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Adalimumab for treatment of severe ulcerative sarcoidosis

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Abstract

Ulcerative sarcoidosis is a rare variant of cutaneous sarcoidosis that may present as ulceration with necrotic yellow plaques on the lower extremities, face, arms, trunk, or genital area. Adalimumab, a human monoclonal anti-TNF antibody, is an emerging treatment for recalcitrant cutaneous sarcoidosis. We describe severe ulcerative sarcoidosis in a 60-year-old woman with chronic ulcerative necrobiosis lipoidica-like plaques on her left arm for over 20 years. Her condition had not responded to previous treatments with hydroxychloroquine, methotrexate, and sulfasalazine. After a four-month course of adalimumab therapy in addition to pentoxifylline and prednisone with taper, the patient had significant improvement in her skin disease.

Keywords: biologics, cutaneous, sarcoidosis

Introduction

Cutaneous involvement of sarcoidosis occurs in 20-35% of patients with variable clinical presentations including ulcerations [1,2]. Ulcerative sarcoidosis represents one of the rarer clinical presentations seen in only 5% of cutaneous sarcoidosis cases [3]. Ulcerative sarcoidosis may be challenging to treat with the first-line treatment agents of topical, intralesional, or systemic corticosteroids and the second-line treatments of antimalarial or cytotoxic agents. We present a patient with severe ulcerative sarcoidosis who, after failing to respond to hydroxychloroquine, methotrexate, and sulfasalazine, improved with adalimumab, pentoxifylline, and a prednisone taper.

Case Synopsis

A 60-year-old woman presented to the dermatology clinic with chronic ulcerative necrobiosis lipoidica (NL)-like plaques of her left arm for over 20 years. These lesions were described as exquisitely painful and the patient had been unable to sleep owing to discomfort. Prior traumatic injuries to the area involved multiple left forearm fractures, left elbow joint disfigurement, and surgery of the left elbow joint.

She was previously treated with hydroxychloroquine, methotrexate, and sulfasalazine by her rheumatologist for nonspecific arthropathy of the left elbow, which did not improve her cutaneous symptoms and were eventually discontinued. She was then treated empirically with cefdinir, minocycline, and clarithromycin, to cover for atypical mycobacterial infection without significant improvement.

Further systemic workup revealed cutaneous sarcoidosis without involvement of other organ systems. Laboratory examinations revealed unremarkable complete blood count with differential (CBC), complete metabolic panel (CMP), angiotensin-converting enzyme, immunoglobulin levels, parathyroid hormone levels, 1,25-hydroxyvitamin D levels, and 25-hydroxyvitamin D levels. The patient was negative for cardiolipin and MPO-PR-3 antibodies. Chest computed tomography (CT) revealed no mediastinal or hilar lymphadenopathy consistent with sarcoidosis and there were no findings of ocular sarcoidosis upon ophthalmic examination. Multiple biopsies of the lesions had been performed, with the most recent biopsy demonstrating naked sarcoidal granulomas

with minimal lymphocytic infiltrate and granulomatous vasculitis, consistent with chronic cutaneous sarcoidosis (**Figure 1**). The histopathologic differential diagnosis included ulcerative necrobiosis lipoidica, foreign body granuloma, and occult infection (although Fite and GMS stains were negative for microbes). Multiple tissue cultures were negative for mycobacterial and fungal infection.

At presentation to our dermatology clinic, she reported significant worsening of her ulcerations with bright pink-to-red erythematous ulcerative, exudative atrophic plaques with elevated violaceous borders over her left forearm, left elbow, and upper left arm (**Figure 2**). The patient was started on adalimumab for chronic cutaneous ulcerative sarcoidosis, along with oral prednisone 1mg/kg with taper for more rapid symptom relief. Pentoxifylline was started owing to the NL-like appearance of the lesions. The patient noticed dramatic improvement after one month of the above therapy with continued improvement thereafter. Her prednisone was successfully tapered over a few months, and the patient continued to have good control of her skin disease. By four months of therapy with adalimumab and pentoxifylline there was near resolution of her ulcerative plaques and residual scarring (**Figure 3**). The patient continued to see improvement of the lesions and only residual scarring remained eight months after initiating treatment.

