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Relapsing polychondritis presented as inner ear involvement

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Abstract
We report a rare case of relapsing polychondritis with an initial symptom of inner ear involvement. This 53-year-old Japanese man experienced a hearing difficulty, tinnitus in both ears, and dizziness of sudden onset, but lacked auricular chondritis at that time, which is the most frequent finding in relapsing polychondritis. Thus it was difficult to reach a correct diagnosis. Steroid therapy, with oral prednisolone 15 mg daily, was effective. Almost two months after we began the steroid therapy, the patient complained of losing interest in his work and reported a hallucination vision on the TV screen, so the dose of prednisolone was decreased to 10 mg. The hallucinations then disappeared, but the serum level of C-reactive protein increased highly. To reduce the dose of prednisolone, we tried low-dose oral methotrexate. However, we had to discontinue it when the patient experienced severe vomiting and diarrhoea. As adjuvant therapy, we then administered Sho-saiko-to, Chinese herbal medicines with few side effects. Symptoms and laboratory abnormalities then improved markedly.

Key words: Hearing loss, sensorineural; Tinnitus; Ear cartilages, infection; Steroids; Methotrexate

Introduction

Relapsing polychondritis (RP) is characterized by the destruction of cartilage in various parts of the body. The main clinical feature is an auricular chondritis, manifested by sudden onset of redness, swelling, and warmth of the cartilaginous portion of the external ear, and rarely, the sudden onset of audio-vestibular symptoms. It is difficult to diagnose RP in most cases until the development of auricular chondritis.

Steroid therapy is the most accepted treatment for RP. Other agents include non-steroidal anti-inflammatory drugs, colchicine, chlorambucil, cyclophosphamide, azathioprine, and cyclosporin-A, administered individually or in combination. However, these drugs may have serious side-effects.

We report a case of RP with inner ear involvement as the initial symptom. As adjuvant therapy, we also administered Sho-saiko-to (Tsumura, Tokyo, Japan) a Chinese herbal medicine. Symptoms were alleviated and laboratory abnormalities returned toward normal.

Case report

A 53-year-old Japanese man came to a local hospital because of sudden onset of hearing difficulty, tinnitus which was more pronounced on the left side, and dizziness on February 20, 1994. He was told he had no significant abnormalities. Because the symptoms persisted, he consulted a local practitioner March 25. Audiometry revealed low-tone sensorineural hearing loss. He was treated for inner ear disease by intravenous injection of hydrocortisone sodium succinate, 100 mg daily for six days, and 50 mg daily for three days. His hearing difficulty and dizziness improved, but on April 6, he experienced sudden onset of redness and diffuse swelling of the left auricle, and, two weeks later, the right auricle became similarly involved. He was then referred to our hospital and was admitted on April 25. The patient did not notice any symptoms of the eyes, skin or joints before admission. Both auricles were swollen and light purple in colour (Figure 1). The external

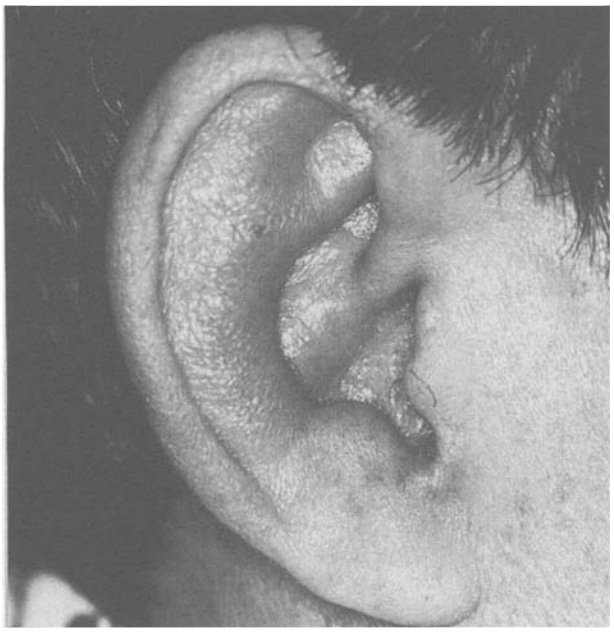


FIG. 1
Auricular chondritis in subacute phase, demonstrating swelling limited to the cartilaginous portion of the external ear.

