Case Report

A Rare Case of Epithelial-Myoepithelial Carcinoma Breast in A Young Female with HER2neu Positivity

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Abstract

Epithelial-myoepithelial tumors of breast are biphasic neoplasms, with dual participation of epithelial and myoepithelial components. It is a very rare tumor, common in elderly females. EMC breast resembles its salivary gland counterpart, which itself forms less than 1% of all salivary gland tumors. Herein, we report one such rare case of EMC breast in a young female with aberrant HER2 positivity, a feature not yet reported in literature.

Keywords:

Epithelial-myoepithelial carcinoma, adenomyoepithelioma, Her2

Introduction

Epithelial-myoepithelial tumors of breast, as the name reflects are biphasic neoplasms, with dual participation of both the epithelial as well as the myoepithelial components. There can be variation in the form that either of the components being benign or malignant.[1,2] The latest World Health Organisation [WHO] classification of breast tumors includes pleomorphic adenoma, adenomyoepithelioma as benign forms of this tumor and adenoid cystic carcinoma, malignant adenomyoepithelioma or "epithelial-myoepithelial carcinoma" as the malignant counterparts. [3,4]

When both the luminal epithelial and outer myoepithelial components are malignant, the term epithelial-myoepithelial carcinoma [EMC] is preferred. It is a very rare entity and extensive literature search revealed only few case reports. Mammary EMC

resembles its counterpart in the salivary gland, which is also rare (less than 1% of all salivary gland tumors), but relatively more common when compared to mammary EMC.[5–7]

EMCs are seen in elderly females, mostly in their six to seventh decade in the reported cases so far, however the present case is of a young female in her third decade of life.[1,5,6,8,9] None have been reported in males. The patients present with long standing breast mass, with recent increase in size. It is believed to arise from benign adenomyoepithelioma, but de novo cases have also been reported.[1,5,10,11]

The EMC breast needs to be differentiated from benign adenomyoepithelioma based on features like invasion at the periphery of the tumor, cellular pleomorphism, areas of necrosis and increased mitotic activity.[7,12] This differentiation is of utmost importance as the adenomyoepitheliomas do not metastasize, though they may recur locally, while EMCs have the potential to metastasize hematogenously to various organs like lung, and liver. Metastasis to lymph nodes is uncommon in EMCs, therefore axillary lymph node dissection is not indicated. The role of radiotherapy and chemotherapy is yet to be established as only few reported cases are available.[1,2,13]

Herein, we report one such rare case of EMC in a young female with aberrant HER2 positivity, which is the first case in literature in our knowledge. Our focus is on its histopathological and immunohistochemical findings that the pathologists need to be familiar with, to be able to recognize and report this uncommon challenging entity which has potential to metastasize.

Case Report

A 37-year-old female, with no known comorbidities presented with history of swelling and dull aching pain in her left breast of 3 months duration. There was no history of fever or and discharge fro, the left breast. The lump was palpable with clear border and non tender on palpation in the lower-inner quadrant of her left breast. On clinical examination, the mass measured 4 cm in size. Ultrasonography, revealed a large, multiseptate, solid-cystic lesion of volume 110 cubic cm with internal echoes, in the lower inner quadrant. The mass was excised and sent for histopathological examination at a separate facility where it was diagnosed as a case of Intracystic papillary carcinoma/ Invasive papillary carcinoma breast.

The blocks of the case were sent to our tertiary care center for review. Histologically, the sections revealed a solid-cystic lesion. The cyst was lined by a bimodal population of luminal epithelial cells present in glandular arrangement and abluminal myoepithelial cells present in sheets. The epithelial cells were large, having moderate amount of eosinophilic cytoplasm, high nuclear to cytoplasmic ratio, marked nuclear pleomorphism with hyperchromatic nuclei and prominent nucleoli. The myoepithelial cells appeared clear to spindled, with moderate nuclear atypia. Mitotic figures were noted. Focal areas of mucin production was also seen. The surrounding areas were fibrotic with presence of sheets of foamy histiocytes and cholesterol clefts. The tumor was seen infiltrating into the adjacent breast parenchyma and adipose tissue at focal areas. Areas of stromal hyalinization were seen. No lymphovascular invasion or perineural invasion was identified. No ductal carcinoma in situ was noted.

