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Bilateral Pleural Effusions as a Rare Presentation of Necrotizing Sarcoid Granulomatosis

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Data Interpretation D
Manuscript Preparation E
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Patient: Female, 56-year-old
Final Diagnosis: Necrotizing sarcoid granulomatosis
Symptoms: Cough • fatigue • weight loss
Clinical Procedure: —
Specialty: Pulmonology

Objective: Rare disease

Background: Necrotizing sarcoid granulomatosis is a rare granulomatous lung disease characterized by sarcoid-like granulomas, vasculitis, and variable degrees of necrosis. It most commonly involves the lungs and shares significant clinical and radiographic overlap with sarcoidosis, infection, vasculitis, and malignancy, often resulting in diagnostic delay. Pleural involvement is uncommon, and pleural effusions are not considered a typical feature of the disease.

Case Report: A 56-year-old woman from Brazil presented with 2 weeks of nonproductive cough and fatigue. Initial imaging revealed a moderate-to-large right pleural effusion and a small left effusion. Thoracentesis yielded a lymphocyte-predominant exudative effusion with negative cytology and cultures. Despite empiric antibiotic therapy, symptoms and pleural effusions recurred. Positron emission tomography- computed tomography (PET-CT) demonstrated intensely hypermetabolic pleural-based masses and consolidations. Video-assisted thoracoscopic wedge biopsy revealed focally necrotizing granulomatous inflammation with vasculitis; cultures were negative, and no malignancy was identified, confirming necrotizing sarcoid granulomatosis. The patient was treated with systemic corticosteroids, resulting in marked clinical and radiographic improvement.

Conclusions: NSG is a rare, poorly understood, and often under-recognized entity that often ends up being diagnosed on biopsy after extensive workup. Our case raises the possibility of necrotizing sarcoid granulomatosis presenting with bilateral pleural effusions in addition to nodular lesions. Though much uncertainty remains on how to treat these patients, increased awareness of necrotizing sarcoid granulomatosis may help avoid delays in diagnosis, unnecessary antimicrobial exposure, and patient anxiety associated with extensive testing.

Keywords: Biopsy • Sarcoidosis • Steroids • Vasculitis

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Introduction

Necrotizing sarcoid granulomatosis (NSG) is a rare disease characterized by sarcoid-like granuloma, vasculitis, and variable degrees of necrosis first described in 1973 by Dr. Averill Liebow [1]. Since its initial description, fewer than a few hundred cases have been reported in the literature, underscoring its rarity and the limited understanding of its etiology and pathogenesis [2].

NSG shares several radiological and clinical features with sarcoidosis, but unlike sarcoidosis is marked by sarcoid-like granulomas, vasculitis, and extensive areas of necrosis [3]. It most commonly involves the lungs but can present in other organs such as the skin and central nervous system. Clinically, patients may be asymptomatic or present with nonspecific symptoms such as cough, dyspnea, chest pain, fever, or fatigue, frequently leading to diagnostic delay or misclassification.

Typical imaging findings include solitary or multiple bilateral pulmonary nodules, patchy infiltrates, or mass-like consolidations, occasionally with cavitation. Hilar or mediastinal lymphadenopathy may be present but is not universal [1]. These features overlap substantially with sarcoidosis, granulomatosis with polyangiitis, malignancy, and infectious granulomatous diseases, making NSG a diagnosis of exclusion that often requires histopathologic confirmation [4].

Pleural involvement in NSG has been infrequently described, and pleural effusions are not considered a typical feature of the disease. This case was previously presented in abstract form by our team [5]. Herein, we provide the full case report of this exceedingly rare presentation of NSG, initially presenting with bilateral pleural effusions in addition to nodular pulmonary lesions.

Case Report

A 56-year-old woman from Brazil with a history of hypertension and hypothyroidism presented with a 2-week history of non-productive cough and fatigue. She denied any past or present tobacco use, vaping, or significant environmental exposures. Despite her symptoms, she remained physically active and continued to perform her usual household activities.

