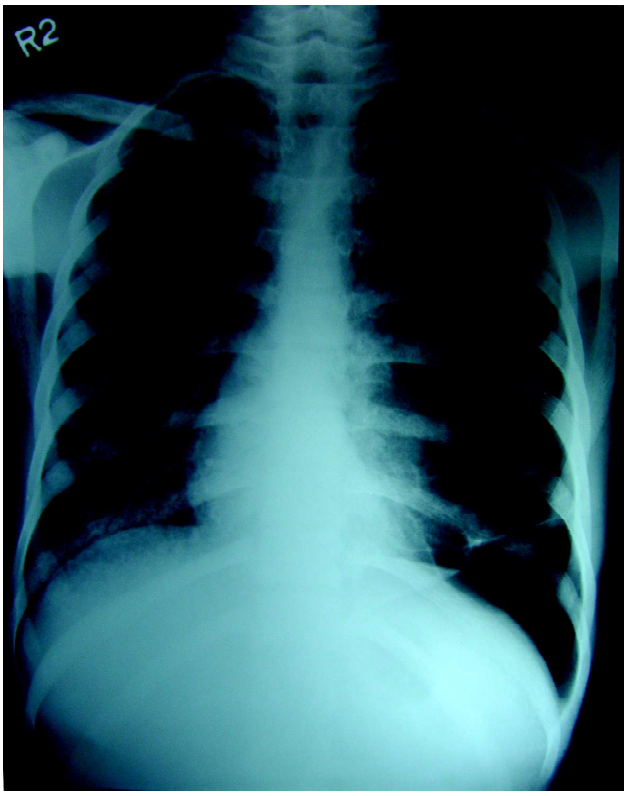

Fig. 1: *Chest Roentgenogram showing left-sided pneumothorax pushing the trachea and heart towards the right.*

Diagnosis

Early recognition of tension pneumothorax is very important because an emergency thoracentesis is the only treatment and is life-saving. It is not wise to waste precious minutes in waiting for a radiological confirmation, because the clinical presentation and physical findings are quite sufficient to establish the diagnosis. If there is any doubt, and the patient is hypoxic, it is necessary to administer supplemental oxygen.

Always remember, the diagnosis of tension pneumothorax should be suspected in[2]:

1. Patients receiving mechanical ventilation.

2. Those patients who have a pneumothorax.

3. Patients whose condition suddenly deteriorates after a procedure known to cause a pneumothorax.
4. Patients in whom difficulty is encountered in mechanical ventilation during cardio-pulmonary resuscitation.

Clinical confirmation of diagnosis

Take a large bore needle. Attach it to a three-way stopcock which is in turn attached to a 50 ml syringe which is partially filled with sterile normal saline solution. Now, insert the needle into the pleural space through the second anterior intercostal space and withdraw the plunger from the syringe. In case of tension pneumothorax, air will immediately rush outward through the fluid in the syringe.

If a tension pneumothorax is confirmed, the needle should be left in place and in communication with the atmosphere until air ceases to exit from the syringe. Additional air can be withdrawn from the pleural space with the syringe and the three-way stopcock[2]. However, preparations should be made for the insertion of a chest tube immediately.

If no bubbles escape from the syringe, then the patient does not have a tension pneumothorax, and the needle should be withdrawn from the pleural space[2].

Differential diagnosis

1. The sudden onset of chest pain and dyspnoea may simulate:
   - Myocardial infarction.
   - Pulmonary embolism.
   - Pulmonary infarction.
   - Perforated peptic ulcer.
2. Extensive bullous emphysema ("vanishing lung").
3. Pneumomediastinum.
4. Pneumopericardium.

To clinch the definitive diagnosis of pneumothorax, a lateral decubitus chest film with the affected lung uppermost is mandatory. Practically, even minute amounts of air can be seen in such a film.

Treatment

Treatment depends on the size of the pneumothorax. If small, observation is sufficient; if large, closed drainage with a chest tube is necessary[3].

Principles of management[12]:

1. Maintenance of a clear airway.
2. Maintenance of adequate ventilation.
3. Oxygen therapy.
4. Treatment of the cause, i.e., removal of air from the pneumothorax.
5. Use of controlled ventilation: If, inspite of treatment, ventilation remains inadequate, the use of controlled ventilation – either through an endotracheal tube or a tracheostomy – becomes necessary.

The goal of treatment:

1. To evacuate air from the pleural space.
2. To initiate steps to prevent recurrence.

When there is no communication between the pleural space and the lung/airways, then air is reabsorbed at a rate of 1.25% of the total radiographic volume of the hemithorax per day. Thus, a 50% collapse of the lung will take 40 days to re-absorb completely once the pneumothorax is closed, i.e., no air leak persists[1, 13].

Treatment options

1. **A small or shallow pneumothorax** – less than 20% collapse – can usually be left to absorb spontaneously; this takes about a month. A few days of rest or limitation of activity for manual workers is all that is required, and it will absorb progressively.
2. **Any type of large pneumothorax** – more than 20 per cent collapse and accompanied by dyspnoea[1] – needs to be aspirated using a suitable gauge needle, a large syringe, and a two-way tap. Sometimes an artificial pneumothorax refill apparatus is also used so as to bring the intra-pleural pressure to minus 5 to minus 15 cm. H_2O. This type of aspiration can be repeated as and when required.

3 **In the presence of a continual leak.** A plastic or rubber catheter is inserted anteriorly in the second intercostal space approximately 5 cm. from the sternal border. The catheter is to be connected to an underwater-seal bottle. This helps evacuate the air and initiate a local irritative pleurisy. Under local anaesthesia, a self-retaining catheter of the Malecot type (size 22-28) stretched on an introducer is inserted through a cannula in the 4th or 5th intercostal space just behind the anterior axillary line, provided there are no adhesions to the chest wall in this site. Lateral pleural adhesions and persistence of an apical pneumothorax may require insertion of the catheter in the anterior chest wall, usually in the second intercostal space. The intercostal tube is usually left *in situ* for 24 hours after full re-expansion of the lung has been achieved, i.e., a total period of 3 – 4 days in most cases[1]. A tube in the chest is quite painful and analgesics are necessary—if there are no contraindications like asthma, severe bronchitis, or emphysema – to make the patient comfortable.

4 **In a case of tension pneumothorax.** Here, the leak in the lung is valvular. Therefore, a positive air pressure may build-up in the pneumothorax so that the heart and mediastinum are progressively displaced to the opposite side, and the patient becomes increasingly breathless and cyanotic. The condition is instantly relieved in emergency by insertion into the pleural cavity, of a blunt ended, wide-bore needle—or any needle available—connected to underwater drainage or to a finger cot slit so that it acts as a one-way valve or safety valve and should be followed as soon as possible by the removal of all the air[1]. If the valvular mechanism continues to function, the tension element will recur and the needle must then be replaced with either an indwelling needle of the Foster-Carter type, or by an intercostal catheter (Malecot type), connected to a water-sealed suction (Fig. 2) until the lung re-expands and seals off the leak[9].

5 **When there is a large air leak and aspiration proves inadequate.** Here, a thoracotomy with suturing of the damaged lung/ bronchus is necessary.

N.B.: *In all cases where a chest tube has been inserted, the rule of thumb is that the tube should not be removed till bubbling in the underwater-seal bottle is absent on coughing, and the lung has re-expanded. Also, the tube should not be left in one position for more than seven days. But if the tube is still required, it should be replaced through a new puncture 2 cm. away*[7].

Tube thoracostomy

Nearly every patient with a secondary spontaneous pneumothorax should initially be managed by tube thoracostomy. Even if the pneumothorax is small, its evacuation can lead to a rapid improvement in symptoms. Arterial blood gases (ABG) usually improve within 24 hours of instituting tube thoracostomy[14].

If the patient has respiratory failure necessitating mechanical ventilation, a chest tube should definitely be placed because the pneumothorax is likely to enlarge during mechanical ventilation. Tube thoracostomy is less efficacious in secondary than in primary pneumothorax, however. In primary spontaneous pneumothorax, the lung usually expands, and the air leak ceases within 3 days. In secondary spontaneous pneumothorax due to chronic obstructive lung disease, the mean time for the lung to re-expand is 5 days[15].

Open thoracotomy

When spontaneous pneumothorax is due to rupture of an emphysematous bulla, then open thoracotomy is resorted to and the bulla is surgically removed.

Pneumothorax in patients on mechanical ventilation[16]

The development of a tension pneumothorax can be life-threatening during mechanical ventilation, since with each breath the pressure within the pneumothorax becomes greater, compromising both ventilatory and cardiovascular function.

Most clinicians are familiar with the signs of tension pneumothorax during volume ventilation because of the continually increasing PIP (peak inspiratory pressure). With pressure ventilation, the changes could be imperceptible. Since PIP is constant, V_T (tidal volume) decreases as the pneumothorax increases, but its decrease is limited by the eventual equilibration of pressure in the thorax and in the

airway. That is, the pneumothorax may not extend to the degree seen with volume ventilation. With pressure ventilation, the first indication that a problem has occurred is frequently a deterioration in blood gases. With volume ventilation, the effects of a tension pneumothorax are immediate, dramatic, and usually rapidly recognised. However, with pressure ventilation, the response is less dramatic and more difficult to recognise. Careful monitoring of the patient's physical condition, blood gas data, and chest x-rays is needed to identify a pneumothorax.