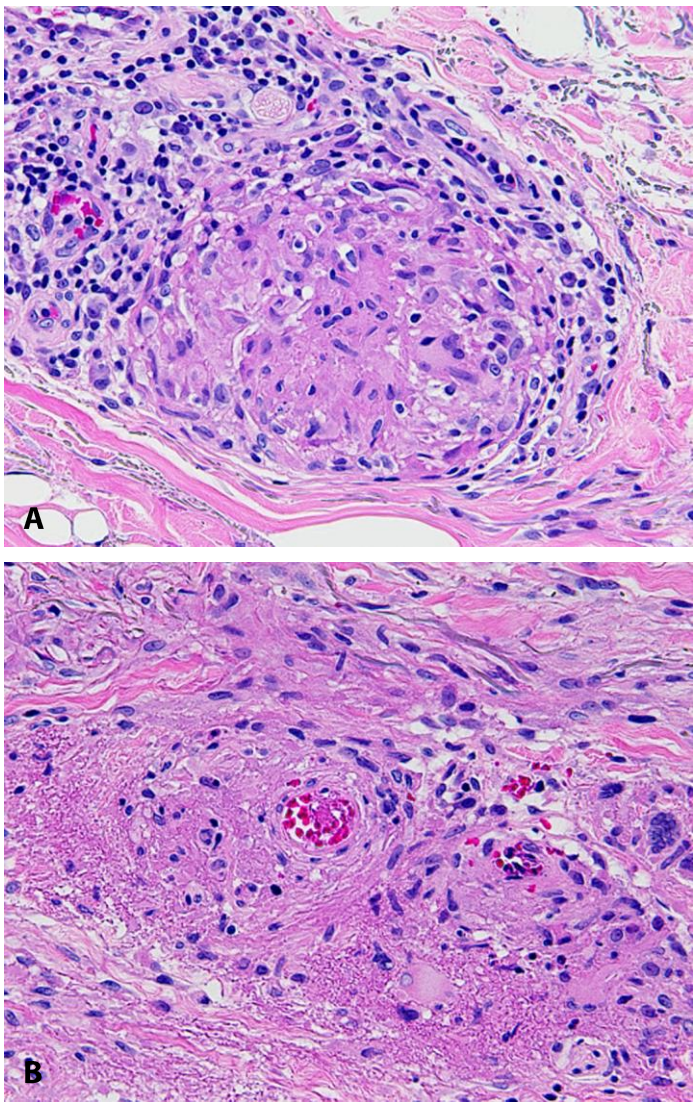

Figure 1 *H&E histopathologies in left arm punch biopsies:* ***A)*** *sarcoidal granulomas, 200×;* ***B)*** *granulomatous vasculitis, 200×.*

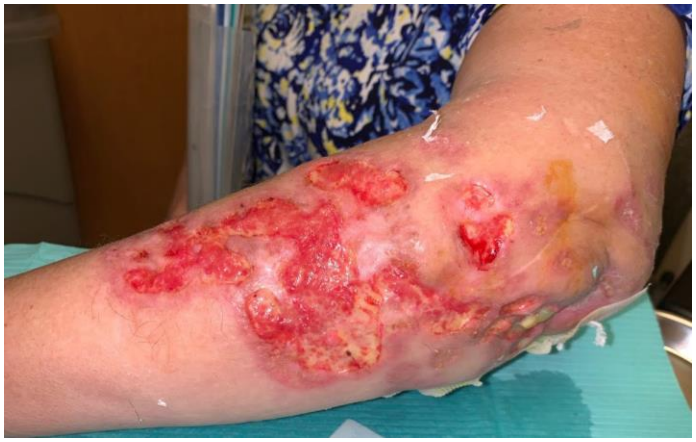

Figure 2 *Painful, ulcerative plaques on the patient's left arm prior to treatment.*

Case Discussion

Clinicopathologic findings as well as exclusion of other etiologies of granulomatous disease are required for diagnosis of sarcoidosis. As there is no single reliable diagnostic test, a multi-systemic approach must be taken to assess for signs of other organ involvement. Initial diagnostic workup may include obtaining chest radiography or CT, abdominal ultrasound or CT, renal ultrasound, CBC, CMP, brain natriuretic peptide, and ophthalmologic evaluation [4]. Biopsies of affected organs may be necessary to reveal pathologic evidence of noncaseating granulomas consistent with sarcoidosis.

