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CASE REPORT

A extremely rare case of cervical intramedullary granuloma due to *Brucella* accompanied by Chiari Type-1 malformation

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ABSTRACT

Chiari Type-1 malformation is displacement of the cerebellar tonsils through the foramen magnum into the cervical spine and usually does not exceed the level of C2. It is 50-70% associated with syringomyelia. Nervous system involvement due to brucellosis is called neurobrucellosis, and neurological involvement rate has been reported an average of 3-5%, ranging between 3% and 25% at different series. Intramedullary abscess or granuloma due to *Brucella* is extremely rare. Hence far, six cases have been reported in the literature and only two of these cases were reported as intramedullary granuloma. This case is presented in order to remind the importance of the cervical cord granuloma which was presented once before in the literature and to emphasize the importance of evaluation of patient history, clinical and radiological findings together in the evaluation of a patient.

Key words: *Brucella*, cervical region, Chiari Type-1 malformation, spinal intramedullary granuloma

Introduction

Chiari malformation is a congenital anomaly of hindbrain with displacement of brain stem and cerebellum into the cervical canal. Chiari malformation is divided into four types. Type-1, 2 and 3 include herniation of hindbrain at different degrees in the posterior fossa. There is also cerebellar hypoplasia or aplasia in Chiari Type-4. Chiari Type-1 malformation is displacement of the cerebellar tonsils through the foramen magnum into the cervical spine and usually does not exceed the level of C2. It is 50-70% associated with syringomyelia. The most common complaint is headache, and sensory loss, motor loss, sleep apnea, lower cranial nerve abnormalities, upper-motor neuron symptoms may occur.

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Brucellosis is a zoonosis, caused by *Brucella* bacteria, which can involve many tissues and system in humans and lead to different clinical circumstances. Brucellosis is transmitted by direct contact with infected animals or ingestion of unpasteurized milk and milk products of infected animals. High fever, sweating, muscle and joint pain are most common symptoms. Brucellosis is an endemic systemic infectious disease in Middle East, India, Mexico, Caribbean, Eastern Europe, Central, and South American countries and Mediterranean Basin (Turkey, Portugal, Spain, Italy, Greece, Southern France, North Africa).[1] Nervous system involvement due to brucellosis is called neurobrucellosis, and neurological involvement rate has been reported an average of 3-5%, ranging between 3% and 25% at different series.[2-4] Neurological situations in neurobrucellosis are highly variable and may be in the form of meningitis, encephalitis, myelitis-radiculoneuritis, brain abscess, epidural abscess, spinal abscess, granuloma, demyelinating and meningovascular syndromes.[1] Neurobrucellosis can cause significant morbidity and mortality if not detected and treated early. There is no specific symptom of brucellosis due to involvement of the spinal cord, clinical findings occur due to compression of the spinal cord by abscess or granuloma and early diagnosis is difficult unless there is compression. Intramedullary abscess or granuloma due to *Brucella* is extremely rare. Hence far, six cases have been reported in the literature[4,5] and only two of these cases were reported as intramedullary granuloma.[5,6] This case is presented in order to remind the importance of the cervical cord granuloma which

was presented once before in the literature and to emphasize the importance of evaluation of patient history, clinical and radiological findings together in the evaluation of a patient.

Case Report

19-year-old male patient was admitted to our clinic complaining of numbness in the right arm and leg. From patient's history, it was learned that the patient had numbness in right arm and a leg for about 15 days, difficulty in walking and holding objects, the patient had been admitted to another center with these complaints and diagnosed with Chiari Type-1 malformation and syringomyelia after brain and cervical magnetic resonance imaging (MRI) and that the operation had been proposed. In addition, it was learned that the patient had been diagnosed with brucellosis 6 months ago with complaints of fever, night sweats, nausea and vomiting and he had had rifampicin, cotrimoxazole treatment for about a month and he had discontinued the treatment due to improvement of his complaints. Physical examination of the patient revealed 36°C fever, 120/70 mmHg blood pressure and 82/min pulse rate and systemic examination was normal. Neurological examination revealed right hemihypoesthesia and right hemiparesis (grade: 4/5).

Laboratory tests were as follows; white blood cell count: 9610/mm^3 (N: 4500-11000) (72.6% granulocytes, 20.3% lymphocytes, 5.1% monocytes), hemoglobin 15.6 g/dl (N: 12-16), platelet count: 224,000/mm^3 (N: 130.000-400.000), C-reactive protein <3 mg/L (N: 0-6), erythrocyte sedimentation rate: 2 mm/h (N: 0-20), creatinine 0.7 mg/dl (N: 0.3-1.4). Cervical MRI of the patient revealed Chiari malformation Type-1, spinal cord edema which is hyperintense on T2-weighted series and isointense on T1-weighted series between C2 and C4 vertebral levels, nodular enhancing intramedullary lesion at the level of C2 vertebra [Figure 1a-c]. Intramedullary tumors, granulomatous infections, were considered in the differential diagnosis. Because of previous brucellosis diagnosis and early cessation of treatment, *Brucella* tube agglutination test was performed, and rose Bengal test was found positive, and *Brucella* tube agglutination test was found positive at 1/1280 titer. Lumbar puncture (L/P) was performed regarding neurobrucellosis. Cerebrospinal fluid (CSF) biochemistry examination revealed 110 mg/dl protein, 45 mg/dl glucose (simultaneous blood glucose is 98 mg/dl), 100/mm^3 (16% granulocytes, 84% lymphocytes) cell count. CSF *Brucella* tube agglutination was positive at 1/8 titer. CSF cultures were negative.

