DOI - 10.37951/CEREM-2021-V2I1-40-42

REVIEW ARTICLE

SARCOMAS AND OTHER NON-EPITHELIAL BREAST TUMORS: A LITERATURE REVIEW

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ABSTRACT

Non-epithelial malignant breast diseases are responsible for about 1% of all breast tumors. The most common primary non-epithelial breast cancers are sarcomas and lymphomas. Among sarcomas, the malignant phyllodes tumor is the most common. The macroscopic aspect of sarcomas shows tissue with a firm consistency, ranging from bronze to gray, with soft, cystic and other hemorrhagic areas. Histologically, these tumors are hypercellular, proliferation in fibroblastic spindles, atypical cells and highly anaplastic of intermediate to high degree. Histological grading is important for treatment and prognosis. Hematogenous dissemination is the most common and the involvement of axillary lymph nodes is not frequent among sarcomas. The most frequent sites of metastasis are the lungs, bones and liver. The treatment for primary breast sarcomas is wide excision with adequate and free margins. Lymphadenectomy is not recommended unless there are clinically suspect lymph nodes. Radiotherapy and chemotherapy can be considered, but they have an uncertain role.

KEY-WORDS: BREAST CANCER; SARCOMA; MALIGNANT PHYLLODES TUMOR

INTRODUCTION

Mesenchymal lesions of the breast are a rare group of benign and malignant lesions. They may appear primarily or be iatrogenically induced. The clinical presentation and epidemiology are confused with that of breast carcinomas, compromising patients of both sexes and in a large age group. The formation of a palpable mass or breast asymmetry is commonly the most frequent presentation. The prognosis and treatment vary extraordinarily depending on the histopathological diagnosis [1].

Mass-forming lesions with favorable biological behavior of the breast are represented by nodular fasciitis, benign vascular lesions, pseudoangiomatous stromal hyperplasia, myofibroblastoma, desmoid fibromatosis, inflammatory myofibroblastic tumor and lipoma [2].

Malignant mesenchymal neoplasms of the breast can be primary or secondary. Primary neoplasms are those that appear sporadically and spontaneously in the breast parenchyma, the most frequent of which is Phyllodes Tumor of the breast. Secondary neoplasms are those that originate after some type of treatment already instituted in the mammary gland. The most frequent histological type is angiosarcoma, which may be secondary to radiotherapy or late consequence of lymphedema of the arm or breast [3].

The Phyllodes Tumor of the breast is historically called Cystossarcoma Phyllodes for presenting morphological characteristics of leaf-like growth and with the formation of cysts due to rapid growth with necrosis and cystic degeneration. It is a neoplasm with variable biological behavior, characterized by a mass-forming mesenchymal proliferation with a biphasic element - mesenchyme and epithelium [4].

Despite the infrequent presentation in the breast, there is a group of non-epithelial lesions that include hematolinfoid lesions and melanoma. These are rare primitive lesions of the breast, that is, the majority of cases diagnosed in the breast represent systemic diseases with secondary involvement of this organ. Mass-forming breast lesions and metastases from other organs to the breast parenchyma should be remembered in the differential diagnosis. The main organs involved in this situation are cancers of the contralateral breast, stomach, colorectal tract, lung and ovary (Table 1) [1].

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MALIGNANT TUMORS	HISTOLOGICAL TYPES
MESENQUIMAL BREAST NEOPLASMS	• Phyllodes tumor • Angiosarcoma • Osteogenic sarcoma • Embryonic breast rhabdomyosarcoma • Lymphangiosarcoma associated with lymphedema • Primary sarcoma of the stroma of the breast • Various sarcomas (stromal sarcoma, leiomyosarcoma, liposarcoma, malignant fibrous histiocytoma, Ewing's sarcoma and fibrosarcoma).
HEMATOLOGICAL TUMORS	• Large, diffuse B-cell non-Hodgkin's lymphoma • Hodgkin's lymphoma • Solitary plasmacytoma • Anaplastic large cell lymphoma (T cells) associated with silicone implants.
MELANOMA OF THE BREAST	• Primary cutaneous melanoma
METASTASES TO THE BREAST	• Contralateral breast • Melanomas • Lung cancer • Gastric and colorectal cancer • Ovarian cancer

Table 1 - Differential diagnosis of other non-epithelial breast neoplasms.

