Letters to the Editor

Failure of unicondylar knee replacement in a patient with psoriatic arthropathy

Sirs,

Unicondylar knee arthroplasty is a well-documented alternative for osteotomy in the treatment of locally restricted osteoarthritis in young patients (1, 2). In the case of inflammatory arthritides, the situation is disappointingly different (3). Here we would like to report a case that emphasizes the importance of proper evaluation of the patient's joint symptoms when a unicondylar arthroplasty is considered in a psoriasis patient.

A 55-year old male building contractor had had psoriasis for 20 years but he had never experienced any joint symptoms that would have been considered psoriatic arthritis. He had successfully undergone demiarthroplasty 3 years previously in his left knee with osteoarthritis being the indication. However, during a period of a few months when the patient had worked on all fours, the knee had developed worsening pain and swelling that ultimately led to the rupture of a Baker's cyst. A month later the pain still continued and he sought medical advice.

Knee aspiration disclosed cloudy synovial fluid, which was considered purulent. As CRP was high (Fig. 1) and the patient had fever, infection of the knee prosthesis was suspected and intravenous antibiotics were commenced. Because septic fever continued, demiprosthesis was removed and the joint was debrided a week later. None of the bacterial cultures taken were positive.

After the operation, CRP and ESR remained still relatively high and the knee remained symptomatic despite the extended use of intravenous antibiotics (Fig. 1). Therefore the patient was referred to a rheumatologist, who detected synovitis in the wrists, elbows and the contralateral knee as well. Psoriatic arthritis was diagnosed and antibiotics were changed to antirheumatics (prednisolone 15 mg o.d., sulphasalazopyridine 1 gm b.i.d.), which led to remission of the joint symptoms.

After 3 months of treatment the patient received a total knee implant to his left knee. The Knee Society Knee Scores (4) after 6 and 12 months of follow-up were 100 and 70, respectively. To control the disease that continued in other joints, methotrexate (15 mg once a week) with folic acid was initiated and at the moment infliximab is under consideration.

Inflammatory arthritides are considered relative contraindications for unicondylar arthroplasty (1-3). Estimates regarding the prevalence of arthritis among patients with skin psoriasis have varied between 6% and 42% (5, 6). Still, it may be difficult to diagnose inflammatory monoarthrits in a patient, who is old enough to have osteoarthritis (5, 7). It is also possible that both diseases occur in the same joint. This is one possible explanation for the failure of knee replacement in the present case. Another alternative is more tragic: deep Köbner phenomenon refers to development of psoriatic arthritis in a joint which is subjected to trauma (7). It is possible that the synovial membrane of the joint that was operated on responded with psoriatic synovitis to the trauma inflicted by arthroplasty. The subsequent removal of the demiprosthesis might have renewed the Köbner phenomenon and induced the onset of arthritis in other joints. Considering the later progression of the disease (Fig. 1), it can be regretted that the patient did not receive total knee prosthesis in the primary arthroplasty, in particular as it has been reported that total removal of the hyaline cartilage from an already inflamed joint leads to the amelioration of arthritis (8, 9).

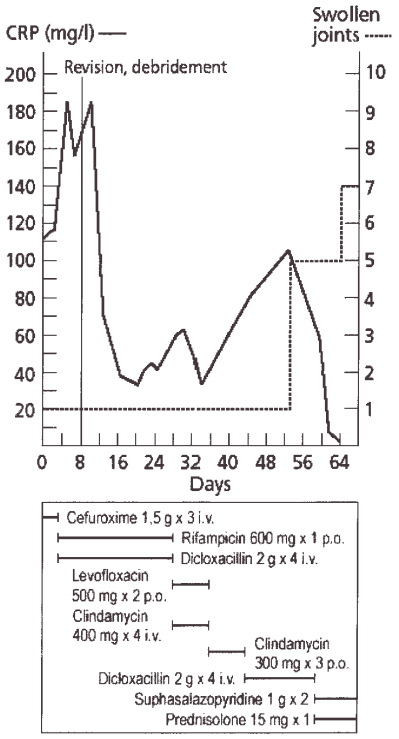

Fig. 1. The effect of various antibiotics and antirheumatic drugs on C-reactive protein level (CRP) during the first 68 days of active treatment. A count of swollen joints is also shown.

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Reprints will not be available from the authors.

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Cyclosporine in addition to infliximab and methotrexate in refractory rheumatoid arthritis

Sirs,

In this letter we report the results of a trial aimed at evaluating whether the addition of cyclosporine A (CsA), an agent often used in the combination therapies for rheumatoid arthritis (RA) (1), is a feasible option in cases of RA refractory to the association infliximab and methotrexate (MTX).

