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REVIEW ARTICLE

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A new syndrome: multiple dislocations of distal interphalangeal joints associated with interstitial pneumonia, Sjögren's syndrome, and positive autoantibodies

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Abstract A 54-year-old woman and a 64-year-old man consulted our clinic for dislocation of the distal interphalangeal (DIP) joints. They both had been diagnosed as having Sjögren's syndrome. In addition, interstitial pneumonia had been detected several years earlier in both cases. Antibodies to SSA/Ro (52 kDa) and Jo-1 were detected in their sera, but serum CK and aldolase levels were normal. There were no eruptions, and muscle strength was normal in both patients. The combination of the following six conditions, i.e., (1) multiple dislocations of DIP joints, (2) interstitial pneumonia, (3) Sjögren's syndrome, (4) positive anti-SSA antibodies (52 kDa), (5) positive anti-Jo-1 autoantibodies, and (6) children with hypermobile joints is quite rare and not observed frequently. Existence of the above six conditions in two patients is even rarer. Therefore, the probability that all six conditions would coincidentally coexist in each of the two separate subjects is virtually zero. In this article, we propose a novel clinical complex – multiple dislocations of DIP joints, interstitial pneumonia associated with Sjögren's syndrome, and positive anti-SSA and anti-Jo-1 antibodies (DIPSSJ) – as a new syndrome of which clinicians should be aware. Because the children of both patients had hypermobile joints, the syndrome may be partially genetic.

Key words Anti-Jo-1 · Anti-SSA · Interphalangeal joints · Multiple dislocations

Introduction

Joint symptoms are commonly reported in rheumatic diseases. In patients with connective tissue disease, deforming arthritides have been reported,[1–3] part of which is associated with autoantibodies.[1,2] There are also several inheritable diseases that cause arthropathy.[4] We previously described a patient with multiple dislocations of the distal interphalangeal (DIP) joints, interstitial pneumonia associated with Sjögren's syndrome, and positive anti-SSA/Ro and anti-Jo-1 antihistidyl tRNA synthethase autoantibodies.[5] We recognized that the coexistence of such conditions is very rare; however, one individual complicated by multiple rare conditions is not a sufficient basis on which we could propose a new syndrome.

Recently, we described the second patient with almost the same clinical complex.[6] In addition, children of both patients have hypermobile jonts. In this article, we describe those two patients and propose a new syndrome named DIPSSJ.

Case 1

A 50-year-old Japanese woman was admitted to our clinic with swollen and painful DIP joints in March 1999.[5] She had noticed dislocation of the DIP joints 5 years earlier. The patient had also noticed hypermobility of her DIP joints at 14 years of age. In 1993, the patient noted pain in all the DIP joints and dryness of the eyes and mouth. At that time, however, a radiograph of her hands revealed neither erosive changes nor dislocations of the fingers joints (Fig. 1). She was diagnosed as having Sjögren's syndrome by ophthalmological examination and lip biopsy. Chest radiography and CT demonstrated interstitial pneumonia in the lower lung fields (Fig. 2).

On admission, there was no hyperelasticity or eruptions of the skin. Muscle strength was normal. All DIP joints were dislocated (Figs. 3A,B, 4). Her 18-year-old son demonstrated hypermobile joints. According to the revised criteria for the diagnosis of benign joint hypermobility syndrome,[4] in both hands, the son was able to (1) passively dorsiflex the fifth metacarpophalangeal joint beyond 90° and (2) oppose the thumb to the volar aspect of the ipsilateral forearm. Thus, he had hypermobile joints with a

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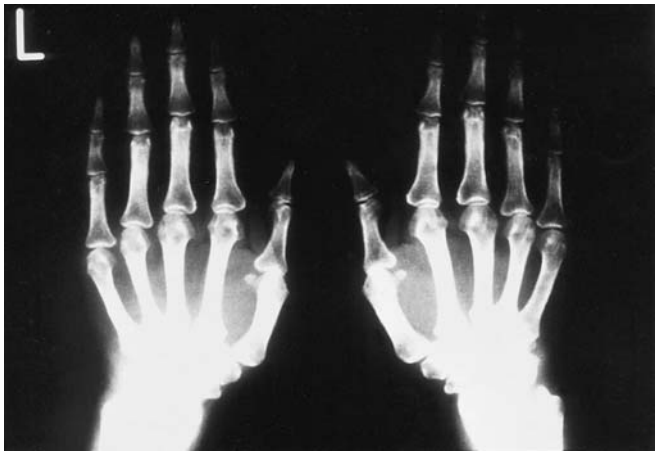