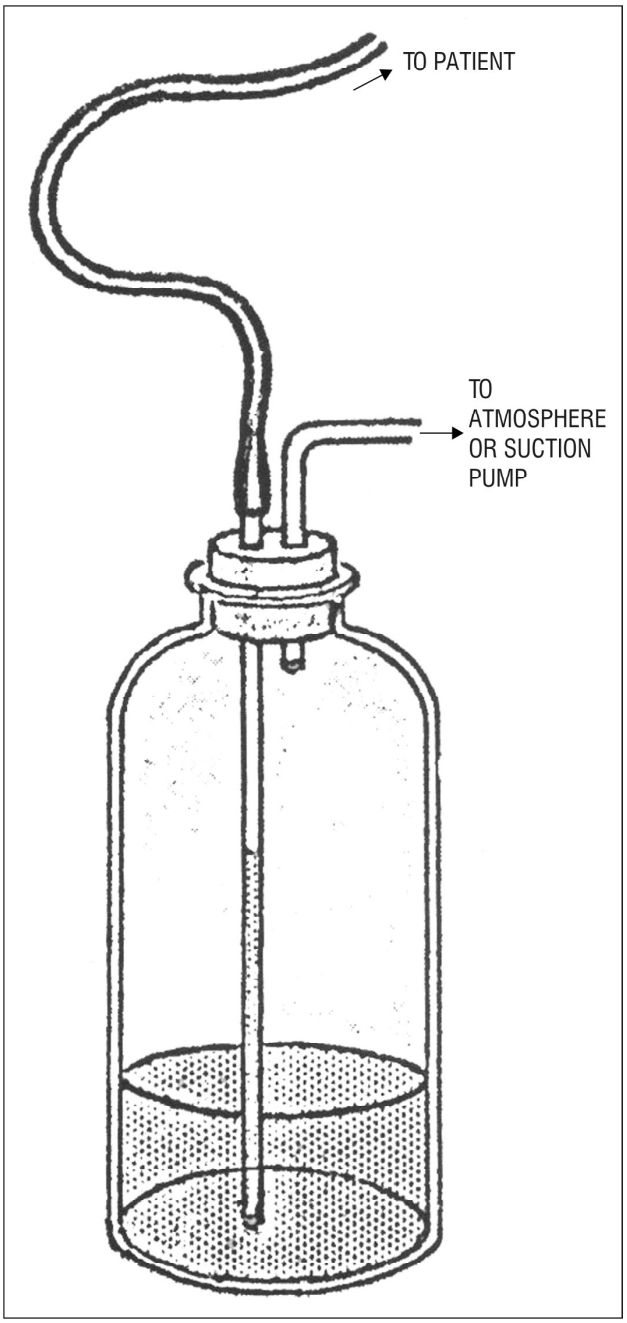

Fig. 2: *A water-sealed drainage bottle. The intrapleural drainage tube is carried down under a measured quantity of saline or antiseptic solution and the negative pressure within the chest causes the fluid to rise up the tube in a meniscus which swings with respiration. The open-ended tube may be connected with a suction pump[9]. (Adapted from Flavell G. Pulmonary Resections. An Introduction to Chest Surgery. London. Oxford University Press, 1957.)*

Recurrence

Recurrences are frequent and the onset of pneumothorax is unpredictable[7]. About 20 per cent of cases of spontaneous pneumothorax recur, most of them within a year. A few cases become chronic, i.e., persisting for 3 months or longer, because of the development of a broncho-pleural fistula (BPF)[1].

Prevention of recurrence

Prevention is important since recurrences could seriously affect the quality of life of a patient and even endanger it. In cases where recurrences have occurred more than three times, it is advisable to go in for pleurodesis[17], i.e., adhering the lung to the chest wall by artificial means. For this, there are two methods:

1. **Surgical:**
   a. A trusted method is to do a pleurectomy wherein the parietal pleura is peeled off. Thereafter, all lung cysts which are larger than a marble are excised and sutured at the base[7].
   b. If the leak from the lung is large and treatment with an intercostal tube is not effective, then a thoracotomy is done with the objective of suturing or excising the ruptured cyst. In some cases a lobectomy is necessitated.
2. **Medical:** This method is resorted to in cases of obstinate pneumothorax. It is effected by instillation into the pleural cavity of an irritant substance which induces a bland pleurisy and subsequent pleural adhesions[1]. Here, silver nitrate and poudrage (iodised talc or kaolin) are used for pleurodesis. However, silver nitrate has been found to be very painful. Though poudrage is also painful, it is preferred by some as the treatment of choice in cases of recurrent pneumothorax. The distribution of the talc or kaolin over the pleural surfaces is carried out visually at thoracoscopy under general

anaesthesia. In most cases, a first or second recurrence on the same side is treated by a further intercostal tube[1].

Complications[3]

1. Haemothorax.
2. Cardiovascular compromise secondary to tension pneumothorax.
3. Broncho-pleural fistula.

Treatment of other complication[1]

1. **Severe bleeding** into the pleural space may occur due to:
   a. Traumatic pneumothorax.
   b. Spontaneous pneumothorax due to rupture of a pleural adhesion (haemopneumo-thorax).

This is managed by an emergency thoracotomy to evacuate the clot and to secure the source of bleeding. Blood transfusion also could be required.

2. **Infection of the pleural space** caused by traumatic pneumothorax or spontaneous pneumothorax may lead to empyema (pyopneumothorax). Infection could be tuberculous or non-tuberculous, e.g., staphylococcal infection. This is treated by immediate aspiration of the effusion and the institution of appropriate chemotherapy.
3. **Atelectasis** may complicate any type of pneumothorax and also delays expansion of the lung. This is managed by:
   a. Physiotherapy, which helps remove viscid secretions.
   b. Bronchoscopy and distension of the collapsed lobe with positive pressure using a cuffed endotracheal tube.
   c. Antibiotic cover is necessary because a collapsed lobe will certainly become bronchiectatic if it is not re-expanded, and so long as collapse persists, antibiotic cover must be continued[9].
4. Respiratory failure could occur in those patients whose respiratory reserve was impaired before the development of pneumothorax. The best option to treat this is to effect a rapid re-expansion of the lung.
5. Surgical emphysema[7]: This could be produced by a rib end penetrating the pleura and damaging the lung. If the pleural cavity is non-adherent, a pneumothorax will develop and air can escape through the torn pleura into the tissues around the fracture and so up the muscle planes of the chest wall, on to the neck, face, arms, abdomen, scrotum, and legs. The eyelids close and the appearance of the patient is grotesque. The fine, silky crepitus of air in the tissues is easily recognisable to the touch and is tender. Treatment is that of the underlying pneumothorax. The air can be milked out of the tissues by squeezing it towards needles inserted in the subcutaneous tissues. This complication is frightening both to the patient and the relatives, but provided the cause is treated, is not serious and reassurance should be given.

Follow-up

It is necessary to follow-up all cases of pneumothorax for at least one year with X-rays taken every three months.

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CASE REPORT

JIACM 2008; 9(1) : 51-2

Bell's Palsy – A Rare Association with Hepatitis A

*Ashok Swaroop**, Naveen Parihar*, Sachin Jain**

Abstract

Bell's palsy is a unilateral lower motor neuron (LMN) type of facial paralysis. Various aetiological agents are associated with it including hepatitis A virus, the rare one. This association is found in our case, hence reported due to its rarity.

Introduction

Bell's palsy caused by hepatitis A virus is a rare clinical entity, only few cases have been reported till date.

Here we are reporting a case of Bell's palsy associated with hepatitis A. Hepatitis A was diagnosed clinically by fever, headache, mild icterus, and serological tests. While Bell's palsy was diagnosed by LMN type unilateral (right side) facial paralysis after excluding other common causes.

Case report

A 24-year-old male presented with three days history of fever, headache, and yellowish discolouration of urine.

One day after admission he had weakness over right side of face which was sudden in onset and progressive. He was unable to close his right eye, unable to hold water in mouth; also, there was watering from right eye and dribbling of saliva from right angle of mouth. His face became asymmetrical with loss of wrinkles over right side of forehead.

He had no complaint of earache, ear discharge, noise intolerance and vesicles in ear; he had no history of rash, cough, weight loss, cold exposure.

ENT examination revealed LMN type right side facial paralysis.

The haematological and biochemical profile showed S. bilirubin 2.8 mg/dL, ALT 300 IU, AST 220 IU, PT (INR) 1.2, rest of the profile was normal.

In serological tests, hepatitis A, total antibody (HAV, total) was reactive (positive), and other possible tests for hepatitis and Bell's palsy such as Herpes simplex virus (1 + 2) IgM, HBsAg, IgM anti-HBc, anti-HCV, IgM anti-HEV, and HIV (1 and 2) were negative.

MRI of head done the next day to rule-out any tumour or intracranial pathology, showed a small mucosal polyp in the right maxillary antrum. X-rays of both mastoid regions were also normal.

The patient was managed conservatively for both disease

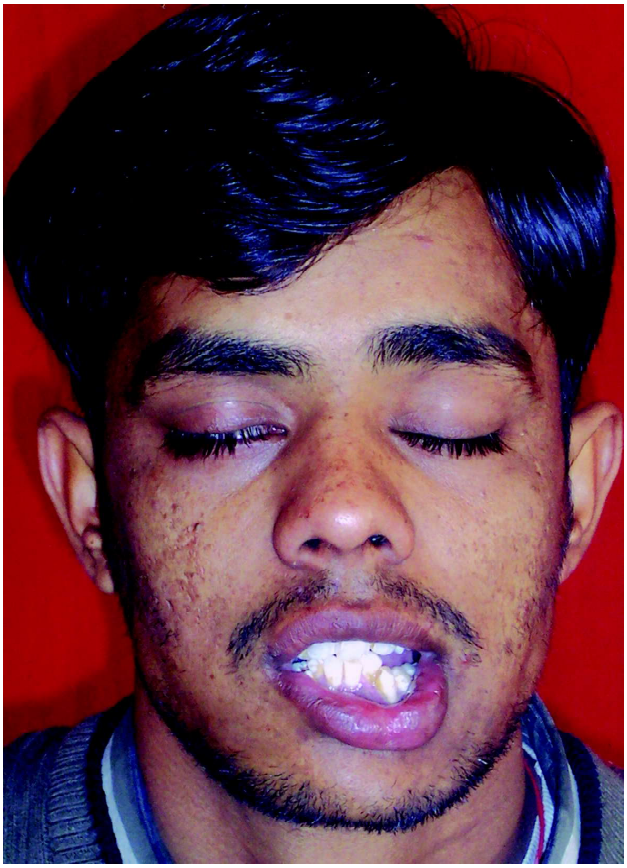

Fig. 1: *Photograph showing right-sided LMN-type facial paralysis (Bell's Palsy).*

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J.L.N. Medical College and Associated Group of Hospitals, Ajmer, Rajasthan.

processes, and he improved gradually. Levels of S. bilirubin and enzymes returned to normal in 10 days, and facial weakness improved in 22 days. Considering facial paralysis as a complication of hepatitis A, steroids were not given.

