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IP Journal of Diagnostic Pathology and Oncology

Journal homepage: https://www.jdpo.org/

Case Report

Metaplastic squamous cell carcinoma caricaturing as tuberculous mastitis-A vicissitude of clinical diagnostic misadventure

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ARTICLE INFO

Article history:
Received 29-04-2023
Accepted 18-05-2023
Available online 22-06-2023

Keywords:
Tuberculous mastitis
Mimic of tuberculous mastitis
Metaplastic
Squamous cell carcinoma
Ulceroproliferative growth of breast

ABSTRACT

Background: Tuberculous mastitis and invasive breast cancers are known to co-exist or occur in the breast independently of each other, albeit the former being less common in developed countries. Tuberculous mastitis with its clinical presentation and morphological features can caricature invasive breast carcinoma. The overlapping features of tuberculous mastitis and metaplastic squamous cell carcinoma often lead to, if no due clinical diligence and discretion is used, bewildering misinterpretation with the vicissitude of diagnostic implications of tuberculous mastitis ensuing catastrophic and perilous ramifications.

Case Report: A 42-year-old woman presented with exophytic growth with extensive areas of ulceration. Clinically, the lesion was diagnosed as disseminated tuberculous mastitis based on clinical and morphological features, which was surgically resected. On histological examination, the lesion was diagnosed as invasive metaplastic squamous cell carcinoma.

Conclusion: The case being presented here displays the vagary involved in clinical diagnosis of tuberculous mastitis inasmuch as it often shares clinical and morphological features with a devastatingly perilous variant of invasive duct carcinoma, metaplastic squamous cell carcinoma, the inadvertent eschewing of or misapprehending of which may engender devastating prognostic implications.

1. Introduction

The adult female breasts are a site of various inflammatory conditions and neoplastic conditions. Infectious inflammatory conditions are common including tuberculous mastitis, the latter being very rare in Western countries and of late, in developing countries. Tuberculous mastitis is not less frequent in developing countries of Africa and Asia with the overall incidence of tuberculous mastitis among surgically treated cases being 0.025 per cent in developed countries to four per cent in developing countries.[1] In India, tuberculous mastitis is still prevalent, though not frequent, and its reported incidence in India is three per cent.[2] Tuberculous mastitis presents clinically and morphologically in various forms: nodular, disseminated, sclerosing, and generalized miliary form with an additional variant being tuberculous mastitis obliterans.[3] All morphological forms culminate in caseating necrosis and abscess formation with focal ulceration of the overlying skin and formation of sinuses except sclerosing variant of tuberculous mastitis.[1,4]

When tuberculous mastitis presents as an extensive ulceroproliferative growth with or without sinus formation to emulate morphologically invasive breast carcinoma, the diagnosis of such proliferative lesion with extensive ulceration carries an intrinsic risk of over diagnosis of a non-existent malignancy. The converse could also be veritable where an invasive breast carcinoma may caricature itself

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https://doi.org/10.18231/j.jdpo.2023.021

clinically and morphologically as tuberculous mastitis.[5]

Invasive breast carcinoma manifests in various morphological patterns with variation in their biological behavior. Based on this invasive breast carcinoma is categorized into invasive duct carcinoma, no specific type or not otherwise specified [NOS], and invasive breast carcinoma, special variants or special types.[6–9] The special variants of invasive duct carcinoma are unique group of malignant lesions of breast, which not display characteristically different morphological patterns but also have extremes of prognostic implications with some having favorable clinical outcome, while others carrying very poor prognostic outlook.[7]

One of the rare variants of special types of invasive duct carcinoma is metaplastic squamous cell carcinoma of breast. Metaplastic squamous cell carcinoma constitutes 0.25-1 per cent of invasive duct carcinoma of breast, which is an aggressive tumor with a prognosis worse than triple negative invasive duct carcinoma of breast.[9–13] In the present study, a case report of metaplastic squamous cell carcinoma of breast carcinoma which masqueraded as tuberculous mastitis is being presented.

