A rare presentation of necrotizing sarcoidosis

Nirali Sheth | Umaima Dhamrah | Branden Ireifej | David Song | Penpa Bhuti | Jagbir Singh | Henry Fan | Sibghatallah Ummar | Vikash Jaiswal | Nishan Babu Pokhrel

1Department of Internal Medicine, Icahn School of Medicine at Mount Sinai Elmhurst Hospital Center, Queens, New York, USA
2Department of Internal Medicine, PNS Shifa Hospital, Karachi, Pakistan
3Department of Research, Larkin Community Hospital, South Miami, Florida, USA
4Department of Internal Medicine, Tribhuvan University Institute of Medicine, Kathmandu, Nepal

Correspondence
Nishan Babu Pokhrel, Department of Internal Medicine, Tribhuvan University Institute of Medicine, Maharajgunj, Kathmandu, Nepal.
Email: nishanpokhrel1@iom.edu.np

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Abstract
Sarcoidosis is a disease with unknown aetiology and pathogenesis which affects young adults and is usually a non-necrotizing granulomatous disease seen in histology. Variants of the disease, such as necrotizing sarcoidosis, were first described by Liebow in 1973 and are rarely seen. This case report describes the case of a 60-year-old Bengali female who presented with vague symptoms and was found to have chronic granulomatous inflammation with foci of calcifications involving the lungs, liver and spleen consistent with necrotizing sarcoidosis.

KEYWORDS
extrapulmonary sarcoidosis, granulomatous disease, necrotizing granuloma, necrotizing sarcoidosis

INTRODUCTION
Sarcoidosis is a disorder of multiple organ systems with unknown aetiology. However, the most common manifestation is that of restrictive pulmonary disease. Sarcoidosis without pulmonary symptoms manifests in less than 10% of cases, in which case, the most common sites of involvement would be the skin, eyes and reticuloendothelial system. To diagnose sarcoidosis without pulmonary involvement, the step-wise approach would be to first identify the organs affected and are amenable to biopsy. A biopsy result with non-caseating granulomas would typically be diagnostic of sarcoidosis.

CASE REPORT
We present the case of a 60-year-old female from Bangladesh with a medical history of hypertension and diabetes who presented with hypercalcaemia associated with weakness and dizziness for the past 3 weeks. The patient had no known harmful exposure. She was a lifetime non-smoker.

She was initially seen at another hospital 1 month ago, where it was found that she had a calcium level of 15 mg/dl, which was treated with intravenous fluids and calcitonin.

On primary evaluation, the patient reported dizziness and headaches associated with nausea. Two months before the patient’s admission, she was independent in all her activities of daily living; however, she rapidly deteriorated to being confined to her bed due to fatigue and headaches. The patient also had 20 lb of weight loss in the past 2 months.

Notable labs include calcium of 14.2, parathyroid hormone (PTH) was suppressed at 5, the PTH-related peptide was normal and 25-hydroxy vitamin D was suppressed at 19, but 1, 25-dihydroxy vitamin D and angiotensin-converting enzyme (ACE) were elevated to 149 and 99, respectively. Alkaline phosphatase elevated at 214. HIV, tuberculosis, histoplasmosis, coccidiomycosis and hepatitis B and C were ruled out. The patient was started on continuous fluid to treat hypercalcaemia.

Computerized tomography (CT) scans of the chest and abdomen/pelvis with contrast showed questionable cirrhosis, splenic and liver hypodense lesions and hilar lymphadenopathy.
Subsequent positron emission tomography (PET)-CT scan showed diffuse heterogeneously increased uptake in the spleen and liver, and avid cervical, thoracic and abdominal lymphadenopathy. Magnetic resonance imaging (MRI) brain was performed to rule out any central nervous system involvement due to persistent complaints of headache. Due to normal MRI with no focal neurologic deficits, and improvement in symptoms, a lumbar puncture was not indicated. An endobronchial ultrasound (EBUS) was done which demonstrated focal necrotizing granuloma in the right lung and focal calcified granuloma of the right mediastinum. Acid-fast bacilli (AFB) and Grocott-Gomori's methenamine silver stain were both negative. Pulmonary function tests were done and showed non-specific ventilatory defect with normal lung volumes and gas exchange. A diagnosis of invasive necrotizing sarcoidosis was made.

The patient was started on prednisone 40 mg daily and trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis for Pneumocystis Carinii pneumonia. The patient improved the next day and was discharged with a 4-week course of 40 mg oral prednisone daily and TMP-SMX three weekly, and was advised to follow-up with pulmonology, cardiology and ophthalmology for surveillance due to complications of sarcoidosis. At the 1-, 3- and 6-month follow-up with pulmonology, the patient reported improvement in symptoms on prednisone taper. Hypercalcaemia had resolved to 9 mg/dl.

**DISCUSSION**

Sarcoidosis is an infiltrative, inflammatory non-caseating granulomatous process. It can very rarely present as necrotizing granulomas. Necrotizing sarcoid granulomatosis (NSG) primarily affects the lungs and presents as nodular masses of confluent sarcoid-like granulomas with extensive necrosis and vasculitis.

It is more common in Caucasians than African-Americans with the median age being 42 years. Classically, sarcoidosis presents in patients 20–60 years of age with non-specific symptoms such as dry cough and fever. However, up to 30% of patients with sarcoidosis can present with extrathoracic symptoms such as uveitis, erythema nodosum or lupus pernio. It has also been reported in the literature to present as a purely extrathoracic syndrome in 10% of patients. Our patient had an unusual clinical presentation, with no overt symptoms other than generalized malaise, headache as well as hypercalcaemia. The only significantly positive values were that of elevated ACE levels and 1, 25-dihydroxy vitamin D. Negative AFB stains, absence of lytic lesions on imaging and normal PTH, urine and serum protein electrophoresis levels ruled out other differential diagnoses, including tuberculosis, primary hyperparathyroidism, malignancy and multiple myeloma. Eventually, a CT scan with contrast revealed hilar lymphadenopathy and hypodensities in the spleen, resulting in a PET scan and EBUS to confirm our diagnosis.

Sarcoidosis can present with a wide variety of symptoms; thus, it may be difficult to discern the diagnosis from a wide spectrum of disorders that can present with similar symptoms. Radiologically, NSG can present as cavitary lesions, ill-defined consolidations or a solitary nodule or a mass. It shares pathological features with classic sarcoidosis and Wegener’s granulomatosis, leading to difficulty in timely diagnosis. To date, the aetiology of sarcoidosis remains nebulous. A definitive diagnosis relies on pathological evidence demonstrating non-caseating granulomas.

There are a few case reports discussing NSG; however, this topic needs extensive research to establish aetiologies in different population groups and diagnostic criteria to aid in prompt diagnosis and treatment. NSG should be considered within the differential diagnosis of granulomatous diseases, and knowledge of this variant is essential in order not to rule out sarcoidosis due to the presence of necrosis.
AUTHOR CONTRIBUTION
Nirali Sheth, Umaima Dhamrah, Branden Ireifej, David Song, Penpa Bhuti, Jagbir Singh and Sibghatallah Ummar wrote the manuscript. Henry Fan, Vikash Jaiswal and Nishan Babu Pokhrel performed critical edits, revised the draft and prepared the final version of this manuscript which was approved by all authors.

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CONFLICT OF INTEREST
None declared.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no data sets were generated or analysed during the current study.

ETHICS STATEMENT
The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

ORCID
Vikash Jaiswal https://orcid.org/0000-0002-2021-1660
Nishan Babu Pokhrel https://orcid.org/0000-0002-4278-5753

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