Neurobrucellosis: A report of two cases
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Abstract
Neurobrucellosis is a rare complication of brucellosis, a common zoonosis with multisystem involvement. Its clinical presentation is quite heterogeneous and diagnosis requires a high index of suspicion in patients from endemic areas. We present two cases of neurobrucellosis with widely varying clinical involvement from a tertiary center in Pakistan.

Our case report emphasizes that neurobrucellosis should be considered in evaluation of patients with unexplained neurological symptoms.

Keywords: Brucellosis, Neurobrucellosis.

Introduction
Human brucellosis is a zoonotic disease that is endemic in many parts of the world. Neurobrucellosis is a rare but a serious complication is seen in 1.7% of adult and 0.8% of paediatric patients. Clinical manifestations are diverse with involvement of both the central and peripheral nervous system. Diagnosis is based on symptoms and signs of neurological disease and raised CSF brucella antibody titers. We report two cases of neurobrucellosis diagnosed at our center and discuss the challenges in clinical and laboratory diagnosis. The consent of the subjects of the two cases for publication had not been taken as the case series is being written as retrospect and patients are now lost to follow up. Further no personal identifying information has been divulged in both cases.

Case-1
A 13 years old girl presented in June 2015 at Shifa International Hospital Islamabad with high grade fever, headache, backache and vomiting for 3 days. She was previously healthy and was doing frequent horse riding in a local club.

On examination neck stiffness was positive. Rest of the physical examination was essentially unremarkable.

CSF analysis showed WBC count 320 cells/µL (polymorphs 80%, lymphocytes 20%), protein 138 mg/dL and glucose of 38mg/dLs. Magnetic resonant imaging (MRI) of the brain showed post contrast leptomeningeal enhancement.

The provisional diagnosis of meningoencephalitis was made. She was given IV ceftriaxone and was discharged home after 5 days to complete 10 days of therapy but returned within 48 hours with para paresis, urinary retention and left facial and third nerve palsies.

Repeat CSF analysis showed WBC 235 cells/µL (polymorphs 20%, lymphocytes 80%), protein 221 mg/dL and glucose of 8 mg/dL. MRI brain showed interval worsening and increase in degree of leptomeningeal enhancement. MRI dorsolumbar spine showed leptomeningeal enhancement suggestive of spinal leptomeningitis and arachnoiditis.

MTB DNA by PCR results were negative. CSF HSV PCR was negative. Both the serum and CSF samples were positive for brucella abortus antibodies at titers of 1:320.

We administered combination therapy with ceftriaxone, doxycycline and rifampicin. Streptomycin was also given for 2 weeks. The patient completed 6 months therapy. Eventually she made full neurological recovery with no residual deficit at 9 months follow-up.

Case-2
A 40 year old male presented in March 2015 at Shifa International Hospital Islamabad with complaints of high grade fever and headache for 7 days and progressively weakness and increasing drowsiness with decreased urine output for 2 days.

On examination he was drowsy with temperature of 101°F. Neck stiffness was positive but rest of the neurological and systemic examination was unremarkable.

His initial laboratory evaluation revealed white cell count of 16100/µL with neutrophils 82%, lymphocytes 16%, haemoglobin 12.76 g/dl and platelet count 380000/µL, blood urea nitrogen (BUN) 107 mg/L, creatinine of 10.26 mg/dL and uric acid 17. A urinalysis revealed moderate haematuria and +3 proteinuria. All viral and bacterial cultures were negative. Renal biopsy revealed acute tubulointerstitial nephritis. CSF analysis showed WBC count 35 cells/µL (polymorphs 20%, lymphocytes 80%), protein 152 mg/dL and glucose of 48 mg/dL. CT of the brain showed no intracranial pathology. Both the serum and CSF samples were positive for brucella miltantis antibodies at titers of 1:320.
We administered a triple combination therapy with ceftriaxone, doxycycline, and rifampin to the patient and haemodialysis was initiated. He had a favourable clinical response to treatment with gradual improvement in drowsiness in first week of treatment. Creatinine improved with gradual normalization of urine output.

Rifampin was stopped after 6 weeks and Doxycycline and Ciprofloxacin were continued for 6 months. During the followup for last one and a half year his renal function has remained normal with gradual resolution of proteinuria.

Discussion

Brucellosis is a wide spread multisystemic zoonotic infection caused by Gram-negative bacteria of the genus brucella. Symptoms may be protean and diagnosis requires a high index of suspicion in patients from endemic areas.

Neurobrucellosis is a rare but severe complication of systemic brucellosis. While meningitis is the most common clinical form of infection, clinical manifestations are many and may include encephalitis, myelitis, polyradiculoneuropathy, cranial nerve palsies, spinal cord compression and demyelinating or vascular disease of the CNS making diagnosis challenging. Our case 1 showed spine involvement with arachnoiditis.2

Gold standard for diagnosis of neurobrucellosis is positive CSF culture, yet its yield is often low being positive in <25% in most cases.4 Diagnosis is confirmed by detection of specific antibodies in CSF using ELISA, indirect coombs test or standard agglutination techniques.5 In both presented cases, CSF culture showed no growth after 6 weeks of incubation and diagnosis was made by detection of brucella antibodies in blood and CSF using standard agglutination technique.

Examination of the cerebrospinal fluid (CSF) typically reveals an elevated protein concentration, a depressed glucose concentration, and a moderate leukocytosis with lymphocytic predominance.2 Essentially similar CSF findings are seen in TB meningitis, necessitating the need for confirmatory tests to differentiate between the two. There has been a case report of an adolescent Pakistani girl with neurobrucellosis misdiagnosed and mistreated as TB meningitis considering only consistent CSF findings, in the absence of positive TB cultures.5

The best treatment regime for neurobrucellosis remains controversial with no consensus regarding optimal antimicrobial regimen and appropriate duration of treatment. Triple regimens of antimicrobials for 3-9 months with an average of 6 months are recommended. Combination may include rifampicin, doxycycline, cotrimoxazole, ceftriaxone and aminoglycosides.2,4

The prognosis of neurobrucellosis is generally good with complete recovery in the majority of patients after receiving appropriate therapy. However, cases of severe neurological sequelae have been reported.4

Renal involvement in brucellosis is extremely rare manifesting as acute interstitial nephritis, pyelonephritis, and IgA nephropathy which may cause proteinuria, haematuria, and pyuria. It may also cause caseating granulomas and calcifications.7 Patients with brucella glomerulonephritis almost always have, proteinuria, and/or azotemia, but exact diagnosis is generally established with resolution of the clinical findings after antibiotic treatment for brucellosis.8 In case 2, microscopic haematuria, proteinuria, and increased BUN and creatinine levels were detected during the initial laboratory analysis while renal biopsy revealed acute tubulointerstitial nephritis.

Conclusion

In conclusion, the two cases presented had widely varying clinical involvement which can interfere with prompt diagnosis of neurobrucellosis. Our case report highlights the importance of considering neurobrucellosis in the differential diagnosis of patients with unexplained neurological disease.

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References