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*Research Paper*

# A case and literature review of Relapsing polychondritis

Anna Zhou[1], Xindi Li[2], Lin Zhao[2], Yonghong Liu[2], Heng Zhou[2], Huabing Wang[2], Tian Song[2] and Xinghu Zhang[2]*

[1]Beijing Children hospital Capital Medical University
[2]Department of Neurology, Beijing Tiantan Hospital Capital Medical University, No. 6 Tiantanxili Dongcheng District, Beijing, China.

*Corresponding author. E-mail: xhzhtiantan@hotmail.com. Tel: +86 13911296676.

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**ABSTRACT**

This study aims to describe the clinical manifests, CSF features and brain MRI characters of patients with relapsing polychondritis (RP) and central nervous system (CNS) involvement presented as encephalitis. Seven cases with RP and CNS involvement were enrolled from 2011 to 2015. RP was diagnosed upon the modified McAdam criteria and CNS dysfunction secondary to RP decided by clinical manifests, CSF analysis and brain MRI. Of the seven (7) cases, three (3) confirmed RP, while four (4) were probable. All of the RP patients with CNS involvement were presented as encephalitis. The common clinical features of CNS involvement were fever and headache, while brain MRI findings were in diversity. The CNS symptoms were relieved after steroid. CNS involvement in RP has no specific findings both in symptoms and brain MRI findings. When one patient presented with encephalitis has extra-CNS manifestations such as eye and ear abnormalities, CNS involvement of RP should be suspected.

**Keywords:** Relapsing polychondritis (RP), central nervous system (CNS), encephalitis.

## INTRODUCTION

Relapsing polychondritis (RP) is a rare auto-immune systemic inflammatory disease characterized by recurrent episodes of inflammatory and progressive destruction of the cartilaginous structures of the nose, ears, joints and tracheobronchial tree; it also affects the eyes, inner ear, kidneys bloods vessels (Lahmer et al., 2010). It was first described by Jaksch-Wartenhorst in 1923 and was named by Pearson in 1960. The annual incidence of the disease is about 3.5 cases per million, with greater than 600 cases worldwide, and the average age when diagnosis is 44-51 years old (Adliff et al., 1997).

Clinically, the disease can involve the CNS and lead to neurological dysfunction. CNS involvement manifests in diversity including encephalitis. Ohta (2004) reported the first case of RP with non-paraneoplastic limbic encephalitis, which presented fever, headache, mental disorder, epilepsy, weakness and dizziness etc easily misleading to encephalitis. The reports about CNS involvement of RP are relatively rare. Here, we reported seven cases with RP who presented clinical manifestations similar to encephalitis in order to explore clinical presentation, CSF and brain MRI characters of RP patients with CNS involvement.

## MATERIALS AND METHODS

In this series, 7 RP patients were diagnosed as CNS involvement in the Department of Neurology, Beijing Tiantan Hospital from January, 2011 to December, 2015. RP was diagnosed upon McAdam modified criteria which was set up in 1976. McAdam criteria suggests that a diagnosis of RP is almost certain if three out of the following six criteria are fulfilled: (a) bilateral auricular chondritis; (b) nasal chondritis; (c) respiratory tract chondritis; (d) non-erosive seronegative polyarthritis; (e) ocular inflammation and (f) audiovestibular damage (McAdam et al., 1976). Afterward, a McAdam criterion was modified. Upon modified criteria, RP can be diagnosed if fulfilling one of the following criteria: (a) at least three of the clinical criteria stated in McAdam criteria; (b) chondritis at two or more separate anatomic

