# Necrotizing Sarcoid Granulomatosis With Skin and Pulmonary Involvement

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*We present a rare case of necrotizing sarcoid granulomatosis (NSG) with skin and pulmonary involvement. NSG with extrapulmonary involvement occurs infrequently, and reports involving skin manifestations in NSG are even more rare.*

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Necrotizing sarcoid granulomatosis (NSG) was first described by Liebow[1] in 1973 as one of 5 forms of pulmonary angiitis and granulomatosis unrelated to infection or connective tissue disorders. Definitions of the following 5 forms are based on histologic structure and other features of natural history: (1) classical Wegener granulomatosis (WG); (2) limited angiitis and granulomatosis of the Wegener type; (3) lymphomatoid granulomatosis; (4) NSG; and (5) bronchocentric granulomatosis. The distinctive features of NSG include the following: (1) histologically, sarcoid-like granuloma, granulomatous angiitis, and varying degrees of necrosis; (2) radiologically, multiple pulmonary nodules or ill-defined infiltrates but no enlarged nodes; and (3) clinically, symptoms (ie, cough, fever, sweating, malaise, dyspnea, pleuritic pain) with minimal physical signs. Extrapulmonary involvement in NSG is rare. We present a rare case of NSG with histologic confirmation of skin involvement.

## Case Report

A 55-year-old woman with prior medical history of childhood poliomyelitis presented with a 7-year history of skin lesions on her forearms and a 4-year history of a chronic nonproductive cough. The skin lesions were asymptomatic and slowly increased in size. Results of a physical examination revealed a 6.5×6-cm graftlike oval plaque on the left forearm in which a circumferential ridge bordered a pink band with central pallor and punctuate erythematous macules (Figure 1). Three smaller erythematous annular plaques were present on both forearms. In addition, the patient demonstrated a geographic and scrotal tongue. The patient had no lacrimal gland enlargement and no lesions within scars. No evidence of lymphadenopathy was detected.

A chest x-ray revealed streaky nodular densities in the right upper lobe of the lung and a computed tomographic scan of the chest demonstrated upper lobe nodules (right greater than left); however, no lymphadenopathy was detected. A nodule in the right lung was excised, and histopathologic examination identified numerous noncaseating necrotizing and nonnecrotizing granulomas. A skin biopsy specimen from the left forearm showed similar changes, with pseudoepitheliomatous hyperplasia and a granulomatous superficial infiltrate with areas of central necrosis (Figure 2). No vasculitis was noted from either biopsy, and no foreign material was seen with a polarizer.

All cultures and direct smears from the lung and skin biopsies for fungi, mycobacteria, and nontuberculous bacteria were negative. Results of periodic acid-Schiff, Fite, and methenamine silver stains were negative. Angiotensin–converting enzyme was 73 U/L (reference range, 8–52 U/L), C-reactive protein was 8.2 mg/L (reference range, <3 mg/L), and anticardiolipin antibodies were positive at 78 GPL (reference range, 0–14 GPL). The purified protein derivative was negative. On laboratory examination, the serum protein electrophoresis, rheumatoid factors, ferritin, rapid plasma reagin, erythrocyte sedimentation rate, complete blood count with differential, basic metabolic panel including serum calcium level, liver function tests, thyroid-stimulating hormone, antinuclear antibody, antiextractable nuclear antigen, anti-DNA antibodies, and lupus anticoagulant were all within reference range. Antineutrophil

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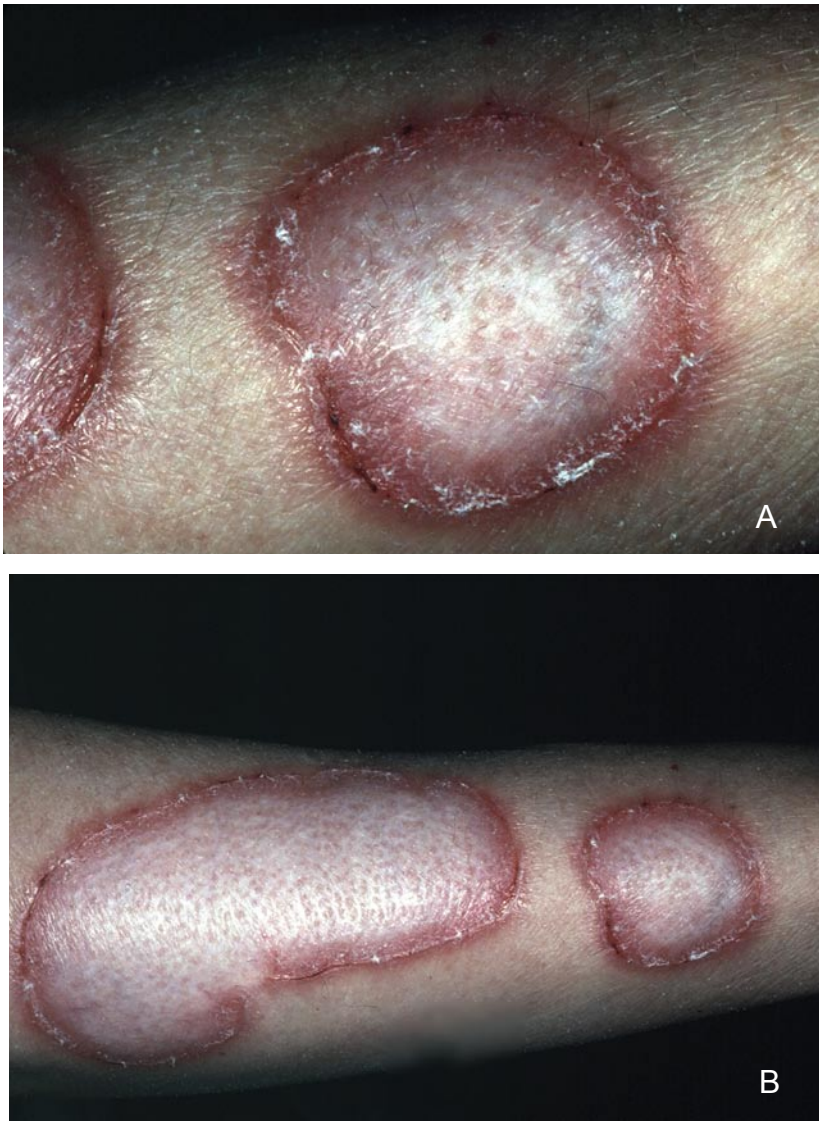


