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CASE REPORT

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Ankylosing spondylitis associated with vitiligo: a case report

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Abstract Vitiligo is a very common disease and is suspected to be autoimmune in its pathogenesis. Many autoimmune complications, such as Hashimoto's thyroiditis, are reportedly associated with vitiligo. The pathogenesis of ankylosing spondylitis (AS) is also suspected to be autoimmune, triggered by some infection. We report a 56-year-old man with concurrent vitiligo and AS, and suggest that both diseases could have a common autoimmune background.

Key words Ankylosing spondylitis (AS) · Seronegative spondyloarthropathy · Vitiligo

Introduction

Vitiligo is a dermatological condition characterized by localized or diffuse depigmented patches on the skin. It is a common disorder, affecting approximately 0.5%–2% of the general population without any significant racial, sexual, or regional distinction.[1,2] Although the pathogenesis of vitiligo is still unknown, it has been suggested that autoimmune mechanisms may be involved. Vitiligo has often been described as a complicating factor in a number of diseases. It is frequently associated with disorders of the autoimmune system and with the presence of serum antibodies that react with organ-specific autoantigens of the thyroid or stomach. Furthermore, a few patients have antibodies that cross-react with epidermal melanocytes.[3]

Ankylosing spondylitis (AS) is a relatively rare disease in Japan compared with Caucasian populations. It may also have an autoimmune etiology, with pathogenesis following infection with some triggering bacteria, such as *Klebsiella*. There have been very few reports of patients with concurrent vitiligo and AS, although an autoimmune mechanism is a feature common to both diseases. We describe a patient with vitiligo and associated late-onset AS.

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Case report

A 54-year-old man was admitted to our Division in March 2001 with a 5-year history of spinal pain of unknown origin and synovitis of some limb joints. His past medical history and his family history were negative for spondyloarthritis and other HLA-B27-associated syndromes. He denied any history of conjunctivitis, uveitis, diarrhea, urethritis, psoriasis, or cardiac symptoms. Nonsegmental vitiligo had been present around his forehead, posterior neck, bilateral wrists, and ankles since his 48th year (Fig. 1).

A physical examination showed bilateral arthritis of his shoulders, wrists, coxae, metacarpophalangeal, proximal interphalangeal, and knee joints. Chest expansion and spine movements were moderately restricted. Schöber's test showed a positive result of 3 cm. Otorhinolaryngological and ophthalmological tests showed no abnormalities. Laboratory evaluation showed an erythrocyte sedimentation rate (ESR) of 114 mm/h, C-reactive protein (CRP) level of 9.4 mg/dl, serum IgA level of 432 mg/dl, fasting plasma glucose (FPG) level of 150 mg/ml, and 10.7% HbA1c (normal ranges: ESR < 20 mm/h, CRP < 0.3 mg/dl, IgA 77–348 mg/dl, FPG 70–110 mg/ml, HbA1c 4.3%–5.8%). Assays for rheumatoid factor, antinuclear antibodies, anti-thyroid peroxidase antibody, anti-microsomal autoantibodies, and anti-glutamic acid decarboxylase antibody were negative. Thyroid function was normal and the patient's diabetes mellitus was non-insulin-dependent. HLA typing showed A2, B35, B70, Cw3, DR6, and DR12 antigens.

Spinal radiographs were normal. No AS features were seen at any spinal segment. Radiographs of his bilateral sacroiliac joints showed joint-space narrowing and ankylo-

sis. Radiographs of his knees and feet revealed slight new bone formation with erosion (enthesopathy) at the sites of attachment of the quadriceps tendon, patella, ischial tuberosity, plantar fascia, and Achilles tendon (Fig. 2). Gascintigraphy showed bilateral arthritis in his shoulders, wrists, knees, hips, and sacroiliac joints. Bone scintigraphy showed uptake in his spine, iliac bone, shoulders, and sacroiliac joints (Fig. 2). He met the modified New York criteria for AS.[5] We diagnosed late-onset AS accompanied by severe peripheral arthritis.

The patient has been treated with diclofenac sodium at 75 mg/day, ampiroxicam at 27 mg/day, and salazosulfapyridine at 1 g/day since March 14, 2001. His arthritis improved gradually, and he was discharged on April 20, 2001, with CRP and ESR levels of 3.57 mg/dl and 91 mm/h, respectively. After discharge, his CRP and ESR levels decreased to 1.91 mg/dl and 68 mm/h, respectively, in May; 0.57 mg/dl and 24 mm/h, respectively, in June; and 0.37 mg/dl and 15 mm/h, respectively, in July 2001, although the extent of his vitiligo remained unchanged.

