CASE REPORT

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Disseminated Brucellosis: A Diagnostic Enigma

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Abstract

Brucellosis is a zoonotic infection caused by gram negative bacillus of the Brucella genus. Brucellosis is transmitted through cuts and abrasions or inhalation of aerosols, or by ingestion of unpasteurised milk or milk products. Osteoarticular involvement is the most frequent complication of brucellosis. Neurobrucellosis may develop at any stage of the disease and may have widely variable manifestations. A patient with disseminated Brucellosis with subgaleal abscess involving occipital bone, neck cellulitis, meningoencephalitis and lumbar spinal discitis has been reported here.

Key words: Brucella, occipital bone abscess, cellulitis, meningoencephalitis, spinal discitis.

Introduction

Brucellosis also known as undulant fever, Mediterranean fever, or Malta fever is a zoonotic infection transmitted to humans by infected animals like sheep, cattle, goats, pigs, etc. Brucella spreads to tissues rich in elements of reticuloendothelial system, such as the joints, central nervous system, cardiovascular system and respiratory system[1]. We report a case of disseminated Brucellosis with meningoencephalitis, neck cellulitis, subgaleal abscess involving occipital bone and lumbar spinal discitis.

Case report

This 54-year-old gentleman from Kerala (India), a known patient of type 2 diabetes mellitus and systemic hypertension presented to our hospital with complaints of high grade fever with chills and backache for a duration of one week prior to admission. He was initially taken to a local hospital where the blood reports revealed thrombocytopenia (23,000/cumm). The patient developed breathlessness two days prior to admission. He had icterus, neck rigidity, diffuse oedema over the neck and bilateral infrascapular crackles.

Routine blood investigations revealed neutrophilic leukocytosis with thrombocytopenia, hyperbilirubinaemia, transaminitis, elevated C reactive protein and elevated procalcitonin (Table I). Viral markers were negative. Dengue IgM was positive. Initial arterial blood gas analysis showed metabolic acidosis with lactic acidosis. Saturation was maintained with noninvasive ventilation. A diagnosis of severe dengue was made. His platelet count gradually improved and normalised by the end of first week (Table I, II).

However, he continued to have fever and his total leucocyte count was gradually increasing (Table I, II). Blood culture sent at admission grew Klebsiella. At this point the diagnosis considered was Dengue fever with a health care-associated infection. The patient was initiated on intravenous piperacillin tazobactum, oral doxycycline, tab oseltamavir and other supportive measures. In the next few days the patient's general condition worsened and he gradually became obtunded. His fever was persisting. He was screened for other tropical fevers like scrub typhus and rickettsial infection and the reports were negative.

We proceeded with a Computed tomogram (CT) of the head which revealed brain atrophy. There were no vegetations seen on the echocardiogram.

Diffuse thickening of skin and subcutaneous tissue over the nape of neck suggestive of cellulitis was noted on ultrasonogram. CT scan of the neck revealed mild thickening of retropharyngeal soft tissue and diffuse inflammation of posterior cervical fascia and subcutaneous fatty tissue of the nape of neck. There was no obvious collection.

Antibiotics were escalated to inj. meropenem and vancomycin. Since the patient continued to be febrile and had altered sensorium, cerebrospinal fluid analysis was performed, which showed polymorphic pleocytosis (total count - 90 cells/cumm with 60% polymorphs) and the culture was sterile. By the 4th to 5th day of antibiotics, his fever came down.

Magnetic resonance imaging (MRI) of the brain and neck was done which revealed left occipital subgaleal collection and a collection in the posterior neck at C3 - C5 level (Fig. 1, 2). Even though an attempt to aspirate the collection was made, the radiologists opined that the collection was too small to be aspirated.

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Table I: Biochemical and haematological assays.

