Case Report

Metaplastic Tumour of the Breast: A case presentation

Khushboo Dewan*, Kiran Agarwal, O. P. Pathania

Department of Pathology, Lady Hardinge Medical College and Associated hospitals, DIZ Industrial area, New Delhi, India

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ABSTRACT

Metaplastic carcinoma (MPC) is a rare breast neoplasm with an incidence of 0-2.5%. Metaplastic spindle cell carcinoma should always be considered in the differential diagnosis of atypical spindle cell proliferations of the breast. We describe the diagnostic challenge posed by a MPC (Spindle cell type) in differentiating it from a Phyllodes tumour (PT) with epithelial hyperplasia on a trucut biopsy. Conventionally, CK and Vimentin co-expression by spindle cells is taken as an evidence for a diagnosis of MPC, but recently, heterogenous CK expression by spindle cells in MPC has been described. Therefore, in such a setting it is not advisable to make a definitive diagnosis of either MPC or PT on a trucut biopsy. However, a few histological and immunohistochemical considerations may help us in deciding the diagnosis. Histologically, blending of squamous cells with spindle cells, presence of extensive lymphocytic infiltrate, keloid-like stromal areas and presence of DCIS, favour the diagnosis of MPC over PT. Absence of CK, EGFR, p63 expression and positive CD34 and bcl-2 expression by spindle stromal cells favours PT over MPC.

***Corresponding author:**
Dr Khushboo Dewan, 26, Amit Apartments, Sector-13, Rohini, Delhi - 110085, India
Phone: +91-9289008474
E-mail: khushboodewan@gmail.com

Introduction

Metaplastic carcinoma (MPC) is a rare breast neoplasm with an incidence of 0-2.5%.[1] It encompasses a group of neoplasms characterized by differentiation of the neoplastic epithelium into squamous cells and/or mesenchymal-looking elements, including but not restricted to spindle cells.[1] Metaplastic spindle cell carcinoma should always be considered in the differential diagnosis of atypical spindle cell proliferations of the breast.[1]

The spindle cell lesions of the breast have always been a diagnostic dilemma, more so on trucut biopsy. We describe the diagnostic challenge posed by a MPC (Spindle cell type) and its differentiation from a Phyllodes tumour (PT) with epithelial hyperplasia on a trucut biopsy. The histological features and an immunohistochemical (IHC) panel useful for distinguishing the two entities are discussed here.

Case Report

A 54 year old female patient presented with a painless lump in the right breast for 15 days duration. On examination, a 4x3 cm well defined, freely mobile, hard lump was palpable in the upper outer quadrant of the breast. There was no associated lymphadenopathy.

A mammogram and ultrasonogram of the right breast revealed a centrally located, irregular, high density speculated lesion measuring 4x3.5 cm with nipple-areolar extension, retraction and periareolar skin thickening, suggestive of a BIRADS V lesion. In the left breast, multiple, well defined, iso-dense lesions were noted in the periareolar region, suggestive of BIRADS III lesion.

On histopathology, the trucut biopsy section showed presence of crush artefacts. The areas with preserved morphology were composed predominantly of closely-packed bland spindle cells arranged in fascicles. The spindle cells were elongated with tapered edges and possessed moderate amount of pale, eosinophilic cytoplasm, centrally placed slender nuclei with inconspicuous nucleoli. Interspersed within the stroma were occasional islands, ducts and cords of round, plump cells. The nuclear morphology of cords and ducts could not be ascertained because of their paucity and compression by surrounding stroma. Few nests of squamous epithelial cells with mild atypia were also seen. Differential diagnosis of biphasic spindle cell tumours of the breast-MPC and PT with epithelial hyperplasia were considered. Immunohistochemistry was done by avidin-biotin method using monoclonal mouse anti-human ER, PR (Dako Cytomation, Norden A/S, Glostrup, Denmark, dilutions 1:40,1:40 respectively), CK, EGFR, CD34, bcl-2 (Dako Cytomation, Norden A/S, Glostrup, Denmark, dilutions 1:50,1:100,1:50,1:50 respectively), Vimentin (Diagnostic Biosystems, dilutions 1:200), polyclonal rabbit anti-human HER-2/neu (Dako Cytomation, Norden A/S, Glostrup, Denmark, dilutions 1:100). The tumor was triple negative as it was negative for ER, PR and HER-2/neu. Diffuse vimentin positivity was seen in spindle cells and cords of plump cells, whereas the glands were negative. CK was positive in normal-appearing glands and cords of plump, round cells but negative in spindle cells. The spindle cells were negative for CD 34, bcl-2 and EGFR. Due to co-expression of vimentin and CK in cords of plump cells, possibility of MPC was considered. An urgent excision of the lump was advised as the possibility of PT could not be ruled out completely.

