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Brucella meningoencephalitis with hydrocephalus masquerading as tuberculosis

Vishwanath Sathyanarayanan*, Bekur Ragini, Abdul Razak, M Mukhya prana Prabhu

Department of Internal Medicine, Kasturba Medical College, Manipal, Karnataka, India

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ABSTRACT

Neurobrucellosis is a rare form of localized brucellosis usually with no systemic manifestations. We report a rare case of brucellosis presenting as meningoencephalitis associated with hydrocephalus. This patient had a lymphocytic predominant CSF and was initially treated with empirical anti tubercular therapy and steroids. A week later, when his CSF culture grew Brucella species, the treatment was changed to a combination of streptomycin, doxycycline and rifampicin and the patient improved with this therapy. This case illustrates the need to consider neurobrucellosis as a close differential diagnosis of neurotuberculosis in endemic areas when the patient presents with meningo encephalitis with lymphocytic CSF.

1. Introduction

Brucellosis rarely presents with involvement restricted to nervous system. Human brucellosis especially neurobrucellosis is rarely reported in India, where animals are raised in large numbers with low hygiene and hence the disease is expectedly endemic. Clinical spectrum of neurobrucellosis is varied, several areas of the nervous system, both central and peripheral can be involved. Identification of the specific neurologic syndromes is important as the response to treatment is better in the acute form when compared to the chronic form, which is more indolent and requires longer duration of therapy. No clear cut classification system exist till date for the spectrum of clinical syndromes is quite varied. In this rare case report of neurobrucellosis, we also discuss regarding the existing classification systems and a short review of treatment recommendations existing till today. Awareness of the conditition and performance of appropriate serological and microbiological tests will differentiate neurobrucellosis from chronic infections especially tuberculosis.

2. Case report

A 29 year old shop-keeper with post-polio flaccid paralysis of both lower limbs was brought to the emergency department with altered sensorium for the past 1 day. There was history of intermittent fever since 2 months. Fever used to be there for 1-2 days, followed by afebrile period for 4-5 days only to recur again. History of loss of appetite, night sweats and loss of weight were also present. No history of headache, vomiting or joint pain. There was history of cattle rearing but no consumption of raw milk from cows. On examination he was conscious, febrile (100° F), not verbalizing or obeying commands, pulse was 70/min, respiratory rate was 18/min, SpO_2 98% on room air and BP was 140/80 mmHg. Head was turned to right side with clenched teeth and tonically flexed upper limbs noted. Pupils were 3 mm symmetrical in size but not reacting to light and marked neck stiffness was present. Cardiovascular, respiratory and abdomen examination were normal. Bystanders claimed this state since the last night. The clinical condition was suspected to be status epilepticus secondary to meningoencephalitis. With intravenous diazepam seizure aborted and he was dilantinised.

*Corresponding author: Dr.Vishwanath Sathyanarayanan, #1, OPD Block, Department of Internal Medicine, Kasturba Medical College, Manipal-576104, Karnataka, India.
Tel:+91-820-2922236, +91-9008417949
Fax: +91-8252-2571927
E-mail: docvishu@gmail.com

Full blood count revealed WBC count 15 400/cumm, 80% neutrophils.The blood biochemistry, urine routine, chest X-ray and ECG were normal.A CT head (Figure 1) showed mild hydrocephalus with meningeal enhancement. A guarded lumbar puncture was done. CSF analysis showed 160 WBCs with 99% lymphocytes. CSF-glucose was low (29 mg/dL), protein was high (157 mg/dL). Cerebrospinal fluid-adenosine deaminase activity (CSF-ADA) was 21 IU/L. CSF-PCR for *Mycobacterium tuberculosis* was negative. Patient was started on empirical antitubercular therapy in view of 2 months history of fever, meningitis, communicating hydrocephalus and lymphocytic predominance of CSF, with four drugs [Isoniazid (H), Rifampicin(R), Pyrazinamide (Z) and Ethambutol (E)] and dexamethasone and Ceftriaxone. Serum was tested for *Brucella* agglutinins by standard tube agglutination test (STAT) and the titer was 320. A week later, Brucella species was isolated from CSF by BacT/Alert automated blood culture system.