Fig. 1. Case 1. Radiograph of the patient's hands in 1993

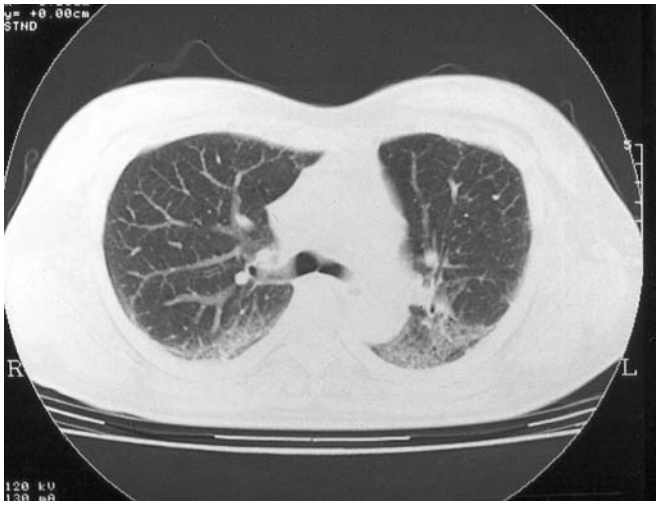

Fig. 2. Case 1. Chest CT revealed interstitial pneumonia in 1993

hypermobility score of 4, although his DIP joints were not dislocated.

Clinical data for the patient were as follows: erythrocyte sedimentation rate (ESR) 53 mm/h, white blood cell count (WBC) 9200/μl, hemoglobin 11.8 g/dl, serum protein 8.2 g/dl (γ-globulin 30.4%), lactate dehydrogenase (LDH) 492 U/l, creatinine kinase (CK) 189 U/l (reference range, 10–110 U/l), aldolase 5.7 U/l, C-reactive protein (CRP) 0.2 mg/dl, and rheumatoid arthritis particle agglutination (RAPA) 1:320 positive. Antinuclear antibody titer was 1:80, and antibodies against SSA (52 kDa) was 4× (by a single radial immunodiffusion method) and Jo-1 was positive by an Ouchterlony method. Anti-SSB/La, anti-ribosome P, anti-U1RNP, and anti-Scl-70 antibodies were negative. Other antiaminoacyl tRNA synthetase (PL-7, PL-12, EJ, OJ, and NJ) antibodies were all negative. HLA types were A24 (9), B54 (22), Cw1, and DR4. Electromyography findings were normal. Arthrodesis was performed. Histological studies of synovial tissue revealed nonspecific chronic synovitis, bone resorption, and bone degeneration (Figs. 5, 6).

