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CASE REPORT

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A case of relapsing polychondritis with bilateral sensorineural hearing loss and perforation of the nasal septum at the onset

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Abstract A 33-year-old woman suffered from epistaxis and perforation of the nasal septum. Based on a biopsy of nasal mucosa, Wegener's granulomatosis was suspected initially. Her nasal symptoms improved spontaneously, but tinnitus, hearing loss, and dizziness appeared within 3 months. Laboratory analyses revealed no inflammation, and antineutrophil cytoplasmic antibodies were negative. Audiometry revealed bilateral sensorineural hearing loss. A second biopsy of the nasal septum showed an inflammatory change in the cartilage. Thus we diagnosed early-stage relapsing polychondritis.

Key words Perforation of nasal septum · Polychondritis · Sensorineural hearing loss

Introduction

Relapsing polychondritis (RP) is a rare disease that is characterized by recurrent inflammation in the cartilaginous tissues of the entire body. The clinical manifestations of RP are diverse and may include auricular chondritis, saddle nose, polyarthritis, and respiratory disturbance. At present, no specific test for RP is available. Therefore, it is very difficult to correctly diagnose RP at the early stage.

In this report we present a case with characteristic symptoms of nasal septum perforation and bilateral audiovestibular damage, which arose during the first episode of RP. The disease course and the combination of symptoms led us suspect RP and succeed in early diagnosis.

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Case report

A 33-year-old woman suffered from intense pain of the nose at the end of December 2005. She did not consult a doctor, however, because at the time she was living abroad and unable to explain her symptoms in English. She took acetaminophen daily for about 10 days, while enduring the pain, but she lost 10 kg in weight. In early January 2006, after epistaxis had continued for 4–5 days, she found that her nasal septum was perforated. The nasal pain gradually ameliorated, but a burning sensation remained in the deep portion of the nasal cavity and head. When she returned to Japan in February 2006, she experienced general malaise, thirst, and night sweats in addition to mild nasal pain.

An otolaryngologist performed computed tomography (CT) and a biopsy of the nasal mucosa. The biopsy revealed only nonspecific granulation tissue, but the CT imaging displayed a defect in her nasal septum, which led the physician to suspect Wegener's granulomatosis (WG). In March 2006 she experienced vertigo, tinnitus, and decreased hearing and was admitted to our hospital.

Because she was diagnosed with epilepsy and obsessive-compulsive disorder at the age of 14, she was taking benzodiazepines and selective serotonin reuptake inhibitors (SSRIs). Furthermore, the patient was diagnosed with Graves' disease when she was 31 years old. The radioisotope therapy that she subsequently received was followed by hypothyroidism. She was allergic to aspirin and cefixime. She was a current smoker, with a history of about 1 pack of cigarettes per day for 8 years, and drank 10 cans of beer or 5 measures of liquor every other day. She had a family history of rheumatic disease; her maternal grandmother and aunt had rheumatoid arthritis.

Physical examination revealed bilateral mild hearing loss, nasal septum perforation (Fig. 1A) without saddle nose deformity, and swelling of one left cervical and one submandibular lymph node, both of which were 5 mm in diameter, but no ocular symptoms. Her vital signs were normal, and chest and abdominal examinations revealed no abnormal findings. She complained of arthralgia in both

Table 1. Laboratory findings on admission

Urine		**Blood chemistry**	
Protein	(+/–)	TP	7.2 g/dl
Occult blood	(–)	Alb	4.4 g/dl
Sugar	(–)	AST	23 mU/ml
RBC	<1/HPF	ALT	24 mU/ml
WBC	<1/HPF	BUN	16.0 mg/dl
Squamous epithelium	10–19/HPF	Creatinine	0.44 mg/dl
ESR	13.3 mm/h		
Hematology		**Serology**	
WBC	5800/μl	CRP	0.0 mg/dl
Ne.	56.4%	RF	30 IU/ml
Mo.	11.2%	MMP	21.0 ng/ml
Ly.	29.1%	ANA	40× (homogeneous, speckled)
Eos.	2.5%		
Hb	13.7 g/dl	MPO-ANCA	< 1.3 EU
Hct	40.3%	PR3-ANCA	<3.5 EU
PLT	27.9×10^4/μl	HLA-DR	DR-4/DR-8

