

RARE PRESENTATIONS OF NEUROBRUCCELLOSIS

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ABSTRACT

Neurobrucellosis (NB) is one of the most serious complications of brucellosis, as a chronic granulomatous zoonotic infection. It may be acute or chronic with central and / or peripheral nervous system involvement. Pediatric NB is usually acute central form. We report a nine years old girl as a case of NB with sudden onset of hemi paresis, aphasia and bilateral sensory neural hearing loss.

KEY WORDS: Brucellosis, Hearing loss, Hemi paresis.

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INTRODUCTION

Brucellosis is a chronic granulomatous zoonotic infection that may transmit to human. It is still a public health problem in Iran with an incidence rate of about 34-105/ one hundred thousand population in different provinces.^{1,2} Neurobrucellosis (NB) is an uncommon complication of brucellosis with pediatric risk of about 0.8%.³

Paediatric neurobrucellosis usually involves the central nervous system and it is usually of acute presentation, with duration of symptoms between 0.5-8 weeks.³

We report a nine years old girl as a case of NB with bilateral sensory neural hearing loss, sudden onset of hemi paresis and aphasia.

CASE REPORT

A nine years old girl with complaint of malaise, anorexia, nausea, and vomiting for two weeks, sudden onset of left hemi paresis and aphasia was admitted in pediatric neurology ward of our Hospital. Physical examination at first, revealed bilateral 8th cranial nerve involvement decreased muscle force

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Table-I: Serial CSF analysis of the reported case with neurobrucellosis

	First	Second 3th day	Third 7th day	4 th 2nd month	5 th 6th onth
WBC/cc	2	50	70	30	0-1
Poly		20%	95%		
Lymph	100%	80%	5%	100%	
RBC/cc	2	0	180	10	0
Glucose mg/dl	20	10	70	18	27
Simultaneous	150	120	127	122	110
Blood glucose mg/dl					
Protein mg/dl	370	480	240	184	172
Gram stain	Neg	Neg	Neg	Neg	Neg
Culture	Neg	Neg	Neg	Neg	Neg

(4/5) and increased deep tendon reflex (DTR) of left lower extremity. Early laboratory tests including CBC, ESR, electrolytes and LFT were at normal limits, but CSF analysis had some abnormalities (Table-I).

Brain CT revealed mild communicating hydrocephaly and brain MRI showed patchy hyperintense areas in pons, periventricular white matter, parietal, temporal, and frontal lobes in T2W images (Fig-1,2). At first with impression of Acute Disseminated Encephalomyelitis (ADEM), she was treated with methylprednisolon without any improvement. She developed fever and nuchal rigidity after third day of treatment and was referred to infectious ward.

According to clinical and lab findings, tuberculous meningitis was considered and anti TB drugs (PZA, ETB, INH and RIF) and dexametasone was prescribed.

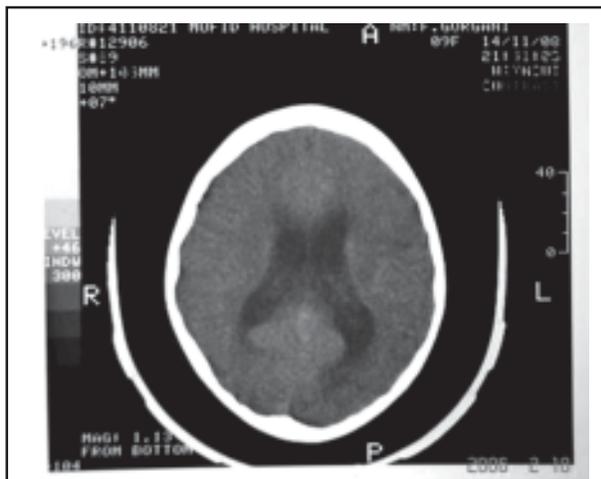


Fig-1: Brain CT revealed mild communicating hydrocephaly

Four days after anti-TB therapy, we received the following results: negative TB- PCR in CSF, serum wright titer of 1/ 2560 with CSF wright titer of 1/ 20, therefore we discontinued anti-TB drugs except rifampin and added cotrimoxazole and doxycycline to previous drugs with diagnosis of NB. Dexametasone was discontinued after one month but antibiotics were continued up to six months according to clinical state and CSF analysis result.

Lumbar puncture was repeated on third day, 7th day, second month and 6th month later when treatment was discontinued. Hemiparesis and aphasia recovered after one month but sensoryneural hearing loss did not improve despite of therapy.

