Relapsing Polychondritis with Encephalitis: A Case Report and Literature Review

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Abstract

We herein report the case of a 39-year-old man who developed bilateral auricular chondritis, conjunctivitis, and central neurological symptoms. He was diagnosed with encephalitis associated with relapsing polychondritis (RP) based on the findings of an ear cartilage biopsy, cerebrospinal fluid examination and magnetic resonance imaging. Although oral prednisolone (60 mg/day) was administered, the initial steroid therapy did not improve his symptoms. In contrast, methylprednisolone (mPSL) pulse therapy followed by prednisolone gradually ameliorated his condition. There were no episodes of recurrence during the two-year follow-up period. A review of the literature revealed that meningoencephalitis and encephalitis are rare, but important, complications of RP responsive to mPSL pulse therapy.

Key words: encephalitis, relapsing polychondritis, steroid pulse therapy


Introduction

Relapsing polychondritis (RP) is a rare autoimmune disease characterized by the presence of systemic and progressive inflammation and destruction of cartilaginous tissues (1). Although the etiology is unknown, type II collagen and matrilin-1 are considered to be potential candidates for target antigens (2). The clinical manifestations of RP include recurrent chondritis of the ears, nose, larynx and tracheobronchial tree, while less frequent manifestations include cardiac, neurological and renal diseases (1).

Peripheral and central nervous system (CNS) involvement is uncommon in cases of RP (3). To our knowledge, RP-associated meningoencephalitis and encephalitis, demonstrated clinically and on neuroimaging, have been reported in only 18 cases in the English literature (4-19). We herein report a case of RP with encephalitis and review similar previously reported cases.

Case Report

A 39-year-old Japanese man with a three-month history of pain and swelling in both ears and bilateral conjunctival hyperemia was admitted to a different hospital due to headache and general pain. He had no past history related to immunological diseases. In the outpatient clinic, RP was suspected based on the patient’s clinical presentation and high level of serum C-reactive protein (CRP, 9.38 mg/dL). He...
was treated with oral prednisolone (PSL) for six weeks, during which time the dose was gradually reduced from 60 to 20 mg/day. On admission, the serum CRP level was 5.28 mg/dL and antinuclear and anti-neutrophil cytoplasmic antibodies were negative. Oral PSL was administered at a dose of 60 mg/day. However, this initial steroid therapy did not improve the patient’s symptoms, and he subsequently experienced episodes of wandering and violence. Computed tomography findings of the head were unremarkable except for thickening in both ears (Fig. 1). Brain magnetic resonance imaging (MRI) was considered to be unremarkable. Initially, a diagnosis of steroid-induced psychiatric symptoms was suspected, and the dose of oral PSL was gradually tapered to 20 mg/day. However, the patient’s psychiatric symptoms did not improve. Because the initial steroid therapy was considered to be insufficient to suppress the high disease activity state with suspected RP-associated encephalitis, he was treated with methylprednisolone (mPSL) pulse therapy (1,000 mg/day for three days) starting on day 30 after admission. Consequently, the bilateral conjunctival hyperemia disappeared during the treatment with mPSL pulse therapy, after which the patient was referred to our hospital. At that time, the serum CRP level was 15.04 mg/dL.

On admission, the patient’s body temperature was 37.2°C. His height and weight were not measured due to these psychiatric symptoms. He was unable to communicate with medical staff. Both ears were swollen; however, no abnormal findings were observed in the heart, abdomen or lungs, including airway stenosis. A neurological examination revealed general acceleration of deep tendon reflexes. Laboratory blood tests showed an improvement in the inflammatory reaction after the administration of mPSL pulse therapy (CRP, 1.52 mg/dL). The cerebrospinal fluid (CSF) contained 19 leukocytes/μL (all mononuclear cells), with a protein level of 71 mg/dL and a glucose level of 80 mg/dL. Cultures and polymerase chain reaction (PCR) testing of the CSF for bacteria and herpes viruses were negative, and oligoclonal bands were absent. The CSF levels of interleukin-6 and tumor necrosis factor-α were 20.5 pg/mL and <0.5 pg/mL, respectively. Fluid-attenuated inversion recovery (FLAIR) images and T2-weighted MRI of the brain revealed high signal intensity lesions in the bilateral subcortical white matter, thalamus, middle cerebellar peduncle and corpus callosum (Fig. 2A). An ear cartilage biopsy showed moderate infiltration of inflammatory cells, primarily lymphocytes, around capillary vessels (Fig. 3).