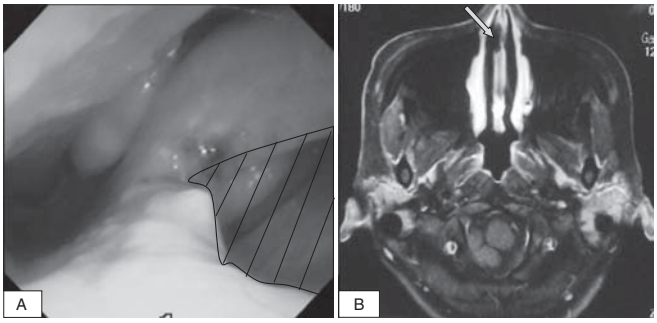

Fig. 1. A Laryngoscopic image of the nasal septum perforation, and **B** enhanced magnetic resonance imaging of the head. The *shaded portion* in **A** is the defect in the nasal septum, and the *arrow* in **B** indicates the same defect

shoulders, knees, and ankles, but no joints were swollen or hot. When 18 tender points of fibromyalgia were pressed, she felt pain in 12 of the points.

Laboratory analyses showed no evidence of active inflammation or renal dysfunction, but rheumatoid factor and antinuclear antibody were slightly positive (Table 1). Enhanced magnetic resonance imaging of the head revealed that the anterior part of the nasal septum was defective and the posterior part of the nasal septum and medial walls of maxillary sinus were thickened, but there was no invasive mass lesion (Fig. 1B). An X-ray CT of the chest and laryngoscopy showed no lesion of the respiratory tract. Systemic bone scintigraphy displayed no abnormal accumulation of radioisotope. X-ray CT of the bilateral temporal bone revealed no destructive change in the middle and inner ear, although an audiogram showed bilateral hearing loss by both air and bone conduction (Fig. 2A). Bekesy audiometry revealed a temporary threshold shift, which suggested retrolabyrinthine hearing loss (Fig. 3A). Moreover, a vestibular function test exhibited a disturbance in her sense of balance (Fig. 4A).

We doubted the tentative diagnosis of WG, because there were no laboratory findings of inflammation, antineutrophil cytoplasm antibodies (ANCA) were negative, and the disease course seemed to spontaneously regress. A biopsy of the nasal septum was performed again, and it revealed inflammatory cell infiltration into the cartilage with fibrosis (Fig. 5). Thus, we changed the diagnosis to RP.

Corticosteroid therapy (prednisolone) was commenced. The initial dose of 50 mg/day was maintained for 2 weeks and then tapered 5 mg each week thereafter. Her hearing loss was exacerbated for the 2 weeks between admission and the beginning of corticosteroid therapy (Fig. 3B). Six weeks later, however, the results of hearing tests and a vestibular function test were improved (Figs. 2C, 3B, 4B). Her complaints of vertigo and tinnitus disappeared, and she reported improved hearing.

Discussion

The diagnosis of RP is quite difficult, especially at the early stage. Trentham and Le reported that the mean delay from symptom onset until diagnosis was 2.9 years, and one-third of patients went to more than five physicians before successful diagnosis.[1] In our case, we successfully diagnosed RP during the early stage and expected to inhibit progression of symptoms by RP. There are several reasons why RP is difficult to diagnose. First, RP is a very rare disease. Its annual incidence is estimated to be about 3.5 per million.[2] In addition, the symptoms of RP at the onset vary from case to case. According to the diagnostic criteria of McAdam et al.,[3] more than three of the following six symptoms are required: auricular chondritis, polyarthritis, nasal chondritis, ocular inflammation, respiratory tract chondritis, and audiovestibular damage. However, the incidence of each of these symptoms is less than 50% at the onset of RP. A study of 337 RP cases revealed the incidences of each of the symptoms (Table 2).[4]

