The Journal of Laryngology & Otology
October 2001, Vol. **115,** pp. 836–838

Large vessel arteritis in relapsing polychondritis

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Abstract
A healthy 58-year-old woman presented with recurrent swelling and pain of the nose and both auricules. Bruits were heard over both carotid arteries. Magnetic resonance angiography revealed stenosis of both internal carotid arteries. Relapsing polychondritis was diagnosed. These symptoms improved after treatment with prednisolone and azathioprine. Although relapsing polychondritis is sometimes associated with systemic vasculitis, large vessel arteritis is rare and can negatively affect prognosis. We conclude that the detection of systemic vascular lesions, including those involving the central nervous system, can play an important role in the diagnosis of relapsing polychondritis and that early treatment is essential for a good outcome.

Key words: Polychondritis, Relapsing; Carotid Stenosis; Vasculitis, Central Nervous System

Introduction

Relapsing polychondritis is a rare disease characterized by recurrent inflammation of cartilage in multiple sites. Patients with relapsing polychondritis infrequently present with central nervous system (CNS) complications such as cranial neuropathy, confusion, seizure or cerebellar ataxia.[1] A vasculitic process can lead to CNS involvement. Neuropathologic changes indicate diffuse vasculitis of the small arteries and arterioles.[2] Rarely, however, relapsing polychondritis is associated with vasculitis of large vessels in the CNS. We report a rare case of relapsing polychondritis with transient stenosis of both internal carotid arteries.

Case report

In June 1996, a 58-year-old woman experienced nasal swelling and pain with rhinorrhoea. The symptoms subsided within one month but returned after a few months. A saddle-nose deformity developed. In May 1997, the patient had rubor, pain, and swelling of the left pinna, associated with swelling of the nose. Because of a high fever and persistent throbbing pain in the left temporal region, she was admitted to our hospital.

The body temperature was 38.0°C, and the blood pressure 100/50 mmHg. She had a saddle-nose deformity, which was red and swollen, and there was redness, oedema, and tenderness of the left auricle (Figure 1a). Bruits were heard over both carotid arteries. The temporal arteries were not dilated or tender. Neurological findings were unremarkable. A complete blood count showed a leukocytosis of 13 300 cells per cubic millimeter with 76.6 per cent neutrophils. The erythrocyte sedimentation rate was 157 mm per hour, and the C-reactive protein concentration was 11.60 mg/dL (normal, ⩽0.4 mg/dL). The rheumatoid factor was negative. The urinary acid mucopolysaccharide concentration was elevated (4.9 mg/day; normal range, 2.0–3.0 mg/day). The results of computed tomography (CT) and magnetic resonance imaging (MRI) of the brain were normal, but ^{99m}Tc-ethyl-cysteinate-dimer-single-photon-emission computed tomography showed decreased cerebral blood flow in the left temporal lobe. Moreover, stenosis of both internal carotid arteries was detected on magnetic resonance angiography (MRA) (Figure 2a). The left auricular chondritis resolved spontaneously within two weeks, but the nasal chondritis and left temporal headache showed no improvement. The left auricular chondritis subsequently recurred, and right auricular chondritis, tinnitus, and vertigo with horizontal left-beating nystagmus developed. The clinical and histological features led to a diagnosis of relapsing polychondritis. A biopsy of the ear cartilage showed severe, diffuse infiltration by polymorphonuclear and mononuclear inflammatory cells, destruction of the collagen matrix, and replacement of normal cartilage by fibrous granulation tissue. The temporal headache as well as the auricular and nasal chondritis improved slightly after treatment with 60 mg/day of prednisolone, but recurred after the dose was tapered to 50 mg/day. Intravenous steroid-pulse therapy with 1,000 mg/day of methylprednisolone was given for three days, and the symptoms resolved completely. Treatment with 60 mg/day of prednisolone was then begun. After two weeks, her condition deteriorated again, and 2 mg/kg/day of azathioprine was given concomitantly. All the symptoms resolved after about two weeks (Figure 1b). The stenosis of both internal carotid arteries on MRA and the carotid bruits had also disappeared (Figure 2b).

Discussion

The cardinal symptoms of relapsing polychondritis are recurrent inflammation of cartilaginous structures, usually manifested as auricular and nasal chondritis in patients in their 40s and 50s. It may be associated with ocular symptoms, such as conjunctivitis, or with cochleovestibular dysfunction.[3] In our patient, relapsing polychondritis could be diagnosed because the diagnostic criteria of McAdam *et al.*[4] were satisfied with respect to vestibular dysfunction with recurrent bilateral auricular and nasal chondritis. In

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Accepted for publication: 20 April 2001.