After being diagnosed with cervical intramedullary granuloma due to *Brucella*, 600 mg/day rifampicin, 200 mg/day doxycycline and 320/1600 mg/day co-trimoxazole treatment was started by the department of infectious diseases. After 2 weeks, a control L/P was performed. CSF biochemistry examination revealed 93 mg/dl protein, 47 mg/dl glucose, 50/mm^3 (4% granulocytes, 96% lymphocytes) cell count and CSF *Brucella*

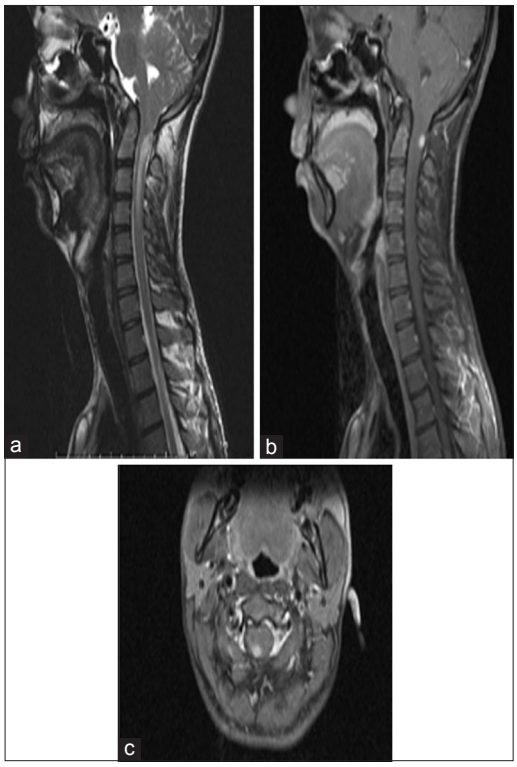

Figure 1: (a) Sagittal T2-weighted, (b) sagittal contrast-enhanced T1-weighted and (c) axial contrast-enhanced T1-weighted cervical spinal magnetic resonance imaging revealed Chiari malformation Type-1 and syringomyelia and/or spinal cord edema which is hyperintense on T2-weighted series and isointense on T1-weighted series between C2 and C4 vertebral levels, nodular enhancing intramedullary lesion at the level of C2 vertebra

tube agglutination was negative. Complaint of numbness in the right side was partially reduced under treatment. At the 2nd month of the therapy, decrease in size of the granuloma and regression of cord edema were seen on cervical MRI. At 6 months of treatment, the patient's complaints and neurological examination completely resolved and granuloma was found to be completely disappeared, and minimal edema was seen on cervical MRI [Figure 2a and b] The patient's antibiotic therapy was terminated due to complete clinical, laboratory and radiological improvement at 6th month. The existence of Chiari I malformation was most probably a coincidence rather than a sequel and follow-up for Chiari malformation was scheduled.

Discussion

Brucellosis is the most common zoonotic infection in the world and is still endemic in our country. Infection spreads to organs such as bone marrow, kidney, spleen, lymph nodes, liver that are particularly rich in the reticuloendothelial system and central nervous system involvement may be by direct hematogenous way and due to spondylitis.

Most common complication of brucellosis due to involvement of the central nervous system is meningitis and rate increases

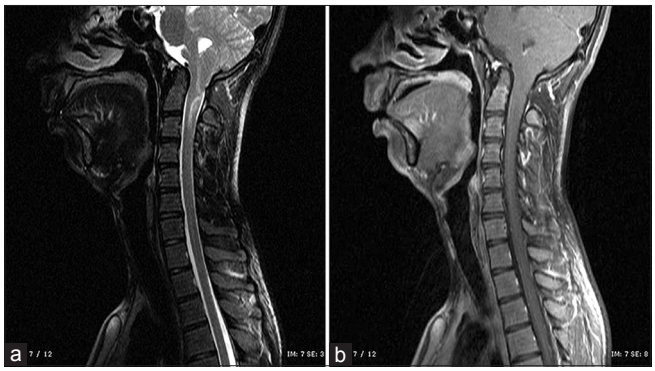

Figure 2: At 6 months of treatment, the patient's complaints and neurological examination completely resolved and granuloma was found to be completely disappeared, and minimal edema was seen on cervical spinal magnetic resonance imaging; (a) sagittal T2-weighted and (b) sagittal contrast-enhanced T1-weighted

to about 50%. Intramedullary abscess or granuloma is an extremely rare complication, and only six cases have been reported in the literature.[5]

