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Coexistence of Carcinoma and Granulomatous Inflammation in Breast and Axillary Lymph Nodes: A Case Reports

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ABSTRACT

Breast carcinoma is the most common malignancy and leading cause of cancer-related deaths in women worldwide. However, breast carcinoma with an associated granulomatous inflammation in the same breast and axillary lymph nodes is unusual. This simultaneous occurrence of both diseases can complicate the neoplastic process. We present a series of four cases of invasive breast carcinoma with an associated granulomatous reaction in the breast and ipsilateral axillary lymph nodes. It is seen that axillary lymph node enlargement in cases of breast carcinoma is not always caused by metastasis of cancer. Various granulomatous lesions are Tuberculosis, sarcoidosis, brucellosis, foreign body reactions, cat scratch disease, lymphoma, and AIDS. It can also cause axillary lymphadenopathy. The presence of granulomas in association with malignancies should be further evaluated, particularly in regions with a high prevalence of Tuberculosis in developing countries like India, for the possibility of coexistent Tuberculosis, as this may alter the postoperative management and prognosis of the patient. Accurate diagnosis is crucial for downstaging breast carcinoma, identifying curable cases, and enabling effective management of both conditions.

1. Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death in women worldwide.[1] In breast carcinoma patients, the most common cause of axillary lymph node enlargement is metastasis of ipsilateral breast cancer.[2] However, finding breast carcinoma accompanied by granulomatous inflammation in the same breast or in the ipsilateral axillary lymph nodes is uncommon. Enlargement of axillary lymph nodes in such patients of breast cancer is not always due to metastasis of carcinoma. Many granulomatous lesions like Tuberculosis, sarcoidosis, brucellosis, foreign body reactions, cat scratch disease, lymphoma, and AIDS can cause axillary lymphadenopathy. Therefore, the presence of granulomas along with breast malignancy warrants further careful investigation, especially in areas with high tuberculosis prevalence, to rule out coexistent infection. Tuberculosis is quite common in India. Although the coexistence of breast carcinoma and Tuberculosis in the same patient is rare, it worsens the neoplastic process.[3, 4] Thus, accurate diagnosis is crucial for appropriate down-staging of breast carcinoma and for identifying the potentially curable cases.

2. Case presentation

Case 1

An 80-year-old woman presented with complaints of an irregular and hard mass in the left breast for a 5-month duration. The contralateral breast appeared normal, and examination of both axillae revealed a hard, mobile, and nontender node palpable in the ipsilateral axilla. She attained Menopause at the age of 48 years. She did not have any significant family history. On physical examination, a 4.5 X 3cm nontender, irregular mass, hard in consistency, adherent to the overlying skin, was present in the upper outer quadrant of the left breast. FNAC of the left breast mass showed ductal cell carcinoma. She underwent a modified radical mastectomy. The pathological specimen measured 12x6.5x4cm with an overlaying skin flap measuring 10x4.5cm. On serial sectioning, grey-white growth was identified, measuring 3.5x2.8x2cm. Microscopic examination revealed invasive ductal carcinoma, NOS type. Two of the five axillary nodes examined showed caseating granulomatous lymphadenitis and tumor cell infiltration. Acid-fast bacilli were detected on Ziehl-Nelsen staining. The patient was immediately put on ATT and received chemotherapy, followed by adjuvant radiotherapy. The patient did not complete the course for ATT and lost follow-up.

