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Case Report

Every Granulomatous Lesion is Not Classified as Tuberculosis. Isolated Sarcoidosis Breast with Comprehensive Review of Literature

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Abstract

Background: Sarcoidosis is an inflammatory disease characterized by forming granulomas in various organs. It affects the lungs, lymph nodes, skin, and eyes in most cases, but isolated breast involvement is rare, with only a limited number of cases reported in the medical literature. Patients with breast sarcoidosis may be asymptomatic or present with a palpable breast lump, which can mimic common breast conditions such as breast fibro adenoma, abscess or breast carcinoma. Thus, accurate diagnosis is crucial to avoid unnecessary antibiotic usage and surgical procedures.

Case Presentation: A 39-year-old nonlactating female with diabetes mellitus presented with pain and swelling in the right breast for 1 year to the breast clinic at our institute without fever, chills, rigors or discharge. The patient had taken multiple courses of antibiotics with no symptomatic relief this year. On referral to the Department of Internal Medicine at SKIMS, the patient had a history of erythema nodosum (EN). The results of the present general examination and left breast examination were normal however, the right breast examination revealed a solid mass measuring approximately 2× 2 cm in the upper outer quadrant with normal skin and no palpable axillary lymph nodes. Her baseline investigations were normal, including complete blood count and chemical and urine examinations. Ultrasonography of the right breast revealed diffusely scattered hypoechoic areas in the retroareolar region and outer quadrant with features of peridal mastitis and multiple duct dilatation with thick contents. Mammography revealed mild asymmetrical enlargement of the right breast with BIRADS 3 morphology. The patient was managed with incision drainage. Aspirated pus samples for microbiological testing (AFB staining, Gram staining and culture, CB-NAAT, MTB culture) were negative. Mantoux test urine for AFB smears, chest X-rays, IGRAs, and vasculitic profiles (ANA, P-ANCA, C-ANCA, and anti-CCP) were negative. However, angiotensin-converting enzyme (ACE) levels and 24-hour urinary calcium levels were elevated. Computed tomography of the chest and abdomen was normal. Histopathological findings from a true cut biopsy of the right breast lesion revealed noncaseating granulomas infiltrating the breast tissue with many foreign body giant cells. AFB and CBNAAT of the biopsy were negative. The patient was diagnosed with primary breast sarcoidosis and managed with oral prednisolone and azathioprine. On follow-up, the mass size decreased, and the pain substantially improved.

Conclusion: Considering that sarcoidosis in a patient who presents solely with breast pain and swelling is rare but clinically suspicious, a thorough evaluation can guide patients to reach a proper diagnosis, which can significantly improve the overall prognosis.

Keywords: Sarcoidosis; Erythema Nodosum; Angiotensin Converting Enzyme

Introduction

Sarcoidosis is a rare condition first identified in Sarcoidosis is a rare condition that was first identified in disease, characterized by noncaseating granulomas, that affects multiple organs in the body, primarily the lungs. More common in women aged 25 to 40 years, it has a prevalence rate ranging from 5 to 40 cases per 10,000 people, varying by region [2]. Patients with sarcoidosis typically experience general symptoms such as fatigue, fever, and weight loss, as well as respiratory symptoms, with dyspnea being the most common [3]. However, many patients remain asymptomatic, and most cases experience spontaneous remission without treatment [4]. Histologically, sarcoidosis is marked by accumulating noncaseating granulomas in various organs, primarily the lungs and lymph nodes, leading to inflammation and potential organ damage [5]. Cases where sarcoidosis manifests outside the commonly affected organs can be difficult to recognize, often resulting in delays in diagnosis [6]. In fewer than 1% of cases, sarcoidosis appears solely as an unusual isolated mass in the breast, with only a limited number of cases documented in the literature [7,8]. Thus, although rare, sarcoidosis should be considered in the differential diagnosis when a breast mass is detected, alongside more common conditions such as breast cancer, to ensure timely diagnosis and improved prognosis. In this report, we present a sporadic case of primary sarcoidosis diagnosed solely through an isolated breast mass.

