MRI Findings of Intracranial Tuberculosis of Three Cases at Different Stages and Locations

Farklı Evre ve Lokalizasyonda Intrakranyal Tüberkülozu Olan Üç Olgunun MRG Bulguları: Olgu Sunumu

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Abstract

Central nervous system (CNS) tuberculosis is an infectious disease process that continues to be a prevalent endemic problem in certain world regions. Intracranial tuberculomas are space-occupying masses of granulomatous tissue which generally emerge with the symptoms of meningeal irritation and increased intracranial pressure. We have reported magnetic resonance imaging (MRI) features of three cases of intracranial tuberculosis that were at different stages and locations. The involvement of the CNS by tuberculosis (Tbc) occurs often in the form of the tubercular meningitis and tuberculoma. The tuberculoma form is more common. The presence of a ring enhancing low signal lesions on T1 weighted images or a transient hyperintense signal on T2 weighted images in MRI of the patients who have tuberculosis elsewhere in the body or live in region where tuberculosis is endemic should suggest CNS tuberculosis. (Marmara Medical Journal 2011;24:203-7)

Key Words: Tuberculosis, Brain, MRI

Özet


Anahtar Kelimeler: Tüberküloz, Beyin, MRG

Introduction

Central nervous system tuberculosis is an infectious disease process that continues to be a prevalent endemic problem in certain world regions. Recently, the incidence of tuberculosis has been on the rise because of the increased incidence of acquired immunodeficiency syndromes.¹² Intracranial tuberculomas are space-occupying masses of the granulomatous tissue which are uncommon in patients with active tuberculosis and generally emerge with the symptoms of meningeal irritation and increased intracranial pressure. It develops in approximately 1% of all patients with active tuberculosis and 4.5–28% of those with tubercular meningitis.¹ It occurs as a result of hematogenous spread from a primary focus of infection.

Here we report features of magnetic resonance images (MRI) of three cases of intracranial tuberculosis that were in different stages and locations.
Case Reports

Case 1: An 18 year-old male patient was admitted with complaints of headache and fever. His symptoms started two weeks ago and he had been given a treatment for upper respiratory tract infection in another hospital. His symptoms did not last. On admission, general physical examination was within normal limits. There was no abnormal finding in the examination of his chest and abdomen including respiratory sounds and lymph nodes. On neurological examination, he was sleepy and his orientation and cooperation were poor. Any other signs of the meningeal irritation were not detected except neck stiffness. Risk factors for tuberculosis (Tbc) (like human immunodeficiency virus (HIV), alcohol abuse, diabetes mellitus (DM), immune suppressive drug use, family history) were not detected.

Routine blood examination was within normal ranges. There were certain amounts of Escherichia coli in culture from his urine. Two weeks after parenteral administration of antibiotics, bacteria from the urine culture disappeared.

Cerebrospinal fluid obtained by lumbar puncture, revealed a white blood cell count of 3800 /mm$^3$ (80% mononuclear leukocyte, 20% polymorpho-nuclear leukocyte) red blood cell count of 520/mm$^3$, a protein concentration of 3753 mg/dl, glucose level 10 mg/dl (serum glucose level 76 mg/dl) but no oligoclonal bands. Ceftriaxone in a daily dose of 4 g/iv (2x2gr) and acyclovir in a daily dose of 1500mg/oral (3x500 mg) was started. After 5 days, patient’s fever decreased.

