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Case Report

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Relapsing Polychondritis Presented with Encephalitis Followed by Brain Atrophy

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Relapsing polychondritis (RP) is a rare autoimmune disease that is characterized by inflammatory reaction of unknown etiology and destruction of cartilaginous structures. Characteristic symptoms of this disease include cartilage inflammation of the ear, nose, larynx, trachea, bronchi, joints, eyes, heart and skin. Concomitance with neurologic symptom is very rare in RP, and the detailed underlying mechanism of neurological involvement associated with RP is not fully understood. We herein described an unusual recurrent case of inflammatory brain lesions associated with RP, with attention to clinical manifestations, autoimmune disease involvement, and therapeutic effects.

Key words: Relapsing polychondritis, Encephalitis, Brain atrophy, Multiple sclerosis, Neuromyelitis optica

INTRODUCTION

Relapsing polychondritis (RP) is a rare autoimmune disease that is characterized by inflammatory reaction of unknown etiology and destruction of various cartilaginous structures [1, 2]. Characteristic symptoms of this disease include cartilage inflammation of the ear, nose, larynx, trachea, bronchi, peripheral joints, eyes, heart and skin [2].

However, other systemic manifestations may be observed in patients with RP such as arthralgia, unilateral or bilateral episcleritis, non-specific fever, anorexia, and weight loss; therefore, RP is sometimes misdiagnosed, with a potentially fatal prognosis [1, 2].

Neurological symptoms have rarely been reported, and include cranial nerve palsy, stroke, and meningoencephalitis [2-4].

However, the detailed underlying mechanism of neurological involvement associated with RP is not fully understood. In addition, recurrent inflammatory brain lesions associated with RP have not been reported. Herein, we describe an unusual case of RP presenting with recurrent inflammatory brain lesions.

CASE REPORT

A 33-year-old man presented with headache, decreased mentation, memory impairment, dysarthria, and excessive sleepiness. On presentation at our department, detailed assessments of cognition and motor and sensory function were not possible because of deteriorated mental status and hearing

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difficulty. He denied past medical history of immune-related or neurological diseases, and also there was no familial history of immune-related disease.

Brain magnetic resonance imaging (MRI), using fluid-attenuated inversion recovery (Fig. 1A) and gadolinium-enhanced T1-weighting (Fig. 1B), revealed multiple high-signal lesions with enhancement in the bilateral cerebral cortex, subcortex, and deep white matter.

Cerebrospinal fluid (CSF) analysis showed leukocytosis (white blood cells 20, lymphocytes 58%) and increased protein (64.1 mg/dl). In addition, blood test revealed increased C-reactive protein (CRP) concentration (6.07 mg/l) and white blood cell (WBC) count (17660/ul).

Because of a possibility of immune-related inflammatory brain disease including multiple sclerosis (MS), neuromyelitis optica (NMO), autoimmune encephalitis and vasculitis, we performed specific laboratory tests and evaluated IgG index, oligoclonal band, autoimmune antibodies, targeting neuronal cell surface antigens, ion channels (voltage-gated potassium channels), ligand-gated ion channels (N-methyl-D-aspartate [NMDA], α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid [AMPA], and gamma-aminobutyric acid [GABA]-b receptor channels) and also tested for rheumatoid factor, lupus anticoagulant, anti-SSA/SSB, and anti-neuromyelitis optica (NMO) antibodies; there were no specific abnormalities.

Interestingly, physical examination showed swollen and stumpy earlobes with tenderness (Fig. 2), and a diagnosis of relapsing polychondritis (RP) was confirmed by tissue biopsy of auricular perichondrium, which revealed abundant lysozyme-positive macrophages, consistent with RP (Fig. 3).

The patient started treatment with 1,000 mg methylprednisolone intravenous (IV) bolus for 5 days, followed by oral prednisolone (1 mg/kg/day).

After high-dose steroid treatment, the patient's mentality, headache, hearing difficulty and language functions gradually recovered. Since then, he had received immunosuppressive treatment with methylprednisolone 16 mg and azathioprine 100 mg.

However, although he remained on medication, his symptoms recurred 6 months later. On the second admission, he was lethargic and emotionally labile and had focal neurologic deficits of dysarthria and clumsiness. A follow-up MRI showed newly developed, small, T2 high-signal intensities in the right posterior basal ganglia, left external capsule and both temporal lobe with suspected brain atrophy and ventricular dilatation (Fig. 1C). A follow-up CSF study showed normal results