Discussion

Neurological complications in infectious hepatitis are rare. On reviewing literature, the first case with neurological complications in infectious hepatitis was reported as early as 1944 by Lischer[1]. Then in 1945 Byrner and Taylor described 5 cases of jaundice with neurological signs, and one of these had myelitis[2]. In 1968, Rao *et al* reported myelitis and neuritis in an epidemic of infectious hepatitis in Delhi[3].

Cranial nerve abnormalities that have been associated with acute viral hepatitis include sensory (trigeminal), motor (seventh and ninth), visual and hearing disturbances[4-6]. Bell's palsy is an idiopathic, unilateral, peripheral facial paralysis of acute onset. It is characterised by the patient being unable to close an eye, dribbling of saliva from angle of mouth, facial asymmetry, inability in frowning and raising the eyebrows, epiphora, hyperacusis, and loss of taste.

Aetiologically, it is idiopathic; however, various causes such as infections (viral, bacterial), vascular ischaemia, hereditary, autoimmune disorders, have been associated[7].

The most common aetiological agent is Herpes simplex virus[7]. Hepatitis A virus can cause many neurological complications; facial nerve involvement has been reported but not well associated[8].

Our case also presented with unilateral LMN type facial paralysis of sudden onset with all the clinical features except hyperacusis and loss of taste sensation, with clinical features of hepatitis and serological positivity for HAV total. The patient was managed conservatively, and complete recovery of hepatitis (normal S. bilirubin, ALT, AST) and facial paralysis was recorded.

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CASE REPORT

JIACM 2008; 9(1): 53-6

Insulinoma – A Case Report and Review of Diagnostic Modalities

Vinaya Poornima, Ajit Mahale**, Ashwini Kumar***, Subas Chandra****, Kalyan Paudel*****

Abstract

Insulinoma is a rare clinical entity and is usually benign, single, and small in size. The hallmark of this disorder is fasting hypoglycaemia with high endogenous insulin secretion. Early localisation of the disease is essential to prevent lethal hypoglycaemia. We report a case of insulinoma in a 60-year-old female and review of diagnostic modalities to localise the tumour.

***Key words:** Insulinoma, Islet cell tumours, Hypoglycaemia, Diagnosis of insulinoma.*

Introduction

Insulinomas are the most common pancreatic islet cell tumours that arise from the beta cells within the islets of the Langerhans. The incidence is 0.4 per 100,000 person-years, i.e., 4 cases per million per year[1]. They are uncommon with female preponderance, the average age of presentation being fifth decade of life[2]. They are typically sporadic, solitary, and less than 2 cm in diameter[3]. Diagnosis of this pathology relies on clinical features alongwith laboratory tests and imaging investigations to aid in localisation. We present a case of an insulinoma in a 60-year-old female and the diagnostic modalities available to localise it.

Case report

A 60-year-old female presented with an episode of dizziness and movement deficiency of all her four limbs. She had similar recurrent episodes for 7 years. The symptoms resolved after eating. She denied having seizures, galactorrhoea and diabetes but she noticed increased appetite over the past few years. She had no family history of diabetes, thyroid or pituitary disease. She had never smoked cigarettes or consumed alcohol. There were no prescription medications at the time of her evaluation. Her physical examination revealed a well-nourished female with normal vital signs. She weighed 79 kg with body mass index (BMI) of 42 kg/m^2. She had predominance of fat in her abdominal area. Her abdomen was soft and non-tender with no palpable masses or organomegaly.

A serum glucose level determined in the emergency department was 36 mg/dl (normal range: 70 – 110 mg/dl). She received intravenous glucose and her symptoms promptly resolved. Laboratory evaluation showed low overnight fasting plasma glucose of 60 mg/dl, elevated insulin of 40.39 mU/l (normal range, 1.7 – 31 mU/l). A urine screen for sulphonylurea was negative. Her pituitary adrenal axis was intact. Plasma thyroid-stimulating hormone level was within normal range. In view of the clinical picture and laboratory data, the clinical impression was that of an insulinoma.

Abdominal ultrasound (US) revealed an isoechoic to hypoechoic lesion at the junction of the body and tail of the pancreas (Fig. 1). A computed tomography of the abdomen with contrast using pancreas protocol demonstrated a well-defined 2.1 x 1.6 cm soft-tissue density mass at the junction of the body and tail of the pancreas. The lesion was isodense on plain scan (Fig. 2) and showed

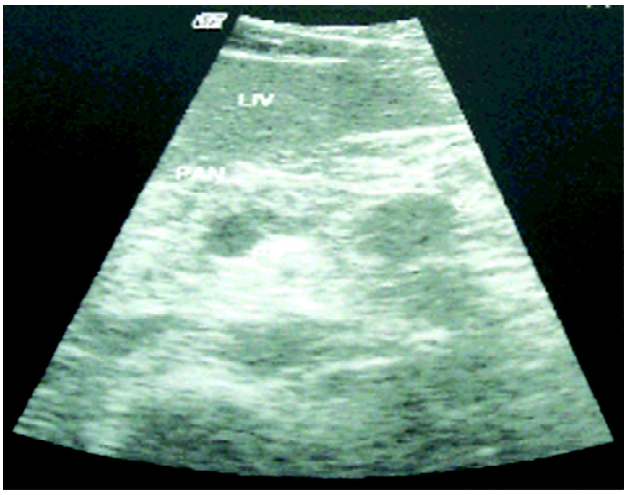

***Fig. 1:** Ultrasound image showing a hypoechoic lesion at the junction of the body and tail of the pancreas.*

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enhancement in arterial phase (Fig. 3), and appeared isodense to pancreas in venous phase of the contrast study. MR study of the pancreas demonstrated an area of altered signal intensity at the junction of the body and tail of the pancreas appearing hypointense on T1 weighted images and hyperintense in axial SPGR and axial GRE post-contrast images (Fig. 4).

The patient underwent pancreatic exploration with enucleation of the pancreatic mass. Immediately after removal of the mass, her glucose level increased to 140 mg/dl. Post-operative glucose levels were consistently greater than 100 mg/dl and she experienced no further hypoglycaemic episodes. Histopathological evaluation of the pancreatic mass was consistent with insulinoma (Fig. 4). The patient was discharged in good health with proper glucose level.

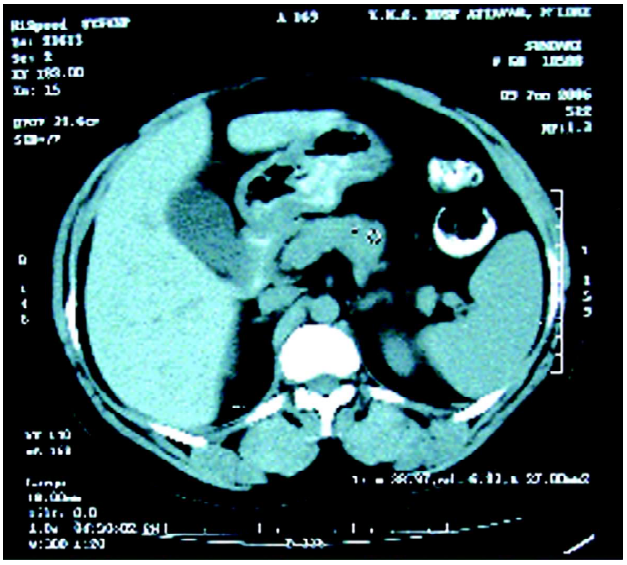

Fig. 2a: *Non-enhanced computed tomography (CT) of the abdomen showing a lesion at the region of the body and tail of the pancreas.*

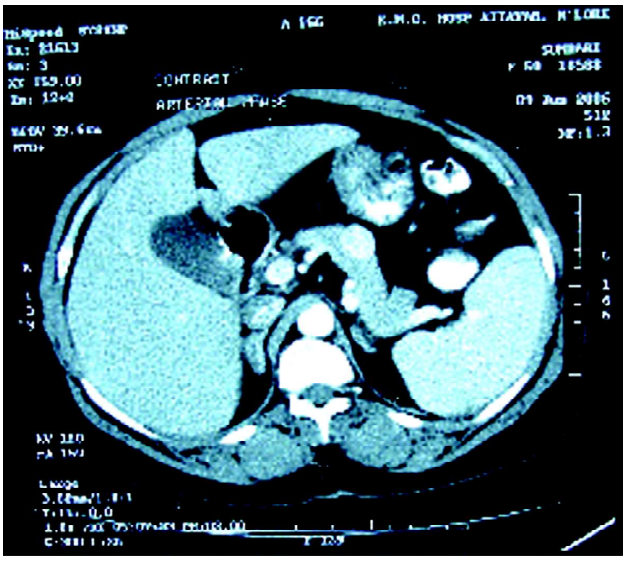

Fig. 2b: *Contrast-enhanced CT of abdomen showing enhancement of the lesion during arterial phase.*