Case 2

A 56-year-old woman presented with complaints of a lump in the left breast of 4 months duration. On physical examination, a 6X4.5cm lump was palpable in the upper inner quadrant of the left breast with multiple, matted palpable nodes in the ipsilateral axilla. The contralateral breast and axilla were normal clinically as well as radiologically. She was a known case of Type-2 Diabetes Mellitus. She gave a history of breastfeeding all three children for

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more than one year each. She attained Menopause at the age of 50 years. She was clinically staged as T3N2M0 after a complete workup. She underwent a modified radical mastectomy. The pathological specimen showed a growth on gross examination measuring 4.5x3.8x3.5 cm. A total of 11 axillary lymph nodes were identified from the received specimen of MRM. A microscopic examination of multiple sections showed features of Invasive ductal carcinoma with chronic granulomatous inflammation in surrounding breast parenchyma and fibrofatty tissue. Of the eleven axillary lymph nodes identified, six showed evidence of tumor cell metastasis. Out of these positive six lymph nodes, two showed features of simultaneous chronic granulomatous lymphadenitis- possibly tubercular. The remaining five lymph nodes showed features of reactive lymphadenitis. Pathological staging was T2N2. Acid-fast bacilli was seen on ZN staining. Post-operatively, on the recommendation of their chest physician, she was started on Anti Tubercular Therapy. She also received six cycles of chemotherapy and radiotherapy to the chest wall. Presently, she is disease-free and is being followed up. Here, the coexistence of Tuberculosis with breast carcinoma led to an overestimation of tumor size and impacted the staging of the carcinoma.

Case 3

A 53-year-old woman presented with complaints of a lump in the left breast for one and a half years, and she had gone through Menopause 2 years back. No significant history or family history was elicited. On examination, the patient had a 4.5x3cm lump in the central area of the left breast. The lump was nontender, hard in consistency, and slightly mobile, with ulceration of the overlying skin. Nipple retraction was also seen. The ipsilateral axillary lymph nodes were palpable. After completing work, the patient underwent modified radical mastectomy and axillary lymph node dissection. The pathological examination of the specimen revealed a growth measuring 4.5x4.5x3cm and 28 lymph nodes identified in the separately received axillary fat. Microscopic examination showed invasive breast carcinoma. 17 out of 28 lymph nodes showed metastasis, and four lymph nodes showed features of chronic granulomatous lymphadenitis- tubercular. The oestrogen and progesterone receptors were strongly positive. The patient received adjuvant treatment with tamoxifen and ATT.

