Radiological Case Report / Caso Clínico

## Breast Sarcoidosis: An Unusual Manifestation

Sarcoidose da Mama: Uma Manifestação Incomum

# Susana L Rodrigues<sup>1</sup>, Beatriz Freixo<sup>1</sup>, Ana Teresa Aguiar<sup>1</sup>, Andreia Coutada<sup>2</sup>, Conceição Leal<sup>2</sup>, Hálio Duarte<sup>1</sup>

<sup>1</sup>Serviço de Imagiologia, Instituto Português de Oncologia Francisco Gentil, Porto, Portugal <sup>2</sup>Serviço de Anatomia Patológica, Instituto Português de Oncologia Francisco Gentil, Porto, Portugal

#### Address

Susana L Rodrigues Serviço de Imagiologia Instituto Português de Oncologia Francisco Gentil R. Dr. António Bernardino de Almeida 865 4200-072 Porto, Portugal e-mail: sulopes1234@gmail.com

Received: 31/07/2022 Accepted: 14/11/2022 Published: 27/09/2023 © Author(s) (or their employer(s)) and ARP 2023. Re-use permitted under CC BY-NC. No commercial re-use.

### Abstract

Breast involvement in the context of systemic sarcoidosis is rare and may mimic a malignant lesion. Imaging studies contribute to the detection of breast lesions but are not useful in establishing a definitive diagnosis. Thus, malignancy must be excluded by histological biopsy in order to confirm the early diagnosis. We report a case of breast involvement by sarcoidosis in a 63-yearold woman with known systemic sarcoidosis. Mammography shows multiple oval masses with microlobulated edges and high density, without microcalcifications. Ultrasonographically, they correlated to solid hypoechoic masses with microlobulated contours, in both breasts, findings that were considered suspicious for malignancy. Breast Magnetic Resonance Imaging (MRI) showed multiple bilateral enhancing masses. Histological examination confirmed breast involvement by sarcoidosis.

#### Keywords

Breast; Sarcoidosis; Granulomatosis disease; Mammography; Ultrasound; Magnetic resonance.

#### Resumo

O envolvimento mamário no contexto de sarcoidose sistémica é raro e pode mimetizar uma lesão maligna. Os estudos de imagem contribuem para a deteção de lesões mamárias mas não são úteis no estabelecimento de um diagnóstico definitivo. Assim, a malignidade deve ser excluída por biópsia histológica de forma a confirmar precocemente o diagnóstico.

Reporta-se um caso de envolvimento mamário pela sarcoidose numa mulher de 63 anos com sarcoidose sistémica conhecida. A mamografia mostra múltiplos nódulos ovalados, de bordos microlobulados e elevada densidade, sem microcalcificações associadas. Ecograficamente correspondiam a nódulos sólidos hipoecogénicos, de contornos microlobulados, em ambas as mamas, achados que foram considerados suspeitos de malignidade. A Ressonância Magnética mamária realizada mostrou múltiplas massas bilaterais com realce de contraste endovenoso. O exame histológico confirmou o envolvimento mamário pela sarcoidose.

#### Palavras-chave

Mama; Sarcoidose; Doença granulomatosa; Mamografia; Ultrassonografia; Ressonância magnética.

## **Case Description**

A 63-year-old-female patient presented with multiple palpable nodules in both breasts. She had a clinical history of systemic sarcoidosis. Physical examination revealed multiple palpable indurations in both breasts. There were no skin changes nor nipple discharge. No axillary or supraclavicular lymphadenopathy were noted.

Bilateral mammography (Fig. 1) showed multiple oval high-density masses, with microlobulated margins, measuring less than 15 mm, in all quadrants of both breasts (BI-RADS 4b), without calcifications. Ultrasonography (Fig. 2) showed multiple oval, hypoechoic, heterogeneous solid masses with microlobulated margins, parallel to the skin (BI-RADS 4b). A left axillary lymphadenopathy was noted at ultrasound examination.

MR (Magnetic Resonance) imaging was performed to determine the extension of the disease and to identify target lesions for an accurate biopsy. MR imaging revealed several oval hypointense masses on T1 and T2-weighted images with circumscribed margins in both breasts. These masses demonstrated homogeneous enhancement on dynamic contrast-enhanced fat-saturation T1-weighted MR imaging. Kinetic curves study (Fig. 3) showed some masses with rapid initial uptake followed by a plateau phase (Type 2 curve) and others showed a rapid enhancement with washout pattern (Type 3 curve), both being considered of concern for malignancy.

