Aseptic Meningitis with Relapsing Polychondritis Mimicking Bacterial Meningitis

Hiroaki Yaguchi¹, Kazufumi Tsuzaka¹, Masaaki Niino², Ichiro Yabe² and Hidenao Sasaki²

Abstract

Relapsing polychondritis (RP) is a rare multisystem autoimmune disease. Though meningitis in RP is not common, some cases with cerebrospinal fluid (CSF) pleocytosis of the lymphocyte cells have been reported. Of the 18 previously reported cases, two cases demonstrated pleocytosis of polymorphonuclear leukocytes (PMN) in the CSF. In addition, cases with a decreased glucose level in the CSF were also seen. Our case also demonstrated pleocytosis of PMN in CSF mimicking bacterial meningitis. In the clinical field, as it is not possible to obtain a culture of CSF on admission day, the glucose level and cellular fraction are considered important. Therefore, meningitis in RP should be considered as a differential diagnosis of bacterial meningitis.

Key words: aseptic meningitis, relapsing polychondritis, polymorphonuclear leukocytes, cerebrospinal fluid (CSF), bacterial meningitis


Introduction

Relapsing polychondritis (RP) is an episodic and progressive inflammatory disease of cartilaginous structures, including the elastic cartilage of the ear and nose, hyaline cartilage of the peripheral joints, fibrocartilage at axial sites, and cartilage of the tracheobronchial tree (1). Multiple neurological abnormalities including meningitis can occur during the course of RP (2, 3) and these have recently attracted the attention of neurologists and subsequently numerous meningitis patients have been reported. Some cases showed pleocytosis with a predominance of polymorphonuclear leukocytes. It is important to look upon meningitis in RP as a differential diagnosis of bacterial meningitis.

Case Report

A 56-year-old woman treated with a bronchodilating agent developed an acute onset of headache, followed by bilateral ear swelling and diplopia. On admission, the patient’s body temperature was 38.8°C, blood pressure 109/60 mmHg, and respiratory rate 22/min. Her general examination revealed a saddle nose, bilateral ear swelling and a stenotic sound of the upper respiratory tract. Laryngotracheal stenosis was observed with a laryngoscope. Neurological examination revealed neck stiffness and left abducent nerve palsy. Consciousness disturbance and pathological reflexes were not detected. Deep tendon reflexes were present and symmetrical. Muscle tone was normal. A superficial and deep sensory disturbance was not detected. The patient’s cerebellar function and gait were also normal. There was no muscular atrophy or involuntary movement.

The blood count showed 22,900 leukocytes with 92% polymorphonuclear leukocytes (PMN), 2,870,000 red cells and 413,000 platelets per cubic millimeter. Serum electrolytes, creatinine, glucose, coagulation tests, liver functional tests, lactate dehydrogenase, and creatine kinase were normal. C-reactive protein (CRP)(24.72 mg/dL) and the erythrocyte sedimentation rate (ESR) (160 mm/h) were elevated. Serum IgG was 1,685 mg/dL. Laboratory data associated with collagen disease were all within the normal range. Cul-

¹Department of Neurology, Kushiro Rosai Hospital, Kushiro and ²Department of Neurology, Hokkaido University Graduate School of Medicine, Sapporo

Received for publication February 17, 2009; Accepted for publication July 7, 2009
Correspondence to Dr. Ichiro Yabe, yabe@med.hokudai.ac.jp
A biopsy sample of the left ear cartilage shows perichondrial inflammation with neutrophils, plasma cells and lymphocytes (Hematoxylin and Eosin staining ×10). Neutrophils in the areas of cartilage destruction (Hematoxylin and Eosin staining ×40).

Figure 1.