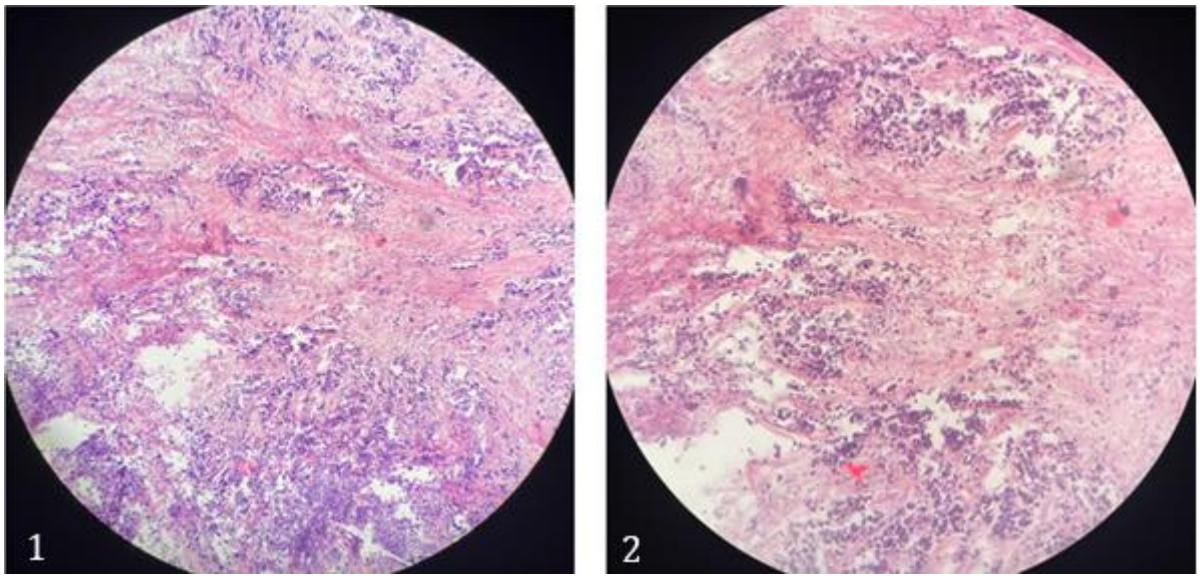
Case 4

A 42-year-old woman presented with complaints of a lump in the right breast of 6 months duration. On clinical examination, a 3.5X3cm lump that was nontender, hard in consistency, irregular margins, and slightly mobile with normal overlying skin was palpable in the upper outer quadrant of the right breast. Ipsilateral axillary lymph nodes were also palpable. The contralateral breast and axilla were unremarkable on examination. She breastfed his children for one and a half years to two years. She gave a history of normal menstrual cycles. Family history was insignificant. There was no history of Tuberculosis or its contact. She underwent a core needle breast biopsy and was diagnosed with invasive ductal carcinoma of the breast. After a complete workup, she was operated on for modified radical mastectomy with axillary lymph node dissection and was clinically staged as T2N1M0. The gross examination of the MRM specimen showed a growth measuring 3.8x3.5x2cm. Six lymph nodes were identified in the attached axillary fat. Histopathological examination from growth showed invasive duct carcinoma, NOS type. All six lymph nodes were free from tumor infiltration. However, four nodes showed features of tubercular granulomatous lymphadenitis comprising caseating granulomatous aggregates of epithelioid cells and Langhans' type of giant cells.

The remaining two lymph nodes showed features of reactive hyperplasia. So, the pathological staging of the MRM specimen was T2N0. ZN Staining for Acid-Fast Bacilli was positive. On IHC, the tumor was Her2neu positive and ER, PR negative. She was started on antitubercular therapy (ATT) along with six cycles of adjuvant chemotherapy followed by adjuvant radiotherapy. She was doing well on follow-up. In this case, if TB in the ipsilateral axilla was diagnosed preoperatively, the clinical staging of breast carcinoma would be T2N0M0 instead of T2N1M0, and the patient would have been offered breast conservative surgery considering the young age of the patient. However, clinical over-staging led to the loss of this opportunity.

Table 1. Shows the microscopic features of all four cases.

Case	Breast	Ipsilateral Axillary Lymph Nodes
Case 1	Invasive ductal carcinoma, NOS type	2/5 lymph nodes showed caseating granulomatous lesions along with infiltration by tumor cells.
Case 2	Invasive ductal carcinoma with chronic granulomatous inflammation in surrounding breast parenchyma and fibrofatty tissue	6/11 lymph nodes showed evidence of metastasis of tumor cells. Out of these positive six lymph nodes, 2 showed features of simultaneous chronic granulomatous lymphadenitis- possibly tubercular.
Case 3	Invasive ductal carcinoma, NOS type	17/28 lymph nodes showed metastasis, and four lymph nodes showed features of chronic granulomatous lymphadenitis- tubercular.
Case 4	Invasive ductal carcinoma, NOS type	All 6 lymph nodes were free from tumor infiltration, but four nodes showed features of tubercular granulomatous lymphadenitis, comprising caseating granulomatous aggregates of epithelioid cells and Langhans' type of giant cells.



Figs. 1 and 2. Invasive breast carcinoma at 100X and 200X respectively.

