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Magnetic Resonance Imaging Findings of Pediatric Neurobrucellosis

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Abstract

Brucellosis is an endemic disease often observed in the Mediterranean and Middle East regions. Systemic brucellosis is the most frequent clinical form of this infection; however, hematogenic spread may result in the focal form of the disease. Neurobrucellosis is a rare disease seen in 0, 5-25 % of the adults with systemic brucellosis. 0,8 % of the children affected by systemic brucellosis are reported to have neurological complications. A 16 year old female applied with the complaints of headache, vomiting, bilateral hip and knee pain, and inability to walk. Physical and laboratory examination, brain computed tomography (CT) brain and cervical spinal MRI were carried out as well as the magnetic resonance spectroscopy (MRS) of the lesion areas in the brain. On MRI hydrocephaly in 3rd, 4th and lateral ventricles, atrophic dilatation in bilateral hemispheric cortical sulcuses were seen. On T2W and FLAIR images, hyperintense focal nodular lesions not accompanied by pathological contrast enhancement were detected on parietal subcortical white matter and the periventricular deep white matter. Dural thickening and contrast enhancement on the bilateral parietal region were observed. On cervical spinal MRI, leptomeningeal enhancing was at the level of C1-C7. On MRS applied to lesions in brain (TE 136 and 31 ms), lactate peak at 1.3 ppm was observed. In the differential diagnosis of central nervous system diseases in children living in endemic regions, neurobrucellosis should be kept in mind, though observed rarely. In these cases, the neurological system involvement that cannot be demonstrated via CT, can be shown with MRI effectively.

Key words: Neurobrucellosis, magnetic resonance imaging, magnetic resonance spectroscopy, pediatric

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Introduction

Brucellosis, also called as "ondulant fever" or "malta fever" is an endemic disease often observed in Mediterranean and Middle East regions. Infection can be transmitted to humans through direct contact with infected animals and consumption of unpasteurized milk and milk products. Although it is primarily a zoonotic infection, it can also affect human health and various organ systems. Characteristically, an acute bacteriemic phase and subsequently a chronic period containing various tissues are observed [1]. Systemic brucellosis is the most frequent clinical form of this infection; however, hematogenic spread may result in the focal form of the disease. Neurobrucellosis is a rare disease observed in 0, 5-25 % of the adults with systemic brucellosis. While observed in children quite seldom, 0,8 % of the children affected with systemic brucellosis are reported to have neurological complications [2].

The clinical presentation, laboratory diagnosis and the treatment of the disease is widely discussed; nevertheless, the number of the publications about its radiological findings is limited.

In this study, we aim to present the magnetic resonance imaging (MRI) findings of the central neural system (CNS) involvement of brucellosis observed rarely at the pediatric age group.

Case Report

A 16-year-old female applied with the complaints of headache, vomiting, bilateral hip and knee pain, and inability to walk. She has had these complaints for two months. She suffered from vomiting without bile 2-3 times per day, from time to time rising fever, severe hip and knee pain and headache, responding to painkiller. She was given antibiotics by the doctor she applied with abovementioned complaints. However the patient did not use the treatment properly and no important improvement was observed on her complaints. By the increased vomiting and lack of appetite, she lost weight. Subsequently, the patient's situation did not show any improvement and in general patient, who was not able to walk without support, was refered to our clinic.

During the physical examination of the patient, pale skin, cachectic appearance, clear atrophy and motor weakness on upper and lower extremity muscles, glove and stocking sensory loss, stiff neck were observed. By walking, she swayed from side to side. The deep tendon reflexes

in lower extremity distals were hypoactive. Cardiopulmoner system and abdomen examinations were ordinary.