DISCUSSION

Brucellosis caused by intracellular gram-negative bacteria of the genus brucella, is

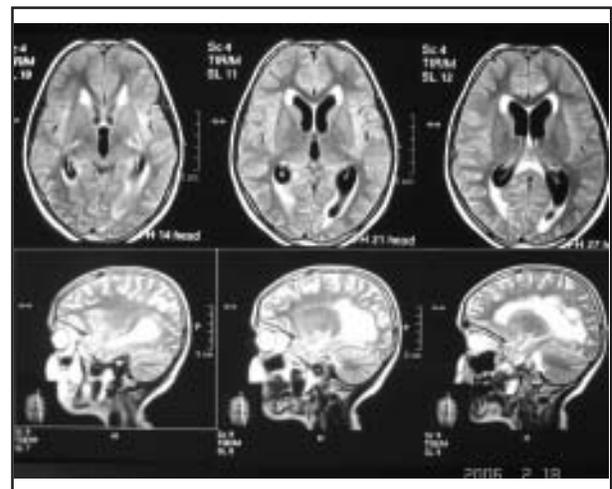


Fig-2: Brain MRI showed patchy hyperintense areas

transmitted to human through consumption of meat, raw milk or infected milk products, contact with infected animals or through the respiratory tract, abraded skin or conjunctiva.^{4,5}

This world wide disease with estimated incidence of half a million annually, is endemic in middle east area, western Asia, Africa and Latin America.⁶⁻⁸ It is still a major health problem in Iran with incidence of about 34-105/ 100000.^{1,2}

NB is an uncommon complication of this disease with incidence of 0.8% and 7% in children and adults' respectively.³ It may be acute or chronic with central and / or peripheral nervous system involvement. Pediatric NB is usually acute central form and peripheral neuropathy has not yet been reported in childhood NB.³

NB may present with brain abscess, subarachnoid hemorrhage, cranial nerve involvement and other sensory or motor abnormalities.^{3,7} The patient may be manifested with meningeal irritation, deep tendon hyperreflexia or areflexia with or without constitutional symptoms.³ Also brucella meningitis has been described without fever, neck stiffness or abnormal CSF findings.³ As regards our patient's clinical, laboratory and imaging findings, ADEM, TB meningitis and NB were suggested. History of recent infectious illness or immunization, increased CSF myelin protein, increased CSF/serum IgG ratio and thrombocytosis which can be found in ADEM helps to differentiate ADEM from NB.⁹ In addition, Intraparenchymal subcortical enhancement that may be found in ADEM has not yet been described in NB.¹⁰

History of contact with index case, positive PPD, abnormal CXR and positive CSF PCR or Culture can help to differentiate TB meningitis from NB. Basilar enhancement and communicating hydrocephalus are most prevalent imaging findings in TB meningitis and could also be found in NB.¹¹

CNS abnormalities in NB are of three types: white matter involvement, inflammatory changes and vascular insult.¹⁰ White matter

involvement may mimic other inflammatory or infectious diseases such as ADEM, Multiple Sclerosis (MS) and lyme disease, but involvement of corpus callosum in MS and intraparenchymal subcortical enhancement in MS, ADEM and lyme disease have not yet been described in NB.¹⁰

The criteria necessary for definite NB diagnosis include:

- * Increased protein in CSF and lymphocyte pleocytosis
- * Positive CSF culture for brucella or positive brucella IgG agglutination titer in the blood and CSF.
- * Response to specific chemotherapy with a significant drop in the CSF lymphocyte count and protein concentration.
- * Dysfunction not explained by other neurologic diseases,⁵ so our patient had all definite NB criteria.

Increased WBC count with PMN predominance of CSF after four days anti-TB therapy in our patient (third LP) can be explained with Jarish – herxheimer like reaction and release of excess brucella endotoxin which can augment the immune response.³ Habeeb and coworkers reported an eight year old boy with brucella meningitis who demonstrated a arisch-Herxheimer-like reaction, presented with clinical deterioration following the commencement of antibrucella treatment, associated with increased pleocytosis and shift from lymphocytic to polymorphic predominance. However this picture may be modified if steroids have been used.³

CSF glucose is not a reliable index for evaluation of response to therapy in NB as our patient had hypoglycorrhathia despite of completion of treatment.¹² Hearing loss is among the rare complications generally occurring with neurobrucellosis, mostly of sensorineural type.¹³ It appears that hearing loss in brucellosis is possibly due to involvement of the central auditory pathways although a mixed-type hearing loss after *Brucella* infection has been reported.¹⁴ Several studies have suggested that cerebral inflammation caused by infections, or

avascular neural tissue resulting from reflex spasm caused by endotoxins, can be the cause of hearing loss in brucellosis.⁵ Treatment should be initiated as soon as possible to prevent permanent hearing loss and later relapses and long-term combination therapy is required in such cases. Mc Lean et al reported that four of 18 cases treated for neurobrucellosis suffered from permanent hearing loss.¹⁵ Unfortunately sensoryneural hearing loss did not improve in our patient despite of therapy.

