The patient, a 46-year-old black woman, was referred to the dermatology clinic at Washington University, St Louis, Mo, for evaluation of reddish-purple nodules on her face and shins. The patient’s medical history was significant for hypothyroidism and an arrhythmia. Findings from a punch biopsy from her right nasal ala showed confluent granulomas with central caseous necrosis in the dermis. Findings from a wedge biopsy specimen from her right shin showed granulomas in the dermis and subcutis with necrotizing foci. Acid-fast bacteria and Giemsa stains of both specimens were negative for mycobacteria and fungal organisms. Because of continued concern that she had an infection, an excisional biopsy specimen from the right leg was taken. Tissue culture for bacteria, mycobacteria, and fungi failed to grow any organisms. Histologic examination of this specimen revealed a septal panniculitis consistent with a diagnosis of erythema nodosum. Despite the caseating granulomas found on histologic examination of the specimens from the initial 2 biopsies, a diagnosis of sarcoidosis was made based on exclusion of an infectious etiology and the clinical appearance of the lesions.

Further evaluations included a complete blood cell count with differential cell count and complete metabolic panel, both of which revealed no significant abnormal findings. The patient had no reaction to purified protein derivative but did react to *Candida* antigen. A computed tomographic scan of her chest revealed a 4-mm nodule in the left upper lobe of the lung and a 1.3-cm left axillary lymph node. A 2.2-cm rim-enhancing lesion in the right hepatic lobe consistent with a hemangioma was noted. Pulmonary function tests revealed a forced expiratory volume in 1 second (FEV₁) of 1.72 (72% predicted of normal for the patient’s age group) and a forced vital capacity (FVC) of 2.02 (70% predicted), with an FEV₁/FVC ratio of 85%. Her diffusion capacity of carbon monoxide was 65% predicted of normal for her age group. These abnormalities in the findings were not felt to be clinically significant by the patient’s pulmonologist.

The patient was treated with minocycline hydrochloride, 100 mg twice daily, and 0.05% clobetasol propionate cream. The minocycline therapy was discontinued after she developed headaches and tinnitus. The patient subsequently developed ulcerations of the nodules on her legs. Findings from a repeated biopsy from an ulcerating nodule on her left leg revealed a granulomatous panniculitis.

Acid-fast bacteria and Giemsa stains were again negative for mycobacteria or fungal organisms, as were tissue cultures for bacteria, mycobacteria, and fungi. Antineutrophil cytoplasmic antibodies were not detected in her blood.

The patient was treated with Unna wraps and 0.05% clobetasol ointment to her legs and continued treatment with 0.05% clobetasol cream to her face. A 3-week trial of 40 mg of prednisone daily led to modest improvement. She subsequently failed treatment with hydroxychloroquine sulfate (Plaquenil; Sterling Winthrop Inc, New York, NY), 200 mg, twice daily; pentoxifylline, 400 mg, 4 times daily; and multiple intralesional injections of triamcinolone acetonide (Kenalog; Bristol-Myers Squibb Co, New York, NY), 5 mg/cm², to the nose. Physical examination at this time revealed reddish-purple nodules on her nose ([Figure 1](#)), eyebrows, chin, and upper lip, as well as numerous hyperpigmented patches and nodules with atrophic centers and erosions on her legs ([Figure 2](#)). An alternative treatment was needed.

Current treatment options for sarcoidosis focus on inhibition of proinflammatory cytokines that maintain the T helper (Th) 1 immune response. There is no universally accepted treatment for sarcoidosis. Systemic agents such as oral corticosteroids are often effective, but long-term therapy is limited by a multitude of serious adverse effects. Steroid-sparing agents such as methotrex-
ate, antimalarial drugs, pentoxifylline, allopurinol, and thalidomide have been shown to be beneficial for select patients, but their use is limited because of significant toxic effects of their own, as well as inconsistencies in efficacy. To our knowledge, there has been 1 small, uncontrolled study that evaluated minocycline in the treatment of sarcoidosis with benefit. However, a randomized, placebo-controlled study evaluating minocycline in the treatment of sarcoidosis is lacking.

Our patient had failed local therapy with topical clobetasol and intralesional Kenalog. She failed systemic treatment with Plaquenil and pentoxifylline and did not tolerate minocycline. Long-term treatment with systemic corticosteroids or methotrexate was felt to be unwarranted because of the risk of serious long-term sequelae. Consequently, a safe and effective therapy was needed.

Treatment with adalimumab (Humira; Abbott Laboratories, Abbott Park, Ill) was proposed as an alternative to treatment with systemic corticosteroids and methotrexate. Adalimumab was administered subcutaneously at a dose of 40 mg once weekly. The patient continued therapy with Plaquenil and pentoxifylline. After 5 weeks of therapy, the nodules on her eyebrows, chin, and upper lip had resolved, and the nodules on her nose were much improved. The nodules and erosions on her legs were significantly improved as well. After 10 weeks of therapy, the nodules on her nose showed further flattening (Figure 3). The erosions on her legs were fully healed, and the nodules were softer and flatter (Figure 4). The patient did not experience any adverse events.

