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Case Report

Malignant Myoepithelioma of the Breast: Clinical Pathological Findings and Review of the Literature

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Abstract

Introduction: Malignant myoepithelioma of the breast is a tumor of infrequent presentation, in the literature and in published case reports is formed by polygonal cells with diffuse pattern or malignant spindle cells with myoepithelial differentiation. Sixty cases have been reported in the indexed literature; because of this scarcity of cases the knowledge of its biological behavior and the treatment that should be offered in this type of tumor is unknown.

Case report: We present a clinical case of a 45-year-old woman, who was admitted to the National Cancer Institute (INCAN) with a breast cancer with histology of infiltrating clear cell carcinoma, which presented an exophytic fungating lesion fixed to deep planes, occupying the internal inferior quadrant of the left breast and bone and pulmonary metastases. On slide review he reported a dense neoplasm of polygonal cells with diffuse pattern, eosinophilic cytoplasm, oval nuclei, obvious nucleoli and atypical mitotic figures. The tumor cells were immunoreactive for EMA, S-100, MSH6, MSH2, PMS2, PMS1, CKIT. With these data, myoepithelial breast carcinoma was diagnosed. First a local excision was performed, with surgical bed enlargement. Continuing with palliative chemotherapy, with platinized salts and taxanes, followed by consolidation chemoradiotherapy and maintenance chemotherapy, with which a progression-free survival of 25 months was achieved, progressing to the pulmonary level with a rechallenge of the initial chemotherapy achieving a partial response at present.

Conclusions: Currently in malignant myoepithelioma of the breast the treatment approach is unknown, for diagnosis the use of immunohistochemistry is essential. Survival of malignant myoepithelioma of the breast is unknown, however, in the present case a progression-free survival of 25 months has been achieved.

Keywords: Malignant myoepithelioma; Breast carcinoma; Immunohistochemistry; Chemotherapy; Systemic recurrence

Introduction

Breast myoepithelioma is a rare entity and its biological behavior is uncertain, of which only 60 cases have been reported in the indexed literature [1]. Myoepithelial cells in the breast are located between the epithelial cells and the basement membrane of the mammary duct system. Myoepithelial cells have characteristics similar to smooth muscle cells, but also to epithelial cells because they present cytokeratin intermediate filaments [2,3]. It's most frequent location is in the salivary gland, extra salivary presentations can be seen in the breast, lung and skin [4-7]. In the Tavassoli publication it is mentioned that there are five types of lesions that derive from myoepithelial cells, these are: adenoid cystic carcinoma, pleomorphic carcinoma, multifocal myoepitheliosis, adenomyoepithelioma and malignant myoepithelioma [8]. With respect to malignant myoepithelioma, the previously reported cases are reported to be composed of a solid infiltrating proliferation of voluminous, atypical spindle cells, with eosinophilic cytoplasm and unusual nuclei and with identifiable mitotic figures [9,10]. The diagnosis of malignant myoepithelioma is usually difficult and immunohistochemical studies with positivity for actin, S-100 protein and low molecular weight cytokeratins are required to reach it [11,12]. In breast cancer, concurrent radiotherapy has been shown to achieve a 5-year disease-free survival of 76.9% and increased overall 5-year survival to 84.2%. In different clinical stages as has been demonstrated in our experience [13]. Going so far as to induce senescence in both cancerous and normal cells, it seems pertinent to target senescent cells and eliminate them from local tissue [14], giving opportunity for maintenance therapy. For these reasons, we present a clinical case with malignant myoepithelioma of the breast with initial metastatic disease. A partial response was achieved and disease-free survival was achieved with maintenance with capecitabine.

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Case Presentation

A 45-year-old postmenopausal woman was admitted to the National Cancer Institute (INCAN) with a 15 cm × 12 cm lesion in the left breast, which was biopsied at another institution with a histopathological report of infiltrating clear cell carcinoma. On examination, a fixed fungal exophytic lesion was observed in deep planes, which occupies the lower internal quadrant of the left breast (Figure 1).

