Multiple bilateral pulmonary nodules masquerading as pulmonary metastasis; a case of nodular sarcoidosis

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Type of article: Case report

Abstract
Sarcoidosis is a multi-system inflammatory disorder of unknown etiology that is manifested by the presence of non-caseating granulomas. Multiple pulmonary nodules are rare presentations of sarcoidosis. We report a case of nodular sarcoidosis in a young male of Middle-East origin who had initially presented with bilateral painful ankle edema. His chest X-ray showed multiple bilateral pulmonary nodules. A high resolution computed tomography scan of the chest demonstrated multiple pulmonary nodular lesions and also mediastinal and hilar lymphadenopathy. Subsequent biopsies revealed non-necrotizing granuloma with multinucleated giant cells indicative of sarcoidosis. An appropriate work-up was done to confirm the true nature of the nodules and facilitate treatment.

Keywords: Sarcoidosis, Multiple Pulmonary Nodules; Neoplasm Metastasis

1. Introduction
Sarcoidosis is a multi-organ inflammatory disease of unknown etiology, which is manifested by non-caseating granulomas in the affected organs (1). The disease most commonly affects young and middle-aged adults in the age group of 20-40 (2). It can involve any organ in the body. However, it is more likely to involve some organs than others, and it frequently presents in the lungs (almost 90%) and mediastinal lymph nodes involvement, skin lesions, and ocular disease. Bilateral symmetrical hilar lymphadenopathy, often accompanied by right paratracheal nodes with or without pulmonary infiltrations is the most characteristic radiographic feature of sarcoidosis on chest X-ray (2, 3). High resolution computed tomography (HRCT) scans usually show micro nodules with perilymphatic distribution in the early stage of the disease and parenchymal fibrosis in the late stages (4). Atypical patterns on chest imaging have been reported in patients with sarcoidosis. Nodular sarcoidosis is a rare presentation of pulmonary sarcoidosis that usually manifests as multiple pulmonary nodules (less than 3 cm) or masses (more than 3 cm) on the chest X-ray and CT scan (1, 3, 5). Nodular sarcoidosis has a favorable prognosis, and pulmonary nodules usually resolve spontaneously (3). Appropriate workup may detect the true nature of pulmonary nodules and, hence, facilitate their treatment. There have been several case reports on nodular sarcoidosis mimicking metastatic lung neoplasia. In this report, we elucidate a case of sarcoidosis with multiple pulmonary nodules masquerading as metastatic lesions on chest X-ray and HRCT.

2. Case presentation
2.1. Clinical presentation
A 31-year-old man presented to the Department of Internal Medicine with a 10-day history of bilateral painful ankle edema. Physical examination on admission revealed bilateral swollen ankles that were painful with active motion.
Passive motions were painless, which was suggestive of bilateral periarthritis. He did not report any constitutional symptoms, such as fever, weight loss, or sweating. With regard to the patient’s age and bilateral periartheritis of the ankles, an initial diagnosis of Lofgern’s syndrome (acute sarcoidosis) was made.

2.2. History
The patient reported a past history of morphine addiction. He was a nonsmoker, and his past medical history was unremarkable.

2.3. Laboratory and imaging findings
The chest X-ray showed multiple bilateral pulmonary nodules and also bilateral hilar lymphadenopathy (Figure 1). The findings of abdominal and pelvic ultrasound were normal. HRCT of the chest and abdominal CT scanning were performed for further evaluation of pulmonary nodules and a probable source of pulmonary metastases. The HRCT demonstrated multiple, bilateral, well-defined parenchymal nodules, predominantly peripheral in distribution. Also, mediastinal and hilar lymphadenopathy were observed (Figure 2). The spirometry and pulmonary function tests showed normal dynamic lung volume and also normal diffusing lung capacity. Bronchoscopy demonstrated no evidence of endobronchial lesions. Tissue stain and culture of bronchial aspirate for microorganisms, mycobacteria, or fungi were negative. The total cell count in the Broncho alveolar lavage content was 68 mm3 with 82% alveolar macrophages, 14% lymphocytes, and 10% eosinophils. Transbronchial lung biopsy showed non-necrotizing granuloma with multi-nucleated giant cells (Figure 3).

2.4. Treatment and follow-up
The diagnosis of nodular sarcoidosis was made based on the histopathological findings, and the patient was started on steroids. The level of serum angiotensin-converting enzyme was decreased to 15 with remarkable clinical, laboratory, and radiological improvements on subsequent evaluations.

