Sustained response to infliximab in 2 patients with refractory relapsing polychondritis.

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Unclassified Early Arthritis Is Often Spondyloarthropathy

To the Editor:

We read with interest the recent editorial by Prof. H.R. Schumacher. Our team recently published a long-term follow-up study of seronegative oligoarthritis. Of 441 patients with recent (<6 mo) arthritis, 64 had rheumatoid factor negative seronegative oligoarthritis (<5 swollen joints). All patients except 2 did not fulfill the American College of Rheumatology criteria for rheumatoid arthritis (RA) at onset. At 23-year follow-up we noted that 40 (62.5%) patients had had putative features of spondyloarthropathy. However, only one patient with HLA-B27 developed bilateral sacroiliitis. Ankylosing spondylitis often begins with joint (knee) and is considered as seronegative oligoarthritis. Patients also seem to accept it.

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Dr. Schumacher replies

To the Editor:

I appreciate the comments of Kaarela, et al. They direct our attention to their important work that adds further support to the relatively benign course of much initially unclassified oligoarthritis.

I especially want to emphasize the comment that their patients seem to accept a “diagnosis” of “seronegative oligoarthritis.” Eventually, we may be able to give more definite diagnoses and prognoses, but for now I hope we will not try to force patients into diagnoses of rheumatoid arthritis or even spondyloarthropathy, as those without full-blown features may do well with more conservative therapies.

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Effect of a Diet Program on Lipid and Lipoproteins, Body Weight, Nutrient Intakes, and Quality of Life in Patients with Systemic Lupus Erythematosus

To the Editor:

We read with interest the article by Shah and colleagues. In their randomized study of patients with systemic lupus erythematosus (SLE) they demonstrated that a cholesterol-lowering diet was highly accepted by their patients and was accompanied by a significant and sustained improvement in their quality of life after 12 weeks.

Despite these findings, only a modest decrease in total (−6%) and low density lipoprotein (LDL) cholesterol (−2%) was achieved at the end of study, contrasting with a more prominent reduction in very low density lipoprotein (VLDL) cholesterol (−34%) and triglycerides (−24%). Nevertheless, dietary intervention should be considered as a first-line intervention in all SLE patients who present a pattern of dyslipoproteinemia secondary to corticosteroid therapy, although its beneficial effect would be more evident in those with higher doses of this drug.

Unfortunately, in the study, an undesirable reduction of 4% was also detected in high density lipoprotein (HDL) cholesterol. It should be pointed out that low HDL, the benign lipoprotein, is one of the most common findings in the “lupus pattern of dyslipoproteinemia” and has an inverse association with cardiovascular risk in SLE. For this reason the authors recommended including in future dietary intervention physical activity as a treatment modality to improve HDL concentrations.

We would like to extend this proposition to include antimalarials. Indeed, we recently demonstrated an increase in HDL levels with continuous use of chloroquine diphosphate in SLE patients, regardless of the use or not of prednisone. This increase in HDL was also observed in rheumatoid arthritis after 6 months of exclusive use of hydroxychloroquine, reaching a 15% increase after 12 months.

Finally, the relevance of this diet program on lipid profile needs further clarification, since at least one-half of the patients in each studied group were receiving cholesterol-lowering therapy. It is important to elucidate if these drugs achieved their maximum improvement in every patient included in the study, in order to define if some of the effect observed could be attributed to these drugs.

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REFERENCES
To the Editor:

Earlier, Kavanaugh and colleagues\(^5\) also reported an increase in HDL diphosphate in SLE patients increases HDL levels regardless of prednisone modality based on their recent findings that continuous use of chloroquine diphosphate on lipoprotein profile in lupus patients with and without therapy. J Rheumatol 2001;28:780-5.

Drs. Borba and Bonfa propose adding antimalarials as another treatment modality to improve HDL concentrations. As Drs. Borba and Bonfa point out, high density lipoprotein (HDL) cholesterol decreased by 4% at the end of the study. This decrease, however, was not significant in the diet group at the end of the study and neither was the change in total and LDL cholesterol ratio. Nevertheless, since low HDL has an inverse relationship with cardiovascular disease in SLE\(^1\), we recommended including physical activity, a well known way of increasing HDL cholesterol, as a treatment modality to improve HDL concentrations.

Drs. Borba and Bonfa propose adding antimalarials as another treatment modality based on their recent findings that continuous use of chloroquine diphosphate in SLE patients increases HDL levels regardless of prednisone use\(^1\). Earlier, Kavanaugh and colleagues\(^2\) also reported an increase in HDL levels (7.6%), although not significantly, in SLE patients taking 800 mg of hydroxychloroquine. Antimalarials thus may be an alternative strategy, especially for SLE patients who are unwilling or unable to exercise enough.

Drs. Borba and Bonfa’s final comment was to clarify whether some of the changes in lipids and lipoproteins seen in our diet subjects were due to the cholesterol-lowering drugs that 4 of them were taking. We believe that the improvement seen in our diet subjects was caused by the dietary intervention and not related to the cholesterol-lowering agents, since they had been taking cholesterol-lowering drugs for an average of 7.1 months (5.4–17.2 mo) before entering the study and thus should have already achieved their maximum improvement attributed to the drugs. Also, the dose remained constant in each subject before and during the study.

