Case report

Abnormal brain MRI signals in the splenium of the corpus callosum, basal ganglia and internal capsule in a suspected case with tuberculous meningitis

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Abstract

The patient was a 34-year-old man who visited the hospital with chief complaints of headache, fever, and disturbance of consciousness. In view of his clinical condition, the course of the disease, and results of examination, he was diagnosed with viral meningitis and treated accordingly. However, his clinical condition worsened, and MRI revealed abnormal signals in the splenium of the corpus callosum, in the basal ganglia and in the internal capsule, as well as the presence of severe inflammation in the base of the brain. Since he had a high ADA level in the cerebrospinal fluid and was consequently suspected to have tuberculous meningitis, he was placed on antitubercular agents. Then, his clinical condition began to improve. Additional steroid pulse therapy further improved his condition, and abnormal signals in the splenium of the corpus callosum and the basal ganglia resolved. This patient seems to be a valuable case suggesting that an immune mechanism contributed to the occurrence of central nervous system symptoms associated with tuberculous meningitis.

Introduction

Meningitis that has a predilection for the base of the brain is known to be a manifestation of tuberculosis in the central nervous system (CNS). In addition, tuberculosis in the CNS appears as various diseases including tuberculoma, vasculitis, cerebral infarction, cranial neuritis, hydrocephalus, and allergic tuberculous encephalopathy (1,2). Among them, it has been speculated that allergic tuberculous encephalopathy is caused by an immune mechanism based on molecular mimicry between a *tubercle bacilli* antigen and a myelin antigen of the CNS. However, such an encephalopathy is extremely rare. We recently examined and treated a suspected case of tuberculous meningitis with reversible, abnormal signals in the splenium of the corpus callosum, the basal ganglia and the internal capsule. In view of his clinical course, this disease may be classified as allergic tuberculous meningitis, which is strongly associated with an immune mechanism. To our knowledge, there are no other reported cases of tuberculous meningitis with similar MRI changes. Such a case is rarely seen and of considerable interest because it is suggestive in analyzing CNS symptoms associated with tuberculous meningitis.

Case report

Patient: A 34-year-old man

Chief complaints: Headache, fever, and disturbance of consciousness.

Family history: Nothing in particular to be described.

Past history: Nothing in particular to be described.

History of present illness: He had a headache and fever beginning on February 10, 2005, and was admitted to a local hospital on February 15. His cerebrospinal fluid (CSF) suggested the presence of meningitis; opening pressure, 180mmH_2O; cell count, 981/μl (monocytes, 90%); protein, 171 mg/dl; glucose, 45 mg/dl; Cl, 117 mEq/l. In addition, abnormal signals were detected in the splenium of the corpus callosum on MRI. On February 18, he was admitted to the neurosurgical department of the author's hospital under suspicion of a brain tumor with dissemination over the meninx. On February 19, disturbance of consciousness occurred, and he was transferred to the author's department on suspicion of meningitis.

Physical examination at the time of transference to the department (2/19, day 1): The patient was 175 cm tall and weighed 81 kg. His blood pressure was 120/90 mmHg, he had a regular pulse rate of 110 beats/min and no cardiac murmurs were heard. His body temperature was 39.4°C.

Neurological findings at the time of transference (2/19, day 1): Disturbance of consciousness (E2V2M5 on Glascow Coma Scale (GCS)) and nuchal rigidity were observed. No disorders were detected in the brain and the nervous system. Deep tendon reflexes were normal. Pathological reflexes were negative.

Blood examination at the time of transference: Except for findings indicating mild inflammation (WBC, 10,300/μl; CRP, 0.53), results of the blood count and biochemical

examinations were normal. All serological examinations on autoantibodies, such as RF, anti-nuclear antibody, anti-SS-A/SS-B antibody, and PR3/MPO-ANCA, were negative. Glucose tolerance was normal: The fasting blood sugar was 90 mg/dl, and the HbA1c level was 4.4%. Titers of candidal antigen and β-D-glucan were normal.

CSF examination (2/21, day 3): The opening pressure was 300 mm H_2O, cell count was 630/μl (monocytes, 84%), protein and glucose concentrations were 295 mg/dl and 35 mg/dl, respectively (simultaneous blood glucose level, 90 mg/dl). The bacteriological and mycological cultures of the CSF were negative, and the mycobacterium culture was repeatedly negative through the eighth week.