The patient has a family cancer history of a father who died of gastric cancer, two maternal aunts who died of breast cancer and a paternal uncle with lung cancer undergoing treatment. She has a

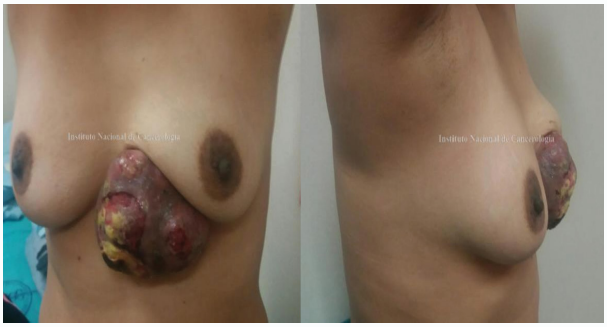

Figure 1: Fungal exophytic lesion was observed in deep planes of the left breast.

personal history of arterial hypertension in treatment with losartan and hydrochlorothiazide and diabetes mellitus II in treatment with metformin. Menarche occurred at age 11. A PET-CT (PET/CT) revealed a voluminous solid lesion dependent on the lower quadrant of the left breast, measuring 11.5 cm × 9.0 cm, with hyperdense tissue associated with hypermetabolism with SUVmax 16.9. Both hemithoraces, with multiple suspicious and non-specific solid nodules, the representative one is located in the left upper lobe, measuring 6 mm with SUVmax 1.1. Lytic lesion in the head of the right femur with SUVmax 7.9. Left axillary lymph nodes at Berg levels I- III, 28 mm with SUVmax 4.6 (Figure 2). Slides from another institution compatible with myoepithelial carcinoma with extensive necrosis, without vascular- lymphatic invasion, were reviewed. IHQ: S-100: +, CKAPM: +, EMA: +. Left lymph node biopsy compatible with carcinoma. The patient was classified with CD IV, the case was discussed in a multidisciplinary team, where it was concluded that the patient would benefit from performing a wide local excision + enlargement of the surgical bed. Subsequently, she receives palliative chemotherapy with carboplatin 2 AUC and paclitaxel at 80 mg/m^2 weekly for 6 cycles, followed by consolidation chemoradiotherapy with cisplatin 30 mg/m^2 and gemcitabine 200 mg/m^2 weekly, which are radio sensitization doses, based on our previously reported experience [13]. 18 F-FDG PET/CT (PET/CT) of reevaluation with postoperative changes at the level of the anterior thorax and left axillary lymph node chain, in both lungs no secondary nodules are observed and in the head of the right femur a lytic lesion with SUVmax 2.2 reaching partial response. She started maintenance with Capecitabine monodroga at 2.5 Gr every 24 hrs for 21/7 for 25 cycles, reaching a progression-free survival of 24 months, subsequently presenting bone and lung progression. Demonstrated by PET CT (Figure 3). Due to good response to previous treatment, she receives carboplatin 2 AUC, paclitaxel 80 mg/m^2 and zolendronate 4 mg. for 7 cycles achieved partial response, with a progression-free survival of 23 months (Figure 4).

Results

Findings

A 12.5 cm × 10 cm × 8 cm tumors with extensive areas of necrosis, ulceration, lateral dermal extension, compromises up to the sternal periosteum and costal cartilage, a positive surgical bed is reported, which is why it is expanded, macroscopically indurated 20 mm axillary nodes.

Histopathology and immunohistochemistry

Malignant myoepithelioma with ulcer and skin infiltration, tumor

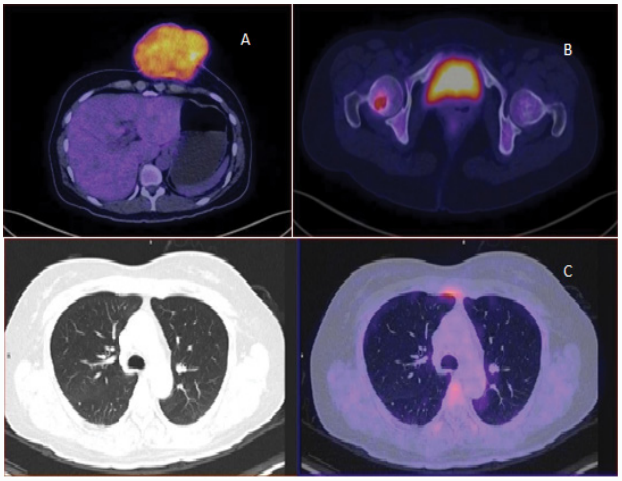

Figure 2: 18 F-FDG PET/CT before receiving surgical and systemic treatment. In axial slices (A) lesion in the thorax dependent on the left breast. (B) Lytic lesion at the femoral level. (C) Secondary lesion in the lung field.