Parameters	Day 1	Day2	Day 3	Day 5	Day 7	Day 8	Day 9	Day 12
Haemoglobin g/dl	13.2	11.6	11.4					11.2
Total leucocyte count/mm^3	12,700	13,700	13,500	14,300	17,500	20,400		12,000
Differential count	N83L10 M5E2							
Platelet/mm^3	15,000	26,000	21,000	58,000	1.38 L	2.24 L		
Blood urea mg/dl		60.3						
Creatinine mg/dl	1.14	1.0	0.83	0.69		0.55		0.61
Total bilirubin mg/dl	4.66	3.98		2.86				
Direct Bilirubin mg/dl	2.91	2.5		1.51				
Total protein G/dl	5.84	5.49		5.89				
Albumin G/dl	3.13	2.87		2.71				
Aspartate aminotransferase U/L	75	75		48				
Alanine Aminotransferase U/L	54	55		43				
Alkaline phosphatase U/L	249	159		157				
Creatinine phosphokinase microgm/l	124.5		74.3					
Lactate mmol/l	5.7							
Magnesium mg/dl	2.16							
Phosphorus mg/dl	2.69							
INR	1.14							
C reactive protein mg/dl	418.4	348.4				156.3		
Procalcitonin		7.15						
Urine albumin	1+							
Glycated haemoglobin %		8.4%						
Lactate dehydrogenase U/L							813.2	

Table II: Biochemical and haematological assays.

	Day 14	Day 17	Day 20	Day 23	Day 28	Day 30	Day 33	Day 50	7 month
Haemoglobin g/dl	11.9		11.9	11.4	9.7	9.4	10.6	11.7	
Total leucocyte count per mm^3	9,500		12,600	14,500	11,200	9,290	7,600	10,200	
Platelets per mm^3	4.21		3.64 L	3.69L	3.9L	4.41 L		4.67 L	
Erythrocyte sedimentation rate mm/hr					40		105	90	36
Creatinine	0.58		0.53			0.62		0.49	
Total bilirubin U/L	0.76			0.61	0.59		0.6		
Direct bilirubin U/L	0.26			0.24	0.2		0.17		
Total protein G/dl	6.85			6.46	6.74		7.9		
Albumin G/dl	2.9			2.58	2.72		3.37		
Aspartate Aminotransferase U/L	90		489	34	26		16		
Alanine aminotransferase U/L	153		263	86	61		13		
Alkaline phosphatase U/L		188			187	179		120	
Creatine phosphokinase microgm/l	81.6		38.6		101.1	50.7	40.1		
T3 ng/ml (69 - 215)					131				
T4 microgm/dl (5.2 - 12.7)					7.55				
TSH micro IU/ml (0.4 - 8.9)					1.84				
INR					0.98				

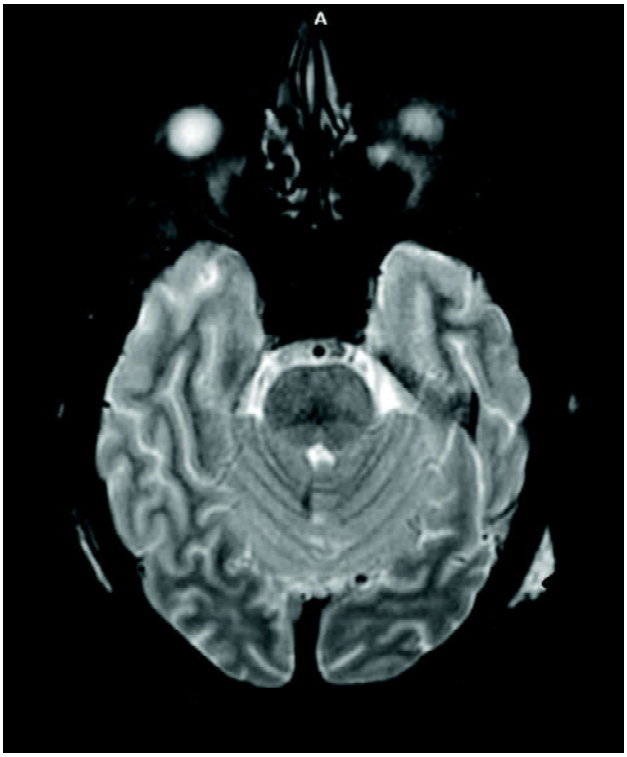

Fig. 1: *MRI brain depicting subgaleal collection in left occipital bone.*

The patient's general condition improved, his neck stiffness subsided and he was recuperating well.