The routine blood biochemical and urine examinations were in normals. At lumbar puncture; yellow appearance, pressure 14 cmH2O, glucose 6 mg/dL (simultaneously blood glucose 109 mg/dL), protein 647 mg/dL, 300 cells/mm3 (90% polymorphonuclear leucocyte) in strain microscopy. Blood and CSF cultures were negative and in brucellar agglutination tests, brucellosis antibodies were determined (Rose Bengal positive, Wright 1/60, Coombs anti-serum 1/1280). Blood brucellosis antibody titre; 1/320, CSF brucellosis antibody titre; 1/160) Tuberculosis PCR and acid-fast staining were negative in CSF and gastric fluide. Venereal disease research laboratory (VDRL) was negative.

In electromyographic exam of the right lower and upper extremity; deceleration was found in motor transmission in bilaterally sciatic and left tibialis posterior nerves. Motor transmission was negative in bilaterally peroneal nerves.

The case was examined with brain and cervical spinal MRI and MRS in lesion areas in the brain. MRI was performed on a 1.5 T scanner (Gyroscan, Intera Master, Philips, Best, Netherlands). T1-weighted (TR/TE: 450/10ms) axial, T2-weighted (TR/TE: 4850/120ms) axial and sagittal, and fluid attenuated inversion recovery (FLAIR) coronal images were obtained. On MRI hydrocephaly in 3rd, 4th and lateral ventricles, atrophic dilatations in bilateral hemispheric cortical sulcuses were seen. On T2W and FLAIR images, hyperintense focal nodular lesions not accompanied by pathological contrast enhancement were detected on parietal subcortical white matter and the periventricular deep white matter. Dural thickening and contrast enhancement on the bilateral parietal region were observed (Figure 1A-C). On cervical spinal MRI, leptomeningeal enhancing was at the level of C1-C7. On MRS applied to lesions in brain (TE 136 and 31 ms) by using the point resolved spectroscopy technique, Lactate peak at 1.3 ppm was observed (Figure 2). N-Acetyl aspartate, choline and creatine were within normal limits.

Figure 1. Axial (A), sagittal (B) T2 weighted images and coronal FLAIR image (C). Hyperintense white matter lesions on left frontal and bilateral parietal subcortical and the periventricular deep white matter.

