CASE REPORT

Breast lumps: a rare site for rheumatoid nodules

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SUMMARY

Granulomatous mastitis (GM) of the breast is a rare benign inflammatory disease and its presentation closely mimics breast cancer. Its diagnosis is mainly based on histology and there is no consensus agreement regarding its management. We report a case of a 60-year-old woman presenting with a right breast lump associated with a history of rheumatoid arthritis and raised rheumatoid factor. Following triple assessment (history and examination, imaging and biopsy), GM was diagnosed and she was treated conservatively.

BACKGROUND

Breast lumps are a common presenting symptom in primary care; it is important to recognise the different causes of breast mass to efficiently establish an appropriate management plan and accurately rule out malignancy.¹

Granulomatous mastitis (GM) is a rare, chronic, benign inflammatory disease of the breast.² It is a difficult diagnosis to establish due to its close clinical and radiological resemblance to breast carcinoma.^{2,3} Diagnosis can only be confirmed histologically and it is a difficult condition to treat with no consensual treatment regimen, partially as a result of its unclear aetiology, pathogenesis and rarity. Fistulae and abscess formation can further complicate treatment.² Corticosteroids, methotrexate and wide local excision are all possible treatments for GM.

Autoimmune disease may contribute to the development of GM, and raised rheumatoid factor (RF) levels have been found in patients with GM, but not all studies have reproduced these findings and, thus, a direct association with RF levels is debated.⁴ Granulomas have a variety of causes, classified into: infectious, vasculitic, immunological, hypersensitive and due to leucocyte oxidase defects, chemicals and neoplasia, or, broadly, infective and non-infective.⁵ Rheumatoid arthritis (RA) is an important cause of granulomas but tuberculosis (TB) is the most common cause worldwide.⁶ The differentiation of RA from other causes of granuloma (TB and malignancy) is important, particularly due to their differing management.

We aim to describe the clinical features, radiological and histopathological findings, and management of a rheumatoid nodule in the breast with a case report.

CASE PRESENTATION

A 60-year-old woman presented to a 'one-stop' breast clinic with a breast lump in the outer quadrant of her right breast (10 o'clock position) for 2 months (figure 1). There was a history of long-standing right nipple inversion prior to this but no

Figure 1 A non-tender, firm breast lump highly suspicious of breast cancer in the upper outer quadrant of the right breast.

discharge or pain. She had no family history of breast cancer or benign breast disease. She was a non-smoker and had hormone replacement therapy, which was stopped 15 years earlier.

Her medical history included RA, asthma, pulmonary fibrosis, hypertension, hiatus hernia and idiopathic thrombocytopenic purpura (ITP). She was previously on methotrexate and folate tablets for RA, but these were discontinued 1 month earlier as a result of intolerable side effects. Her medication included an ACE inhibitor, calcium channel blocker, a proton pump inhibitor and nebulisers.

On clinical examination, a 1×1 cm, non-tender, firm, poorly mobile lump was palpable in the right outer quadrant at 10 o'clock position, with a palpable right axillary lymph node highly suspicious of breast cancer, her left breast appeared normal.

She had a mammogram and an ultrasound scan (USS), followed up with a wide-bore needle biopsy as part of triple assessment.

INVESTIGATIONS

USS of the right breast demonstrated hypoechoic, irregular lesions without vascularisation (figure 2) with acoustic shadowing measuring 10×9 and 9×7 mm, respectively, suggestive of multifocal carcinoma.

Figure 2 An ultrasound scan of the right breast with hypoechoic, non-vascularised irregular lesions.

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The mammogram revealed a moderately dense right breast with benign calcifications and mixed density but no suspicious features of malignancy.

Core biopsies revealed non-caseating, non-vasculitic granulomas including numerous neutrophil infiltrations (figure 3). An area of fibrinoid necrosis surrounded by a palisade of macrophages and scattered chronic inflammatory cells was seen. There was no evidence of Langerhans cells, epithelial hyperplasia, atypia or malignancy. A diagnosis of GM as a result of RA was made. Fine-needle (FNA) aspiration cytology of the lymph node was carried out, which revealed normal cytology.

