ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 7 | July - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

METAPLASTIC CARCINOMA OF BREAST MASQUERADING AS ANGIOSARCOMA- A CASE REPORT WITH REVIEW OF LITERATURE

Pathology

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ABSTRACT

Metaplastic carcinoma of the breast (MCB) is a rare but aggressive type of breast cancer that is characterised by the differentiation of neoplastic epithelium into squamous cells and mesenchymal- looking elements (spindle cells, cartilage, bone, rhabdomyoma). The differential diagnosis depends on the metaplastic component. Here we report a case of a 60-year-old female, who presented with a clinically malignant right breast lump of eight months duration. Histomorphology suggested angiosarcoma. But immunohistochemistry proved that to be metaplastic carcinoma –spindle cell type.

KEYWORDS

Metaplastic Carcinoma, Rare Breast Malignancy, Breast Carcinoma, Immunohistochemistry, Triple-negative

INTRODUCTION:

Metaplastic carcinoma represents 0.25-1% of breast cancers. They present in women older than 50 years of age. MCBs are a heterogeneous group of malignancies that can exhibit multiple morphologies. The differential diagnosis is broad as their glandular component may be partially or replaced by a nonglandular component(s), which may differentiate along the squamous, spindle, chondroid, and other lineages[1]. Immunohistochemical evidence of carcinomatous differentiation is extremely helpful in the differential diagnosis when the tumour has predominant spindle cell morphology with no identifiable epithelial component as in our case. The tumour shows rapid growth, and they are usually triple-negative and has limited therapeutic options[2].

CASE REPORT:

A 60-year-old lady presented with a rapidly growing lump in the right breast of 8 months duration. There was no nipple discharge. There was no history of any fever, loss of appetite or significant weight loss /bone pains. She has breastfed two children. There was no history of any hormone intake in the past. She attained menopause at 48yrs. There was no history of any comorbidities or surgeries. There was no family history of any malignancy.

Physical examination showed a well defined, firm, partially mobile fungating mass in the subareolar region involving the nipple and areolar complex, measuring 8 x 10 cms in the right breast (Figure 1). The surrounding skin showed mild oedema and redness. On palpation, the mass was tender and firm. The lesion was not attached to the chest wall. There were no lymph nodes palpable in the right axilla and supraclavicular region. Examination of the left breast and axilla were unremarkable. Routine haemogram, peripheral smear, ESR, electrolytes, renal function test, liver function test, ECG were all within normal limits

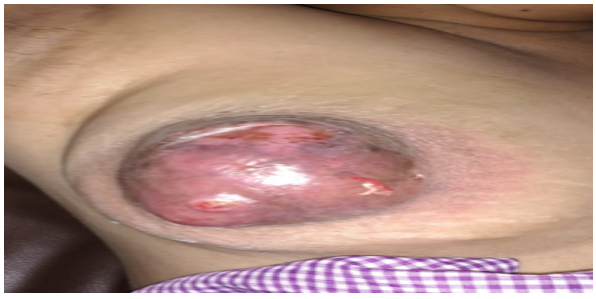

Figure 1- Clinical Image Of The Right Breast Lump

USG report suggested a well defined heterogeneously hyperechoic lesion in the right breast involving nipple-areola, suggestive of neoplastic aetiology, BIRADS 4 B. CT scan showed lesion involving the right breast with right axillary lymphadenopathy. Chest Xray & CT showed no lung /bony lesions. Fine needle aspiration showed adequate cellularity and was diagnosed as duct carcinoma. A core needle biopsy was done and was reported as poorly differentiated malignancy. The patient underwent modified radical mastectomy under general anaesthesia. There was no intraoperative or postoperative complication.

We received the right Modified Radical Mastectomy specimen measuring 25 x 12 x 8.5cm. External examination showed an ellipse of skin measuring 15 x 9 cm. A large ulcerative growth measuring 7 x 5.5 cms was seen involving the nipple and areola complex. Cut sections showed an ill-defined infiltrating grey white tumour measuring 7.5 x 7 x 6 cms with large areas of haemorrhage & necrosis. Surrounding breast parenchyma showed extensive areas of fibrotic thickening (Figure 2). The overlying skin was stretched over the tumour, shiny and ulcerated. The deep margin was free. A total of 23 lymph nodes were isolated from the axillary tail; none appeared grossly involved.