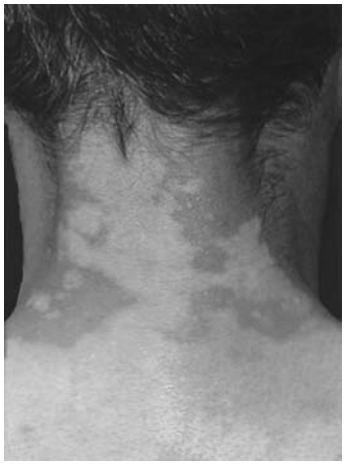

Fig. 1. Nonsegmental vitiligo occurred around the posterior neck

Discussion

Vitiligo is very common all over the world. There are two common types[4] that differ in their clinical manifestations and courses. Type A is caused by autoimmune mechanisms, and type B results from dysfunction of the sympathetic nerves in the affected area. Nonsegmental vitiligo (type A) is approximately three times more common than segmental vitiligo (type B). The onset of type A may occur at any age, whereas type B generally affects only children. The activity of type B usually ceases after a year, after it has spread over the particular dermal area. In contrast, type A develops during the life of the adult patient, with new lesions appearing in a symmetrical pattern.[4] Although there are few spe-

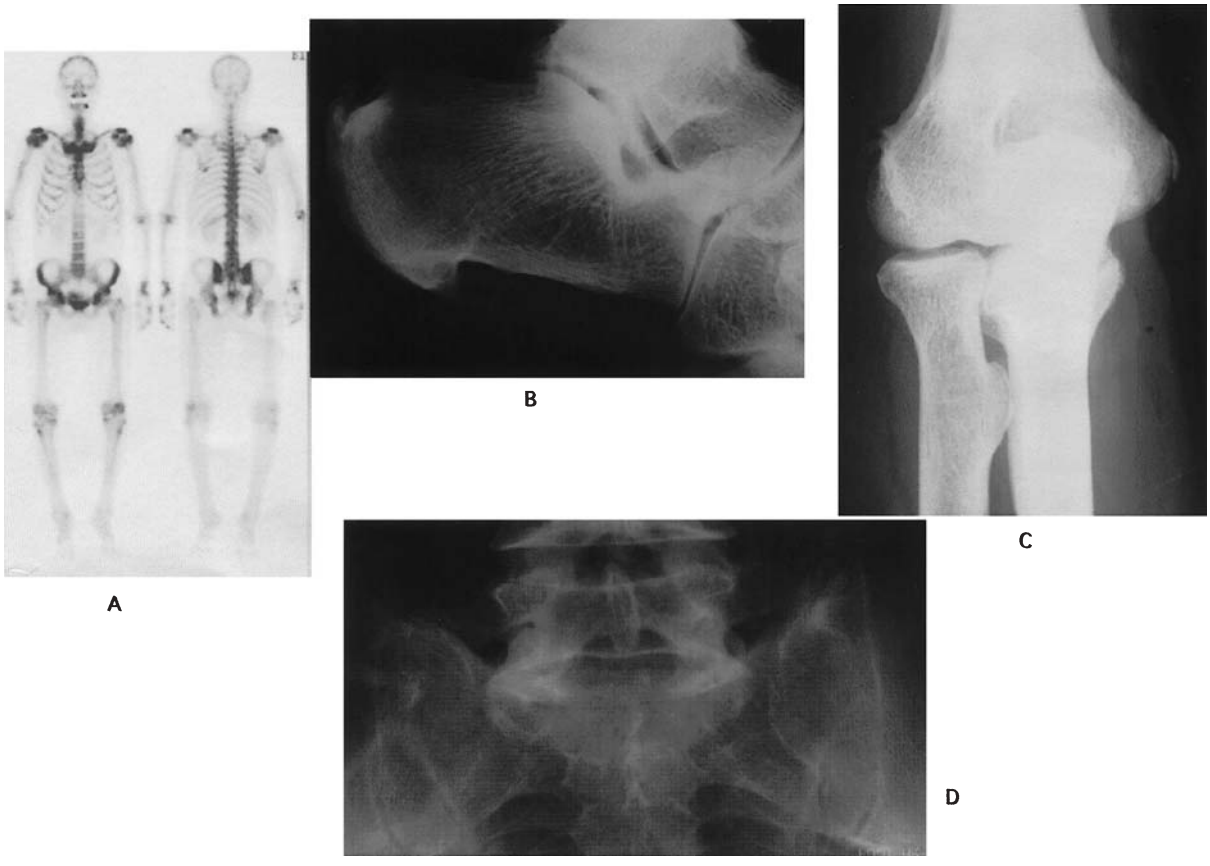

Fig. 2. Bone image showing sacroiliac arthritis and enthesopathy. **A** Bone scintigraphy. **B** X-ray of left Achilles tendon attachment site. **C** X-ray of right elbow. **D** X-ray of lower spine and sacroiliac joint

cific reports of treatment, there is one report of a splenectomy for autoimmune pancytopenia that unexpectedly alleviated the associated vitiligo.[5] This report also suggested that an autoimmune mechanism might be involved in the pathogenesis of vitiligo.

Type A vitiligo has been reported in association with many kinds of diseases, including collagen diseases and several endocrine diseases of an autoimmune nature.[2,4,6,7] Our patient had concurrent vitiligo and AS, and we wondered if both diseases occur together more frequently than by chance. We performed a Medline search of the available literature and found no reported cases. However, we found some cases of the coexistence of vitiligo with spondyloarthritis (SpA), and a suggestion that vitiligo may have a higher incidence with cases of SpA compared with controls.[8,9] The SpA complex includes interrelated diseases such as AS, Reiter's syndrome, reactive arthritis, psoriatic arthritis, arthritis associated with inflammatory bowel disease, and a group of undifferentiated forms.[10–12] Padula et al. suggested that vitiligo and SpA do not coexist by chance and that vitiligo should be included in the list of diseases associated with SpA.[13] They reported that 8 (3.4%) patients (including two with AS) of 234 patients with SpA (including 43 patients with AS) had vitiligo, whereas 5 (1.06%) of 468 controls had vitiligo ($P < 0.05$).[13]