Nervous system involvement due to brucellosis can be acute and chronic, and can cause different clinical presentations ranging from minimal local disease to diffuse disease. This variable atypical presentation can also be caused by mycobacterium tuberculosis, *Leptospira* species, *Borrelia burgderferi*, so these can cause difficulties in the differential diagnosis of neurobrucellosis. Hemophilus meningitis, central nervous system syphilis, paralytic poliomyelitis, lymphocyticchoriomeningitis and spinal tumors should also be considered in the differential diagnosis.[7] In our case, differential diagnosis becomes more difficult due to the presence of Chiari Type-1 malformation and possible misdiagnosis of cord edema with syringomyelia. Granulomatous reaction due to infection in the spine is more common in tuberculosis. Spinal cord compression due to tuberculosis is 26.7%, and this rate is reported as 10.5% in *Brucella*.[8]

Diagnostic criteria of neurobrucellosis are unexplained neurological symptoms, >1/160 titer blood *Brucella* agglutination, positive CSF *Brucella* tube agglutination test at any titers, protein and lymphocyte increase in CSF and dramatically responding to antibiotic treatment.[9,10] Similarly, in our case, right hemiparesis associated with intramedullary granuloma, *Brucella* blood agglutination test positivity at 1/1280 titer, CSF *Brucella* tube agglutination test positivity at 1/8 titer and improvement of neurological deficits by antibiotic treatment confirm the diagnosis.

There is no specific antibiotic regimen and duration in medical treatment of neurobrucellosis. The generally accepted protocol is together application of two or three drugs that can pass the blood-brain barrier (rifampicin, trimethoprim-sulfamethoxazole, ceftriaxone, etc.) along with doxycycline for a couple of months (3-12 months).[11] In our case, rifampin, doxycycline, and co-trimoxazole were in combination for 6 months, and clinical, radiological and laboratory findings improved.

Al-Sous *et al*. reported that clinical and radiological correlation of neurobrucellosis is variable.[12] Radiological findings of neurobrucellosis were classified under four main headings: Normal findings, inflammation (abnormal contrast enhancement), white matter changes and vascular changes. Inflammation in neurobrucellosis is radiologically determined by granulomas and contrast enhancement of meninges, perivascular area and lumbar nerve roots. In our case, Chiari Type-1 malformation with edema between C2 and C4 vertebral levels and intramedullary localized nodular enhancing lesion at the level of C2 vertebra were detected by radiological imaging.

Spinal involvement due to *Brucella* is mostly extramedullary, and six intramedullary cases have been reported in the literature. Vajramani *et al.* detected an abscess at the level of conus in a patient with paraplegia, patient's laboratory findings were found to be compatible with neurobrucellosis and the agent was reported as *Brucella* melitensis from the surgical drainage sample.[4] Bingöl *et al.* reported that clinic and radiological findings had been improved after medical treatment for about 4 months in a patient with intramedullary granuloma and surrounding edema at T5 level.[6] In the case of intramedullary dermoid cyst reported by Cokça *et al.*, the agent was *Brucella* abortus, and medical treatment was given following surgical drainage of abscess.[13] Helvaci *et al.* surgically drained and gave medical treatment to the patient who had been diagnosed with neurobrucellosis with intramedullary abscess at T11-T12 level and laboratory findings. Clinical symptoms of the patient were improved.[14] Nas *et al.* reported that the patient with intramedullary granuloma at C1-C2 level had only received medical treatment and recovered without sequelae.[5] Novati *et al.* reported complete relief of a patient with a 15 mm diameter focal abscess at dorsal spinal cord and growth of *Brucella* melitensis in blood and bone marrow culture after 6 months of antibiotic treatment.[15] In our case, with 6 months of antibiotic treatment of intramedullary granuloma, which is a rare complication of brucellosis, radiological and clinical improvements were seen.

Treatment of spinal brucellosis includes bed rest, nonsteroidal antiinflammatory drugs, antibiotics and surgical intervention. Initially, neurological symptoms were considered as an indication for surgery, but in recent years surprisingly good response to medical treatment led to consideration of surgery as a last option.[6] However, involvement of multiple spine levels, spinal cord compression and instability are indications for early surgical intervention.[16] In our case, due to small size of the lesion and lesion being granuloma instead of abscesses, surgical treatment was not considered in the first place. In addition, due to the patient being previously diagnosed with brucellosis and clinical and laboratory findings supporting the diagnosis of brucellosis, no biopsy was done.

Conclusions

In *Brucella* endemic areas, in patients presenting with intramedullary mass, neurobrucellosis should be considered. The quality of the imaging methods is also important in the differential diagnosis. Follow-up only with medical therapy in patients without neurological deficit is adequate, whereas implementation of a combined surgical and medical therapy is appropriate in patients with neurological deficit.

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