

Neurobrucellosis in a 9-year-old girl

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ABSTRACT

Brucellosis is a zoonotic multi-organ infectious disease most frequent in developing countries. Neurobrucellosis a quite rare but serious complication of brucellosis in the pediatric age group manifests with different neurological symptoms and signs. In the present case a 9-year-old girl was referred to our centre with a 9-months history of headache and back pain, facial nerve palsy and right upper limb weakness. She had undergone ventriculoperitoneal shunting surgery due to communicating hydrocephalus. Magnetic resonance imaging revealed a spinal extramedullary intradural mass, two epidural collections in the cervical spine and thickening/abnormal enhancement in the basal cisterns with invasion to medulla and pons. The patient's serum and cerebrospinal serologic tests were found positive for brucellosis. The patient was successfully treated by anti-brucella antibiotic therapy.

CASE REPORT

CASE REPORT

A 9-year-old girl was admitted to our centre with complaints of neck pain, left facial and upper limb weakness. She had a history of frontal headache, back pain and repetitive vomiting since nine months before admission. Two months ago she had underwent a VP shunting surgery in another hospital due to communicating hydrocephalus which was revealed after she was evaluated on account of loss of consciousness (Fig. 1). She was referred to our hospital for further evaluation.

The patient had no history of problem during pregnancy or birth. She had normal motor, cognitive and speech development and complete vaccination. No other history of hospital admission or surgery was mentioned. She had never received blood transfusion. She used no medication and had no allergies. Her parents were healthy and she had no siblings. Her vital signs and physical examination were normal. On her neurologic exam she had left central facial nerve palsy.

CBC showed lymphocytic predominance (White Blood Cell count 9450/mL: polymorphonuclear cells 47%, and lymphocytes 43%) with normal Hemoglobin level and Platelet Count. Erythrocyte Sedimentation Rate was 14 (normal range 1-10). C-reactive protein was 1 mg/L (normal range <5). PPD test, IGRA and TB PCR were negative. Blood culture was negative.

Brain CT scan revealed effects of previous shunting but no remained hydrocephalus. Brain MRI demonstrated thickening and abnormal enhancement in basal cisterns including suprasellar cistern that had invaded medulla and pons (Fig. 2 a, b, c) with ring enhancing lesions in the pons. Total spinal MRI revealed an enhancing extramedullary intradural mass at T7-T8 level (Fig. 2 d) and extensive intrathecal/meningeal nodular enhancement. Cervical spine images showed two fluid intensity anterior epidural collections with enhancing walls (Fig. 2 e, f). The intrathecal and meningeal nodular enhancement was more pronounced in

lumbosacral portions of spine, with diffuse cauda equina nerve root enhancement. Regarding the thick enhancement of basal cisterns, the findings were suggestive of granulomatous diseases of infectious or non-infectious origin or tumoral diseases with CSF seeding or metastases.

She underwent L5-S1 laminectomy to provide samples of intrathecal nodules. During surgery the lesion was found to be of infectious origin. Samples of pus, meningeal tissues and CSF were sent for analysis.

The CSF sample revealed 60 WBC/mL (normal range 0-8) with 80% lymphocytes and 20% polymorphonuclear cells, no bacteria, protein level 1880 mg/dl (normal range 15-45) and glucose level below 20 mg/dl (normal range 50-80). This was suggestive of infections such as Tuberculosis or fungal infection. CSF culture showed no growth for bacteria or fungus.

A couple of days later her manifestations aggravated with fever, coffee ground vomiting, wheezing, decreased level of consciousness and left spastic hemiparesis. Brain CT scan imaging demonstrated slit ventricles, diffuse edema of brain parenchyma and no hydrocephalus. The patient was started on Ceftriaxone, Vancomycin, phenytoin, pantoprazole and vitamin K.

Blood and CSF re-sampling were performed after aggravation of patient's status. White Blood Cell count was 11530/mL (polymorphonuclear cells 63% and lymphocytes 28%). C - reactive protein was 3.5 mg/L. Erythrocyte Sedimentation Rate was 28 mm/H. Other routine tests were normal. Blood, Urine and CSF cultures showed no growth. The CSF analysis revealed 4 WBC/mL, 267 RBC/mL, glucose 31 mg/dl, protein 211 mg/dl and no bacteria.