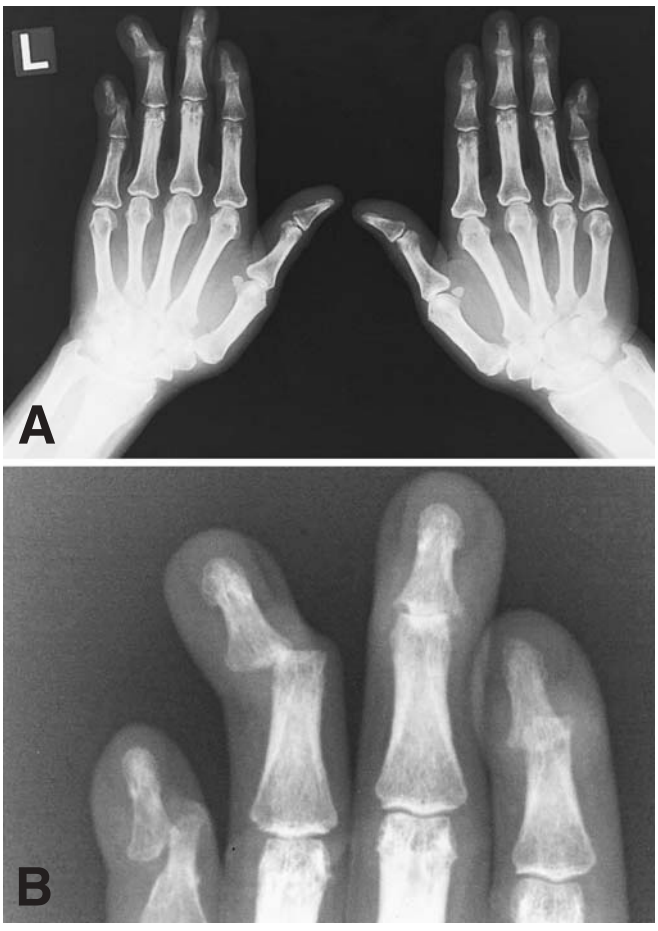

Fig. 3. Case 1. **A** Radiograph of the patient's hands at admission. **B** Multiple dislocations of distal interphalangeal (DIP) joints

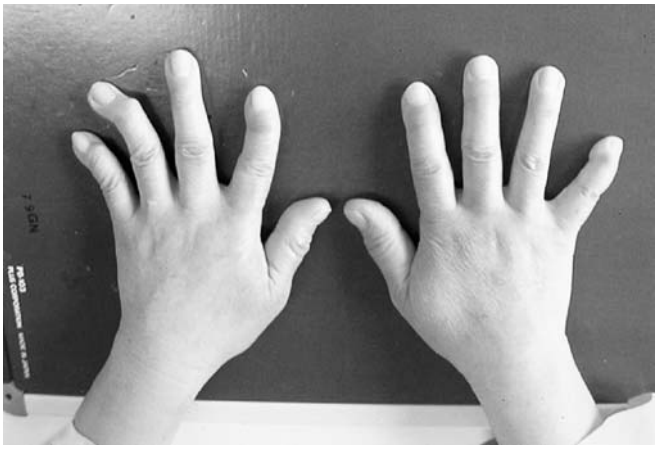

Fig. 4. Case 1. The patient's hands, showing dislocations of DIP joints at admission in 1999

Case 2

A 64-year-old Japanese man, who was not related to case 1, visited our outpatient clinic in May 2000 for dyspnea and polyarthralgia.[6] He had polyarthralgias of the wrist and DIP

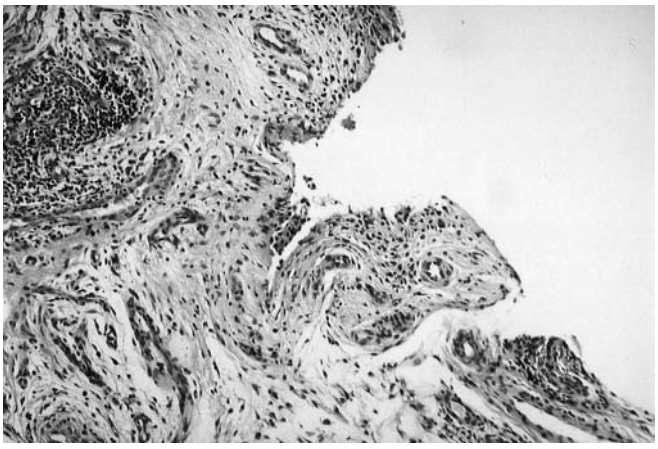

Fig. 5. Case 1. Histological section (H&E stain) of synovial tissue from DIP joint in the left fourth finger. Fibrinoid necrosis with proliferated lining cells, lymphocytes, and sparse plasma cells are observed. There is no lymphoid nodular formation

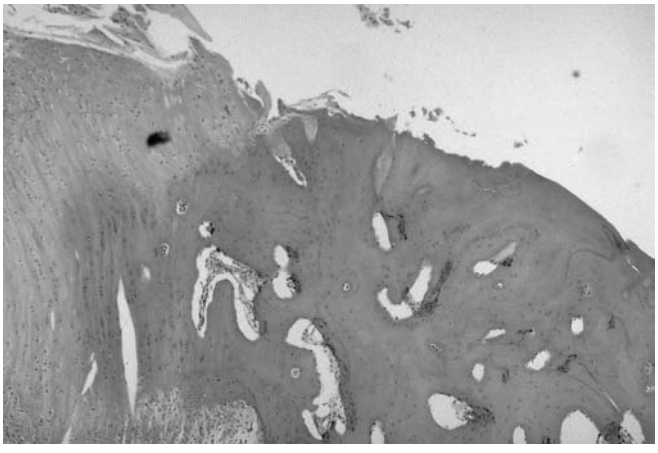

Fig. 6. Case 1. Histochemical staining (H&E) of bone from the middle phalanx of the third finger. Bone resorption and degeneration, but no cartilage, can be seen

