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Case Report Open Access

A Metaplastic Carcinoma of Ectopic Breast in Axilla Mimicking a Cutaneous Epidermoid Carcinoma: A Differential Diagnosis not to Disregard

Berrada S[1]*, Elhamri L[1], Rais H[1], Quaboul M[2], Benchamkha Y[2] and Khouchani M[3]

[1]Department of Pathology, FMPM-UCA, CHU Mohammed VI, Marrakech, Morocco
[2]Department of Plastic and Reconstructive Surgery, FMPM-UCA, CHU Mohammed VI, Marrakech, Morocco
[3]Department of Radiotherapy, FMPM-UCA, CHU Mohammed VI, Marrakech, Morocco

Abstract

Metaplastic carcinomas (MC) of the breast constitute a heterogeneous group of tumors, characterized by the presence of squamous or sarcomatoid differentiation. It is a rare type of malignant epithelial neoplasm that arises from the breast, and whose diagnosis is based on histology and immunochemistry. Location in ectopic breast tissue (EBT) in axilla is extremely rare, and when it ulcerates, it can mimic squamous cell carcinoma of skin. We report an unusual clinical case of a 61-year-old woman with metaplastic carcinoma in axillary ectopic breast, falsely diagnosed as a squamous cell carcinoma of skin.

Keywords: Breast; Metaplastic carcinoma; Ectopic breast tissue; Squamous cell carcinoma of skin

Abbreviations: MC: Metaplastic Carcinoma; EBT: Ectopic Breast Tissue; WHO: World Health Organization; IHC: Immunohistochemical; EGFR: Epidermal Growth Factor Receptor

Introduction

Metaplastic carcinoma (MC) encompasses a group of neoplasms characterized by differentiation of the neoplastic epithelium into squamous cells and/or mesenchymal-looking elements [1,2] including but not restricted to spindle, chondroid, osseous, and rhabdomyoid cells according to the fourth edition of the world Health Organization (WHO) classification of tumours of the breast, published in 2012 [3]. It is a very rare neoplasm accounting for 0.2–5% of all invasive breast cancers [4-7]. The ectopic breast tissue (EBT) result of alterations in mammary development and growth et may occur along primitive milk line, from axilla to groin. The most common location is axilla comprising 55-65%. EBT can be the site of pathologic process or physiologic change affecting the normal breast tissue. To date, a few cases of metaplastic carcinoma have been published, especially in this rare location. The aim of this study is to discuss the clinical, histological, immunohistochemical, therapeutic features as well as the differential diagnosis of a metaplastic carcinoma in an axillary EBT and compare them with literature data.

Case Presentation

We report the case of 61-year-old patient with no family history of cancer. She was consulted for a right axillary lump evolving for 4 months, gradually increasing in volume. The initial physical examination revealed the presence of a right ulcerated and burgeoning axillary mass measuring 6 cm in diameter, well limited and painful on palpation. It was adherent to the skin but movible in relation to the deep plane. There were no inflammatory sign in the right breast or retraction of the nipple and/or areola. The left breast showed no abnormalities. There were no right or left axillary lymph nodes. A thoracoabdominal pelvic computed tomographic scan was performed and revealed the presence of a voluminous mass with extensive necrosis in right axillary breast associating to a infracentimetric axillary lymphadenopathy. The patient had a wide excision with axillary node dissection. The pathological examination revealed poorly differentiated and infiltrating squamous cell carcinoma of skin. The resection margins were healthy and there were no positive lymph nodes. But the radiotherapist was convinced the tumor was of mammary origin, the reason why he requested a reexamination of the slides. Histologic observations revealed infiltrative malignant tumour composed of nests and glandular structures of epithelial cells. The tumour cells were large-sized, clear cytonuclear atypia with mitotic activity. Some cells had abundant eosinophilic cytoplasm and a large, often vesicular, nucleus evoking the presence of squamous differentiation. This proliferation was admixed with chondroid matrix containing lacunar spaces and rare chondrocytes. The stroma was myxoid and desmoplastic. There was a perineural and vascular invasion. The resection limits were healthy. Eight lymph nodes were explored, and involvement was found zero node negative/8 node explored. The immunohistochemical analysis (IHC) identified expression of cytokeratin (AE1/AE3).

The tumour cells also displayed nuclear expression of P63 and cytoplasmic expression of anti Epidermal Growth Factor Receptor EGFR. There were intense nuclear expression (40%) of KI67. The tumor was unreactive to estrogen receptor (ER) and progesterone receptor (PR) and did not express human epidermal growth factor receptor 2 (HER2). The final diagnosis was metaplastic carcinoma with chondroid differentiation in EBT in axilla.

Discussion

The primary milk line develops in the human embryo at 6-week gestation. This line forms a ridge of ectoderm joining the bases of the upper and lower limb buds on either side of the ventral trunk from the

***Corresponding author:** Sofia Berrada, Department of Pathology, FMPM-UCA, CHU Mohammed VI, 40000, Marrakech, Morocco, Tel: +212524339899; E-mail: sfberrada@gmail.com

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mid-axilla through the normal breasts and then inferiorly to the medial groins 5 [8]. Ectopic breast tissue (EBT) arises when the primitive mammary tissue fails to regress after the development of mammary ridge except in the pectoral region [9]. It can occurs anywhere along the milk lines (Figures 1-3) mostly in axilla [10].