The pathology samples provided from meningeal tissues consisted of no malignant cells, acid fast bacilli or fungus but it indicated the presence of histiocytes. The CSF flow cytometry showed no abnormal immunophenotype.

Brain and cervical MRI imaging had no change in comparison with previous imaging. The history of unpasteurized dairy products consumption was inquired which was confirmed along with a history of brucellosis in the patient's mother.

The Wright agglutinations test, 2ME test and Coombs Wright test in the serum were positive at a titer of 1/80 (positive: $\geq 1:80$ for Wright and $\geq 1:40$ for 2ME test and Coombs Wright) following which the antibiotics were discontinued and a regimen of Rifampin 15 mg/kg/day and Cotrimoxazole 10 mg/kg/day was started with the impression of Neurobrucellosis.

Two days after the initiation of treatment hemiparesis gradually improved. No fever was detected. CSF and Blood cultures were still negative after 6 days. Streptomycin 50mg/kg/day was added to the anti-Brucella regimen and Cotrimoxazole was replaced with Doxycycline 5mg/kg/day. CSF culture in Castaneda and BACTEC culture media showed

no growth. The repeat blood Wright agglutination test, 2ME test and Coombs Wright test after 2 weeks were positive at a titre of 1/320, 1/160 and 1/320 respectively. In addition the CSF Wright agglutination test was positive at a titer of 1/640. The patient was discharged with oral antibiotics including Rifampin 15mg/kg/day, Cotrimoxazole 15 mg/kg/day and Doxycycline 5 mg/kg/day.

On follow-up visit one month after the initiation of treatment, symptoms had improved. Brain MR imaging demonstrated partial improvement of the basal cistern enhancement and thickening and also mildly smaller brain stem enhancing lesions. Spinal meningeal/intrathecal nodular enhancement also persisted with smaller size. Three months later (four months after beginning of anti-brucellosis treatment), however, imaging findings showed marked improvement (Fig. 2, Fig. 3) with minimal remained abnormal enhancement and nodularity. At this visit patient had no clinical complaint and achieved a normal function. No abnormality was detected on clinical exam.

DISCUSSION

Etiology & Demographics:

Brucellosis is an infectious zoonotic disease which is transmitted to humans via consumption of contaminated products of domestic animals and unpasteurized dairy products in particular [1]. The high risk areas worldwide include the Mediterranean basin, Mexico, South and Central America, Eastern Europe, Asia, Africa, the Caribbean and the Middle East [2]. Neurobrucellosis is a rare and serious complication of the disease. The pediatric neurobrucellosis unlike the nervous system infection in adults which can manifest as acute or chronic, usually presents itself with acute symptoms [3]. Despite its 7% prevalence in adult patients with brucellosis, neurobrucellosis is quite rare in the pediatric age group and consists about 0.8% of brucellosis cases [4]. Nevertheless in an endemic area for brucellosis and its complications such as Iran [5] (the country from which the case is presented), neurobrucellosis should be considered in patients with pertinent symptoms.

Clinical & Imaging findings:

One difficulty in diagnosing brucellosis is the vast range of signs and symptoms it can present with and their un-specificity. Brucellosis symptoms and signs include arthralgia, fever, fatigue, sweating, lack of appetite, weight loss, myalgia, chills, upper and lower back pain, nausea and vomiting, abdominal pain, headache, cough, epistaxis, scrotal pain, psychosis, depression, confusion, hearing loss, ataxia, lower limb weakness, splenomegaly, hepatomegaly, lymphadenopathy, osteoarticular involvement, CNS involvement, stiff neck, endocarditis, cardiovascular involvement, skin lesion, rash, peritonitis, epididymo-orchitis, prostatitis and genitourinary system involvement [6]. The involvement of the nervous system can lead to meningitis, encephalitis, meningoencephalitis, cerebellar dysfunction, radiculitis, myelitis, epidural abscess, meningovascular disease, involvement of cranial nerves, seizure, brain abscess,

and demyelination problems [4,7]. More rare cases have presented with hydrocephalus, intracranial hypertension, papilledema, recurrent transient ischemic attacks, pseudotumor cerebri and diabetes insipidus [3,7-11].