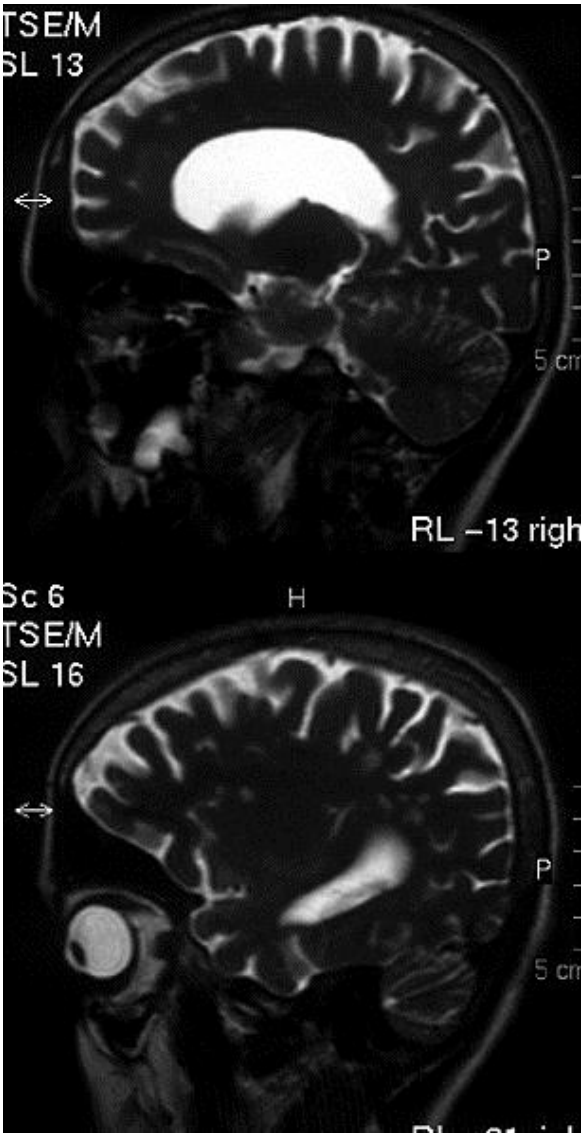
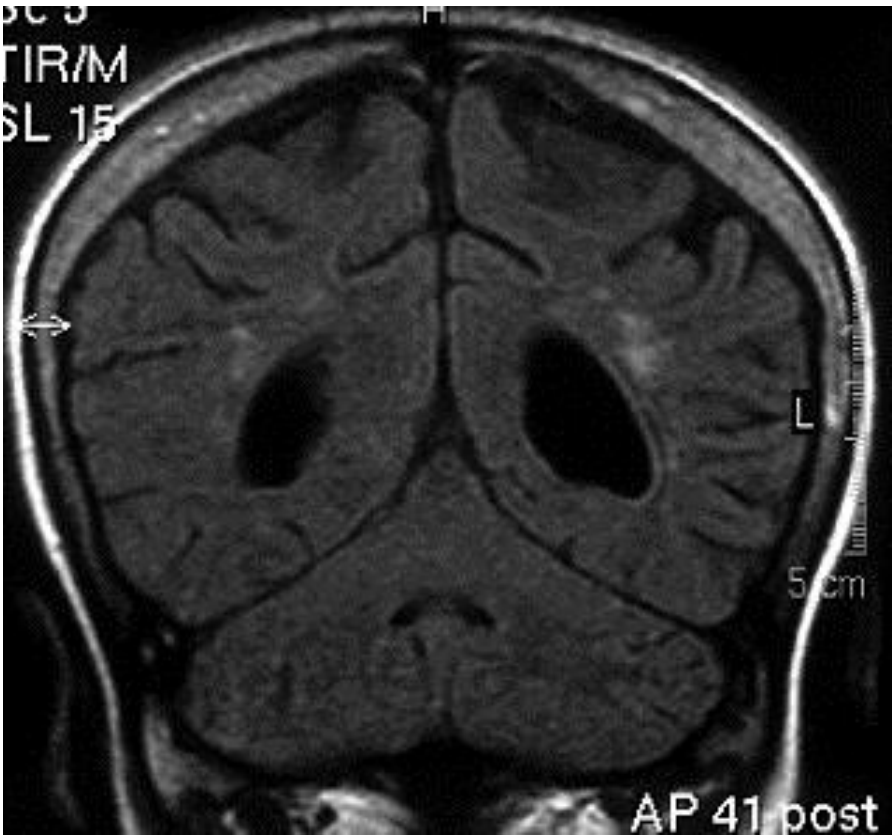


Figure-1A.



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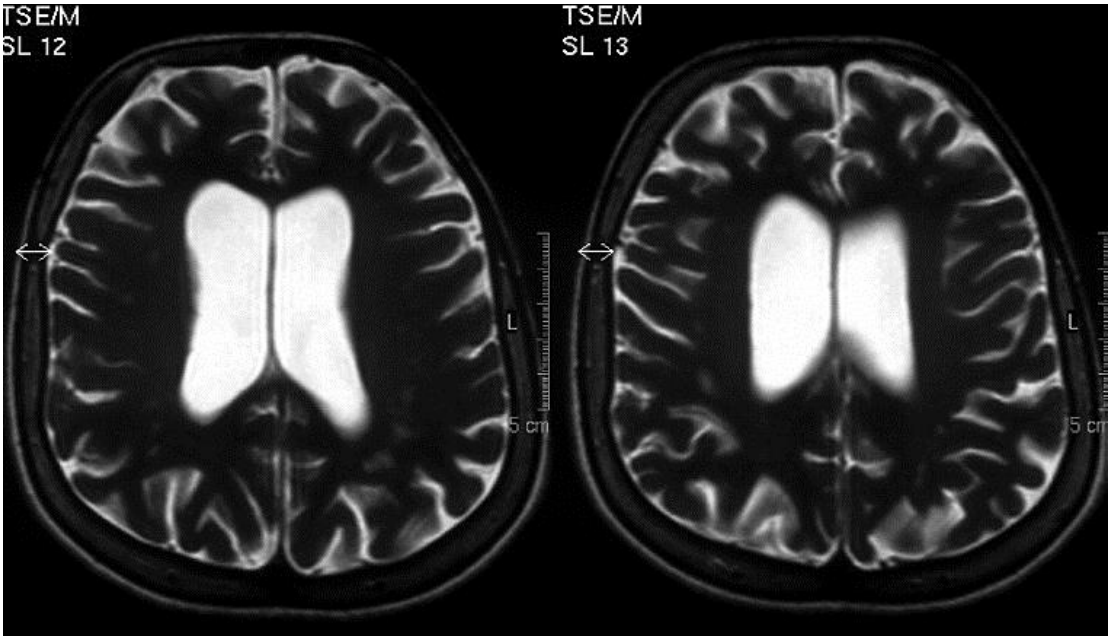