The tuberculin skin test was positive. Although the diagnosis of tuberculosis infection was not ensured, an anti tuberculosis drug treatment Rifampin (RIF) in a daily dose of 600 mg/oral, Isoniazid(INH) in a daily dose of 300 mg/oral, Pyrazinamide(PZA) in a daily dose of 1500 mg/oral and Ethambutol (ETB) in a daily dose of 900 mg/oral were started 3 days after the start of ceftriaxone (2x2gr) and acyclovir (3x500mg) treatment. Contrast enhanced brain MRI examinations (1.5 Tesla, Gyroscan Intera, Philips Medical Systems, Netherland) were performed on our patient. A flair image in the axial plane, T1 weighted images in the axial and sagittal planes, T2 weighted images in the axial and coronal planes, contrast enhanced sagittal and coronal T1 and contrast enhanced magnetization transfer contrast T1 weighted images in the axial plane were taken. The brain MRIs showed lesions in the pons, splenium of the corpus callosum, the left side of the mesencephalon, with hyperintensity on T2-weighted(W) and isointensity on T1 weighted images(WI) (Figure 1a). After administration of gadolinium (Gd) based contrast media, enhancement of the leptomeninx without the lesions previously described were detected. IV pulse steroids were started due to these lesions. 10 days later MR scans were repeated. Lesions in the pons, mesencephalon, thalamus and corpus callosum were resolved (Figure 1b). Contrast enhancement of the leptomeninx was also decreased. CSF culture for M. tuberculosis complex was positive so diagnosis of Tbc was confirmed after three weeks.

A 4th nerve paralysis developed during the treatment of first month, brain MRI with gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA) demonstrated tuberculomas with ring enhancement in the preoptin and suprasellar cisterns and cerebellar tentorium when the patient was in the third month of antituberculous treatment (Figure 1c).

Case 2: A 25 year-old male patient was admitted with the complaints of headache, gait imbalance and right sided facial weakness. He had been given the treatment of lung tuberculosis two weeks earlier.

Figure 1. Axial T2 Weighted images (a) Shows hyperintense signal on the left side of the mesencephalon (arrow) and (b) the signal disappeared 1 week later after IV pulse steroid treatment. (c) Tuberculomas with ring enhancement appeared 4 months later in the right tentorium on coronal T1 Weighted image with Gd-DTPA enhancement (arrow).

Figure 2. T2 weighted image in the axial plane (a) shows a hyperintense lesion with a small hypointense core (long arrow) surrounded by a slightly hypointense capsule (short arrow) and (b) Axial T1 weighted image with Gd-DTPA enhancement shows intense capsular enhancement of the lesion (c) 15 months later the size of the lesion was decreased. (d) Shows the hypointense signal of the central core on T2 weighted image was increased (arrow).
Vital signs, such as pulse, blood pressure, and body temperature were within normal ranges. Rales in both lungs especially on the right were detected on auscultation. On neurological examination, a slight gaze limitation in the downward and medial direction in the right eye was observed. A Hess chart examination revealed slight palsy of the right trochlear nerve. A right hemi-sensory disturbance including the face was detected. He exhibited a slight right hemiparesis. Deep tendon reflexes were not exaggerated.

Routine blood examination showed an increase in the white blood cell count of 12000/mm³, C-reactive protein of 11mg/dl, erythrocyte sedimentation rate (ESR) of 42 mm within first hour. Chest X-Ray and thorax computed tomography (CT) were interpreted as positive evidence of active tuberculosis. There was a certain amount of Mycobacterium tuberculosis in a culture from his sputum was detected.

A brain CT revealed a high-density lesion of 3 cm in diameter with a central low density spot in the right half of the middle pons. Brain MRI showed that this lesion was 3x2 cm in diameter, with a small central hypointense core surrounded by slightly hyperintense capsule and hypointense area on T1WI, hyperintensity with bright hypointense core surrounded with a slightly hypointense capsule and hyperintense area on T2WI. Gd–enhanced MRI presented an intense capsular enhancement of the lesion (Figure 2a, b). There was no other lesion on MRI study. A pontine tuberculoma was considered as the primary diagnosis. Pulse IV steroid was started. MRI scans were repeated 6 and 15 months later. A significant reduction in the size of the lesion and of the perilesional edema was detected (Figure 2c). Central hypointensity signal of the lesion on T2 weighted sequence was increased (Figure 2d).

Case 3: A 21 year-old female patient was admitted with the complaints of headache, cough and seizure. She was under treatment for lung tuberculosis started 1 month prior to admission for an MRI examination. She was also taking an antiepileptic drug (Carbamazepine 400mg/day) started 2 weeks earlier.

