Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid



Case Report

Leprosy-an unusual cause of a suspicious nodule on mammography

Christine Flis^a, Colan M. Ho-Yen^b, Alexander Polson^c, Ula Mahadeva^c, Stephen L. Walker^{d,e,*}

^a South West London Breast Screening Service, St George's Healthcare NHS Trust, Tooting, London, UK

^b Department of Cellular Pathology, St George's Healthcare NHS Trust, Tooting, London, UK

^c Department of Histopathology, Guy's and St Thomas' Hospital NHS Foundation Trust, London, UK

^d Hospital for Tropical Diseases and Department of Dermatology, University College London Hospitals NHS Foundation Trust, London, UK

^e Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

ARTICLE INFO

Article history: Received 26 July 2021 Revised 27 August 2021 Accepted 27 August 2021

ABSTRACT

A routine mammogram identified changes thought to be due to a lymph node, which was confirmed on biopsy. The lymph node was infiltrated with macrophages and showed fragmented acid-fast bacilli. The patient had been treated for leprosy some years before and was still taking thalidomide for erythema nodosum leprosum. Leprosy-associated lymphadenopathy may be identified on routine breast screening.

© 2021 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

Case report

A 48-year-old woman was recalled following mammographic screening for a new well-defined rounded density in the upper outer quadrant of the left breast (Figure 1). The abnormality in the left breast was graded M3 (indeterminate but probably benign findings). She had been assessed 8 years previously for microcalcification in the right breast, which was biopsied and shown to be benign.

A breast examination performed was unremarkable. Ultrasound showed a $5 \times 5 \times 2$ mm hypoechoic nodule (Figure 2), corresponding to the mammographic density, which was thought to represent a lymph node. The left axilla was also scanned, which showed reactive-looking lymph nodes.

An ultrasound-guided core biopsy was taken, which showed fatty breast tissue and parts of a lymph node. The lymph node had preserved architecture, but showed infiltration by macrophages with abundant clear or lightly eosinophilic cytoplasm with large cytoplasmic vacuoles (Figure 3a, b). There were no neutrophils present. In the cytoplasm and vacuoles were numerous fragmented bacilli consistent with previous treatment. The fragmented bacilli were diffusely positive on a modified Ziehl–Neelsen (ZN) stain (Wade–Fite stain) (Figure 3c; bacterial index 5; more than 100 bacilli per oil immersion field). The ZN stain was negative. A modified ZN stain is necessary to make the diagnosis, as the bacterial cell wall of *Mycobacterium leprae* is less resistant to the solvent used in a conventional ZN stain (Cassidy and Chapman, 2019). The addition of peanut oil to the xylene protects the lipid coat, resulting in retention of the stain. The findings were in keeping with treated lepromatous leprosy (LL), although it takes many years for the remnants of dead *M. leprae* to be cleared from affected tissues following successful antimicrobial therapy (Ganapati et al., 1997).

The patient had been diagnosed with lepromatous leprosy 6 years previously and had been treated with 24 monthly doses of rifampicin, ofloxacin, and minocycline. The course of the disease had been complicated by severe chronic erythema nodosum leprosum (ENL) requiring thalidomide. ENL is a multisystem, immunemediated inflammatory response to *M. leprae* antigen and is characterized by painful skin nodules, fever, and other organ involvement including lymphadenopathy (Polycarpou et al., 2017; Walker et al., 2015). The high bacterial load characteristic of lepromatous leprosy is a risk factor for ENL, which is frequently chronic (Pocaterra et al., 2006). Lymphadenopathy has been reported to occur in 14.7% of individuals (Walker et al., 2015).

Intramammary lymph nodes (IMLN) are one of the most common benign findings at screening mammography. IMLN are seen in about 5% of mammographic studies (Meyer et al., 1993). IMLN with typical features identified on mammography are considered a benign finding, but those with a small or absent hilum, thickened



^{*} Corresponding author: Stephen L. Walker, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK.

E-mail addresses: cflis@nhs.net (C. Flis), Colan.HoYen@stgeorges.nhs.uk (C.M. Ho-Yen), alexander.polson@gstt.nhs.uk (A. Polson), ula.mahadeva@gstt.nhs.uk (U. Mahadeva), Steve.walker@LSHTM.ac.uk (S.L. Walker).

https://doi.org/10.1016/j.ijid.2021.08.068

^{1201-9712/© 2021} The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)



Figure 1. Bilateral mammograms showing a well-defined rounded density (circled) in the upper outer quadrant of the left breast. Previously assessed microcalcification is noted in the right breast.