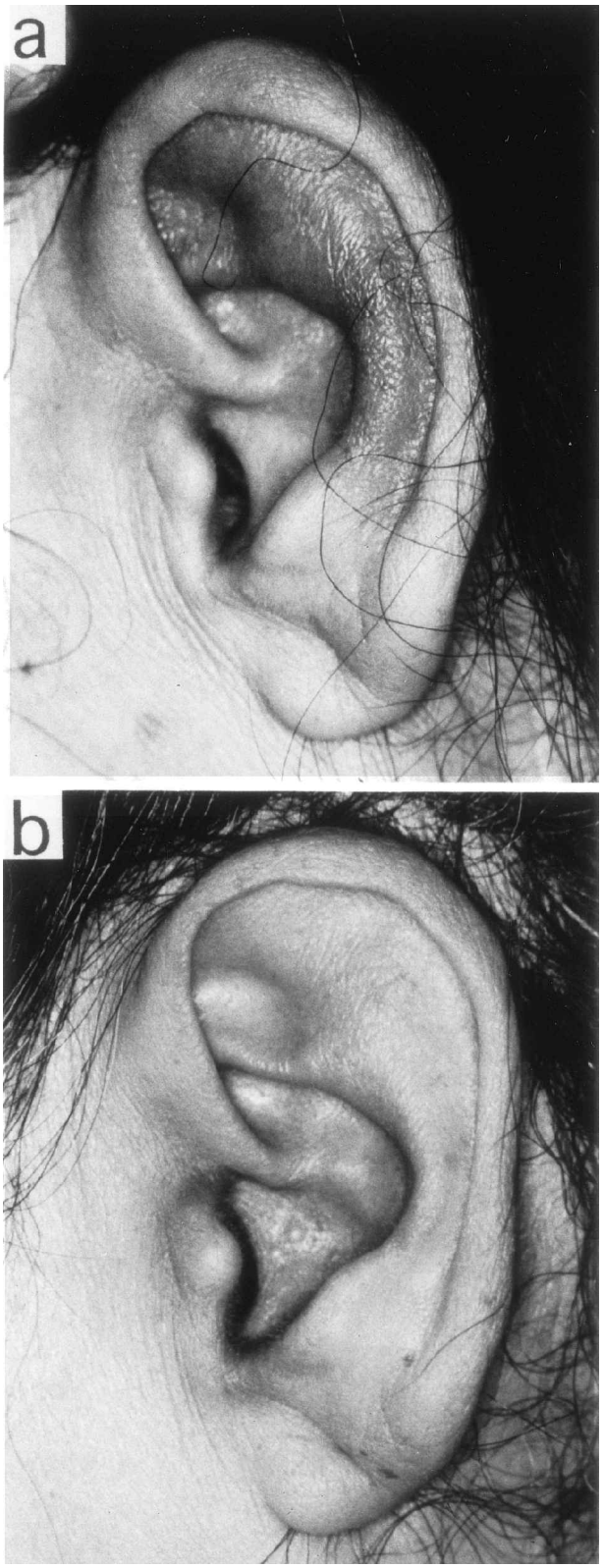

FIG. 1

Auricle before and after treatment. (a) The auricle, excluding the ear lobe, is reddened and swollen. (b) The redness and swelling has disappeared after treatment.

addition, chondritis was found in a biopsy specimen of the auricle. Audio-vestibuliar manifestations of relapsing polychondritis developed in 46 per cent of patients. Such manifestations may be bilateral or unilateral, are usually of