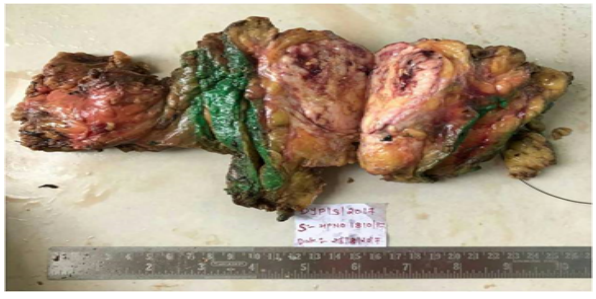

Figure 2 Gross Specimen, Cut Section

On microscopy, sections showed an infiltrating neoplasm comprising of pleomorphic oval to spindle cells in short fascicles, lining cleft like spaces, and in patternless discohesive sheets with large areas of haemorrhage and necrosis. (Figure 3) Individual tumour cells were highly pleomorphic, with high N:C ratio, hyperchromatic nuclei and scant cytoplasm. In areas, cells revealed intracytoplasmic lumina with RBCs.(Figure 4) Mitosis was 3-4 /HPF with the presence of atypical mitosis. No glandular, squamous or differentiated mesenchymal components identified. All surgically resected margins were free of tumour. Twenty-three lymph nodes isolated from the axillary tail were free of tumour.

On H&E sections, we faced diagnostic difficulty as it was a malignant spindle cell tumour of the breast without glandular component. The morphologic diagnosis was angiosarcoma. Differential diagnosis considered were metaplastic breast carcinoma, malignant phyllodes tumour and primary breast sarcoma.

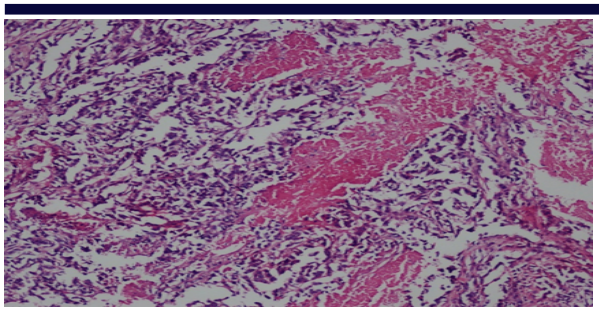

Figure 3 Spindle Cell Areas With Necrosis And Haemorrhage (H&E X100)

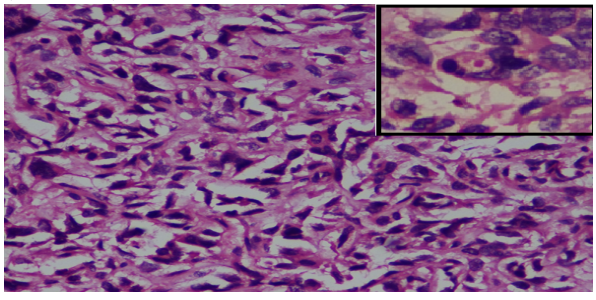

Figure 4. Pleomorphic Cells Lining Cleft Like Spaces (H&E X400). Intracytoplasmic Lumina With RBC (in set)

Immunohistochemistry was done. The tumour cells were positive for AE1/AE3, p63 and vimentin. They were negative for SMA, S100, CD34, ER, PR and HER2. (Figure 5). Ki 67 index was 40%. The case was diagnosed as Metaplastic carcinoma (spindle cell carcinoma). The tumour was classified as pT4bN0M0 according to the American Joint Committee on Cancer, eighth edition.

