LETTER

Leflunomide for the treatment of systemic lupus erythematosus: Comment on the article by McMurray

To the Editor:

Dr. McMurray did an extensive review of nonstandard and adjunctive medical therapies for systemic lupus erythematosus (SLE) (1). However, he does not mention the use of leflunomide for treatment of SLE. To support the notion that leflunomide is helpful in managing patients with SLE, 2 patients are described for whom leflunomide helped to achieve remission.

Patient 1 is a 56-year-old woman who first presented in October 1999 with a 6-year history of Raynaud's phenomenon, intermittent pleuritis, and migratory active arthritis. In 1985, discoid lupus, lymphopenia, antinuclear antibody (ANA) positivity, and sun sensitivity had already been noted by a physician at a local university center. The patient had been treated with glucocorticosteroids and azathioprine in the past, but at the time of her first visit had received homeopathic medications only. Physical examination revealed bilateral swelling of the proximal interphalangeal and metacarpophalangeal (MCP) joints and wrists, as well as unilateral knee effusion. Laboratory evaluation documented hypothyroidism; mild lymphopenia; ANA titers of 1:10240 with a speckled pattern; anti–DNA antibodies of 62 IU/ml (normal = 5 IU/ml); and positivity for RNP, Sm, IgG, and IgM anticardiolipin antibodies. Urinalysis was normal. C3 and C4 complements were both mildly reduced, and the erythrocyte sedimentation rate (ESR) was markedly elevated at 120 mm/hour. Therapy with prednisolone 7.5 mg/day, hydroxychloroquine (HCQ) 400 mg/day, and methotrexate (MTX) 20 mg/week was started, in addition to thyroxin, calcium, and vitamin D supplementation.

Despite the fact that the HCQ dose was reduced and subsequently discontinued because of the patient's agitation, her condition improved. Prednisolone could be reduced to 5 mg/day, but mild arthritis and synovitis persisted. Because disease was believed to be not adequately controlled, and the patient repeatedly expressed the wish to further reduce use of glucocorticosteroids, in March 2000 leflunomide was started, with a loading dose of 100 mg on 3 consecutive days, followed by 10 mg/day thereafter. The patient's arthritis disappeared within 4 weeks, MTX was reduced to 15 mg/week, and prednisolone could be tapered to 1 mg/day. Eight months after initiation of leflunomide, the patient's ESR was reduced to 30 mm/hour, and anti–DNA antibodies were reduced to 6.5 IU/ml. There has been no recurrence of arthritis with a followup so far of 16 months.

Patient 2 is a 54-year-old woman who presented in May 1998 with a 2-year history of sun sensitivity and swelling of her hands and feet. Physical examination revealed a malar rash, synovitis at the wrists, and tender MCP and metatarsophalangeal joints. Laboratory evaluation revealed an ANA titer of 1:640 with a speckled pattern, SSA positivity, and low-titer RNP antibodies. Prednisolone at 12.5 mg/day (the dose the patient had been receiving for 2 years) was continued, and MTX therapy was initiated at 15 mg/week. The dosage of MTX had to be split into 2 weekly doses because of nausea but was not continued after August 1998. The patient did not return until November 1999, at which time she complained of increased arthritis and synovitis, despite treatment with 17.5 mg/day of prednisolone and sulfasalazine prescribed by another doctor. Hydroxychloroquine at 400 mg/day and leflunomide at 20 mg/day (after a loading dose of 100 mg/day for 3 consecutive days) were started. The patient reported a drastic improvement within 3 weeks, with disappearance of synovitis. She discontinued HCQ after 2 months and was still in remission, with 5 mg prednisolone and 20 mg/day leflunomide, in July 2000.

In the first case, leflunomide was added to MTX. In the second case, it was given for a short period in combination with HCQ but then was continued alone, all in addition to low-dose glucocorticosteroid therapy. In both cases, leflunomide helped to control arthritis and reduced the need for glucocorticosteroids. Both patients responded within a few weeks with remission of their arthritis. In one patient, who showed elevated anti–DNA antibodies, a near normalization of the anti–DNA antibody level that paralleled normalization of the ESR was observed.

Although many practicing rheumatologists admit to having treated SLE patients with mild to moderate disease with leflunomide—most often when arthritis dominates, and treatment with methotrexate and hydroxychloroquine have failed or were not tolerated—there have been only two other uncontrolled open label observational reports of its use in SLE. Peteral and colleagues reported preliminary data of 11 patients with mild to moderate SLE who were treated with leflunomide in conjunction with baseline glucocorticosteroids, indicating a tendency toward reduced disease activity (2). Remer et al. recently published their experience with 18 patients in whom SLE disease activity was not adequately controlled by concurrent or prior medications (3). Ten of the 14 patients who completed 3 months of leflunomide had an improvement in symptoms. Reduction of ESR, anti-DNA antibodies, and required glucocorticoid dosage occurred or was possible in some patients—similar to the two patients described above. Further, larger prospective trials seem indicated to more clearly define the potential role of leflunomide in managing patients with SLE.

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