Successful treatment of SAPHO syndrome with leflunomide. Report of two cases

Sirs,

SAPHO (Synovitis, Acne, Pustolosis, Hyperostosis, Osteitis) is characterized by aseptic bone and joint lesions, associated with skin involvement. Usually anterior chest pain is present at the early stage. Enthesis involvement was in most cases the first event leading to hyperostosis (1,2). We report two cases of SAPHO treated with leflunomide, with improvement of joint complaints and of skin lesions.

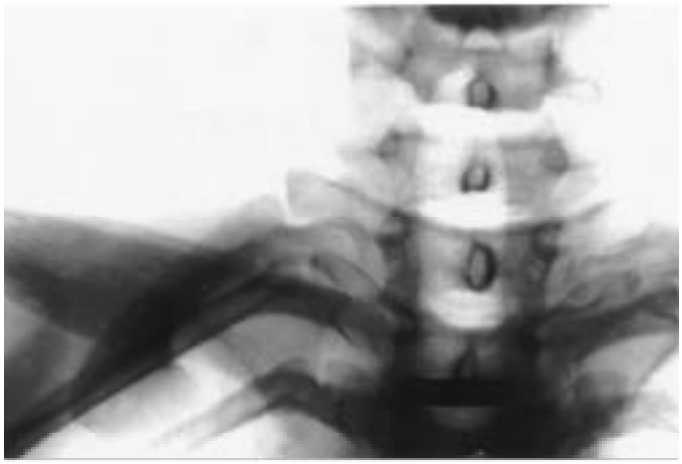
Case no. 1. A 17-year-old Caucasian boy with acne conglobata was admitted for fever, weight loss, swelling of right clavicle. His symptoms appeared one year ago. No history of psoriasis in his family. HLA typing was A3A9B7B35Cw4. Radiographs revealed hyperostotic changes of right clavicle with double track picture (Fig. 1), and right sacroiliitis. Bone scintigraphy showed increased uptake in right clavicle, manubriosternal, pubis and right sacro-iliac joint. A diagnosis of SAPHO syndrome was made and the patient was treated with diclofenac b.i.d. and injection of triamcinolone in sternal joints, with limited efficacy. Therefore, the patient was discharged on leflunomide (20 mg oad), diclofenac (100 mg) and rest. After 2 weeks the spine stiffness disappeared, after 1 month the swelling of right clavicle disappeared, the patient reported a total relief of cutaneous and osteoarticular symptoms, and diclofenac was withdrawn. At present, after 18 months the patient is in total remission with leflunomide 20 mg oad alone, which appears to be well tolerated. He presents only scars of acneic lesions.

Case no. 2. A 22-year-old Caucasian male was admitted for arthralgias, restricted spine movement, neck pain and anterior chest pain, swelling and tenderness of wrists, ankles, manubrio-sternal region. The onset of this symptomatology began 7 months ago. He suffered from acne conglobata. HLAtyping was not performed. Bone scintigraphy showed increased uptake in manubriosternal, condrosternal, sacro-iliac joints, ankles and knee. A diagnosis of SAPHO syndrome was made but the patient refused steroid therapy. Therefore he was discharged on leflunomide 20 mg oad and diclofenac 50 mg b.i.d. After 5 weeks the patient reported improvement of articular symptoms, with partial reduction of acneic lesions. Diclofenac was stopped. At present, after 9 months, the patient is in total remission. He complains only a mild nausea after taking leflunomide.

Wagner has demonstrated in histologic investigations of bone biopsy specimen in SAPHO patients an amounts of TNFα production (3).These findings provided several authors with a rationale for using TNFα blocking agents to treat successfully SAPHO patients (3-5). Leflunomide suppress pyrimidine synthesis, and recently significantly decreased expression of ICAM-1, TNFα and IL-1β was detected in synovial tissue samples from patients with RA after leflunomide treatment (6), accompanied by reduced cytokine synthesis by activated macrophages (7). The compound has recently been shown to be useful for the treatment of recalcitrant cases of psoriasis and psoriatic arthritis (8).