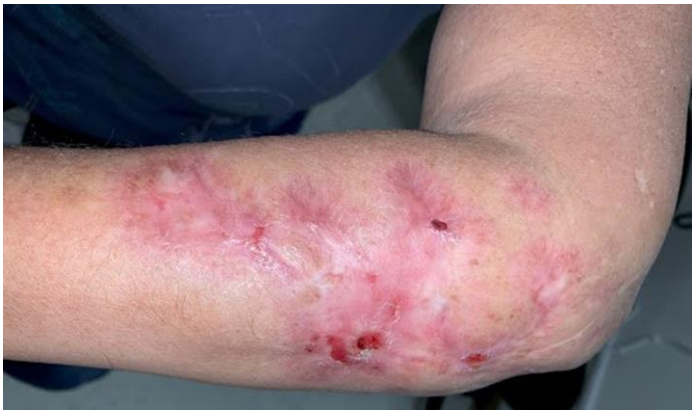

Figure 3 *Significant improvement with resolution of ulcerations and residual scarring after four months of therapy.*

Ulcerative sarcoidosis presents a therapeutic challenge owing to variable clinical responses and associated toxicities. In cases in which first-line and second-line therapies of corticosteroids and antimalarial or cytotoxic agents have failed, respectively, the biologics infliximab and adalimumab are a considerable treatment option. A recent subset analysis from a randomized, double-blind, placebo-controlled trial of patients treated with infliximab for chronic pulmonary sarcoidosis revealed 12 infliximab-treated patients observed improvement of their cutaneous sarcoidosis in terms of desquamation and induration after 24 weeks compared to the 5 placebo-treated patients [5]. However, two of the patients' lesions reappeared. Additionally, a handful of case reports have documented successful treatment of cutaneous sarcoidosis using adalimumab [6-10]. Fewer case reports have documented successful treatment of ulcerative sarcoidosis with adalimumab [6,7,9,10].

Conclusion

In this case, we observed clinical resolution of a rare subtype of recalcitrant cutaneous sarcoidosis with adalimumab in addition to pentoxifylline and prednisone with taper. We conclude that adalimumab represents a viable therapeutic option for chronic, severe ulcerative sarcoidosis that has failed other therapeutic options.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Karadag AS, Parish LC. Sarcoidosis: A Great Imitator. *Clin Dermatol*. 2019;37:240-54. [PMID: 31178106].
2. Caplan A, Rosenbach M, Imadojemu S. Cutaneous Sarcoidosis. *Semin Respir Crit Care Med*. 2020;41:689-99. [PMID: 32593176].
3. Powell E, Rosen T. Ulcerative Sarcoidosis: A Prototypical Presentation and Review. *Cutis*. 2017;100:312-6. [PMID: 29232421].
4. Soto-Gomez N, Peters JI, Nambiar AM. Diagnosis and Management of Sarcoidosis. Am Fam Physician. 2016;93:840-8. [PMID: 27175719].
5. Baughman RP, Judson MA, Lower EE, et al. Infliximab for Chronic Cutaneous Sarcoidosis: A Subset Analysis from a Double-Blind Randomized Clinical Trial. *Sarcoidosis Vasc Diffuse Lung Dis*. 2016;32:289-95. [PMID: 26847095].
6. Hashemi DA, Rosenbach M. Ulcerative Sarcoidosis. *JAMA Dermatology*. 2019;155:238. [PMID: 30566195].
7. Philips MA, Lynch J, Azmi FH. Ulcerative Cutaneous Sarcoidosis Responding to Adalimumab. *J Am Acad Dermatol*. 2005;53:917. [PMID: 16243166].
8. Wanat KA, Rosenbach M. Case Series Demonstrating Improvement in Chronic Cutaneous Sarcoidosis Following Treatment with TNF Inhibitors. *Arch Dermatol*. 2012;148:1097-100. [PMID: 22986883].
9. Judson MA. Successful Treatment of Lupus Pernio with Adalimumab. *Arch Dermatol*. 2011;147:1332-3. [PMID: 22106129].
10. Heffernan MP, Smith DI. Adalimumab for Treatment of Cutaneous Sarcoidosis. *Arch Dermatol*. 2006;142:17-9. [PMID: 16415380].