The right breast lumpectomy specimen measured 8x8x7 cm and revealed a solid, white growth measuring 4.5x4x4 cm with few myxoid areas. Microscopically, the tumour was infiltrating into the surrounding fat and was composed predominantly of spindle cells arranged in fascicles, running in a storiform as well as herringbone pattern. Focally the spindle cells showed moderate pleomorphism with mitotic count- 3/10hpf. No heterologous elements were seen. Foci of epithelial hyperplasia were also present. With these microscopic findings of moderate stromal hypercellularity and pleomorphism but mitotic figures <10/10HPF, grading of PT was uncertain and therefore further sectioning was done. Further sections however revealed larger areas of ducts and cords of plump, round epithelial cells, some even covering the entire section. Few of these epithelial cells also exhibited anisonucleosis, high nucleo-cytoplasmic ratio and prominent nucleoli. Foci of squamous differentiation were seen, blending imperceptibly with the surrounding epithelial cells at places. The spindle cells lying in immediate vicinity of epithelial islands were plumper than those at the periphery, representing a transition between the round, epithelial cells and slender, stromal cells. Stroma also showed myxoid change and dense collagen fibres forming keloid-like areas with moderate lymphocytic inflammatory infiltrate. Surrounding breast parenchyma also showed epithelial hyperplasia, at places with atypia and also ductal carcinoma in situ (DCIS). The above findings cumulated together favoured a diagnosis of MPC over PT. On IHC, CK expression was not only confined to the ducts and squamous islands but was also seen in the surrounding plump spindle shaped cells. These plump spindle cells co-expressed vimentin and were negative for CD 34, bcl-2 and EGFR. Although present in most, but many ducts did fail to express calponin, implying their neoplastic nature. A final diagnosis of MPC (spindle cell type) was signed out.

