

Case Report

Seronegative Oligoarthritis Preceding Psoriasis by 9.5 Years

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We report a case of psoriatic arthritis where oligoarthritis preceded the skin lesions. A 57-year-old man complained of left third-finger pain. Laboratory examinations were negative for anti-cyclic citrullinated peptide antibodies and rheumatoid factor; he was treated for suspected rheumatoid arthritis. Six years later, X-ray revealed enthesitis of his fingers and wrist joint. At 9.5 years after the initial visit, skin lesions appeared in the left auricular region and buttock and dermatopathology findings indicated psoriasis vulgaris. The final diagnosis was psoriatic arthritis. In cases of seronegative oligoarthritis, psoriatic arthritis must be considered because some patients demonstrate osteoarticular lesions preceding skin lesions.

Key words: enthesitis, psoriatic arthritis, seronegative oligoarthritis, classification criteria for psoriatic arthritis

Psoriatic arthritis (PsA), a chronic inflammatory arthritis, is characterized by cutaneous psoriasis, enthesitis, and axial and peripheral joint damage. Moll and Wright [1] described five clinical subtypes of PsA: oligoarticular, polyarticular, distal, arthritis mutilans, and spondyloarthritis. PsA is easily diagnosed in the presence of skin lesions, but the diagnosis becomes difficult when arthritis precedes the appearance of skin lesions. Generally, the average interval between arthritis onset and psoriatic skin lesions onset was 4.4 years in a previous report [2]. Here, we report a case of psoriatic arthritis in which oligoarthritis preceded the skin lesions by 9.5 years.

Case Presentation

A 57-year-old man presented with a complaint of painful swelling of his left third metacarpophalangeal (MCP) joint over the previous 2 months. He was a

known hypertensive on treatment. Physical examination revealed swelling over the left third MCP joint and tenderness on flexion. Other joints appeared normal. His initial laboratory examination (Table 1) showed a normal white blood cell count and C-reactive protein (CRP) level. His erythrocyte sedimentation rate (ESR) was slightly elevated (17 mm/h; reference value: 2-10 mm/hr). Rheumatoid factor (RF), antinuclear antibody, and anti-cyclic citrullinated peptide antibody were negative. Serum matrix metalloproteinase-3 (MMP-3) was within the normal limit (86.1 ng/ml; reference value: 36.9-121.0 ng/ml).

Initial radiographs of both hands showed no bony erosions or joint space narrowing in the MCP, proximal interphalangeal joints (PIP), distal interphalangeal joints (DIP), or wrist joints (Figures 1A, 1B). Magnetic resonance imaging (MRI) of the left third finger revealed a diffusely thickened flexor synovium with edematous changes and diffuse enhancement on T1-weighted images and joint fluid in the axial view of

Table 1 Laboratory findings at the initial visit

Parameter	Value	Normal	Parameter	Value	Normal
WBC, cells/ μ l	4,530	3,590–9,640	Total protein, g/dl	7.7	6.6–8.0
Neutrophil, %	66.9	41–75	Albumin, g/dl	4.5	4.1–5.1
Lymphocyte, %	24.5	21–51	AST, U/l	24	13–33
Eosinophil, %	1.1	0.2–8.4	ALT, U/l	27	8–42
Basophil, %	0.7	0.2–1.8	LDH, U/l	177	119–229
Monocyte, %	6.8	3–8	ALP, U/l	408	115–359
RBC, cells $\times 10^4$ / μ l	439	400–552	γ -GTP, U/l	59	10–47
Plt, cells $\times 10^4$ / μ l	30.2	14.8–33.9	BUN, mg/dl	14	8–20
CRP, mg/dl	0.27	≤ 0.3	Creatinine, mg/dl	0.69	0.6–1.1
ESR, mm/h	17	2–10	Uric acid, mg/dl	5.3	3.7–7.5
RF, IU/ml	<5.0	≤ 10	MMP-3, ng/ml	86.1	36.9–121.0
ANA	10.5	20	Anti-CCP antibody, U/ml	1.1	<4.5

WBC, white blood cell; RBC, red blood cell; Plt, platelet; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor; MMP-3, matrix metalloproteinase-3; CCP, cyclic citrullinated peptide; AST, aspartate transaminase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; ALP, alkaline phosphatase; γ -GTP, gamma-glutamyl transpeptidase; BUN, blood urea nitrogen.

