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CASE REPORT

Takeo Sakuta · Yoshitaka Morita · Joe Sakai
Atsunori Kuwabara · Norio Komai · Tatsuo Fukushima
Tamaki Sasaki · Akio Tabuchi · Naoki Kashihara

A case of Vogt-Koyanagi-Harada disease that developed relapsing polychondritis

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Abstract We report the case of a 56-year-old Japanese man with Vogt-Koyanagi-Harada disease in whom pain and diffuse swelling of the left auricle and bilateral episcleritis developed 3 years after diagnosis. Biopsy of the left ear showed acute chondritis, leading to another diagnosis of relapsing polychondritis. Additionally, he was found to carry human leukocyte antigen DR4, which has been reported to be associated with these inflammatory conditions. To our knowledge, our patient is the first reported case of the occurrence of relapsing polychondritis and Vogt-Koyanagi-Harada disease.

Key words Autoimmune disease · Relapsing polychondritis · Vogt-Koyanagi-Harada disease

Introduction

Relapsing polychondritis is an autoimmune disease of unknown etiology, which is characterized by recurrent inflammation and destruction of cartilage structures and connective tissue. Some cases have been associated with other autoimmune disorders.[1,2] Vogt-Koyanagi-Harada disease is a rare disorder characterized by uveitis and neurologic and cutaneous abnormalities, including tinnitus, vertigo, headache, meningoencephalitis, vitiligo, alopecia, and poliosis.[3,4] It is considered to be a cell-mediated autoimmune disease against liberated melanocytic cellular antigens,[5] and occurs most frequently in orientals and heavily pigmented individuals.[3,4] We describe here an interesting case of Vogt-Koyanagi-Harada disease in a patient who developed relapsing polychondritis.

T. Sakuta · Y. Morita (✉) · A. Kuwabara · N. Komai · T. Fukushima · T. Sasaki · N. Kashihara
Division of Nephrology and Rheumatology, Department of Internal Medicine, Kawasaki Medical School, 577 Matsushima, Kurashiki 701-0192, Japan
Tel. +81-86-462-1111; Fax +81-86-462-1199
e-mail: morita@med.kawasaki-m.ac.jp

J. Sakai · A. Tabuchi
Department of Ophthalmology, Kawasaki Medical School, Kurashiki, Japan

Case report

A 53-year-old Japanese man presented with bilateral panuveitis in 1999. He was diagnosed as having Vogt-Koyanagi-Harada disease, and successfully treated with transient administration of systemic corticosteroid. In August 2002 he was admitted to our hospital with a 3-day history of fever and bilateral episcleritis. Four months prior to his admission, he started to note pain and diffuse swelling of the left auricle sparing the ear lobe (Fig. 1A). The right ear was noted to be normal. He reported no headache, tinnitus, or vertigo. His body temperature was 37.7°C, blood pressure 110/60 mmHg, and heart rate 72 beats/min. He showed pain and swelling of bilateral wrist joints. There was no abnormality in other joints. The nose, larynx, and trachea were all clinically normal. Skin examination exhibited diffuse vitiligo of the anterior and posterior trunk (Fig. 1B). There was no poliosis in the eyebrows, eyelashes, or scalp hair. Cardiac examination revealed the absence of murmurs. Laboratory findings were erythrocyte sedimentation rate 126 mm/h, C-reactive protein 15.1 mg/dl (normal <0.5), hemoglobin 11.7 g/dl, white blood cell count 8000/μl, and platelets 36.3×10^4/μl. Liver, renal tests, and serum complement concentration were normal. Antinuclear antibodies, antineutrophil cytoplasmic antibodies, and rheumatoid factors were negative. Human leukocyte antigen (HLA) typing demonstrated the presence of antigens DR4 and DR9. No abnormalities were detected by urine analysis, stool examination, wrist joint radiography, chest radiography, electrocardiogram, or echocardiogram. An ophthalmic evaluation revealed bilateral episcleritis and a change in the retinal pigment epithelium, resulting in a red fundus (Fig. 1C). This retinal finding, so-called sunset glow fundus, and his cutaneous abnormality, vitiligo, supported the previous

diagnosis of Vogt-Koyanagi-Harada disease. Biopsy of the left ear showed degenerated cartilage with inflammatory mononuclear cell infiltration (Fig. 1D). This finding with his clinical symptoms led to another diagnosis of relapsing polychondritis. Treatment with prednisolone 20 mg/day immediately reduced fever, polyarthritis, bilateral episcleritis, and left auricular chondritis. The patient was discharged from the hospital in apparently good health. During an attempt to taper prednisolone, chondritis and episcleritis recurred once. However, at the time of this report, he remains clinically well, taking prednisolone 10 mg/day.