We presumed that we were dealing with a bacterial infection since patient was responding to our treatment and we continued the intravenous injections for 14 days and then stopped. The leucocyte count improved, C-reactive protein came down, renal functions normalised and the transaminitis improved (Table II).

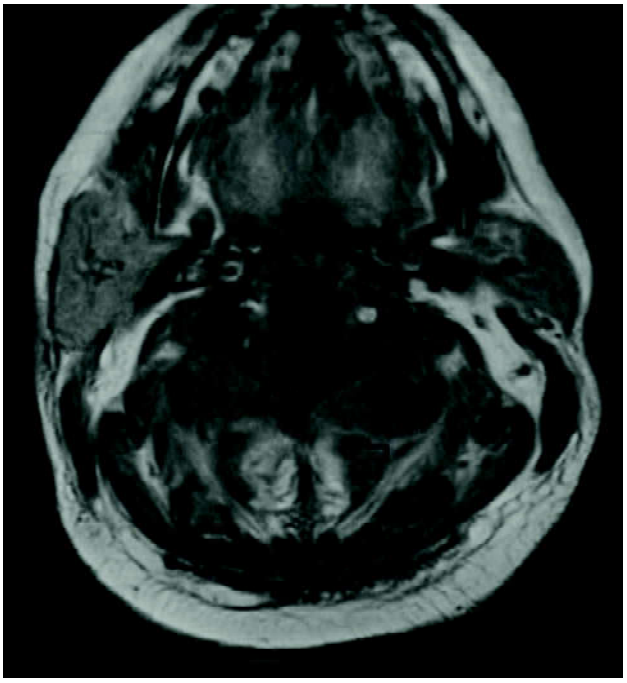

Fig. 2: *MRI neck showing intermuscular collection at C3 - C5.*

Within a few days of stopping the antibiotics, the patient had recurrence of fever. He was re-evaluated for the cause of fever and all the possible causes for a health care infection were addressed and remedial measures were instituted. Repeat blood cultures were sterile. Patient continued to have fever with rising leukocytosis. Even though we could not pin point any source of infection we restarted on meropenem considering a possibility of health-care associated Gram-negative bacterial infection and he became afebrile.

Patient was mobile by then and he noticed that he had severe back ache with pain radiating to the right lower limb. Clinical examination revealed tenderness at L5. MRI of lumbosacral spine revealed L5-S1 infective spondylodiscitis with epidural soft tissue (Fig. 3, 4). A CT guided biopsy of the spinal cord lesion was done. AFB (acid fast bacilli) smear and TB PCR was negative. Brucella IgM antibody was borderline positive. Brucella agglutination also was reactive. Focal areas of small collection of epitheliod cells depicting an attempted granuloma were noted on histopathology (Fig. 5). Pathologists opined that these granulomas can be consistent with Brucellosis in the given clinical setting. On reviewing the history, we learnt that he consumed boiled milk and had no history of exposure to cattle. Even though Kerala state of India is not an endemic area, it was noted that he was earlier working in a Middle-Eastern country which is known to be an endemic area for Brucellosis.