Blood tests revealed elevated RF of 74.9 iU/mL (normal range 0–20.0), antinuclear antibodies (ANA) and anti-CCP antibodies were normal. Platelets were low, consistent with ITP. White cell count (WCC), erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) levels were normal.

A combination of normal inflammatory markers (WCC, ESR and CRP) make infectious sources unlikely as the aetiology of the GM, and the non-caseating nature histologically rules out TB. Elevated RF levels point towards RA for the cause of GM.

DIFFERENTIAL DIAGNOSIS

The most important differential diagnosis to exclude was breast carcinoma, but other diagnoses included benign breast disease such as breast cyst, fat necrosis, mastitis and fibroadenoma.

Other causes of GM were important to consider, infectious or non-infectious: TB, Wegener's granulomatosis, giant cell arteritis, duct ectasia, sarcoidosis and polyarteritis nodosa.

TREATMENT

The patient was treated conservatively.

OUTCOME AND FOLLOW-UP

The patient was followed by the rheumatologist and due to see the breast team if she developed any further problems.

DISCUSSION

GM, a rare benign inflammatory breast disease, was initially described in 1967 by Veyssiere *et al.*⁷ However, their work was further established in 1972 by Kessler and Wolloch,⁸ who described the clinical features and histology of GM. The disease is mostly seen in women of reproductive age with an average mean age of 37 years;² our patient presented at 60 years and,

Figure 3 H&E stain at ×100 magnification of a non-caseating granuloma.

while the condition can affect postmenopausal women, they are rare with reports of only 5% of patients with GM aged >60 years.⁹ A possible explanation may be the discontinuation of methotrexate in our patient causing a flare-up of RA presenting as a breast nodule.

While many factors have been implicated in the aetiology of GM: infections (eg, TB, mycotic, virus, parasitic), autoimmune conditions (eg, RA, giant cell arteritis, Wegner's granulomatosis), sarcoidosis, hyperprolactinoma, α -1 antitrypsin deficiency, diabetes mellitus and smoking, no consensus on aetiological processes exists.^{2 4 10} Autoantibody serological tests have been elucidated with GM, our patient had a raised RF level, a finding supported by Özel *et al.*² who reported raised RF levels for 6/8 patients and raised ANA levels for 2/8 patients; in contrast, Asoglu *et al.*¹¹ revealed negative RF and ANA levels in their 18-patient report. Clearly, autoantibody levels may not be useful in raising clinical suspicion for GM, but a raised level should increase suspicion in presence of a breast lump.

GM remains a challenging diagnosis to be made clinically, due to its close resemblance to breast malignancy. Patients commonly present with a painful, firm, tender, unilateral mass that can occur in any breast quadrant; it can also present with skin changes, such as skin thickness, erythema, nipple retraction, sinus and abscess formation.^{2 3} Enlarged axillary lymph nodes have been reported; a case series found 14 patients (41.7%) with enlarged nodes, a finding noted in our case study, but USS findings did not raise suspicion of malignancy.³

Radiological findings, similarly, resemble those of breast carcinoma, making diagnosis difficult. Mammography findings are variable, but, most commonly, focal asymmetric density with an ill-defined mass is noted.^{3 12} Our case supported these findings with moderate density in the right breast in addition to calcifications. The literature reports that the most common USS findings are of a single irregular hypoechoic mass, although multiple masses have also been reported; areas of heterogenic echogenicity and parenchymal deformities have been described.^{3 12} Multiple, clustered hypoechoic lesions with elevated autoantibodies would raise the possibility of GM. Our case supported these findings with non-vasculitic, irregular hypoechoic lesions, but these observations are noted in breast carcinoma. It is clear, then, that mammography and sonography lack the specificity to distinguish between GM and breast carcinoma, and it remains a diagnosis of exclusion.