2. Case Report

A 42-year-old female presented with a large ulcerated fun gating mass in the lower and outer quadrant of the left breast, which measured 12x10 cm; the nipple and areola were not identifiable and were obscured completely by the ulceroproliferative lesion. The ulceroproliferative lesion was diffusely reddish and fleshy in appearance as it was covered with hemorrhagic material. On further fixation, the lesion appeared as a grayish-white and fleshy ulcerated fungating mass with thickened margins.

On general physical examination, the right breast was clinically unremarkable. Additional important clinical findings were bilateral axillary as also generalized lymphadenopathy.

Moreover, the general clinical history of the patient included loss of appetite and loss of weight since a few months. Dyspnea on exertion and dry cough were the latest clinical features for one month. Significant past history included the patient having generalized lymphadenopathy two years back, the High-Resolution Computed Tomography (HRCT) of which revealed retroperitoneal necrotizing lymphadenitis suggestive of tuberculosis. Axillary lymph node excision biopsy had revealed predominately necrotic granulomatous lesion, albeit confirmation of tuberculosis was not by other sensitive ancillary studies such as molecular not made. She was treated with anti-tuberculous drugs for a year. She remained unresponsive to the treatment, and during this period, she noticed a nodular lump in the upper outer quadrant of the left breast which gradually enlarged to become an ulcerated fungating growth involving most of the left breast to attain the present size.

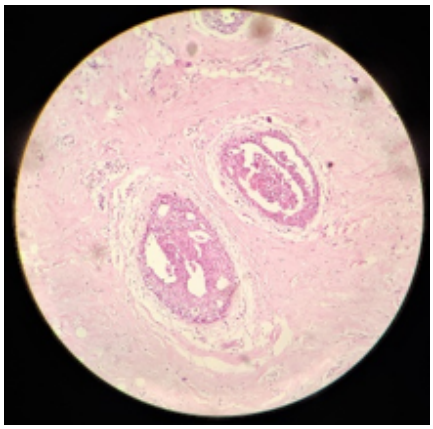

Fig. 1: 40X, H & E stain Photomicrograph showing ductal epithelial hyperplasia with diffuse squamous metaplasia.

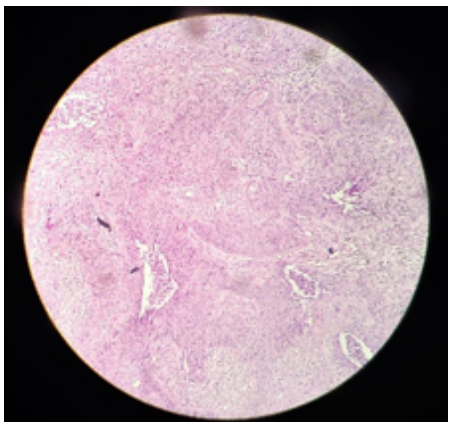

Fig. 2: 40X, H & E stain Photomicrograph showing nests and cords of squamous epithelial with moderate to severe dysplastic changes interspersed by delicate stromal hyperplasia with focal myxoid change**.**

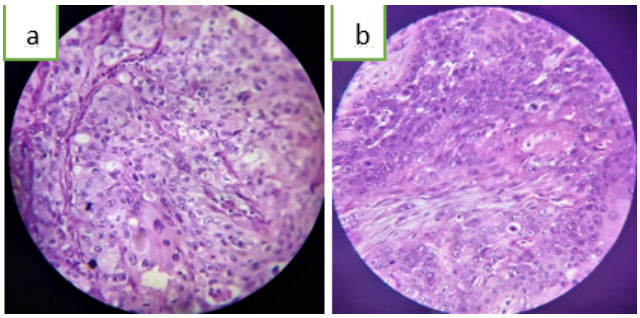

Fig. 3: a,b: 40X, H & E stain Photomicrograph showing sheets and nests of squamous epithelial cells displaying moderate to marked nuclear atypia and increased mitotic activity including few atypical mitosis.