MRI of the brain (2/17): Abnormal slight hyperintensity signals of an ovoid shape were found in the splenium of the corpus callosum on FLAIR MRI. The intensity of the abnormal signals was markedly high on diffusion-weighted MRI. However, they had no contrast enhancement (Figures 1a-c).

The clinical course after admission (Figure 2)

The patient was considered to have viral or mycotic meningitis, because the headache and fever preceded the disturbance of consciousness, monocyte-dominant pleocytosis was found, and the glucose level was only slightly decreased in the CSF. The MRI findings were not considered contradictory to the diagnosis of infectious meningitis. He was consequently started on aciclovir, panipenem/betamipron (PAPM/BP), ceftriaxone

(CTRX), fosfluconazole (fosFLCZ), and an immunoglobulin–preparation. As the disturbance of consciousness worsened on day 3, he underwent barbiturate therapy in the intensive care unit and was assuaged. On day 7, the number of cells in the CSF had increased slightly. FLAIR MRI on the same day revealed uneven, slight hyperintensity signals not only in the splenium of the corpus callosum, but also in the posterior limbs of the bilateral internal capsules, the heads of the caudate nuclei, and the lenticular nuclei. The presence of severe meningitis in and around the brainstem was suspected, since linear high intensity images were found on the surface of the brainstem on gadolinium-enhanced FLAIR MRI (Figures 1d, e). These findings coupled with the lack of effect of the described medication, led us to consider the possibility that the patient had tuberculous meningitis. He was therefore placed on antitubercular agents (i.e., 2 g pyrazinamide (PZA), 750 mg ethambutol (EB), 0.5 g isoniazide (INH) and 450 mg rifampicin (RFP)). The adenosine deaminase (ADA) level in his CSF on day 7 was unknown at this time, but was later reported to have been 91.41 IU/l, markedly high compared to the normal level (below 9.0 IU/l). The genome of *tubercle bacilli* was not detected by nested PCR in his CSF, nor were abnormal findings suggestive of tuberculous infection obtained in the general examination. As an outer portion of the left kidney was not well contrast-imaged on abdominal CT examination, the presence of kidney tuberculosis was suspected. Cultures of his gastric juice, CSF, urine, and sputum were negative for *tubercle bacilli*, and the bacilli genome was not detected by PCR in these specimens. His tuberculin reaction (PPD skin test) was negative.

After administration of the antitubercular agents was started, both protein and ADA levels in the CSF decreased and the glucose level was corrected, indicating a conceivably high possibility that he had tuberculous meningitis. In addition, the abnormal image in the left kidney was resolved.

On day 18, aciclovir and fosFLCZ were withdrawn, and barbiturate therapy was discontinued. However, he was deeply comatose (E1V1M1 on GCS) on day 21, and the electroencephalogram was dominated by slow waves at 3-4 Hz. MRI on the same day showed that although the high intensity images on the surface of the *medulla oblongata* had been resolved, abnormal images in the splenium of the corpus callosum remained, and high intensity signals in the bilateral internal capsules and basal ganglia were slightly enlarged (Figures 1f, g). The ADC values in abnormal intensity lesions were low. Since the CSF indicators were improving at this stage, we considered that the activity of tuberculous meningitis was lowered, and that the lesions in the internal capsule and the basal ganglia occurred secondarily by a certain immune mechanism. We therefore started steroid pulse therapy from the same day. On day 27, the consciousness level recovered to E4V4M6 on the GCS, and purposeful voluntary movements of extremities were observed. Since steroids were evidently effective from a clinical point of view, steroid pulse therapy was repeated. On day 35, his consciousness became lucid, and his CSF indicators were normal. He received rehabilitation for diminution of muscle power and finally left the hospital on day 91 (June 2005) when he was capable of walking with the aid of a stick. He was then followed up and was maintained on the

four–antitubercular agents. In September 2005, abnormal brain MRI signals in the splenium of the corpus callosum and basal ganglia were found to have disappeared (Figure 1h), and his CSF remained normal. His medication was consequently reduced to only RFP and INH. He is still under medical surveillance. Based on follow-up observations as of April 2006, he could walk without any aid and had no evident neurological deficits.

Although the results of microbiological investigations were negative, very high ADA levels in the CSF and the high clinical success of anti-tubercular agents strongly suggest a diagnosis of tuberculous meningitis.