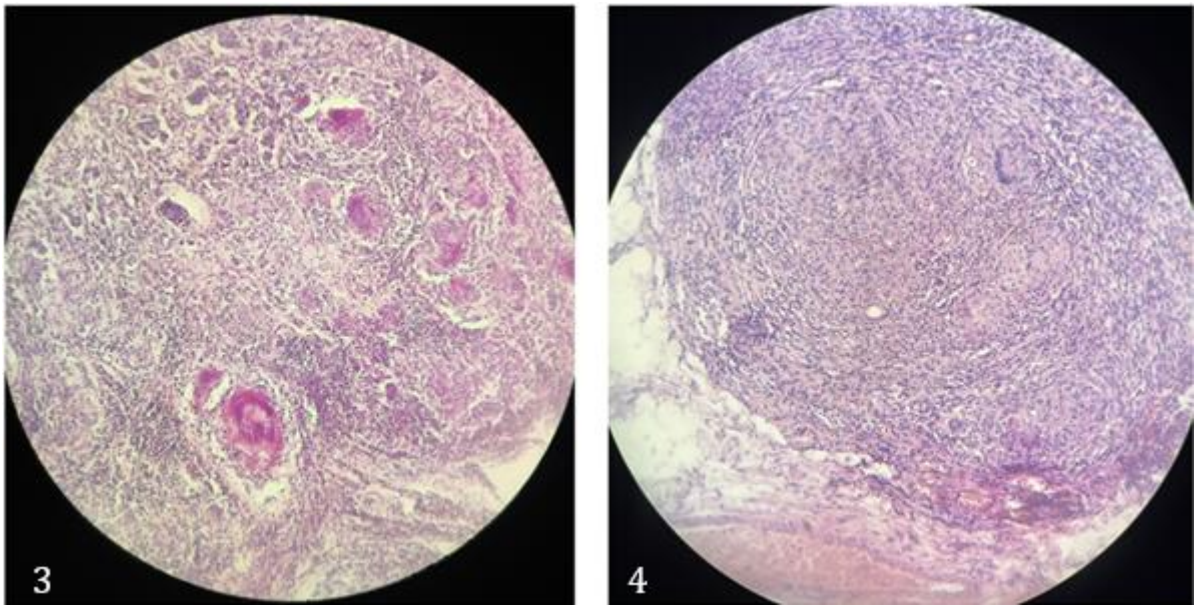


Fig. 3. Axillary lymph node showing coexistence of tumor infiltration and granulomatous aggregate 100X. Fig. 4. Axillary lymph node showing tubercular granulomatous aggregate 100X.

3. Discussion

Tuberculosis infecting organ systems other than the lungs is defined as extrapulmonary Tuberculosis. Breast tuberculosis is also a type of extrapulmonary TB (EPTB). The first documented case of breast tuberculosis was reported by Sir Astley Cooper, who referred to it as "scrofulous swelling of the bosom."[5] The incidence is estimated to be 0.1% of breast diseases in developed countries, but it rises to 3% to 4% in countries where Tuberculosis is endemic, such as India and Africa.[6] An American pathologist, Warthin, first reported the simultaneous occurrence of breast carcinoma and Tuberculosis in the same patient in year 1899.[7] Review of the literature showed that the first ever large study examining the coexistence of breast carcinoma and Tuberculosis was published by Kaplan et al. in 1974.[8] In this study total 14,742 cases of breast carcinoma were examined for breast TB and 28 cases were found to be simultaneously infected with Tuberculosis; prevalence was calculated as 19/10,000. However, there was no discussion about the same coexistence of carcinoma and Tuberculosis in the ipsilateral axillary lymph nodes. For surgeons, the breast and axilla are considered inseparable parts of a whole. This perspective is rooted in the high rates of axillary metastases in breast cancer. Therefore, the coexistence of carcinoma and Tuberculosis should be carefully evaluated in both breast and axilla. This study included all four cases with this fundamental concept in focus. Various permutations and combinations of possible clinical situations can be witnessed in the coexistence of breast TB and carcinoma, listed as breast carcinoma and tuberculous mastitis, carcinoma in the breast with axillary tuberculous adenitis, carcinoma in the breast with axillary tuberculous adenitis and metastatic tumour infiltration, and carcinoma in the breast with both tuberculous mastitis and axillary tuberculous adenitis. Simultaneous occurrence of carcinoma and Tuberculosis can affect the neoplastic process

