Rheumatoid Leptomeningitis: Radiological Alteration of Cerebral Hypoperfusion and Subarachnoid Lesions

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Abstract

A 56-year-old man with rheumatoid arthritis developed emotional lability and myoclonic seizure in the left arm, followed by fever and generalized convulsion. Brain magnetic resonance imaging (MRI) revealed leptomeningeal lesions with abnormal enhancement. MRI lesions were localized predominantly in the right cerebral subarachnoid spaces. Electroencephalogram showed epileptogenic focus at the right frontal and central points. After administration of valproate sodium improved convulsion and myoclonus, single photon emission computed tomography (SPECT) using N-isopropyl-p-123I-iodoamphetamine was performed. Brain SPECT displayed hypoperfusion predominantly in the right cerebral hemisphere. Cerebrospinal fluid (CSF) disclosed mild pleocytosis and marked elevations of interleukin-6 levels. Repeated CSF analyses showed cytology of class I and negative results for infectious pathogens. Methylprednisolone pulse therapy (1 g for 3 days, iv) and subsequent prednisolone administration (daily 50 mg, po) ameliorated neurological symptoms dramatically. Prednisolone was tapered to 20 mg/day for 5 months. Leptomeningeal MRI lesions were attenuated gradually followed by restoration of cerebral hypoperfusion on SPECT. He was diagnosed as rheumatoid leptomeningitis (RLM). Although clinical features of RLM exhibited variable deficits of the central nervous system (CNS), MRI failed to detect the corresponding CNS lesions. We first highlighted neuroradiological changes of cerebral hypoperfusion and leptomeningeal lesions in RLM. These neuroimages of our patient supported that leptomeningeal inflammation and the adjacent cerebrocortical ischemia could cause encephalitis-like symptoms in RLM patients.

Key words: rheumatoid leptomeningitis, encephalitis-like symptoms, MRI, leptomeningeal lesion, SPECT, cerebral hypoperfusion

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Introduction

Rheumatoid leptomeningitis (RLM) is a rare complication of rheumatoid arthritis (RA). RLM causes a variety of central nervous system (CNS) deficits, including mental changes, epileptic seizures and hemiparesis. Previous reports have suggested that brain magnetic resonance imaging (MRI) had benefits for excellent detection of leptomeningeal involvement in RLM patients (1-12). Otherwise, MRI failed to display brain parenchymal abnormalities in most of RLM patients (1-11). Although cerebrocortical damages are speculated to trigger encephalitis-like symptoms in RLM patients, the corresponding lesions have not been proved radiologically. Here we highlighted a RLM patient who had reversible changes of brain hypoperfusion on single photon emission computed tomography (SPECT), along with leptomeningeal lesions on MRI.

Case Report

A 56-year-old man developed arthralgia in the left shoulder, the left elbow, the wrists, the fingers and the right hip. Serological tests showed higher levels of C-reactive protein (CRP) and positive reaction of RA hemagglutination (RAHA) test. He was diagnosed as stage I of RA and re-
Figure 1. (A, B) Diffusion-weighted and (C, D) fluid-attenuated inversion recovery images show subarachnoid hyperintensity signal areas. (E, F) Leptomeningeal enhancement on T1-weighted imaging after gadolinium administration. Leptomeningeal lesions are found predominantly in the right cerebral hemisphere.

cieved treatment with methotrexate (6 mg/week) and salazosulfapyridine (1.0 g/day). After 2 months, he had emotional lability and myoclonic seizure in the left arm. Three days later, fever and generalized convulsion (10 minutes) occurred. Acute meningoencephalitis was suspected and he was admitted to our department. Physical examination showed blood pressure of 128/78 mmHg and body temperature of 38.2°C. There were no arthralgia and joint swelling. Neurological examination revealed mild degree of consciousness disturbance and intermittent myoclonus in the left arm. Frequency of myoclonic seizures was 10-20 times for daily time and duration of an attack was 1-2 minutes. No seizures occurred during nocturnal sleep. Blood laboratory examination disclosed CRP of 5.1 mg/dL (normal < 0.08), erythrocyte sedimentation rate of 45 mm/hour (normal of 3-15), rheumatoid factor of 18 IU/mL (normal < 10) and RAHA of ×160 (normal < ×40) and matrix metalloproteinase-3 of 299 ng/mL (normal < 121). Serum levels of soluble interleukin-2 receptor (sIL-2R) and ferritin were increased to 996 U/mL (normal of 220-530) and 1,791 ng/mL (normal of 6.2-138), respectively. Cerebrospinal fluid (CSF) analyses suggested an initial pressure of 220 mm H2O, cell count of 26 mononuclear cells/mm3, total protein of 47 mg/dL, and interleukin-6 levels (IL-6) of 202 pg/mL (normal < 12.1). On repeated CSF studies, cytology was class I. Infectious pathogen tests, including herpes simplex
Figure 2. (A) Lateral right, (B) lateral left, (C) medial right and (D) medial left views of easy Z-score imaging system. SPECT shows cerebral hypoperfusion predominantly in the right cerebral hemisphere.

