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Case Report

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Sarcoidosis of the Breast

***(Running title:** Breast sarcoidosis)*

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Abstract

Sarcoidosis is a systemic granulomatous disease that can affect any organ including the lungs. lymph nodes, skin, and eyes, Breast involvement is extremely rare that poses unique diagnostic and management challenges and often misdiagnosed. A 44-year-old woman presented with a right breast mass detected by physical examination without any other systemic or respiratory symptoms. other symptoms. Laboratory findings were within normal limits. Chest x-ray and CT showed bilateral hilar lymphadenopathy. Mammography revealed a heterogenous mass in the right upper quadrant. Pathologic examination of the needle aspiration biopsy sample revealed non-caseating granulomatous inflammation. Transbronchial biopsy pathology displayed non-caseating granulomatous inflammation compatible with sarcoidosis. The serum ACE level was 84 IU/ml. Final diagnosis was sarcoidosis with breast involvement.

This case highlights the diagnostic challenges and management strategies for this atypical presentation of sarcoidosis. Our patient underscores the importance of recognizing breast sarcoidosis to avoid unnecessary surgical interventions and to optimize patient management. The main target is to review clinical presentation, diagnostic approaches, treatment options, and implications for patient care in breast sarcoidosis.

Keywords: *Sarcoidosis, breast sarcoidosis, diagnosis.*

Introduction

Sarcoidosis is characterized by the formation of non-caseating granulomas, primarily affecting the lungs but capable of involving virtually any organ system. Breast involvement, although uncommon, can manifest as palpable masses, skin lesions, or asymptomatic findings on imaging studies. Breast sarcoidosis is reported to occur in 0.2% to 2% of patients with sarcoidosis, and the majority of cases are females that are typically between 30 to 60 years of age coinciding with almost the same demographic features of breast carcinoma in general (1-3). The incidence appears to be higher in certain ethnic groups, particularly African Americans, reflecting broader trends seen in sarcoidosis epidemiology.

The rarity of this condition often leads to misdiagnosis, particularly when the breast masses are considered primarily for malignant processes. Breast sarcoidosis is quite uncommon but as it occurs in the same age group of patients with breast carcinoma displaying similar features including almost the same symptoms and signs, it may easily mimic malignancy leading to diagnostic challenges. This case report will present clinical features, diagnostic strategies, and treatment options for sarcoidosis affecting the breast emphasizing the importance of considering sarcoidosis in the differential diagnosis of breast lesions.

Case report

A 44-year-old woman with a medical history of hypertension presented to the breast outpatient clinic with a painless in her right breast noticed one month ago and dry cough. Her personal and family history did not disclose any disease of concern. Physical examination revealed normal pulmonary and cardiac findings other than a firm, irregular mass approximately 2 cm in diameter in the upper outer quadrant of the right breast with no associated lymphadenopathy. Mammography demonstrated a suspicious mass with irregular margins, prompting a biopsy. Pathologic examination of the core needle biopsy revealed a non-caseating granulomatous inflammation compatible with sarcoidosis. Immunohistochemical staining was inconclusive for malignancy, leading to further investigation. The patient was consulted to the internal medicine clinic.

Serum biochemistry was within normal limits except for a mildly elvated ERS of 36 mm/h. ECG showed sinus rhythm and a normal cardiac axis. Chest x-ray and thorax CT revealed bilateral hilar lymphadenopathy consistent with stage I sarcoidosis. Further evaluation included serum angiotensin-converting enzyme (ACE) levels, which were elevated **(**86 IU/ml**),** and a bronchoscopy with biopsy confirmed the diagnosis of sarcoidosis demonstrating non-caseating granulomas with a BAL CD_4/CD_8 ratio of 4.2 and lymphocytosis. In ^{18}F-FDG-PET/CT revealed mediastinal and hilar lymph nodes along with multiple nodules in both breasts with diameters between 2 to 3 cm and SUVmax values ranging from 3.2 to 4.6 consistent with granulomatous inflammation (Figure 1).

