BRIEF REPORT

COEXISTENT GOUT AND SYSTEMIC LUPUS ERYTHEMATOSUS

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We are unaware of any previous report concerning the coexistence of gout and systemic lupus erythematosus (SLE). Since gout is a relatively common disease affecting over 500,000 Americans (1), it seems likely that it would occur in some patients with SLE. In fact, on the basis of disease prevalence data (2), approximately 100 cases of coexistent gout and SLE might be expected in the United States (Table 1). This report documents the first known case of coexistent gout and SLE, and the various factors that may contribute to the lack of association between these diseases are discussed.

Case Report. The patient was a 48-year-old white man who was first seen at the Ann Arbor Veterans Administration Medical Center in November 1979 with nephrotic syndrome. He had a 10-year history of intermittent arthralgia of the ankles, feet, hands, and elbows, a 15-year history of intermittent urticaria, a positive LE cell test, and hypocomplementemia. The patient had been treated with 5–10 mg prednisone per day for 5 years. In 1978 he developed hypertension, 10-pound weight gain, and proteinuria. The serum uric acid was 13 mg/100 ml. He was placed on diuretics and continued on low dose prednisone, but by 1979 severe peripheral edema and fatigue developed. The patient denied a history of Raynaud's phenomenon, mucosal ulcerations, alopecia, and photosensitivity.

The physical examination was remarkable for a blood pressure of 215/105 and 4+ pitting edema up to the knees. Laboratory data included hemoglobin 11.3 gm/100 ml, hematocrit 31.7%, white blood count 5,300, platelets 220,000, BUN 25 mg/100 ml, creatinine 1.9 mg/100 ml, uric acid 11 mg/100 ml, creatinine clearance 70 ml/minute, 18 gm/proteinuria per 24 hours, microscopic hematuria, antinuclear antibody positive at 1:40 with a homogeneous pattern, DNA binding 81.5% (normal up to 25%), total hemolytic complement (CH50) 87 (normal 104–188), C3 79 (normal 85–191), and normal C4. Radiographs of the hands and ankles were unremarkable. Results of renal biopsy disclosed severe mixed diffuse proliferative and membranous glomerulonephritis with subepithelial and subendothelial deposits and myxovirus-like bodies on electron microscopy.

The patient was placed on prednisone 60 mg/day, propranolol 80 mg/day, furosemide 320 mg/day, and hydralazine 100 mg/day. Over the next 6 months, the prednisone was tapered to 20 mg/day. During that time, he began to complain of intermittent mild metatarsalgia. In June 1980, the patient developed tenderness, warmth, swelling, and erythema over the right first metatarsophalangeal (MTP) joint and metatarsal bone. Passive flexion and extension of the first MTP joint were painless. His temperature was 38.1°C and white blood count was 6,500, and a presumptive diagnosis of cellulitis was given. The patient was placed on intravenous nafcillin for the next four days. His right foot improved somewhat, but subsequently the left first MTP joint and metatarsal area became similarly erythematous, painful, and swollen. The serum uric acid was 10.8 mg/100 ml, and the CH50, C3, C4, and DNA binding were normal. An x-ray of the right foot revealed an erosion with overhanging margins at the head of the first metatarsal bone and another erosion at the second MTP joint (Figure 1). Aspiration of synovial fluid from the left first MTP joint yielded white blood cells filled with negatively birefringent needle-shaped crystals consistent with monosodium urate. Nafcillin was stopped, indomethacin was begun, and the inflammation in the feet resolved over the next several days.

Discussion. This patient had a well established diagnosis of SLE manifesting as biopsy proven nephritis, arthralgias, and urticaria, and characterized by the presence of elevated DNA binding values and hypo-

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Table 1. Expected concurrence of gout and systemic lupus erythematosus in the United States (1,2)

	Prevalence	Expected concurrence
SLE		
Women	0.10%	
Men	0.011%	
Gout		
Women	52,500	
Men	482,500	
Total	535,000	
Gout + SLE		
Women	52, 500 × 0.10%	52
Men	482,500 × 0.011%	53
Total		105

complementemia when the disease was active. Proof that he had gout occurred on finding crystals of uric acid in the joint aspiration. That he did not have concomitant infection was proved by the rapid resolution of the pain and swelling on indomethacin alone.

A search through the medical literature reveals that there are no other reports of coexistent gout and SLE. The age and sex disparity between the two diseases and the rarity of SLE itself are probably the major reasons for the negative association. In addition, the lack of such cases may be due in part to possible underdiagnosis of gout in lupus patients. Gout may not be suspected in a patient whose arthritis is attributed to established SLE.

Alterations in the complement system may be an additional important factor that inhibits the development of gout in the milieu of SLE. It has been demonstrated that the complement system may play an integral role in the pathogenesis of gouty arthritis. Incubating sodium urate crystals in human serum activates the complement cascade, evidenced by a consumptive depletion of complement components including C3 (3). Some patients have decreased C3 levels in the synovial fluid of the involved joint during an acute attack (4). Complement also enhances phagocytosis of sodium urate crystals and generates chemotactic activity, both of which help mediate the acute inflammatory response in gout (5). Animals depleted of complement exhibit diminished urate-induced inflammation (6). Thus, there is evidence that synovial fluid complement may be an important mediator of urate-induced inflammation, and a characteristic of patients with SLE is a marked decrease in synovial complement levels, even when the serum C3 level is normal (4). If urate crystals require near normal levels of synovial complement to induce inflammation, then the presence of decreased complement levels in SLE may pose a barrier to urate-induced inflammation and make the coexistence of gout and SLE very unlikely.

