Relapsing Polychondritis Presenting with Meningoencephalitis and Dementia: Correlation with Neuroimaging and Clinical Features

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Abstract-

Purpose: Relapsing polychondritis (RP) is a rare systemic autoimmune disease affecting cartilaginous and non-cartilaginous structures. Neurological involvement is rarer but results in profound disability. Early identification and treatment of underlying RP may promote neurological recovery.

Case Report: We illustrated a 53-year-old man diagnosed with dementia. Neuroimaging and cerebrospinal fluid studies disclosed meningoencephalitis. "Prominent ear sign" was evident on diffusion-weight magnetic resonance imaging. After glucocortisone administration, the improvement of clinical manifestations was closely correlated subsequent neuroimaging findings.

Conclusion: The importance of better understanding of this disease in terms of the prevention of further tissue damage in patients with RP cannot be overemphasized.

Key Words: relapsing polychondritis, auricular chondritis, meningoncephalitis, dementia, prominent ear sign

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INTRODUCTION

Relapsing polychondritis (RP) is a rare multisystem disorder affecting cartilaginous tissue including the hyaline cartilage of joints and the fibrocartilage of extra-articular location, as well as proteoglycan-rich structures such the media of the arteritis and eye [(1)]. Its pathogenesis appears to be an immune-mediated reaction against collagen type II [(2)], collagens type IX and XI [(3)]. Corticosteroid remains a mainstay of medical treatment of RP. Clinical features of RP are protean dependent on tissue involvement. Early identification of PR and prompt intervention might be beneficial for its prognosis. Nervous system involvement can manifest as meningoencephalitis [(4)], dementia [(5)], stroke [(6)], and parkinsonism [(7)]. Awareness of RP may prevent subsequent disability secondary to irreversible brain or nerve tissue damage.

We report a case with meningoencephalitis and dementia that RP could be allowed in the differential diagnosis on account of the unique feature of bilateral

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auricular hyper signal intensity on diffusion-weighted imaging (DWI).

CASE REPORT

A 53-year-old man with mental deterioration for 8 months presented with memory impairment, place disorientation, difficulty in verbal communication, reduced calculation ability, and poor performance in routine job task. Inappropriate mood response was persecuted by his wife. Formerly an introverted man, the patient began to be hyper talkative and to feel more physically active than he did before. He denied swallowing problem, but weight loss from 58 to 45 kg within one year. Under the impression of dementia, cranial computed tomography (CT) scan was conducted and it showed unremarkable finding at out-patient clinic of Neurology. Brain single-photon emission computed tomography (SPECT) imaging with ^{99}m Tc-ethylene cysteine diethylester [ECD] ligand demonstrated reduced uptake in bilateral temporal and left frontal lobes which is indicative of decreased perfusion/metabolism in these areas. Thus, he was admitted for further investigation to exclude the diagnosis of frontotemporal dementia. On admission, a detailed history was obtained from the patient's wife. Because the patient displayed intermittent word-finding deficits, he mumbled when he tied to say something. Memory impairment would improve with cueing. He didn't pass interlocking pentagon copying and clock drawing test. Calculation skill was profoundly impaired as well. There is neither primitive reflex nor urinary incontinence. No abnormal neurological examination was shown regarding muscle strength, deep tendon reflex, sensory modalities, cerebellar function, and gait.

Laboratory investigation for dementia revealed negative findings including thyroid function profile, B12 level, rapid plasma regain for syphilis, and human immunodeficiency virus survey. Brain magnetic resonance imaging (MRI) with gadolinium enhancement disclosed high signals in the bilateral auricles on DWI (Fig. 1A) and abnormal leptomeningeal enhancement and multiple nodular enhancement on T1-weighted MRI (Fig. 1B), and multiple high signals in the above mentioned nodules on T2-weighted fluid attenuated inversion recovery (T2 FLAIR). Metastatic brain lesion or infectious disease was suspected from brain MRI findings. Cerebrospinal fluid (CSF) examination revealed white cell count 38/cmm, lymphocyte 29/cmm, protein 108 mg/dL, and glucose 66 mg/dL (serum glucose 124 mg/dL). Microbiology for CSF studies excluded bacterial, fungal, or tuberculosis infection. Tumor marker survey of serum or CSF cytology didn't detect any evidence of neoplasm.