On immunohistochemistry, the biphasic nature of the tumor was highlighted with CK7 and p63 immunostains. While CK7 immunopositivity was seen diffusely and strongly in the luminal epithelial cells, the surrounding myoepithelial cells were positive for p63. The tumor cells were negative for estrogen receptor (ER, 0/8 Allred Score) and progesterone receptor (PR, 0/8 Allred Score) but showed strong membranous immunoreactivity for HER2neu (3+, ASCO score). The Ki-67 proliferation index was also increased (~15%).

Based on the above histological and immunohistochemical features, a final diagnosis of Epithelial-Myoepithelial Carcinoma Breast was made. Since the lady had undergone only lumpectomy, a completion mastectomy was performed at our centre which did not reveal any residual tumor. The patient is on regular follow-up since last seven months and is disease free.

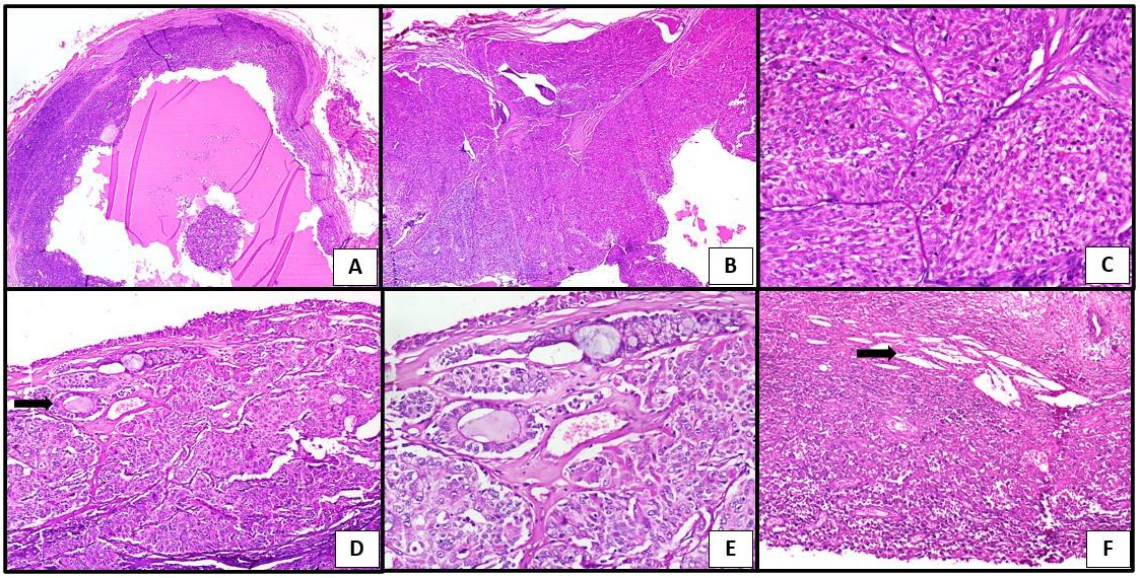

Figure 1

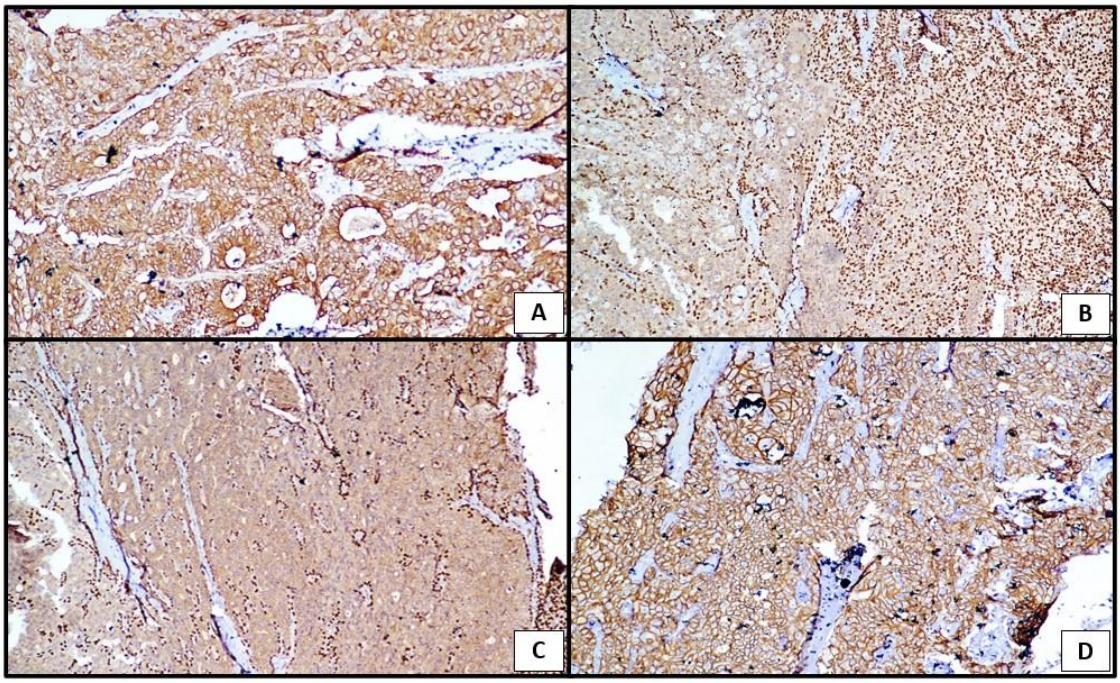

Figure 2

Discussion

EMC is a rare tumor, with only a few case reports in the literature. The latest WHO (5th) classification of breast tumors has placed it in the category of adenomyoepitheliomas with carcinoma. This category includes carcinoma from luminal epithelium (ductal carcinoma), carcinoma from myoepithelium (myoepithelial carcinoma) and carcinoma from both epithelium and myoepithelium (epithelial-myoepithelial carcinoma) [1,3,7,14].

EMCs can have pushing or infiltrative type of margins. Being a mixture of both malignant epithelial and myoepithelial cells, its immunohistochemistry also exhibits the biphasic nature of this tumor. The luminal epithelial cells express CK7 and EMA, while the outer layer of myoepithelial cells express SMA, p63, SMMHC, CD10, Calponin and CK5/6 [1,11].

