Reversible Posterior Leukoencephalopathy Syndrome in p-ANCA-associated Vasculitis

Yasutaka Tajima and Akihisa Matsumoto

Abstract

The perinuclear antineutrophilic cytoplasmic antibody (p-ANCA) is closely associated with rapidly progressing glomerulonephritis, microscopic polyangiitis, and allergic granulomatous angiitis. While mononeuropathy due to vasculitis is a well-known neurological manifestation of these conditions, manifestations involving the central nervous system (CNS) have rarely been reported. Our patient presented the very characteristic CNS lesion of reversible posterior leukoencephalopathy syndrome (RPLS) which has often been associated with hypertension, eclampsia, cyclosporine neurotoxicity, and other diseases (1). The patient also developed the recently established disease entity, Takotsubo cardiomyopathy (2).

Key words: reversible posterior leukoencephalopathy syndrome, p-ANCA, MRI

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Case Report

The patient was a 76-year-old woman who had developed a high-grade fever that persisted for over one month, and the cause was unknown. Three days before being referred to our hospital, she had experienced diplopia and left sided ptosis. As no other neurological abnormalities were apparent, mononeuropathy of the left oculomotor nerve was suspected. Her blood pressure was 110/76 mmHg and physical examinations were not remarkable. Laboratory examinations revealed an increased C-reactive protein (CRP) level and physical examinations were not remarkable. Laboratory examinations revealed an increased C-reactive protein (CRP) level and erythrocyte sedimentation rate. The white blood cell (WBC) count was 19,700 /mm$^3$ (Baso.0.7%, Eos 1.1%, Gran 72.7%, Lym 15.6%, and Mono 9.9%). Rheumatoid factor (RF) (231 IU/ml) and p-ANCA (643.2 U/ml) levels were highly elevated. In systemic examinations, no infection that could have caused the persistent high-grade fever was noted. Initially, her cranial magnetic resonance image (MRI) and magnetic resonance angiography (MRA) examinations demonstrated no significant changes. Analysis of the cerebrospinal fluid showed a normal protein content (30 mg/dl) and number of cells (2/mm$^3$).

On the basis of these findings, the patient was diagnosed with isolated oculomotor neuropathy associated with p-ANCA-positive vasculitic syndrome and the administration of oral prednisolone was started (60 mg/day). Soon after starting this treatment, the high-grade fever subsided and the movement of her left eye and ptosis were greatly improved. At seven days however, the patient suddenly began to complain of a headache and her consciousness was disturbed. Her blood pressure was 136/86 mmHg, which did not represent a significant change. Brain MRI examinations revealed high fluid attenuated inversion recovery (Flair) and T2 signal intensities in the bilateral parietal, occipital and right frontal lobes (Fig. 1A, B). However, there were no significant signal alterations in the diffusion-weighted image (DWI) and no apparent changes in the diffusion coefficients (ADC) map. MRA examinations revealed dilated intracranial vessels as compared with previous images (Fig. 1C). Posterior leukoencephalopathy associated with p-ANCA positive vasculitis was suspected and one gram of methylprednisolone was administered. On the following day, her blood oxygen level dropped rapidly and a chest x-ray showed pulmonary congestion. In echocardiography, poor motion of the left ventricular wall was observed, indicating Takotsubo cardiomyopathy, and the patient was transferred to the intensive care unit. With further steroid treatment, after three weeks, the previously observed high Flair and T2 signal intensity lesions had disappeared, the dilation of intracranial vessels was no longer apparent and p-ANCA had fallen to 152 U/ml (Fig. 1D, E, F). Though her conscious-
Figure 1. Flair (A) and T2 (B) MRI showed high intensity signals in the right frontal, bilateral parietal and occipital areas, indicating the posterior leukoencephalopathy syndrome. MRA (C) revealed dilatation of intracranial vessels. After three weeks, though the chronic ischemia had progressed slightly, the previously observed high intensity signal lesions had almost disappeared in Flair (D) and T2 (E) images, and no vascular dilation was obvious (F).

Discussion

The pathogenesis of ANCA-related vasculitis is very complicated, and several mechanisms are considered to be involved together in its development (3). In the present case, since DWI and the ADC map showed no significant signal alterations, vascular edema was suspected rather than cytotoxic edema (4, 5). Damage to the endothelium may lead to an increase in vascular permeability and extravasation which can break the blood-brain barrier and eventually result in uncontrollable vasogenic edema. In this regard, we feel that the dilatation of intracranial vessels seen in the present case, especially that of the peripheral small arteries, must be significant. Vasospasm has often been seen in RPLS associated with hypertension, but the MRA findings suggest vasodilatation in the present case. The mechanism is unclear, but failed autoregulation of the affected cerebral blood vessels might be involved.

Additionally, we feel that the Takotsubo cardiomyopathy observed was highly significant. This disease entity represents a relatively new concept and its pathogenesis remains to be determined, though coronary artery spasms, myocarditis, an over-response to catecholamine and stress have been postulated as causes. The present case suggests that it can also be associated with p-ANCA-positive vasculitis.
References


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