Case Presentation

Informed and written consent was obtained from the patient. This is the first case report of BCS reported in the Kashmir Valley, India. A 39-year-old female with a 5-year history of type II diabetes mellitus, two live births, and no lactation since her last childbirth four years ago presented to the medical outpatient department (OPD) of Sher-I-Kashmir Institute of Medical Sciences Soura Srinagar India with complaints of pain and swelling in her right breast for one year. She reported no fever, chills, discharge, or rash. Initially evaluated in the surgical clinic at our hospital, she was treated for a breast abscess with a two-week course of oral antibiotics. Later, she developed painful red nodules on her lower limbs and was prescribed NSAIDs and amoxicillin-clavulanate. She experienced some symptomatic relief for three months but returned with persistent right breast pain and swelling. On physical examination, a solid 2×2 cm mass was noted in the upper outer quadrant of the right breast, with normal overlying skin, no palpable axillary lymph nodes, and a normal left breast. The results of routine investigations, including complete blood count, liver and kidney function tests, and blood sugar level tests, were within normal limits. Ultrasonography of the right breast revealed multiple small organized abscesses (each at approximately 10 cc) with signs of inflammatory mastitis and mild ductal dilation. The patient underwent incision and drainage, and aspirated pus samples were collected for microbiological testing (Gram staining, culture, AFB staining, CB-NAAT, MTB culture), which were negative. Histopathology of the breast lesion revealed a benign inflammatory lesion with fibrocollagenous tissue infiltrated by lymphocytes, neutrophils, plasma cells, and histiocytes. Following surgery, the patient developed sinus discharge at the incision site, with postsurgical discharge. She returned to the medical OPD due to unresolved symptoms. Examination revealed multiple scars but no active discharge. A 2×3 cm lobulated lesion with mild tenderness was palpated in the upper outer quadrant of the right breast. Her general physical examination was normal. Blood tests revealed normocytic normochromic anaemia (HB 9.8 g/dl), an ESR of 17 mm in the first hour, and normal liver and kidney function tests. Glycemic control was within normal limits (HbA1c 6.5%). Additional tests, including a Montaux test, urine AFB smears, chest X-ray, and vasculitis profile (ANA, P-ANCA, C-ANCA, Anti-CCP), were also negative. Notably, her ACE level was elevated at 115 U/L (normal range: 20–70 U/L), and her 24-hour urinary calcium level was elevated at 8.52 mmol/24 hours (normal range: 2.50–7.50 mmol/24 hours). Radiological findings from ultrasonography of the right breast indicated a linear subcutaneous hypoechoic tract extending into the glandular soft tissue at the 2 o'clock position, with multiple organized microabscesses, the largest measuring 29×19 mm. Some collections showed a branching pattern, with hypoechoic areas lacking definitive liquefaction, suggesting chronic granulomatous mastitis (GM). Her chest X-ray appeared normal, and no lymphadenopathy was observed in the neck, axillae, or abdomen on ultrasound. Both contrast-enhanced CT (CE-CT) scans of the chest and abdomen and high-resolution CT (HR-CT) images of the chest were normal. Mammography of the bilateral breasts revealed asymmetrical enlargement of the right breast with BIRADS ACR type 3 morphology on the right side and BIRADS ACR type 2 morphology on the left side. The right breast also reveals diffusely scattered lumps with predominantly obscured backgrounds. However, there was no retraction of the nipple or skin thickening. A core biopsy of the right breast tissue revealed noncaseating epithelioid granulomas infiltrating the breast tissue, with numerous foreign body giant cells, Schaumann bodies, and multinucleated giant cells with intracellular inclusions. The features were consistent with haemorrhage and chronic granulo-

matous pathology, indicating sarcoidosis. AFB staining of the biopsy sample was negative. Given her symptoms (right breast mass and erythema nodosum), elevated ACE levels increased 24-hour urinary calcium, and histopathological findings, the patient was diagnosed with isolated breast sarcoidosis. The patient was prescribed a three-month course of prednisolone (0.5 mg/kg), which resulted in significant improvement in her symptoms. Follow-up ultrasonography revealed tiny hypoechoic nodules at the 8–9 and 8–12 o'clock positions, the largest measuring 6–7 mm, with evidence of a healed tract at the 2 o'clock position. Steroid treatment was subsequently tapered, and the patient is currently on a maintenance dose of prednisolone 10 mg/day and azathioprine 50 mg twice daily.