Upon arrival to the emergency department, she was afebrile, tachycardic, and saturating 94% on room air. Physical examination revealed diminished breath sounds in the right lower lung field. Laboratory studies showed a normal cell count, normal pro-B-type natriuretic peptide (pro-BNP), and normal procalcitonin. Extensive testing was obtained, which was largely unremarkable (**Table 1**). Initial chest computed tomography (CT) demonstrated a moderate-to-large right-sided pleural effusion and a small left-sided effusion (**Figure 1**). A diagnostic and therapeutic thoracentesis was arranged, yielding 1 L of straw-colored, lymphocyte-predominant exudative fluid; cytology and cultures were negative. The patient was empirically treated with ceftriaxone and doxycycline for community-acquired pneumonia and discharged home a few days after symptomatic improvement was noted.

Follow-up was arranged at the outpatient pulmonary clinic. Symptoms recurred, and imaging showed re-accumulation of

Table 1. Selected laboratory workup.

Test/parameter	Result
WBC	9×10^3/μL
Hemoglobin/hematocrit	10.8 g/dL / 34.4%
Platelets	397×10^3/μL
BNP	76 pg/mL
Procalcitonin	0.06 ng/mL
TSH	0.19 μIU/mL
Pleural fluid analysis	Exudate, lymphocyte-predominant
Gram stain/culture/cytology	Negative
Flow cytometry	Negative
Anti-CCP, ANA, RF	Negative
QuantiFERON (TB)	Negative
Paracoccidioides antibody	Negative
MTB complex PCR, AFB	Negative
Fungal cultures, histoplasma Ag	Negative
HIV Ag	Negative
Anaerobic culture	Negative
1,3 Beta-D-Glucan, fungitell	Negative
pANCA, cANCA	Negative
ACE	Low
Vitamin D (1,25 and 25-OH)	Normal

BNP, B-type natriuretic peptide; TSH, thyroid-stimulating hormone; WBC, white blood cell count; H/H, hemoglobin/hematocrit; Anti-CCP, anti-cyclic citrullinated peptide; ANA, antinuclear antibody; RF, rheumatoid factor; TB, tuberculosis; AFB, acid-fast bacilli; MTB, *Mycobacterium tuberculosis;* AFB, acid-fast bacilli; Ag, antigen; pANCA, perinuclear anti-neutrophil cytoplasmic antibody; cANCA, cytoplasmic anti-neutrophil cytoplasmic antibody; ACE, angiotensin-converting enzyme.

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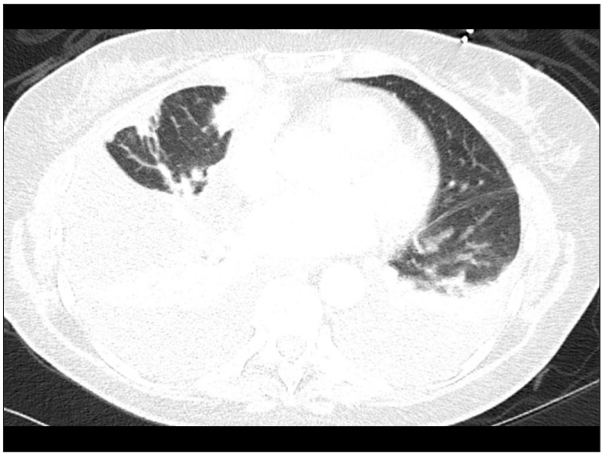


Figure 1. Initial non-contrast chest CT showing bilateral pleural effusions and nodular opacities. CT, computed tomography.



Figure 2. Follow-up chest CT 1 month later showing resolution of bilateral pleural effusions with development of parenchymal and subpleural consolidation. CT, computed tomography.

pleural fluid. Positron emission tomography (PET)-CT revealed intensely hypermetabolic bilateral pleural-base masses/consolidation, raising suspicion for malignancy vs granulomatous infection. Due to diagnostic uncertainty, a video-assisted thoracoscopic surgery (VATS) with wedge resection of the left upper lingula and left lower lobe was scheduled. Tissue cultures including bacterial, fungal, and acid-fast bacilli were negative. Pathologic examination revealed confluent, well-formed epithelioid granulomas with focal areas of necrosis, accompanied by granulomatous vasculitis involving small- to medium-sized vessels. The inflammatory infiltrate was composed predominantly of histiocytes and lymphocytes, without significant eosinophilia. No cytologic atypia or malignant cells were identified. Special stains and ancillary studies were negative for infectious organisms. Overall, these findings were consistent with NSG. While in the hospital, she was started on prednisone 40 mg daily and discharged with a taper over 4 weeks to a minimum of 10 mg daily. Follow-up chest imaging a month later demonstrated marked improvement of parenchymal opacities and nodules, as well as resolution of pleural effusions (**Figure 2**).