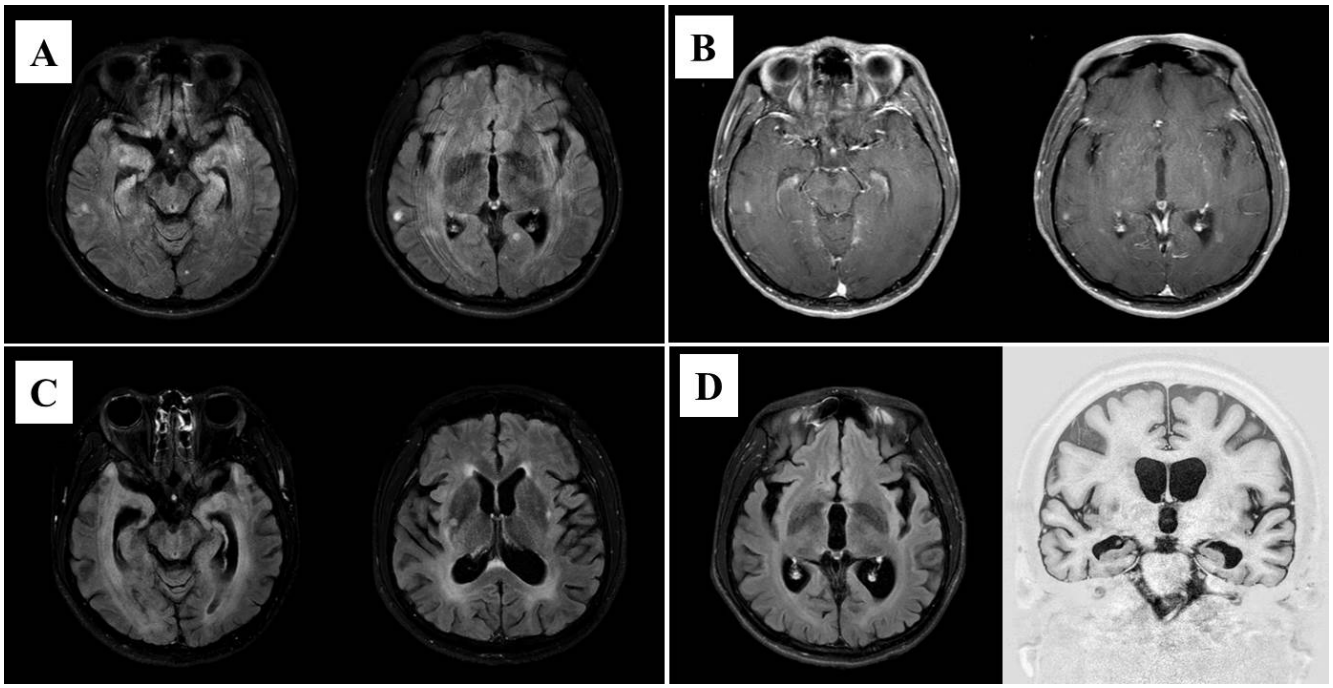

Fig. 1. Brain magnetic resonance imaging (MRI), using fluid-attenuated inversion recovery (A) and gadolinium-enhanced T1-weighting (B), revealed multiple high-signal lesions with enhancement in the bilateral cerebral cortex, subcortex, and deep white matter. After 6 months later, a brain MRI showed newly developed, small, T2 high-signal intensities in the right posterior basal ganglia, left external capsule and both temporal lobe with advanced brain atrophy (C). And a recent followed-up brain MRI showed aggravated brain atrophy with third and lateral ventricular dilatation (D).

without leukocytosis. The patient started treatment again with 1,000 mg methylprednisolone IV bolus for 5 days, followed by oral prednisolone (1 mg/kg/day) with mycophenolate and cyclophosphamide.

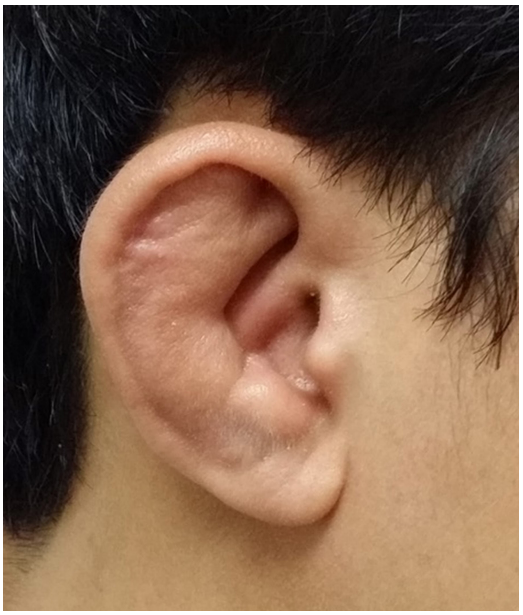

Fig. 2. Characteristic swollen and stumpy earlobes indicative of relapsing polychondritis in our patient.

After high-dose steroid treatment, the neurological manifestations have remained well-controlled but brain atrophy with ventricular dilatation had progressed on follow-up brain MRI (Fig. 1D).

DISCUSSION

We herein described an unusual recurrent case of inflammatory brain lesions associated with RP, with attention to clinical manifestations, autoimmune disease involvement, and therapeutic effects.