Review of the Literature and Discussion

No literature related to isolated sarcoidosis of the breast is available in India. Our study is the first case reported from the region. Sarcoidosis is a multisystem granulomatous disease with an unknown cause [9]. Breast involvement in sarcoidosis is rarely reported and occurs exclusively in women. A study among 382 female patients revealed 7 cases of breast cancer (1.8%) and 3 cases of breast sarcoidosis (0.8%), which are comparable to the rates reported in Lower's series [14]. The main characteristics of our case was similar to those of the patients described in Table 1 and Table 2. Our study correlated with known cases of sarcoidosis of the breast reported in the literature globally [15-19]. In this study, we excluded patients with a history of breast carcinoma, as well as those with incidental findings of regional sarcoidosis-like reactions in breasts removed due to carcinoma, along with all differential diagnoses. Notably, comparative analysis was challenging because patients were assessed via either a pathological or radiological approach rather than a clinical approach. On imaging, breast sarcoidosis typically appears as an irregular and/or spiculated mass on mammography and as an irregular Hypoechoic mass on ultrasound [20]. Axillary lymph nodes are also involved, but our study did not. not show any lymphadenopathy. Only 35 cases that histologically prove sarcoidosis of the breast [15] have been identified in recent years. Clinically, breast sarcoidosis may present as a painful breast mass, with less common symptoms, including nipple inversion and axillary lymphadenopathy. On mammography, it may appear as a spiculated, ill-defined, or well-defined mass, whereas on ultrasound, it typically presents as a hypoechoic mass [20]. The overlap in clinical presentation and radiological features makes distinguishing granulomatous mastitis from breast cancer challenging, emphasizing the critical role of histopathological examination for an accurate diagnosis. Diagnosis is confirmed through a core biopsy that reveals noncaseating granulomas without indications of nearby malignancy. Numerous cases of idiopathic granulomatous mastitis have been reported, occurring most frequently in parous women aged 30–40 years, typically within a few years postpartum or during pregnancy [21]. Some of these patients also present with extramammary symptoms such as erythema nodosum, arthralgias, and episcleritis, which may represent a mild or incomplete form of sarcoidosis [21]. Our results also revealed elevated 24-hour urinary calcium and ACE levels, which are correlated with the other rare cases reported in very few international studies [14,15]. Management of breast sarcoidosis generally aligns with that of both pulmonary and extrapulmonary sarcoidosis, with glucocorticoids being the preferred treatment option in both cases [22].

Case Reference	Age	Parity	Manifestation of BS	Positive biopsies for Sarcodiaosis	Radiology	ACE level	Treatment
Kaddoura., *et al.*	27	0	Bilateral Fatigue, fever, weight loss, multiple firm-hard masses that were tender on palpation. The masses were felt at 5, 11, and 8	Breast	USG with core biopsy, CT, Chest X-ray	High	Oral prednisolone Azathioprine
Marques de Mattos., *et al*. [16]	21	0	Fever, left breast involvement and bullous skin lesions	Breast	USG, CT, MRI, mammography	None	Corticosteroids
Aseel Abuhammad., *et al*. [17]	31	NG	Unilateral GMENA syndrome, who presented with a painful nodule of the left breast.	Breast	CT	None	Corticosteroids
Meriem Rhazari [18]	50	NA	Bi lateral BI-RADS V and BI-RADS IV Diabetic fever, night sweats, and Preservation of her general condition. multiple lymphadenopathies	Breast	USG, CT, MRI, mammography	None	Corticosteroids
RichmondRonald Gomes [19]	35	1	Unilateral, pregnant, non diabetic, non hypertensive with right breast abscess.	Breast	Chest X-ray, CT Scan	High	Corticosteroids

Table 1: Literature review and summary of the clinical characteristics of isolated patients with breast sarcoidosis.

Case Reference	Age	Associated Features	Duration of Symptoms	Histology	Lab investigations	Outcome/ Duration
Aseel Abuhammad., *et al*. [17]	31	Unilateral GMENA syndrome, nodule of the left breast. bilateral EN on the lower extremities.	1 Month	Histopathologic examination of the breast tissue exhibited noncaseating granulomas.	CRP, ESR, WBC count, PPD	Complete Resolution
Kaddoura., *et al*. [15]	27	Bilateral Breast Involvement with Rash on the right thigh.	6 months	Fine-needle aspiration (FNA) showed an inflammatory process with granulomatous formation.	ACE Levels	Complete Resolution
Marques de Mattos., *et al*. [16]	21	Unilateral nodule occupying the lateral quadrants of the left breast and bullous lesions, along with phlogistic signs in the same topography	2 Months	Fibroadipose tissue showing numerous non caseating granulomas with neutrophilic microabscesses and Langerhans-type giant cells, suggesting chronic granulomatous mastitis, which may correspond to sarcoidosis.	Urinary Calcium	Complete Resolution
Meriem Rhazari [18]	50	Bilateral BI-RADS V and BI-RADS IV Diabetic fever, night sweats, and Preservation of her general condition. multiple lymphadenopathies	2 Months	(presence of granuloma without caseous necrosis in 3 different organs: lymph node, salivary glands, and mammary glands).	CRP, Blood Ionogram, KFT, LFT, Viral Serologies, TST	Complete Resolution
Richmond Ronald Gomes [19]	35	Unilateral, pregnant, non diabetic, non hypertensive with right breast abscess arthralgias and myalgias	7 days	Non caseating granulomas	CRP, ESR, CBC, ANA, dsDNA	Complete Resolution

Table 2: Literature review and summary of the clinical characteristics of isolated patients with breast sarcodiosis.
KFT= kidney function test, LFT= liver function test, ESR= erythrocyte sedimentation rate, CBC = complete blood count, ANA= antinuclear antibodies, ds-DNA= double-stranded DNA, ACE= angiotensin-converting enzyme.