Figure-1C.

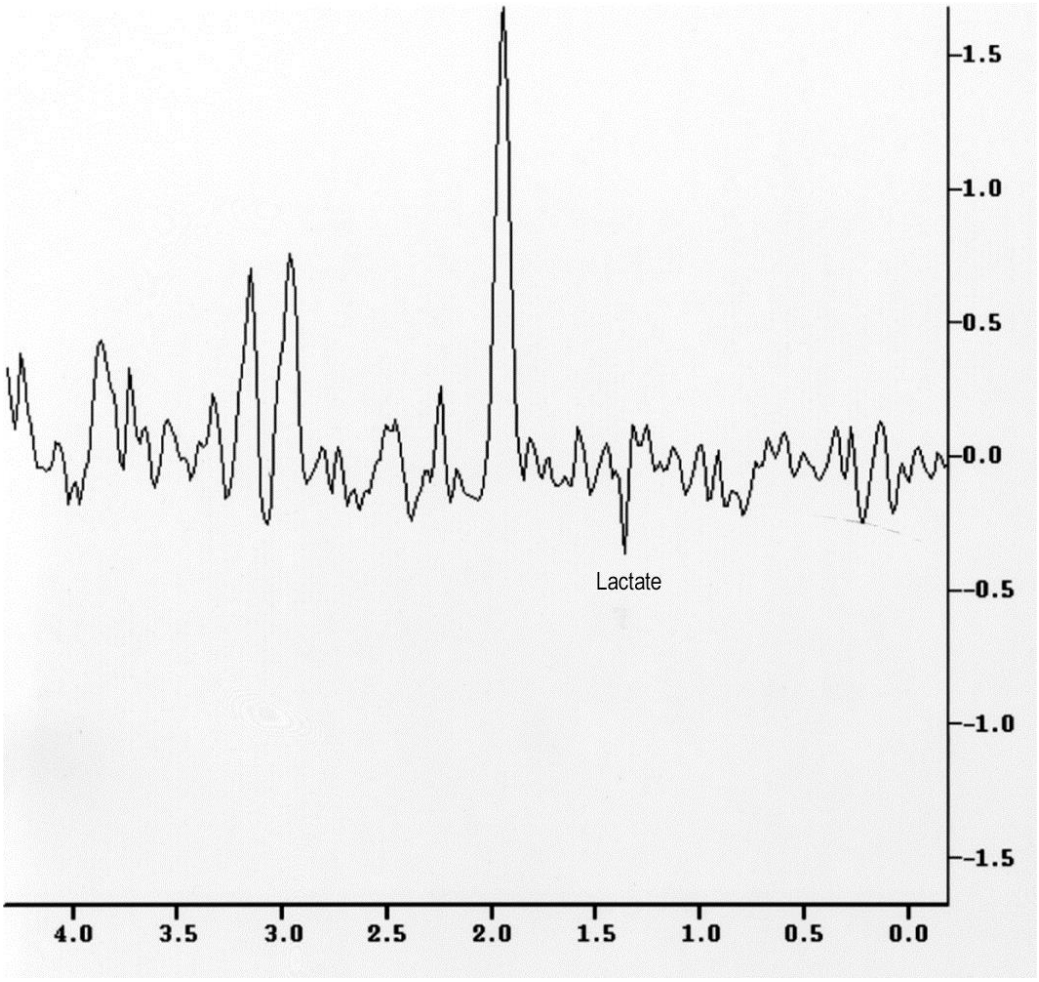

Figure 2. MR spectroscopic analysis (TE 136 ms). Lactate signal at 1.3 ppm was observed on parietal white matter lesions.