Discussion

NSG is a rare and incompletely understood granulomatous lung disease with overlapping features between sarcoidosis and vasculitis. Sarcoid-like granulomas with varying degrees of necrosis and vasculitis are the typical histopathologic hallmarks [3]. Because of its rarity and nonspecific clinical presentation, NSG remains a diagnostic challenge and is frequently mistaken for infection or malignancy.

Patients may be asymptomatic or have nonspecific respiratory complaints such as cough, dyspnea, chest pain, or fatigue [6]. Constitutional symptoms, including low-grade fever or weight loss, may occur but are not universal. In our case the subacute and nonspecific presentation was consistent with prior descriptions. Additionally, the absence of smoking history, environmental exposures, or significant infectious markers further complicated early differential diagnosis, as these features neither strongly supported nor excluded more common etiologies. In a small case series, patients were typically young adults presenting with pleuritic chest pain, with imaging demonstrating solitary or multiple pulmonary nodules, often accompanied by mediastinal lymphadenopathy and, notably, frequent pleural involvement [7].

Radiographically, NSG typically presents as solitary or multiple pulmonary nodules [1]. Pleural involvement with associated pleural effusion is rare. A previous case described a patient with constitutional and respiratory symptoms, including cough, dyspnea, and pleuritic chest pain, in whom imaging demonstrated a loculated pleural effusion with associated lymphadenopathy, initially raising concern for tuberculosis despite negative microbiologic studies. Definitive diagnosis was ultimately established only after histopathologic evaluation revealed necrotizing granulomas consistent with NSG, with subsequent clinical and radiographic improvement following corticosteroid therapy [8]. In our patient, a lymphocyte-predominant exudative effusion with negative cytology and sterile cultures argued against bacterial pneumonia or metastatic disease but did not establish a definitive diagnosis. Re-accumulation of pleural fluid after the initial thoracentesis supported the presence of an ongoing inflammatory vs neoplastic process.

Follow-up PET-CT demonstrated hypermetabolic lesions in addition to the pleural-based masses. While PET avidity is often associated with malignancy, it is well recognized that

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granulomatous diseases, including sarcoidosis and NSG, can demonstrate intense fluorodeoxyglucose uptake due to active inflammation [9]. Additional etiologies such tuberculosis and endemic fungal diseases were considered. Despite extensive microbiologic testing, including bacterial, fungal, and acid-fast bacilli cultures, no infectious cause was identified in this patient.

Definitive diagnosis of NSG requires histopathologic confirmation. The hallmark features include sarcoid-like granulomas with central necrosis and granulomatous vasculitis involving small- to medium-sized vessels [10]. Unlike classic sarcoidosis, NSG demonstrates more prominent necrosis and vasculitic changes, yet lacks the widespread systemic involvement typical of primary necrotizing vasculitides. In this case, VATS with wedge biopsy established the final diagnosis, highlighting how resource intensive and invasive the diagnosis of NSG can be when less invasive modalities are nondiagnostic and clinical uncertainty persists.

Management of patients with NSG has not been standardized due to its rarity, but literature suggests corticosteroids as the mainstay of treatment in symptomatic patients or those with progressive disease [4]. Previous cases demonstrate rapid clinical and radiographic improvement with steroid treatment, as seen in our patient whose follow-up imaging showed marked improvement of consolidations [11]. Some patients may experience spontaneous remission, while others have a relapsing course requiring prolonged or repeated immunosuppression. Prognosis tends to be favorable, but long-term data on follow-up after treatment remains scarce.

Conclusions

Necrotizing sarcoid granulomatosis is a rare, poorly understood, and often under-recognized entity that often ends up being diagnosed on biopsy after extensive workup. Clinical and radiographic presentations can resemble malignancy, infection, vasculitis, and sarcoidosis.

Our case raises the possibility of NSG presenting with bilateral pleural effusions in addition to nodular lesions. Though much uncertainty remains on how to treat these patients, increased awareness of NSG may help avoid delays in diagnosis, unnecessary antimicrobial exposure, and patient anxiety associated with extensive testing.

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Department and Institution Where Work Was Done

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Patient Permission/Consent Declarations

Written informed consent was obtained from the patient for the publication of this report and any accompanying images or data.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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