**Figure 1.** A 6.5×6-cm graftlike oval plaque on the left forearm (A and B).

cytoplasmic antibodies directed against proteinase 3 and myeloperoxidase (cytoplasmic antineutrophilic cytoplasmic antibody and perinuclear antineutrophilic cytoplasmic antibody, respectively) were not detected. Results of an electrocardiogram were normal.

The patient was started on prednisone 40 mg daily for pulmonary symptoms and over time was increased to a peak dose of 150 mg every other day. After several years of no clinical improvement and the development of corticosteroid-induced diabetes mellitus, prednisone was discontinued. The patient was then started on thalidomide 50 mg twice daily, which was discontinued after several months because of leukopenia. Throughout this time, topical steroids were applied to the skin lesions with no substantial change. The patient's current regimen of hydroxychloroquine sulfate 200 mg twice daily has dramatically improved the skin lesions, and no new lesions have developed. All findings from ophthalmologic examinations have shown no conjunctival lesions, iritis, uveitis, or iris granulomas. Radiologic evidence of lung disease has shown only minimal increases in nodular opacities throughout the course of her disease and no other systemic symptoms of sarcoidosis have been present.

## Comment

We report a rare, histologically confirmed case of NSG with skin and pulmonary involvement. The histopathology of the skin and lung was repeatedly interpreted as necrotizing granulomas, strongly suggesting infection; however, results from all cultures and stains were repeatedly negative. WG, lymphomatoid granulomatosis, and bronchocentric granulomatosis were excluded clinically or histologically. Although biopsy results did not show signs of angiitis, all other findings