Extensive literature search shows only about 40 cases of malignant adenomyoepithelioma of breast. These cases mostly occurred in adult to elderly females, usually post-menopausal with mean age of 63 years [1,3,7,13]. All cases were diagnosed as adenomyoepithelioma with carcinoma except for one which was diagnosed as EMC ex pleomorphic adenoma [7]. Some of the cases showed Ductal Carcinoma In Situ component. Estrogen and progesterone receptor status was found to be negative in most of the cases, except few showing hormone receptor positivity [1–3,5,8,11]. HER2 status was negative in all cases except one case report by Hu et al. [11]. Our case also uniquely showed diffuse membranous HER2 positivity. Metaplastic carcinomas comprising of EMC as a histologic variant have also been reported [5,6]. Lymph node metastasis was not present in all cases reported so far including the present case. Occasional cases had worse outcome in the form of local recurrence and distant metastasis to lung, brain, bone, thyroid and mediastinal lymph nodes [1,2,5,8,11]. A comparative summary of all the case reports of EMC available in literature has been shown in Table 1.

The present case of a rare histopathologic subtype of carcinoma breast was unique due to presentation at a younger age as compared to the other cases where the patients are post-menopausal. Also, present case shows a rarer HER2neu positivity (3+, ASCO score) which is not commonly found in this variant as compared to the other case reports. This gene is considered as a prognostic factor in breast cancer. Although it is not an independent marker. When used in conjunction with ER, it forms an important marker which is also an important gene for molecular targeted therapy.