We reviewed the patient's history from out-patient clinic chart record. He had suffered from three episodes of bilateral auricular erythema and pain before. Rheumatologist also noticed ocular inflammation and multiple joint pain affecting bilateral knee and fingers. RP was established before the onset of dementia. Studies concerning connective tissue diseases were all negative except rheumatoid factor measured as 116 IU/ml (normal < 20 IU/ml).

Meningoencephalitis and dementia associated with RP was highly suspected. He was started on pulse therapy with intravenous methylprednisolone as 1 gram daily for 3 days and maintenance with oral prednisolone in the dosage of 1 mg/kg. Two weeks later, his calculation ability

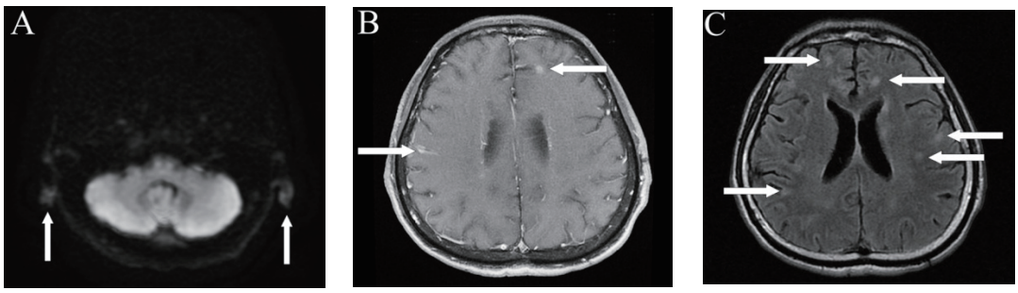

Figure 1. Initial MRI of the brain on admission. (A) DWI showed a hyper signal in bilateral auricles. (B) Leptomeningeal enhancement and multiple nodules were demonstrated on T1WI with contrast and fat suppression. (C) T2WI FLAIR showed multiple small hyper signal nodules in bilateral frontal lobes.

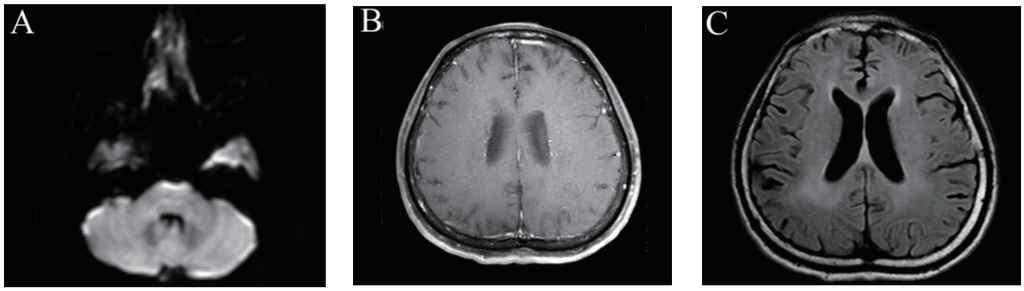

Figure 1. Follow-up MRI of the brain after 6 weeks. (A) DWI showed that the hyperintense signal in the bilateral auricles had disappeared after 6 weeks of treatment. (B) T1WI with contrast and fat suppression showed substantial reduction of multiple enhanced nodules. (C) T2WI FLAIR also showed that all of the small nodules had disappeared.

became improved and he also displayed less troublesome in verbal communication. Sequential brain MRI studies were conducted six weeks later. Bilateral auricular hyper signal intensities on DWI resolved (Fig. 2A). Leptomeningeal enhancement and multiple nodular lesions also became less which corresponded to his clinically improvement (Fig. 2B and 2C).