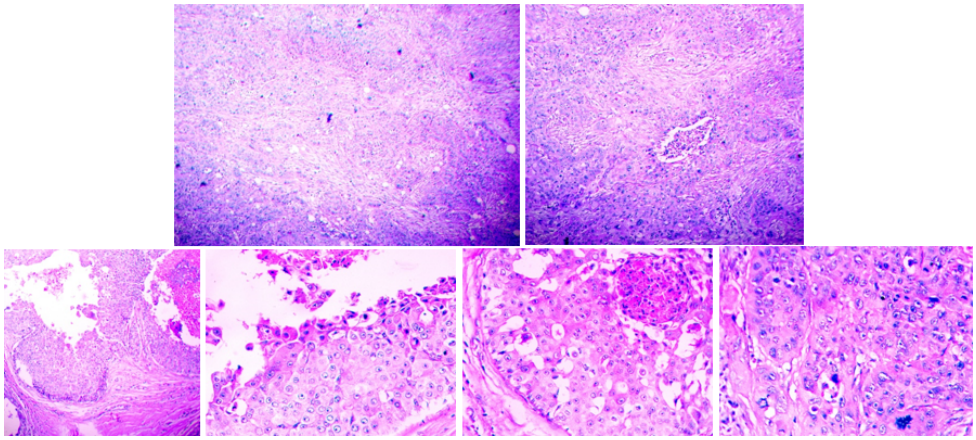

Fig. 4: 20X:photomicrograph showing nests and sheets of moderately to poorly differentiated squamous cells with scattered bizzare nuclei with increased mitotic activity with focal areas of necrosis. (First row images are 20X magnification, second row images are 40X magnification.)

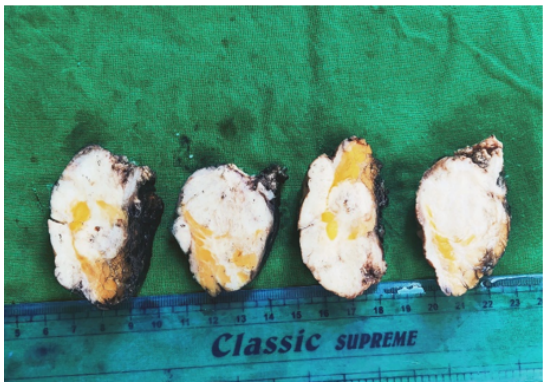

Fig. 5: Gross photomicrograph of cut section of the lesion, pearly white and firm.

Fig. 6: Clinical photomicrograph showing extensive ulcero - proliferative lesion of the breast.

Fine Needle Aspiration Cytology (FNAC) study of cervical lymph nodes revealed non-specific reactive lymphadenopathy. Molecular study such as CB-NAAT of samples obtained through fine needle aspiration of lymph node was negative for mycobacterium tuberculosis.

Other ancillary screening tests for tuberculosis such as Mantoux test and sputum Acid-fast Bacilli (AFB) did not show evidence of extrapulmonary or pulmonary tuberculosis. X-ray chest showed mild pleural effusion.

With considerable cumulative evidence of past history, clinical presentation, and imaging studies, the ulcero-proliferative lesion of the breast was diagnosed as tuberculous mastitis. The left breast along with the mass was excised by modified mastectomy and the excised specimen was sent Histopathology laboratory of Pathology department of a tertiary care teaching hospital in Dahanu. The specimen of mastectomy was not accompanied by axillary nodes. On Gross examination, it was apparently reddish and fleshy when it was received. After further fixation, it was ulceroproliferative lesion which was gray-white to focally pearly white and nodular; firm with irregular thickened and slightly rolled out margins. The nipple and areola were not discernible since the ulcerated areas involved most of the breast tissue sparing only thin marginal areas of the breast. Microscopically, the lesion consists of sheets and nests of squamous epithelial cells with highly pleomorphic nuclei with brisk mitotic activities. Focal areas of necrosis were also noted. No evidence of neoplastic cells forming ductal structures or the presence of intraductal carcinoma is noted, though some areas show intraductal squamous metaplasia with mild hyperplastic changes. Lymphovascular and perineural invasion was also noted Thus, a diagnosis of metaplastic squamous cell carcinoma of breast (Grade III) was arrived at. All the resected margins were involved by tumour infiltration except the inferior margin. Depending on the

size of the tumour, grade, and undetermined status of lymph node and distant metastasis, American Joint Committee on Cancer (AJCC) staging of the tumour was assigned as per College of American Pathologists (CAP) protocol: pTNM stage pT4apNxpMx (AJCC manual, 8^{th} edition, 2018). The patient was referred to a higher center for further advanced clinical management.