Sarcoidosis is a multisystem disease affecting the lungs, eyes, lymph nodes, skin, gastrointestinal tract, heart, musculoskeletal system, kidneys, and central nervous system. Cutaneous involvement occurs in approximately 25% of patients with sarcoidosis, with morphologic traits of lesions varying widely. Lupus pernio, violaceous papules and plaques, subcutaneous nodules, ichthyosis, alopecia, and verrucous growths may all be seen.

It is hypothesized that persistent exposure to a specific, low-potency antigen catalyzes the proinflammatory cascade seen in sarcoidosis. The classic noncaseating granulomatous infiltration seen with sarcoidosis is composed primarily of macrophages and CD4+ T cells. These cells secrete proinflammatory cytokines, such as interleukin (IL) 12, interferon gamma (IFN-γ), and tumor necrosis factor α (TNF-α), which direct naive T lymphocytes to differentiate into activated T cells. Therefore, sarcoidosis is maintained by a dominant, polarized T cell immune response.

Tumor necrosis factor α is a proinflammatory cytokine that is produced by macrophages, lymphocytes, and
neutrophils. It is known to induce other proinflammatory cytokines, such as IL-1, IL-6, and IL-8. It also acts on the endothelium to promote leukocyte migration into sites of inflammation. Increased levels of TNF-α have been demonstrated in alveolar macrophages of patients with pulmonary sarcoidosis. Inhibition of TNF-α-induced inflammation could effectively treat sarcoidosis.

This hypothesis is supported by a review of the MEDLINE database from 1966 to the present, which reveals 15 reports of the successful treatment of cutaneous and extracutaneous sarcoidosis with infliximab and 1 report of cutaneous sarcoidosis responsive to etanercept. A small phase 2 trial of etanercept in the treatment of pulmonary sarcoidosis was initiated, but it was terminated early because of excessive treatment failures. However, 5 of 17 subjects were considered treatment successes.

Infliximab is a chimeric, monoclonal antibody directed against TNF-α and is currently approved by the US Food and Drug Administration (FDA) to treat rheumatoid arthritis and Crohn disease. Etanercept is a dimeric fusion protein consisting of the extracellular ligand-binding domain of the human TNF receptor linked to the Fc portion of human IgG, and is currently approved by the FDA to treat psoriasis and psoriatic arthritis.

In the 15 reports on the use of infliximab for sarcoidosis, 6 patients had cutaneous disease. All patients received infliximab, 5 mg/kg, and had a marked or complete response after the fourth infusion (4 to 12 weeks). One patient with lupus pernio and arthropathy had a marked response after 2 months of treatment with 25 mg of etanercept twice weekly. All 7 of these patients received concomitant immunosuppression, making comparison of the time to response between these patients and ours difficult.

In these reports, treatment with infliximab and etanercept was generally well tolerated and safe. In the phase 2 trial of etanercept to treat patients with pulmonary sarcoidosis was initiated, but it was terminated early because of excessive treatment failures. However, 5 of 17 subjects were considered treatment successes.

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In these reports, treatment with infliximab and etanercept was generally well tolerated and safe. In the phase 2 trial of etanercept to treat patients with pulmonary sarcoidosis, there were 2 serious adverse events. One patient, who was treated with etanercept for 9 months, developed a localized intestinal lymphoma 8 months later. Another patient, who was treated with etanercept for 12 months, developed a nasopharyngeal extramedullary plasmacytoma. Both patients were successfully treated. A patient with a very complicated case of sarcoidosis developed a venous thrombosis at a hemodialysis catheter site and multiple necrotizing skin ulcerations on her legs after 6 weeks of treatment with infliximab. Workup revealed circulating anticoagulation antibodies. Antinuclear antibodies and anti-double-stranded DNA antibodies were not found in the patient’s serum.

To our knowledge, there have been no reports describing the treatment of sarcoidosis with adalimumab. Adalimumab is a fully human, monoclonal antibody directed against TNF-α. Given that adalimumab targets the same cytokine as infliximab and etanercept, one would expect that adalimumab may also be effective in the treatment of sarcoidosis. Treatment with adalimumab has advantages over infliximab in drug delivery. Adalimumab is administered subcutaneously once weekly or every other week by the patient at home, which most patients find to be convenient. Patients can be instructed on proper injection technique at an office visit. Infliximab, by contrast, is delivered intravenously in the physician’s office. This requires routine office visits and vital sign monitoring by a health care professional. Infusion reactions, such as allergic reactions (pruritus, urticaria) and cardiopulmonary effects (hypotension, hypertension, tachycardia), occur in about 9% of patients. In addition, because adalimumab is fully human, patients may be less likely to form antibodies against the medication. Adalimumab is approved by the FDA for the treatment of moderate to severe rheumatoid arthritis and is, therefore, available on the market.

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