Discussion

Hypoglycaemia is a common medical emergency. Among hospitalised patients, it is most common in those with

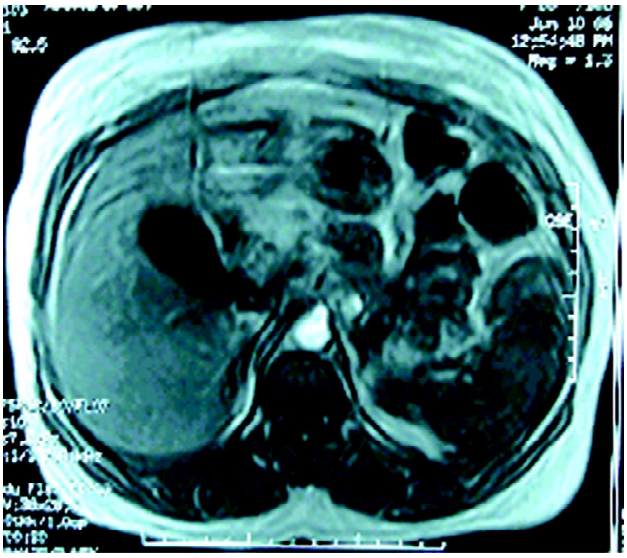

Fig. 3a: *Axial, T1-weighted fat sat MR image shows a hypointense area at the junction of the body and tail of the pancreas.*

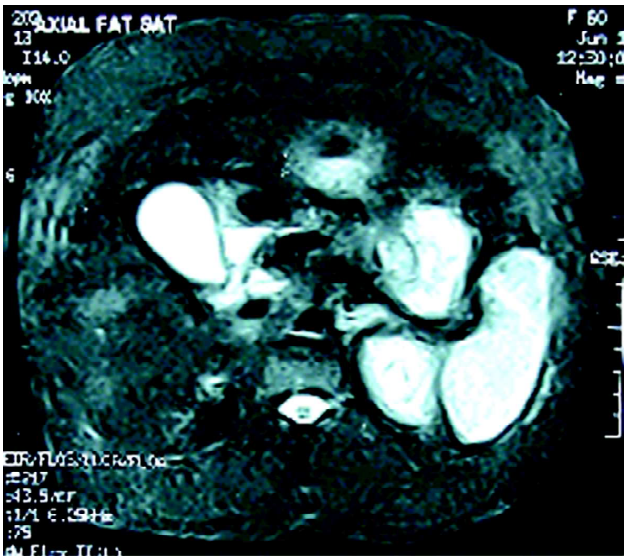

Fig. 3b: *Axial SPGR MR image shows hyperintensity of the same lesion.*

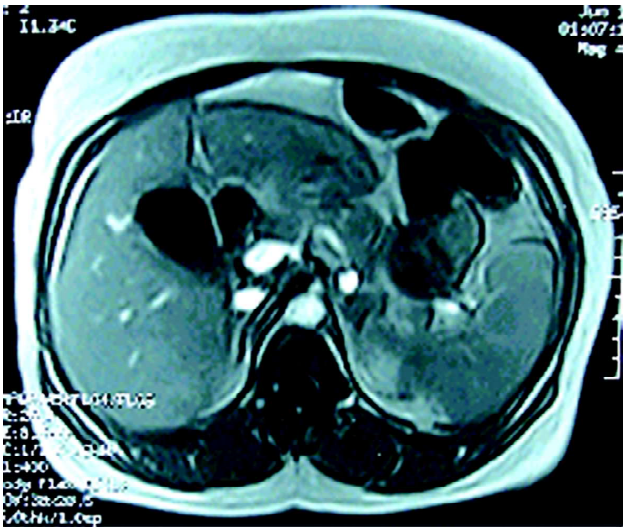

Fig. 3c: *Axial GRE post-contrast image showing hyperintensity of the lesion.*

diabetes, but also occurs in patients with renal insufficiency, liver disease, malnutrition, congestive heart failure, sepsis, or cancer[4]. Diabetes on treatment with insulin is an important cause of hypoglycaemia among ambulatory groups. Factitious or surreptitious use of insulin or sulphonylurea drugs is probably the most common cause of hypoglycaemia among patients who do not have diabetes[5].

Occasionally, hypoglycaemia can be induced by endocrine tumours, including pancreatic tumours that secrete insulin and non-islet-cell tumours that secrete insulin-like growth factors.

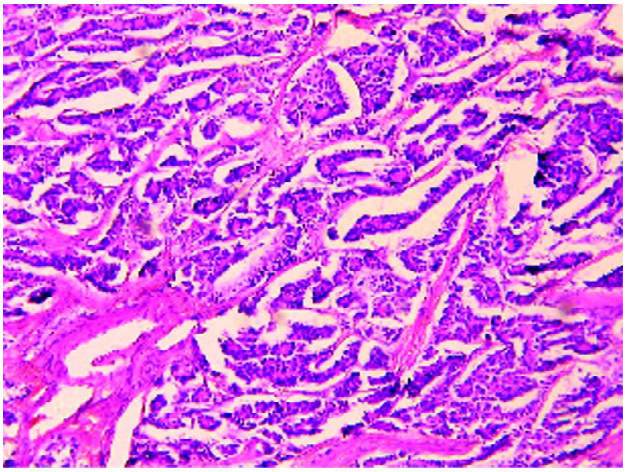

Fig. 4: *Microscopic features of the insulinoma: tumour cells arranged in ribbon-like trabeculae, and acinar pattern in the background of pink homogeneous amyloid.*

Symptoms of hypoglycaemia include both neurogenic symptoms from adrenergic stimulation and neuroglycopenic symptoms as a direct result of a decrease in brain substrate (Table I)[1].

Table I: Signs and symptoms of hypoglycaemia[1].

Neurogenic-mediated	Neuroglycopenic-mediated
Diaphoresis	Warmth
Hunger	Weakness
Tingling sensations/paraesthesia	Difficulty in thinking/confusion
Shaking/tremulousness	Tiredness/drowsiness
Palpitations/tachycardia	Faintness/dizziness
Nervousness/anxiety	Difficulty in speaking
	Blurred vision
	Stupor/coma

The diagnosis of insulinoma is suggested by hyperinsulinaemia in the presence of hypoglycaemia and reversal of the symptoms by administration of glucose (Whipple's triad). Our patient displayed several characteristics typical for insulinoma. She had a 7-year history of symptoms similar to the presenting symptoms to emergency department.

In patients with insulinoma, there is continued secretion of insulin despite a lower glucose level. Insulin is synthesised as a single-chain precursor proinsulin – which is cleaved into a peptide and insulin, both of which are secreted in equimolar concentrations. Diagnostic criteria for insulinoma include a serum insulin concentration of more than 6 microU/ml, a detectable concentration of serum C peptide, and a high proinsulin concentration, concomitant with symptoms of hypoglycaemia and blood glucose concentration of less than 45 mg per deciliter during fasting[5]. Hypoglycaemia induced by sulphonylurea may have an identical presentation like an insulinoma; a negative screening for sulphonylurea is required to confirm the diagnosis.

Once a clinical and biochemical diagnosis is established, the imaging modalities are used for localisation of tumour. Transabdominal ultrasound sometimes reveals a mass in the region of pancreas. Endoscopic ultrasound has been found to be more selective, detecting solitary insulinomas in 80% of surgically proven cases; the sensitivity drops below 40 – 60% with tumour in the tail

of the pancreas[6]. Expertly performed intraoperative ultrasonography assists in tumour localisation and in delineating important related anatomy. Intraoperative palpation and ultrasound are the gold standard for localising an insulinoma with a reported success rate of 96 – 100%[3].

Dual-phase contrast spiral CT scan is more sensitive than other non-invasive imaging studies; six of seven biochemically proven tumours ranging from 6 – 18 mm were detected by dual-phase spiral CT scan. Insulinomas appear as well-circumscribed hypointense foci on fat saturation T1-weighted images and markedly hyperintense on STIR images. The markedly uniform enhancement in the arterial phase of gadolinium chelate injection helps to identify the lesion. MRI is said to be superior to CT for localisation of insulinoma. However, in our study, CT images are superior than MRI images. Standard localisation procedures including CT, ultrasound, and MRI may be negative due to small size of these lesions[1]. Insulinoma tumour cells contain less insulin and secretary granules than normal B cells, but have higher levels of proinsulin. Typical granules or even agranular cells are frequent in histology pictures.

Intra-arterial calcium stimulation with pancreatic venous sampling has recently emerged as a very sensitive and specific localisation procedure[1]. Because of the highly vascular nature of these tumours, angiography has been used successfully. It has been observed that insulin is released from insulinomas but not from normal pancreatic islets upon stimulation with calcium. Serum insulin level has been found to increase abruptly two-to-seven-fold when calcium is infused into the artery supplying the insulinoma; whereas the injection into an artery not supplying the tumour has resulted in no increase in insulin[1].

Insulinomas are usually benign and relatively small (< 2 cm) solitary tumours; however, 5.8 to 15% of the tumours are malignant. Studies have shown that the diagnosis of an insulinoma is often delayed despite the improvement of laboratory and diagnostic techniques. The interval from the onset of symptoms to diagnosis ranges from one month to 30 years (median = 24 months)[1,7]. Our patient was diagnosed after 7 years of onset of symptoms.

Insulinoma is the most common type of tumour causing hypoglycaemia inspite of being a rare clinical entity. About 90% of insulinomas are benign, and it is important to remove this tumour surgically as it can cause potentially lethal hypoglycaemia[8].

