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### <u>Case Report</u> Neurobrucellosis in a 17 years Girl Presenting as Chronic Meningitis and Paraparesis: A Rare Case Report

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#### Introduction

Brucellosis is a disease of livestock animals such as cattle, swine, goats, sheep, dogs and humans are the accidental hosts. Human brucellosis is a known occupational hazard among adults working with livestock however, most cases in children are associated with consumption of unpasteurised milk products. It causes more than 5,00,000 human infections per year worldwide<sup>1</sup>. In the state of Himachal Pradesh (India), the seroprevalence of brucellosis among occupationally exposed human beings was observed to be  $6.66\%^{1}$ . Symptoms can be acute or insidious and are usually nonspecific. Serious manifestations of brucellosis include endocarditis, meningitis, osteomyelitis and spondylitis. Invasion of nervous system occurs only in 1 to 4 % of patients. Neurological complications include encephalitis, myelitis, meningoencephalitis, peripheral and cranial neuropathies, subarachnoid haemorrhage, psychiatric manifestations, brain abscess, and demyelinating syndrome<sup>2</sup>.

#### **Case Report**

We present a case of a 17 year female adolescent who presented with 10 days history of fever, headache, altered sensorium and one episode of seizure. Her bowel and bladder habits were normal. There was history of undocumented weight loss, loss of appetite and night sweats for the last 4 months. The patient belonged to a rural area of district Chamba, Himachal pradesh and her family was associated with livestock rearing. She used to consume raw milk of goat. On examination she was thin built, had neck stiffness and disc hyperaemia bilaterally on fundus. Kernig's sign was positive. There were no other localising signs on systemic examination. Her analysis was suggestive of pyogenic CSF meningitis and CT scan brain was normal. She was treated with intravenous ceftriaxone for 14 days after which she improved however her papilledema did not settle. So she was advised for two weekly follow up regarding papilledema however she was lost to follow up.

After 6 months she again presented in ER with complaints of progressive lower limb weakness for the last four months. There was history of severe frontal headaches on and off. No history of altered sensorium, abnormal body movements, any cranial nerve involvement or loss of sensations. Her bowel and bladder habits were normal.

## JMSCR Vol||08||Issue||07||Page 06-08||July

General physical examination was grossly normal. On nervous system examination, our patient was conscious, co-operative and well oriented to time place and person. Examination of cranial nerves revealed no abnormality except bilateral papilledema and bilateral sensorineural hearing loss. Motor examination revealed normal muscle bulk, flaccidity in lower limbs, grade IV power in all muscles of lower limbs, symmetrically absent deep tendon reflexes, and bilaterally flexor plantar response. Sensory examination was normal. No meningeal signs were present. On investigations haemoglobin was 12.6 gm% and total leukocyte count was 4170/mm<sup>3</sup>. Biochemistry showed normal blood glucose and renal and liver functions. Cerebrospinal fluid (CSF) analysis had 280 cells: 70 percent polymorphs; proteins: 200 mg/dL; glucose: 35 mg/dL (concomitant blood glucose: 96 mg/dL); CSF was negative for acid fast bacilli by ZN stain. Chest X-ray was normal. As a part of fever workup her blood sample was sent to Department of Veterinary Microbiology, College of Veterinary and Animal Sciences, Palampur (Himachal Pradesh) for diagnosis of brucellosis. Blood sample was positive for Rose Bengal test. SAT was positive and was more than 1:160. Subsequently MRI brain was done. On T1W restricted diffusion (infarcts) in periventricular white matter in right frontal lobe (centrum semi-ovale) likely to be lacunar infarcts of right frontal lobe. Minimal leptomeningeal enhancement in bilateral frontal plane and temporal lobe (figure 1). MRI spine was normal. Investigative workup for tuberculosis, sarcoidosis, lyme disease and syphilis was negative.



Figure 1: MRI film of the same patient.

We started her on iv ceftriaxone for three weeks hospitalisation period and doxycycline 100 mg BD and cotrimoxazole (160 mg trimethoprim) BD each for 4 months. There was a dramatic clinical improvement during the hospital stay of 3 weeks.

#### Discussion

Brucellosis is primarily a reticuloendothelial system (RES) disease, and the most common site involved is the osteoarticular. Additionally, hematologic system, central nervous system, cardiopulmonary system and genitourinary system can be involved. Neurobrucellosis is an infrequent complication of brucellosis. The frequency of neurobrucellosis has been reported as  $0.5\%-25\%^3$ . Diagnosis of neurobrucellosis is usually made 2-12 months after the onset of symptoms in most cases<sup>4</sup>. It is mainly diagnosed based on clinical sign and symptoms, microbiological and/or biochemical evidence from cerebrospinal fluid. Erdem et al, defined chronic Brucella meningitis on the basis of following criteria: (1) The manifestation of clinical neurological symptoms for over 4 weeks. (2) The presence of typical CSF evidence with meningitis (protein concentrations >50 mg/dL, pleocytosis over 10/mm<sup>3</sup>, and CSF glucose to serum glucose ratios <0.5). (3) Positive

### 2020

# JMSCR Vol||08||Issue||07||Page 06-08||July

bacterial culture or serological test results for brucellosis in CSF (positive Rose Bengal Test or serum tube agglutination) or in blood (positive Rose Bengal Test and serum tube agglutination with a titer  $\geq 1/160$ ) or positive bone marrow culture. (4) Nonappearance of any alternative neurological diagnosis CSF culture, when positive, is considered the gold standard in the diagnosis of neurobrucellosis<sup>5</sup>. laboratory However, serological approaches are the mainstays in the diagnosis of neurobrucellosis due to the relatively lower efficacy of bacterial culture. Our patient fulfilled all the four criteria of neurobrucellosis as laid in the case definition by Erdem et  $al^5$ .

For treatment there is no consensus for choice of antibiotic, dose, and duration of the treatment for neurobrucellosis. Dual- or triple-combination therapy with doxycycline, rifampicin, trimethoprim-sulfamethoxazole, streptomycin, or ceftriaxone for >2 months (3–6 months) has been recommended<sup>6</sup>.

#### Conclusion

India is one of the many endemic countries for brucellosis and a high degree of suspicion is required along with experience to diagnose neurobrucellosis, otherwise patients may be partially treated as meningitis or may present as chronic meningitis with complications. Also simplified diagnostic criteria and readily available serologic testing is required in a low resource areas as ours.

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