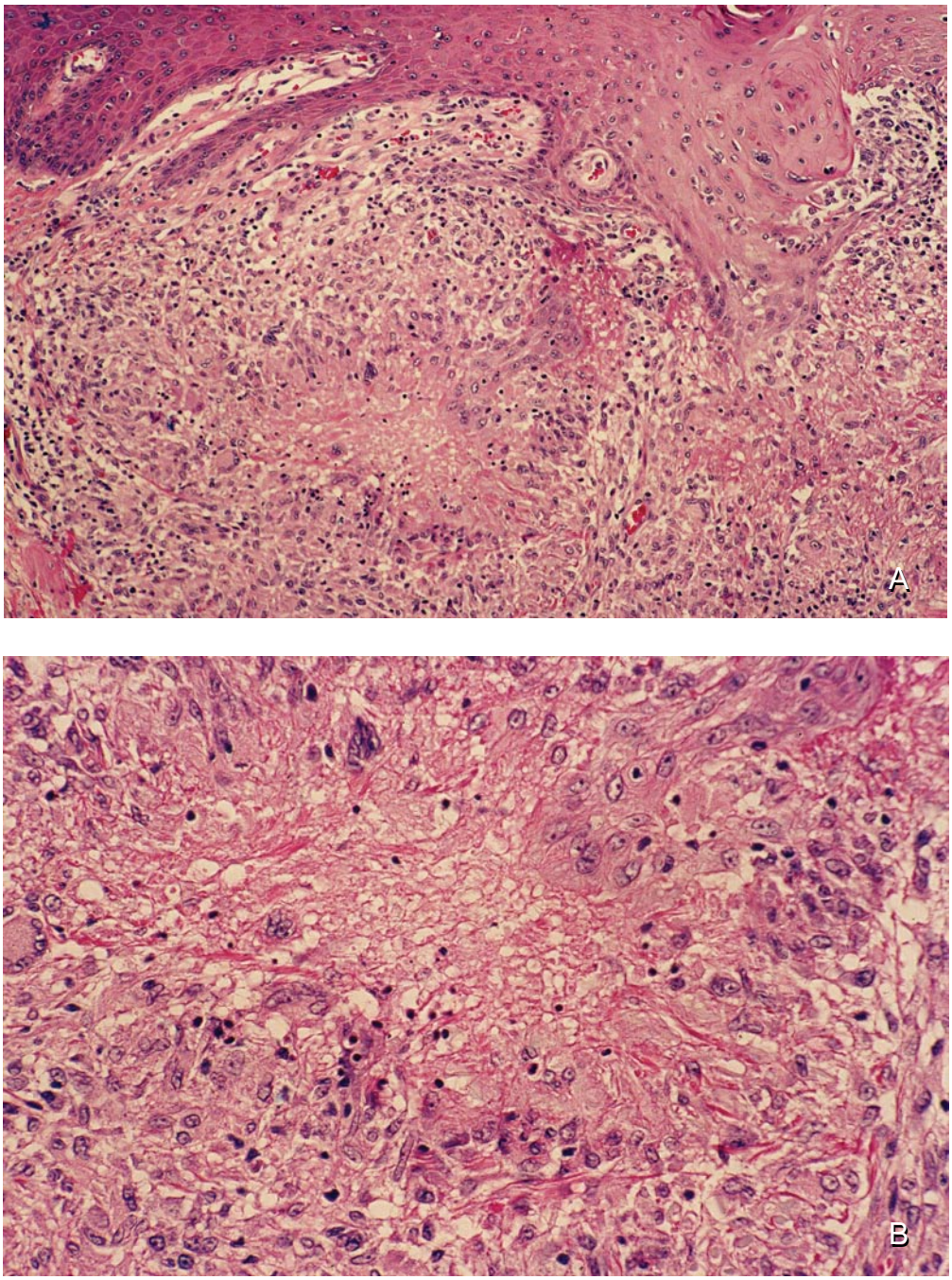


**Figure 2.** A skin biopsy specimen from the left forearm showing pseudoepitheliomatous hyperplasia overlying a granuloma with central necrosis (H&E, original magnification ×10)(A). Same biopsy specimen, with a central area of tissue necrosis containing some cellular debris and surrounded by granulomatous inflammation (H&E, original magnification ×40)(B).

led us to speculate that this is a case of a benign variant of sarcoidosis—an NSG.

Most cases of NSG involve the lungs. Extrapulmonary involvement rarely occurs with NSG but predominantly involves the eyes and central nervous system.[2] However, cases have been reported involving the skin, kidney, lacrimal gland, gastrointestinal tract, liver, and spinal column.[3] Although sarcoidosis by definition is noncaseating, focal central necrosis within granulomas are not infrequently seen in classic sarcoid.[2] NSG is considered to be a subset of sarcoidosis, with only one case of dermal involvement in the literature.[2]

The nature of NSG has been one of much debate. Although Liebow[1] initially described NSG as a separate form related to WG, the lack of systemic vasculitis or renal or upper respiratory tract involvement, as well as its benign nature, strongly disprove this explanation.[4] Liebow's[1] alternative proposition that NSG is a variant of sarcoidosis has been pursued extensively. Popper et al[5] compared clinical and histologic features of 10 cases from

3 institutions. Their study failed to find any granulomatous vasculitis, a hallmark of WG.[5] Popper et al[5] described the extensive granulomatous vasculitis of NSG as the cause of the disease's characteristic coagulative necrosis and classified NSG as a variant of sarcoidosis.

The disease classification debate continues in case studies of NSG. These case studies are important because therapeutic modalities differ between the disease forms. Spiteri et al[6] supported the belief that NSG is a variant of sarcoidosis, with distinctive characteristics capable of control via steroids alone.[7] In contrast, the majority of patients with WG require treatment with a combination of corticosteroids and cyclophosphamide.[8] Although NSG may be considered benign and responsive to corticosteroids, cases have been reported in which NSG with extrapulmonary involvement was the source of severe morbidity and protracted clinical course.[9] Although our patient never had a remission of her skin lesions while on prednisone or any other medication, her disease has not progressed and new skin lesions have not appeared. She remains stable only on hydroxychloroquine sulfate therapy.

Only one other case of NSG involving the skin has been reported in the literature.[2] The patient presented with pulmonary symptoms, later developing multiple, well-circumscribed, hard and nontender subcutaneous nodules on the limbs and face. A biopsy of the skin nodules revealed both subcutaneous and dermal well-circumscribed epithelioid and giant cell granulomas with areas of richly neutrophilic geographical necrosis. Vessels within the areas of neutrophil infiltrate showed focal destruction of the elastin layer. The patient was initially treated with high-dose steroids and, after 3 months, all inflammatory markers normalized, subcutaneous skin nodules and lymphadenopathy resolved, and the size of the cavitation and nodules decreased. The patient continued treatment with low-dose steroids and remained well after 2 years of treatment.[2]

## Conclusion

We report a rare case of NSG with distinctive skin manifestations characterized by annular graftlike plaques. It is important to consider NSG in the differential diagnosis of necrotizing granulomatous disease in the skin if associated pulmonary disease exists.

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