Clin Rheumatol (2000) 19:67–69

Clinical Rheumatology

Case Report

Gouty Arthritis in a Female Patient with Mixed Connective Tissue Disease

C-M. Huang

Division of Rheumatology and Immunology, Department of Internal Medicine, China Medical College Hospital, Taichung, Taiwan, ROC

Abstract: Gout with systemic lupus erythematosus (SLE) or progressive systemic sclerosis (PSS) has rarely been reported, whereas mixed connective tissue disease (MCTD) with the demonstration of intra-articular monosodium urate crystals has never been reported. We describe an unusual case of MCTD (SLE–PSS) in a 37-year-old woman who developed acute gouty arthritis. Arthrocentesis and synovianalysis may be necessary to differentiate gout from the arthropathy of MCTD.

Keywords: Gouty arthritis; Mixed connective tissue disease; Progressive systemic sclerosis; Systemic lupus erythematosus

Introduction

Gout and systemic lupus erythematosus (SLE) are both common rheumatic diseases, whereas mixed connective tissue disease (MCTD) is relatively rare. The prevalence of MCTD in Taiwan is not known. An epidemiological study on rheumatic disease in Japan [1] reported a prevalence of 2.7% for MCTD, compared with 20.9% for SLE, 5.7% for progressive systemic sclerosis (PSS) and 4.9% for polymyositis–dermatomyositis (PM–DM).

The relatively rare occurrence of coexistent gout and SLE suggests that either clinicians miss the diagnosis of gout or that SLE or the therapy for SLE protects against gout [2–6]. To the best of our knowledge, MCTD (SLE–PSS) and gout have not been reported before. Herein, we describe a case of gouty arthritis in a patient with MCTD.

Correspondence and offprint requests to: Dr C-M. Huang, Division of Rheumatology and Immunology, Department of Internal Medicine, China Medical College Hospital, 2 Yue Der Road, Taichung, Taiwan, ROC. Tel: 886-4-2052121, ext 1223; Fax: 886-4-2034608.

Case Report

A 37-year-old woman first noticed painful swelling and morning stiffness of both the finger and wrist joints in August 1994. Under the diagnosis of rheumatoid arthritis (RA), she was treated with a non-steroidal anti-inflammatory drug (NSAID) and low doses of prednisolone with effective relief of the symptoms. In February 1995 she developed right pleural effusion, Raynaud's phenomenon and thickening of the skin on both hands. She was admitted to a local hospital and diagnosed with PSS.

This patient visited the emergency room of our hospital on 26 August 1995, complaining of arthritic pain in the knees, wrists and hands. Shortness of breath, lower-leg edema and Raynaud's phenomenon were also noted. On admission, laboratory analyses revealed a haemoglobin level of 103 g/l, with a positive indirect Coombs' test. Urinalysis showed no haematuria or proteinuria. Antinuclear antibody (ANA) at a titre of 1 : 5120 was detected, with a speckled staining pattern. Assays for antibody to Sm and double-stranded DNA were both negative. An anti-ribonucleoprotein (RNP) antibody test was strongly positive (detected by counter-immune electrophoresis), at a titre of 1 : 512. The levels of C3 and C4, 44 mg/dl (normal 88–201) and 12 mg/dl (normal 16–47) respectively, were both below normal. Radiographs of the chest indicated right pleural effusion. Echocardiography showed moderate pulmonary hypertension (pulmonary arterial pressure 45 mmHg). A

diagnosis of MCTD (PSS–SLE) was thus established and she was treated with D-penicillamine 500 mg/day, nifedipine 30 mg/day and prednisolone 10 mg/day for 20 days. After being discharged, the patient received regular treatment in our outpatient department.

On the second admission to our hospital on 14 September 1996, the patient complained of right knee pain and swelling for 3 days. A physical examination revealed tenderness, swelling and redness of the right knee joint with a limited range of motion (Fig. 1). There was taut, thick skin on her hands, fingers (Fig. 2), feet, legs and face. Her fingers were cold and pale, accompanied by Raynaud's phenomenon. Laboratory values were: erythrocyte sedimentation rate (ESR) 54 mm/h, white blood cell count 12.6 $\times$ 10^9/l, haemoglobin 88 g/l, platelet count 422 $\times$ 10^9/l, creatinine 0.9 mg/dl (79.8 μmol/l), 24-h urine protein 0.6 g, 24-h uric acid 380 mg/dl, creatinine clearance 84 ml/min, uric acid 6.5 mg/dl (390 μmol/l), IgG 2580 mg/dl (normal 694–1618), IgA 66 mg/dl (normal 68–370) and IgM 330 mg/dl (normal 60–263). The ANA assay was positive at a titre of 1 : 2560 with a speckled pattern. Anti-Scl 70, anti-Ro and anti-RNP antibody assays were also positive, but anti-Sm, anti-DNA and anti-La antibodies were not detected. Results of a cryoglobulin test were negative and anticardiolipin antibody titres of IgG and IgM were all within normal limits. X-ray studies revealed soft-tissue swelling, but no calcification or degenerative destructive changes, in the right knee joint.