DISCUSSION

Because of rarity of RP, there is lack of awareness about this disease. Trentham and Le reported that the mean delay from clinical presentation to diagnosis was 2.9 years [8]. However, disability and fatal outcome can occur if left untreated. It is paramount to get acquainted with the diagnosis of RP. The diagnosis of RP relied on characteristic clinical features. There are three diagnostic criteria for relapsing polychondritis including McAdam et al. [9], Damiani et al. [10], and Michet et al. [11]. Our patient developed auricular chondritis (AH), polyarthritis, and ocular inflammation. Neurological symptoms responded to steroid therapy. According to all of the above three diagnostic criteria, RP can be established.

AH is the most frequent and unique feature in RP. Our patient presented with AH in a recurrent manner to reflect a relapsing inflammatory nature. Bilateral auricles with hyper signal intensity on DWI also subsided after steroid therapy. "Prominent ear sign" on DWI [12] may play an important role on the identification of AH among patients with RP. Wang et al. also reported abnormal signal in the bilateral auricles on DWI in 2 of 4 cases [4]. To our knowledge, this case illustrates a reversible "prominent ear sign" for the first time. Auricular biopsy can be avoided in order to reduce additional cosmetic deformity.

Although nervous system manifestations are not included in the criteria of RP, central or peripheral nervous system can be affected. Despite of its only 3% in patients with RP [13], neurological disability may be debilitating. Meningoencephalitis has been mostly reported in many articles and was reviewed by Wang et al. [4]. Most of them disclosed aseptic CSF pleocytosis and response to steroid use. Brain MRI abnormalities are non-specific for meniongoencephalitis of RP. In our case, leptomeningeal infiltration and multiple subcortical nodular enhancements and abnormal CSF data were identified to support the notion of meningoencephalitis. Almost complete resolution was accompanied by steroid therapy. Initial cranial CT scan didn't reveal any abnormality which might be due to the superiority of MRI to demonstrate the detail and differences between different soft tissues. However, brain ECD-SPECT scan disclosed a reduction of cerebral blood flow in several regions which are compatible with clinical presentations of dementia.

In general, prognosis of PR depends on the affected location, the severity of inflammation, and the timing of medical intervention. Fatal outcome can occur among patients with RP. Common causes of death are cardiovascular or respiratory complications. A variety of cardiovascular morbidity may result in a potential lethal consequence [14]. The majority of cardiovascular disease arises from the mechanism of vasculitis which affects vessels of all size. Detailed monitoring of cardiovascular

events may reduce a fatal outcome. Airway chondritis also represents a life-threatening condition. Up to 50 % of RP patients eventually will develop respiratory tract affection. Symptoms initially manifest in an ambiguous fashion, but RP can lead to tracheobronchial collapse and airway obstruction. Chest CT scan was suggested to conduct in all patients with RP. Our patient's chest CT scan showed unremarkable finding [15]. Great awareness of neurological, respiratory, or cardiovascular manifestations in RP may initiate a more aggressive treatment. Medication for RP is largely empiric since randomized clinical trial is almost impossible for a rare disease. Based on clinical trials for systemic vasculitis, intravenous pulse methylprednisolone is delivered by the dosage of 1 g/d for 3 consecutive days followed by oral prednisone maintenance. Relapses tend to occur if steroid is reduced too rapidly. When clinical response to steroid is not achieved or relapse occurs, the second-line drugs including cyclophosphamide and azathioprine are required [16].

In summary, RP is a rare, disabling, potentially fatal, but treatable autoimmune disease. Early diagnosis and treatment may prevent serious tissue damage of the vital organ. It is a multisystem disorder including brain. Neurologists should put RP in the differential diagnosis in the setting of meningoencephalitis with dementic presentation.

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