Brucella's susceptibility to Meropenem could possibly

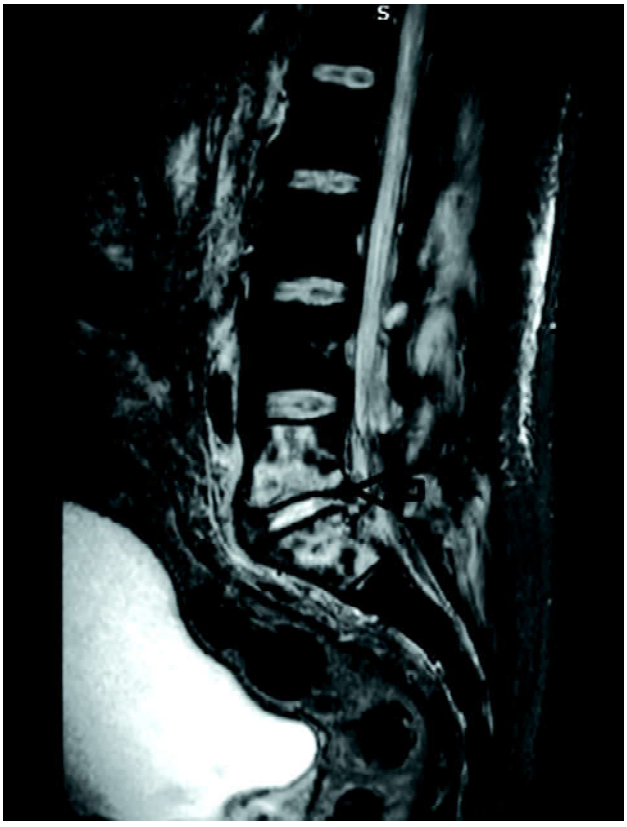

Fig. 3: *MRI of the lumosacral spine revealing L5 S1 discitis with paraspinal collection.*

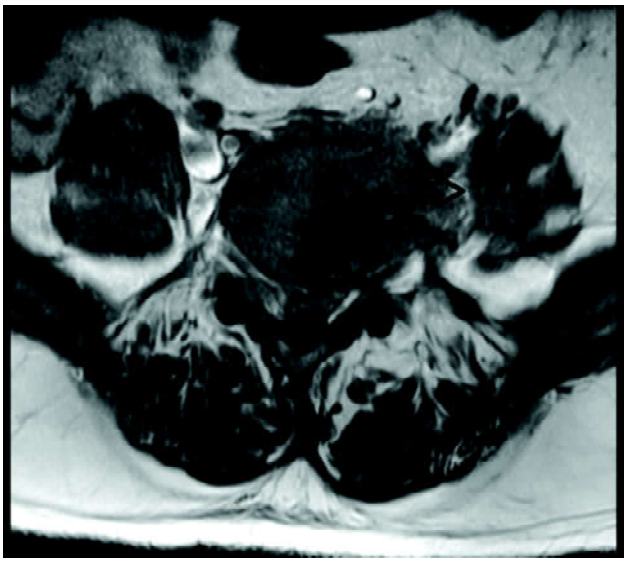

Fig. 4: *Paraspinal collection.*

explain the defervescence of fever while on Meropenem. We stopped Meropenem and initiated him on intramuscular streptomycin (21 days), tab doxycycline, and tab rifampicin. His condition gradually improved. He remained afebrile thereafter. An MRI done 6 weeks later revealed reduction