Discussion

Since no specific tests for relapsing polychondritis and Vogt-Koyanagi-Harada disease are available, both diseases must be diagnosed on clinical findings. In 1976, McAdam et al. proposed diagnostic criteria of relapsing polychondritis, requiring three or more of the following clinical criteria: (1) recurrent chondritis of both auricles, (2) nonerosive inflammatory polyarthritis, (3) nasal chondritis, (4) ocular inflammation, (5) respiratory tract chondritis, and (6) cochlear and/or vestibular dysfunction.[1] In 1979, Damiani and Levine suggested the diagnosis of relapsing polychondritis is certain if three of McAdam's sign exist, if one of McAdam's signs is accompanied with biopsy confirmation, or if chondritis in two or more separate anatomic locations occurs that responds to steroids or dapsone.[6] Our case satisfied the criteria of Damiani and Levine.

Vogt-Koyanagi-Harada disease is a systemic disorder with variable clinical manifestations at different times within the overall disease course. Taking into account these features, diagnostic criteria and nomenclature of Vogt-Koyanagi-Harada disease by an international committee were published in 2001: (1) no history of penetrating ocular trauma or surgery preceding the initial onset of uveitis, (2) no clinical or laboratory evidence suggestive of other entities, (3) bilateral ocular involvement, (4) neurologic-auditory findings, and (5) integumentary findings.[7] Based on these criteria, our case was defined as incomplete Vogt-Koyanagi-Harada disease because the patient did not note any history of neurologic or auditory symptoms.

