Remitting symmetric seronegative synovitis with pitting edema associated with B-cell non-Hodgkin's lymphoma

Sirs,

Cantini *et al.* have recently reviewed the literature concerning paraneoplastic remitting seronegative symmetrical synovitis with pitting edema (RS3PE) (1). We report here a further case of RS3PE associated with B-cell non-Hodgkin's lymphoma (NHL).

A 64-year old woman presented in June 1999 with a 4-week history of marked swelling of both hands and feet. She also complained of fever (< 38.5°C), mild weight loss, pain and stiffness of the shoulder and pelvic girdles, and Raynaud's phenomenon. At the physical examination pitting edema of the hands and feet and tenosynovitis of the finger flexors were observed. No signs of skin, eye or urogenital tract disease were detected. Laboratory investigations showed a erythrocyte sedimentation rate (ESR) of 86 mm/hr, C-reactive protein (CRP) 20.2 mg/dL (n.v. < 0.5), normocytic anemia (10.8 g/dL), and seropositivity for HCV-Ab+. Rheumatoid factor and antinuclear antibodies were negative. Other assays, including serum lactate dehydrogenase (LDH) and β_2-microglobulin, also yielded normal results. The HLA phenotype was A2, A74, B44, B57. X-rays of the hands, feet and sacro-iliac joints were normal.

The patient was thoroughly evaluated for a possible paraneoplastic syndrome: the only abnormality found was a hepatic hilar adenopathy 15 mm in diameter, disclosed by abdominal ultrasonography and diagnosed as a lymph node caused by HCV infection. The patient failed to respond to indomethacin, but dramatic improvement was obtained within 8 days with methylprednisolone 8 mg /5 days a week. Fever disappeared and a complete and persistent remission of the distal edema and marked improvement of the girdle pain and stiffness were seen. However, due to the persistence of a raised CRP and mild left knee synovitis the therapy was not tapered.

Two months later intermittent fever and polyarthrosynovitis involving the proximal interphalangeal and metacarpophalangeal joints, wrists, knees, and left elbow reappeared. CRP was 26.8 mg/dL and haemoglobin 9.6 g/dL. Liver enzymes and LDH were normal. No signs of infections were observed. Abdominal ultrasonography was unchanged. Steroids were increased to 20 mg 5 days a week, and sulphasalazine and hydroxychloroquine were added. The fever disappeared, morning stiffness and polyarthritis greatly improved, haemoglobin rose (11.7 g/dL) and CRP decreased (4.3 mg/dL).

In November 1999 the fever reappeared. Haemoglobin was 9.5 g/dl, CRP 14.7 mg/dL, LDH 435 IU/L (n.v. < 230) and β_2-microglobulin 4.0 mg/L (n.v. < 2.5). Abdominal ultrasonography demonstrated a coeliac hypo-anhechogenic adenopathy 50 x 31 mm diameter and 3 hilar adenopathies of 20, 27 and 27 mm. Ultrasound-guided fine-needle biopsy demonstrated a large cell NHL of B-cell origin (CD20+). Clinical staging did not show supra-diaphragmatic involvement. Only very rare CD20+ lymphomatous large cells were observed in the bone marrow biopsy. After a first cycle of polychemotherapy with CHOP, the fever disappeared. When last evaluated, in July 2000, the NHL was in complete remission and the patient was no longer receiving steroids. No signs of arthritis or polymyalgia were present and there was no residual flexor contraction of the fingers. CRP was within normal limits.

The possibility of a clinical picture indistinguishable from RS3PE and induced by an occult neoplasm has been clearly identified for solid cancers (1), but is less evident for B-cell malignancies. Only 3 other cases of RS3PE associated with B-cell lymphoproliferative disorders have been reported. However, just one was similar to the case described here, in that RS3PE preceded the diagnosis of NHL, although it differed in that there was a complete lack of response to low-dose steroids (2). In our patient, the prompt and persistent disappearance of distal swelling suggested at first that it was a truly "remitting" syndrome. The persistence of a raised CRP and the reappearance of fever after an interval, however, were clues for an association with an occult malignancy. This hypothesis had already been considered at presentation due to the presence of systemic signs.

The other 2 cases reported in the literature were quite different: RS3PE arose in patients with long-standing, untreated, low-grade B-cell lymphoproliferations. In one (3) the rapid achievement of a persistent remission of the rheumatologic syndrome with a short course of low dose steroids suggested a chance association between the two disorders. In the other (4), the picture was caused by diffuse lymphomatous marrow involvement and periostitis of the bone adjacent to synovitis, suggesting a direct role of NHL in its pathogenesis. This is at variance from what is commonly observed in RS3PE, which is usually due to diffuse tenosynovitis. In our patient induction of the synovitis by inflammatory cytokines (in this case, perhaps secreted by lymphomatous cells) might be hypothesised.

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Fabry's disease mimicking familial Mediterranean fever

Sirs,

We describe a patient with Fabry's disease whose diagnosis was made on the basis of kidney biopsy findings. Given the clinical features and ethnic background of the patient, familial Mediterranean fever (FMF) was the most probable diagnosis prior to the biopsy. Although several reports have noted the similarities between the clinical findings of Fabry's disease and various rheumatic disorders (1), we are unaware of any report suggesting mimicry between Fabry's disease and FMF.

A 20-year-old male patient from central Turkey was referred to our hospital with proteinuria. His past medical history included recurrent painful attacks in the abdomen and distal extremities, accompanied by fever of 6 years duration. He had been treated with non-steroid anti-inflammatory drugs during the painful episodes. On admission, his blood pressure was 110/70 mmHg and he had markedly dried skin; the rest of the examination was normal. Urinalysis showed proteinuria with acellular urine and daily urinary protein excretion was 1.6g. All other biochemical, haematological and immunological parameters were normal except for the erythrocyte sedimentation rate (ESR), which was 50 mm/hr.