Discussion

The patient reported in this article had tuberculous meningitis, which progressed subacutely and was accompanied by lesions in the splenium of the corpus callosum, the basal ganglia and internal capsule. He was initially treated under a diagnosis of viral or mycotic meningitis. Since he had a high ADA level, responded favorably to antitubercular agents, and was refractory to other medication, however, there is a high possibility that he had tuberculous meningitis. The fact that *tubercle bacilli* DNA was not detected in his CSF by nested PCR does not seem to contradict this diagnosis. About 20% of the patients who are highly likely to have tuberculous meningitis have been reported to be negative for detection of the bacillary genome by nested PCR (3).

Lesions in the basal ganglia and the internal capsule accompanying tuberculous meningitis are found in numerous patients with vasculitis and vasculitis-associated cerebral infarct. In about 75% of them, the internal striatal artery and the paramedian thalamic artery are affected (2). MRI changes seen in these patients are irreversible, however. Concerning reversible changes, Wakai et al. reported a case of tuberculous meningitis transiently presenting with symmetric linear lesions in the bilateral thalamus (4). They discussed the correlation between vasculitis of minute blood vessels and edema as a possible cause of the transient changes. Lesions in the basal ganglia and the internal capsule in the present study were more extensive than those reported by Wakai et al. and resolved in response to steroid therapy. Although patients with demyelinating disorder who showed MRI changes similar to those described in this study have been reported (5), there have been no previous reports of patients with tuberculous meningitis. Because the ADC values were low, we could not completely rule out ischemia caused by vasculitis. However, the reversible clinical course of our patient suggests a contribution of demyelination, caused by an immune mechanism such as acute disseminated encephalomyelopathy (ADEM), rather than ischemia due to vasculitis, to the occurrence of the disease.

Transient abnormal MRI signals similar to those detected in the splenium of the corpus callosum in the present patient were reported previously as ovoid symmetric lesions in the central portion of the splenium of the corpus callosum (6). MRI findings of the lesions were described as markedly high signal intensities with the ADCmap

demonstrating decreased ADC values on diffusion-weighted images, slight high intensity signals on T2- and FLAIR-weighted images, and isointensity or slight low intensity signals on T1-weighted images. MRI changes found in the present study are in agreement with those. Influenza encephalopathy, rotavirus infection, hemolytic uremia syndrome, and medication with antiepileptics have been reported to underlie occurrence of such lesions. Tuberculous meningitis has not been shown to be an underlying disease. These transient signals were considered to reflect transient cellular edema or intramyelinic edema, and to occur by an immune mechanism, in which IL-6, cytokines, and antigen-antibody reactions are involved (7). There have been many case reports of various disorders with isolated splenial lesions, but there are only a few cases with other lesions in addition to the splenial lesions (5-10). The lesion in the basal ganglia resolved with the same time course as did that in the corpus callosum, suggesting the possibility that these two lesions had a common pathogenic mechanism.

The lesions in the basal ganglia and the splenium of the corpus callosum observed in this study supervene only rarely in tuberculous meningitis. In view of its time course, we believe an immunologic process followed the tuberculous meningitis. The number of patients with tuberculosis is increasing recently, and tuberculous meningitis is not a rare disease. It is important in diagnosing and treating patients with this disease that particular attention be directed to the presence of cerebral symptoms caused by an immune mechanism.

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Legends

Figure 1; Brain MRI findings of our case.

FLAIR (a), diffusion weighted (b) and gadolinium-enhanced T1 weighted (c) brain MRI

on February 17. FLAIR and diffusion weighted MRI showed high intensity signals in the splenium of the corpus callosum without gadolinium enhancement. On the 7th hospital day, gadolinium-enhanced FLAIR MRI showed an enhancing lesion on the surface of the medulla oblongata (d) and scattered lesions in the basal ganglia and splenium of the corpus callosum (e). On the 21st hospital day, the enhancing lesion on the surface of the medulla oblongata disappeared following tuberculous chemotherapy in gadolinium-enhanced FLAIR MRI (f), while scattered lesions in the internal capsule were still distinguishable (g). It has been reported that gadolinium-enhanced FLAIR images may be useful for detecting superficial abnormalities, such as meningial disease, because they do not demonstrate contrast enhancement of vessels with slow flow as do T1-weighted images (11,12) . In September, 2005, the high intensity lesions in the basal ganglia and the splenium of the corpus callosum disappeared following steroid therapy (h).