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TABLE I
LABORATORY DATA ON ADMISSION

WBC	6000	RF	<20 (<20)
RBC	395×10^4	LE test	(–)
Hb	11.5 g/dl	ANA	<20 (<20)
Ht	36.5%	Anti-DNA ab	1 IU/ml (<7)
CRP	0.4 mg/dl	Anti-Mt ab	<20 (<20)
T Protein	7.4 g/dl	Anti SS-A Ab	0.2
Albumin	55.5%	Anti SS-B Ab	0.0
α 1 globulin	3.7%	ESR (1hr/2hr)	30/68
α 2 globulin	14.5%		
β globulin	11.6%		
γ globulin	14.7%		

CRP; C-reactive protein. T Protein; Total protein. RF; Rheumatoid factor. LE test; Lupus erythematosus test. ANA; Anti-nuclear antigen. Mt; Mitochondria. SS-A; Sjögren syndrome A. ESR; Erythrocyte sedimentation rate.

ear canal and tympanic membrane appeared normal. No abnormalities were apparent in the nose nor larynx. Table I shows the laboratory data on the day of admission. The erythrocyte sedimentation rate was accelerated and there was mild anaemia. Markers for autoimmune disease were not elevated. Figure 2 shows the audiogram obtained on March 25 and on April 25. Hearing of the right ear improved from 49 to 15 dB. The patient could not stand with his eyes closed. A caloric test showed a moderate decrease in the response of the right ear. The eye tracking test, horizontal optokinetic nystagmus, and an MRI study were normal. Auditory brainstem response examination revealed no abnormalities in wave intervals I–V.

Figure 3 shows the patient's clinical course. Steroid therapy was withheld for one week after admission so that a biopsy could be performed. Figure 4 shows the results of histopathological examination of the right auricle, including infiltration of neutrophils into the cartilage. On May 2, the patient developed conjunctivitis and treatment with prednisolone 10 mg daily was begun. The dosage was increased to 20 mg daily when no improvement was noted. One month after admission, the inflammation was almost under control with oral prednisolone, 15 mg daily. The patient was discharged on May 26, but the diminished hearing acuity and the intensity of the tinnitus were unchanged.

At the beginning of July, he complained of losing interest in his work and reported a hallucination vision of bubbles on the TV screen. These symptoms were believed to be side effects of the steroid, so the dose of prednisolone was decreased to 10 mg. The hallucinations then disappeared. After this decrease in dosage, his serum level of C-reactive protein (CRP) increased to 6.7 mg/dl (<0.5). He did not notice any significant worsening of symptoms. One month later, however, he began to complain of stiffness of the fingers. In October, we reduced the dose of prednisolone and instituted oral methotrexate (MTX) 7.5 mg per week, with 5 mg of prednisolone given daily. Just after

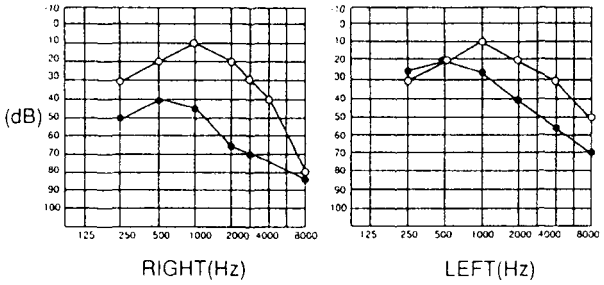


FIG. 2
Audiogram. ●—● Mar. 25th., ○—○ Apr. 25th.