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CASE REPORT

JIACM 2008; 9(1) : 57-60

Atypical Manifestation of Sacral Tuberculosis as Cauda-conus Syndrome

VPS Punia, Satish Kumar***

Abstract

Tuberculosis is a major health problem in India and globally. Skeletal tuberculosis though common, involves the sacrum very rarely. Our case presented with gluteal pain, weakness of lower limbs and urinary retention. MRI spine revealed a sacral lesion. This case report intends to emphasise that sacral tuberculosis, being itself rare, may present atypically as cauda-conus syndrome and chemotherapy may be required for 12 to 15 months and not merely for 6 months.

Key words: Cauda-conus syndrome, Sacral tuberculosis, Anti-tuberculous therapy.

Introduction

Skeletal tuberculosis accounts for about 10 per cent of extra-pulmonary tuberculosis, and roughly half of them are in the vertebral column[2]. Thoraco-lumbar region is the most common site for spinal tuberculosis. Lumbo-sacral tuberculosis accounts for only 2 to 3% of all cases of spinal tuberculosis[1, 2]. In our knowledge, only a few cases of sacral tuberculosis have been reported. We present here a case of spinal tuberculosis with isolated involvement of sacrum with atypical clinical presentation.

Case report

A 21-year-old female presented with acute onset of pain in both gluteal regions of a duration of 4 days; it was severe in intensity and was aggravated by movements and change in posture with radiation to postero-lateral aspect of the thigh, calf, and upto heel bilaterally. It was associated with retention of urine on next day followed by weakness of both lower limbs – the left being weaker than the right. Their was no h/o weakness of upper limbs, dysphagia, dysphonia, visual loss, headache, vomiting, convulsion, facial weakness, or any abnormal movement. There was history of low grade fever, malaise, and significant weight loss in the last 2 months. Around two months prior to this episode, the patient had a cervical abscess resulting in a sinus with overlying scar tissue.

On clinical examination, our patient was of average build with pallor and a scar over the anterior neck with serous discharge and cervical lymphadenopathy. Respiratory, cardiovascular, and abdominal system examination was normal. Neurological examination revealed that findings were localised to the lower limbs. Bulk and tone was normal in both lower limbs. In the left lower limb, power was 3/5 grade around hip joint and ankle joint, while it was 4/5 grade around the knee joints. In right lower limb power was 4/5 grade around hip, knee, and ankle joint. Knee jerk was normal while ankle jerk was absent bilaterally. Superficial abdominal reflexes were present. Plantar reflex was absent bilaterally. Pain and temperature sensation was impaired in the L5 – S1 distribution in both lower limbs. Perianal and perineal anaesthesia was present. Urinary bladder was full and distended for which patient was catheterised. No gibbus or kyphosis was found on examination of the spine. Straight-leg raising (SLR) test was positive.

On investigation, haemoglobin was 8.7 gm/dl, ESR – 60 mm/1 hour; other biochemical parameters were normal. HIV I and II ELISA was negative. Mauntoux test was positive with an induration of 20 x 15 mm. Histopathologic examination of cervical lymph node and sinus was suggestive of tuberculous pathology. Culture and sensitivity of pus from cervical sinus did not yield acid-fast bacilli. X-ray of lumbo-sacral spine lateral and AP views and X-ray chest PA view were normal. Magnetic resonance imaging (MRI) of lumbo-sacral spine revealed osseous destruction and signal alteration involving left sacral ala and left half of S2 – S4 spine. There was associated prevertebral collection from S1 – S3 level and large posterior epidural collection tracking from D12 – S2 level

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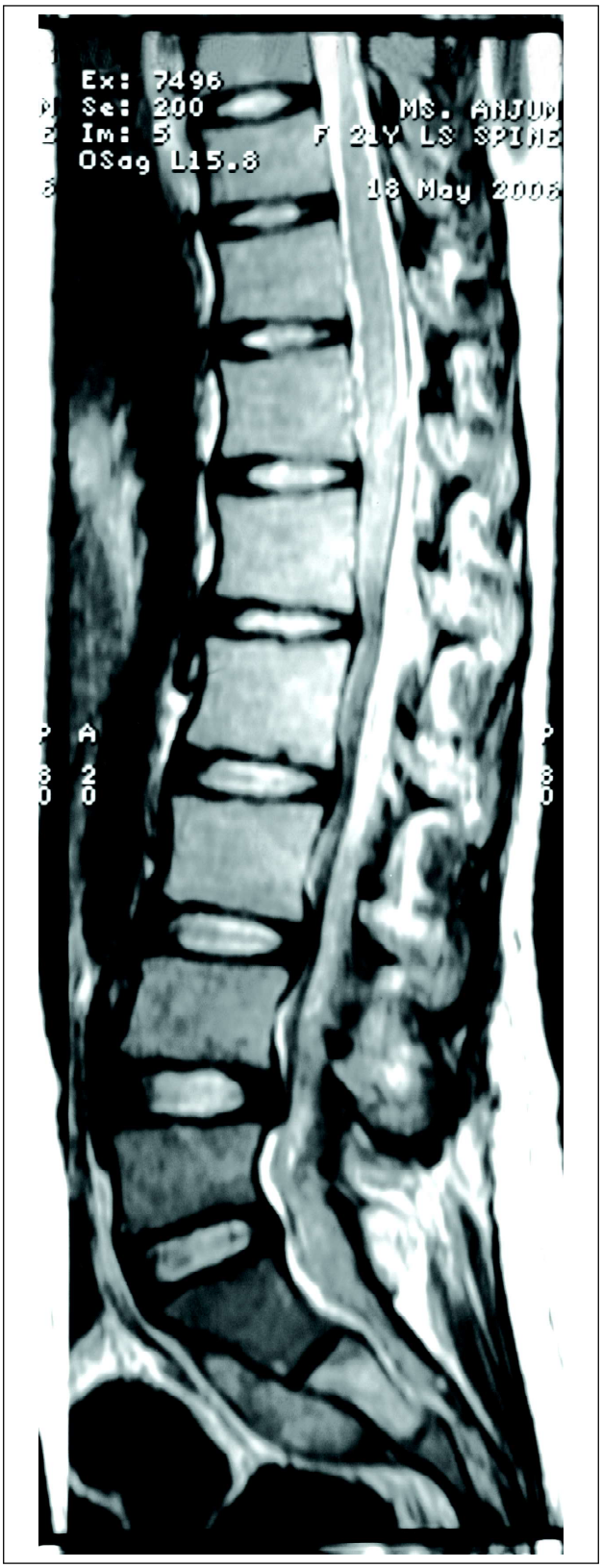

Fig. 1: *MRI of lumbo-sacral spine showing sacral lesion with pre-vertebral and posterior epidural collection.*

causing conus compression. The patient developed bed-sores and hence biopsy material was not taken from sacral lesions.

On the basis of history, clinical examination and detailed investigations, a diagnosis of Pott's disease of the spine with tuberculous lymphadenitis of neck was made. Anti-tuberculous therapy (ATT) was started and continued for one year with regular monthly follow-up.

The patient improved with complete resolution of cervical lymphadenopathy with sinus and improvement in power of both lower limbs upto grade 5/5. Sensory impairment and urinary retention persisted. MRI of lumbo-sacral spine was repeated which showed complete resolution of prevertebral and epidural collections. Sacral lesions had not cleared completely. The patient was prescribed ATT for 6 more months with concomitant physiotherapy and regular follow-up.

Discussion and review of literature

Tuberculosis is a major health problem in India and globally. Tuberculosis of the spine occurs by the hematogenous spread of infection from pulmonary or extra-pulmonary sites. Pulmonary infection is detected in around 50% of cases of spinal tuberculosis[1]. After reaching the vertebrae, *M. tuberculosis* affects anterior portion of the body near intervertebral disc. It may reach cortex, destroy the

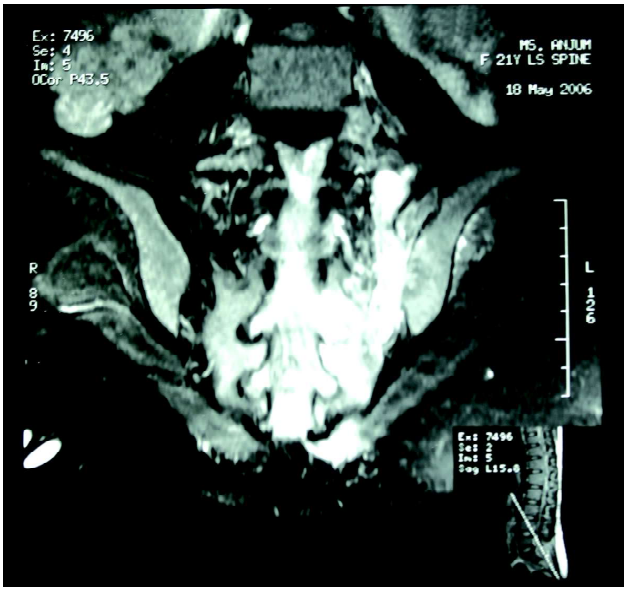

Fig. 2: *MRI of sacrum showing signal alteration in left sacrum.*

intervertebral disc, and fragment the adjacent vertebral body[2]. Sacrum is a rare site for tuberculosis. With the rise in the number of AIDS patients and emergence of multi-drug resistant tuberculosis, tuberculosis should be considered as one of the possibilities in lesions present in odd areas of the human body[1].