The case we present here did not match the criteria described by McAdam et al.[3] but was diagnosed based on the criteria of Damiani and Levine,[5] which are concordant with those of McAdam et al. Damiani and Levine's diagnostic criteria, however, are also satisfied when more than one of the six symptoms is accompanied with positive histology or more than two symptoms respond to corticosteroids or dapsone therapy. These broader criteria increase the chance of correctly diagnosing RP. In cases of RP, the affected lesion shows the following histologic course: (1) the cartilage matrix loses basophilic staining; (2) the inflammatory cells infiltrate the cartilage and chondrocytes become vacuolated and necrotic; and (3) the cartilage is replaced by fibrous tissue.[1] Biopsies, however, often result in only nonspecific granulation tissue, as the first biopsy in our case. The pathognomonic findings for RP may be not easy to obtain.

Another reason why the diagnosis of RP is quite difficult is the lack of a specific laboratory test. Several reports have indicated a relationship between human leukocyte antigen (HLA) and the onset of RP. For instance, Zeuner et al. re-

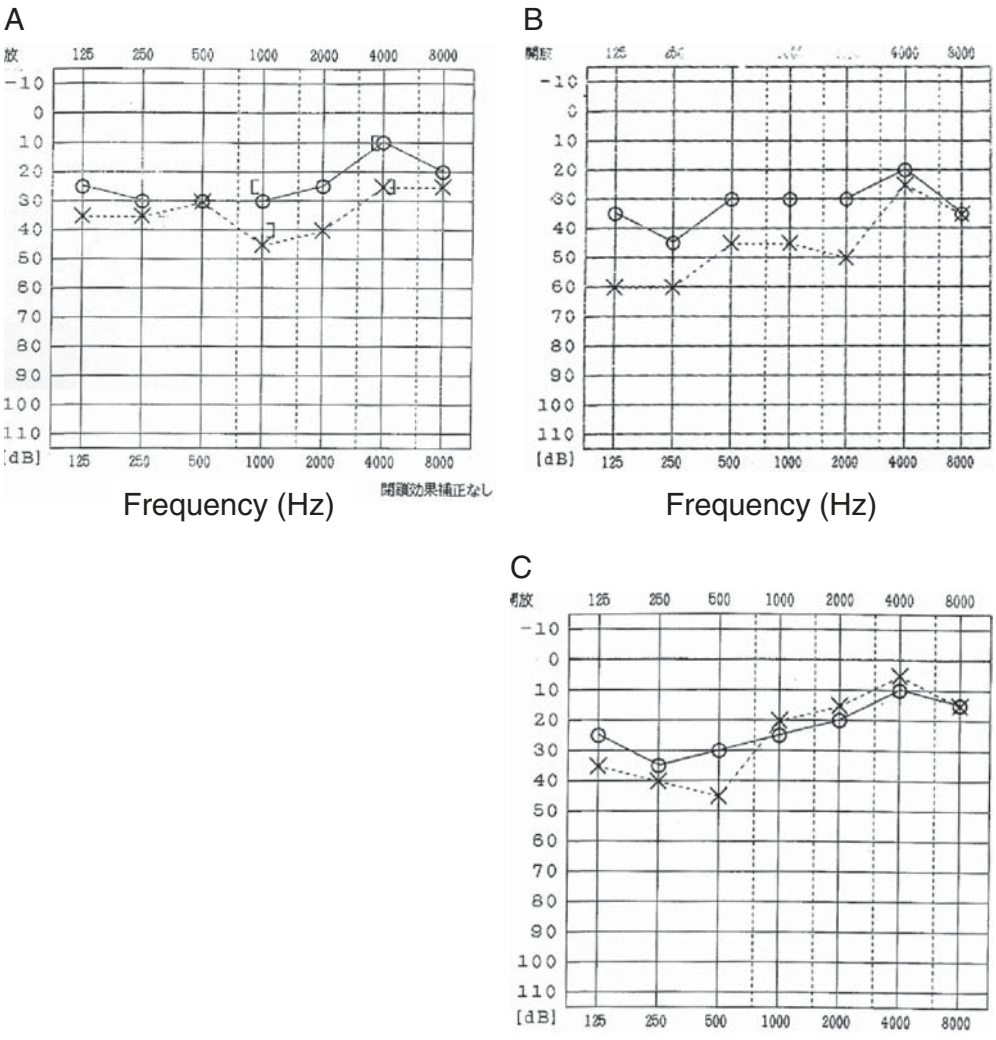

Fig. 2. Audiograms **A** at admission, **B** just before the administration of corticosteroids, and **C** 6 weeks after the commencement of the therapy. The *circles* and *crosses* indicate hearing levels by air conduction of the right and left ear, respectively. The *squares without right edges* and *without left edges* indicate hearing levels by bone conduction of the right and left ear, respectively