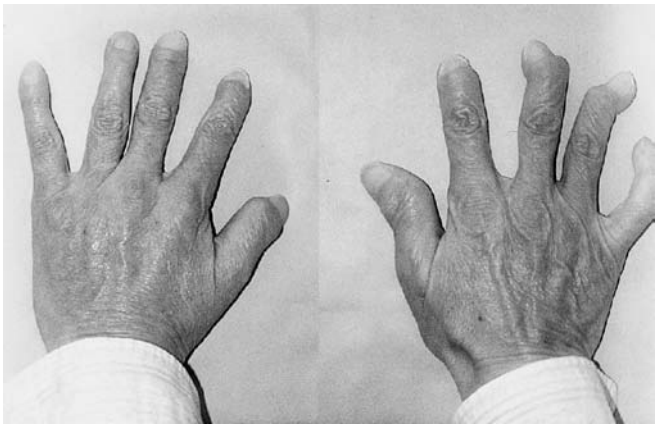

Fig. 7. Case 2. The patient's hands, showing dislocations of DIP joints at admission in 2000

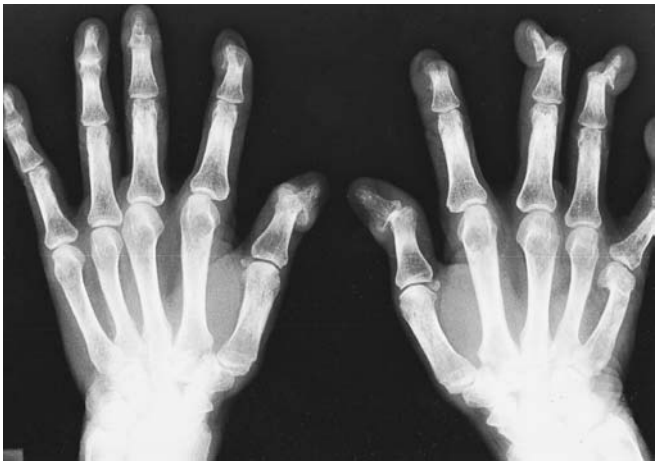

Fig. 8. Case 2. Radiograph of the patient's hands in 2000

joints with Raynaud's phenomenon in 1986 and had contacted our outpatient clinic for the first time in 1987. At that time, his hand radiograph demonstrated dislocations of DIP joints of the right second, third, and fifth and left second fingers, but there were no erosive changes. Chest radiography revealed interstitial pneumonia at both lung base areas. Pulmonary function study showed moderate restrictive lung disease.

In 1991, he noticed dry eyes and mouth. Raynaud's phenomenon had been persistent for the past 14 years. Throughout the clinical course, there was no myalgia or erythema. His skin was not sclerotic, and his muscle strength remained normal. Laboratory data were positive for anti-SSA [33.5 by enzyme-linked immunosorbent assay (ELISA)] and anti-JoI antibodies (by immunodiffusion), but negative for anti-SSB and anti-U1 RNP antibodies. Serum CK and aldolase levels were normal. The patient was diagnosed as having Sjögren's syndrome by ophthalmological examinations. He had been treated with indomethacin and tocopherol nicotinate until he stopped those medications in 1994.

