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Granulomatous response within draining axillary lymph nodes in patients with Breast cancer: A series of 4 cases

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ABSTRACT

Granulomatous response associated with breast cancer and within the draining lymph nodes is an extremely rare phenomenon. In this study, we are presenting a series of 4 cases of invasive ductal carcinoma showing both caseating and noncaseating granulomas within the ipsilateral draining axillary lymph nodes. We also discussed the pathogenesis of granulomatous response and its clinicopathologic significance.

Key words: Granulomatous reaction; Invasive ductal carcinoma; Axillary lymph node

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INTRODUCTION

Granulomatous inflammation which is a form of chronic inflammation; is defined by the collection of activated macrophages, sometimes with the presence of T lymphocytes and necrosis.[1] It is an immune mechanism against infections, such as mycobacteria, some fungi and parasites, and a few nonneoplastic conditions, such as Crohn's disease, sarcoidosis, Wegener's granulomatosis.[2] Some malignancies are known to harbor granulomas, such as Hodgkin lymphoma, certain non-Hodgkin lymphomas, Seminoma of testis, Ovarian dysgerminoma, Renal cell carcinoma and few sarcomas.[3,4] A granulomatous response in the draining lymph nodes of cancers is a rare occurrence and they sometimes contain tumor cells at the center. The etiology of this phenomenon is mostly unknown but it is thought to be due to immunological response to tumor antigens.[5] In a country like India, where the incidence of mycobacterial tuberculosis is high, it is difficult to distinguish tubercular granulomas from nonspecific granulomas, especially in case of caseating granulomas.

There are few case reports and articles reporting this phenomenon due to its rare occurrence. Here we are presenting a series of 5 cases of invasive ductal carcinoma showing both caseating and noncaseating granulomas within the ipsilateral draining axillary lymph nodes with a brief discussion of the pathogenesis of granulomatous response and its clinicopathologic significance.

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MATERIALS AND METHODS

Duration and place of study: From March 2018 to March 2023, Department of Pathology, CMSDH, Kolkata. The modified radical mastectomy (MRM) specimens received in our department of pathology were subjected to thorough grossing according to common alerting protocol followed by routine tissue e-processing method. The hematoxylin and eosin-stained slides both from the breast tissue and axillary lymph nodes were examined under a microscope. The axillary lymph nodes which showed the presence of granulomas were stained with Ziehl-Neelsen (ZN) stain.

CASE PRESENTATION

Case-1

A 50-year-old female presented clinically with a hard lump in the lower quadrant at the 6 o'clock position of the left breast with multiple axillary lymph node enlargement.

We received an MRM specimen measuring 31×19×4 cm^3 in size with an axillary tail measuring 8×6×1 cm^3. The cut section shows the presence of unifocal growth measuring 4×2.5×1.5 cm^3 in size with the largest axillary lymph node measuring 2 cm in diameter.

Case-2

A 46-year-old female presented with a hard and fixed breast lump on the right side involving the supero-lateral quadrant. MRM specimen received for histopathological examination measuring 6.5×6×2 cm^3 in size just below the nipple areola with retraction of the nipple. Multiple axillary lymph nodes were identified, the largest measuring 1 cm in maximum dimension.

Case-3

A 35-year-old female presented with a hard right breast lump in the upper inner quadrant measuring 3×2×1 cm^3 in size. In addition to this another small lump measuring 1 cm in diameter is present at a 6 o'clock position. Only two enlarged lymph nodes in the axillary tail were identified, a larger one measuring 1.8 cm in diameter.

Case-4

A 62-year-old female presented with a hard lump in the left breast with the presence of skin ulceration and multiple satellite nodules on the overlying skin of the left breast. Multiple axillary lymph nodes were identified with the largest one measuring 8 cm in diameter.

RESULTS

On histopathological examination of the tumor tissue, the diagnosis was given as Invasive carcinoma of the breast (Figures 1a, 2a, 3a, 4a). Interestingly, histopathological examination of the axillary lymph nodes showed multiple enlarged epithelioid granulomas with caseous necrosis at the center (Figures 1b, 2b, 3b, 4b) along with scattered Langhans giant cells. ZN stain of the sections from the corresponding lymph nodes were negative for acid-fast bacillus (AFB) (Figures 1c, 2c, 3c, 4c). So the final diagnosis was given as a granulomatous response in the draining axillary lymph nodes of breast carcinoma.

