Cite as: Jaguś D, Yafimtsau I, Mlosek RK, Jonczak L, Roszkowska-Purska K, Dobruch-Sobczak K: Sarcoidosis of the breasts – when should it be considered? A case report. J Ultrason 2022; 22: e136–e139. doi: 10.15557/JoU.2022.0022.

Submitted: 08.07.2021
Accepted: 24.11.2021
Published: 13.04.2022

Sarcoidosis of the breasts – when should it be considered? A case report

Dominika Jaguś[1], Ivan Yafimtsau[2], Robert K. Mlosek[3], Luiza Jonczak[4], Katarzyna Roszkowska-Purska[5], Katarzyna Dobruch-Sobczak[6]

[1] *Department of Diagnostic Ultrasound, Faculty of Medicine, Medical University of Warsaw, Warsaw, Poland*
[2] *Students' Research Association at the Department of Diagnostic Ultrasound, Faculty of Medicine, Medical University of Warsaw, Warsaw, Poland*
[3] *Department of Diagnostic Ultrasound, Faculty of Medicine, Medical University of Warsaw, Warsaw, Poland*
[4] *Clinical Department of Allergology, Lung Diseases and Internal Diseases, Central Clinical Hospital of the Ministry of Interior, Warsaw, Poland*
[5] *Department of Pathology, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland*
[6] *2nd Department of Radiology, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland*

Correspondence: Dominika Jaguś, Zakład Diagnostyki Ultrasonograficznej, Wydział Medyczny, Warszawski Uniwersytet Medyczny, Ludwika Kondratowicza 8, 03-242 Warszawa; e-mail: derapunzel@gmail.com

DOI: 10.15557/JoU.2022.0022

Keywords
sarcoidosis; granulomas; ultrasonography; breast diseases; granulomatous mastitis

Abstract

Sarcoidosis is a systemic inflammatory disease of unknown aetiology. Given its complex clinical presentation, the disorder frequently causes diagnostic challenges. In most cases, the primary manifestation is in the lungs and mediastinum. Breast involvement as the primary manifestation of sarcoidosis is rare, accounting for less than 1% of cases. The authors present the case of a 44-year-old woman whose disease first manifested as multiple non-specific BIRADS 4 lesions in both breasts, accompanied by axillary lymphadenopathy, detected by ultrasound examination. The lesions were not visible on mammography. The course of the disease was clinically silent, with intermittent remissions, until the complete resolution of focal breast lesions on ultrasound after two years of follow-up. The paper presents an algorithm for the management of multifocal breast pathology with associated lymphadenopathy, which led to the prompt verification of sarcoidosis.

Introduction

Given the heterogeneity of presentations, the diagnosis of sarcoidosis is a challenge to both clinicians and diagnosticians. Multiorgan involvement, varied imaging findings and diverse clinical features frequently contribute to prolonging the time to diagnosis. Serious complications of untreated sarcoidosis include pulmonary fibrosis, cardiac arrhythmias, and damage to the central nervous system[(1)]. Therefore, prompt diagnosis is crucial for the further clinical course of the disease. The reported case shows that individualised approach is required of medical teams to achieve satisfactory treatment outcomes.

Case report

A 44-year-old woman, who had annual prophylactic breast ultrasound scans, without any complaints or palpable breast lesions, presented for a breast ultrasound during lactation. The examination revealed a few small focal lesions with uneven margins, up to 7 mm in size, arranged in a non-parallel configuration, with small blood vessels along their periphery. The foci were characterised by reduced echogenicity, with no enhancement or acoustic shadow visible behind the lesions. The foci were located primarily in the outer quadrants

of both breasts. No calcifications were seen within the lesions, and on ultrasound elastographic images they all appeared soft (E_{max} <20 kPa) (Fig. 1A–C). In addition, enlarged hypoechoic lymph nodes, up to 21 mm in length, with thickened, hypoechoic cortical layers, up to 4 mm thick, with preserved rich hilar vascularisation and no visible sinuses, were identified in both axillary fossae (Fig. 1D). On mammography, glandular structures were predominant, without abnormal thickening or microcalcifications.