Physical examination and imaging results were inconclusive to establish a definitive diagnosis and they were unable to exclude malignancy. Therefore, the patient underwent 14-Gauge core-needle ultrasound guided biopsies on both breasts, targeting the most suspicious lesions. Histological examination revealed multiple non-caseating granulomas (Fig. 4). Ziehl-Neelsen test was negative for the presence of mycobacteria, ruling out tuberculosis. The final histologic diagnosis was sarcoidosis of the breast.

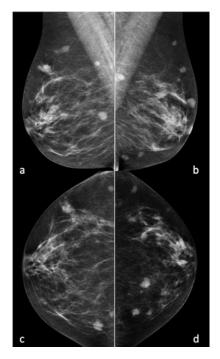


Figure 1 – Mediolateral oblique (a and b) and craniocaudal (c and d) views revealing multiple oval masses with microlobulated margins in both breasts.

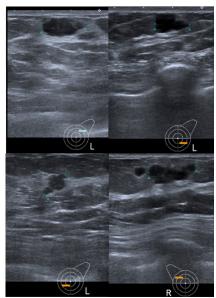


Figure 2 – Gray scale ultrasonography images showed multiple hypoechoic heterogeneous masses with microlobulated margins in all quadrants of both breasts.

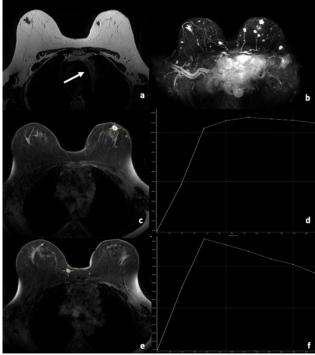
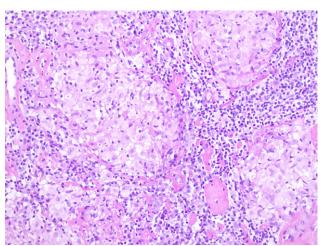


Figure 3 – Axial breast MRI. (a) T2 MR-weighted image shows bilateral hypointense masses with circumscribed margins. It also shows mediastinal lymphadenopathy (arrow) (b) MIP reformatting shows multiple enhancing masses in both breasts. T1-weighted post-contrast fat-saturation images show an enhancing mass (c) with rapid initial uptake followed by a plateau phase at the kinetic curve study (d). Post-contrast T1 fat-saturated image shows another enhancing mass (e) with rapid initial uptake followed by washout phase at the kinetic curve study (f). Both curves (type 2 (d) and 3 (f), respectively) were suspicious for malignancy.

## Discussion

Sarcoidosis is a chronic multisystemic inflammatory granulomatous disease of unknown etiology manifested by the presence of non-caseating granulomas that can be found in multiple organs and tissues, affecting predominantly the lungs and intrathoracic lymph nodes. Breast involvement by this inflammatory disease is rare and generally occurs in patients with well-known systemic involvement. Primary breast involvement is rare.<sup>1,2</sup>

Lesions often have a similar appearance to malignant masses, which constitute a diagnostic challenge. Diagnosis is based on clinical and



**Figure 4** – H+E 200x - Multiple circumscribed granulomas composed of histiocytes with abundant pink cytoplasm and indistinct cell borders ("epithelioid") with no necrosis. Fibrosis is also present.

radiological findings, and definite diagnosis requires histopathological confirmation with observation of non-caseating epithelioid granulomas<sup>2,3,4</sup> Breast sarcoidosis affects young to middle aged adults, with higher incidence in woman.<sup>5,6</sup> Clinically breast sarcoidosis presents as palpable hard masses with enlarged axillary lymph nodes, often mimicking carcinoma.<sup>2,4</sup>

Mammography, ultrasound and MRI contribute for detection of breast sarcoidosis. Since cancer is far more common than sarcoidosis of the breast, malignancy must always be considered and ruled out.<sup>3</sup>

At mammography breast sarcoidosis most often presents with irregular, ill-defined and/or spiculated masses. On ultrasound, the most common findings of breast sarcoidosis are irregular hypoechoic masses with enlarged axillary and/or intramammary lymph nodes, often considered suspicious for malignancy.<sup>24,5,7,8</sup>