3. Discussion

Adult female breasts are a site of varied neoplastic, infectious and inflammatory lesions. Tuberculosis of breast is one of the rare infectious diseases, which is common in certain endemic areas of Asia and Africa, while it is rare in Western countries with an incidence varying from 0.25 per cent in developed countries to four per cent in developing countries.[1–4] In India, it is still prevalent with the incidence being around three per cent. Granulomatous mastitis (GM) also referred to as granulomatous lobular mastitis (GLM) as it often affects lobular regions, Sarcoidosis, fungal infections such as actinomycosis, parasitic infections such as filariasis, Wegener's granulomatosis, fat necrosis and duct ectasia are differential diagnoses of tuberculosis mastitis.[1–4] Demonstration of Acid-fast bacilli in tissue sections is an essential requisite for the diagnosis of tuberculous mastitis.Invasive carcinoma of breast includes the largest group of malignant tumours of breast, which are a phenotypically heterogenous group of neoplastic lesions that are divided into two categories:[6–9] Invasive carcinoma, not other specified, and invasive carcinoma, special types. One of the rare special types of invasive carcinomas of breast is metaplastic carcinoma of breast, which consists of mixed tumours of epithelial and mesenchymal elements and pure epithelial malignant tumours. Metaplastic squamous cell carcinoma is a very rare variant of metaplastic carcinoma of the breast.[6]

The diagnosis of metaplastic squamous cell carcinoma is an arduous task which is guided by certain pathological criteria for unequivocal diagnosis of squamous cell carcinoma. These pathological criteria include the following:[9,14]

1. Origin of the tumour must not be from on the skin, nipple or adnexal structures of the skin.
2. More than 90 per cent of the tumour must be composed of squamous cell carcinoma.
3. No other neoplastic invasive elements such as ductal or mesenchymal, can be present in the entire sample.
4. Squamous cell carcinoma at other primary sites must be ruled out. Some of the common primary sites of squamous cell carcinoma are lung, larynx, cervix and urinary bladder.[14]

Metaplastic squamous cell carcinoma of breast is a rare variant of invasive duct carcinoma and accounts for one per cent of invasive duct carcinomas of breast.[9–11] Metaplastic squamous cell carcinoma can be of different histological variants—large cell non-keratinizing, keratinizing, acantholytic and spindle cell carcinoma.

The case being presented here is quite interesting in the fact that it was clinically diagnosed as tuberculous mastitis in the backdrop of strongly accessible clinical evidence insofar as the patient had tuberculous lymphadenitis of multiple groups of lymph nodes and was already on anti-tuberculous therapy. It was followed by a modified radical mastectomy of breast minus the axillary lymph nodes. Histopathological examination of the specimen led to the diagnosis of metaplastic squamous cell carcinoma of breast.

Many case reports of metaplastic carcinoma of breast, including pure squamous cell carcinoma have been published in English Medical literature. Luciana Graziano et al[9] published a case of metaplastic carcinoma in a 59-year-old female. Delphine Uwamariya et al [reported a case of metaplastic carcinoma with squamous differentiation. Ana Alicia Tejera Hernández et al reported two cases of metaplastic squamous cell carcinoma in their retrospective study.[12] Ahmed Alzaraa and Neha Dalal[5] and Raveendran Vishnu et al[13] in their separate studies reported the co-existence of invasive duct carcinoma and tuberculous mastitis and the co-existence metaplastic squamous cell carcinoma and tuberculous axillary lymphadenopathy, respectively. All these published reports suggest that metaplastic squamous cell carcinoma occur generally in women between 30-80 years of age, and presents as a palpable nodular mass with rapid growth involving axillary infiltration. Invasive duct carcinomas including metaplastic squamous cell carcinoma often mimic tuberculous mastitis since the clinical and presenting morphological features often overlap and are indistinguishable.