LITERATURE REVIEW

Clinical condition

Sarcomas of the breast usually present as a unilateral, well-defined, relatively painful firm mass. They are rarely bilateral, usually fast growing and larger when compared to epithelial neoplasms of the breast. They vary in size from a few centimeters to giant masses with infiltration and necrosis of the skin [5].

Diagnosis

Like all other breast neoplasms, the diagnosis of breast sarcoma begins with a complete clinical history, careful physical examination, epidemiological history, pathological history and imaging exams [6].

In view of the clinical suspicion of tumor mass, fine needle aspiration (FNAB) is of great importance in the formulation of the diagnosis, considering that it is a low-invasive and low-cost procedure and provides relevant information for the construction of the final diagnosis. Cytopathological examination allows to define the histogenetic lineage of the lesion, whether it is a lesion of epithelial, mesenchymal or hematopoietic origin. It also allows for the assessment of their biological behavior: benign, low malignant or frankly malignant potential [7].

Core biopsy is generally considered to be the procedure of choice for diagnosing sarcomas. However, the gold standard for defining the diagnosis is the pathology of the surgical specimen, as in most sarcomas, not only of the breast, are dependent on sampling [8].

Macroscopically, breast sarcomas are masses of variable size, with infiltrative growth, firm-rubbery consistency, sometimes with calcifications and or cystic degeneration, foci of necrosis, with a grayish-white cut surface with the appearance of "fish meat" [8].

Histologically, the diagnosis of breast sarcoma is always difficult because they are rare lesions and with strict morphological diagnostic criteria recommended by the WHO. Morphologically, the fusocellular pattern with atypias is the most common in most sarcomas. Immunohistochemistry greatly helps in the definition of cell differentiation [1].

Phyllodes tumor shows expression of vimentin in the mesenchymal component and keratins in the epithelial component.

Primary stroma sarcoma of the breast has expression of vimentin and CD10.

Liposarcoma shows S100 protein expression.

Rhabdomyosarcoma has expression of MyoD1 or myogenin.

Angiosarcoma shows expression of CD31, CD34, BNH-9, D2-40 and ERG.

In order to differentiate between primary and secondary angiosarcomas, amplification of the MYC gene gains importance, described more frequently in radioinduced form.

Morphologically, phyllodes tumors can be benign, malignant or boderline. Benign tumors have mild cellular atypias, absence of necrosis, low mitotic activity, less than 4 mitoses per 10 high-magnification fields (HMF) in histology, and expansive growth pattern. Tumors with malignant behavior, on the other hand, present marked stromal overgrowth, severe cell atypias, mitoses above 10 mitoses/ 10 HMF, necrosis and infiltrative growth of adjacent tissues [4].

Tumors with borderline behavior present intermediate characteristics at both ends, but mainly mitosis rates between 4 and 10 mitoses per 10 HMF [5].

Treatment

Surgery represents the modality of choice in the management of sarcomas, when the intention of treatment is curative. Mastectomy is usually necessary for large tumors and/or those that appear in previously irradiated areas. Tumor-free resection margins are the main factor for a long relapse-free survival [1 2].

The use of adjuvant chemotherapy should be evaluated individually taking into account the patient's clinical conditions, age, toxicities to previous therapies, comorbidities and, mainly, the histological type sensitivity to chemotherapy [4 5].

In the case of metastatic disease, the use of palliative chemotherapy follows the same protocols used for soft tissue sarcomas in general [1].

Conclusion

Sarcomas can be primary or the consequence of treating epithelial breast cancer (secondary). Radiotherapy can lead to the development of secondary sarcomas with a latency of more than twenty years. Malignant mesenchymal tumors of the breast are mainly composed of the malignant phyllodes tumor and soft tissue sarcoma. Surgical resection with negative margins is the treatment of choice in most primary sarcomas, especially the phyllodes tumor.

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