Figure 3. (A, B) After 3 months steroid treatment, subarachnoid hyperintensity signal areas are attenuated on diffusion weighted imaging. (C, D) No abnormal enhancement exists on gadolinium-enhanced T1-weighted imaging.
and tuberculosis by polymerase chain reaction assay, bacteria and fungus, were negative. Brain MRI revealed leptomeningeal lesions with abnormal enhancement (Fig. 1A to 1F). Brain magnetic resonance angiography was normal. Electroencephalogram showed θ and δ waves in bilateral frontoparietal regions. The epileptogenic focus was suggestive at the right frontal and central points. Gallium scintigraphy of the whole body revealed no abnormal accumulation. Chest and abdominal computed tomography (CT) were normal. Treatment of valproate sodium (600 mg/day) was started immediately after admission. Two weeks later, myoclonic seizures disappeared. However, emotional lability was impaired and auditory hallucination occurred. We performed brain SPECT using N-isopropyl-p-[123]iodoamphetamine. SPECT displayed mild to moderate degree of cerebral hypoperfusion predominantly in the right cerebral hemisphere (Fig. 2A to 2D). He was diagnosed as RLM based on those clinicoradiological and laboratory courses. Intravenous methylprednisolone pulse therapy (1 g per day for 3 days) and subsequently prednisolone (50 mg/day, po) was administered. One month later, steroid therapy ameliorated neuropsychiatric symptoms remarkably. CSF study showed an initial pressure of 140 mmH2O, cell count of 4 mononuclear cells/mm³ and total protein of 38 mg/dL. Serum levels of sIL-2R (221 U/mL) and CSF levels of IL6 (1.9 pg/mL) were decreased to normal ranges. His neurological symptoms were stable and prednisolone doses were tapered for the following 2 months. Leptomeningeal hyperintensity signal areas were reduced on diffusion-weighted imaging (Fig. 3A, B) and leptomeningeal enhancement became absent (Fig. 3D, E). During the same period, cerebral blood flow was not altered on SPECT. At 5 months after steroid administration, leptomeningeal MRI lesions were diminished (Fig. 4A to 4D) and cerebral hypoperfusion was markedly attenuated (Fig. 5A to 5D). Our patient is currently treated with prednisolone at 20 mg/day. At the follow-up of more than 10 months, there were no laboratory and radiological data indicative of malignant lymphoma.

**Discussion**

We showed neuroradiological changes of cerebral hypoperfusion on SPECT and leptomeningeal lesions on MRI in a patient with RLM. These neuroradiological lesions were distributed dominantly in the right cerebral hemisphere. EEG also suggested the epileptogenic focus at the right frontoparietal regions.

RLM exhibits various neurological deficits due to CNS damages, including mental symptoms, epileptic seizures and focal neurological signs. The clinical features of our patient...
Figure 5. (A) Lateral right, (B) lateral left, (C) medial right and (D) medial left views of brain SPECT. Cerebral hypoperfusion is markedly recovered after 5 months of steroid therapy.

were also neuropsychiatric symptoms and myoclonic seizure. Previous case reports described that brain MRI depicted leptomeningeal lesions in RLM patients (1-12). Otherwise, MRI failed to find out brain parenchymal or cerebrocortical lesions in most of RLM patients (1-11). Only one case revealed an edematous lesion in the frontal lobe on MRI that was suggestive of rheumatoid meningoencephalitis (12). The generation mechanism of these encephalitis-like symptoms remains unclear. Brain MRI and SPECT findings of our patient indicated strongly that leptomeningitis-associated cerebrocortical hypoperfusion could contribute to various CNS symptoms in RLM patients.

In general, the frequency of RLM is extremely rare in RA patients and also its occurrence is not correlated with RA activity or duration. It is of interest that this chronic meningitis has not been pointed out in patients with malignant RA. RLM was affected usually in patients with early (< 2 years) or long duration (> 15 years) of RA (1, 2, 11). These clinical hallmarks of RLM may lead to difficulty for early diagnosis of RLM. Concerning the differential diagnosis of this disease, the common causes of chronic meningitis are known as fungus, mycobacteria and malignant tumors. It was noteworthy that subarachnoid MRI lesions of RLM can mimic leptomeningeal metastases of malignant tumors or acute subarachnoid hemorrhage (13, 14). The clinical differentiation between RLM and malignant lymphoma was important in the present patient. Repeated CSF cytology, whole body CT and gallium scintigraphy suggested no malignant tumors in our patient. At follow-up of more than 10 months, our patient showed no clinical or laboratory data of malignant lymphoma under tapering administration of prednisolone. Finally, these profiles indicated a clinicoradiological diagnosis of RLM in our patient.

In conclusion, we highlighted cerebral hypoperfusion on SPECT and leptomeningeal lesions on MRI. Both neuroimages supported that meningeal inflammatory effects and cerebral ischemia adjacent to leptomeningitis could play a major role in the pathogenesis of meningoencephalitis-like symptoms in RLM patients. Recovery of brain ischemia was confirmed after remarkable attenuation of MRI lesions by long-term steroid treatment. Thus, brain SPECT is a useful tool for the therapeutic evaluation of CNS involvement due to RLM. In addition to MRI, physicians should attempt brain SPECT for assessment of cerebral blood flow damages in RLM patients.

References


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