Figure 3 (a) Axial T1 weighted image with Gd-DTPA enhancement shows a conglomerated mass of multiple ring enhancing tuberculoma. (b) Axial T2 weighted image shows the hypointense core of the tuberculomas. (c) 8 months later number and size of the multiple lesions were decreased. Also the central hypointense signal of the tuberculomas was increased on the T2 weighted image.

Brain MRI scans showed enhancing multiple tuberculomas in the right parietal, bilateral temporal lobes and left cerebellar hemisphere. The largest focus was in the left parietal lobe. The largest tuberculoma was 2 cm in diameter; tuberculomas show a central hypointense core surrounded by slightly hyperintense capsule on T1 WI, and a hyperintense and mostly hypointense core surrounded by a slightly hypointense capsule on T2 WI. Gd–enhanced MRI presented intense capsular enhancement of the tuberculomas (Figure 3a, b). Perilesional edema was detected in the left parietal, temporal and frontal lobes. MRI scans were repeated 6 months later. A marked reduction of the perilesional edema, and of the size and number of the tuberculomas was detected. The central T2 hypointensity of the tuberculomas was also increased (Figure 3 c). Her headache was resolved; incidence of seizure was decreased.

Discussion

CNS tuberculosis is rare; it constitutes 15-50 % of intracranial lesions in developing countries. It is far less common in industrialized countries.

Intracranial tuberculomas are thought to result from hematogenous spread of miliary tuberculosis from a focus elsewhere in the body. Therefore CNS tuberculomas tend to occur in region of higher blood supply such as the frontal and parietal lobes of the cerebrum. Tuberculomas located in the brainstem are rare and account for 2.5-8% of all intracranial tuberculomas in large series. Most cases of pontine tuberculomas accompany supratentorial or meningeal lesions; solitary pontine tuberculomas are rare.

The involvement of the CNS by tuberculosis occurs often in the form of the tuberculosis meningitis and tuberculoma. The tuberculoma form is more common. Tuberculosis meningitis is characterized as a meningoencephalitis, since its pathology encompasses not only the meninges but the parenchyma and the vasculature of the brain as well. The primary pathologic event is the formation of a thick exudate within the subarachnoid space. Occasionally this exudate is localized in the immediate vicinity of a ruptured tubercle. The pathogenesis of CNS tuberculoma is identical to that of tuberculosis meningitis. Instead of rupturing into the subarachnoid space, the initial tubercles continue to grow, walled off from the brain parenchyma and the meninges by a dense fibrous capsule. Perforating arteries running through the cerebro spinal fluid (CSF) may be affected by the inflammatory exudate that result inschemia and infarcts. Transient hyperintense signals seen in our patient 1 was probably due to the transient occlusion of the perforating arteries that are perforating the tuberculoma. However, it was not possible to prove this explanation in our case because MRI angiography was not performed during examination.
As most cranial nerves run through the skull base, they can be affected, producing cranial nerve palsies. Development of a tuberculoma also may cause nerve palsy. Trochlear nerve palsy developing in our patient 1 was probably due to the formation of a tuberculoma.

MRI plays an important role in the diagnosis of intracranial tuberculomas. Tuberculomas have different signal characters at different stages especially on T2 WI.

At early stage of formation of tuberculomas, an inflammatory reaction occurs; the mass has an abundance of giant cells and a capsule that is poor in collagen. At this stage the mass is isointense on T1 and T2-WI and shows some contrast enhancement. At a later stage, the capsule becomes rich in collagen. When small tuberculomas coalesce to become larger lesions they give rise to a low signal on T2 WI because of fibrosis, scar tissue and presence of the free radicals produced by macrophages during active phagocytosis. Our Case 2 had a conglomerate mass of multiple tuberculomas that had a central hypointensity on T2 WI. All tuberculomas show ring or nodular contrast enhancement. The central hypointensity of tuberculomas of our cases 2 and 3 was increased along with decrease in the size of the lesions as the treatment continued. According to the literature this was due to a decrease in water content, central necrosis, an increase in cellularity and in the free radicals of the tuberculoma and possible hemorrhage which is a contributing factor. Kim et al. reported no evidence of hemorrhage on microscopic examination of the tuberculomas that could result in T2 shortening.

