Consider Infliximab, Leflunomide for Sarcoidosis

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KEY BISCAYNE, FLA. — Although antimalarial agents are first-line treatment for cutaneous sarcoidosis, infliximab and leflunomide are showing promise and may be appropriate for refractory patients, Theodore Rosen, M.D., said at the annual meeting of the Noah Worcester Dermatological Society.

Corticosteroids and/or methotrexate are generally second-line therapy for patients who fail to respond to chloroquine or hydroxychloroquine. There are few data, however, to support the use of other drugs that researchers have considered—pentoxifylline, tetracyclines, or isotretinoin, "which we can barely give right now," Dr. Rosen said.

Sarcoidosis occurs 10-20 times more often in black patients, particularly women, and is associated with a mortality rate 15 times greater in blacks than in whites. The condition is rare in patients younger than 4 years, and the peak incidence is between age 20 and 40 years. When there is skin involvement, it suggests a chronic condition with lung and bone involvement. Sarcoidosis is fatal in 5%-10% of cases.

Diagnosis can be challenging. Skin presentations are polymorphic, and include lesions that are lupus pernio, annular, psoriasiform, ichthyosis-like, verrucous, ulcerative, hypopigmented, nodular, or micropapular. "Any skin lesion not otherwise diagnosed should suggest sarcoidosis," said Dr. Rosen, professor of dermatology at Baylor College of Medicine, Houston.

Treatments are aimed at interrupting the immunopathogenesis at various stages. For example, 4 mg/kg per day of chloroquine or 6.5 mg/kg per day of hydroxychloroquine can inhibit antigen presentation. Topical or oral corticosteroids, including 40-80 mg/day of oral prednisone, can suppress granuloma formation. An immunosuppressive agent, such as methotrexate, 30 mg weekly, is another option.

Tumor necrosis factor α (TNF-α) agents also suppress granuloma formation. Infliximab [Remicade] is "where I'm putting my money," Dr. Rosen said. Infliximab appears to offer excellent control, but there are risk and cost considerations, he said. The Food and Drug Administration approved the TNF-α antibody for Crohn's disease and rheumatoid arthritis. For sarcoidosis, Dr. Rosen suggested a dosing regimen of 3-10 mg/kg per dose delivered by intravenous infusion at 0, 2, and 6 weeks, and then as dictated.

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Several studies have shown that infliximab provides a "dramatic and rapid response" for cutaneous lesions, Dr. Rosen said (J. Am. Acad. Dermatol. 2003; 48:290-3; J. Drugs Dermatol. 2003;2:413-4; Chest 2003;124:2028-31; and Arthritis Rheum. 2003;48:3542-3).

He also cited a woman he treated for cutaneous sarcoidosis. She failed treatment with chloroquine and hydroxychloroquine at maximal doses. She also failed treatment with prednisone as well as methotrexate; nor did she show any response to potent topical steroids. Intralesional steroids provided minimal improvement. She tried pentoxifylline and tetracycline regimens, again with no clinical improvement. However, after receiving infliximab 5 mg/kg IV at 0, 2, and 6 weeks, the prominent lesions on her face disappeared.

Long-term safety, possible induction of lymphoma, and risk of infection are concerns with infliximab. Dr. Rosen stressed that physicians must ensure the diagnosis is sarcoidosis and not TB. Cost is another factor with infliximab. He estimated the cost per infusion is $4,500-$9,000.

Leflunomide (Arava) appears promising for sarcoidosis, Dr. Rosen said. The FDA approved the agent for RA. The drug may work for this condition because it inhibits pyrimidine synthesis, decreases TNF-α response, and inhibits monocyte activation by proliferating T cells. A case series of 32 patients with skin, eye, and/or lung involvement showed 80% responded to leflunomide (Sarcoidosis Vasc. Diffuse Lung Dis. 2004;21:43-8). Nausea, headache, hypersensitivity reactions, and hepatic injury are concerns with leflunomide (Dermatology 2003;207:386-9). ■