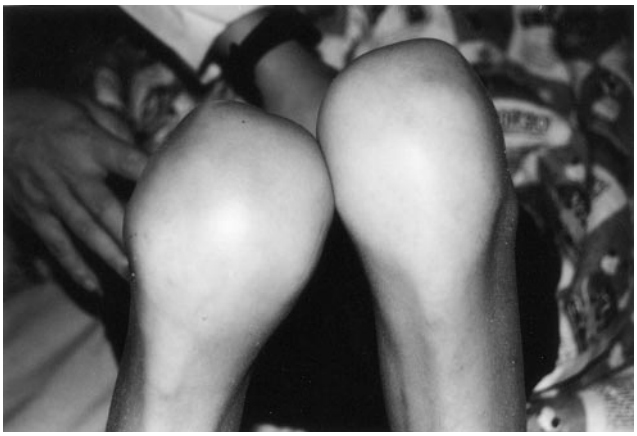

Fig. 1. Painful swelling and redness, with a limited range of motion, over the right knee joint in a 37-year-old woman with concomitant gout and mixed connective tissue disease.

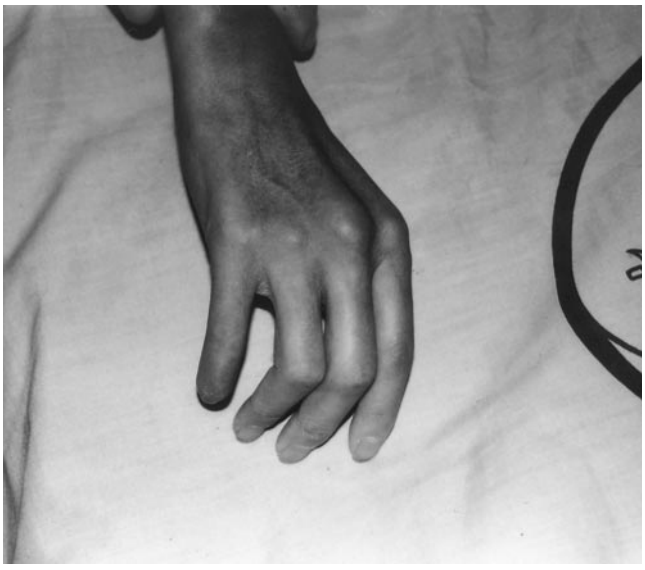

Fig. 2. A 37-year-old woman with thick, taut skin and contracture on the right hand.

About 40 ml of synovial fluid (SF) was aspirated from the right knee. Polarised light microscopy revealed intracellular negatively birefringent needle-shaped crystals, consistent with gout. The SF white blood cell count was 9.4 $\times$ 10^9/l with 56% polymorphonuclear cells and 44% lymphocytes. The patient was treated with sulindac 400 mg/day and colchicine 1.0 mg/day. The swollen knee joint showed improvement 2 days after the start of treatment. One month later, serum uric acid had increased to 7.5 mg/dl, and creatinine was normal at 1.0 mg/dl. The patient remained asymptomatic for 2 months. Symptoms of sepsis and coma developed after an episode of acute pyelonephritis, and she eventually died.

Discussion

MCTD is an overlap syndrome, which consists of SLE, PSS, PM–DM and RA, defined as high titres of circulating ANA with specificity for nuclear RNP antigen. It was first described by Sharp et al. [7] in 1972, and is receiving increasing attention.

Our patient's clinical manifestations of Raynaud's phenomenon, hand oedema and arthritis, acrosclerosis and high titres of anti-RNP antibodies met the criteria for the diagnosis of MCTD [8–9]. Pain, swelling and stiffness of the finger joints are frequently noted in MCTD. Many patients also develop more generalised peripheral joint involvement with swelling, erythema, warmth and tenderness of the knees, ankles, toes, wrists, elbows and shoulders. Radiographs usually show an absence of erosive changes [10]. Gouty arthritis might be mistaken for the arthropathy of MCTD if appropriate radiographic examinations and synovianalysis are not performed. MCTD is consistent with acute gouty arthritis, which was proven in our case when right knee monosodium urate (MSU) crystals were isolated. This is the first case report of MCTD with simultaneous gouty arthritis, based on an extensive literature search.

