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A Rare Case of Primary Multifocal Mucoepidermoid Carcinoma in the Skin of the Breast Masquerading as a Breast Mass

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Abstract

Cutaneous Mucoepidermoid Carcinoma (MEC) of the breast is extremely rare and must be distinguished from MEC originating in the breast parenchyma. Histologically, MEC is characterised by the presence of both solid and cystic components and morphological identification of the three intermixed components of squamoid, intermediate, and mucin cells. Diagnosis may be difficult given the rarity of this disease, the variable clinical presentation and histological heterogeneity. Here we describe the first published case of primary multifocal MEC arising in the skin of the breast and masquerading as a breast mass. Cutaneous MEC may prone to recurrences so wide local excision with pathologic confirmation of tumour-free margins is appropriate and careful follow-up is recommended.

Introduction

Mucoepidermoid Carcinoma (MEC) is the most common histological type of salivary gland neoplasm in children and young adults [1]. MEC can also be found in other sites such as bronchi, thyroid gland and lacrimal sac [2]. The mean age of diagnosis is within the 5th decade. Histologically, MECs are composed of 3 cellular elements in varying proportions: squamous cells, mucous-secreting cells and intermediate cells. It can have mixed cystic and solid components. Prognosis is dependent on clinical stage, site, grading and adequacy of surgical resection. Overall 5 to 10 years survival rates are in the range of 0% to 43% for high grade, 62% to 92% for intermediate grade, and 92% to 100% for low grade tumours [1,3].

Primary MEC of the skin is extremely rare with only around 20 reported cases [4]. It must be differentiated from adenosquamous carcinoma and from cutaneous MEC metastases, as prognosis and behaviour differs [5]. Immunohistochemical staining for p63 may be used to differentiate primary from metastatic MEC [6]. In contrast to MEC originating from the salivary gland, primary cutaneous MEC is more common in males than females [7]. The head and neck regions are the most commonly affected sites, followed by axillae and vulvae. It may present clinically as localised skin change or as a mass lesion with unremarkable overlying epidermis [8,9]. Given its variable clinical presentation and heterogeneous histologic features this rare tumour is often difficult to diagnose. Data on prognosis is limited.

Cutaneous MEC of the breast is especially rare and may present clinically as a palpable lump. It must be distinguished from MEC originating in the breast parenchyma. Primary MEC of the breast is also extremely rare and has a reported incidence of 0.03% [10] 0.3% [11]. Surgical resection to clear margins is the mainstay of treatment. Here we describe the first published case of primary multifocal MEC arising in the skin of the breast and masquerading as a breast mass.

Case Presentation

A 70-year-old female was referred for evaluation of a self-detected right breast lump present for 5 months. The patient's co-morbidities included osteoporosis, carpal tunnel syndrome, hypertension and hypercholesterolemia. She is a non-smoker. Clinical examination findings revealed a non-tender 5 cm subcutaneous mass in the right breast at the 9 o'clock position 12 cm from the nipple.

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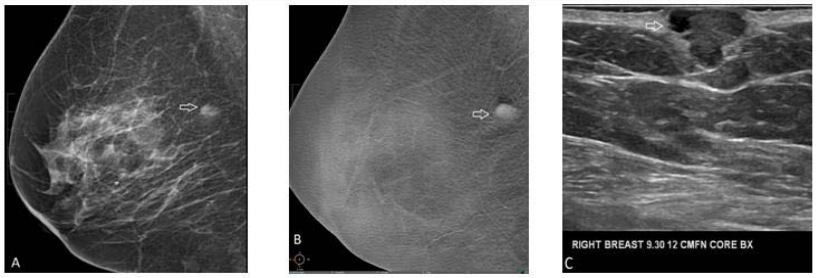

Figure 1: A) Mammogram, right breast mediolateral oblique view: Focal ill-defined density separate from the breast parenchyma. B) Tomogram, right breast mediolateral oblique view: Circumscribed tumour confirmed to be originating from the skin. C) Right breast ultrasound: Well defined lobulated mass with cystic and solid components corresponding to the lesion seen on mammographic and tomographic images.