of breast carcinoma in many ways; first, it can result in over-estimation of tumor size, which can diminish the chances for breast conservation along with over-staging. Second, the palpable lymph nodes resulting from tubercular lymphadenitis may contribute to the overstaging by considering nodal involvement. Additionally, underlying breast tuberculosis can lead to potential complications in operated cases, such as sinus formation, fistulas, or chronic wound infections at the surgical site. Soualili et al.[9] documented a similar case of nonspecific invasive breast carcinoma in a 39-year-old woman, where axillary tuberculous lymphadenitis was found alongside lymph node metastases from the carcinoma, without any evidence of primary breast tuberculosis. Pamateck et al.[10] presented two cases of nonspecific infiltrating breast carcinoma in women aged 35 and 55, where Tuberculosis was discovered in the axillary lymph nodes alongside metastases. There is no established causal relationship between Tuberculosis of the breast and breast cancer, and no scientific evidence suggests that TB has carcinogenic properties or increases the risk of cancer development at any bodily site. Diagnosing the coexistence of Tuberculosis and carcinoma in the breast is tricky because of the overlapping symptoms of weight loss and malaise, which can be mistakenly attributed to breast cancer. Furthermore, radiological imaging of tubercular mastitis often presents nonspecific features that can mimic various breast lesions, including both benign and malignant conditions, making accurate diagnosis challenging. Farrokh et al.[11] concluded in their case report that the coexistence of breast carcinoma and tuberculosis mastitis is extremely rare, but it can present significant challenges in diagnosis and treatment. Clinical symptoms and imaging results often do not differentiate between breast cancer and tuberculosis mastitis, making histological examination crucial for an accurate diagnosis and effective patient management. Some authors linked this coexistence with COVID-19 as cancer patients were a particularly vulnerable group during the COVID-19 crisis, making them more susceptible to various infectious diseases throughout the pandemic. Ramamoorthy et al.[12] recommended that during the COVID-19 pandemic, there is a heightened risk of both latent and active TB. Additionally, immunocompromised individuals with cancer were at an increased risk of TB flare-ups. The simultaneous occurrence of two diseases is uncommon, even in areas with high TB incidence. However, the pandemic has led to a surge in cases involving both conditions. The delay in chemotherapy during this time has contributed to a rise in infectious diseases, including TB. Treating Tuberculosis and cancer of breast simultaneously poses significant challenges in developing countries, primarily due to poor treatment adherence. Two differing treatment approaches for co-existing breast cancer and Tuberculosis have been proposed; Alzaraa et al. suggest performing mastectomy for operable breast cancer, followed by 18 months of anti-tuberculosis (TB) therapy.[13] In contrast, Broughton et al. recommend initiating chemotherapy only after 4 weeks of anti-TB treatment, citing concerns about chemotherapy's immunosuppressive effects.[14] There is no established guideline on when to initiate and how long to administer Anti-Tuberculosis Treatment (ATT) in conjunction with chemotherapy, as insufficient case studies limit existing research. The treatment approach depends on the breast cancer's stage: If operable, radical mastectomy is recommended, followed by 18 months of postoperative antitubercular chemotherapy; if incurable, palliative care combined with antitubercular medication is advised. However, treating co-existing breast cancer and Tuberculosis poses challenges, particularly in developing countries like India, where adherence to dual treatment regimens can be very difficult.

4. Conclusion

It is concluded that in case of coexistence of breast carcinoma and granulomatous inflammation in breast tissue or/and axillary lymph nodes, an accurate diagnosis aids in both down-staging breast carcinoma and identifying potentially curable diseases like Tuberculosis. Axillary lymph node enlargement in breast carcinoma can be attributed to causes other than cancer metastasis. The presence of granulomas along with breast malignancy necessitates meticulous evaluation to consider the potential coexistence of Tuberculosis, which could impact postoperative management and prognosis. Tuberculosis and breast carcinoma share similar clinical and radiological presentations. Confirming the diagnosis relies heavily on histological examination. A high index of suspicion is required for diagnosis, simultaneous treatment of both conditions, and patient counseling to ensure adherence to treatment protocols.

Conflict of Interest

The authors declared that there is no conflict of interest.

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