The primary objective of the study was to evaluate the safety of combined infliximab, CsA and MTX therapy in adult RA patients, but the efficacy of the treatment was also assessed. This pilot, 6-month open-label study was carried out in four Italian Rheumatology centres after the approval of the local Ethics Committees. The inclusion criteria were: a diagnosis of RA (ACR criteria) (2), an age of 18-75 years, no contraindications to the use of CsA, patient's willingness to participate to the study (written informed consent), and an (original) Disease Activity Score (DAS) (3) of ≥ 3.0 despite combined therapy with infliximab (3-5 mg/kg every 6-8 weeks) and MTX (10-15 mg/week) for at least 6 months. The infliximab and MTX doses and times of administration were left unchanged; the initial CsA dose was 3.0 mg/kg/day in 2 oral administrations. Safety and tolerability were evaluated by carefully questioning and examining the patients for adverse events, and by performing all stan-

Table I. The adverse events recorded in the 17 patients during the six months of the trial.

Patient	Adverse event	Time of occurrence	Action	Outcome
FP	Scrotal abscess	Month 5	Antibiotic therapy	Resolution
MCV	None	-	-	-
LS	Creatinine increase	Month 1	CsA discontinued	Resolution
CF	None	-	-	-
AG	None	-	-	-
BN	None	-	-	-
ZMB	Arterial hypertension	Month 3	CsA discontinued	Resolution
RL	None	-	-	-
IB	None	-	-	-
RC	None	-	-	-
PA	Arterial hypertension	Month 1	CsA discontinued	Resolution
MA	Arterial hypertension	Month 1	CsA discontinued	Resolution
RM	None	-	-	-
MN	Nausea	Month 2	None	Resolution
CG	Hypertrichosis	Month 2	None	Persistence
PC	Gingivitis	Month 4	CsA dose reduced	Improvement
CM	Arterial hypertension	Month 1	CsA discontinued	Resolution

dard laboratory investigations at each control visit. Efficacy was measured by using the DAS and the EULAR response criteria (4). Wilcoxon's test was used to compare the mean DAS values.

The study involved 17 patients (11 females and 6 males) with a mean age of 47.8 ± 12 years (range 24-75), and a mean disease duration of 99 ± 48 months (range 28-223). The baseline and final mean doses of CsA were respectively 2.81 ± 0.24 and 2.16 ± 0.23 mg/kg/day. The mean infliximab and MTX doses were respectively 3.0 ± 0.8 mg/kg per infusion and 11.45 ± 3.85 mg/kg/week, and remained unchanged during the study period. As CsA was discontinued in five cases (29.4%), the study was completed by 12 patients; arterial hypertension (defined by systolic/diastolic arterial pressure values greater than 140/90 mm Hg on at least 3 consecutive measurements) in 4 cases and increased serum creatinine in one, were the reasons for the therapy discontinuations. All of the patients of this study were on stable doses of prednisone (2.5 to 7.5 mg/day) and traditional non-steroidal anti-inflammatory drugs (none was on Cox-2 inhibitors) and, in this regard, there was no difference between the patients who developed arterial hypertension and increased serum creatinine and the others. All of the adverse events recorded during the study period are reported in Table I.

The mean DAS (using the last observation carried forward method for dropouts) at the different evaluation times was 6.7 ± 1.15 at baseline, 4.23 ± 1.0 after one month, 3.97 ± 0.97 after 2 months, 3.86 ± 1.0 after 4 months, and 3.53 ± 1.04 after 6 months. The difference in the mean DAS was already significant after one month ($p = 0.005$), remained significant between month 1 and month 2 ($p = 0.03$), and was not significant between month 2 and 4, or between month 4 and 6. The final difference (between baseline and month 6) was highly significant ($p = 0.0004$). At the end of the study period, nine of the 12 patients completing the trial and 1 of the 5 non-completers were responders according to the EULAR criteria, a total of 10 patients (58.8%).

The results of this pilot study seem to indicate that the addition of CsA to infliximab and MTX in patients with long-standing and still active RA is acceptably safe. The adverse events responsible for CsA discontinuation during the six months of the trial were those typical of the drug. Although the study was not designed to evaluate the efficacy of the therapy, it is worth noting that more than half of the patients showed a response according to the EULAR criteria. Similar efficacy results have been shown by the only other published report on the same subject (5).

In conclusion, the addition of CsA to infliximab and MTX seems to be a safe and effective rescue option for RA patients resistant to the double combination. Larger studies and longer follow-up periods are required to confirm these preliminary results.

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Erratum corrige

The paper "The fibrinolytic system components are increased in systemic sclerosis and modulated by Alprostadil (alpha1 ciclodestryn)" by F. Bandinelli, F. Bartoli, E. Perfetto, A. Del Rosso, A. Moggi-Pignone, S. Guiducci, M. Cinelli, C. Fatini, S. Generini, A. Gabrielli, R. Giacomelli, S. Maddali Bongi, R. Abbate, M. Del Rosso, M. Matucci Cerinic, published in Clin Exp Rheumatol 2005; 23(5): 671-677 was funded by grant number 04/2001 of Scleroderma foundation and by the Italian MIUR.