2.5. Ethics of case report
An informed consent was obtained from the patient for publication of this manuscript. The Vice Chancellor for Research, Mashhad University of Medical Sciences approved this case report.
Figure 2. High resolution computed tomography scan of the chest demonstrating bilateral pulmonary nodular infiltrates

Figure 3. Histopathological examination of the lung nodule showing a non-caseating granuloma

3. Discussion
3.1. Clinical presentation
Sarcoidosis is a granulomatous disease of unknown etiology that commonly affects young and middle-aged patients between 20 and 40 (1, 3). The disease can involve any organ system, but pulmonary involvement occurs in more than 90% of patients. Extra-pulmonary involvement, including lymph nodes, skin, eyes, joints, bones, salivary glands, central nervous system, muscles, heart, liver, and spleen also may occur (1, 3, 4). In sarcoidosis, pulmonary involvement occurs in up to 90% of the patients, so the chest X-ray remains a key tool for formulating a diagnosis. Isolated extrapulmonary disease is rare (less than 60% of patients) (1, 3, 5). Because sarcoidosis can involve any organ system, the clinical presentation often is variable. Patients with pulmonary sarcoidosis usually present with
cough and pulmonary dyspnea or skin lesions. Common symptoms are vague, such as fatigue, weight loss, fever, and night sweats. Pulmonary and mediastinal involvement may be asymptomatic in 30-35% of patients, and the disease may be diagnosed as an incidental finding on chest X-ray. Lofgrn’s syndrome is an acute presentation consisting of erythema nodosum, arthritis, and bilateral hilar adenopathy, which occurs in 4 to 34% of patients (2). Pulmonary nodular sarcoidosis was first described in 1952 by McCord and Hyman (6). Nodular lesion on chest X-ray or CT scan is a rare manifestation of pulmonary sarcoidosis, with an estimated prevalence in the range of 2.4 - 4%, as reported by Sharma et al. (5). Atypical manifestation of pulmonary sarcoidosis has been reported on chest imaging and may be seen in 25-30% of patients (3, 7). The disease is prevalent in females, especially in African-American ethnicities, and it is rare in Asian populations (3). Patients with nodular sarcoidosis may present with pulmonary or constitutional symptoms (3, 7, 8), which are not consistently reported in the nodular form of sarcoidosis. Our patient presented with bilateral painful ankle edema.

3.2. Laboratory findings and imaging

In patients with the nodular form of sarcoidosis, pulmonary function tests may be abnormal, but they usually show only a mild functional impairment. Our patient’s pulmonary function test was normal (8). The radiological findings in nodular sarcoidosis are not specific and resemble other nodular pulmonary diseases, especially metastatic lesions and mycobacterial and fungal infections (3, 4, 8). Chest X-ray and CT scan usually show multiple nodules (measuring 1 - 4 cm in diameter) mostly in the peripheral region of the lungs. Cavitating nodules may be seen, and pulmonary lesions may be accompanied by mediastinal lymphadenopathy. On CT scan, sarcoid nodules usually present as bilateral, multiple opacities frequently occupying the peri hilar and peripheral lung zones (3, 4, 9). Small satellite nodules that border the periphery of the larger nodules (galaxy sign) are not specific for sarcoidosis and are reported in other granulomatous disease and malignant lesions (3). Solitary lung nodules or masses are rare manifestations of sarcoidosis (10). Nutting et al. reported a case of nodular sarcoidosis that presented with a single pulmonary mass that mimicked primary bronchogenic carcinoma (7). Radiologists are usually unfamiliar with these atypical and rare imaging findings of sarcoidosis, which may delay making a correct diagnosis and undertaking appropriate management in most of these cases. Diagnosis of nodular sarcoidosis is usually difficult on imaging modalities because the imaging findings may mimic metastatic lung lesions, primary lung malignancy, infectious diseases, and vascular lesions. Bronchogenic carcinoma and metastatic lesions are principle concerns in these circumstances (3, 4, 12, 14). It is usually difficult to discriminate infectious diseases, especially mycobacterium tuberculosis and fungal infections from nodular sarcoidosis based on imaging findings. Hence, tissue biopsies and histopathological studies are always required to confirm the diagnosis of nodular type of sarcoidosis (15). Transbronchial lung biopsy, CT-guided lung biopsy, and vats biopsy can be valuable to achieve a histopathologic diagnosis. In our patient, bronchoscopy and transbronchial lung biopsy was performed, which established the diagnosis of non-caseating granulomatous disease.

3.3. Treatment and follow-up

Nodular sarcoidosis usually has a favorable prognosis, and the pulmonary nodules may resolve either spontaneously or with treatment (1, 3, 8). When needed, treatment is primarily based on systemic corticosteroids. In asymptomatic patients with pulmonary nodular sarcoidosis, a watch and wait approach is suggested, and treatment with steroids should be considered in case symptoms develop or lung function deteriorates. Our patient was treated with steroids, and he responded well, showing clinical improvement and radiological resolution of the pulmonary nodules.

4. Conclusions

Diagnosis of nodular sarcoidosis may be difficult based on imaging findings alone, owing to their similarity with metastatic or primary pulmonary malignancy or other nodular lung lesions, especially infectious diseases. Appropriate work up and histological examination are necessary to achieve a correct diagnosis and, hence, provide appropriate treatment.

Acknowledgments:
The authors gratefully acknowledge the contribution of Ms. M. Hassanpour for editing the manuscript.

Conflict of Interest:
There is no conflict of interest to be declared.

Authors' contributions:
All authors contributed to this project and article equally. All authors read and approved the final manuscript.
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