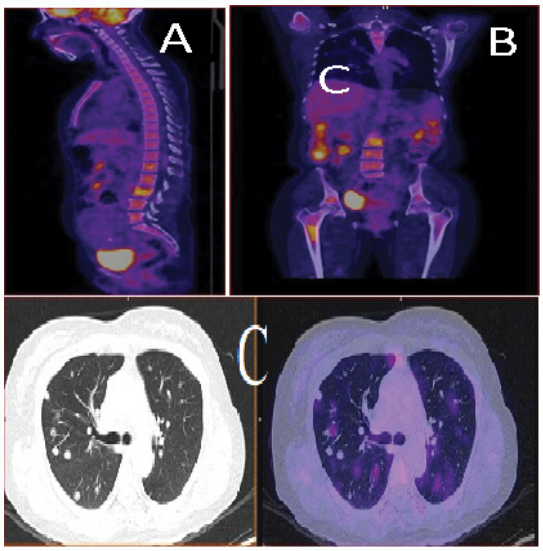

Figure 3: 18 F-FDG PET/CT after surgical and systemic treatment. (A) Sagittal section of metastases at vertebral level. (B) Coronal section of metastases at vertebral level. (C) axial section of secondary lesions in the lung field.

size 12.5 cm × 10 cm × 8 cm, NECROSIS 20%, Surgical edge: negative Lymph nodes: 2/12 positives. EMA: +, S-100:+, MSH6:+, MSH2: +, PMS2:+, PMS1:+, CKIT: +, EGFR: NEG, RE: NEG, HER-2: NEG, KI 67: 40% (Figure 5).

Discussion

Malignant myoepithelioma carcinoma of the breast is a rare pathology and making the diagnosis can be very difficult without the help of immunohistochemistry [15]. The work corresponds to a 45-year-old woman with a 15 cm tumor, with macroscopic findings of extensive areas of necrosis, ulceration, lateral dermal infiltration, affecting up to the sternal periosteum, costal cartilage, and macroscopically indurated 20 mm axillary nodes. Microscopic examination revealed a dense neoplasm of polygonal cells with a diffuse pattern, and these tumor cells have eosinophilic cytoplasm, oval nuclei, obvious nucleoli, and atypical mitotic figures. These features contributed to the diagnosis of malignant myoepithelioma.

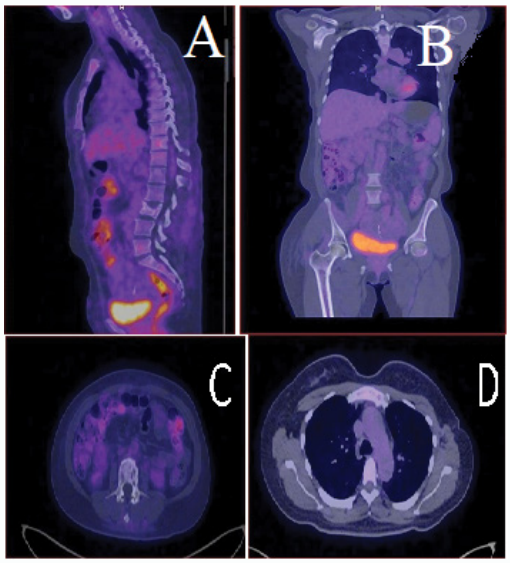

Figure 4: 18 F-FDG PET/CT after systemic treatment with partial response. (A) Sagittal section with response at the vertebral level. (B) Coronal section with response at the femoral level. (C) Vertebral axial section. (D) Reduction of lesions at the lung level.