The young age, the severe course, the good compliance, the handling of dosage and the cost/benefit ratio oriented us to prefer leflunomide with respect other DMARDs, including TNFα-blocking agents. Leflunomide costs 904.87€ /year vs 12,984.81€ / year of Infliximab at dosage of 3 mg/Kg for each infusion for treatment of RA (9). Therefore, in our young patients we preferred leflunomide, with total remission of articular signs and good tolerance. At present the two patients are in good health, and our intention is to stop therapy with leflunomide after 2 years since remission, and then only to supervise periodically these patients.

Fig. 1. Periosteitis and hyperostosis of the right clavicle with double track picture.



S. SCARPATO, *MD*
E. TIRRI, *MD*

Rheumatology Unit, Medicine Dept., Ospedale "Scarlato" di Scafati, ASLSalerno 1, Italy.

Address correspondence to: Dott. Salvatore Scarpato, U.O. Reumatologia, Ospedale "Scarlato", Via Passanti 5, 84018 Scafati (SA), Italy. E-mail: scarpasa@tin.it

References

1. MAUGARS Y, BERTHELOT JM, DUCLOUX JM, PROST A: SAPHO syndrome: a follow-up study of 19 cases with special emphasis on enthesis involvement. *J Rheumatol* 1995; 22: 2135-41.
2. HAYEM G, BOUCHAUD-CHABOT A, BENALI K *et al.*: SAPHO syndrome: a long term follow-up study of 120 cases. *Semin Arthritis Rheum* 1999; 29: 159-71.
3. WAGNER AD, ANDRESEN J, JENDRO MC, HULSEMANN JL, ZEIDLER H: Sustained response to tumor necrosis factor alpha-blocking agents in two patients with SAPHO syndrome. *Arthritis Rheum* 2002; 46: 1965-8.
4. OLIVIERI I, PADULA A, CIANCIO G, SALVARANI C, NICCOLI L, CANTINI F: Successful treatment of SAPHO syndrome with Infliximab. Report of two cases. *Ann Rheum Dis* 2002; 61: 375-6.
5. TUCUNCU Z, MORGAN JR GJ , KAVANAUGH A: Anti-TNF therapy for other inflammatory conditions. *Clin Exp Rheumatol* 2002; 6 (Suppl. 28): S146-151.
6. KRAAN MC, REECE RJ, BARG EC *et al.*: Modulation of inflammation and metalloproteinase expression in synovial tissue by leflunomide and methotrexate in patients with active rheumatoid arthritis. *Arthritis Rheum* 2000; 4: 1820-30.
7. CUTOLO M, SULLI A, GHIORZO P, PIZZONI C, CRAVIOTTO C, VILLAGGIO B: Anti-inflammatory effects of leflunomide on cultured synovial macrophages from patients with rheumatoid arthritis. *Ann Rheum Dis* 2003; 62: 297-302.
8. LIANG GC, BARR WG: Open trial of leflunomide for refractory psoriasis and psoriatic arthritis. *J Clin Rheumatol* 2001; 7: 366-70.
9. SEYMOUR HE, WORSLEY A, SMITH JM, THOMAS SHL: Anti-TNF agents for rheumatoid arthritis *Br J Clin Pharmacol* 2001; 51: 201

Anti-RNApolymerase antibodies in Korean patients with systemic sclerosis and their association with clinical features

Sirs,

In systemic sclerosis (SSc), serum autoantibodies such as anticentromere antibody (ACA) and anti-topoisomerase I antibody (anti-topo I) are helpful markers of certain clinical features. However, Korean SSc patients have shown different characteristics (1): (i) no association between autoantibodies and disease subsets; (ii) much lower ACAprevalence in limited subset (6.7% vs 44% in Caucasians and 37% in the Japanese) (2); and (iii) no significant difference in clinical characteristics between disease subsets, except for more frequent musculoskeletal involvement in limited subset. Therefore, we investigated the prevalence of anti-RNAP antibodies in Korean SSc patients and their association with clinical features.