Based on the clinical manifestations the patients suffering from neurobrucellosis can be divided into four categories: CNS involvement, PNS involvement, combined CNS and PNS involvement and isolated hearing loss. Walid et al. classified the radiologic presentations as follows: normal, inflammation (abnormal enhancement), white matter changes, and vascular changes [12]. Neuroimaging in our patient demonstrated findings associated with inflammation and white matter involvement. The literature review shows that granulomatous formation is rare in the sellar/suprasellar regions [12]. In our patient while no sample was taken from the suprasellar region lesions, the pathologic evaluation of the thickened spinal meningeal layers which were similar to that of the suprasellar region on MRI (Fig 1. a) was consisted of histiocytes and resembled granulomatous formation. These focal lesions however resolved remarkably after treatment. The MR imaging also demonstrated thickening and diffuse meningeal enhancement around the brain stem in our patient. This change which is also indicative of inflammatory reaction has been formerly described [12]. Intraaxial white matter lesions are observed in the brain stem as nodular and ring enhancing lesions. No vascular change was observed. The spinal MR imaging also demonstrated meningeal enhancement, nodular enhancing granulomatous formation intrathecally and nerve root enhancement of cauda equina. Epidural collections are also visible in the cervical spine.

Radiological presentations of neurobrucellosis are also diverse and might be different in each individual. It would be of advantage to be familiar with the different neuroimaging presentations of neurobrucellosis including white matter hyperintense lesions, white matter hypoattenuation, enhancing granuloma, meningeal enhancement, nerve root enhancement, atrophy and also normal brain and spinal imaging [12].

The patient underwent brain and spine MR imaging four months after the initiation of treatment. The focal brain stem lesions which presumed to be granulomas showed remarkable improvement.

Treatment & Prognosis:

Main treatment for neurobrucellosis is regimen of antibiotics including Rifampin 15mg/kg/day, Cotrimoxazole 15 mg/kg/day and Doxycycline 5 mg/kg/day. Despite the disabling symptoms that the patients present with, neurobrucellosis rarely leaves any permanent sequelae provided that adequate treatment is started early and maintained for an adequate time [8,13-15]. However, although our patient unlike most cases of pediatric neurobrucellosis had suffered from a chronic course of disease and her symptoms deteriorated due to delayed diagnosis, her symptoms improved completely after adequate treatment. The prolonged time of diagnosis might be attributable to the nonspecific constitutional symptoms and low level of suspicion despite the high probability of the disease.

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Differential Diagnosis:

Granulomatous meningoencephalitis, mainly tuberculosis (TB), is an important differential diagnosis which can show similar clinical and nervous system imaging findings. There are a few differentiating points such as:

1. Lung involvement may be presented in CXR of patients with TB infection.
2. Presence of gas/air would make brucellosis more likely (Fig 2. e, f); as air/gas is never found in spinal TB or any other granulomatous infection (e.g. sarcoidosis).
3. Spinal TB would often result in spine biopsy for confirmation in such cases; which does not add to the diagnosis for brucellosis and final confirmation is by blood culture or serology.

Another differential diagnosis of neurobrucellosis is meningeal carcinomatosis that demonstrates thickening and diffuse meningeal enhancement in patients with history of cancer. Advanced imaging such as CT perfusion would add value. It helps in differentiation of infection from leptomeningeal metastases, but has limitations.

TEACHING POINT

Neurobrucellosis is a serious complication of brucellosis and despite its rarity it should be suspected with almost any neurologic sign, especially in endemic areas. The clinical and radiological presentations of the disease are extremely diverse and tend to mimic a variety of other conditions, especially TB meningoencephalitis. Hence it is important that brucellosis would be suspected and the history of unpasteurized dairy product consumption would be sought to make early diagnosis by the means of brucella serologic tests.