The first case of sacral tuberculosis described in medical literature was reported by Campbell in 1917. Out of his 19 patients of spinal tuberculosis, 12 had dorsal lesion, 3 lumbar, 1 cervical, and 1 sacral. His patient was a 3-year-old boy who had tubercular lesions in lower lumbar region and sacrum[3]. In 1998, Rajshekaran reported a 15-year follow-up of 53 patients. Of these only 12 had spread disease inferiorly to lumbosacral junction[4]. Pun reported 20-year follow-up of 26 patients of tuberculosis of lumbo-sacral junction. In majority of patients, the disease had started in lumbar spine and descended to the sacrum[5]. In 1985, Dayras reported a case of isolated sacral tuberculosis with lower back pain. In 2004, Wellons reported a case of sacral tuberculosis with lower back pain and difficulty in walking[1]. Our case presented with features of acute cauda-conus syndrome. A case of sacral tuberculosis presenting with acute cauda-conus syndrome is not only atypical, it can cause difficulty and delay in making a diagnosis. Thus, it was a rare and interesting case to be reported in medical literature. In such cases with atypical presentations, detailed history of the illness can provide useful clues for reaching a diagnosis. In our case the patient gave the history of cervical abscess which was followed by scar formation. This provided a very important clue. Histopathology of cervical lymph node and scar confirmed the tubercular aetiology. MRI scan of spine revealed the lesion to be situated in sacrum only. Regarding treatment of spinal tuberculosis we found different opinions in literature. Many workers prescribe chemotherapy for 6 months while some continue it for 9 to12 months[1, 2, 6]. In our patient, the sacral lesions did not heal completely after one year of therapy so we decided to continue rifampicin (450 mg/d) and isoniazid (300 mg/d) till 15 months with regular follow-up.

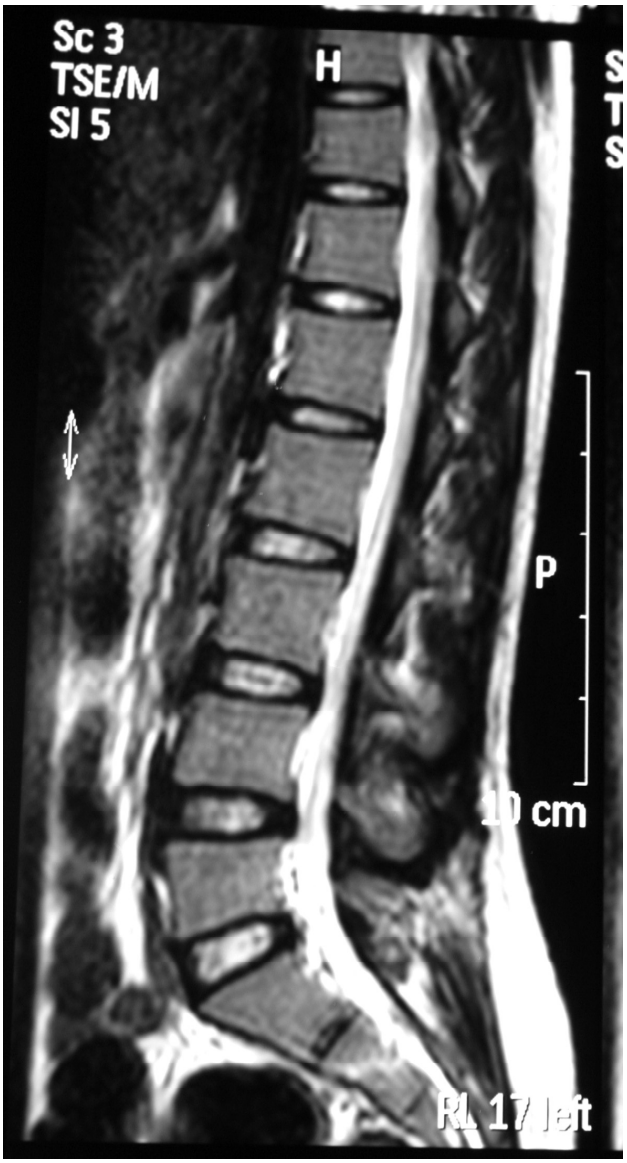

Fig. 3: *MRI showing complete resolution after 12 months of chemotherapy.*

Conclusion

In the evaluation of patients of cauda-conus syndrome, the possibility of sacral tuberculosis should be kept in mind. Treatment of spinal tuberculosis for 6 months may not be enough and continuation of therapy for 12 to 15 months should be considered.

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Lloyd's Test

A black and bearded man named Lloyd
had found a single haemorrhoid
protruding, as they do quite often,
when certain foods that tend to soften
are present with their fibrous mass
down at the gate that some call ass.

Lloyd would, as he had once been shown,
detect when it again had grown
to take up space and he could feel,
akin to a varicocoele,
a blossom fastened by its stem
perhaps a terminus ad quem?

Most mornings Lloyd would take his phone
and sit, with patience, on the throne.
When things fell out he'd raise his voice
to overcome the vulgar noise.

Since action in the bowels vary
from Tom to Dick and Tim and Harry,
one cannot say with certainty
how long a man like Lloyd would be,
and it is true that Lloyd himself
kept novels on his toilet shelf.

Thus if he could not reach his friends
by phone he'd delve into suspense
inside a book, (his legs went numb),
soon it was time to wipe his bum.

Each time, the paper would be crimson
which made him talk like Homer Simpson.
His haemorrhoid would bleed and bleed
sometimes it scared the man, indeed.

Doc Johnson had assured him though
that piles are fine, if you can go
without assistance of some kind.
Stop fretting over your behind.

So Lloyd, who was a college proctor,
did trust implicitly his doctor,
the doc had said that he, as well
had piles that could, 'believe me', swell
and it was just a minor flaw
shared by the doctor's son-in-law.

For twenty-seven happy years
Lloyd did suppress his innate fears,
but then, one day he felt quite faint
so he went home to see his Saint
inside the chapel, and he prayed
his nerves a mess and truly frayed.

The Saint just hung there, on the wall
and nodded slightly, if at all.
But Lloyd had understood the sign,
he opened up a flask of wine
and drank until the morning's dew
because inside he really knew.

They buried Lloyd in early Spring
when squirrels smile and robins sing.
The doc was negligent, you see,
to skip the colonoscopy.

– Dr. Herbert Nehrlich.
(Queensland, Australia)

CASE REPORT

JIACM 2008; 9(1): 61-3

Cardiac Tamponade – A Rare Aetiology

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Abstract

The incidence of pyogenic liver abscess has remained relatively constant during this century despite early diagnosis and treatment of underlying causes and more aggressive antibiotic therapy. Early diagnosis and prompt therapy are essential for reducing the morbidity and mortality associated with a pyogenic hepatic abscess. Reports of complications with pyogenic abscess are rare. Rupture of a liver abscess in the pericardial cavity is seen rarely and that to in association with the Entamoeba histolytica infection; pyogenic abscess rupture in such a way is very rarely reported in the English literature. It is a lethal complication with a very high mortality rate. Here, we report a case of a 53-year-old male with a pyogenic liver abscess (Staphylococcus aureus) with rupture into pericardium and cardiac tamponade, who was successfully managed by medical and surgical interventions.

Key words: Pyogenic liver abscess, Pericardial rupture, Cardiac tamponade.

Introduction

The term hepatic abscess refers to an infection and a resultant localised pus collection coinciding with the destruction of the hepatic parenchyma[1]. Liver abscess has been recognised since the time of Hippocrates. With the availability of antibiotics, McFadzean and associates in Hong Kong advocated closed aspiration and antibiotic drugs for the treatment of solitary pyogenic liver abscess in 1953[2]. Early diagnosis and prompt treatment are essential for reducing the morbidity and mortality associated with a pyogenic hepatic abscess as it extends outside the confines of the liver parenchyma.

Case history

A 53-years-old male was admitted with complaints of pain in the upper abdomen and fever for the last 2 months. This patient was apparently well 2 months back when he had fever which was low-to-moderate grade and had pain in the upper abdomen which was non-colicky and not associated with vomiting or altered bowel habits. 2 months back he was treated on OPD basis, elsewhere. Investigations done had shown mild leucocytosis, normal liver function tests. Ultrasound abdomen was suggestive of left lobe liver abscess. He was prescribed ofloxacin 200 mg twice daily and metronidazole 400 mg thrice daily. Subsequently, the amoebic serology was negative and the family physician advised him to continue ofloxacin for 10 days. Patient was non-alcoholic and did not have any major illness in the past.

Examination

Patient was toxic, febrile, had tachycardia but no icterus. Per abdomen examination revealed tender hepatomegaly. Systemic examination of chest and CVS was unremarkable.

Investigations

On arrival, investigations revealed Haemoglobin 10.9 gm%, TLC – 20,900/cumm, DLC – P85%, L15%, BUN – 18.5 mg%, Cr. – 1.1 mg%, S. bilirubin – 0.6/0.2 mg%, SGOT – 22 IU/l, SGPT– 17 IU/l, SAP – 340 IU/l. Amoebic serology was negative. CT guided aspiration was done and fluid culture grew *Staphylococcus aureus*. Blood culture was sterile. CT abdomen done revealed a large abscess in the left lobe with rupture in the pericardial space with large pericardial effusion, bilateral pleural effusion with subsegmental collapse of the right middle lung. There was no other focus of infection in the abdomen. Echocardiography was done which showed large pericardial effusion with diastolic dysfunction, ejection fraction of 65% and evidence of early cardiac tamponade on doppler study. Repeat amoebic serology was also negative.

Management

The patient was administered injection ticarcillin/clavulanic acid 3.2 gm IV 8 hourly. By 4th day fever and pain in upper abdomen improved. On 5th day the patient became breathless and repeat echocardiography showed early diastolic collapse of the right ventricular free wall, late diastolic compression/collapse of the right atrium alongwith

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swinging of the heart in its sac (all of which were suggestive of cardiac tamponade), and ejection fraction of 45%. Patient had *pulsus paradoxsus* with a BP of 90/60 mmHg. As the patient developed severe left ventricular failure and was dyspnoeic, an urgent sub-xiphoid pericardiocentesis was done. Pericardial fluid was serous and was sterile. Repeat blood culture was also sterile. The antibiotic was continued for 2 weeks and later the patient was given 2 weeks of amoxycillin and clavulanic acid.