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Sustained Response to Infliximab in 2 Patients with Refractory Relapsing Polychondritis

To the Editor:

Relapsing polychondritis (RP) is a rare inflammatory disease of unknown etiology causing recurrent inflammatory reactions in the cartilaginous structures and joints\(^1\). Because precise knowledge of the pathogenesis of RP is lacking, many therapeutic approaches have been reported. There are important clinical similarities and overlaps between RP and rheumatoid arthritis (RA). The decision to use tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)) blocking agents was supported by recent reports of successful use of these agents in different rheumatic diseases, especially RA\(^2\). We describe the results obtained with infliximab in 2 patients with RP over a 9-month period.

A 20-year-old Caucasian woman was diagnosed with RP in November 1997, based on symmetrical auricular and nasal cartilage inflammation, with leakage of the aortic valve, and 3 years of nonerosive seronegative polyarthritis.

Laboratory tests including rheumatoid factor, antinuclear antibody, and antineutrophil cytoplasmic antibody were negative. She had been treated initially with prednisone 20 mg per day, which led to the resolution of the polyarthritis. However, she had repeated relapses of polyarthritis, and satisfactory control of the nasal and auricular symptoms was not achieved, despite multiple treatments including prednisone, hydroxychloroquine, gold salts, azathioprine (2.5 mg/kg/day), D-penicillamine, and methotrexate (MTX; 20 mg weekly).

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Because of polyarthritis relapse, systemic inflammation [erythrocyte sedimentation rate (ESR) 53 mm/h, C-reactive protein (CRP) 42 mg/l], failure to control the ear and nose cartilage inflammation, and hematological toxicity due to azathioprine and MTX, TNF-α blocking therapy was initiated in September 2001. Infliximab 5 mg/kg body weight was selected for TNF-α blockade in addition to prednisone 15 mg per day. Infliximab infusions were given at 0, 2, 6, 14, 22, 30, 38, and 46 weeks. Before each infusion a premedication with intravenous betamethasone 10 mg was given.

After the first infusion CRP decreased to the normal range (Figure 1A) and clinical improvement was observed. No further episode of synovitis occurred and auricular and nasal cartilage inflammation disappeared. Sustained clinical and biological response was observed after 8 infusions, with no adverse events. In addition, the prednisone dose was reduced from 15 to 3 mg per day (Figure 1A).

A 20-year old Caucasian woman was diagnosed with RP in 1993, based on auricular and nasal cartilage inflammation, bilateral episcleritis, and polyarthritis. On examination there was no evidence of cartilage involvement in the respiratory tract. Soon after she developed necrotic cutaneous lesions of the left foot, which led to amputation of the second toe. Histological examination of the toe revealed a necrotizing vasculitis. Laboratory findings were negative. Episcleritis was treated with topical steroids with complete resolution of symptoms. Treatment with 20 mg/day oral prednisone controlled her synovitis, but inflammation of her ears and nose often needed a higher dose. Repeated attempts to reduce steroid dosage below 20 mg per day failed. MTX (25 mg weekly), dapsone, cyclosporine, azathioprine (3 mg/kg/day), and cyclophosphamide were added to her treatment to better control disease and to reduce steroid dose, but all were ineffective. Therefore, TNF-α blocking therapy with infliximab was initiated in October 2001. Infliximab 5 mg/kg body weight was added to prednisone 20 mg per day. Infliximab infusions were given at 0, 2, 6, 14, 22, 30, and 38 weeks. After the first infusion clinical improvement was observed. No further episode of synovitis, episcleritis, or vasculitis occurred and auricular and nasal cartilage inflammation disappeared. CRP decreased to the normal range after 2 infusions (Figure 1B). Sustained clinical and biological response was observed after 7 infusions, with no adverse events. Prednisone dose was reduced from 20 to 8 mg per day (Figure 1B).

RP and RA share several clinical symptoms and signs. Interestingly, Buckner, et al have recently described, in a patient with RP, production of interferon-γ in response to DR1 autologous antigen-presenting cells, although the cytokine profile was dependent on the DRB1 restriction element used. Further, Ohwatari, et al have shown that RP patients exhibited significantly higher levels of macrophage migration inhibitory factor. These findings and reports of successful use of TNF-α blocking agents in RA provided us with a rationale for using these agents to treat 2 RP patients who were unresponsive to immunosuppressive drugs.

Our 2 cases fulfilled McAdam’s and Damiani’s criteria of RP. Both these patients had a history of therapy with immunosuppressive agents, none of which had been sufficient to control clinical symptoms or systemic inflammation. In both cases, repeated relapses required longterm use of steroids. After the first infusion of infliximab, clinical and biological improvement was observed. Prednisone dose was reduced in both cases. Over a 9-month period sustained response was observed, with no adverse event.

Infliximab seems to be an effective therapy for RP that is unresponsive to conventional therapy; it is also useful as a steroid-sparing agent. Longer term controlled studies of TNF-α blocking agents in patients with RP are warranted.

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Figure 1A. Prednisone dosages and C-reactive protein (CRP) levels in Patient 1 during 11 month followup.

Figure 1B. Prednisone dosages and C-reactive protein (CRP) levels in Patient 2 during 9 month followup.