With these findings, the patient was examined for neurobrucellosis, neurosyphilis and tbc meningitis. The medical history, clinical-radiological findings and laboratory results corraleted with neurobrucellosis. Triple antibiotherapy (rifampin, doxycycline, seftiraxon) was given for three months. Neurological symptoms were recovered in follow-ups. One year later, the most of MRI findings disappeared, but white matter changes persisted. On MRS control, choline peak at 3.2 ppm was detected in lasting white matter changes. Lactate peak was not seen (Figure 3).

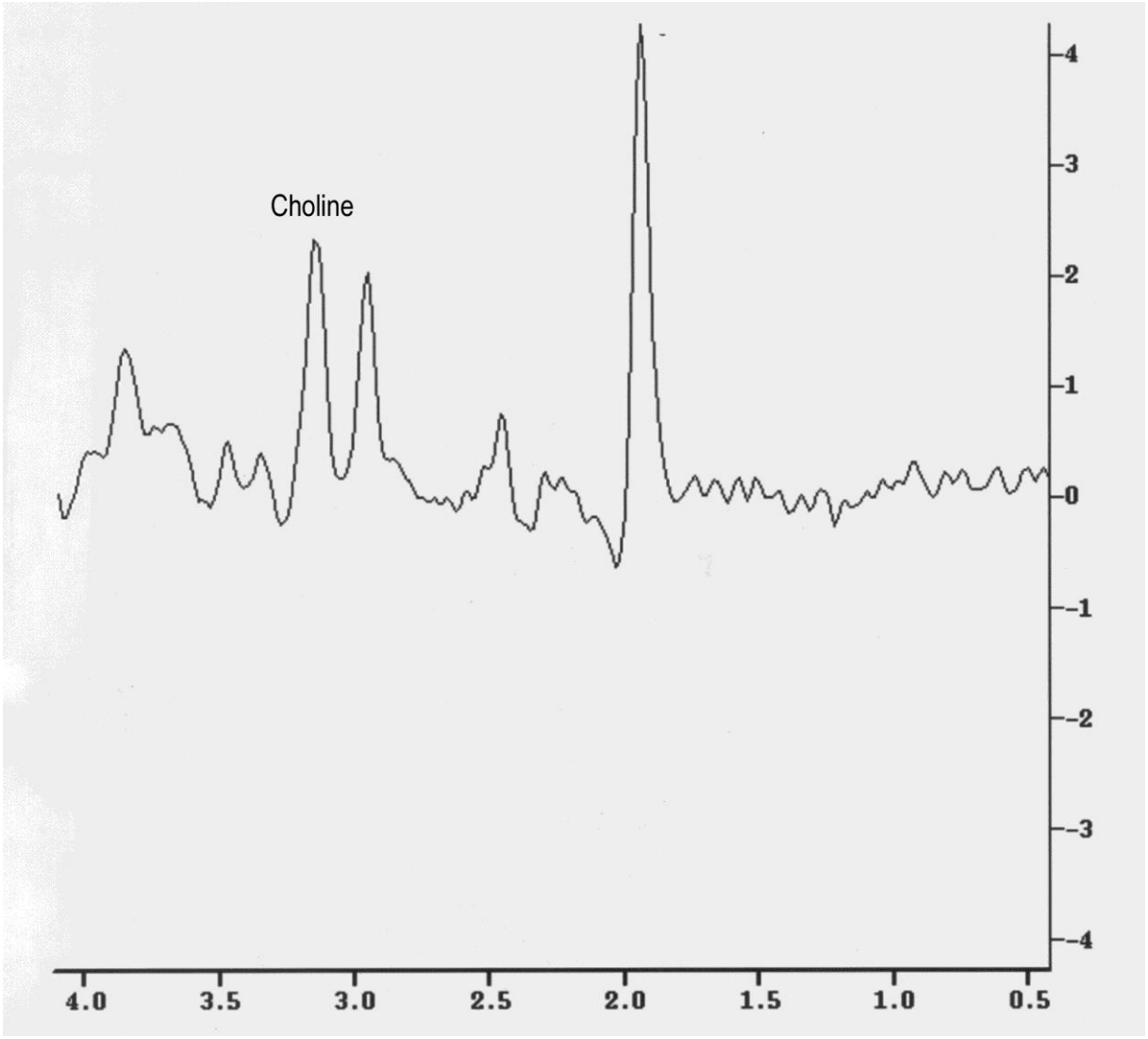

Figure 3. One year later, MRS control (TE 136ms). Choline peak at 3.2 ppm was seen on persisting white matter lesions. Lactate peak was disappeared.

Discussion

Central neural system involvement**,** is a rare complication of brucellosis and it is even rarer at the childhood age group. This is why that it may not be noticed or lately diagnosed. Whereas the adult neurobrucellosis shows acute or chronic presentation, may affect central and/or peripheral neural system; pediatric neurobrucellosis shows acute presentation and usually affects the central neural system [3].

The neurogical complications of brucellosis are meningitis, meningoencephalitis, subarachnoid hemorrhage, myelitis-radiculoneuritis, cerebral and cerebellar abscess, epidural

abscess, meningovascular syndrome, cranial and peripheric neural involvement [4,5]. The clinical presentation of neurobrucellosis in children is meningitis, meningoencephalitis, myelitis and radiculitis. Peripheral neuropathy in children has not been reported [3]. Meningitis is the most frequent clinical form of the disease [6,7].

The main symptoms of neurobrucellosis are fever and headache [8,9]. Neck stiffness, confusion, motor deficit at upper/lower extremity, diplopia, vomiting, weight loss, backpain, and muscle weakness are other symptoms and findings [9,10]. Headache, vomiting, bilateral hip and knee pain, inability to walk, neck stiffness, muscle weakness and weight loss were present in our case.