MRI is useless for excluding malignancy in cases of breast sarcoidosis since these lesions often present as irregular enhancing masses, making it difficult to distinguish from carcinoma.<sup>3</sup> It has also been reported that breast sarcoidosis lesions may demonstrated rapid enhancement and washout kinetic curves, rendering the distinction from cancer very difficult because these kinetics are very similar to those observed in cases of breast carcinoma.<sup>4</sup> Sarcoidosis lesions can also show gradually enhancement over time followed by a plateau phase. Therefore, MRI has not a higher accuracy than mammography or ultrasound in excluding malignancy.<sup>5</sup>

The differential diagnosis of an irregular spiculated mass include malignancy, radial scar, fibrosis, chronic idiopathic granulomatous mastitis, foreign body reactions and fungal or tuberculosis infections. All these pathologies should be excluded.<sup>23,5,9</sup> Consequently, tissue core biopsy confirmation is required to establish a definitive and accurate diagnosis, allowing to differentiate breast sarcoidosis from carcinoma or from other immunological and infectious diseases.<sup>35,10</sup> In presence of granulomas, it is important to recognize other granulomatous disorders, such tuberculosis, Wegener's granulomatosis, or idiopathic granulomatous disease since therapeutic approaches differ.

The definitive diagnosis is based on radiological manifestations, histological confirmation, and assessment of high serum angiotensin-converting enzyme (ACE) levels, which is a specific test used to confirm the diagnosis of primary sarcoidosis.<sup>9,11</sup> The previous diagnosis of sarcoidosis does not exclude malignancy in breast lesions.

Corticotherapy is considered the first line of treatment for sarcoidosis.<sup>10,12</sup> In conclusion, breast sarcoidosis involvement represents an unusual manifestation of this systemic disease, with imaging features mimicking malignancy in all imaging modalities. Patients with known sarcoidosis of the breast with chronic masses, must always undergo core biopsy when presenting with a newly suspicious mass in the breast or axilla to exclude malignant lesions.

#### Ethical Disclosures / Divulgações Éticas

Conflicts of interest: The authors have no conflicts of interest to declare. Conflicts de interesse: Os autores declaram não possuir conflitos de interesse.

*Financing Support*: This work has not received any contribution, grant or scholarship. *Suporte financeiro*: O presente trabalho não foi suportado por nenhum

subsídio ou bolsa.

*Confidentiality of data*: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

*Confidencialidade dos dados:* Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação dos dados de doentes.

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Protecção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

#### References

1. Fitzgibbons PL, Smiley DF, Kern WH. Sarcoidosis presenting initially as breast masses: report of two cases. Hum Pathol, 1985;16:851-2.

2. Sabate J, Clotet M, Gomez A, Heras P et al. Radiologic evaluation of uncommon inflammatory and reactive breast disorders. RadioGraphics. 2005;25:411-24.

3. Isley L, Cluver A, Leddy R, Baker M. Primary sarcoid of the breast with incidental malignancy. Journal of Clinical Imaging Science. 2012;2:46.

4. Kenzel PP, Hadijuana J, Hosten N, Minguillon C, Oellinger H, Siewert C, et al. Sarcoidosis of the breast: mammographic, ultrasound, and MR findings. J Comput Assist Tomogr. 1997;21:439-41.

5. Reis J, Boavida J, Bahrami N et al. Breast sarcoidosis: clinical features, imaging, and histological findings. The Breast Journal. 2021;27:44-7.

6. F Fiorucci 1, V Conti, G Lucantoni et al. Sarcoidosis of the breast: a rare case report and a review. Eur Rev Med Pharmacol Sci. 2006;10:47-50.

7. Mailan M. Cao, Anne C. Hoyt, Lawrence W. Bassett. Mammographic signs of systemic disease. RadioGraphics. 2011;31:1085-100.

8. Gisvold JJ, Crotty T, Johnson R. Sarcoidosis presenting as spiculated breast masses. Mayo Clin Proc. 2000;75:293-5.

9. Banik S, Bishop PW, O'Brien TE. Sarcoidosis of the breast. J Clin Pathol. 1986;39:446-8.

10. Zujić P, Grebić D, Valenčić L. Chronic granulomatous inflammation of the breast as a first clinical manifestation of primary sarcoidosis. Breast care. 2015;10:51-3.

11. Studdy P, Lapworth R, Bird R. Angiotensin-converting enzyme and its clinical significance--a review. J Clin Pathol. 1983;36:938-47.

12. Jammal T, Jamilloux Y, Gerfaud-Valentin M et al. Refractory sarcoidosis: a review. Therapeutics and Clinical Risk Management. 2020;16:323-45.