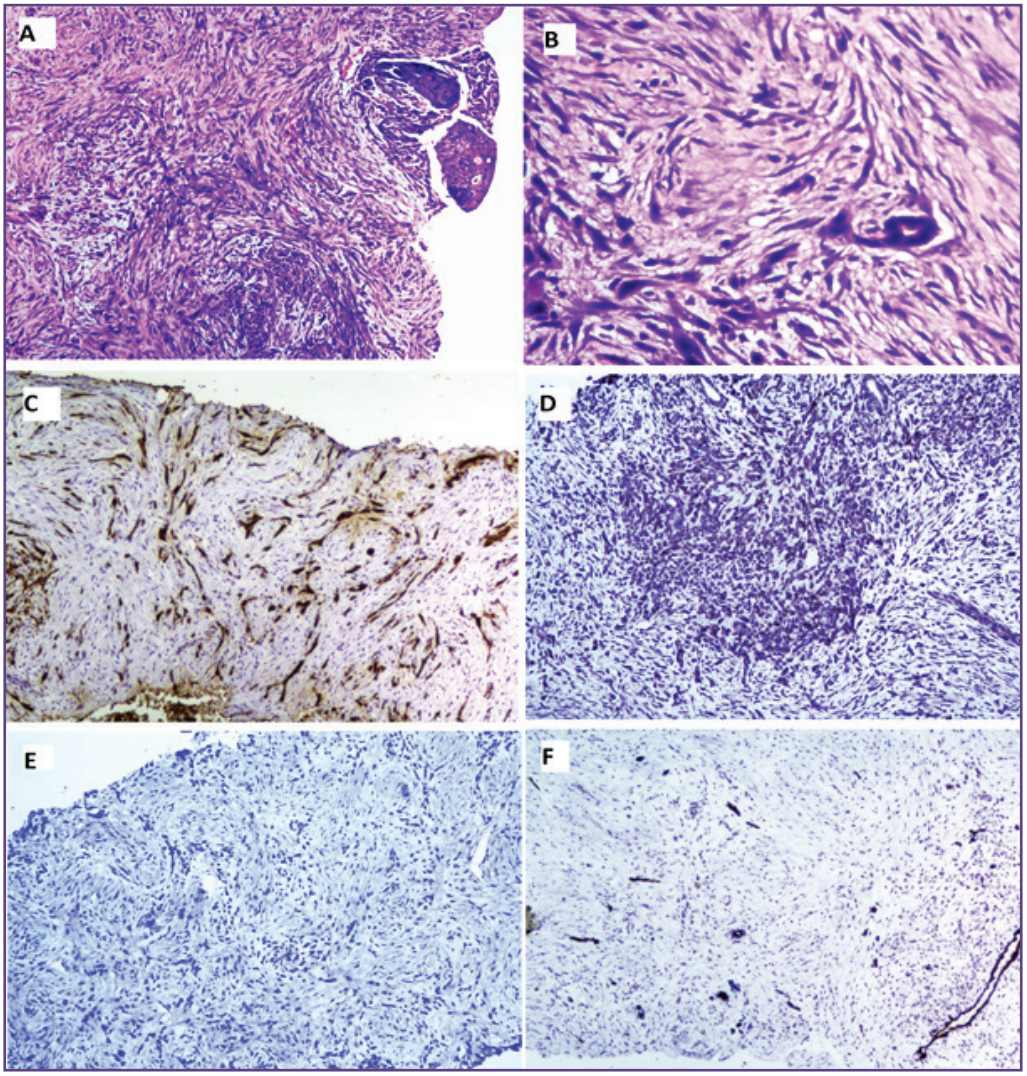

Fig. 1: Trucut biopsy of the breast

- **A) Fascicular arrangement of closely-packed bland spindle cells. Ducts and cords of round, plump cells are interspersed within the stroma. A nest of squamous epithelial cells is also seen (H&E, 10x).**
- **B) High power view showing plump, round cells arranged in ducts and cords (H&E, 10x).**
- **C) CK immunostaining (10X)-Positive in cords of plump, round cells. Negative in spindle cells.**
- **D) Vimentin immunostaining (10X)- Diffuse positive in spindle cells and cords and islands of plump cells. Few negative stained glands are seen.**
- **E) bcl-2 immunostaining (10X)- Negative in spindle cells and cords of plump cells.**
- **F) CD34 immunostaining (10X)- Negative in spindle cells and cords of plump cells. Normal blood vessels serve as positive internal control.**

Discussion

The World Health Organization has classified MPC into low-grade adenosquamous carcinoma, fibromatosis-like metaplastic carcinoma, squamous cell carcinoma, spindle cell carcinoma and carcinoma with mesenchymal differentiation including chondroid and osseous differentiation.[1]

This heterogenous group of tumours is important as it may pose diagnostic confusion with many other spindle cell tumours especially on a trucut biopsy where the quantity of tissue is limited. A predominance of spindle cells with foci of epithelial hyperplasia may be seen in both MPC and PT as in the present case. MPC requires modified radical mastectomy along with axillary dissection and PT is treated with wide local excision.