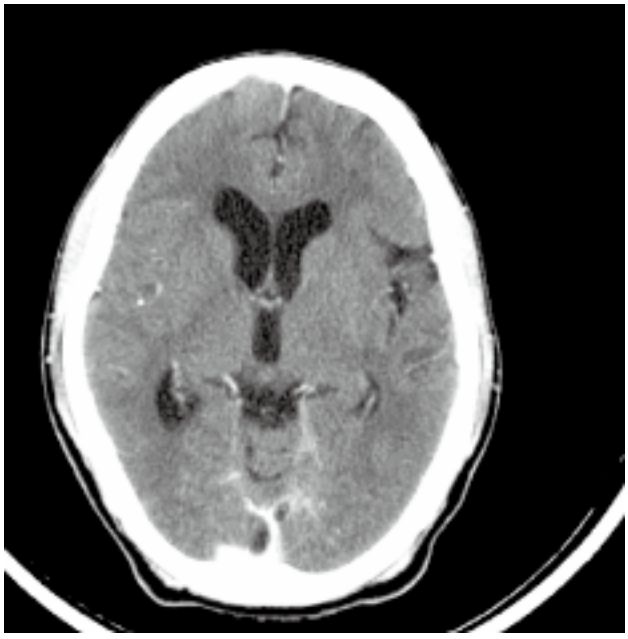

Figure 1. Computed tomography of brain.
It shows meningeal enhancement and mild hydrocephalus.

Following the laboratory confirmation, case was re-evaluated as neurobrucellosis and HZE stopped and dexamethasone continued in view of hydrocephalus and tapered. Streptomycin(S) 750 mg/day i.m was started along with oral doxycycline 200 mg/day. The dose of rifampicin was increased to 600 mg/day and ceftriaxone was continued. Fever subsided, disorientation improved and he started obeying commands from the second day. Seizures did not recur during the recovery period that extended to four weeks. Streptomycin was stopped after two weeks and ceftriaxone stopped after four weeks and then he was discharged symptom free after four weeks. Rifampicin and doxycycline were continued. He was reviewed after one month as an out-patient and found to be symptom free. He was advised to continue rifampicin and doxycycline for 4 more months. Lumbar puncture was repeated after 6 months and CSF sent for culture was reported as sterile. Hence treatment was terminated.

3. Discussion

Brucellosis is a well known zoonosis endemic in Mediterranean, Middle east, Africa Latin America and South west Asia. Humans acquire infection commonly through consumption of unpastuerised dairy products and rarely via cuts and aerosols. Majority of human disease has been due to *Brucella melitensis*. Localized involvement of nervous system (neurobrucellosis) has been observed in only 3-5% of cases in most of the case-series reported world-wide[1]. Nervous system can be involved in various stages of brucellosis i.e. at the onset, during the course of illness, convalescence or months after recovery from acute infection. The effect on nervous system can be due to direct effect of bacilli, cytokines or endotoxins on peripheral nerves, spinal cord, meninges and brain. The whole spectrum of neurological manifestations include meningitis(M)/meningo-encephalitis(ME) as the most common manifestations[2] and rarely cranial neuropathies, peripheral neuropathies, chorea, demyelination, transient ischemic attacks, and psychiatric manifestations.

In 2009, pooled analysis of 187 neurobrucellosis cases with 35 publications from Turkish medical practice revealed varied presentation of neurobrucellosis mimicking various pathologies hence a thorough evaluation of patients is crucial[3]. Neurobrucellosis presenting as acute psychosis[4], thalamic infarction[5], and spastic paraparesis[6] have been reported. First case of neurobrucellosis associated with hydrocephalus was described by Guney F *et al* in 2008 after consumption of fresh sheep cheese, stressing the need to consider neurobrucellosis in any case of hydrocephalus especially from endemic areas of brucellosis[7]. In 2006, Turkish experience based on 452 cases of spinal brucellosis found that the clinical and radiological features are atypical and non specific hence difficulty in identifying them, CT/MRI of spine may be sensitive for diagnosis and follow up[8]. Epidemiological, clinical and imaging findings in brucellosis with osteoarticular involvement by Poubagher *et al* found that MRI is the method of choice for diagnosing osteoarticular and spinal complications of human brucellosis and the closest differential diagnosis for tubercular spondylodiskitis is brucellosis[9].