REFERENCES

1. Corbel MJ. Brucellosis in Humans and Animals. World Health Organization, Food and Agriculture Organization of the United Nations, World Organization for Animal Health; Geneva, Switzerland: 2006.
2. Centers for disease control and prevention. Areas at Risk of brucellosis. www.cdc.gov/brucellosis/exposure/areas.html
3. Altas M, Evirgen O, Arica V, Tutanc M. Pediatric neurobrucellosis associated with hydrocephalus. J Pediatr Neurosci. 2011;5(2):144-6. PMID: 21559164
4. Habeeb YK, Al-Najdi AK, Sadek SA, Al-Onaizi E. Paediatric neurobrucellosis: case report and literature review. J Infect. 1998;37(1):59-62. PMID: 9733381
5. Sofian M, Aghakhani A, Velayati AA, Banifazl M, Eslamifard A, Ramezani A. Risk factors for human brucellosis in Iran: a case-control study. Int J Infect Dis. 2007;12(2):157-61. PMID: 17698385

6. Buzgan T, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evirgen O, et al. Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. *Int J Infect Dis.* 2009;14(6):e469-78. PMID: 19910232

7. Gul HC, Erdem H, Bek S. Overview of neurobrucellosis: a pooled analysis of 187 cases. *Int J Infect Dis.* 2009;13(6):e339-43. PMID: 19428283

8. Akhondian J, Ashrafzadeh F, Toosi M, Hashemi N. A Rare presentation of neurobrucellosis in a child with Recurrent transient ischemic attacks and pseudotumor cerebri (A case report and review of literature). *Iran J Child Neurol.* 2014;8(2):65-9. PMID: 24949055

9. Ozisik HI, Ersoy Y, Refik Tevfik M, Kizkin S, Ozcan C. Isolated intracranial hypertension: a rare presentation of neurobrucellosis. *Microbes Infect.* 2004;6(9):861-3. PMID: 15374008

10. Trifiletti RR, Restivo DA, Pavone P, Giuffrida S, Parano E. Diabetes insipidus in neurobrucellosis. *Clin Neurol Neurosurg.* 2000;102(3):163-5. PMID: 10996715

11. Yilmaz S, Serdaroglu G, Gokben S, Tekgul H. A case of neurobrucellosis presenting with isolated intracranial hypertension. *J Child Neurol.* 2011;26(10):1316-8. PMID: 21551370

12. Al-Sous MW, Bohlega S, Al-Kawi MZ, Alwatban J, McLean DR. Neurobrucellosis: clinical and neuroimaging correlation. *AJNR Am J Neuroradiol.* 2004;25(3):395-401. PMID: 15037461

13. Al Deeb SM, Yaqub BA, Sharif HS, Phadke JG. Neurobrucellosis Clinical characteristics, diagnosis, and outcome. *Neurology.* 1989;39(4):498-501. PMID: 2927673

14. Guven T, Ugurlu K, Ergonul O, Celikbas AK, Gok SE, Comoglu S, et al. Neurobrucellosis: clinical and diagnostic features. *Clin Infect Dis.* 2013;56(10):1407-12. PMID: 23446629

15. Hendaus MA, Qaqish RM, Alhammad AH. Neurobrucellosis in children. *Asian Pacific Journal of Tropical Biomedicine.* 2015;5(2):158-61. DOI: 10.1016/S2221-1691(15)30160-X

FIGURES



Figure 1: 9-year-old girl with neurobrucellosis.

FINDINGS: Primary brain CT scan without IV contrast, axial section at the level of lateral ventricles shows acute hydrocephalus as dilatation of ventricular bodies (asterisk) and adjacent parenchymal hypoattenuation suggestive of interstitial edema (arrow).

TECHNIQUE: CT scan examination of the brain without contrast, using Emotion 16 CT scanner (Siemens, Erlangen, Germany).