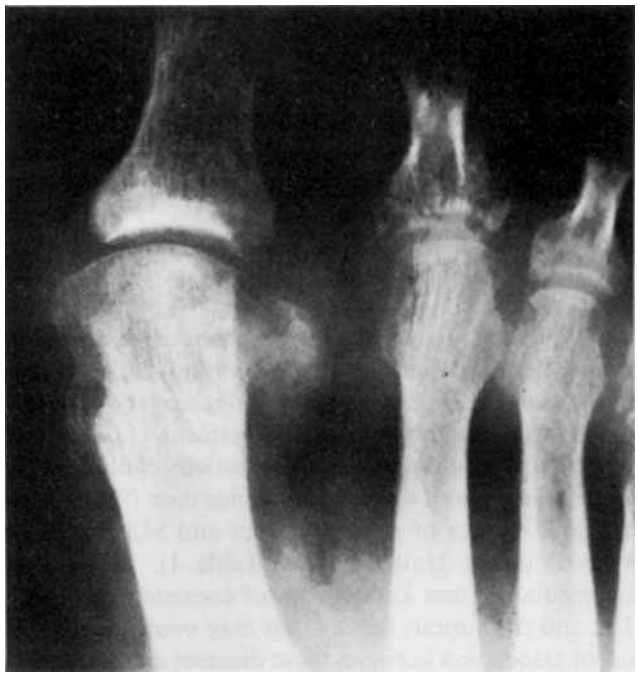

Figure 1. Erosion at the head of the right first metatarsophalangeal joint.

The negative association between gout and rheumatoid arthritis (1,7–11) may similarly involve the reduced synovial fluid complement levels found in rheumatoid arthritis (4), inhibiting the expression of clinical gout.

In conclusion, the rarity of the association of gout and SLE may be due to the disparity of the populations that each disease affects, the rarity of SLE itself, and the clinical difficulty in distinguishing an acute gouty attack from a flare of lupus arthritis rather than any true pathogenetic incompatibility between the two diseases. Conversely, the presence of low synovial fluid complement levels in SLE and rheumatoid arthritis may present an important blockade for the development of gouty arthritis since the presence of synovial fluid complement seems to be required for mediation of this inflammatory process. Further studies of the mechanism of urate-induced inflammation may clarify the reasons for the disassociation between gouty arthritis and SLE.

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ADDENDUM

Since acceptance of this manuscript for publication, we have discovered another case of coexistent

gout and SLE. The patient is a 39-year-old woman with SLE and membranous nephropathy since 1966 who developed tophaceous gout in 1976. The gout is presently controlled with allopurinol, and she has been on maintenance hemodialysis for several months. At the onset of gout, her creatinine was 1.4 mg/100 ml and the uric acid was 12 mg/100 ml

REFERENCES

1. Wallace DJ, Klinenberg JR, Morhaim D, Berlanstein B, Biren PC, Callis G: Coexistent gout and rheumatoid arthritis: case report and literature review. Arthritis Rheum 22:81–86, 1979
2. Fessel WJ: Systemic lupus erythematosus in the community. Arch Intern Med 134:1027–1035, 1974
3. Naff GB, Byers PH: Complement as a mediator of inflammation in acute gouty arthritis. I. Studies on the reaction between human serum complement and sodium urate crystals. J Lab Clin Med 81:747–760, 1973
4. Hasselbacher P: Immunoelectrophoretic assay for synovial fluid C3 with correction for synovial fluid globulin. Arthritis Rheum 22:243–249, 1979
5. Byers PH, Ward PA, Kellermeyer RW, Naff GB: Complement as a mediator of inflammation in acute gouty arthritis. II. Biological activities generated from complement by the interaction of serum complement and sodium urate crystals. J Lab Clin Med 81:761–769, 1973
6. Kellermeyer RW, Naff GB: Chemical mediators of inflammation in acute gouty arthritis. Arthritis Rheum 18:765–770, 1975
7. Talbott JH, Altman RD, Ts'ai-Fan Y: Gouty arthritis masquerading as rheumatoid arthritis or vice versa. Semin Arthritis Rheum 8:77–114, 1978
8. Schwartzberg M, Lieberman DH, Gupta VP, Ehrlich GE: Rheumatoid arthritis and chronic gouty arthropathy. JAMA 240:2658–2659, 1978
9. Jessee EF, Toone E, Owen DS, Irby R: Coexistent rheumatoid arthritis and chronic tophaceous gout. Arthritis Rheum 23:244–250, 1980
10. Rizzoli AJ, Turjeque L, Bankhurst AD: The coexistence of gout and rheumatoid arthritis: case reports and review of the literature. J Rheumatol 7:316–324, 1980
11. Owen DS, Toone E, Irby R: Coexistent rheumatoid arthritis and chronic tophaceous gout. JAMA 197:953–956, 1966