Further course

A repeat CT scan done after 4 weeks showed a large loculated pericardial effusion anteriorly 2.7 cm, laterally 2.4

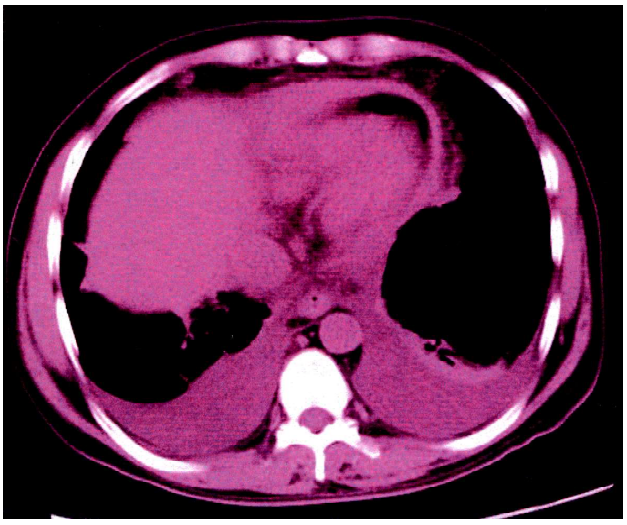

Fig. 1: *Coronal reformatted section reveals a left lobe liver abscess with pericardial effusion and pericardial thickening.*

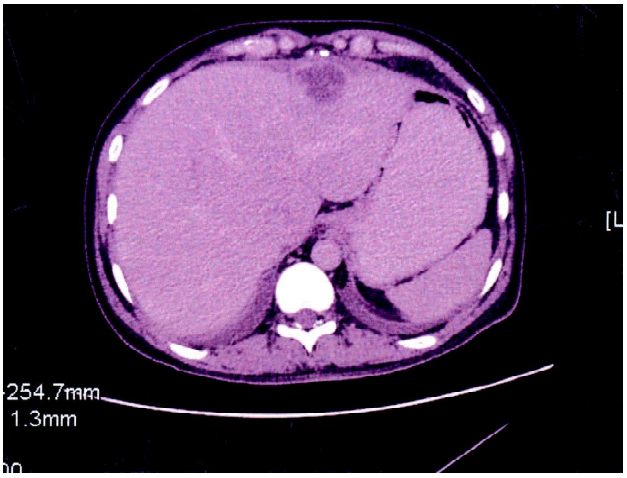

Fig. 2: *Axial CT scan through the level of liver reveals a thick-walled abscess in relation to the left lobe of liver.*

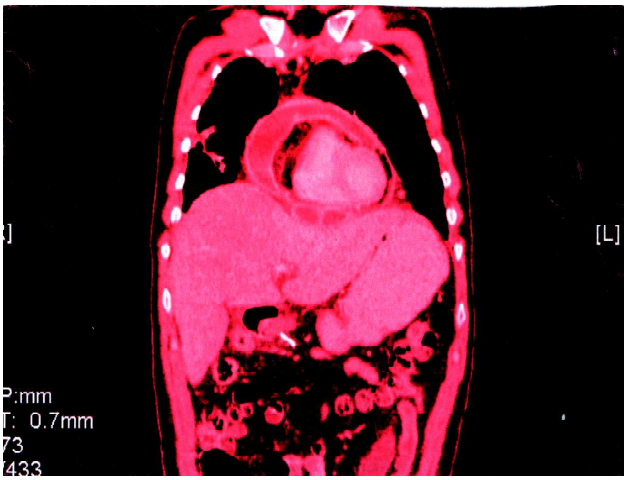

Fig. 3: *Axial section taken through the level of the heart reveals bilateral pleural effusion and pericardial effusion.*

cm, thickened visceral and parietal pericardium. Echocardiography showed normal valves with LVEF of 60%, respiratory variation in trans-mitral and trans-tricuspid flow. In view of effuso-constrictive pericarditis, the patient underwent pericardiectomy. The histology of pericardium showed non-specific inflammation. Post-operatively, echocardiography done showed normal LV function, LVEF 66%, no regional wall motion abnormality, no evidence of constrictive pericarditis or tamponade.

Discussion

The most common organisms causing pyogenic hepatic abscesses are *Escherichia coli*, *Klebsiella*, *Streptococci milleri* and enterococci[2]. In an amoebic hepatic abscess, various complications have been described and the rates of complications have been reported to be 10.3%[3]. Reports of complications in pyogenic hepatic abscess are rare. The various complications associated with pyogenic hepatic abscesses are:

Table I: Complications of pyogenic liver abscess[1].

Complications	No. of cases (n = 21)
Pleuro-pulmonary complications	11 (8.6%)
Rupture into the peritoneal cavity	3 (3.7%)
Vascular complications	3 (3.7%)
Rupture into the pericardial cavity	1 (1.2%)
Rupture into the gastrointestinal tract	1 (1.2%)
Rupture into the retroperitoneum	1 (1.2%)
Rupture into the bile ducts	1 (1.2%)

There is extensive world literature on amoebic liver

abscesses and their complications, but there are only anecdotal reports of complicated pyogenic liver abscess – especially with pericardial rupture – in the English literature. Among the various complications of a hepatic abscess, rupture into the pericardial cavity is quite rare. Whatever literature is available on liver abscess and pericardial rupture is mostly reported with amoebic abscesses. Nevertheless, it is a highly lethal complication with a mortality rate of 60 – 90%[3]. It is usually seen in cases where there is left lobe abscess, as it may rupture into the pericardial cavity through the tendinous portion of the diaphragm. Because of its high mortality, early diagnosis and aggressive medical and surgical treatment are needed. CT scan is an ideal tool for diagnosing hepatic abscesses, and the sensitivity of CT is as high as 97%[4]. On CT, the appearance of a hepatic abscess in continuity with pericardial cavity and increased density of pericardial fluid may be useful in making the diagnosis[3]. Ultrasonography is less sensitive than CT, but is still the first line investigation despite being observer dependent and having limitations due to technical factors[5]. Pericardiocentesis is useful as a diagnostic and initial therapeutic tool. A cardiac tamponade may develop as a result of the accumulation of the contrast material in the pericardial cavity flowing into the hepatic abscess during percutaneous abscess drainage[1]. Treatment for a liver abscess with rupture into the pericardial cavity involves medical and surgical intervention. It involves antibiotics, pericardiocentesis, and pigtail catheter drainage[6]. Aspiration of the accumulated fluid should be performed urgently in cardiac tamponade; repeated aspiration may be needed. Surgical drainage should be done if needed. Emergency pericardiectomy may be required in cardiac tamponade as was done in our patient[7].

Conclusion

Pyogenic liver abscesses are rare in the tropics. With liver abscesses in the left lobe of liver there is a potential risk of rupture into the pericardial cavity and very rarely they may present as cardiac tamponade – a life-threatening complication. Therefore, awareness about this complication and the ability to diagnose and manage this condition by both medical and surgical interventions is essential.

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CASE REPORT

JIACM 2008; 9(1): 64-5

Cerebellar Ataxia – An Uncommon Manifestation of Enteric Fever

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Abstract

Enteric fever is a very common clinical problem dealt with in the day-to-day practice and represents a wide spectrum of acute febrile illness with systemic manifestations. Neurological manifestation is an important, but often underdiagnosed entity of this spectrum. Cerebellar involvement in enteric fever is further uncommon. Here we present one such case of 'the very common' enteric fever that presented with the most uncommon manifestation: cerebellar signs including hypotonia, ataxia, wide gait, dysarthria and impaired coordination, and who recovered gradually over a period of 2 months.

Key words: Hypotonia, Ataxia, Dysarthria.

Case report

A 50-year-old male patient presented with complaints of high grade, intermittent fever for 5 days, alongwith dry cough. Also, he had unsteadiness while walking, and difficulty in speech, which started 1 day prior to presentation. There were no other significant presenting complaints and no history of major medical illness.

On general examination, the patient had a toxic look, with temperature of 102° F, pulse rate of 110/min and BP of 120/74 mmHg. On examination of the CNS, the patient was confused and irritable. His speech was slurred. Cranial nerves and sensory system were normal on examination. He had gross hypotonia in all four limbs, with nearly normal power, and marked ataxia, including truncal ataxia and titubation. Coordination was affected on both sides, with presence of dysmetria, dysdiadokokinesia, and impaired knee-heel test. Pendular knee jerks were elicited bilaterally. On checking for Rhomberg's sign, the patient was unable to stand with his feet together; even with eyes open he had the tendency to sway on all sides. He had a wide-based gait, and tandem walking was not possible. There was no nystagmus.

On investigating the patient, his routine investigations including haemogram, ESR, peripheral smear, urinalysis, and serum biochemistry (RBS, urea, creatinine, and LFT) did not reveal any significant abnormality. Peripheral blood smears checked for malarial parasites were negative. Blood cultures were sent in glucose and taurocholate broths and serum Widal test was performed which was negative. Chest X-ray was normal. MRI of brain done to look into the cause of cerebellar signs also turned out to be normal. Blood culture and sensitivity reports were obtained after 5 days and showed isolation of *Salmonella typhi*, sensitive to ceftriaxone. During the second week of admission, the serum Widal test was repeated and it showed high titres (*S. typhi*: 'O' 1:320, 'H' 1:160). He was now diagnosed to have enteric fever with cerebellar involvement.

After isolation of *S.typhi* on blood culture, the patient was put on ceftriaxone 2g q12h till he became afebrile, and then 1g q12h for another 4 days. The majority of cerebellar signs improved over a period of 2 weeks of hospital stay, but ataxia and dysarthria persisted for 6 weeks. During follow-up, marked improvement was noted in that too.