Tissues of blood, urine and sputum were negative. A CSF study showed 640 cells/mm³ with 94% PMN, glucose 62 mg/dL (blood glucose 125 mg/dL), protein 114 mg/dL, and IgG index 0.47. The opening pressure was 200 mmH₂O. Adenosine deaminase (ADA) and angiotensin-converting enzyme (ACE) were within the normal range. Smear for acid-fast bacilli, Gram stain and Indian ink were negative. In CSF cultures for bacteria, *Mycobacterium tuberculosis* and cytology were also negative. And the other 2 times of CSF studies before PSL therapy showed pleocytosis with a predominance of PML.

Brain MRI, MRA and nerve conduction studies were normal. EEG demonstrated α-actives without a slow wave. A biopsy of the left ear cartilage before prednisone therapy showed inflammation and infiltration of neutrophils, plasma cells and lymphocytes (Fig. 1A, B).

We established a diagnosis of aseptic meningitis with RP. One thousand mg/day of methylprednisolone was given intravenously for three days as a steroid pulse therapy, followed by oral prednisolone (PSL) at 40 mg/day for four weeks (which was then tapered at rate of 10 mg every two weeks). After steroid therapy was initiated, her symptoms improved considerably. Two months later, her physical and neurological symptoms had returned to normal. Serological data demonstrated that WBC, CRP and ESR also returned to normal. On CSF study, 4 cells/mm³, glucose 67 mg/dL and protein 37 mg/dL were detected. Two years after the attack, she was still receiving oral PSL (7.5 mg/day) without recurrence.

**Discussion**

Relapsing polychondritis (RP) is a rare multisystem autoimmune disease of unknown origin characterized by recurrent episodes of inflammation and a progressive destruction of cartilaginous tissues. Elastic cartilage of the ears and nose, hyaline cartilage of the peripheral joints, vertebral fibrocartilage and tracheobronchial cartilage, as well as the proteoglycan-rich structures of the eye, heart, blood vessels or inner ear may all be affected. In most patients RP manifests as a fluctuating but progressive course which eventually results in a significant shortening of life expectancy (3). Central and peripheral nerve system involvement in RP occurs in approximately 3% of patients (2). Various cranial neuropathies as well as headaches, encephalopathy, seizures, hemiplegia, and cerebral aneurysms have been reported (2, 3). The diagnosis was usually established by clinical features, whose criteria are proposed by McAdam et al (1), Damiani and Levine (4), and Michet et al (5). Modifications to the criteria of McAdam et al were made by Damiani and Levine due to the variability of clinical manifestations during the course of this disease. The present patient fulfilled the criteria of both Damiani and Levine (4) and Michet (5).

In this case, the neurological symptoms were meningitis and abducens paralysis. Abducens paralysis seemed to have been a cranial neuropathy because it was improved by the administration of PSL and there was no neurological sign of brain stem involvement or increased intracranial pressure.

The present case showed marked pleocytosis with a predominance of PMN in the CSF. Meningitis and encephalitis in patients with RP including our case have been noted in 17 cases previously reported in the literature (Table 1) (6-21). In the initial reported cases, pleocytosis with a predominance of lymphocytosis in the CSF was described. But in more recent cases, pleocytosis with a predominance of PMN was reported. Eight cases presented pleocytosis with a predominance of lymphocytosis in the CSF (6-16). On the other hand, 3 cases including our case presented pleocytosis with a predominance of PMN leukocytes (17, 18). In addition, in the other 2 cases the level of glucose in the CSF was decreased, and therapy by immunosuppressors including PSL normalized the level of glucose. One case, at the first onset of meningitis, showed pleocytosis of mononuclear cells in the CSF, but the recurrence showed meningitis with pleocytosis of PMN in the CSF (19). In the other case, PMN leukocytes made up nearly half of the leukocytes (20). The efficiency of therapy by immunosuppressors, including PSL, was good except for one case (16). In cases with more inflammation, a predominance of PMN is observed.