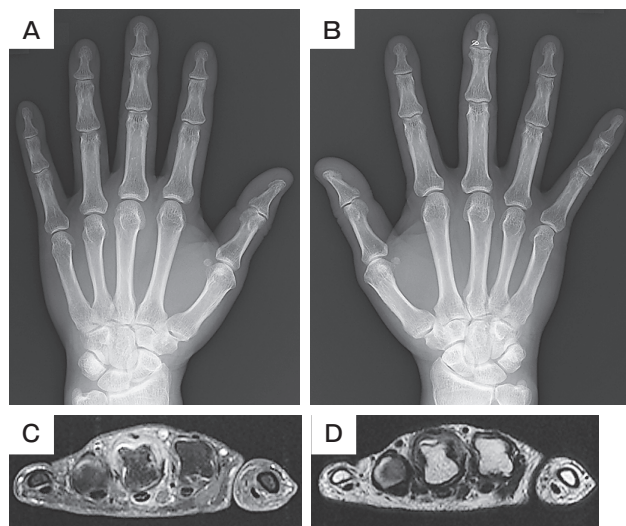


Fig. 1 Radiographs of the left (A) and right (B) hands at the initial visit. Bone erosions and joint space narrowing were not detected in any joint, even in the symptomatic left third metacarpophalangeal (MCP) joint. Magnetic resonance imaging of the left hand showed a diffusely thickened flexor synovium with edematous changes and diffuse enhancement in T1-weighted images (C) and joint fluid in T2-weighted images (D) of the left long MCP joint.

the MCP joint on T2-weighted images (Fig. 1C, 1D). Enthesitis in his left long finger was not detected on either radiograph or MRI.

A confirmatory diagnosis was not made during the first visit. Based on the presentation and findings, treatment for suspected early rheumatoid arthritis was initiated with conventional synthetic disease-modifying

antirheumatic drugs (csDMARDs): 1000 mg/day salazosulapyridine (SASP) and 200 mg/day bucillamine (BUC). The painful swelling of the left third MP joint improved spontaneously, but the swelling of both wrist joints and other finger joints persisted.

The patient was followed-up with annual radiographs. Approximately 6 years after the initial visit, no changes were detected on the radial side of the left third DIP joint (Fig. 2A); however, at 9 years, periosteal new bone formation was observed (Fig. 2B). Ankylosing changes with flexion contractures of the right fifth PIP joint were detected at 6 and 9 years after the initial visit (Figures 2C, 2D). Periosteal new bone formation around the left hamate bone occurred at 6 years (Fig. 3A) and the radial styloid process after 9 years (Fig. 3B). In the right wrist joint, periosteal new bone formation occurred in the distal radius after 6 years (Fig. 3C) and around the radial styloid process and the distal radioulnar joint after 9 years (Fig. 3D). Thus, within 3 years, the periosteal new bone formation had advanced in various joints of the fingers and wrist in both hands. Enthesitis was detected in the triceps tendon insertion at his right olecranon at 7 years from the initial visit and bilateral sacroilitis was also detected at 9 years from the initial visit (Figures 4A, B, C). Well-demarcated, erythematous, scaly plaques appeared over the patient's left postauricular and gluteal area at 9.5 years from the first visit (Figures 5A, 5B). The patient was referred to a dermatologist who diagnosed psoriasis.

Skin biopsy confirmed psoriasis vulgaris (Fig. 6),

and arthritis was finally diagnosed as psoriatic arthritis. At this time point, the Classification Criteria for Psoriatic Arthritis (CASPAR) score was 4: positive for skin psoriasis (2 points), negative rheumatoid factor (1 point), and new bone formation on radiograph (1 point). A CASPAR score of more than 3 points is highly



Fig. 2 Longitudinal radiographic findings of the fingers. The left third distal interphalangeal (DIP) joint at 6 years (A) after the initial visit. After 9 years (B), there was subperiosteal new bone formation (arrow) on the radial side of the DIP joint. Joint space narrowing and ankylosing changes with flexion contracture (arrows) were observed in the proximal interphalangeal joint of the right fifth finger at 6 years (C) and 9 years (D) after the initial visit.