In diagnosis and follow-up, clinical, microbiological and radiological evaluation is important. The definitive diagnosis of neurobrucellosis is the isolation of the organism from CSF. However, this occurs seldom and the diagnosis is made with serological tests [4]. In our case, there was no reproduction in blood and CSF culture and brucellar antibodies were detected in serological tests.

The imaging findings of neurobrucellosis are variable and may imitate other infectious or inflammatory diseases [4,8,10]. Imaging findings reflect the inflammatory or demiyelinating processes or the vascular insult and are not always correlated with the clinical manifestations [8]. Most of the cases with neurobrucellosis were evaluated as normal in CT studies [3,6,9,10]. Yetkin et al. found normal brain CTs in 15 cases of 20 cases with neurobrucellosis [9]. In another study made by Akdeniz et al., brain CTs of 4 patients with neurobrusellosis out of 5 were normal and only in one case brain edema in acute phase was observed [10]. The radiological examinations made by brain CT in children with brucellar meningitis are also usually normal. Rarely brain atrophy, thickening in optic nerves, dilatation of lateral ventricules or cerebellar abscess have been reported [3,4].

MRI is more sensitive than CT and is the most advanced modality with capability to show parenchymal brain lesions and leptomeningeal involvement [4,8]. In a study made by Al-Sous et al., 5 of the 7 CT examinations of neurobrusellosis were evaluated normal. By 2 of them positive findings were found in MRI (1 patient with periventricular white matter changes, 1 patient with meningeal enhancement). In the MR images on 17 patients, 8 cases were normal

and in 9 cases abnormal findings were detected [8]. In our case, the nervous system involvement, which cannot be shown with CT scan, was shown with MRI effectively.