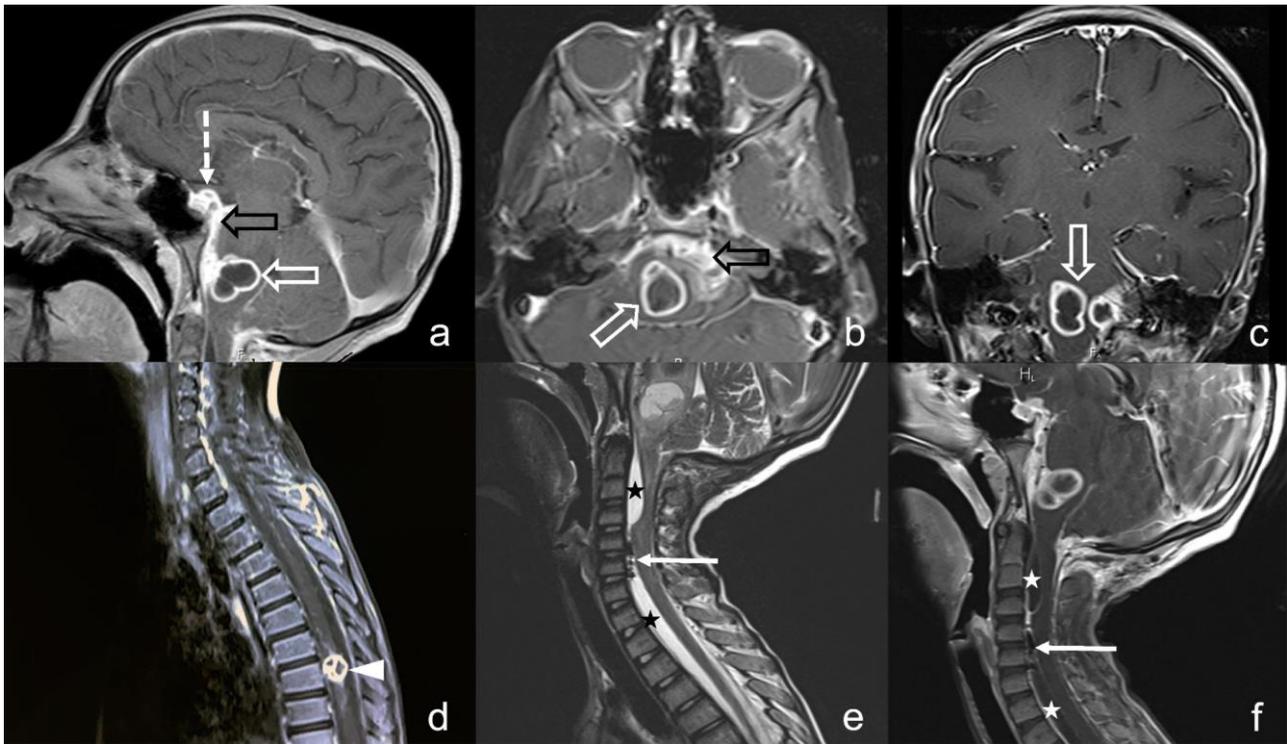


Figure 2: 9-year-old girl with neurobrucellosis.

FINDINGS: In pretreatment brain MRI, sagittal, axial and coronal sections of post contrast T1 weighted images (a, b and c), show thickening and abnormal enhancement in basal cisterns (black arrows) including suprasellar cistern (dashed arrow) with invasion to brain stem and resultant ring enhancing lesions (white arrows). Sagittal post contrast T1 weighted images of thoracic spine MRI (d) revealed a heterogeneously enhancing extramedullary intradural mass at T7-8 level (arrowhead) and more extensive intrathecal/meningeal nodular enhancement. Sagittal cervical spine images in T2 weighted and post contrast T1 weighted sequences (e and f), show two fluid intensity anterior epidural collections with thin enhancing walls (asterisks). Air bubbles are seen in the more inferior collection as signal void foci (thin solid arrows).

TECHNIQUE: MRI examination of the brain and spine, multiplanar post contrast T1 weighted and T2 weighted sequences, using 3.0 Tesla MAGNETOM TIM Trio MR system (Siemens, Erlangen, Germany).