Histologically, it consists of an organized ductal system communicating with its overlying skin. Benign and malignant disease processes that can occur in the orthotopic breast can also arise in ectopic breast tissue. Carcinoma in the axillary EBC is extremely rare, accounting 0.3% of all breasts malignancies [11]. The most common histological subtype in this location is ductal carcinomas [12]. Other histological subtypes can be seen especially medullary and lobular carcinomas [12,13]. The breast cancer presentation of our case is very uncommon, and only a few cases have been reported in the literature. The conclusion of the pathology report was metaplastic carcinoma with chondroid differentiation in the axillary ectopic breast tissue.

Metaplastic carcinoma constitute a specific subtype of breast cancers according to the fourth edition of the WHO classification of tumours of the breast, published in 2012 [3]. It comprises a heterogeneous group of neoplasms the may be either entirely composed of metaplastic elements,

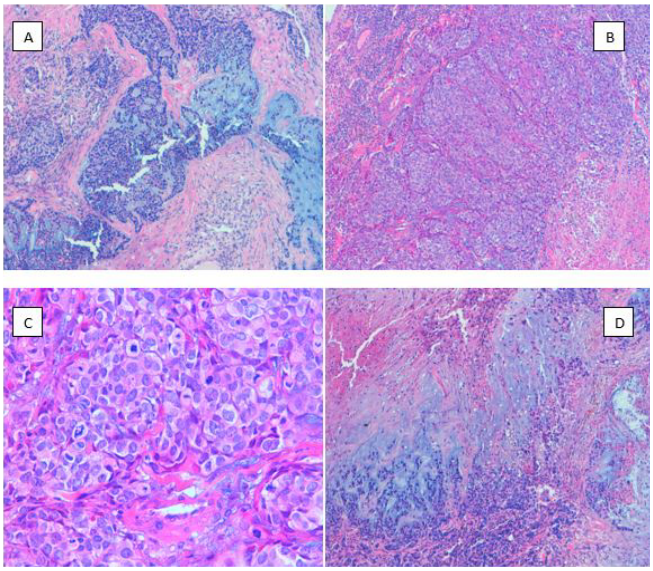

Figure 1: (A and B) Metaplastic carcinoma of breast composed of nests and glandular structures of epithelial cells. The tumour cells were large-sized, clear cytonuclear atypia with mitotic activity. Some cells had abundant eosinophilic cytoplasm and a large, often vesicular, nucleus evoking the presence of squamous differentiation. (**C and D**) This proliferation was admixed with chondroid matrix containing lacunar spaces and rare chondrocytes.

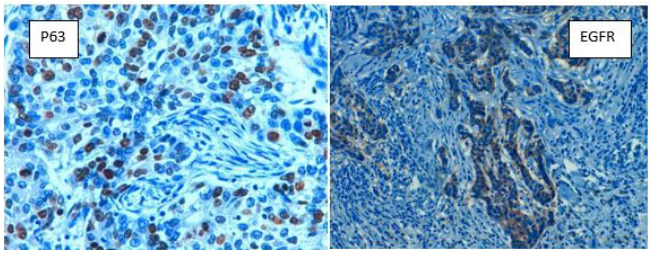

Figure 2: The tumour cells displayed nuclear expression of P63 and cytoplasmic expression of anti Epidermal Growth Factor Receptor (EGFR).

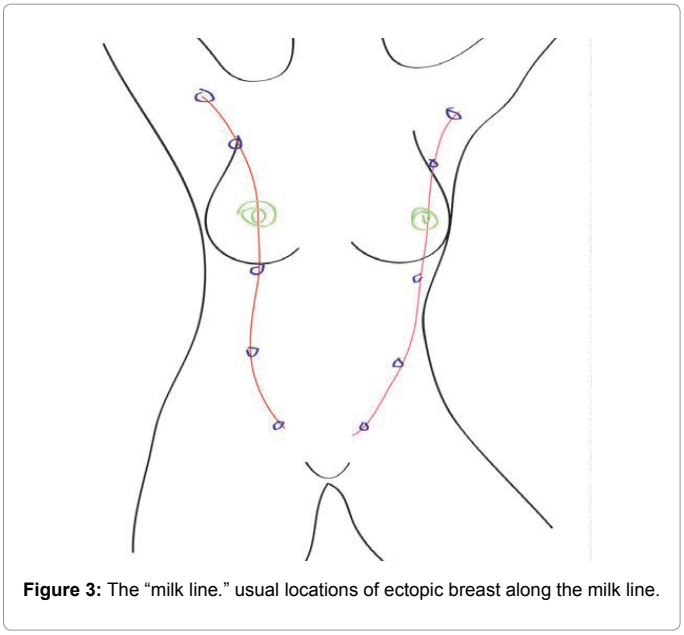

Figure 3: The "milk line." usual locations of ectopic breast along the milk line.

or a complex admixture of carcinoma and metaplastic areas [3]. Their origin has been subject of controversy. The most probable hypothesis is the possible metaplasia of a cell that is epithelial, myoepithelial or totipotent reserve cells in another type of epithelial or mesenchymal cells [10].