**Table 1:** Summary of the clinical information, CSF and blood results in 7 RP cases with CNS involvement.

| Case number | Age (years) | Gender (F/M) | No-CNS symptoms | CNS symptoms | Duration of onset before diagnosis (month) | Diagnosis | Sequence of CNS and no-CNS symptoms | CSF profile | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Opening Pressure ($mmH_2O$) | Leucocytes (/ul) (0-6) | Monocyte (%) | Protein (mg/dl) (15-45) | Glucose (mmol/L) (2.5-4.5) |
| 1 | 26 | M | Auricular chondritis, scleritis, | Fever, headache, mental disorder | 1 | Probable RP | CNS symptoms ahead | 170 | 22 | | 28 | 2.9 |
| 2 | 48 | F | Auricular chondritis, scleritis, arthritis | Fever, headache, dizziness, bulbar paralysis | 0.5 | RP | Simultaneously | 90 | 40 | 60 | 31 | 3.1 |
| 3 | 46 | M | Auricular chondritis, scleritis, | Headache, epilepsy, aphasia, mental disorder | 1 | Probable RP | Simultaneously | 260 | 146 | 58.9 | 85.6 | 3.4 |
| 4 | 41 | M | Auricular chondritis, scleritis, laryngitis | Headache, limb weakness, mental disorder | 12 | RP | CNS symptoms ahead | 200 | 6 | | 60.2 | 3.5 |
| 5 | 46 | M | Scleritis, arthritis | Fever, headache, dizziness, tinnitus, hearing impairment | 5 | Probable RP | CNS symptoms ahead | 190 | 30 | 100 | 30.42 | 4.96 |
| 6 | 51 | M | Auricular chondritis, scleritis, | Headache, dizziness, bulbar paralysis, weakness, decrease of vision, facial paralysis | 24 | Probable RP | CNS symptoms behind | 150 | 15 | | 41.3 | 4.2 |
| 7 | 38 | M | Auricular chondritis, scleritis, nasal chondritis, bronchomalacia | Fever, headache, tinnitus, hearing impairment, facial paralysis, bulbar paralysis, weakness, uroschesis | 12 | RP | CNS symptoms ahead | 150 | 22 | 22.77 | 70.03 | 3.48 |

locations with response to steroids (Chuah and Lui, 2016).

CNS involvement of RP was judged by mainly CNS symptoms besides fulfilling the modified McAdam criteria.

## Clinical information

Seven cases with RP and CNS involvement were included in this study. Among them, four cases were definite RP who fulfilled all the modified McAdam criteria, while 3 cases were probable RP who only fulfilled 2 out of the 6 criteria. The average age of onset of RP was 42.3 (range: 26 to 51) years old, female-to-male ratio was 1:6. The duration of symptoms before diagnosis ranged from fifteen days to two years. Table 1 shows the clinical manifestations of these 7 cases.

In this series, the most common clinical features of RP were scleriti (n=7) and auricular chondritis (n=6) which showed the redness of bilateral eyes and swelling ears (Figure 1). In addition, laryngitis, arthritis, nasal chondritis and bronchomalacia were observed in one or two cases. Skin damage, renal damage or cardiac involvements were not found. All the symptoms of destruction of the cartilaginous structures of the nose, ears, joints and