At this examination, he complained of dyspnea, and his arthralgia had become worse. There were no eruptions or hyperelasticity of the skins, but all the DIP joints were dislocated (Fig. 7). Clinical data were as follows: ESR 26 mm/h, WBC 10100/μl, hemoglobin 12.8 g/dl, serum protein 8.6 g/dl (γ-globulin 28.2%), LDH 308 U/l, CK 97 U/l (reference range, 53–288 U/l), CRP 0.2 mg/dl, RAPA 1:160, antinuclar antibody 1:40 (speckled pattern), and antibodies against SSA (52 kDa) and Jo-1 were positive. Other antiaminoacyl-tRNA synthetase antibodies were all negative. HLA types were A24 (9), A33 (19), B60 (40), B44 (12), Cw3, DR 8, and DR6. All the DIP joints were dislocated, although no erosive changes were shown by hand radiographs (Fig. 8). His 24-year-old daughter had also hypermobile joints with a hypermobility score of 5. In both hands, the daughter was able to (1) passively dorsiflex the fifth metacarpophalangeal joint beyond 90°, (2) oppose the thumb to the volar aspect of the ipsilateral forearm, and (3) place her hands flat on the floor without bending the knees.

Discussion

Here we presented two patients with the following six conditions: (1) multiple dislocations of DIP joints, (2) interstitial pneumonia, (3) Sjögren's syndrome, (4) positive autoantibodies to SSA, (5) positive autoantibodies to Jo-1, and (6) children with hypermobile joints. If we consider whether these six conditions can coexist in each of the two individuals by chance, the probability is estimated to be almost zero. Although these conditions could incidentally occur in one individual, occurrence in the two subjects can more easily be explained by the recognition of a new clinical complex. In addition, because the patients each had offspring with hypermobile joints, we hypothesize that the etiology of the dislocations in these cases is, at least in part, genetic.

Although the anti-Jo-1 antibody of each case was positive, there was no myalgia, no muscle weakness, and no eruptions during their clinical course. In addition, levels of serum CK and aldolase were almost normal in both patients throughout their clinical course. Other autoantibodies against aminoacyl-tRNA synthetases anti-PL-7, PL-12, EJ, OJ, and NJ antibodies[7,8] were not detected when they were screened by the immunoprecipitation method. Therefore, the patients could not be diagnosed as having polymyositis/dermatomyositis (PM/DM).

Association between autoantibodies and deforming arthropathy has been noted in a variety of connective tissue diseases. Oddis et al. have described 12 patients with association of anti-Jo-1 antibody and inflammatory polyarthritis in PM/DM.[1] Four of these patients had a deforming, predominantly nonerosive arthropathy with subluxation of the proximal and distal interphalangeal joints. In contrast, Franceschini et al. reported 13 patients with systemic lupus erythematosus (SLE) who revealed deforming arthropathy of hands.[2] They compared SLE with deforming arthropathy to SLE without deforming arthropathy, and concluded that patients with SLE developing deformities of the hands belong to a special subset with circulating antibodies to SSA, particularly to the 52-kDa component, and to SSB. Characteristics of the deforming arthropathy of the hands were ulnar drift, swan neck deformity of the fingers, Z deformity of the thumb, limited metacarpophalangeal joint extension, buttonhole deformity of the fingers, and scant and asymmetrical joint erosions. Reilly et al. have also reported that the presence of antibodies to U1 RNP correlates significantly with hand deformity such as Jaccoud's type arthropathy in SLE.[3] However, these deformities differ from those of our patients. Because both our cases were positive for anti-SSA and anti-Jo-1 antibodies and negative for anti-U1 RNP and anti-SSB antibodies, the deformation of their hands might be associated with the antibodies against SSA and/or Jo-1.

Recently, it has been reported that synostosis of the proximal interphalangeal or DIP joints is caused by heterozygous mutation in the gene encoding noggin, which binds and inactivates members of the transforming growth factor-β superfamily, although the dislocation in our patients differed from synostosis.[9] Although symmetrical distal polyarthralgia, usually intermittent, is often encountered in Sjögren's syndrome, joint deformities and erosions are rare.[10] Moreover, there are several arthropathies caused by genetic factors such as Marfan's syndrome, Ehlers–Danlos syndrome, Larsen's syndrome, and familial articular hypermobility syndrome.[4] However, such disorders were excluded in our two cases. In addition, neither of our patients had experienced a physical injury that could have caused dislocation of the DIP joints.[11]

In summary, we propose a possible new complex – multiple dislocations of DIP joints, interstitial pneumonia associated with Sjögren's syndrome, and anti-SSA and anti-Jo-1 antibodies, as a new syndrome designated DIPSSJ.

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