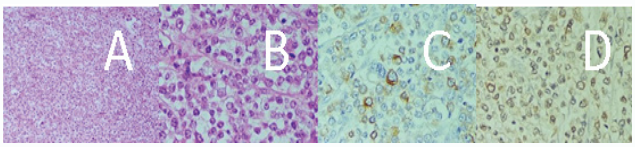

Figure 5: Slide of surgical piece. (A) Hematoxylin-eosin (10x/0.25). Dense neoplasm of polygonal cells with a diffuse pattern. (B) Hematoxylin-eosin (40x/0.65). Tumor cells present an eosinophilic cytoplasm, oval nuclei, evident nucleoli, and atypical mitotic figures. (C) Phenotype of myoepithelial cells. EMA immunohistochemistry (40x/0.65). Neoplastic cells with cytoplasmic staining. (D) S-100 immunohistochemistry (40x/0.65). Neoplastic cells with cytoplasmic staining.

The value of immunohistochemistry is important to reach the diagnosis of malignant myoepithelioma, in the studied sample I present immunoreactivity for the myoepithelial differentiation markers that are S-100 and EMA. This tumor did not mark hormonal or her-2 receptors, being considered a triple negative with a Ki-67 of 40%. In other case reports, they mention that useful antibodies are those directed against CK and myofilaments. These antibodies against high molecular weight CKs (CK5, CK5/6, CK14 and CK17) react to this type of lesions. Other important immunostains are nuclear p63, p53 and S-100, which tends to reach 90% positivity. It is also mentioned that calponin is positive in 86%, desmin in 14% and SMA in 36% [11]. Another type of immunostaining that rarely expresses malignant myoepithelioma is Glial Fibrillary Acidic Protein (GFAP) positivity [16]. Differential diagnosis becomes very difficult and must be performed with immunohistochemical tests.

The differential diagnosis must take into account 3 main entities. The first is that fibromatosis must be taken into consideration, due to how frequent it is in the breast and because it presents proliferation of myofibroblasts and fibroblasts intermingled with stromal collagen. This pathology, by presenting a minimum number of mitosis and pleomorphism, this indicates that it is of a benign type. Regarding the positive immunostains for this, it comes to express actin, desmin and S-100, unlike CK and CD34 do not express them [8,17].

The second is myofibroblastoma due to its characteristics similar to malignant myoepithelioma due to the positivity for smooth muscle myosin heavy chains and CD34, but they are generally negative for CK and S-100 [12].

The third is monophasic sarcomatoid carcinoma because they do not present an epithelial component. This type of neoplasms can express positivity for actin in immunoreactions and this is why differentiation with malignant myoepithelioma is difficult. In order to differentiate between the two, antibodies against keratin of variable molecular weight are required. Sarcomatoid neoplasms behave very similarly to high-grade carcinomas [18,19].

In the literature, malignant myoepithelioma is a rarely reported entity, for this reason the biological behavior of this neoplasm is not fully known. It presents a good response to surgical treatment, with few recurrences at the locoregional level, and metastatic dissemination of the disease is rare [18,20,21].

In the case presented, the patient started with a metastatic disease at the lung level and with a 15 cm × 12 cm tumor in the left breast, for which it was decided by a multidisciplinary team that it was necessary to perform a wide local excision+expansion of the surgical bed. Subsequently, palliative chemotherapy based on carboplatin with paclitaxel was started, which is consistent with the treatment given in other case reports of malignant myoepithelioma of the breast [10-12,22].

Due to the aggressiveness of the disease, it was decided to continue with concurrent chemotherapy with consolidation radiotherapy; in previous experience it was possible to optimize the local control of the disease. Although this type of treatment is not standard, in our experience in breast cancer satisfactory results were obtained. Understanding the determinants of metastasis, as well as epithelial- mesenchymal/cancer stem cell plasticity, therefore, if we control the drivers of plasticity will have a significant impact on survival of people. For this reason, the patient received capecitabine as maintenance, achieving a disease-free survival of 25 months in a metastatic stage [14,23].

Conclusions

Myoepithelial carcinoma of the breast is an extremely rare entity that is difficult to diagnose without immunohistochemistry. In the reported case of a young patient who, despite having an aggressive and metastatic disease at the beginning, a disease-free survival of 25 months was achieved. For all of the above, further research on this entity must be carried out in order to better understand its biology and behavior that allow defining the best oncological treatment.

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