Treatment of psoriatic arthritis with cyclosporin A

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ABSTRACT

The purpose of this study was to determine the efficacy and toxicity of cyclosporin A (CsA) in treatment of patients affected with psoriatic arthritis (PsA).

Methods: This study includes 11 patients with PsA. Clinical and functional parameters are assessed: Ritchie Index, duration of the morning stiffness of joints in minutes, and pain. Laboratory values in serum were checked: SR, CRP, urea, creatinin, cholesterol, trigliceride, electrolyte, and liver enzymes.

Measurements of blood pressure were taken monthly.

Results: With a therapeutic dose of CsA 3 mg/kg/daily we noticed an improvement of clinical parameters, but not of laboratory values.

Conclusion: The investigation showed that CsA in the dosis of 3 mg/kg/daily was efficient and safe in the treatment of PsA.

KEY WORDS

cyclosporin A, psoriatic arthritis, treatment

Introduction

Psoriatic arthritis (PsA, psoriasis arthropathica) is characterized by a negative rheumatoid factor in blood serum and arthritic manifestations. For a long time it was considered a mild form of arthritis. During the last years, however, this opinion has changed. In 1978, Gladman and coworkers (1) reported 40% out of 220 patients with PsA to be suffering from deforming and erosive arthritis, 17% of those with 5 or more affected joints. Arthritic manifestations can be subdivided into five subgroups: 1. Predominantly peripheral mono or asymmetrical oligoarthritis (sausage-like finger), often overlooked; 2. Predominantly distal interphalangeal arthritis; 3. Predominantly symmetrical rheumatoid like polyarthritis: 4. Arthritis mutilans involving fingers and toes. 5. Predominantly spondylitis and/or sacroileitis (2).

In mild cases PsA can successfully be treated with nonsteroid anti-inflammatory drugs (NSAR) and local corticosteroid injections, whereas the so-called second line of medicines are intended for NSAR refractory and progressively destructive forms of PsA (3). As a rule,

patients with minimal skin lesions and an active involvement of joints react positively to treatment using antimalarials, gold salts, D penicillinamin and sulfosalazine (4, 5). In a generalized form of psoriasis, which is accompanied by severe affection of joints, it is logical to use drugs efficacious in both manifestations of this disease. These are methotrexate, retinoids, azathioprine, sulfasalazin and cyclosporin A.

Patients and methods

This study included 11 patients with active peripheral PsA who were unsuccessfully treated with nonsteroid antirheumatics and/or corticosteroids.

We have registered the principal data of each patient. Over a period of 6 months they were treated with CsA in doses of 3mg/kg/daily. At the same time, 4 patients were also receiving lower doses of corticosteroids.

At the beginning and at the end of this study clinical and functional parameters were assessed: Ritchie Index, duration of morning stiffness of joints in minutes, and pain.

Measurements of blood pressure were taken monthly and laboratory values in sera were checked: ESR, CRP, urea, creatinine, cholesterol, triglyceride, electrolyte, and liver enzymes. At the beginning and at the end of this study we have also measured concentration of cyclosporin in serum with fluorescence polarization immuno assay (ABBOTT) method.

Results

Out of 11 patients with PsA included in this study there were 6 females and 5 males of an average age of 51 (34-74).

The results of this study, assessed on the basis of T-student test, revealed a statistically significant lowering of Rithchie Index ($p < 0.05$), of morning stiffness and of pain ($p < 0.05$), but there was no significant lowering of erythrocyte sedimentation rate ($p > 0.05$) and CRP ($p > 0.05$).

One of our patients was subsequently dropped from the test list because of increased blood pressure.

Discussion

PsA is a disease, which includes inflammation of joints, involving about 5% of patients affected by psoriasis. The disease is characterized by a negative rheumatoid factor. In approximately 50% of patients who are HLA B27 positive there also develops spondyloarthropathy, so that PsA is included in the group of seronegative spondyloarthropathies (6).

In the etiopathogenesis of the disease the influence of the immune system has been proven. Immunohistochemical changes of synovial membranes in PsA were described. The infiltration of activated CD4+ T lymphocytes and macrophages is dominating in synovial membranes as well as in the skin. The mononuclear inflammatory infiltration in PsA is smaller than in rheumatoid arthritis (RA), whereas the pathogenetic mechanism causing the inflammation of synovial membranes is probably equal (7).

Moreover, there are also descriptions of numerous irregularities in the subpopulations of circulating lymphocytes during the active phase of the joint disease. In the first place, the percentages of CD8+ T and activated CD 3+ T lymphocytes, as well as of B lymphocytes and killer cells (8) are lowered, while the level of the serum soluble interleukin 2 receptor (S IL-2R) and of IL-6 is increased (9).

Certain studies dealt with the levels of cytokines and their receptors in the synovial fluid of patients with PsA. They established an increased level of IL-1, IL-6, IL-8, and of the tumor necrosis factor receptor (TNFr) (3).

The most important immunosuppressive effect CsA is the blockage of the early stage of T lymphocyte activation, i.e. of the production of cytokines, including IL-2, IL-4, and interferon gamma (3). In addition, CsA acts as a direct anti-inflammatory agent by inhibiting the release of inflammatory mediators from tissue mastocytes, basophil substances and polymorphonuclear cells (3).

There are only few studies assessing effects in vivo on seroimmunological parameters in patients with PsA. After a 6-month treatment they described a significant lowering of the IL-6 level accompanied by significant decrease of joint ailments and of the CRP level. (2) There occurred also a reduction of s IL-2R parallel with a reduced number of swollen and painful joints (3).

Olivieri and coworkers (3) have reviewed 16 studies dealing with the treatment of 170 PsA patients using CsA. Analyses confirmed the safety of such treatment. Only 16 patients (9.4%) stopped taking this medicine due to side effects: nephrotoxicity 10, uncontrolled hypertension 4, gastrointestinal disturbances 2. The authors concluded that CsA was successful in treatment of psoriasis, of both skin lesions and joint symptoms (3).

Sporado and coworkers (10) reported similar positive effects of CsA. The main reason for breaking off the treatment was hypertension (10). In 1989, Gupta and coworkers (11) noted a short period of successful activity of CsA in 6 patients who had been treated for 8 weeks with doses of 6 mg/kg/daily. A few days after the end of the therapy skin efflorescences reappeared, and after two weeks joint symptoms emerged again.

Mazzanti and coworkers (12) treated 8 patients with a combination of CsA (5 mg/kg/daily) and methotrexate (10-15 mg/weekly). After a 6-month treatment they

noted a regression of skin and joint symptoms (12), except in one case.

In all studies published so far only the effect of CsA on the peripheral arthritis has been observed. Likewise, there are few studies evaluating longer lasting effects of CsA on the radiologically verified evolution of the disease (2). One of such studies is a 2-year study by Macchioni and coworkers (13) who have established that CsA controlled the progression of damages inflicted on peripheral joints in 60% of patients with PsA. This presupposes that the normal level of the s IL-2R after a six-month therapy is a reason for assuming a good prognosis of the disease, while SR and CRP lack any prognostic value (1).

The results of our study have also revealed the efficacy and tolerance of CsA in the treatment of PsA. We established an improvement of the clinical parameters of arthritis, measured by Ritchie Index, morning stiffness, and pain in the joints. However, we did not notice any decrease in CRP and in the sedimentation rate of erythrocytes.

During treatment attention must be paid to possible toxic side effects of the drug, including a regular control of the blood count, liver and renal tests, cholesterol, triglyceride, and electrolyte. Of utmost importance are regular measurements of blood pressure. Medical personnel must also be on lookout for other possible side effects.

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