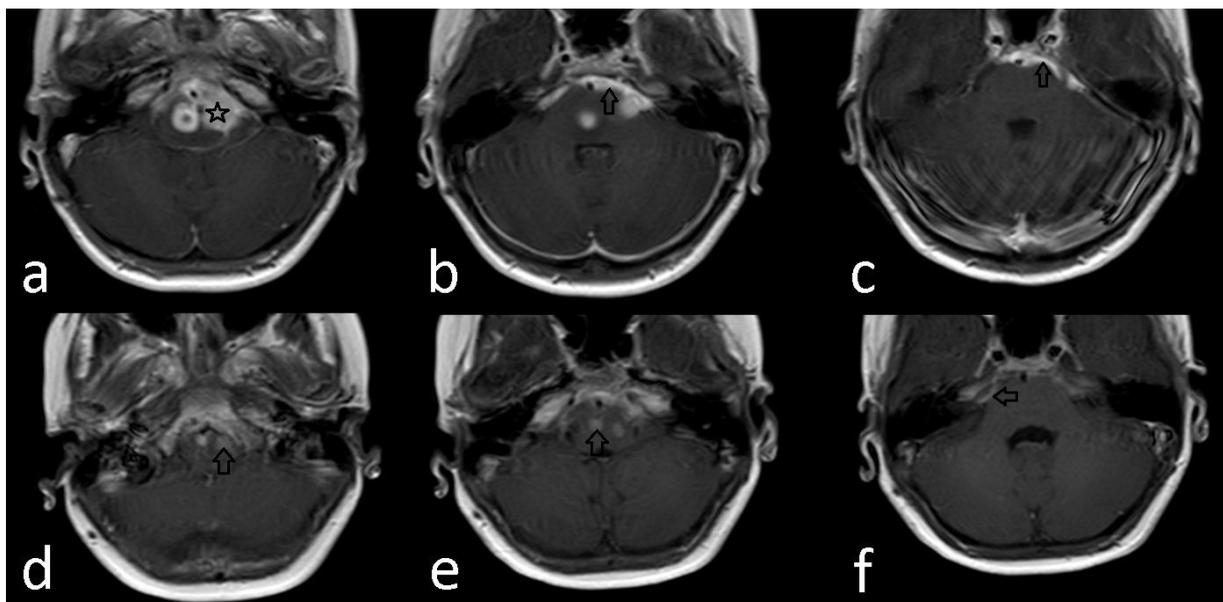


Figure 3: 9-year-old girl with neurobrucellosis (one and four months after treatment).

FINDINGS: One month post-treatment follow up, post contrast T1 weighted brain MRI in axial sections from brain stem at the level of pons and medulla (a, b and c) displays thick prepontine cistern enhancement (arrows) with invasion to brain stem (*). In four month post-treatment follow up, post contrast T1 weighted brain MRI in axial sections (d, e and f) demonstrate significant improvement both in the prepontine cistern enhancement and brain stem lesions (arrows).

TECHNIQUE: MRI examination of the brain, post contrast T1 weighted sequences in axial planes from posterior fossa, using 1.5 Tesla Ingenia MRI system (Philips Healthcare, Netherlands).