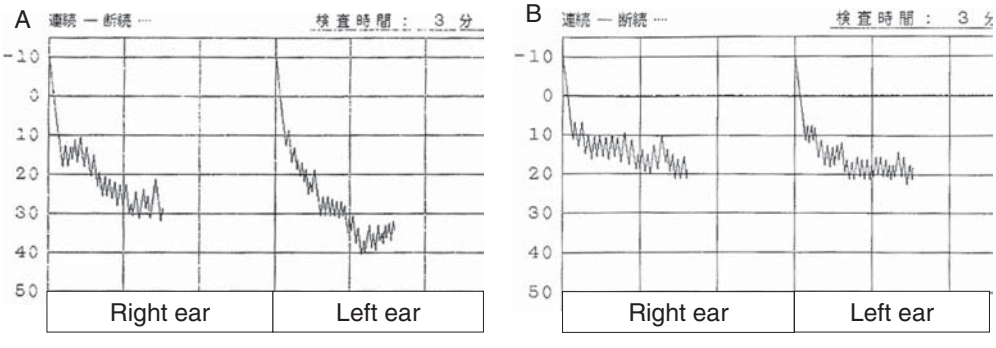

Fig. 3A,B. Bekesy audiometry findings. **A** At admission, with the auditory threshold set to 4000 Hz, the continuous tone shifted from around 20 dB to 30–40 dB. **B** At 6 weeks after corticosteroid therapy was begun, the auditory threshold did not shift

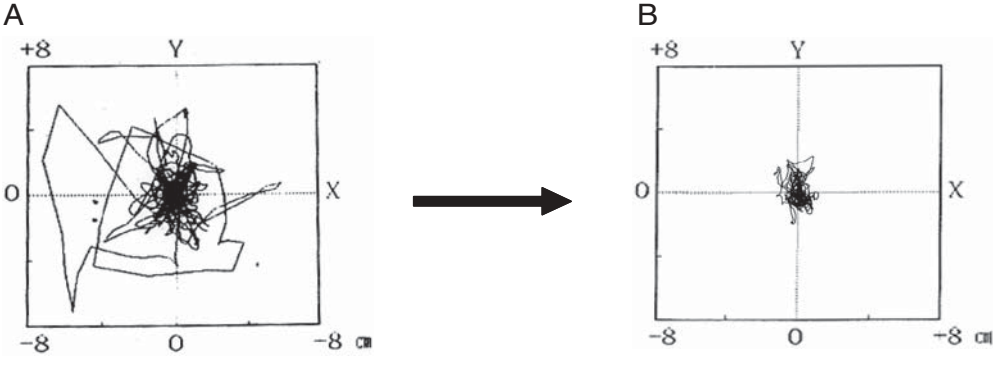

Fig. 4. The vestibular function test **A** at admission and **B** 6 weeks after corticosteroid therapy was begun. These graphs display the fluctuation of the center of gravity when the patient closed her eyes and stood still. The range of fluctuation diminished after the treatment