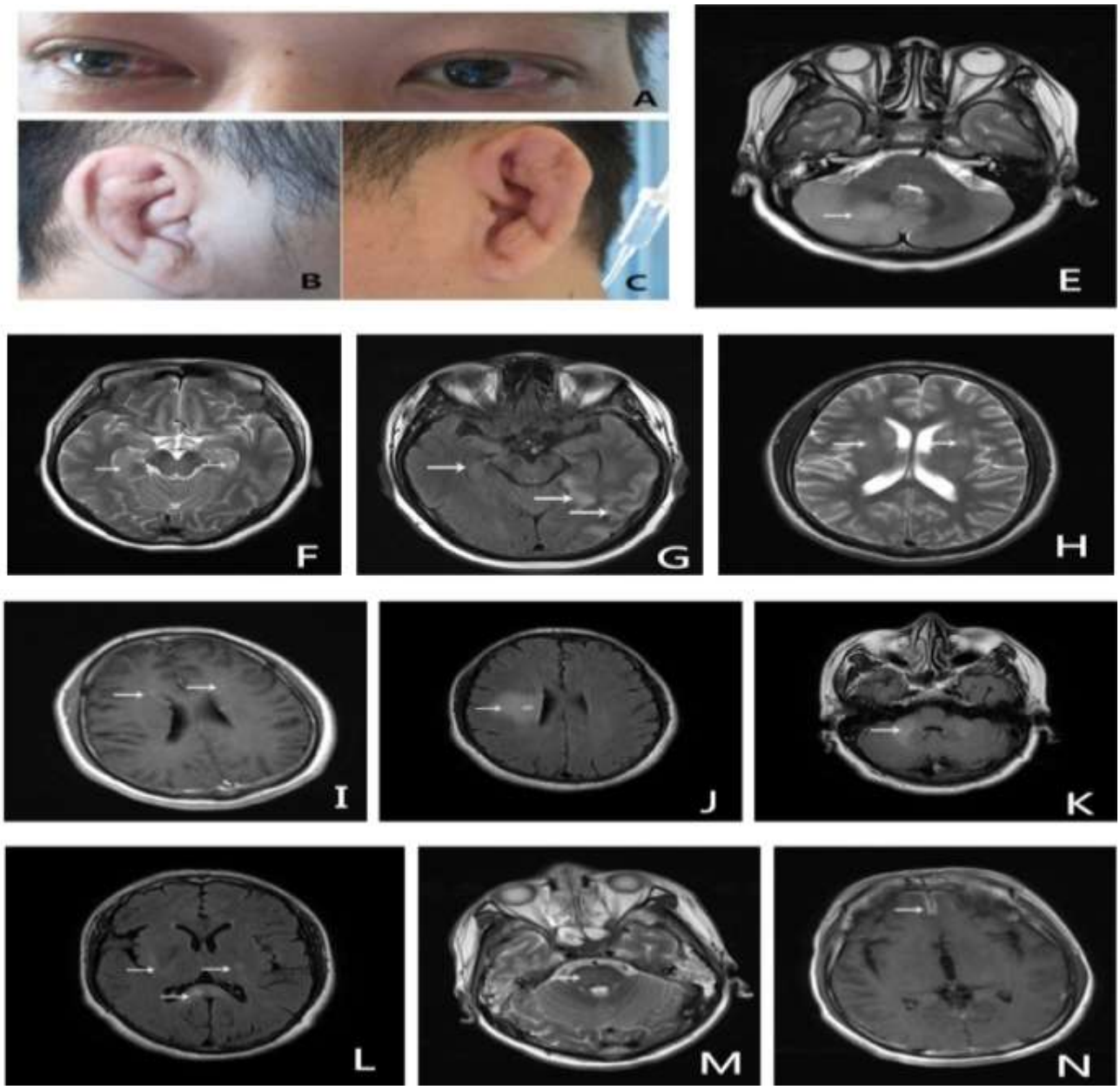


**Figure 1:** Case 4 showed redness of both eyes (A), redness and swelling of both ears (B, C). Brain MRI showed abnormal signals without enhancement in right cerebellum hemisphere, cerebellum vermis (E: T2W image) and bilateral temporal lobes (F: T2W image) in case 2, abnormal signals in bilateral temporal (G:Flair image), left occipital lobe (D: T2W image; E: Flair image; F: CE image) in case 3, multiple abnormal signals with some enhancement in bilateral basal ganglia (H: T2W image), corona radiate and centrum semiovale (I: CE image) in case 4, abnormal signals with some enhancement in right corona radiate (J), right cerebellum hemisphere (K), corpus callosum (L) in case 6 and abnormal signals in pons (M) and meningeal enhancement in anterior longitudinal fissure (N) in case 7.

tracheobronchial tree were relieved after steroid treatment. Headache was found in all cases, with or without fever. The other CNS symptoms included mental disorder, epilepsy, aphasia, bulbar paralysis, decrease of vision, facial palsy, limb weakness and uroschesis (Table 1).

The CNS symptoms and cartilaginous destruction features occurred at the same time in both cases and CNS symptoms appeared before cartilaginous features in four cases. There was also a case where cartilaginous manifests appeared ahead.

### Serum and CSF analysis

Blood WBC counts were elevated in 6 cases, ESR increased in 5 cases and CRP increased in 6 cases. In 3 cases, intracranial

pressure was high. CSF WBC count increased in six cases and protein was elevated in three cases. All the findings in blood and CSF implied the possibility of inflammation in CNS.

**Brain MRI**

All cases got brain MRI scanning. MRI finding was in diversity without specific signs. Two cases had normal MRI. 4 cases had abnormal signals in brain parenchyma (cerebellum: 2 cases (Figure 1E and K), pons: one case (Figure 1M) and cerebral cortex: one case (Figure 1G). Moreover, thalamus, basal ganglia, corona radiate and centrum semiovale and corpus callosum could also be involved (Figure 1F, H, I, J and L). One case had meningeal enhancement in anterior longitudinal fissure (Figure 1N).