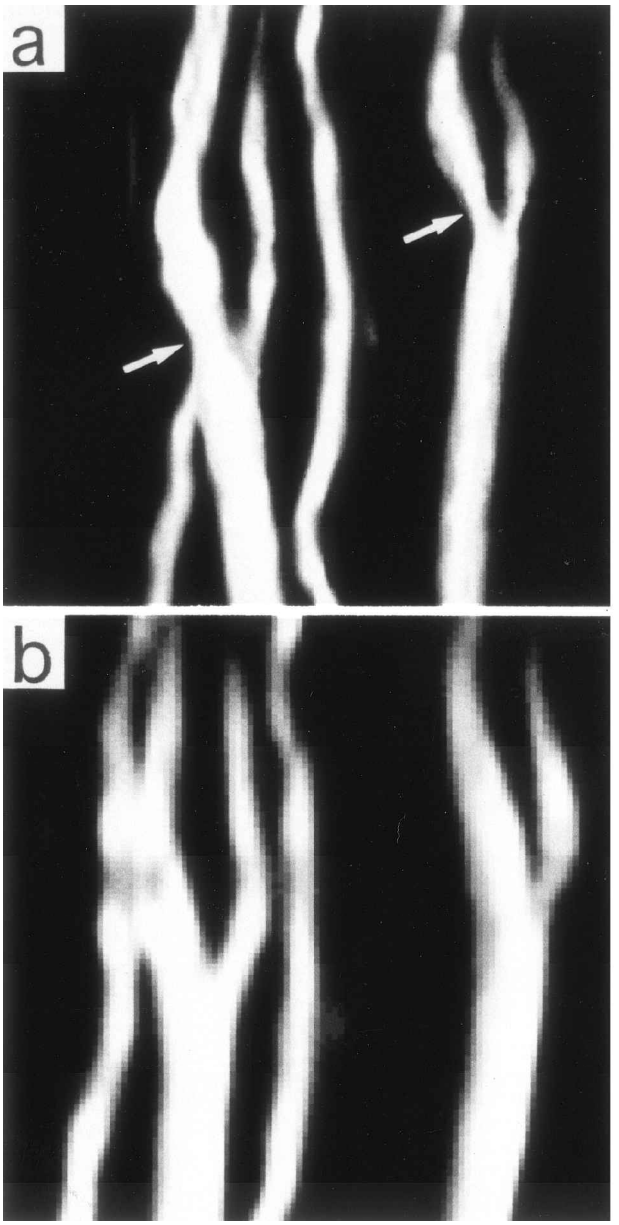

FIG. 2

Cervical magnetic resonance angiographies obtained before and after treatment. (a) Both internal carotid arteries are stenosed (arrows). (b) Stenosis has disappeared after treatment.

sudden onset, and include deafness and tinnitus, with or without vertigo, nausea, vomiting, and nystagmus. Vestibular symptoms typically subside, but perceptive deafness usually persists.[4]

Relapsing polychondritis is often associated with other autoimmune diseases, such as rheumatoid arthritis or systemic lupus erythematosus[5,6] and generally responds to corticosteroid treatment. Chondrocytes and type II collagen components of cartilage matrix may be immunogenic. Antibodies to cartilage and type II collagen have been found in sera from patients with relapsing polychondritis.[7,8] Sensitization to type II collagen induces inflammatory destruction of elastic ear cartilage as well as arthritis in rats.[9,10] Cell-mediated immune responses to cartilage proteoglycans have been demonstrated in patients with relapsing polychondritis.[11] An animal model of relapsing polychondritis (cartilage matrix protein, matrilin-1-

https://doi.org/10.1258/0022215011909125 Published online by Cambridge University Press

induced) has been established.[12] These findings suggest an underlying autoimmune mechanism. In addition, pathological studies have shown that a fundamental abnormality of relapsing polychrondritis is decrease of the mucopolysaccharides derived from cartilage matrix.[13] Although the mechanism is unknown, proteolytic enzymes are activated during active relapsing polychondritis. Acid mucopolysaccharide levels decrease in the cartilage matrix in response to activated proteolytic enzymes, resulting in the degradation of relapsing polychondritis. Therefore, urinary acid mucopolysaccharide levels often increase during active relapsing polychondritis. There was an increase of the urinary mucopolysaccharide in our patient. Relapsing polychondritis also causes lesions in the eye and inner ear, because mucopolysaccharides are an important component of the sclera of the eye, spiral ligament of the cochlea, and basement membrane of the semicircular duct. Although considerable interest has focused on autoimmune disorders and abnormalities of the mucopolysaccharides, studies have yielded conflicting results concerning the pathogenesis of relapsing polychondritis.

Respiratory disturbances associated with the degeneration or collapse of tracheal cartilage affect the prognosis of relapsing polychondritis. The rate of mortality from airway stenosis, however, is not more than 10 per cent; the leading causes of death are infection, systemic vasculitis, and malignancy.[3] Dysmyelopoietic or myeloproliferative syndromes are the most frequent types of malignancy.[14] To date, about 700 cases of relapshing polychondritis have been reported. Few cases were associated with neurological diseases. Neurological complications have recently attracted attention because of their impact on prognosis. The frequency of CNS complications is reported to be high and includes cerebral palsy, mental disorders, headache, and paralytic disorders.[1] Although few histological studies have been done, these symptoms are considered to be associated with inflammation of medium and small arteries and small veins that have been infiltrated by lymphocytes, monocytes, and giant cells.[2] The most common type of systemic vasculitis in relapsing polychondritis is aortitis, which usually leads to aortic insufficiency, aneurysms, and renal dysfunction.[15] By contrast, relapsing polychondritis with large-vessel lesions in the CNS or neck is very rare; only six cases have been reported.[15–20] Rabuzzi *et al.*[17] noted a relation between relapsing polychondritis and vasculitis (large-vessel arteritis) in their report on symptoms that mimic internal carotid artery stenosis and temporal arteritis. Because the temporal arteries could not be examined histologically in our patient, it is not clear whether her condition was complicated by arteritis. Given that she presented with clinical symptoms suggestive of stenosis of both internal carotid arteries with temporal arteritis and that these symptoms resolved as the chondritis improved in response to treatment with steroid and azathioprine, autoimmune mechanisms are likely to have played a role in the development of vasculitis.

Relapsing polychondritis is easily diagnosed on the basis of its clinical characteristics and course, but may be associated with various autoimmune diseases, manifested as organic disorders caused by systemic small-vessel arteritis and phlebitis, as well as with large-vessel stenosis or occlusion. Vascular complications negatively affect the prognosis of patient with relapsing polychondritis. Detection of systemic vascular lesions, especially large-vessel arteritis in the CNS or neck, is therefore necessary so that appropriate treatment of relapsing polychondritis and can be undertaken and therefore hopefully a good outcome will be achieved.

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Dr K. Yamazaki takes responsibility for the integrity of the content of the paper.
Competing interests: None declared