Since NB is a complication of systemic brucellar infection, patients should be given a combination of drugs that are both able to cover current treatment of brucellosis and achieve high levels in CSF. Triple regimens comprising doxycycline, rifampicin and cotrimoxazole are recommended because they have good intracellular and CNS penetration and may act in a synergistic fashion. The actual duration of therapy is predicated by the clinical and CSF response. Some authors also recommend concomitant steroid administration.¹⁶ Steroids have been used in neurobrucellosis when deterioration occurs after initiating antibrucella treatment as well as for optic neuropathy, papilloedema, cranial nerve involvement and arachnoiditis.³

CONCLUSIONS

Persistent aseptic meningitis with unusual presentations such as neurologic deficits should be an alarm signal to physicians to evaluate the patient for TB and brucellosis in endemic areas. In suspected cases, treatment should be started immediately before receiving laboratory results. In addition, every patient with acute paresis or chronic sensorineural hearing loss should be evaluated for infectious causes such as NB if other possible causes are ruled out.

REFERENCES

1. Karimi A, Alborzi A, Rasooli M. Prevalence of antibody to *Brucella* species in butchers, slaughterers and others. *La Revue de Sante' de la Mediterranee orientale* 2003;9:178-84.
2. Haji AM, Rasooli NM, Yaaghoob Z. Evaluation of Epidemiology, clinic, diagnosis and treatment of 505 patients with brucellosis. *Tehran Med Uni J* 2001;59:34-46 .
3. Habeeb YKR, AL – Najdi AKN, Sadek SAH. Paediatric Neurobrucellosis: Case Report and Literature Review. *J Infection* 1998;37:59-62.
4. Sohn AH, Probert WS, G laser CA. Human neurobrucellosis with intracerebral Granuloma caused by a Marine mammal *Brucella* SPP. *Emergency Infectious Diseases* 2003;9:485-8.
5. Kochar DK, Kumawat BL, Agarwal N. Meningoencephalitis in brucellosis. *Neurology India* 2000;48:170-3.
6. Ozturk KT, Kaygusuz I, Kilic S. Investigation of hearing loss in patients with acute brucellosis by Standard and high-frequency and audiometry. *Clin Microbiol Infect* 2005;11:559-63.
7. Kizilkilic O, Turunc T, Yildirim T. Successful medical treatment of intracranial abscess caused by *Brucella* SPP. *J Infection* 2005;51:77-80 .
8. Kyebambe PS. Acute brucella meningomyeloencephalo-spondylosis in ateenage male. *African Health Sciences* 2005;5:69-72.
9. Rust RS. Acute Disseminated Ecephalomyelitis. *E medicine* 2005 Available at <http://www.emedicine.com/neuro/topic500.htm>
10. AL–Sous MW, Bohlega S, AL Kawi MZ. Neurobrucellosis: Clinical and Neuroimaging correlation. *Amer J Neuroradiology* 2004;25:395-401.
11. Munoz FM, Starke JR. Tuberculosis. Behrman RE, Kleigman RM, Jenson HB. *Nelson text book of pediatrics*. 7th ed. New York: Saunders, 2004;958-72.
12. Anlar FY, Yalcin S, Secmeer G. Persistent hypoglycorrhachia in neurobrucellosis. *The Pediatric Infectious Diseases J* 1994;8:747-8.
13. Tuncer I, Akdeniz H, Uygan I. A brucellosis case with ascites, hearing loss and Pancytopenia. *Turk J Gastroenterol* 2002;13(3):168-71.
14. Yildirim A, Bayazit, Namiduru M. Hearing status in brucellosis. *Otolaryngology-Head and Neck Surgery* 2002;12:98-100.
15. Mc Lean DR, Russell N, Khan MY. Neurobrucellosis: clinical and therapeutic features. *Clin Infect Dis* 1992;15:582-90.
16. Mesut, Yilmaz, Resat, Ozaras, Recep, Ozturk (Istanbul University, Turkey), Chapter 10 - Neurobrucellosis: Current Clinical, Diagnostic and Therapeutic Features (pp. 207-220), available on: https://www.novapublishers.com/catalog/product_info.php?products_id=544