In view of the presence of numerous solid lesions in both breasts, the first step involved performing a core-needle biopsy (CNB) of the dominant lesion. Using a 14G needle, three core specimens were taken. The presence of malignant tumour cells was ruled out. Multiple granulomas with multinucleated giant cells, without signs of serous necrosis, were identified. The suspicion of granulomatous lobular mastitis (GLM) was raised, to be differentiated with another disease characterised by granulomas. To this end, a test for bacteria of the genus *Corynebacterium* in the breast material was carried out. The bacteria were not detected. To extend the diagnostic work-up for granulomatous lesions, tissue material was obtained from lymph nodes for histopathological analysis. A CNB procedure was performed using a 14G needle. Three core specimens were taken. Clusters of epithelioid cells with sparse multinucleated giant cells, without features of necrosis, were found. Analysis of the lymph node lesions and the focal lesion in the breast led to the suspicion of sarcoidosis (Fig. 2, Fig. 3). In the next step, the patient was referred for pulmonary consultation. High-resolution computed tomography (HRCT) showed lesions characteristic of sarcoidosis, presenting as small nodules in the middle fields and at the fissures of both lungs (Fig. 4). Histopathological analysis of material taken during bronchoscopy showed fragments of bronchial mucosa with granulomas composed of epithelial and giant cells, without signs of necrosis. Based on these findings, the diagnosis of sarcoidosis was established. The dynamics of the lesions in the breasts was followed up at intervals of several months, for a total of two years. Over that period, the focal lesions in the breasts shrank and grew again until they resolved completely (Fig. 1E–H). The patient remains under the care of the Outpatient Clinic of Pulmonary Diseases and the Outpatient Clinic of Breast Diseases. At the time of diagnosis, she did not require pharmacological treatment.