Figure 2; Clinical course of our case.

PAPM/BP ; panipenem/betamipron, CTRX; ceftriaxone, fosFLCZ; fosfluconazole,

PZA; pyrazinamide, EB; ethambutol, INH; isoniazide, RFP; rifampicin

ADA; adenosine deaminase, GCS; Glascow Coma Scale

Figure 1. Brain MRI findings of our case

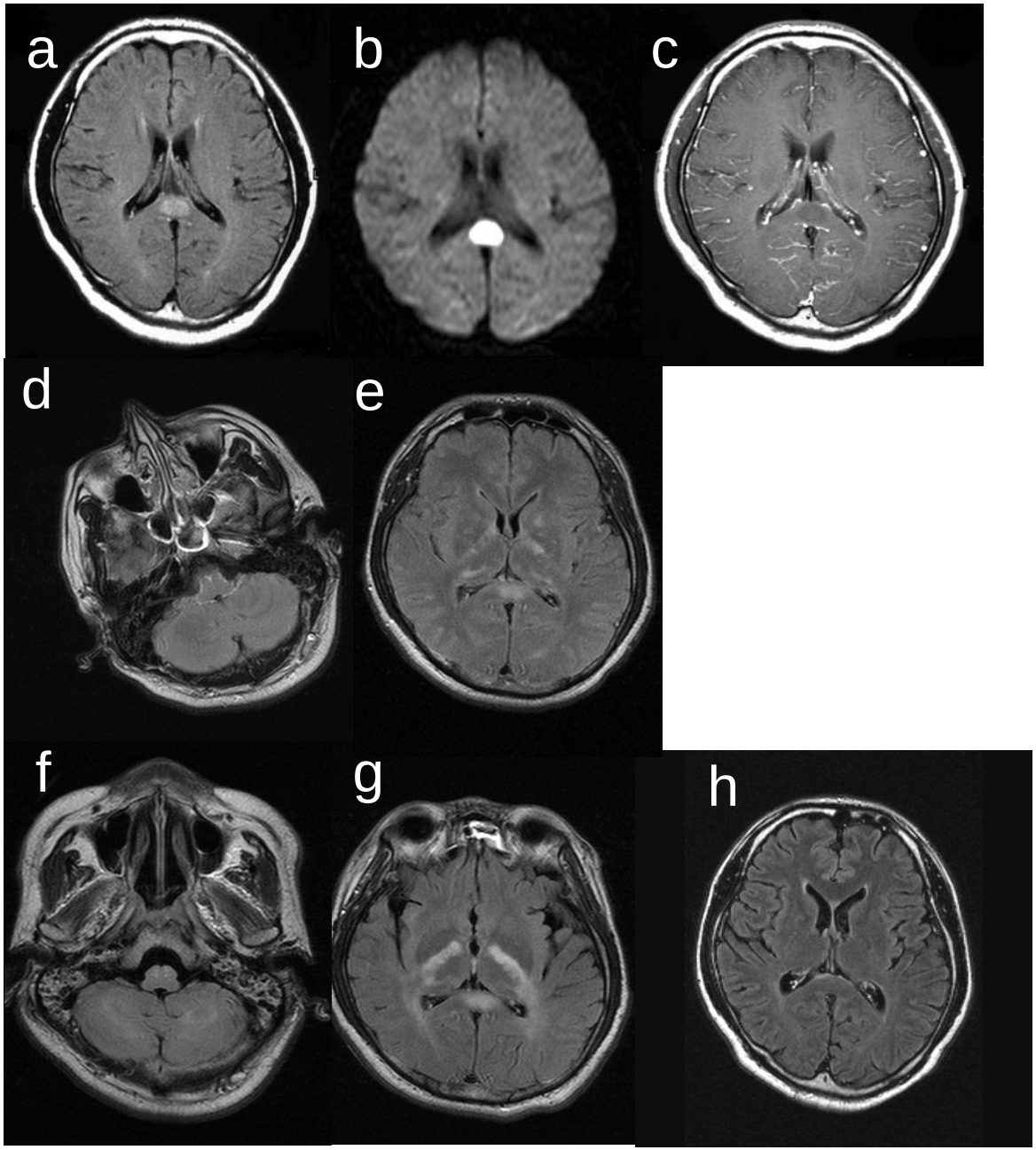

Figure 2. Clinical course of our case