Neurobrucellosis is less commonly reported disease in India although animal brucellosis and seroprevalence in specific areas is well reported. Extensive meningoencephalitis, retrobulbar neuritis and pulmonary involvement was reported from Lucknow[10]. In 2007, hospital based case series of 175 cases of serologically, confirmed cases of brucellosis in Bikaner, Northwest India, the incidence of neurobrucellosis was 18.86%[11]. Recently there are no much reports of cases of neurobrucellosis although incidence of brucellosis is on rise. Majority of people with cattle rearing profession reside in rural India have decreased access to tertiary care centre and lack of awareness among primary care physicians where no specific data regarding incidence and prevalence in humans exist, though theoretically expected to be endemic. Brucellosis closely mimics tuberculosis in its presentation including neurobrucellosis. It is confused for tuberculosis.

Diagnosis of neurobrucellosis rests in neurological symptoms usually unaccompanied by systemic manifestations, positive CSF culture or blood serology and/or positive CSF culture, and CT/MRI abnormalities are variable.

Al Sous MW *et al* found three types of imaging abnormalities in central nervous system in case of neurobrucellosis–inflammation, white matter changes and vascular insult. The white matter changes may mimic other inflammatory/infectious disease such as multiple sclerosis, acute disseminated encephalomyelitis/Lyme disease[12]. Only one case of neurobrucellosis associated with hydrocephalus as a radiological feature of neurobrucellosis has been reported[7]. Patients with unexplained neurological and psychiatric symptoms from endemic areas should raise suspicion of neurobrucellosis[13]. For rapid diagnosis of neurobrucellosis light cycler based real time polymerase chain reaction based assay in CSF samples is more rapid and sensitive than conventional microbiological tests[14].

Treatment of brucellosis is complex requiring protracted administration of more than one antibiotic. Recommendations in 2006 suggested that treatment of uncomplicated brucellosis in non-pregnant adults should be based on a six week regimen of doxycycline combined with either streptomycin for two to three weeks or rifampicin for six weeks[15]. Systematic review and meta analysis of randomized controlled trials in 2008, found that the preferred treatment in brucellosis should be with dual/triple regimens including an aminoglycoside[16]. Doxycycline and rifampicin readily penetrate the blood-brain-barrier (BBB) and achieve good CSF concentrations. Concentrations of amino-glycosides in CSF are therapeutic only when meninges are inflamed. In a new case, when the initial presentation is M/ME, it is wise to consider other common causes and challenge them empirically, until the results of diagnostic work-up arrive. Thus ceftriaxone remains an important initial drug[1,17]. Ceftriaxone is active against brucella *in vitro*, but results of *in vivo* studies have not been compelling. Given the benefit of doubt, it becomes necessary to include ceftriaxone in the initial treatment regimen as it achieves good concentration in CSF.

Neurobrucellosis generally needs prolonged therapy for 3-6 months, but no large trials exist. A recent review of most case-series on neurobrucellosis have still suggested that treatment duration has to be individualized[1], which seems reasonable as the spectrum of neurological manifestations is diverse. Steroids are warranted in special circumstances like our case where there was hydrocephalus. Other manifestations requiring steroids include papilledema, cranial neuropathies, myeloradiculitis, raised intracranial pressure and optic neuropathy[1].

This case presented as pyrexia of unknown origin, with sudden involvement of central nervous system proved to be due to brucellosis can be easily confused with tuberculosis with fever, loss of appetite, weight loss, meningeal signs, CSF picture and CT feature of hydrocephalus. High index of clinical suspicion coupled with appropriate microbiological investigations will improve level of case detection. It will be reasonable to consider neurobrucellosis as differential diagnosis in such circumstances.

In conclusion, in any case of meningitis or meningoencephalitis with lymphocytic predominance in CSF neurobrucellosis is an important close differential diagnosis to neurotuberculosis in endemic places. Though antitubercular drugs are active against Brucella, diagnosis becomes important as neurobrucellosis needs prolonged therapy with those specific drugs that attain good CSF concentration to exert their bactericidal activity. And high index of clinical suspicion coupled with appropriate microbiological investigations will improve level of case detection.

Conflict of interest statement

We declare that we have no conflict of interest.

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