However, given the rarity of breast sarcoidosis, especially as an initial or isolated presentation, further studies are needed to identify the optimal treatment approach. While prognosis varies depending on factors such as disease extent and complications, patients with breast sarcoidosis generally have a favorable outlook with appropriate treatment, often experiencing significant symptom improvement or complete resolution [23]. In our case, the patient was treated with oral prednisolone (tapering over three months) followed by azathioprine, resulting in a reduction in mass size and substantial pain relief. She remained stable with regular follow-up.

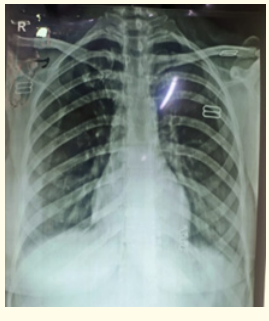

Figure 1: X-ray chest PA view showing normal lung fields with evidence of any hilar prominence.

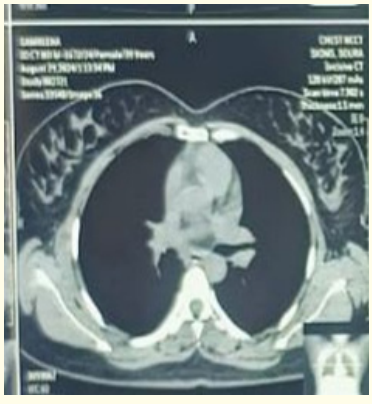

Figure 2: Axial images of the chest CT image in the HR and soft tissue windows showing normal lung parenchyma. Normal hilar with no hilar or mediastinal lymph nodes.

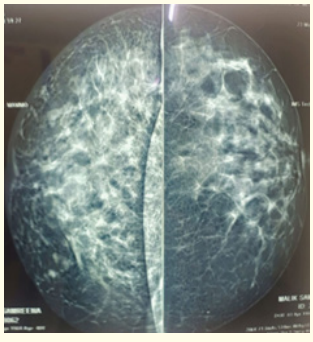

Figure 3: Mammogram craniocaudal view of the bilateral breast showing mild asymmetrical enlargement of the right breast with BIRADS ACR type 3 morphology on the right side and BIRADS ACR type 2 morphology on the left side. The right breast also reveals diffusely scattered lumps with predominantly obscured backgrounds. There was no nipple retraction or skin thickening.

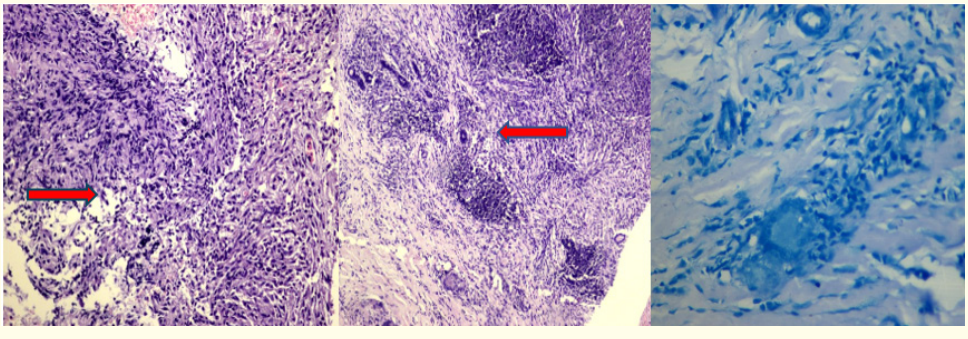

Figure 4: (A) Histologic section showing non-caseating epithelioid histiocytic granulomas with foci of calcification arrows. (B) Histologic section showing multiple noncaseating granulomas with dense lymphoid infiltrates, which are periductal at places [red arrow]. A giant cell can be seen (arrow). (C) Micrograph (ZN stain) showing a Langhan-type giant cell. The special stain for AFB was negative.

Conclusions

Primary breast sarcoidosis is a rare entity, particularly as the initial manifestation of the disease. It is crucial to consider breast sarcoidosis in the differential diagnosis of patients presenting with unexplained breast masses and associated signs.

Ethics Approval

No ethical approval was necessary.

Acknowledgement

Nil.

Conflict of Interest

The authors have no conflicts of interest to declare.

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