The imaging findings of neurobrucellosis are in 4 groups: normal, inflammation (abnormal enhancement), white matter changes, and vascular changes. Inflammation causes granulomatous formation or enhancement of meninges, perivascular space or lumbar nerve roots. Tuberculosis, fungal infection, sarcoidosis are other diseases that need to be discarded with these imaging findings. After the adequate therapy, when the patient is healed clinically, inflammatory process disappears on MRI or CT scans [8].

The white matter changes are observed as hyperintense lesions on T2-weighted and FLAIR images. The white matter changes may be in different patterns, such as periventricular, diffuse peripheral and focal. Although the reason of these changes is not known, they may be related with autoimmune reaction. The white matter involvement may imitate other inflammatory or infectious diseases like multiple sclerosis, acute disseminated encephalomyelitis, and Lyme disease. Nevertheless, in neurobrucellosis cases with white matter changes, enhancing lesions and corpus callosum involvements are not observed. In a study made by Al-Sous et al., 7 cases had white matter changes among 17 brain MRIs and in none of those enhancing lesion and corpus callosum involvement were not detected. In 3 cases out of 7, clinical and CSF findings were recovered after sufficient treatment, but the white matter changes persisted [8].

Unusual clinical and MRI findings of neurobrusellosis were reported too. Leptomeningeal enhancements in the cerebellar hemispheres and T2-hyperintensity at the splenium were shown in a case with unilateral abducens nerve palsy [11]. In a meta-analysis made by Turgut et al., 452 cases with spinal brucellosis reported from Turkey were investigated. Only 3 cases of them were in childhood period. Radiculopaty was most frequent neurological finding and spondylitis or spondylodiscitis was the predominant radiological finding. MRI was found to be more sensitive in detecting the presence of spondylodiscitis than other imaging modalities [12].

In our case, the CT scan was normal. On the brain and cervical MRI, hydrocephaly, brain atrophy, subcortical and periventricular white matter changes, bilateral focal dural thickening and enhancement as well as cervical spinal leptomeningeal enhancement were detected. We did not see enhancement in white matter lesions and corpus callosum involvement.

MRS is a non-invasive method to detect the metabolic alterations of biological systems. It may provide additional information on the diagnosis and progression of several diseases. On MRS, the white matter changes showed lactate peak at 1.3 ppm supporting the infectious process in our case. MRS study made from cerebral lesions in neurobrusellosis cases has not been presented yet. However, Kayabas at al [13] reported MRS features of normal-appearing white matter in patients with acute brucellosis. They detected increased choline (Cho)/ creatine (Cr) ratios in patients with acute brucellosis compared to controls [13].

The objective of treatment is to improve the symptoms, reduce the complications, and prevent relapses. Combined antibiotherapy is recommended and the treatment period can vary upon the localization of the disease [4]. In our case, triple antibiotherapy (rifampin, doxycycline, seftiraxon) was applied for three months. Clinical response was acquired. One year later, MRI findings disappeared out of the white matter changes. On MRS control, lasting white matter changes showed choline peak at 3.2 ppm supporting the demyelination process.

In conclusion, in the differential diagnosis of CNS diseases in children, especially where brucellosis is endemic, neurobrucellosis should be kept in mind, though observed rarely. In these cases, the neurological system involvement that cannot be demonstrated via CT can be shown with MRI effectively. MRS may give additional data during the follow-up of the disease.

Conclusions

Neurobrucellosis is a rare disease seen in 0, 5-25 % of the adults with systemic brucellosis. 0,8 % of the children affected by systemic brucellosis are reported to have neurological complications. In this study, we presented the magnetic resonance imaging (MRI) and MR spectroscopic (MRS) findings of the central nervous system (CNS) involvement of brucellosis observed rarely at the pediatric age group. In the differential diagnosis of CNS diseases in children, especially where brucellosis is endemic, neurobrucellosis should be kept in mind, though observed rarely. In these cases, the neurological system involvement that cannot be demonstrated via CT can be shown with MRI effectively. MRS may give additional data during the follow-up of the disease.

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