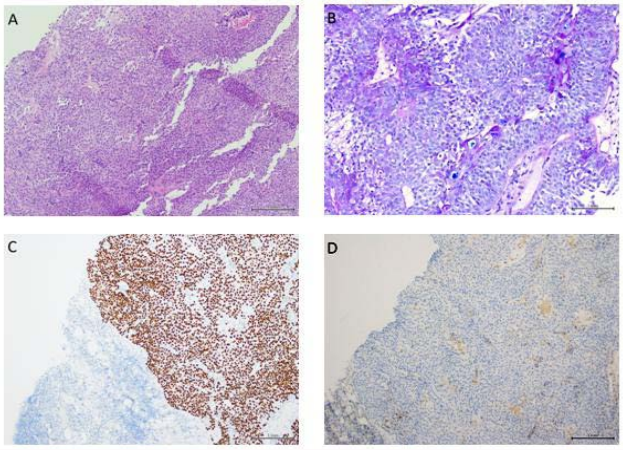

Figure 2: A) The tumour was composed of squamoid and intermediate cells. B) Focal intracytoplasmic mucin was identified with PAS-Alcian Blue stain. C) The cells were strongly positive for p63. D) The cells did not stain with ER.

The overlying skin had dusky discoloration with a papular rash. There was no palpable lymphadenopathy. The remaining skin examination was normal. The head and neck examination was also normal.

Mammography showed a small ill-defined oval density laterally in the right breast (Figure 1A) with tomographic images suggesting it was related to the skin (Figure 1B). Breast ultrasound showed a 12 mm lobulated mixed cystic and solid mass attached to the skin (Figure 1C). There was no increased vascularity or surrounding oedema. The axillae were sonographically normal. It was felt that the breast mass most likely represented an unusual appearance of a sebaceous cyst.

The mass was sampled by 3 × 14 gauge cores. Histology showed a rounded, poorly defined and infiltrative tumour with a biphasic appearance composed of squamoid and intermediate cell morphology (Figure 2A). Alcian Blue and PAS staining highlighted scattered intra-cytoplasmic mucin droplets (Figure 2B). The cells expressed cytokeratin 5/6 and p63 (Figure 2C) and were negative for Estrogen Receptor (ER) (Figure 2D) and smooth muscle myosin stains. The mass was favored to be a MEC and surgical excision was therefore recommended.

The patient proceeded to a wide local excision of the right breast mass. Macroscopically, cut sections revealed a central, well-demarcated, firm, tan and partially cystic mass, measuring 9 mm × 9 mm × 6 mm just deep to the skin and clear of the margins. Histologically, the tumour was located in the dermis of the skin (Figure 3A) with adipose tissue seen at the deep aspect of the excision, and no definite breast lobules identified. The tumour was 12 mm in maximum dimension

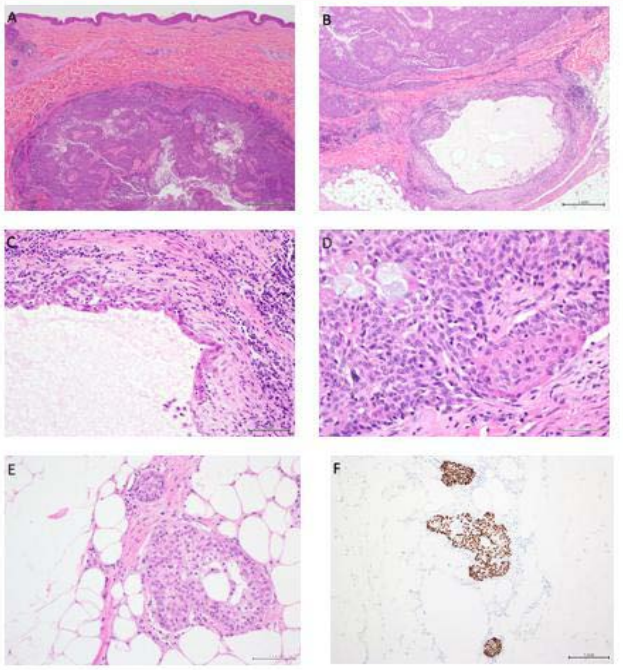

Figure 3: A) Dermal tumour. B) Multi-nodular growth into subcutaneous fat with solid and cystic components. C) Cystic spaces lined by squamoid cells. D) Squamoid, intermediate and mucinous cells. E) Separate focus of tumour confirming multifocal disease. F) Separate focus of tumour demonstrating p63 expression.

with a solid and cystic multi-lobulated architecture (Figure 3B). The cysts were lined by squamous cells (Figure 3C). The solid component was composed of squamoid, intermediate and goblet cells (Figure 3D). The intermediate cells had moderate nuclear atypia and the mitotic count was 2 per 50 high power fields.