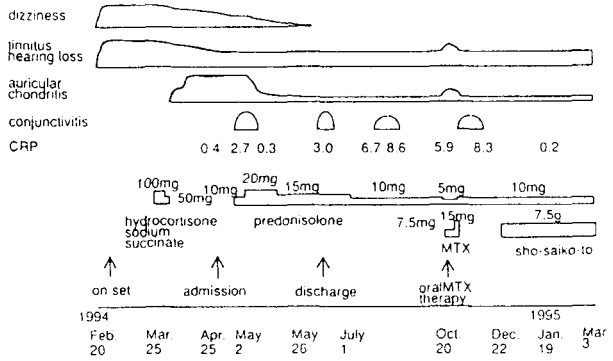


FIG. 3
Clinical course of the patient.

initiating this therapy, swelling of the bilateral auricles developed and the tinnitus increased. The dose of MTX was raised to 15 mg weekly, but had to be discontinued due to severe nausea, vomiting, and diarrhoea. The MTX therapy was stoppd and the dose of prednisolone was increased to 10 mg. In December, we attempted to minimize side-effects by prescribing Sho-saiko-to, a Chinese herbal medicine as adjuvant therapy. After one month on this medication, his symptoms, especially stiffness of the fingers, and laboratory data improved dramatically. The serum CRP level decreased from 8.3 to 0.2. His symptoms are well controlled on 10 mg of prednisolone daily with 7.5 g of Sho-saiko-to daily at the time of writing.

Discussion

Jaksch-Wartenhorst (1923) first described the disease in humans, now referred to as relapsing polychondritis, as an inflammatory reaction in multiple cartilage. In 1976, McAdam *et al.* proposed diagnostic criteria for RP. Damiani and Levine (1979) later proposed an expansion of these criteria. Both sets of criteria are generally accepted throughout the world. Our case was consistent

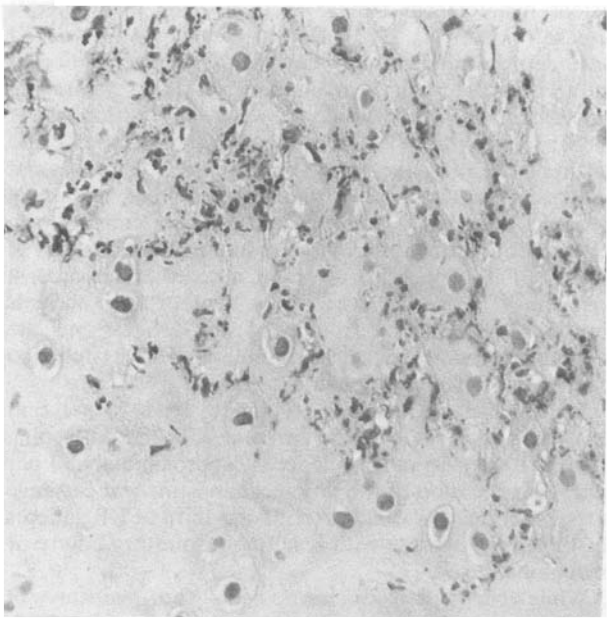


FIG. 4
Histopathological examination of the right auricle, demonstrating infiltration of neutrophils into the cartilage. (H & E; × 400)

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with both sets of criteria. According to McAdam *et al.* (1976), the most common presenting sign was auricular chondritis which was seen in 88.6 per cent of their study population. The incidence of other organ involvement was as follows: polyarthritis or other articular involvement (81 per cent), nasal chondritis (72 per cent), ocular inflammation (65 per cent), respiratory tract chondritis (56 per cent), and audio-vestibular damage (46 per cent). During their clinical course, almost half of the cases presented with audio-vestibular damage. However, the initial involvement of the inner ear is very rare. In most cases, it is difficult to diagnose RP until the development of auricular chondritis. When our patient first presented at the local hospital, he was told that no abnormalities could be found. A second practitioner informed him that his hearing loss and dizziness were probably caused by inner ear abnormality. Because the hearing loss was the only finding, it was difficult to make the correct diagnosis. Few reports in the literature describe inner ear involvement as a primary symptom of RP. Acute bilateral hearing loss, however, would point to RP as a possibility.