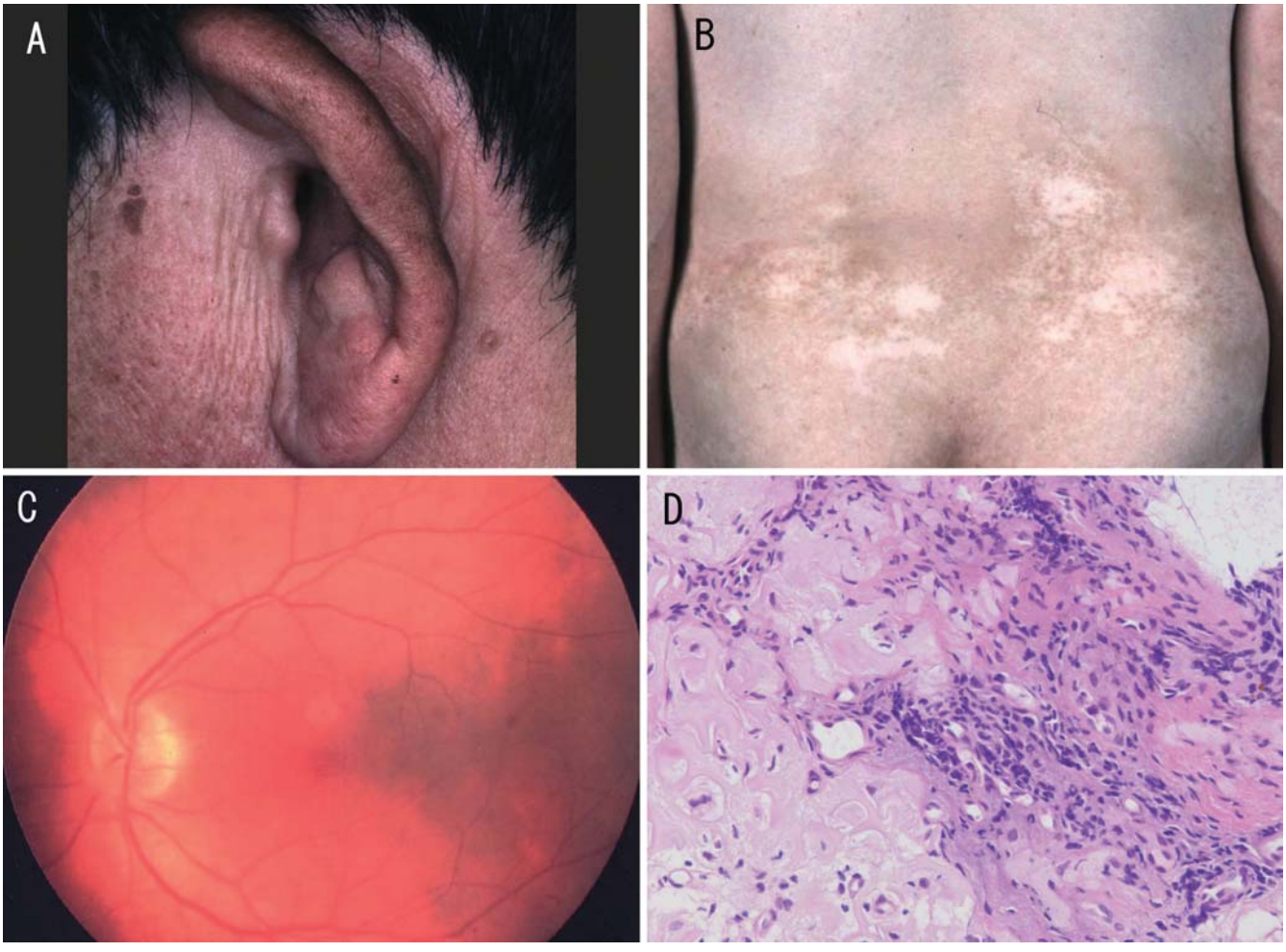

Fig. 1. A Acute auricular chondritis of the left ear. **B** Vitiligo of the posterior trunk. **C** A color fundus photograph of the left eye. **D** Histopathology of auricular cartilage biopsy (H&E stain, ×200)

Ocular manifestations occur frequently in patients with relapsing polychondritis, including proptosis, lid edema, episcleritis/scleritis, corneal infiltrates/thinning, iridocyclitis, retinopathy, and optic neuritis.[8] All ocular symptoms are nonspecific and can be found in a variety of systemic inflammatory diseases. Considering that episcleritis is the most common ocular finding in relapsing polychondritis,[8] and is usually not seen in Vogt-Koyanagi-Harada disease, the bilateral episcleritis that developed in our patient is considered to be associated with relapsing polychondritis. This conclusion is also consistent with the finding that it recurred once with the auricular chondritis. Sunset glow fundus was also seen in our patient, which represents the loss of melanin granules in the choroid and retinal pigment epithelium. It is a characteristic ocular finding in prolonged and/or not well-treated cases of Vogt-Koyanagi-Harada disease,[4] but has never been described in relapsing polychondritis.

The concurrent development of relapsing polychondritis and Vogt-Koyanagi-Harada disease may suggest a genetic influence. Both diseases are thought to be associated with specific HLA-DR molecules, which are known to participate in antigen recognition and processing. A significant increase of HLA-DR4 antigen, which is expressed in our patient, has been demonstrated in relapsing polychondritis and Vogt-Koyanagi-Harada disease.[9,10] These findings support the hypothesis that T-cell-mediated immune response plays an important role in the development of both diseases.

Indeed, recent studies suggest that Vogt-Koyanagi-Harada disease is a T-cell-mediated disease against the tyrosinase family proteins, which is a melanoma antigen expressed by normal melanocytes. T-cell line and T-cell clones that responded to synthetic peptides corresponding to tyrosinase were established from the peripheral blood of patients with Vogt-Koyanagi-Harada disease.[11,12] Furthermore, pigmented rats immunized with these peptides developed an inflammatory disease that resembled clinically and histologically human Vogt-Koyanagi-Harada disease.[5] In relapsing polychondritis, immune response to type II collagen seems to be important. Patients with relapsing polychondritis have demonstrated both autoantibodies and T-cell immune responses to type II collagen.[13–15] Models of relapsing polychondritis in susceptible strains of rats following immunization with type II collagen have been reported.[16,17]

As both relapsing polychondritis and Vogt-Koyanagi-Harada disease have an immunological basis, there are hypothesized associations with other autoimmune disorders such as rheumatoid arthritis and thyroid autoimmune disease.[1–3] However, as far as we can establish from a search of the literature, our patient is the first case of the occurrence of relapsing polychondritis and Vogt-Koyanagi-Harada disease.

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