Although pleocytosis of mononuclear cells in the CSF can
Table 1. Summary of Relapsing Polychondritis Cases with Meningitis

<table>
<thead>
<tr>
<th>References</th>
<th>Age</th>
<th>Leucocytes (PMN/M/L)</th>
<th>Protein (mg/dL)</th>
<th>Glucose (mg/dL)</th>
<th>Treatment Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagashima et al [6]</td>
<td>65 M</td>
<td>302/450 (M+L)</td>
<td>79</td>
<td>65</td>
<td>179</td>
</tr>
<tr>
<td>Hsu et al [7]</td>
<td>71 F</td>
<td>0/110 (M+L)</td>
<td>116</td>
<td>57.6</td>
<td>(-)</td>
</tr>
<tr>
<td>Brod and Booss [8]</td>
<td>30 F</td>
<td>2/43/31</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Stewart et al [9]</td>
<td>52 M</td>
<td>140/200</td>
<td>176</td>
<td>normal</td>
<td>(-)</td>
</tr>
<tr>
<td>Hanslik et al [10]</td>
<td>70 F</td>
<td>5/10/22</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Watanabe et al [12]</td>
<td>60 F</td>
<td>5/0/44</td>
<td>51</td>
<td>normal</td>
<td>(-)</td>
</tr>
<tr>
<td>Yang et al [13]</td>
<td>49 M</td>
<td>55/4/86</td>
<td>87</td>
<td>54</td>
<td>(-)</td>
</tr>
<tr>
<td>Fujiki et al [14]</td>
<td>62 M</td>
<td>40/0/90</td>
<td>98-140</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Kuwabara et al [15]</td>
<td>61 M</td>
<td>13/299/(M+L)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Imamura et al [16]</td>
<td>70 F</td>
<td>0/73(M)</td>
<td>123</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Ragnaud et al [17]</td>
<td>70 F</td>
<td>2340/260 (M+L)</td>
<td>40</td>
<td>37.2</td>
<td>(-)</td>
</tr>
<tr>
<td>Wasserfallen and Schaller [18]</td>
<td>73 F</td>
<td>6460/304</td>
<td>100</td>
<td>39.6</td>
<td>165.6 PSL+CY improvement</td>
</tr>
<tr>
<td>Berg et al [19]</td>
<td>60 M</td>
<td>onset 31/9/109</td>
<td>140</td>
<td>22</td>
<td>(-)</td>
</tr>
<tr>
<td>recurrence 190/10 (M+L)</td>
<td>80</td>
<td>20</td>
<td>(-)</td>
<td>PSL improvement</td>
<td></td>
</tr>
<tr>
<td>Kothare et al [20]</td>
<td>66 M</td>
<td>14/4/8</td>
<td>59</td>
<td>68</td>
<td>(-)</td>
</tr>
<tr>
<td>Fujioka et al [21]</td>
<td>66 F</td>
<td>90</td>
<td>147</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Our case</td>
<td>62 F</td>
<td>601/0/38</td>
<td>114</td>
<td>62</td>
<td>125</td>
</tr>
</tbody>
</table>

PMN: polymorphonuclear cells, M: monocytes, L: lymphocytes, PSL: prednisolone, MTX: methotrexate, CyA: ciclosporin A, AZP: azathioprine, CY: cyclophosphamide, (-): not described

*no registry of cellular fraction

be seen in meningitis with most inflammatory diseases, patients with neuro-Behcet’s disease have increased levels of PMN leukocytes in the CSF on acute exacerbation. In systemic lupus erythematosus (SLE) patients with aseptic meningitis, significantly higher cell counts with neutrophil predominance can occur rarely and this suggests cerebral vasculitis with ischemia (22). In addition, the level of glucose in the CSF is rarely decreased in the neuropsychiatric manifestation of SLE (NP-SLE), which has been reported at a low incidence of between 3% and 8% of patients (22). Thirty percent of RP patients have a complication of autoimmune diseases, such as Behcet’s disease or SLE (23). We speculate that the increase of PMN in the CSF is caused by RP as well as other inflammatory diseases (e.g. neuro-Behcet’s disease, SLE). It is important to note that meningitis with RP can also be the differential diagnosis of bacterial meningitis.

References