MCTD is a chronic systemic inflammatory disease caused by immunological disorders. Hyperuricaemia is not a feature of SLE or PSS [11]; however, many patients with SLE or PSS show hyperuricaemia that necessitates chronic diuretic therapy and leads to chronic

renal insufficiency [6,11]. As our patient did not have renal disease or receive diuretic treatment, gout was surprising.

The low frequencies of gout in SLE and MCTD may be attributable to higher frequencies of both SLE and MCTD in young women and of gout in older men. Several theories about the rarity of the association between gout and SLE have been proposed. In patients with gout, MSU are phagocytised by neutrophils. Chemotactic factors related to complement activation attract additional neutrophils, which produce inflammation [3]. Patients with SLE have a form of leukopenia that is primarily lymphopenic, but with a possible neutropenic component. Another theory [3] that has been suggested is that during active SLE with low complement, the body may be less able to mount an inflammatory reaction to MSU crystals, and complement activation has been shown in MSU crystal-induced inflammation [12]. A third theory [13] is that steroids or immunosuppressive therapy during active disease could block the clinical expression of gout while tophaceous deposits accumulate. These speculations may also apply to our patient with MCTD (SLE–PSS).

In conclusion, MCTD and gout rarely occur together. Recognition of acute gout in patients with MCTD may be difficult because its clinical features may be masked or attenuated by drugs used for MCTD, or it may be mistaken for arthritis in MCTD. However, the possibility of gout must be kept in mind during the evaluation of each form of arthritis in patients with MCTD. Arthrocentesis and analysis of synovial fluid are required for confirmation of the diagnosis of gout.

References:

1. Nakae K, Furusawa F, Kasukawa R, Tojo T, Homma M, Aoki K. A nationwide epidemiological survey on diffuse collagen disease: estimation of prevalence rate in Japan. In: Kasukawa R, Sharp G, editors. Mixed connective tissue disease and anti-nuclear antibodies. Amsterdam, Excerpta Medica, 1987:9–13.
2. McMillen MA, Cunningham ME, Schoen R, Fikrig E. Gout in patients with systemic lupus erythematosus. Br J Rheumatol 1994;33:595–6.
3. Moidel RA, Good AE. Coexistent gout and systemic lupus erythematosus. Arthritis Rheum 1981;24:969–71.
4. Rose EP, Alves LE. Coexistent gout and systemic lupus erythematosus. Arthritis Rheum 1982;25:713–4.
5. Bradley JD, Pinals RS. Tophaceous gout in patients with systemic lupus erythematosus. Clin Exp Rheumatol 1984;2:151–5.
6. Frocht A, Leek JC, Robbins DJ. Gout and hyperuricemia in systemic lupus erythematosus. Br J Rheumatol 1987;26:303–6.
7. Sharp GC, Irvin WS, Tan EM. Mixed connective tissue disease: an apparently distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). Am J Med 1972;52:148–59.
8. Alarcon-Segovia D, Cardiel MH. Comparison between three diagnostic criteria for mixed connective tissue disease. Study of 593 patients. J Rheumatol 1989;16:328–41.
9. Doria A, Ghirardello A, deZambiasi, Ruffatti A, Gambari PF. Japanese diagnostic criteria for mixed connective tissue disease in Caucasian patients. J Rheumatol 1992;21:259–64.
10. Sharp GC, Singsen BH. Mixed connective tissue disease. In: MacCarty DJ, Koopman WJ, editors. Arthritis and allied conditions, 12th edn. Philadelphia: Lea & Febiger, 1993:1213–24.
11. Durback MA, Schumacher RH. Acute gouty arthritis in 4 patients with systemic sclerosis. J Rheumatol 1988;15:1503–5.
12. Hasselbacher P. C3 activation by monosodium urate monohydrate and other crystalline material. Arthritis Rheum 1979;22:571–8.
13. Lalley E, Parker V, Kaplan S. Acute gouty arthritis and systemic lupus erythematosus. J Rheumatol 1982;9:308–10.

Received for publication 15 March 1999
Accepted in revised form 29 July 1999