DISCUSSION

Metastatic sites of breast cancer are primarily the bone, lungs, regional lymph nodes, liver, and brain, bone being the most common site.[6] Axillary lymph node involvement is the most important prognostic factor for patients with breast cancer and predictor of disease-free survival. Overall survival decreases with the increased number of positive lymph nodes.[7] The lymph node reaction to cancer can be the following types: (i) The development of germinal centers and plasmacytic reaction in tumor-draining nodes, (ii) Sinus histiocytosis, (iii) Granulomatous reactions, (iv) Paracortical hyperplasia, and (v) Lymphocytic depletion and nodular alteration of T-cell areas, with increased histiocytic infiltration-seen in the draining nodes of an advanced cancer.[8]

Granulomatous response within the stroma of breast carcinoma and in the draining lymph nodes is a phenomenon not often observed and diagnosed. The etiology of it is mostly unknown and in most of the cases, it is challenging to pinpoint the definitive cause. According to some authors, there is a possibility of T-cell-mediated immunological reaction to soluble tumor antigens which leads to a granulomatous response or an idiopathic foreign body reaction to the necrotic areas of the tumor. Oberman[9] was the first to report three cases of epithelioid granulomas within the stroma adjacent to invasive breast carcinomas, but axillary nodes were not involved. Daroca[10] reported three cases of medullary carcinoma of the breast with granulomas in the stroma. The granulomatous reaction is also seen in tumor-draining lymph nodes with or without accompanied by metastasis.[11,12] According to Hall et al.,[13] granulomatous response in the stroma is due to the necrotic non-viable tumor and the granulomas in draining lymph nodes may be a response to tumor debris. However, the coexistence of infectious and immune-related diseases, such as tuberculosis, sarcoidosis, and fungal infections, may also result in granulomas in association with tumors. In developing countries like India, where tuberculosis has a high incidence, it should always be excluded first, even if associated with a carcinoma.[14] Even though negative

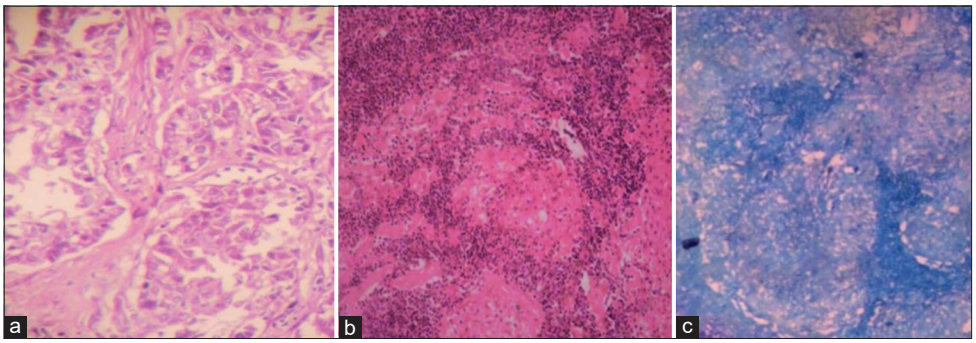

Figure 1: Features of invasive breast carcinoma (a) (H and E, ×400), caseating granuloma in axillary lymph node (b) (H and E, ×100), negative acid-fast bacilli (c) (ZN stain, ×1000)

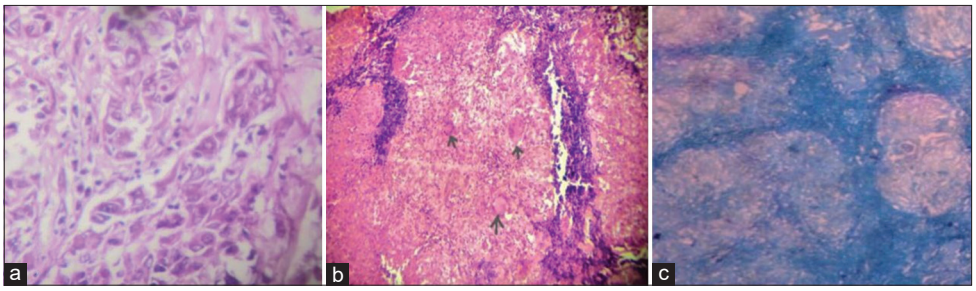

Figure 2: Features of invasive breast carcinoma (a) (H and E, ×400), caseating granuloma in axillary lymph node (b) (H and E, ×100), negative acid fast bacilli (c) (ZN stain, ×1000)