It was evident in some trials that salazosulfapyridine is more effective for treating peripheral AS than the axial subgroup of AS.[14] Therefore, we treated our patient with salazosulfapyridine, and achieved a good response with this therapy. However, it did not affect his vitiligo. Salazosulfapyridine is a well-known agent which to suppresses the activity of rheumatoid arthritis, but the mechanism of this suppression is still unresolved. It may suppress the inflammation of AS nonspecifically without any immune suppression. The difference in the response of AS and vitiligo to the drug can be accounted for by this explanation.

Some infection factor, such as *Klebsiella pneumoniae*, may be the trigger that induces AS associated with the HLA-B27. It is suspected that the HLA-B27 antigen may be the receptor for the triggering infection factor, and/or molecularly mimics the infection factor. Because HLA-B27 antigen is generally very rare (less than 1%) in the Japanese population, AS is a very rare disease in Japan. In this patient, no endocrine disease of an autoimmune nature, such as autoimmune thyroid disease or autoimmune-type diabetes mellitus, was associated, and he had no autoantibodies. Although his is not typical AS because it was late onset with no family history and he was negative for HLA-B27, the pathogenesis of SpA is considered to be the same as that of typical AS. In brief, his T-cell reactivity to some infection factor may have been altered to induce SpA because he had had vitiligo with an autoimmune background for 1 year before the onset of AS.

Some explanations can be considered for this association (so-called vitiligo arthritis). First, when patients who have been suffering from vitiligo with a specific hereditary background that induces vitiligo are infected with some kind of bacterium, the immune response to the bacterium may be altered to induce SpA because of this hereditary background. We believe that this is why the association of SpA and vitiligo is rare. Second, some bacteria that could induce SpA may molecularly mimic epidermal melanocytes. The antibody reactive to these bacteria could also bind melanocytes to induce vitiligo. Because the melanocytes are destroyed by the immune mechanism, vitiligo cannot be resolved with treatment. Third, vitiligo is known to be associated with many autoimmune diseases including collagen diseases.[7,8] Because SpA is also considered to have an autoimmune link, vitiligo and SpA may be different aspects of the same autoimmune background. Fourth, because vitiligo can be associated with a long list of diseases other than autoimmune diseases,[8] SpA may simply be added to that long list without any common background. We consider that the first explanation for the association is the most probable because the patient's AS occurred after vitiligo and the diseases differed in their response to treatment.

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