Discussion

Enteric fever is one of the commonest infections seen in our clinical practice. Neuropsychiatric manifestations are encountered in 10 – 40 % of cases[1]. CNS manifestations secondary to 'enteric encephalopathy' is a well – established entity, with a steady increase in neuropsychiatric complications recorded in the last few years; in some patients these neuropsychiatric symptoms dominate the clinical picture[2]. These manifestations include: confusion, delirium, semi-coma, coma, meningism, mutism, dysarthria, acute toxic psychosis, Parkinsonian rigidity, hemiplegia, cerebellar ataxia, myopathy, generalised myoclonus,

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catatonic schizophrenia, polyneuropathy, hypomania, encephalomyelitis, GB syndrome and transverse myelitis[2].

However, apart from ataxia, presence of other cerebellar signs in our patient – like hypotonia and cerebellar dysarthria – are rare with enteric fever.

In the past 15 – 20 years, reports from India, Nigeria, Indonesia, and other Asian countries have documented a wide spectrum of neurological complications in cases of enteric fever[3]. Why these neuropsychiatric manifestations occur, is still not clear. The exact pathogenesis of these complications is also not known. Certain possible and logical mechanisms are hypothesised to explain these complications, e.g., metabolic disturbances, hyperpyrexia, dehydration and electrolyte imbalance, toxaemia and non-specific cerebral changes in the form of oedema and haemorrhage[4]. A cascade of various pathological processes in the cerebrum leads to an acute diffuse encephalomyelitis, causing enteric fever encephalopathy[5]. Other workers have found that toxaemia is the earliest and commonest neurological complication in enteric fever, but is often under-diagnosed. It can be considered to be an acute brain syndrome, associated with the height of pyrexia and clears quickly after initiating therapy[6].

Cerebellar ataxia may develop in isolation or with other manifestations. Wadia *et al* in 1985 described 28 cases of enteric fever with cerebellar ataxia with 25% incidence in the 1st week and 60% incidence in the 2nd week[7]. Other workers found an incidence of 19 – 44% with a mean onset of 14.8 days (7 – 29) for cerebellar ataxia[8].

CT and MRI studies in these cases will be, by and large, normal – indicating that there is no gross structural damage, and also suggesting the reversible nature of these neurological events. Only medical management with antibiotics, preferably after testing for microbial sensitivity will help to alleviate the neurological complications. Subjective and objective recovery from CNS involvement may be delayed for 6 – 8 weeks, as in this case, for which we found no suitable explanation ; but the recovery is usually complete, with no residual effect.

Thus, in conclusion, it would be worth remembering that one should look for these unusual presentations in enteric fever and more importantly, when investigating a case of cerebellar ataxia with fever, it would be worthwhile to remember that enteric fever forms an important and curable differential diagnosis.

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CASE REPORT

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Rupture of the Sinus of Valsalva to the Right Ventricle

*S Dwivedi *, S Rajpal**, MP Agarwal***, A Aggarwal****, S Khanna******

Abstract

A continuous murmur over left upper chest has many differentials like patent ductus arteriosus, ruptured sinus of Valsalva, aortopulmonary window, coronary AV fistula. The diagnosis has been made simpler since the advent of transthoracic echocardiography and transoesophageal echocardiography. We herewith report a case of ruptured sinus of Valsalva into the right ventricle.

Keywords: RSOV, Echocardiography, Continuous murmur.

Introduction

The differential diagnosis of a continuous to-and flow murmur over left upper chest includes patent ductus arteriosus (PDA), ruptured sinus of Valsalva, coronary arteriovenous (AV) fistula, aortopulmonary window, anomalous origin of left coronary artery from pulmonary trunk. Role of echocardiography has immense diagnostic value in making a correct diagnosis. Many of these conditions can be cured if appropriate and timely surgical intervention is done at an early stage. We herewith report a case of ruptured sinus of Valsalva into right ventricle which was diagnosed by echocardiography.

Case report

A 40-year-old male presented with history of progressively increasing dyspnoea on exertion since the past 3 years. He had low grade fever and two episodes of haemoptysis 6 months ago. He developed a progressively increasing swelling over both lower limbs and abdomen for past 3 months. He denied any history of orthopnoea, joint pains, recurrent chest infections, or cyanotic spells in the past. He was not a known case of diabetes, hypertension, or coronary artery disease. He had been operated for testicular injury 1 year back. Physical examination revealed bilateral pedal oedema, raised jugular venous pressure, pulsatile hepatomegaly and ascites. There was tachycardia with bounding pulse. Blood pressure was 130/50 mmHg in both upper limbs, and 212/70 in both lower limbs (Hill's sign was positive). Pistol shot sounds over femoral artery were present (Traube's sign). Head nodding with pulse was present (de Musset's sign) and dancing carotids were also present (Corrigans sign). Apex beat was palpable in the left 5th intercostal space 1 cm lateral to mid- clavicular line with grade II parasternal heave. A continuous thrill was palpable in the left 3rd intercostal space. Cardiac auscultation revealed a continuous murmur maximally heard over the left 2nd and 3rd intercostal spaces. A pansystolic murmur was heard over the tricuspid area increasing on inspiration. A clinical diagnosis of PDA with tricuspid regurgitation (TR) was kept. However, differential diagnosis of ruptured sinus of Valsalva, coronary AV fistula, aortopulmonary window, and anomalous origin of left coronary artery from pulmonary trunk were also entertained.

Routine investigations revealed Hb = 13.6 gm/dl, TLC = 7,300/cumm, ESR = 10 mm at end of 1st hour. BU = 51 mg/dl, S. creat = 1.4 mg/dl, urine examination was normal, chest X-ray demonstrated marked cardiomegaly. Transthoracic echo revealed ruptured sinus of Valsalva having fistulous tract with right ventricle (Fig.1) with severe aortic regurgitation and moderate TR with moderate left ventricular dysfunction. Colour doppler revealed a continuous flow from ruptured right coronary sinus into right ventricle (Fig. 2). There was no evidence of vegetations. ECG revealed right atrial enlargement with left ventricular enlargement with a diastolic overload pattern. Repeated blood cultures were sterile. Ultrasound abdomen revealed moderate ascites with hepatomegaly and prominent intrahepatic veins. Fundus examination was normal.

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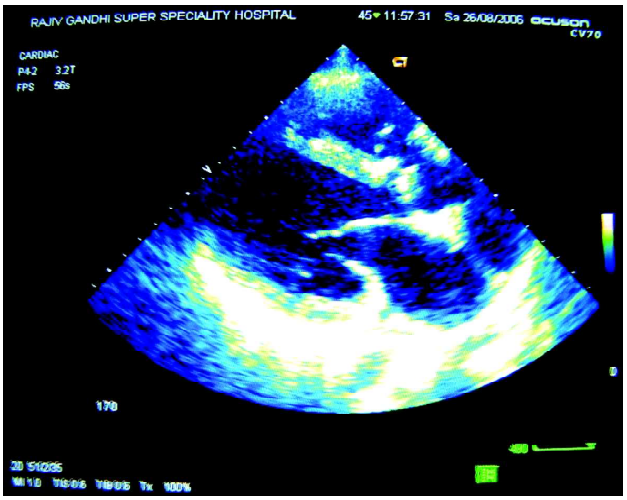

Fig. 1: *Echocardiogram showing the calcified aortic valve and rupture of sinus of Valsalva.*

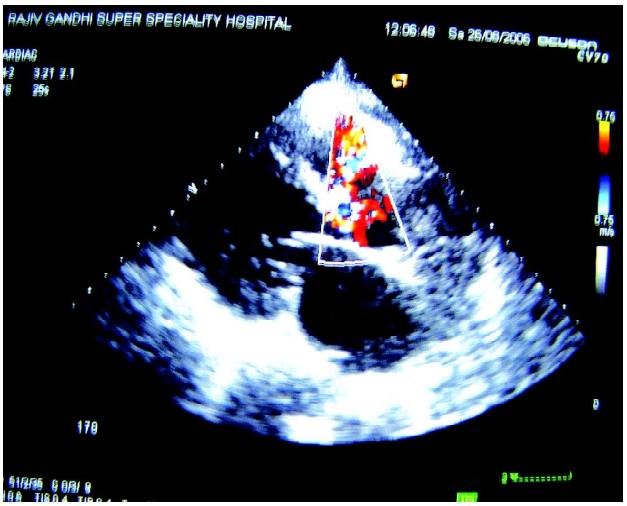

Fig. 2: *Echocardiogram showing the flow of blood from ruptured sinus of Valsalva into the right ventricle.*

Discussion

Aneurysm of sinus of Valsalva in this case appears to be congenital in nature manifesting at this age of 40 years. Embryological basis of this defect is congenital failure of fusion of aortic media with fibrous skeleton of heart through which a sinus of Valsalva aneurysm may develop. This defect typically begins as a blind diverticulum that takes origin from a localised site on one of the coronary sinuses. Substantial majority of ruptures develop after puberty but before 30 years of age. Aneurysm of right coronary sinus is most frequent and ruptures into right ventricular outflow tract. Non-coronary sinus ruptures into the right atrium and left coronary sinus into the pericardial space beneath left coronary artery. Aneurysm of right coronary sinus may produce undermining of aortic valve and may cause incompetence of valve as is present in this case. Some cases may have associated ventricular septal defect. Heart blocks and conduction abnormalities may occur due to protrusion of aneurysm into the interventricular septum[1]. While in most cases illness is known to proceed quickly to decompensated failure, there are few reports of prolonged survival[2]. These lesions may be complicated by infective endocarditis and can be recognised early with transthoracic echocardiography and transoesophageal echocardiography[3]. This defect can be tackled successfully by timely surgical interevention[4]. Thus the importance of early echocardiographic diagnosis of RSOV cannot be overemphasised.

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