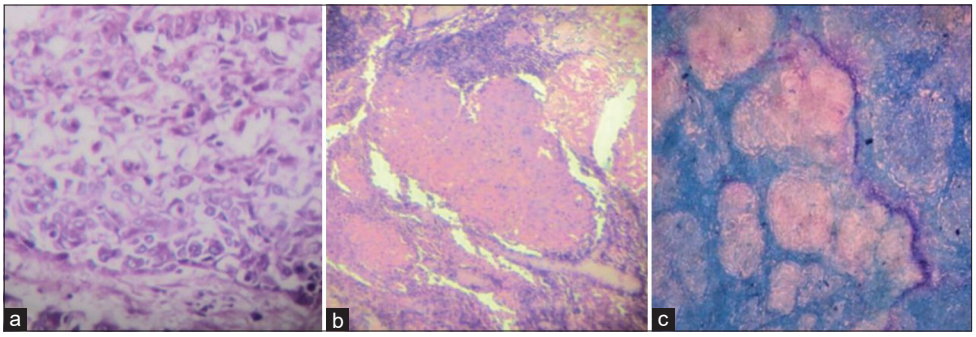

Figure 3: Features of invasive breast carcinoma (a) (H and E, ×400), caseating granuloma in axillary lymph node (b) (H and E, ×100), negative acid fast bacilli (c) (ZN stain, ×1000)

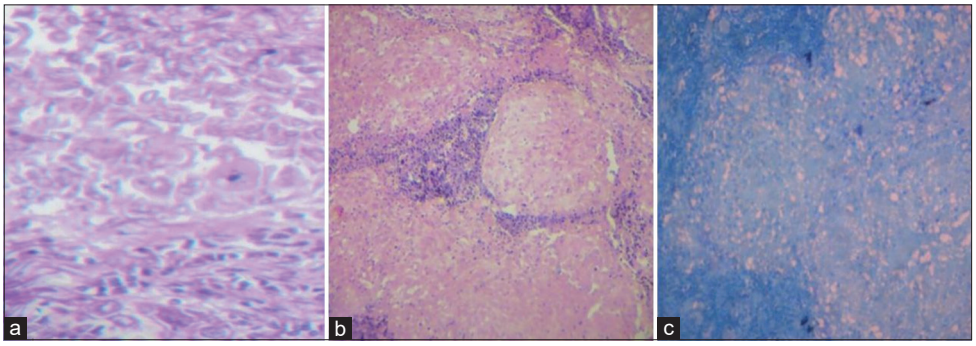

Figure 4: Features of invasive breast carcinoma (a) (H and E, ×400), caseating granuloma in axillary lymph node (b) (H and E, ×100), negative acid-fast bacilli (c) (ZN stain, ×1000)

ZN. Stain cannot rule out the presence of tuberculosis, proper history taking, clinical and radiological findings can help to reach the diagnosis.

Out of our 5 cases, all of them presented clinically with hard lumps and palpable axillary lymph nodes, one of them having skin ulceration and satellite nodules. On histopathological

examination of the breast tumor, the diagnosis was given as invasive carcinoma of the breast, and histopathological examination of the axillary lymph nodes showed multiple enlarged epithelioid granulomas with caseous necrosis at the center along with scattered Langhan's giant cells. ZN stain of those lymph nodal sections was negative for AFB. The final diagnosis was given as granulomatous response in the draining axillary lymph nodes of breast carcinoma.

CONCLUSION

Granulomatous reaction in the draining lymph node is rare but important differential diagnosis of granulomatous lymphadenitis. It is also important predictor of impending metastasis or microinvasive carcinoma. Proper history taking, clinical examination, radiological investigation and special stains (ZN, periodic acid-Schiff, Gomori methenamine silver) can help to differentiate it from other systemic and local causes of granulomatous inflammation.

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RP- Definition of intellectual content, literature survey, prepared the first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation; SM- Concept, design, manuscript preparation, editing, and manuscript revision; SC- Design of study, manuscript preparation and editing UM- Final editing of manuscript ,editing and submission of article.

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