Consider Infliximab, Leflunomide for Sarcoidosis

BY DAMIAN McNAMARA
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Key Biscayne, Fla. — Although antimalarial agents are first-line treatment for cutaneous sarcoidosis, infliximab and leflunomide may be appropriate for refractory patients, Theodore Rosen, MD, said at the annual meeting of the Nooch Wertheim Dermatological Society.

Corticosteroids and/or methotrexate are generally second-line therapy for patients who fail to respond to colchicine or hydroxychloroquine. There are few data, however, to support the use of other drugs that researchers have considered—pentoxifylline, tetracyclines, or colchicine—in patients who 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% of cases.

In the past, researchers considered the presence of granulomas in, for example, the mouse ear or leg to be a marker for cutaneous sarcoidosis. Now, it is known that the presence of granulomas is a marker for sarcoidosis in general, Dr. Rosen said.

There are few controlled studies in patients with cutaneous sarcoidosis. Because there is no specific treatment, “there is no need to examine the choice of initial therapies,” he said.

“Sarcoidosis is generally a disease of young adults,” he said. “Young adults may potentially be interested in oral contraceptives.”

The National Sarcoidosis Society recommends that patients with sarcoidosis use contraceptive methods, including oral contraceptives. Some patients use oral contraceptives as the sole therapy for this condition. But, they warned, “Only a small percentage of patients will achieve completely normal laboratory indices while on contraception alone. The majority of patients will have residual clinical and laboratory evidence of sarcoidosis.”

“Women of childbearing age should use effective contraception,” Dr. Rosen said. “Oral contraceptives can reduce the size of the sarcoidosis lesion.”

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 per kg per dose given every 4 weeks of intravenous infusion at 0, 2, and 6 weeks, and then as needed.

Several trials 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;143-4; Chest 2003;124:2028-31; and Arthritis Rheum. 2003;48:5342-3).

He also cited a woman he treated for cutaneous sarcoidosis. She failed treatment with corticosteroids and methotrexate 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 lesions on her face disappeared.

Long-term systemic 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.

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 release, and activates T cells 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 (Dermatolology 2003;207:386-9).

Tumor necrosis factor (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 per kg per dose given every 4 weeks of intravenous infusion at 0, 2, and 6 weeks, and then as needed.

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