The molecular landscape of breast EMCs is not much explored, however, mutations in HRAS and PIK3CA have been reported in few cases. Similar gene mutations are also found in the EMCs of salivary gland, but larger cohorts need to be studied to establish this fact [5,11,14].

Conclusion

This case report describes a rare case of EMC of breast in a young female which exhibited HER2 positivity, which is an important prognostic and predictive marker with available targeted therapy. This report also highlights the importance of histomorphology and the ancillary technique of immunohistochemistry which if used judiciously can help reach an accurate diagnosis.

Table 1: Review Of Literature

Authors	Year	Patient profile	Histopathological findings	Immunohistochemistry	Intervention	Follow up
Karl et al	2020	76 year old female	EMC with rhabdoid features	CK8/18 + P63 + Myogenin -	Wide local excion	-
Zhu et al	2018	81 year old female	Metaplastic breast carcinoma with EMC and squamous cell carcinoma	34BE12 + (glandular epithelial cells) P63, SMA, S100 + (Myoepithelial cells)	Wide local excision	No recurrence at 18 month follow up
Baum et al	2018	73 year old female	EMC with focal metaplastic spindle cell differentiation	E-cadherin, CK7, GATA-3 + (Epithelial cells) SMM-HC, p63 + (Myoepithelial cells) Ki67- 12% ER, PR, HER2 – CK20 –	Lumpectomy	No recurrence or metastases at 29 month follow up
Hu et al	2021	80 year old female	EMC with solid and papillary architecture	CK7 + (Epithelial) P63 + (Myoepithelial) Ki67- 30% ER, PR – HER2neu 2+ HER2 amplification by FISH	Modified radical mastectomy	No complications or recurrence at 3 months follow up
Shah et al	2011	43 year old female	EMC ex pleomorphic adenoma with squamous metaplasia and keratinous cysts	CK, EMA + (Epithelial cells) SMA, S100 + (Myoepithelial cells)	Wide local excision without axillary lymph node dissection	No recurrence or metastases at 30 months follow up
Gandhi et al	2011	68 year old female	EMC with intraductal papilloma and foci of adenosis	34BE12, CK7, CD117 +(Epithelial cells) p63, S100 + (Myoepithelial cells) SMA – ER, PR, HER2 –	Modified radical mastectomy	No metastasis
Petrozzo et al	2013	60 year old female	Adenomyoepithelioma with focal malignant transformation of epithelial component and more widespread malignant transformation of myoepithelial component	CK7 + (Epithelial cells) P63, S100 + (Myoepithelial cells) ER, PR, HER2 –	Lumpectomy	No tumor recurrence
Zhang et al	2021	64 year old female	Malignant adenomyoepithelioma	CK5/6 + Calponin, p63, S100 + ER, PR, HER2 –	Mastectomy and sentinel lymph node biopsy	No recurrence at 12 months follow up
Kakkar et al	2019	36 year old female	EMC with tubular and solid architecture with areas of necrosis	Pan-CK + (Epithelial cells) CK5/6,SMA,SMMHC, CD10 + (Myoepithelial cells) Ki67- 16% ER, PR + HER2 –	Breast conservation surgery with sentinel lymph node biopsy + with adjuvant Tamoxifen	Disease free at 12 follow up
Sugano et al	2001	82 years old female	Malignant adenomyoepithelioma	SMA, S100 + EMA, keratin + Focal GFAP + Mib-1 40% P53 – ER, PR-	Lumpectomy followed by total mastectomy	No evidence of disease at 24 months
Sugano et al	2001	58 years old female	Malignant adenomyoepithelioma	SMA, S100 + EMA, keratin + GFAP- Mib-1 20% P53 – ER, PR-	Wide local excison	No evidence of disease at 28 months
Present case	2022	37 years old female	Epithelial- myoepithelial carcinoma	CK7+ (Epithelial) P63+ (Myoepithelial) ER, PR- Ki67~15% Her2neu 3+	Lumpectomy followed by completion mastectomy	

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