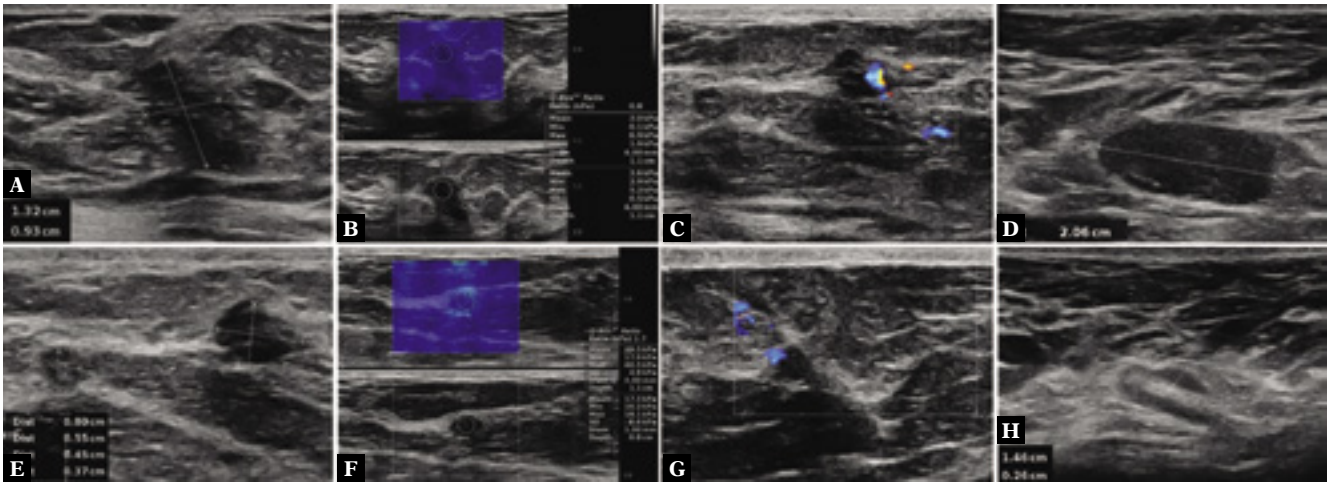

Fig. 1. *Ultrasound findings in a 44-year-old female patient with breast sarcoidosis.* **A–D**. *Pre-biopsy examination,* **E–H**. *Examination performed a year later. B-mode ultrasound revealed a hypoechoic nodule with an irregular margin. Colour Doppler ultrasound showed small blood vessels surrounding the lesion. On shear wave elastography, the lesion appeared soft*

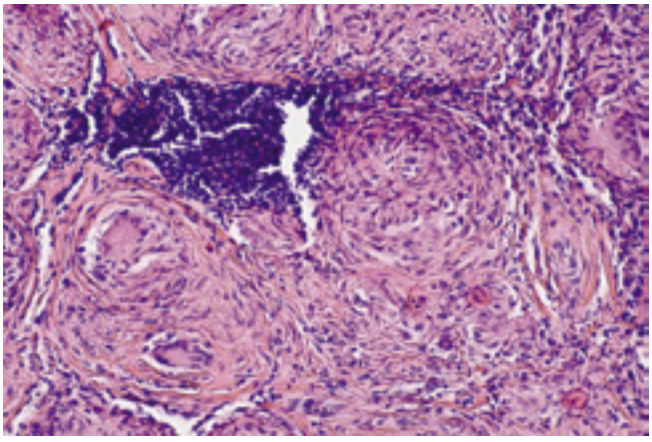

Fig. 2. *Microscopic examination of lymph node tissue showed an aggregation of epithelial cells with multinucleated giant cells, without signs of necrosis. Hematoxylin and eosin staining (10x magnification)*

Discussion

Sarcoidosis is an idiopathic systemic inflammatory disorder which typically occurs in individuals between 20 and 40 years of age[1,2]. In 90% of cases, the disease begins in the lungs or mediastinal lymph nodes, but it can manifest in any organ, including the breasts[3,4]. The diagnosis of sarcoidosis relies on three criteria: compatible clinical or

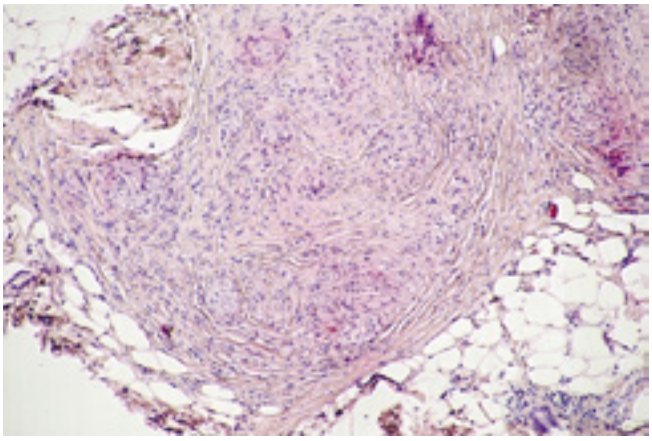

Fig. 3. *Typical features of breast sarcoidosis (5x magnification)*

radiologic presentation, histologically confirmed evidence of noncaseating epithelioid granulomas, and exclusion of other diseases with similar findings (presence of granulomas)[1,5].

In the reported case, the diagnosis of sarcoidosis was further complicated by the unusual location of inflammatory lesions. The literature includes isolated case reports of breast sarcoidosis, accounting for less than 1% of all instances of the disease[2,6].