Cody and Sones (1971) described 11 cases of RP with audio-vestibular involvement. Eight of the 11 cases had sensorineural hearing loss, which was bilateral in five and unilateral in three. Acute onset of sensorineural hearing loss resembles sudden deafness. However, bilateral involvement is very rare in cases of sudden deafness. According to Cody and Sones (1971), three out of 11 cases had conductive hearing impairment, presumably as a result of chondritis of Eustachian tube cartilage with resultant tubal dysfunction. At the time of their study, the cause of sensorineural hearing loss was unknown.

The detection of antibodies against type II collagen and the granular deposits of immunoglobulin and complement at the fibrochondrial junction indicate the possibility of an underlying autoimmune mechanism (Foidart *et al.*, 1978; Bergfeld, 1983). Collagen is the primary extracellular matrix protein of cartilage and mainly forms collagen fibrils, which are largely made up of type II collagen. Furthermore, chronic progressive sensorineural hearing loss has been induced in experimental studies of animals by immunization with purified type II collagen, giving rise to specific anti-type II collagen antibodies and inner ear lesions histologically similar to those seen in Menière's disease (Yoo *et al.*, 1983). Recently, collagen IX and XI were demonstrated to play key roles in the formation of collagen fibrils and in the maintenance of the physiological function of cartilage (Poole *et al.*, 1984; Wotton *et al.*, 1988). Joliat *et al.*, (1992) reported that anti-type II and anti-type IX antibodies were found in a high percentage of patients with Menière's disease, otosclerosis, and strial atrophy. Yang *et al.* (1993) investigated six patients with RP and found autoantibodies against native collagens II and IX in all of them. In addition, autoantibodies against collagen XI were detected in the sera of four patients showed. However, the source of autoantigen and the mechanism that triggers the immunological dysfunction leading to RP have not been determined.

Mortality associated with RP ranges from 28 per cent (McAdam *et al.*, 1976) to 50 per cent (Cohen and Rapini, 1986), with an overall incidence of approximately 30 per cent. Inflammation of the laryngeal and tracheal cartilage is the main cause of death. About one-third of RP patients die of airway collapse with resulting respiratory failure or pneumonia.

While corticosteroids have been the mainstay of treatment, other agents with high potential for side-effects have been used either alone or in combination. Sismanis *et al.* (1994) administered low-dose oral MTX in an attempt to reduce its toxicity in treating five autoimmune sensorineural hearing loss. Tinnitus and hearing fluctuation improved in all patients with a minimum of side effects. However, our patient developed severe nausea, vomiting, and diarrhoea on MTX, 15 mg per week. These disparate responses to MTX are probably attributable to racial differences. For example, the dose recommended by the United States Food and Drug Administration for treating rheumatoid arthritis is 7.5 mg to 15 mg per week (Weinblatt *et al.*, 1990), whereas a dose of 5 mg orally per week is recommended for treating that disease in Japan (Shinozawa *et al.*, 1990).

Sho-saiko-to, a Chinese herbal medicine, proved to be effective as adjuvant therapy in our patient. This substance consists of seven crude ingredients extracted from herbs and is used in the treatment of various diseases. It reportedly acts as an immunopotentiator by activating macrophages and enhancing interleukin 1 production as well as enhancing antibody production by B lymphocytes (Yamashiki *et al.*, 1992). Recent *in vivo* and *in vitro* studies have reported its chemopreventive effects and its role as a biological response modifier. In addition, Sho-saiko-to was shown to have anticarcinogenic effects in rats (Tatsuta *et al.*, 1991). Herbal medicine produces fewer side-effects and thus can be administered for a longer period of time than more toxic agents. It appears that this herbal medicine will be tried in a wider range of clinical applications.

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