The use of MRI has been looked at in assisting with the diagnosis of GM. A case series reported that MRI did not provide any further information for differentiating GM from breast carcinoma; however, only 3/19 cases had MRI and with such a small sample size, the pattern recognition can be difficult and inaccurate.¹³ It has been reported that MRI could be helpful in excluding carcinoma but, as such, that it does not play a role in the diagnosis of GM.¹⁴

Typically, a chronic inflammatory process comprising: lymphocytes, epithelioid histiocytes, plasma cells, multinucleated giant cells and, occasionally, neutrophils with microabscess formation are seen histologically in confirmed GM.^{10 15} Rheumatoid granulomas have an area of fibrinoid necrosis with homogenous giant cells, early palisading of surrounding histiocytes and substantial stromal fibrosis.¹⁶ The combination of fibrinoid necrosis and elevated RF levels favoured RA as the aetiology of the granuloma. The non-caseating nature of the granuloma and the absence of Langerhans cells ruled out TB; the absence of epithelial hyperplasia and atypia ruled out malignancy. Other infectious causes were unlikely with normal WCC, ESR and CRP levels, and no clinical signs of infection (night sweats, fever and malaise).

There is no consensus on the optimum management of GM. Some authors suggest that surgical management is the best treatment. Wide local excision (WLE) provides an exact diagnosis and treatment. However, recurrence rates after a WLE vary considerably, ranging from 5.5% to 50%.³ GM complicated with abscess formation means that WLE is not possible. Spontaneous resolution of GM abscesses, however, have occurred in 50% of cases without any treatment after a mean interval of 14.5 months.¹⁷ In cases without spontaneous resolution or fistulae, a short course of antibiotics and corticosteroids to reduce the mass prior to excision have been proposed. Corticosteroids alone have been shown to be an effective treatment in 87% of patients without a relapse.¹⁸ However, there is no consensus on the timing, duration and dosing of corticosteroid administration, and infective causes of GM must be excluded.

Conservative management has been advocated by some authors, with treatment with incision and drainage in those with non-resolving abscess formation. This prevents the need for surgery when there is a chance for recurrence.¹⁹ However, due to the close clinical and radiological resemblance of GM to breast carcinoma, histological sampling is required for diagnosis, and conservative treatment would make exclusion of carcinoma difficult.

There is no accepted optimal treatment plan for GM, but it seems WLE and corticosteroid is advocated. The rarity of the condition and the variability of clinical presentation make it difficult to standardise a treatment regimen. Further research with randomised controlled trials needs to be conducted comparing conservative management with WLE and WLE combined with different corticosteroid regimens to provide an evidence base for a GM treatment pathway.

A meta-analysis in 2008 reported a reduction in breast malignancy incidence in patients with RA compared the general population, with a standardised incidence ratio of 0.84 (95% CI 0.79 to 0.90).²⁰ A finding reported in other observational studies.²¹ However, due to the observational nature of these studies, a cause and effect relationship cannot be established. Nevertheless, it may be concluded that patients with RA are at a lower risk of breast malignancy and, consequently, GM is a more likely diagnosis in patients presenting with a breast lump.

Learning points

- Granulomatous mastitis (GM) is a rare chronic inflammatory disease in the breast, with no consensus on management.
- GM should be suspected in patients with a history of chronic inflammatory condition (such as rheumatoid arthritis) presenting with a new breast lump.
- Autoantibody levels may be helpful for raising suspicion of GM in patients with chronic inflammatory conditions and should be measured; however, definitive diagnosis is only ascertained from biopsy and histopathological assessment.
- The close clinical and radiological resemblance of GM to breast cancer indicates GM is a diagnosis of exclusion.

In conclusion, GM is a disease that closely resembles breast cancer clinically and radiologically. Patients with RA seem to be less likely in developing breast carcinoma, and GM should be suspected when a new breast lump is the presenting symptom. There is currently no consensus on treatment. A histological diagnosis is required to tailor a treatment plan to the individual, whether it is conservative or surgical.

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