Metaplastic carcinoma is diagnosed in postmenopausal women, and the average age at presentation is 55 years. It presents similar clinical features and imaging aspects to other estrogen-receptor (ER)-negative invasive carcinomas of no special type (NST) [14,15], hence the importance of histological analysis, which makes possible histochemical analyses. Macroscopically, metaplastic carcinomas tend to be relatively large tumours, compared to invasive carcinomas NST, with a mean size of 3.9 cm (range, 1.2 to >10 cm) [16]. They can either be well-circumscribed or show an indistinct or irregular border. Cystic degenerative changes are not infrequent [17].

Histologically, metaplastic carcinoma represent various morphological features and all them can be seen in EBT However, several classifications have been proposed, namely that of the who 2012 which distinguishes : low-grade adenosquamous carcinomas, fibromatosis-like metaplastic carcinomas, squamous cell carcinomas with acantholytic variant, spindle cell carcinomas, metaplastic carcinomas with mesenchymal differentiation and mixed metaplastic carcinomas. Our case corresponds to the entity metaplastic carcinomas with mesenchymal differentiation characterized by the presence of carcinomatous areas, which can be in the form of glandular tubules, solid clusters and/or foci of squamous differentiation, associated with an admixture of mesenchymal components, including chondroid, osseous, rhabdomyoid and even neuroglial differentiation [14,18,19]. Those mesenchymal components can either appear differentiated with minimal atypia to exhibiting frankly malignant features that to some extent recapitulate the patterns found in true sarcomas of the soft tissues. In such tumours, true chondroid differentiation or chondroid matrix is often found, which aligns with our case.

A more accurate diagnosis is reached mainly using immunohistochemistry. Usual markers are high-molecular-weight keratins, especially keratins 5/6 and 14, and AE1/AE3; have high

sensitivity and specificity to identified the epithelial differentiation. Low-molecular-weight keratins are commonly negative [20]. P63, which is expressed in > 90% of metaplastic breast carcinomas, has proven to be a useful marker for the identification of these tumours and for their differentiation with other spindle and mesenchymal malignancies [14,21]. In our case the tumour cells were immunoreactive for P63 and cytokeratin. The overexpression of EGFR was found in 76% of cases, in which only 37% were amplified in *in-situ* hybridation. In our patient, the EGFR was over expressed but not amplified. The majority of these tumours are ''triple-negative'' and basal phenotype, which are characterised by the absence of expression of ER, PR and HER2 [22,23]. However, a study of 286 cases of metaplastic carcinoma of breast proved that were positive [24]. In another recent study, 5,2% were immunoreactive to ER 5,2% to PR and 10,5% HER2 positive status [25]. The main differential diagnosis depend essentially on the type of metaplasia, but generally the presence of an adenocarcinomatous component allows the diagnosis of metaplastic carcinoma. The location in EBT of axilla can be misleading, especially in case of squamous metaplasia and can mimic squamous cell carcinoma of skin or metastasis from other sites [26]. In our clinical presentation, the first biopsy favored a squamous cell carcinoma of skin. But a reexamination of the slides, associated with an immunohistochemical complement allowed rectifying the diagnosis. However, other differential diagnosis must be ruled out especially phyllodes tomours, primary sarcoma of breast, desmoid fibromatosis, nodular fasciitis and myofibroblastoma.

Metaplastic carcinoma of breast remains aggressive. However, lymph-node metastases are significantly less frequently found in this group of neoplasm than in invasive carcinomas NST of similar size and grade [14,27]. In a way akin to other triple-negative breast cancers, distant metastases can be found in the absence of lymph-node metastases, and preferentially affect the brain and lungs. During the diagnosis, our patient had no lymph node involvement or distant metastases. The deficient prognosis of ectopic axillary breast cancer originates from the delay diagnosis and the earlier lymph node extension due to the adjacency of the tumor and lymph nodes. To date, there is no standard strategies therapy for MBC. Generally, the treatment is similar to the invasive carcinomas NST and consists on breast surgery, with axillary node dissection followed by radiotherapy that should be used to minimize local recurrence. The role of chemotherapy in MCB was unclear and it can be used in some metastatic cases. Hormonal therapy and targeted therapy were ineffective because these tumours are generally with a ''triple-negative'' and basal phenotype (negative for ER, progesterone receptor (PR) and HER2). If the EGFR were positive, treatment by tyrosine kinase inhibitors could be effective [25]. Further clinical trials are necessary to study these new therapies afin de establishing a therapeutic consensus for this group of tumours.

Conclusion

We describe a case of a patient with metaplastic carcinoma in EBT in axilla which is extremely rare. This location can simulate squamous cell carcinoma of skin, but a thorough histopathological examination, alongside a thoughtful recommendation of careful immunohistochemical markers are necessary to reach the right diagnosis.

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