**Treatment and follow-up**

All of our patients were given intravenous methylprednisolone (500 mg/d, 5 days) or dexamethasone (20 mg/d, 7 days), thereafter, oral prednisone (60 mg/d) followed and tapered gradually. After steroid therapy, both CNS and no CNS symptoms improved remarkably.

**DISCUSSION**

RP is a rare disease with the incidence of approximately 3.5 per million/year (Cantarini et al., 2014). CNS involvement in RP is estimated to occur with an incidence of 3% RP patients (Kent et al., 2004).

Encephalitis is one of the manifestations of CNS involvement, which was first reported by Ohta et al. (2004). Besides encephalitis, other manifestions of CNS involvement included headache, seizures, hemiplegia, aseptic meningitis, and cerebral aneurysms (Cantarini et al., 2014). In our series, symptoms of CNS involvement included fever, headache, mental disorder, dizziness, weakness or speech difficulty.

Due to lack of specific biomarkers, the diagnosis of RP is still a challenge. McAdam criteria (McAdam et al., 1976) is now widely accepted in which RP is mainly diagnosed based on clinical features including auricular and nasal chondritis, ocular inflammation, non-erosive inflammatory polyarthritis, respiratory tract chondritis and audiovestibular damage. A definite RP is made when three of six clinical features are present along with the histological findings of affected cartilage which are loss of basophilic staining of the cartilage matrix, perichondrial inflammation and eventual destruction of cartilage replaced by fibrotic tissue (Ohta et al., 2004). In our patients, two cases had three clinical features, while the others had two. All of them lacked tissue biopsy. It should be stressed that all of our patients had auricular chondritis and ocular inflammation which may be a symbol of RP.

Patients with CNS involvement in RP sometimes have CSF profiles mimicking meningoencephalitis. Wang et al. (2011) described 4 patients with RP who were suspected of meningoencephalitis upon elevated WBC and protein in CSF. All of our patients were considered as viral encephalitis or meningitis at the local hospital based on the elevation of WBC count (4 cases) and increase of protein content (2 cases) in CSF.

These findings remind us that encephalitis should be carefully differentiated. One should pay much attention to extra-CNS manifestations which maybe a clue of final diagnosis, for example, swelling nose, cauliflower ears and redness eyes are helpful to the diagnosis of RP.

The pathogenesis of RP arises from an immunologic reaction to type II collagen with specific circulating antibodies present in approximately two-thirds of patients with RP (Childs et al., 2012). The mechanism of CNS involvement in RP may be related to vasculitis (Hsu et al., 2006). However, Kashihara et al. (2009) found positive anti-CluR antibodies in sera and CSF of a RP patient with limbic encephalitis, thus, mechanism of CNS involvement in RP may be complicated.

Brain MRI is an important tool in neurological disorders. In a report, some RP patients presented with encephalitis had lesions in the temporal lobes on brain MRI (Kao et al., 2007) which is similar to our patients. We also found the lesions in cerebellum hemisphere and cerebellum vermis which had never been reported in previous literatures. Four of our patients showed multiple lesions in the thalamus, basal ganglia, corona radiate and centrum semiovale, which were similar to the report of Massry et al. (1995) and Hatti and Giuliano (2014).

Ducci et al. (2016) reported a RP patient with neurological symptoms who had diffuse thickening of the dura in the frontal lobes similar to three of our patients. These findings show that brain MRI findings in CNS involvement of RP are not specific. Glucocorticoids are effective to RP. Intravenous pulse methylprednisolone (1 g/d for 3 consecutive days) is a common option followed by oral prednisone (Nadeau, 2002). Our cases improved remarkably after steroid. However, the optimal dose and the duration of steroid are still uncertain. Further study is needed.

**Conclusion**

In summary, CNS involvement in RP has no specific findings both in symptoms and brain MRI findings. The diagnosis is still difficult. However, when one patient presented with encephalitis has extra-CNS manifestations such as eye and ear abnormalities, CNS involvement of RP should be suspected. Immunotherapy including steroids and immunosuppressants may be a choice. Long-term follow-up is necessary.

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