Following admission to our hospital, the patient was treated with intravenous PSL at a dose of 40 mg/day. Empirical treatment for herpes encephalitis was also initiated while awaiting the PCR diagnosis. Two weeks after the start of the initial mPSL pulse therapy, the patient’s symptoms considerably improved. Intravenous mPSL (1,000 mg/day for three days) was again administered, followed by intravenous PSL at a dose of 40 mg/day for three weeks. Consequently, the patient’s symptoms slowly improved, and the intravenous and oral PSL doses were gradually tapered.
Follow-up brain MRI performed three months after admission showed that multiple lesions had nearly disappeared (Fig. 2B). All of the patient’s symptoms improved four months after the initial mPSL pulse therapy, and he was discharged. At that time, the dose of oral PSL was tapered to 17.5 mg/day. At the two-year follow-up visit, he continued to receive oral PSL (9 mg/day), with no recurrence of symptoms.

**Discussion**

The current patient was diagnosed with RP according to Damiani’s diagnostic criteria, including bilateral auricular chondritis, ocular inflammation, histologic confirmation and a positive response to corticosteroids (1, 3). Encephalitis associated with RP was suspected in this case due to the CSF pleocytosis and the brain MRI findings, and the administration of mPSL pulse therapy followed by PSL gradually improved the patient’s symptoms, with no recurrence of symptoms during the two-year follow-up period.

RP is a rare autoimmune disease characterized by the presence of systemic and progressive inflammation in different cartilaginous structures; the spectrum of clinical presentations may vary from intermittent episodes of painful auricular and nasal conditions to severe progressive multiorgan damage (1). Although CNS involvement due to vasculitis is rare, RP has been reported to be associated with aseptic meningitis, meningoencephalitis, encephalitis, and ischemic stroke (3). To our knowledge, there have been 18 cases of RP-associated meningoencephalitis and encephalitis demonstrated clinically and on neuroimaging in the English literature (4-19). The clinical features of the previously reported cases and the present case are summarized in Table.

Among these cases, the age of onset was between 29 and 73 years (mean, 55 years). Interestingly, the male-to-female ratio was 16:3, and 58% of the patients (11 of 19) were reported from Asian counties [seven from Japan (5, 7, 10, 11, 13 and our case), two from China (16), one from Taiwan (6) and one from Korea (17)]. The interval between the onset of meningoencephalitis and encephalitis and the onset of RP ranged from six days to four years. In two patients, typical RP symptoms were not noted at the onset of meningoencephalitis and encephalitis.

Most patients exhibited predominantly mononuclear pleocytosis in the CNS, and the brain MRI findings were characterized by the presence of bilateral high signal intensity lesions on FLAIR and T2 images in the medial temporal lobe, including the hippocampus, or subcortical and periventricular deep white matter. It should be noted that repeated MRI was required to obtain these findings in some cases (5, 8), including our case. The brain lesions in such cases became obvious on MRI images obtained several weeks after the onset of the initial neurological symptoms. In the autopsy case reported by Yan et al. (8), the histopathological findings were often more extensive than those suggested by the MRI features.
Simultaneous auricular and brain biopsies performed in two patients showed active inflammation with chondritis and meningoencephalitis. Although perivascular cuffing around the meningeal and intracerebral vessels was observed with an increased vascular wall thickness, these histological features were not specific for vasculitis (7). Brain autopsies performed in three cases showed neuronal loss and gliosis in the hippocampus with leptomeningeal lymphocytic infiltrates (8), non-specific meningoencephalitis without evidence of vasculitis (12) and non-specific subacute and chronic inflammation of the meninges and both white and grey matter spreading cortically (18). Although vasculitis is assumed to be the cause of CNS involvement in patients with RP (16), the above-mentioned observations do not support this assumption. In addition, obvious risk factors were not noted in the previously reported cases or our current case of RP-associated meningoencephalitis and encephalitis. The etiology of these CNS complications in cases of RP therefore remains unknown, although the disease appears to originate from autoimmunity (16). Autoantibodies to glutamate receptor GluR ε2 and neutral glycosphingolipids are detectable in the CSF and sera obtained from some patients with limbic encephalitis associated with RP (13, 20). However, we were unable to examine the presence of these autoantibodies in our patient.

All patients, except for one with uncontrolled diabetes mellitus, were treated with high-dose steroids either with or without additional immunosuppressive agents. Of the 18 patients treated with high-dose steroids, including mPSL pulse therapy, 11 showed significant improvements in their neurological symptoms (from within one week to three months), four demonstrated no improvements in symptoms and three died five to 18 months after disease onset. In two of the cases in which the patients died (8, 12), more intensive and/or timely treatment was likely required.

In summary, meningoencephalitis and encephalitis are rare but serious complications of RP. Providing an early diagnosis and treatment with mPSL pulse therapy is important for obtaining a better outcome.

The authors state that they have no Conflict of Interest (COI).

References