Tuberculomas have a feature that can mimic other space occupying lesions, such as malignant gliomas, brain abscesses, cysticercus granulomas, metastatic cancers or lymphomas. They are encapsulated, avascular and slow growing, with areas of necrosis and very occasionally calcification. More than half attach to the dura matter and may resemble meningiomas. About one third of tuberculomas are multiple. Intracranial tuberculomas are more common in patients who are seropositive for HIV compared with HIV seronegative patients. Signs and symptoms in the clinical process of brain tuberculomas are generally silent, and the complaints gradually increase. These patients have low-grade fever and headache. CSF analysis shows lymphocytosis, elevated levels of protein and normal to low levels of glucose as in our patient 1. However, the hypointensity or isointensity that is frequently seen in the central portion of tuberculomas on T2 WI can differentiate these patients from pyogenic abscesses, which usually have a central hyperintensity on T2 WI.

However, MRI findings are not crucial for diagnoses of CNS tuberculomas in all patients. In these situations Del Brutto and Mosquera suggested that an antituberculous agent could be a useful diagnostic tool rather than radiological studies. But as in our case 1, development or enlargement of tuberculomas has been reported in the literature. The pathogenesis behind the paradoxical progression or the development of intracranial tuberculomas in patients given antituberculosis medication is not clearly understood. A common belief is that the paradoxical response has an immunological basis. The infected hosts develop hypersensitivity to an array of mycobacterial proteins. Tuberculostatic drugs cause destruction of mycobacterial structures and liberation of bacillary proteins. These provoke a delayed hypersensitivity immune reaction. In the CNS micro tuberculomas grow slowly and become encapsulated after a latent period, resulting in paradoxical progression of existing lesions. This may be supported by an accompanying immunological phenomenon, namely the local perilesional secondary granulomatous vasculitis associated with intimal proliferation and degeneration of vessel walls with occlusion of the vessel lumen, this reduces the penetration of the tuberculostatic drug into the lesions. Concomitant corticosteroid therapy along with the antituberculous agents may promote the antimicrobial efficacy and interrupt this vicious circle. This may explain the clinical improvements in many cases after treatment with glucocorticosteroids.

The most important factor affecting the prognosis of CNS tuberculosis is an early start of therapy. Although intensity and duration of the treatment varies from case to case, INH, Rif with PZA or ETB and streptomycin are used as the first line drugs for CNS tuberculosis. Our three patients treated with a combination of Rif, INH, PZA and ETB which was given both for lung and CNS tuberculosis. A minimum of 12 months of therapy is necessary in order to obtain the optimum response. The duration of the therapy may be extended up to 30 months according to the patient’s response. In case of persistence or progression of the clinical symptoms, contrast enhanced (CT) or MRI should be performed. Changing the drug regimen is not necessary. In such cases systemic corticosteroids are worthwhile and effective as adjuvant therapy for 4 to 8 weeks.

A tuberculosis skin test and the QuantiFERON-TB tests have been used in the diagnosis of latent Tbc but they have some limitations. CSF examination is still the gold standard and the key to the diagnosis of intracranial tuberculosis. Patients whose CSF analysis shows lymphocytosis, elevated levels of protein and low levels of glucose should alert us to intracranial tuberculosis. The presence of a ring enhancing low signal lesions or nonenhancing transient hyperintense signal on T2 WI of the patients who have tuberculosis elsewhere in the body or live in region where tuberculosis is endemic should suggest CNS tuberculosis. In suspicious cases antituberculous treatment must be started to confirm the diagnosis. It should be kept in mind that some lesions show paradoxical expansion and that new tuberculomas may develop under the treatment. Increase in a central hypointense signal on T2 WI may be a sign of the resolution of the tuberculoma. This article is a good overview of MRI findings of intracranial tuberculosis.

References