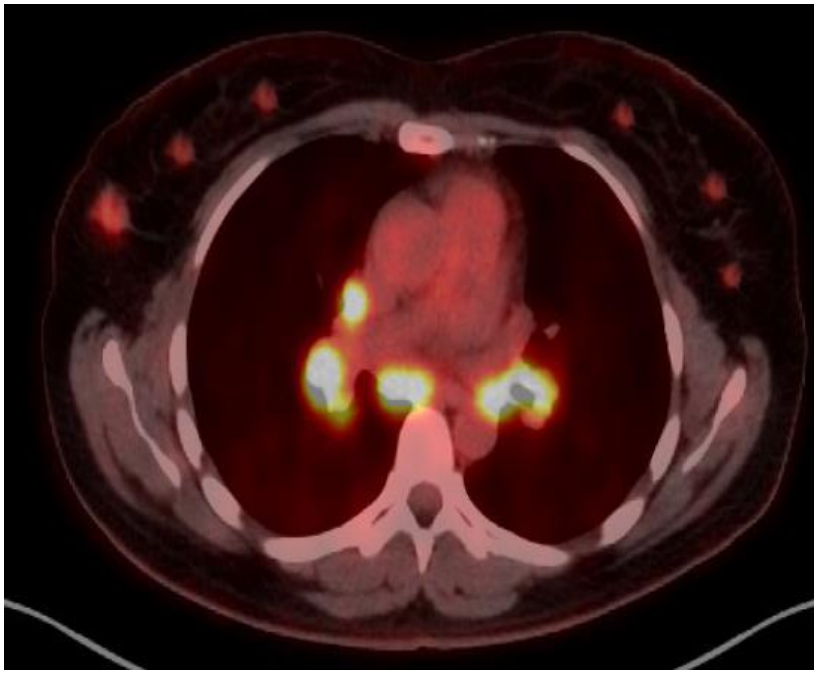

Figure 1: ^{18}F-FDG PET/CT revealing mediastinal, hilar lymph nodes, and multiple nodules in both breasts compatible with granulomatous inflammation.

Pathologic examination of the needle aspiration biopsy sample of the 3 cm nodule revealed non-caseating granulomatous inflammation compatible with sarcoidosis. Given the patient's history of dry cough, high serum ACE level, imaging, and the histopathologic findings a diagnosis of sarcoidosis with breast involvement was made. During follow-up, the patient had improvement in dry cough with inhaled steroid treatment and stable breast nodules.

Discussion

Breast sarcoidosis is an extremely rare entity with an approximate incidence of %1 around the world and often presenting as a palpable mass that can mimic breast cancer. Conventional laboratory and imaging modalities contribute to the detection of breast lesions, but scarcely ensure a definite diagnosis. Histological assessment is required almost in all patients over imaging assessments for an early and timely diagnosis to avoid unjustified interventions or treatments (1-5). Malignancy should be excluded as a primary differential diagnosis while in the presence of granulomatous inflammation, other granulomatous disorders such as tuberculosis, Wegener's granulomatosis, or idiopathic granulomatous mastitis should be excluded since the treatment strategies are imprescriptibly different. This case report clarifies the current clinical assessment and differential diagnosis of breast sarcoidosis that underscores the importance of considering sarcoidosis in the differential diagnosis of breast lesions, particularly in patients with previously unknown systemic sarcoidosis presenting with respiratory symptoms and an unnoticed breast nodule. The rarity of this condition along with its extremely similar clinical profile with breast carcinoma often leads to a delayed diagnosis, particularly when such breast masses are considered primarily for malignant processes or if they are indeed malignant. In this patient, the associated FDG-PET/CT findings consistent with granulomatous inflammation were the exclusive diagnostic feature in this patient.

The etiology of breast sarcoidosis remains unclear, though it is thought to be associated with immune dysregulation and exposure to environmental antigens (6-8). Granuloma formation results from an exaggerated immune response, potentially triggered by infectious agents or allergens. The presence of non-caseating granulomas in breast tissue can arise from hematogenous dissemination or localized immune responses (9-12). Histologically, breast sarcoidosis exhibits a distinctive pattern of lymphocytes and giant cells within granulomas. The prognosis of breast sarcoidosis is generally favorable, with many patients experiencing resolution of symptoms and lesions, particularly with appropriate treatment. However, outcomes can vary based on the extent of disease and the presence of concurrent systemic sarcoidosis.

This patient presents crucial hallmarks for the clinicians. In a patient presenting with prevailing with respiratory symptoms and a breast nodule sarcoidosis is preliminary diagnosis. A breast nodule associated with sarcoidosis is an extremely crucial diagnostic challenge. The hallmark of breast sarcoidosis lies in the clinician's failure to overlook breast cancer, which may present with similar clinical and even radiological features. The key point for diagnosis was the presence of multiple nodules in both breasts on PET/CT images and their low tracer uptake associated with granulomatous inflammation. It is obvious that in patients with a previously known history of sarcoidosis or presenting with clinical symptoms and radiologic manifestations compatible with sarcoidosis, there does not exist any difficulty for confirmation or identification of breast sarcoidosis although a pathologic identification with exclusion of malignancy is absolutely required.

Conclusion

Breast sarcoidosis, although rare, presents a significant and a noteworthy diagnostic challenge. Increased awareness is essential for early recognition and management. Given its potential to mimic malignancy, a thorough diagnostic approach is critical to avoid unnecessary surgical interventions. Ongoing research into pathophysiology and sarcoidosis treatment will further enhance our understanding to improve patient outcomes. Our case highlights the rare occurrence of breast involvement in sarcoidosis and the potential for misdiagnosis as malignancy or vice versa. Clinicians should maintain a high index of suspicion for sarcoidosis in patients presenting with breast masses,

especially in the context of other systemic and particularly the respiratory symptoms not to misdiagnose breast sarcoidosis or malignancy. FDG-PET/CT may emerge as the hallmark of a definite diagnosis in such cases. Increased awareness of this condition will facilitate timely diagnosis and appropriate treatment, ultimately improving patient outcomes.

Author contributions:
Cuneyt Tetikkurt designed and wrote the manuscript.
Halil Yanardag installed the dermographic analysis.
Muammer Bilir assembled the patient findings.

Conflicts of interest
The authors declare that they do not have any conflicts of interest to declare associated with this study and state explicitly that any kind of potential conflicts do not exist.

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