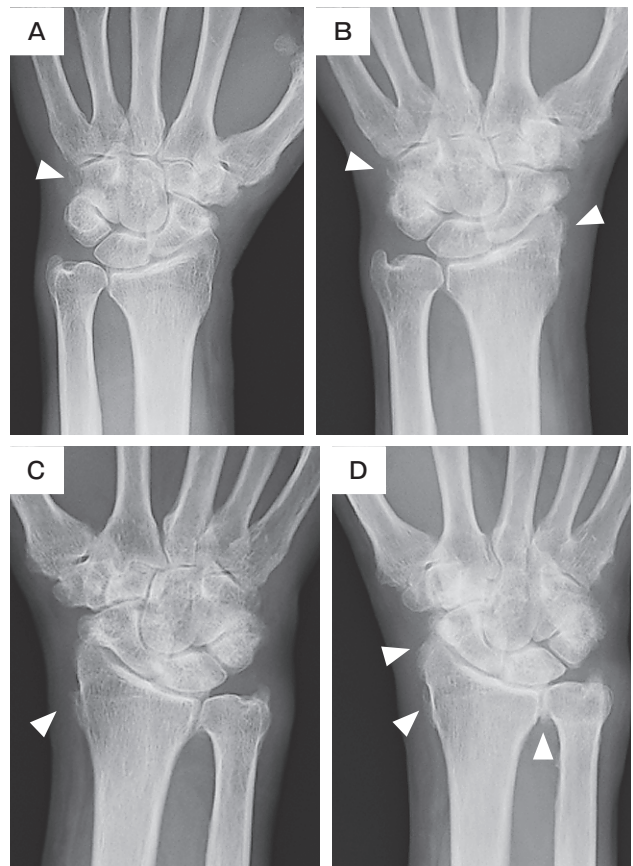


Fig. 3 Longitudinal radiographic findings of the wrists. At 6 years after the initial visit, periosteal new bone formation (arrowheads) occurred adjacent to the left hamate (A) and right distal radius (C); at 9 years after the initial visit, such formation was observed adjacent to the left radial styloid process (B), and in the right radial styloid process and distal radioulnar joint (D).

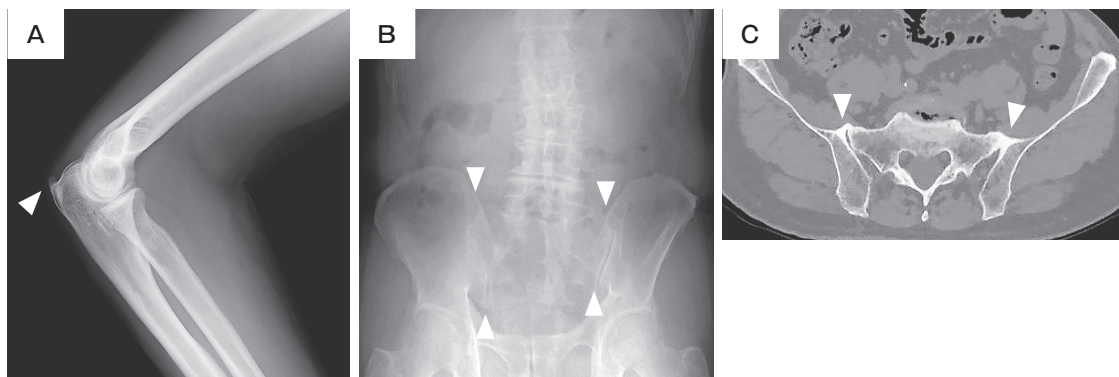


Fig. 4 Enthesitis of the elbow joint and axial lesions of the lumbar spine and sacroiliac joint. Radiological lateral view of the right elbow joint at 7 years after the initial visit. Enthesitis (arrowhead) was observed at the triceps tendon insertion of the olecranon (A). The radiographical anteroposterior view of the lumbar spine and sacroiliac joint (B) and computed tomography of the sacroiliac joint (C) at 9 years after the initial visit showed bilateral sacroiliitis (arrowheads) but no bamboo spine.

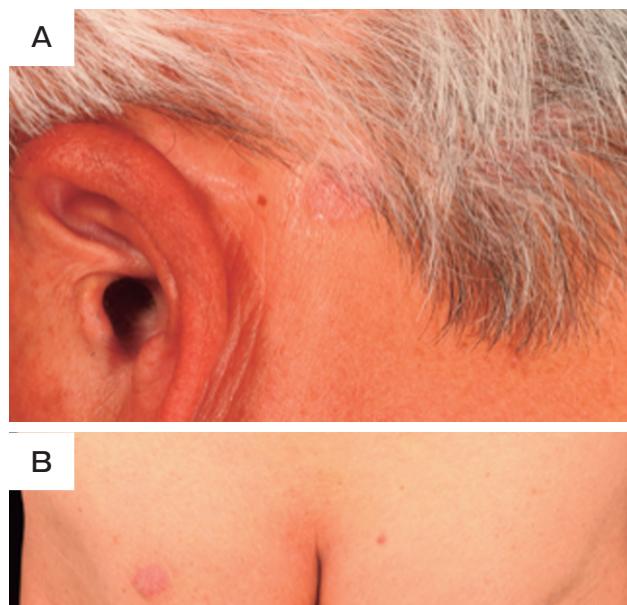


Fig. 5 Clinical cutaneous manifestations. Well-demarcated, erythematous, scaly plaques were present on the left postauricular (A) and left gluteal regions (B).