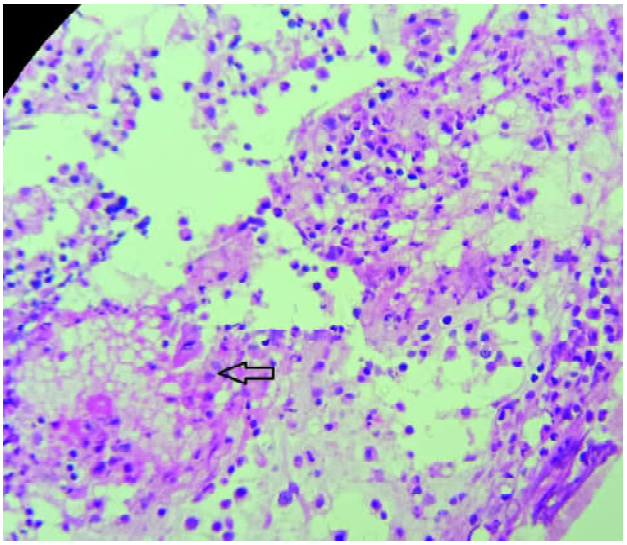

Fig. 5: *Histopathology showing focal areas of collection of epitheloid cells.*

in oedema and reduction in epidural soft tissue at L5 - S1. Doxycycline and rifampicin were given for a total duration of 12 weeks. There was resolution of neurological deficit and radicular pain and his ESR returned to normal. He was further followed-up for 6 months and he continued to remain asymptomatic.

Looking back, we could assemble the pieces of the jigsaw puzzle. This patient indeed had presented with dengue infection as he had presented with significant thrombocytopenia in the backdrop of dengue serology positivity. His platelets improved within a week which was what we expected in dengue infection. We did not refute the presence of Klebsiella bacteraemia at presentation as he came in from another health care facility. However, that did not explain the neck cellulitis, meningoencephalitis, and subgaleal collection. Brucellosis is a multisystem disorder which can cause osseous involvement including skull bone, skin and soft tissue infection, meningoencephalitis, and spinal discitis. Clinical resolution following therapy for brucellosis reiterated our diagnosis.

Discussion

This patient had a multisystem involvement of brucellosis including osseous, cutaneous, and nervous system involvement.

The various neurological involvement of Brucella noted in literature are encephalitis, meningoencephalitis, radiculitis, myelitis, peripheral and cranial neuropathies, subarachnoid haemorrhage, and psychiatric manifestations[2,3]. Signs and symptoms of meningeal involvement are nonspecific in neurobrucellosis and meningeal signs are infrequently present [4]. Our patient had meningoencephalitis. According to Kochlar *et al* the criteria necessary for definite diagnosis of neurobrucellosis are: (i) neurological dysfunction not explained by other neurologic diseases, (ii) abnormal CSF indicating lymphocytic pleocytosis and increased protein, (iii) positive CSF culture for *Brucella* organisms or positive *Brucella* IgG agglutination titre in the blood and CSF, and (iv) response to specific chemotherapy with a significant drop in the CSF lymphocyte count and protein concentration[5].

Osteoarticular involvement is the most frequent complication of brucellosis, and can occur in 10% to 85% of the patients infected with the disease[6]. The spine is one of the most common organs involved in brucellosis infection with a rate of 2% - 54%, and the lumbar vertebrae are the most frequently affected[7]. Sohn *et al* reported an unusual case of occult Brucella osteomyelitis involving the skull[8]. This patient had subgaleal abscess involving occipital bone and lumbar discitis with radiculopathy.

Chronic ulcerations and subcutaneous abscesses have also been described in brucellosis[9]. The neck abscess in this patient resolved completely with treatment.

The essential element in the treatment of all forms of human brucellosis is the administration of effective antibiotics for an adequate length of time. Uncomplicated cases can be treated with doxycycline 100 mg twice a day for six weeks + streptomycin 1 g daily for two to three weeks or doxycycline 100 mg twice a day for six weeks + rifampicin 600 - 900 mg daily for six weeks[10]. IDSA (Infectious disease society of America) also suggest doxycycline with rifampicin for treatment of Brucella osteomyelitis[11]. The WHO recommends that drugs which penetrate blood brain barrier like rifampicin or co-trimoxazole should be added to the standard regimen of doxycycline plus streptomycin in the treatment of central nervous system complications of brucellosis. The optimal duration of treatment for neurobrucellosis has not been determined; however, most authorities recommend a minimum of six to eight weeks, and possibly longer, depending on the clinical response[10].

Conclusion

Brucella is a multisystem disease with variable presentation. A high index of suspicion is required to diagnose Brucellosis. Brucellosis should be considered in the differential diagnosis of a multisystem involvement in patients returning from an endemic area.

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