There was a separate focus of the same tumour, 1 mm in maximum dimension, approximately 12 mm superior to the main mass (Figure 3E). This was confirmed to be the same tumour by immunohistochemistry (Figure 3F). The theory that the separate focus represented lymphatic invasion was tested by immunohistochemistry for CD31 and CD240. Lack of staining around the tumour nests confirmed that this represented a separate invasive focus. The diagnosis of multifocal intermediate grade MEC in the skin of the breast was rendered. Post-operative MRI of the head and neck and a computed tomography scan of the chest showed no metastatic focus and no mass lesions in the mucosal surfaces of the head or neck to suggest a primary minor salivary gland tumour and so the diagnosis of a primary multifocal MEC of the skin of the breast was

assumed. There has been no complication or disease recurrence on clinical examination or ultrasonography of the breast over 6 months of follow-up.

Discussion

We report the first published case of primary multifocal MEC arising from the skin of the breast. The primary cutaneous MEC in this case presented clinically as a breast mass with overlying localised skin change. The lesion was initially thought to clinically represent an unusual sebaceous cyst with differential diagnoses including breast neoplasm involving the skin. Elsewhere in the literature, MECs of the skin have been described as a mass beneath an unremarkable epidermis [8] or a skin lesion most commonly located in the head or neck region [5]. The rarity and variability in the clinical presentation of primary cutaneous MEC makes it a difficult tumour to recognise.

Furthermore, histologically, MEC is characterised by the presence of both solid and cystic components and morphological identification of the three intermixed components of squamoid, intermediate, and mucin cells [1]. Given this heterogeneity, core biopsy has the potential to limit diagnosis given the sample is only of a small part of the target lesion. The very low reported incidence of MEC in the breast region has partly been attributed to the tendency of MEC to masquerade as other processes [11]. A pitfall for pathologists would arise if the core biopsy material had only sampled the squamous lined wall of one of the cysts and failed to demonstrate the solid tumour. If this were to have occurred, the lesion may have been misdiagnosed as squamous metaplasia in fibrocystic change or as part of the wall of a sebaceous cyst.

Alternatively, if the core biopsy had demonstrated only a solid spindled intermediate to squamoid component without mucinous cells, the lesion may have been misdiagnosed as metaplastic carcinoma. These diagnostic pitfalls can be avoided by remembering the diagnosis of MEC and obtaining an adequate tissue sample of the lesion in core biopsy material. Mucin stains can be useful in identifying the presence of mucin in a squamous and intermediate cell predominant sample.

Once a diagnosis of MEC has been obtained in this rare location, the possibility of secondary metastasis to the skin of the breast from a breast, salivary gland, peri-bronchial or other primary must be considered. Clinical examination with imaging of the head, neck and chest may assist in excluding a distant primary. Clinical examination and medical imaging in this case did not detect an alternative primary site. In addition, in this case the tumour stained positively for p63, which has been shown to be a significant indicator of cutaneous primary in comparison to a cutaneous metastasis from salivary gland or other primary.

Cutaneous MEC is thought to originate from dermal adnexal structures [12]. It is known that many tumours have a viral driver effect, and causal links between MEC and Cytomegalovirus (CMV) have been suggested [13]. Subsequent CMV immunostain in our case did not highlight any infected cells.

There is limited data regarding disease progression and prognosis in cutaneous MEC. In one paper, patients treated with surgery appear to have remained disease-free for over 3 years with the longest reported survival of 19 years [9].

Cutaneous MEC can be prone to multiple local recurrences and only rare metastases [14]. Perhaps there is multifocal disease underlying the recurrences. We demonstrated multi-focality in our case, therefore wide excision of these tumours to clear margins is appropriate. The role of sentinel node biopsy in these cases is unknown. In one case study of primary breast MEC a low grade tumour did metastasis to the sentinel nodes and follow-up of recurrence free period was only for 3 months [10]. The role of radiotherapy and chemotherapy in the treatment of primary cutaneous MEC is unknown. Given the rarity of this tumour and the lack of well-established treatment guidelines, careful follow-up with imaging and clinical examination is recommended. We have opted for 6 month ultrasound after surgery, followed by annual mammography and ultrasound. The role of breast MRI in these cases is unknown.

Conclusion

In conclusion, we report the first case of primary multifocal MEC arising in the skin of the breast. Cutaneous MEC in this region is a rare entity to consider in the differential diagnoses for a breast lesion. Diagnosis may be difficult given the rarity of this disease, the variable clinical presentation and its histological heterogeneity. Cutaneous MEC may be multifocal and prone to recurrences so wide local excision with pathologic confirmation of tumour-free margins is appropriate and careful follow-up is recommended, especially in intermediate and high grade lesions.

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