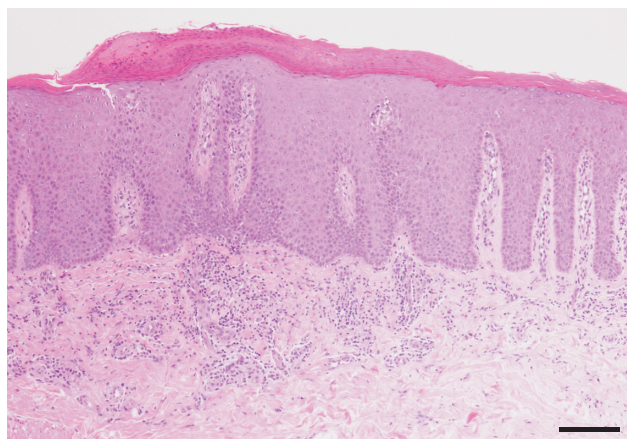


Fig. 6 A skin biopsy specimen obtained from the scaly erythema in the buttock showed hyperkeratosis with parakeratosis, acanthosis with club-shaped rete ridges, and Munro's microabscesses in the stratum corneum (scale bar 100 μ m, hematoxylin and eosin staining).

specific and fairly sensitive for psoriatic arthritis [3].

After the diagnosis of psoriatic arthritis, the patient's skin lesions improved with steroid ointment. His arthritis was not as active and he did not feel that his activities of daily living were seriously impaired; hence, methotrexate and biological DMARDs, such as adalimumab and infliximab, were not administered. At the last

follow-up, he was still being treated with SASP and BUC (csDMARDs). He provided written informed consent to have the details of his case published.

Discussion

The present case demonstrated that osteoarticular lesions can precede manifestations of psoriasis with a long time lag (9.5 years in this case). Typical skin lesions are key findings for a diagnosis of PsA, but some studies have shown that arthritis precedes the appearance of skin lesions in 5-11% of cases [4, 5], making the diagnosis difficult in such patients.

In another recent case report of a 48-year-old man, the time interval from osteoarticular manifestation to skin lesions was 2 years [6]. Over time the patient developed dactylitis, supporting the diagnosis of PsA. In the present case, the time interval from osteoarticular manifestation to skin lesions was 9.5 years, much longer than that in the previous case. However, Nanke *et al.* reported the case of a 45-year-old man with PsA in whom osteoarticular lesions preceded PsA by 20 years [7]. This patient complained of lumbar pain, not peripheral joint pain.

In another report, a 26-year-old man was diagnosed as having PsA based on unilateral plantar forefoot pain and swelling. Radiographs showed nonspecific subchondral bone changes at a few metatarsophalangeal joints of the involved foot. As that case illustrated, it can be challenging to diagnose PsA due to the lack of specific serum markers in the absence of dermatologic changes of psoriasis [8]. In our case, peripheral joint swelling and pain gradually appeared preceding psoriasis vulgaris.

CASPAR assessment is applied to patients with established inflammatory articular disease. The criteria for psoriatic arthritis are met if the patient scores at least 3 points from the following categories: current psoriasis (scored 2, all other categories are scored 1), a history of psoriasis (unless current psoriasis was present), a family history of psoriasis (unless current psoriasis was present, or there was a history of psoriasis), dactylitis, juxta-articular new bone formation, rheumatoid factor negativity, and nail dystrophy [3].

The present case showed asymmetrical oligoarthritis with periosteal new bone formation and negative RF. There were no skin lesions, dactylitis, or nail dystrophy. This case was assigned a CASPAR score of 2 until

psoriatic eruptions appeared. The diagnosis was delayed as the patient had no skin lesions at the first presentation, and the typical skin lesions did not appear until 9.5 years after arthritis onset.

The European League Against Rheumatism and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis recommend csDMARDs as the initial therapy after nonsteroidal anti-inflammatory drugs and local therapy failure for active disease, followed, if necessary, by a biological DMARD or a targeted synthetic DMARD [9, 10]. In the present case, csDMARDs were not very effective, since CRP was still 0.8 to 1.5 mg/dl, so we consider that this patient may eventually require advanced agents such as methotrexate or tumor necrosis factor inhibitors such as adalimumab and infliximab.

In conclusion, for all cases of asymmetrical oligoarthritis with negative RF, we recommend periodic follow-up for early detection of articular changes and skin lesions. In particular, enthesitis of the fingers and wrists on a radiograph indicates the existence of PsA. Based on the present case, the onset of skin lesions might lag behind articular involvement by up to 9.5 years.

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