Initially, based on the ultrasound findings, a proliferative process within the breast was considered. On ultrasound imaging, the focal lesions in the breasts were consistent with BIRADS 4 category, with a malignancy risk of 2–95%[7]. The procedure of choice was CNB of the dominant breast lesion. Considering that the lesions were numerous and small in size, while the patient was still lactating, it was decided that a single focal lesion would be evaluated, and the histopathological diagnostic work-up would be extended to the remaining lesions, if necessary. In the next stage, in order to specify the type of granulomatous disease, the diagnostic procedure was extended to include CNB of the axillary lymph nodes. The histopathological findings revealing granulomatous lesions without signs of necrosis narrowed down the range of possible pathologies and ruled out their malignancy.

Tuberculous lesions were considered in the differential diagnosis, but the possibility was abandoned based on the identification of noncaseating granulomas. Subsequent diagnostic work-up of pulmonary lesions detected no presence of acid-fast bacilli in the bacteriological examination of bronchoalveolar lavage (BAL)[8,9].

In view of the suspicion of granulomatous mastitis (GLM), culture of a histopathological specimen was done, excluding infection with bacteria of the genus *Corynebacterium*. In the absence of clinical signs of breast inflammation, no other inflammatory factor was taken into account in the diagnosis, also considering a different microscopic image[10,11].

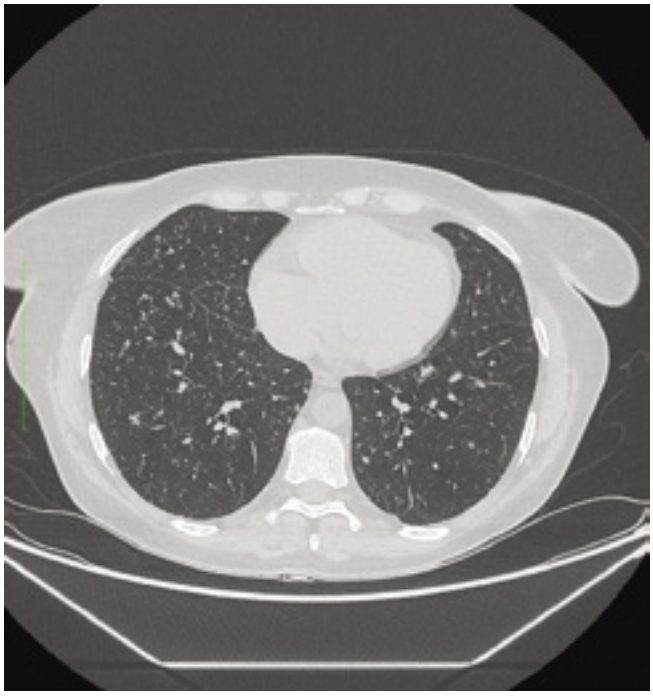

Fig. 4. *Axial CT scan showed small perivascular nodules in the middle and lower lobes of the right lung, consistent with sarcoid granulomas*

Idiopathic granulomatous mastitis (IGM) is more common in the postpartum period. Even though the patient gave birth two years before the appearance of the breast lesions, she was still lactating at the time of diagnosis. The characteristic manifestations of IGM include lobular mastitis with microabscesses, and inflammatory changes and damage to the mammary ducts[12–15]. The histopathological material did not show any changes specific to this disease entity.

The results of HRCT of the chest and histopathological examination of the mucosal sample obtained during bronchoscopy confirmed the presence of changes pathognomonic of sarcoidosis. Moreover, by excluding other possible causes of the lesions, all three criteria for the diagnosis of pulmonary sarcoidosis with breast involvement were met.

The diagnosis was additionally confirmed by the clinical course, which was characterised initially by partial and eventually complete remission of the inflammatory lesions. The literature reports show that – depending on the stage – pulmonary lesions may resolve spontaneously in up to 90% of patients[5]. The case reported here, though isolated, is consistent with previous literature findings. Over the two-year follow-up, the patient experienced several remissions of the lesions, followed by their recurrence. Ultimately, the abnormalities resolved completely both in the breasts and axillary lymph nodes.