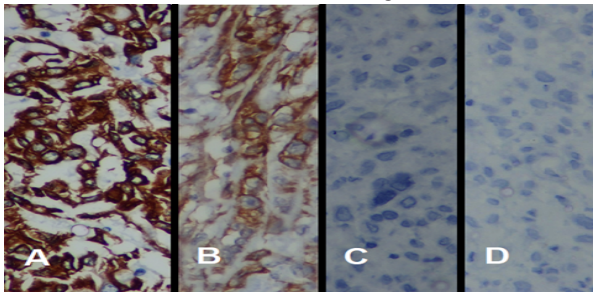

Fig 5 IMMUNOHIS TO CHEMISTRY (A) AE1/AE3, (B) Vimentin , (C) CD34, (D) ER

Postoperatively the patient underwent radiation therapy. No endocrine treatment or chemotherapy was administered as the diagnosis was confirmed to be metaplastic carcinoma which is triple-negative. The patient is asymptomatic and disease-free at three years of follow-up

DISCUSSION:

Metaplastic carcinoma encompasses a group of neoplasms characterised by differentiation of the neoplastic epithelium into squamous cells and mesenchymal-looking elements, including but not restricted to the spindle, chondroid, osseous, and rhabdomyoma cells. These neoplasms may be either entirely composed of metaplastic elements, or by a complex admixture of carcinoma and metaplastic areas. The World Health Organization (WHO) recent classification system for MCB includes low-grade adenosquamous carcinoma, fibromatosis-like metaplastic carcinoma, squamous cell carcinoma, spindle cell carcinoma, and carcinoma with mesenchymal differentiation[3]. Metaplastic carcinomas except for low grade adenosquamous and fibromatosis-like variants have a high propensity for metastasis, are characteristically aggressive, and chemoresistant[1].

The differential diagnosis is broad in MCB when an identifiable atypical epithelial or carcinomatous component is not present. Immunohistochemical evidence of carcinomatous differentiation is extremely helpful in the differential diagnosis in this situation. Immunohistochemical analysis of metaplastic carcinomas has revealed that > 90% of these cancers are negative for ER, progesterone receptor (PR) and HER2, and express keratins 5/6 and 14, and EGFR. P63 is expressed in > 90% of metaplastic breast carcinomas. Keratins and p63 are negative in phyllodes tumours and positive in metaplastic breast cancers. SMA, S100 and CD34 help to exclude other mesenchymal tumours. Microarray-based gene-expression profiling has demonstrated that metaplastic breast tumours are preferentially classified as of basal-like subtype.

Lymph-node metastases are significantly less frequently found in metaplastic breast cancers than in invasive carcinoma NST. Metaplastic breast cancers have lower response rates to conventional adjuvant chemotherapy and a worse clinical outcome than those of other forms of triple-negative breast cancers [4,5] Post-surgery chemotherapy regimens are different for Metaplastic carcinoma, angiosarcomas and primary breast sarcoma. Malignant phyllodes need only surgery. Exact subtyping is important because of the difference in treatment and prognosis of each entity.

A study by Amy E McCart Reed and Sunil R Lakhani, whole-exome sequencing was performed in metaplastic Carcinoma. Breast cancer driver genes were the most frequently altered in this cohort: TP53 (21/30 cases), PIK3CA (10/30 cases), PTEN (7/30 cases), and NF1 (4/30 cases)[4].

Except lowgrade adenosquamous and fibromatosis-like variants, metaplastic carcinomas are typically aggressive, chemoresistant, and have a high propensity for metastasis[1]. Clinically, patients are more likely to present with large primary tumours (higher stage), distant metastases and overall, have shorter 5-year survival compared to Invasive Carcinomas of no special type[5]

CONCLUSION

Metaplastic carcinoma is a rare tumour of the breast . It poses diagnostic difficulty when it exhibits exclusive spindle cell morphology as in our case . Differential diagnoses considered was angiosarcoma, metaplastic breast carcinoma, malignant phyllodes tumour and primary breast sarcoma. Immunohistochemistry unravelled the epithelial nature of the tumour. It diagnosed it as spindle cell carcinoma, Categorisation of these tumours by extensive sampling and immunohistochemistry is important as these are different in treatment, follow up and prognosis. Future investigations aimed at understanding the link between the phenotypic diversity of MCBs, protein and gene expression profiles and their relationship with prognosis will be important to develop effective and personalised therapies.

Consent

Informed written consents were obtained from the patient for the publication of this case report along with the images.

Declaration Of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship:- Nil.

Conflicts Of Interest There are no conflicts of interest.

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