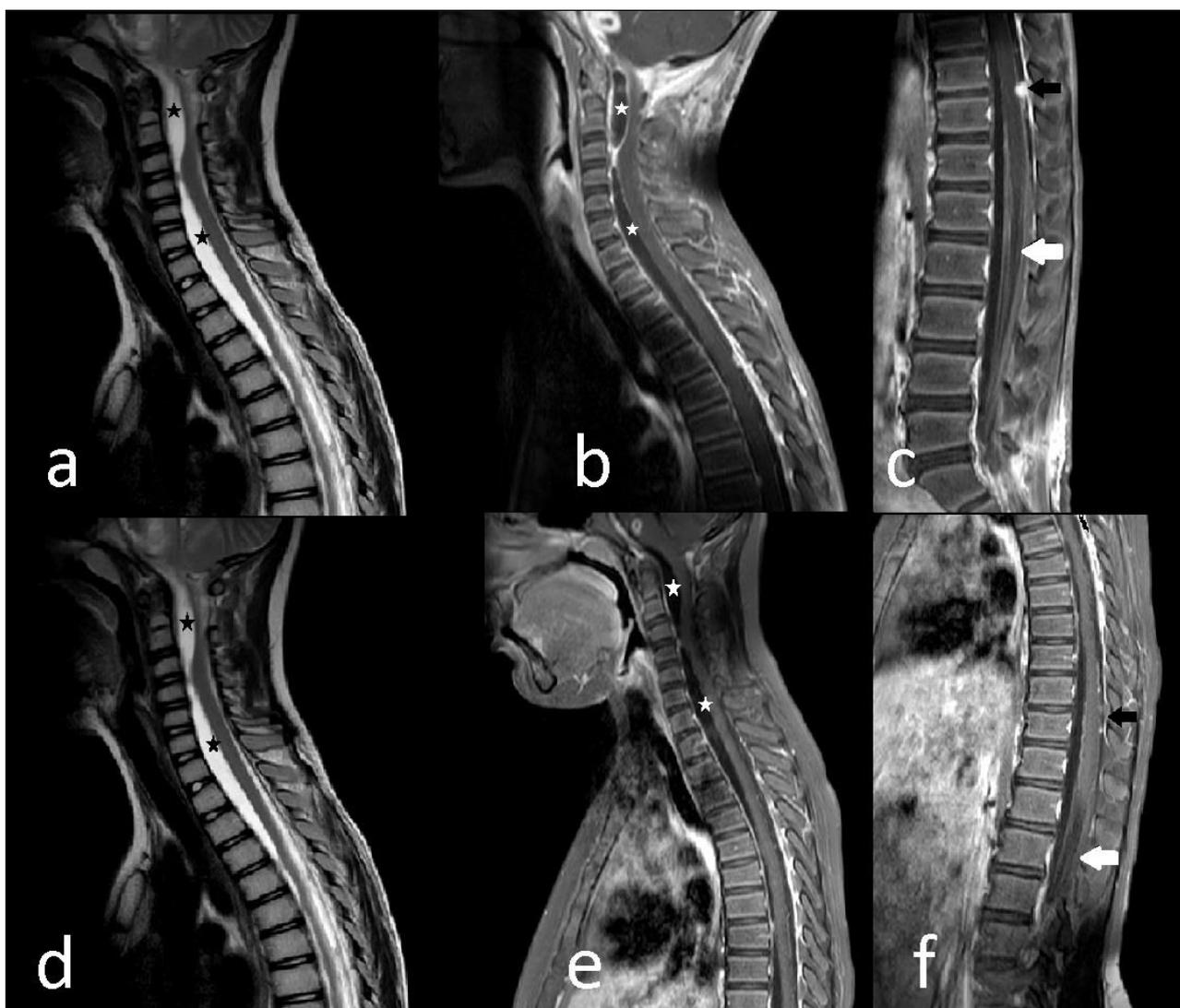


Figure 4: 9-year-old girl with neurobrucellosis (one and four months after treatment).

FINDINGS: Sagittal section T2 weighted MRI images from cervical spine (a and d) and sagittal section post contrast T1 weighted images from cervical spine (b and e) and lumbar spine (c and f) are presented. First row images are taken one month after initiation of treatment and second row images, after four months. Two epidural collections anterior to the cervical spinal canal (*) become smaller without mural enhancement after four months of treatment. The intrathecal nodular enhancement (black arrows) and cauda equina enhancement (white arrows) are also almost resolved four months after treatment.

TECHNIQUE: MRI examination of the brain, T2 weighted and post contrast T1 weighted sequences in sagittal planes from spine, using 1.5 Tesla Ingenia MRI system (Philips Healthcare, Netherlands).

Etiology	Bacterial genus <i>Brucella</i>
Prevalence	7% in adult brucellosis cases and rare in the pediatric age group and consists of 0.8% of brucellosis cases
Age predilection	More common in adults
Risk factors	Ingestion of unpasteurized milk or undercooked meat
Treatment	Antibiotic drugs
Prognosis	Rarely leaves any permanent sequelae provided that adequate treatment is started early and maintained for an adequate time
Finding on imaging	Different in each individual including white matter hyperintense lesions, white matter hypoattenuation, enhancing granuloma, meningeal enhancement, nerve root enhancement, atrophy and also normal brain and spinal imaging

Table 1: Summary table of neurobrucellosis

DDx	X-ray	CT	MRI	Postcontrast	Scintigraphy	PET
Granulomatous meningoencephalitis (e.g. Tuberculosis)	CXR may show lung involvement	Absent air/gas	Parenchymal granuloma, meningeal thickening	Enhancing granuloma, meningeal enhancement, nerve root enhancement	Not specific	Not specific
Meningeal carcinomatosis	CXR may show primary disease or pulmonary metastases	Not specific	Meningeal thickening	Meningeal enhancement	Not specific	Not specific

Table 2: Differential diagnosis table for neurobrucellosis

ABBREVIATIONS

CBC = Complete Blood Count
 PPD = Purified Protein Derivative
 IGRA = Interferon Gamma Release Assay
 TB PCR = Tuberculosis Polymerase Chain Reaction
 CT = Computerized Tomography
 MRI = Magnetic Resonance Imaging
 CSF = Cerebrospinal Fluid
 CNS = Central Nervous System
 PNS = Peripheral Nervous System

KEYWORDS

Neurobrucellosis; Brucellosis; Pediatric; Nervous System; MRI

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