Figure 2. Ultrasound images showing a well-defined hypoechoic nodule corresponding to the mammographic abnormality, which was suspicious for a lymph node.

cortex, or ill-defined margins warrant a biopsy to exclude neoplasia (Bitencourt et al., 2019).

Leprosy has been reported to cause a granulomatous mastitis (Pandhi et al., 2012). There are no reports of suspicious mammographic changes associated with leprosy (Murray et al., 1984). However, it is well recognized in sarcoidosis, another granulomatous disease. Following close liaison between the breast, radiology, histopathology and infectious diseases services, the patient was re-

assured that the changes identified were benign and needed no further intervention.

Early detection of breast cancer in low and middle-income countries has been identified as a priority by the Global Breast Cancer Initiative (Anderson et al., 2021). Improved access to breast screening services in settings where leprosy is endemic means that incidental findings associated with the disease such as those reported here will need to be recognized.



Figure 3. (a) A lymph node containing clusters of histiocytes (arrows) (haematoxylin and eosin). (b) A higher power view of the histiocytes, many of which have a vacuolated cytoplasm (arrows) (haematoxylin and eosin). (c) Numerous fragmented bacilli are present within the cytoplasm of the histiocytes, in places forming clumps ('globi', arrows) (modified Ziehl–Neelsen stain (Wade–Fite)).

Acknowledgements

We are grateful to our patient who reviewed the manuscript and provided written informed consent for publication. Dr Nilukshi Wijesuriya, Consultant Pathologist, St George's Healthcare NHS Trust, reviewed the pathology and contributed to the interpretation.

Declarations

Funding source: The authors received no specific funding for this work. Payment of publication fees was supported by the Hospital for Tropical Diseases Charitable Fund, which had no role in the decision to publish, or in the preparation of the manuscript.

Ethical approval: No ethical approval was required.

Conflict of interest: The authors have no conflicts to declare.

References

Anderson BO, Ilbawi AM, Fidarova E, Weiderpass E, Stevens L, Abdel-Wahab M, et al. The Global Breast Cancer Initiative: a strategic collaboration to strengthen health care for non-communicable diseases. Lancet Oncol 2021;22(5):578–81.

- Bitencourt AG, Ferreira EV, Bastos DC, Sperandio VA, Graziano L, Guatelli CS, et al. Intramammary lymph nodes: normal and abnormal multimodality imaging features. Br J Radiol 2019;92(1103).
- Cassidy DP, Chapman J. An unusual cause of lymphadenopathy: when AFB staining is not enough. Blood 2019;134(1):93.
- Ganapati R, Pai VV, Shroff HJ, Gandewar K. Rate of decline in bacterial index in leprosy; observations after three different chemotherapeutic interventions. Int J Lepr Other Mycobact Dis 1997;65(2):264–6.
- Meyer JE, Ferraro FA, Frenna TH, DiPiro PJ, Denison CM. Mammographic appearance of normal intramammary lymph nodes in an atypical location. AJR Am J Roentgenol 1993;161(4):779–80.
- Murray KA, McLelland BA, Job CK. Early leprosy with perineural proliferation. Arch Dermatol 1984;120(3):360–1.
- Pandhi D, Verma P, Sharma S, Dhawan AK. Borderline-lepromatous leprosy manifesting as granulomatous mastitis. Lepr Rev 2012;83(2):202-4.
- Pocaterra L, Jain S, Reddy R, Muzaffarullah S, Torres O, Suneetha S, et al. Clinical course of erythema nodosum leprosum: an 11-year cohort study in Hyderabad, India. Am J Trop Med Hyg 2006;74(5):868–79.
- Polycarpou A, Walker SL, Lockwood DN. A Systematic Review of Immunological Studies of Erythema Nodosum Leprosum. Frontiers in immunology 2017;8:233.
- Walker SL, Balagon M, Darlong J, Doni SN, Hagge DA, Halwai V, et al. ENLIST 1: An International Multi-centre Cross-sectional Study of the Clinical Features of Erythema Nodosum Leprosum. PLoS Negl Trop Dis 2015;9(9).