RP is a rare autoimmune disease of unknown etiology, characterized by inflammation and deterioration of cartilage [1-5]. The pathomechanism is thought to be related to an immune-mediated attack on particular proteins that are abundant in cartilage [1, 5, 6]. Coexisting autoimmune diseases have been reported to include systemic vasculitis, rheumatoid disease, lupus erythematous, Sjogren's syndrome, Behcet's disease, ankylosing spondylitis, psoriatic arthritis, and polymyalgia rheumatic [1-6]. Therefore, RP can disrupt the blood-brain barrier (BBB), and consequently become a pathogenic cause of recurrent autoimmune encephalitis. Usually, therapies for RP typically involve medications to suppress the immune-associated inflammations. Corticosteroid is initially used via oral or intravenous administration, and a few

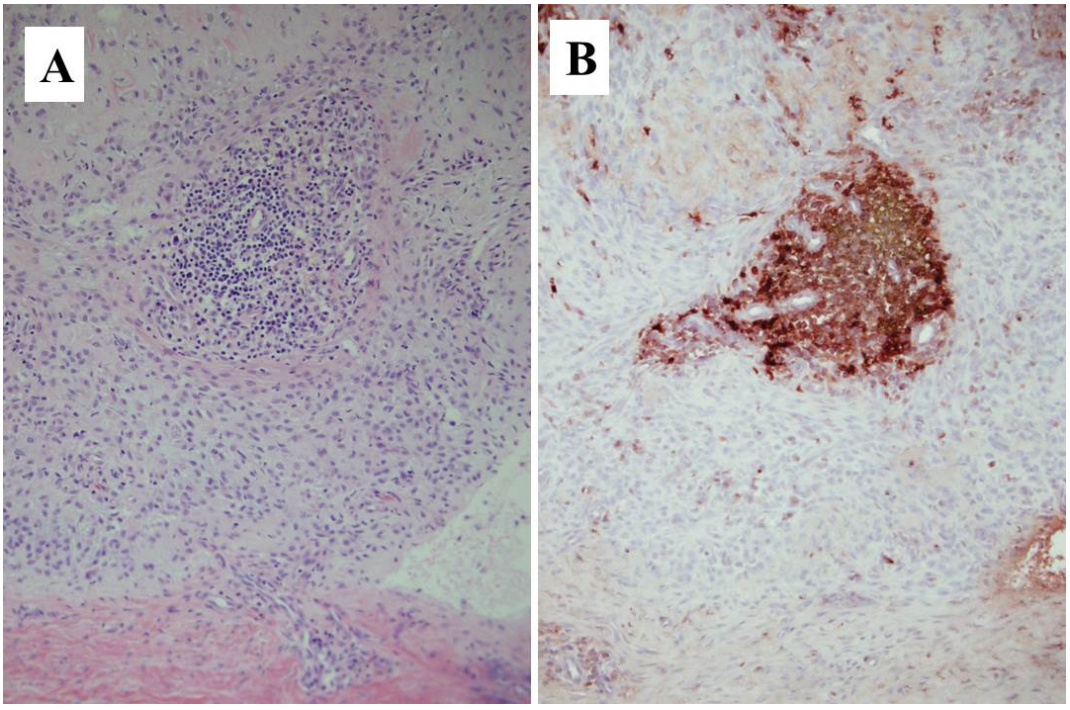

Fig. 3. Tissue biopsy of auricular perichondrium revealed abundant macrophages (A, H&E) with lysozyme-positivity (B, lysozyme immunohistochemistry) consistent with relapsing polychondritis.

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immune-suppressants such as azathioprine, methotrexate or cyclophosphamide may be used to suppress the immune reactions and minimize doses of steroid [1-6].

Concomitance with neurologic symptom is very rare in RP and only occurs in 3% of patients with RP, furthermore the detailed underlying mechanism of neurological involvement associated with RP is not fully understood [4-6]. The common neurological manifestations following RP are cranial nerve palsies involving the facial and trigeminal nerves, and also encephalitis, myelitis, polyneuropathy, seizures and multifocal areas of enhancement consistent with cerebral inflammation have been rarely reported [1-6]. Therefore, RP presenting with neurological symptoms can be easily misdiagnosed and treated incorrectly, although RP is potentially fatal, and early diagnosis and treatment may reduce morbidity and mortality [1-6]. Fortunately, our patient did not showed serious systemic manifestations of respiratory difficulty by tracheal chondritis, ocular inflammation and cardiovascular involvement. He just revealed mild systemic symptoms of arthritis, bilateral auricular chondritis and hearing difficulty.

In addition, this unusual case serves to remind clinicians that recurrent cerebral inflammation with multifocal enhancement which look like those of multiple sclerosis (MS), neuromyelitis optica (NMO), vasculitis and autoimmune encephalitis, can be found in RP [7, 8]. For treating MS and NMO, various disease-modifying therapies (DMTs) and immunosuppressants have been developed and are with significant therapeutic efficacy [7, 8]. This case also suggests that complete evaluation with physical examination, brain MRI, rheumatic autoantibodies, and CSF study are warranted to investigate the possibility of various autoimmune diseases, before administering DMTs or immunosuppressants.

In conclusion, our patient showed recurrent CNS inflammation, followed by neurological symptoms of headache, hearing difficulty, lethargic state, memory impairment, and dysarthria, and early diagnosis followed by high-dose steroids and immunosuppressant have markedly improved his neurological symptoms and MRI findings. However, proper management of the patient with RP will be needed to prevent another recurrence of CNS inflammation and further brain atrophy.

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