Conclusions

The reported case provides evidence for the clinical polymorphism of sarcoidosis. The authors highlight the

importance of an individualised approach in diagnosing this systemic disease which, if left untreated, results in a significantly reduced quality of life for the patient. Moreover, the development of breast lesions as a primary symptom of the disease emphasises the role of preventive breast ultrasound in women. Good collaboration between diagnosticians, pathologists and clinicians is essential for a successful treatment outcome.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Acknowledgements

We would like to thank the Patient (IM) for her consent to the publication of her case report.

Author contributions

Original concept of study: DJ, RKM, KD-S. Writing of manuscript: DJ, IY, KD-S. Analysis and interpretation of data: DJ. Final acceptation of manuscript: DJ, IY. Collection, recording and/or compilation of data: DJ, LJ, KR-P, KD-S. Critical review of manuscript: RKM, KD-S.

References

1. Thomas KW, Hunninghake GW: Sarcoidosis. JAMA 2003; 289: 3300–3303.
2. Zujić PV, Grebić D, Valenčić L: Chronic granulomatous inflammation of the breast as a first clinical manifestation of primary sarcoidosis. Breast Care (Basel) 2015; 10: 51–53.
3. Lazarus A: Sarcoidosis: epidemiology, etiology, pathogenesis, and genetics. Dis Mon 2009; 55: 649–660.
4. Stefański M, Stefańska M, Bruliński K: Etiologia, patogeneza i diagnostyka sarkoidozy – przegląd piśmiennictwa. Med Rodz 2016; 19: 98–105.
5. Hunninghake GW, Costabel U, Ando M, Baughman R, Cordier JF, du Bois R, Eklund A, Kitachi M, Lynch J, Rizzato G, Rose C, Selroos O, Semenzato G, Sharma OP: ATS/ERS/WASOG statement on sarcoidosis. American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomatous Disorders. Sarcoidosis Vasc Diffuse Lung Dis 1999; 16: 149–173.
6. Gisvold JJ, Crotty TB, Johnson RE: Sarcoidosis presenting as spiculated breast masses. Mayo Clin Proc 2000; 75: 293–295.
7. Mendelson EB, Böhm-Vélez M, Berg WA, Whitman GJ, Feldman MI, Madjar H *et al.*: ACR BI-RADS® Ultrasound. In: ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. 5th ed. Reston, VA, American College of Radiology, 2013: 128–130.
8. Galego MA, Lage G, Shekhovtsova M, Duarte R: Tuberculosis of the breast: an uncommon presentation of an old disease. BMJ Case Rep 2019; 12: e227014.
9. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E *et al.*: Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: diagnosis of tuberculosis in adults and children. Clin Infect Dis 2017; 64: 111–115.
10. Oddó D., Stefanelli A, Villarroel A, Méndez GP: Coryneform bacteria in granulomatous lobular mastitis: morphological diagnosis in breast biopsies. Int J Surg Pathol 2019; 27: 380–386.
11. Zhou F, Yu L-X, Ma Z-B, Yu Z-G: Granulomatous lobular mastitis. Chronic Dis Transl Med 2016; 2: 17–21.
12. Banik S, Bishop PW, Ormerod LP, O'Brien TE: Sarcoidosis of the breast. J Clin Pathol 1986; 39: 446–448.
13. Chirappapha P, Thaweepworadej P, Supsamutchai C, Biadul N, Lertsithichai P: Idiopathic granulomatous mastitis: a retrospective cohort study between 44 patients with different treatment modalities. Ann Med Surg (Lond) 2018; 36: 162–167.
14. Patel RA, Strickland P, Sankara IR, Pinkston G, Many W Jr, Rodriguez M: Idiopathic granulomatous mastitis: case reports and review of literature. J Gen Intern Med 2010; 25: 270–273.
15. Velidedeoglu M, Kilic F, Mete B, Yemisen M, Celik V, Gazioglu E *et al.*: Bilateral idiopathic granulomatous mastitis. Asian J Surg 2016; 39: 12–20.