4. Conclusion

Tuberculous mastitis rarely occurs in the breast even in countries where tuberculosis is still endemic. When it is present with one of its distinctive morphologic patterns of presentation as a nodular mass it may caricature invasive metaplastic carcinoma of breast including squamous cell carcinoma with its characteristic phenotypic features of nodular growth progressing to diffusely ulcero-proliferative mass as in the present case, the diagnosis of such lesions becomes vexatious and challenging and if not diligent with strong clinical history and compelling clinical evidence it might lead to the vicissitude of clinical diagnostic misfortune. Histopathological examination remains the quintessential mainstay and gold standard of diagnosis, which helped in rescinding the clinical diagnosis of tuberculous mastitis for an unequivocal diagnosis. Active and effective interaction between clinicians, radiologists and pathologists is incumbent for a veritable and incontrovertible diagnosis and thereby clinical management of such formidable, intricate lesions.

5. Conflict of Interest

There are no conflicts of interest in this article.

6. Source of Funding

None.

References

1. Bani-Hani KE, Yaghan RJ, Matalka I, Mazahreh TS. Tuberculous mastitis: a disease not to be forgotten. *Int J Tuberc Lung Dis*. 2005;9(8):920–5.
2. Tauro LF, Martis JS, George C, Kamath A, Lobo G, Hegde B, et al. Tuberculous mastitis presenting as breast abscess. *Oman Med J*. 2011;26(1):53–5.
3. Venyo AKG, Venyo LKG, Khan AN. Tuberculosis of the breast: A review of the literature. *J Med Sci Technol*. 2015;4(2):178–91.
4. Puneet, Tiwary S, Ragini R, Singh S, Gupta S, Shukla V, et al. Breast Tuberculosis: Still Common In India. *Internet J Trop Med*. 2004;2(2):1–4.
5. Alzaraa A, Dalal N. Coexistence of carcinoma and tuberculosis in one breast". *World J Surg Oncol*. 2008;6:29. doi:10.1186/1477-7819-6-29.
6. Tavassoli FA, Devilee P. Pathology and Genetics: Tumours of the Breast and Female Genital Organs", WHO Classification of Tumours series. Lyon, France: IARC Press; 2003.
7. Mills SE, Carter D, Greenson JK, Reuter VE, Stoler M. Sternberg's Diagnostic Surgical Pathology. 5th Edn. Lippincott Williams & Wilkins; 2010.
8. Rosai JR, editor. Ackerman's surgical pathology. 10th Edn. New York, Mosby: Elsevier; 2011.
9. Graziano L, Filho PG, Bitencourt AGV, Soto DB, Hiro A, Nunes CC, et al. Metaplastic squamous cell carcinoma of the breast: A case report and literature review" 1. *Rev Assoc Med Bras*. 2016;62(7):618–21. doi:10.1590/1806-9282.62.07.618.
10. Flikweert ER, Hofstee M, Liem S. Squamous cell carcinoma of the breast: a case report. *World J Surg Oncol*. 2008;6:135. doi:10.1186/1477-7819-6-135.
11. Uwamariya D, Nyampinga C, Nsenguwera AY, Rugwizangoga B. Metaplastic Carcinoma of the Breast with Squamous Differentiation: A Case Report:from the University Teaching Hospital of Kigali (CHUK), Rwanda. *Case Rep Pathol*. 2020;p. 4806342. doi:10.1155/2020/4806342.
12. Hennessy BT, Krishnamurthy S, Giordano S, Buchholz TA, Kau SW, Duan Z, et al. Squamous cell carcinoma of the breast". *J Clin Oncol*. 2005;23(31):7827–35.
13. Vishnu R, Gurushankari B, Balamourougan K, Elamurugan TP, Sureshkumar S, Muthukumarassamy R, et al. Coexistence of metaplastic carcinoma of the breast with tuberculous axillary lymphadenopathy: A rare occurrence". *Int J Adv Med Health Res*. 2020;7:35–8.
14. Peter RP, Hoda S. Rosen's Breast Pathology. 4th Edn. Philadelphia. Lippincott, Williams and Wilkins; 2014.

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Cite this article: Pardeshi KG, Basalingappa HM, Kadam SA, Sampat N, Bhonsle V, Valand AG. Metaplastic squamous cell carcinoma caricaturing as tuberculous mastitis-A vicissitude of clinical diagnostic misadventure. *IP J Diagn Pathol Oncol* 2023;8(2):97-101.