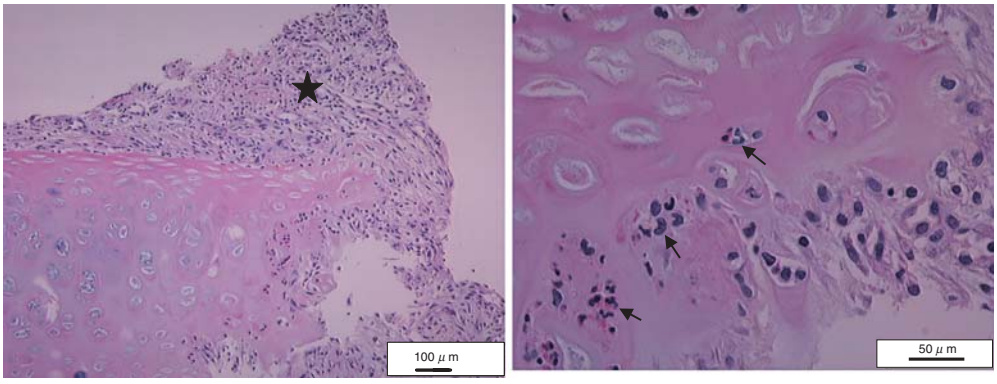

Fig. 5. Micrographs of the nasal septum biopsy using low-power (**left**) and high-power (**right**) light microscopy. Fibrosis with dense inflammatory cells surrounding the cartilaginous tissue (*star*) and infiltration of inflammatory cells into cartilage (*arrows*) are seen. H&E staining; *bar* indicates magnification

Table 2. Incidences of major relapsing polychondritis symptoms

Symptom	Presenting (%)	Cumulative (%)
Auricular chondritis	43	89
Arthritis	32	72
Nasal chondritis	21	61
Ocular inflammation	18	59
Respiratory tract chondritis	23	55
Reduced hearing	7	40
Vestibular dysfunction	4	28

Data from the study by Kent et al.[4]

ported that 36 of 60 patients (60%) were positive for HLA-DR4, whereas only 52 of 204 control subjects (25%) were positive.[6] They concluded that susceptibility to RP was significantly associated with HLA-DR4 ($P < 0.001$, RR = 3.5). Other studies revealed that type II collagen antibody was useful for the diagnosis of RP, although only 20%–33% of patients were positive for this antibody[1,7,8] and this rate should decrease in the remission phase of RP.

Our case was first diagnosed with WG. The incidence of nasal manifestations in WG (e.g., nasal crusting, bloody nasal discharge) is 62%–70%.[9] Noritake et al. reviewed 50 patients with Wegener's granulomatosis and found RP in 2 patients (4%).[10] We questioned the diagnosis of WG, however, because laboratory analyses were negative for ANCA and the disease course had regressed without immunosuppressive therapy. Although nasal septum perforation or sensorineural hearing loss is quite rare in the early stage of RP, some studies have reported that either of these symptoms could appear at the onset of RP without other characteristic symptoms (e.g., auricular chondritis, respiratory tract chondritis).[11–13] Our patient's compliant of arthralgia did not indicate any sign of polyarthritis caused by RP, because we obtained normal findings for MMP-3 and systemic bone scintigraphy. Because she had 12 tender points of fibromyalgia, there is a possibility that fibromyalgia may be accompanied by RP.

According to a report of nine RP cases, the incidence of sensorineural hearing loss was much greater than that of conductive hearing loss (seven vs two cases).[14] In contrast, the most frequent otologic finding in WG was otitis media, and the incidence of sensorineural hearing loss was only 13%.[15] The audiovestibular manifestations in our case were consistent with the characteristics of RP. Thus, when diagnosing RP, it appears to be important to differentiate whether hearing loss is conductive or sensorineural.

The mechanisms of audiovestibular damage by RP remain unclear. Issing et al. reported that antilabyrinthine antibodies were detected in the serum of a RP patient with audiovestibular dysfunction.[16] These autoantibodies or autoreactive T cells may induce inflammation or apoptotic cell death in the inner ear. In our case, the temporary threshold shift revealed by Bekesy audiometry showed that hearing loss was due to a retrolabyrinthine lesion. Based on this result, we speculated that a circulatory disorder due to vasculitis in the artery that feeds the acoustic nerve may be one of causes for sensorineural hearing loss in RP. However, there are no other reports in which sensorineural hearing loss with RP was analyzed by Bekesy audiometry. Thus, further studies are required to confirm the relationship between retrolabyrinthine hearing loss and RP.

Conclusion

We report a case of relapsing polychondritis with bilateral sensorineural hearing loss and perforation of the nasal septum at the onset of RP. We successfully diagnosed RP during the early stage by focusing on the disease course and the combination of symptoms and performing a second biopsy.

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