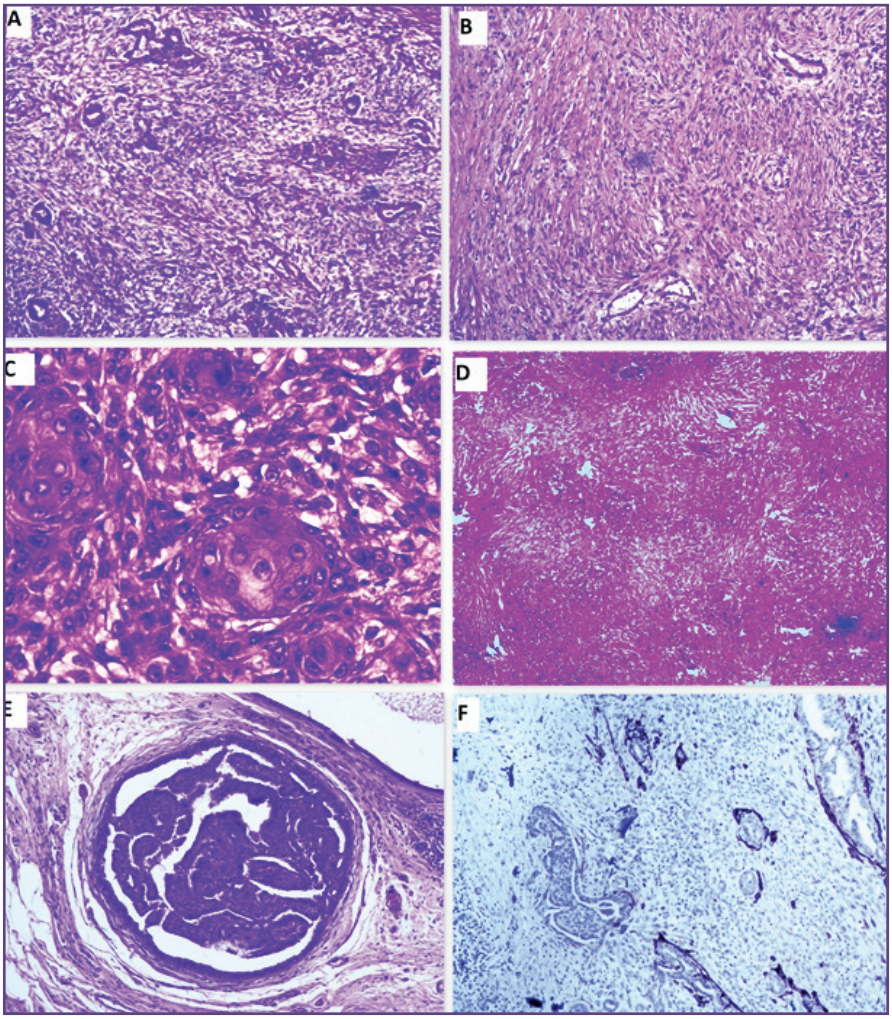

FIG. 2: Right breast lumpectomy

- **A) H and E (10X)- Ducts and cords of plump, round epithelial cells. The spindle cells lying in immediate vicinity of these ducts are plumper than those at the periphery**
- **B) H and E (40X)- High power view of the plump, epithelial cells. Few cells exhibit anisonucleosis, high nucleo-cytoplasmic ratio and prominent nucleoli.**
- **C) H and E (40X)- Foci of squamous differentiation, blending imperceptibly with surrounding epithelial cells.**
- **D) H and E (10X)- Spindle cells arranged in fascicles, running in a storiform pattern**
- **E) H and E (10X)- Focus of DCIS**
- **F) Calponin immunostaining (10X)- Positive in many ducts but few negatively staining ducts are also seen.**

Conventionally, CK and Vimentin co-expression by spindle cells is taken as an evidence for the diagnosis of MPC. CK is a useful marker however it is packed with its own limitation of heterogenous expression by stromal cells in MPC.[2,3] Therefore, even a focal and low intensity of CK expression should be sufficient to arouse a differential diagnosis of MPC especially on trucut biopsy. A focal and patchy cytoplasmic staining for various keratins may also be seen in stromal cells in 2-30% cases of PT.[4]In the present scenario, a panel of CK, Vimentin, bcl-2, CD 34, p63 and EGFR should be used in the differentiation of the two entities. CD 34 has been specifically found to be expressed by stroma of PT in most cases, but never in MPC.[2,3] bcl-2 is not so categorical in differentiating the two entities, although present in 100% of PT cases, it has also been found to be expressed in few odd cases of MPC.[2] p63, a homologue of p53 and a myoepithelial marker, has a sensitivity and specificity of 85% and 99% respectively for MPC.[3,5]Recently, EGFR overexpression and gene amplification has been described in both epithelial and spindle cell component of MPC.[6,7]

In the present case, a focal and patchy CK positivity and negativity for CD34 and bcl-2 on trucut biopsy did favour, but was insufficient to conclude a diagnosis of MPC. The final answer was only provided by the wide local excision. Although many sections from the tumour comprised only of the spindle cells similar to trucut biopsy, other sections did show considerable amount of admixed epithelial-squamous as well as ductal component. In these sections, the CK was not only positive in epithelial islands but also in the adjacent lying plump spindle cells that co-expressed vimentin. CK and Vimentin co-expression, CD34 and bcl-2 negativity in the spindle cells, coupled with DCIS in the periphery of the main tumour was confirmatory for MPC.

Some histopathological features may be helpful in diagnosis of metaplastic carcinoma on trucut biopsy. The close imperceptible blending of squamous cells with surrounding spindle cells has been described previously in MPC.[8]In addition a densely collagenised keloid-like stroma and lymphocytic infiltrate are also seen in spindle cell (metaplastic) carcinoma.[1,8] Despite extensive literature research, the above mentioned histological features were not described in PT. Presence of in situ component in the surrounding breast as was seen in present case also favours MPC. In study by Tan et al, only a single case of PT with DCIS was found among the 335 cases of PT studied.[9]

Conclusion

To summarize, one should be cautious in giving a definitive diagnosis of either PT or MPC on trucut biopsy. Absence of an epithelial phenotype and focal CK expression immunohistochemically is insufficient to rule out the possibility of MPC. Histologically, blending of squamous cells with spindle cells, presence of extensive lymphocytic infiltrate, keloid-like stromal areas and presence of DCIS, favour the diagnosis of MPC over PT. Absence of CK, EGFR, p63 expression and positive CD34 and bcl-2 expression by spindle stromal cells favours PT over MPC.

Abbreviations

MPC- Metaplastic Carcinoma

PT-Phyllodes Tumor

IHC-Immunohistochemistry

Acknowledgements

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None

Competing Interests

None declared

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