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Diagnostic and therapeutic pitfalls with primary breast sarcoma: A case report and review of the litterature

Pièges diagnostiques et thérapeutiques d'un sarcome mammaire primitif : cas clinique et revue de la littérature

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Cas clinique

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Mots clés : Tumeurs phyllodes du sein, sarcome primaire du sein, diagnostic, traitement.

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ABSTRACT

Primary breast sarcomas are rare and aggressive tumours that represent less than 1% of breast neoplasms. An 18-year-old female presented with a right breast mass, histology of which revealed a benign phyllodes tumour. After a multidisciplinary consultation, a right mammectomy with axillary curage was indicated. Histopathological and immunohistochemical analysis of the operative specimen were in favour of a grade 2 primary sarcoma with cutaneous and axillary extension. The post-mastectomy course was marked by tumour recurrence. Diagnostic and therapeutic difficulties are related to the young age, clinical presentation and histopathology of this entity.

RESUME

Les sarcomes primaires du sein sont des tumeurs rares et agressives qui représentent moins de 1 % des cancers du sein. Il s'agissait d'une patiente de 18 ans présentant une masse mammaire droite, pour laquelle l'histologie révélait une tumeur phyllode bénigne. Après réunion de concertation multidisciplinaire, une mammectomie droite avec curage axillaire a été indiquée. L'analyse histopathologique et immunohistochimique de la pièce opératoire étaient en faveur d'un sarcome primitif grade 2 avec extension cutanée et axillaire. L'évolution post mastectomie a été marquée par une récidive tumorale. Les difficultés diagnostiques et thérapeutiques sont liées au jeune âge, à la présentation clinique et à l'histopathologie de cette entité.

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Introduction

Breast masses in children and adolescents are generally of a benign nature [1]. The most common mass is fibro-adenoma which constitutes 30–50% of breast masses [1, 2]. Malignant tumours are extremely rare in this age group, with phyllodes malignant tumour being the most common [3]. Primary breast sarcoma is extremely rare, accounting for less than 1% of all breast cancer cases [3,4]. It usually occurs in postmenopausal women, with most of the reported cases being between 45 to 50 years [5]. We report the case of a primary breast sarcoma in a female adolescent, and discuss through a review of the literature, the diagnostic pitfalls associated with this entity which constitutes a diagnostic dilemma for pathologists.

Case presentation

This is an 18-year-old nulligravid female patient with no significant past medical nor family history, who presented with a rapidly growing, painless mass in the right breast of about four months duration before her first consultation. Physical examination initially revealed a firm, non- tender, mobile mass of about 9cm occupying both right external quadrants. The overlying skin and nipple-areola complex were normal, and there were no palpable axillary lymph nodes. The left breast was normal. Breast ultrasound revealed two hypo-echogenic heterogeneous masses of the right breast measuring 75x65x58mm and 38x25x20mm with regular borders, classified ACR BI-RADS 4 (American College of Radiology - Breast Imaging Reporting & Data System). Analysis of a fine needle aspiration of the right breast showed cytopathological aspects of a fibro-adenoma. A right breast lumpectomy was done in November 2022 with findings; a poorly defined mass of about 10cm. Histopathology analysis of the mass confirmed a periductal fibro-adenoma without malignant lesions. The postoperative course was unremarkable and patient was discharged.

Progress was marked three months later by an exponential recurrence of the right breast mass. This time, physical examination revealed breast asymmetry with the right breast being increased in size, ulceration at the union between both outer quadrants, peri-areolar hyperpigmentation and orange-peel appearance on inspection of the right breast. On palpation, there was a firm and tender mass of about 20cm occupying all the four quadrants of the right breast, and fixed to the chest wall. Ipsilateral lymph nodes were difficult to assess due to the mass. Examination of the left breast was unremarkable, and there were no palpable lymph nodes on the left as well (**Figure 1**).

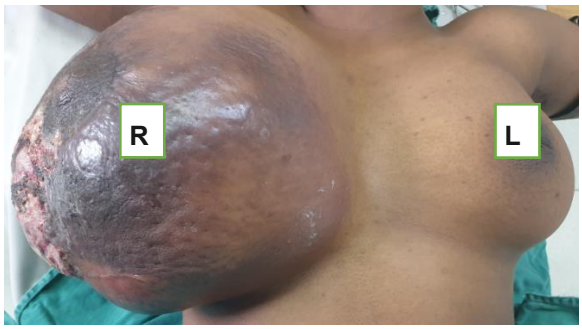

Figure 1*: clinical appearance of the large ulcerated righ breast following initial lumpectomy (R= Right and L= Left)*

Following this recurrence of the right breast mass, a second histological reading of the mass post lumpectomy was requested, which revealed a benign phyllodes tumour. Another breast ultrasound was also done which revealed an oval hypo-echogenic heterogeneous mass of 107x105x81mm with irregular borders, posterior acoustic shadowing, long axis oblique to the cutaneous plane, mixed vascularisation on Doppler, infiltration of overlying fatty tissue and skin, with modification of breast architecture and no lymphadenopathy, classified ACR BI- RADS 5. After a multidisciplinary consultation meeting, a right total mastectomy with ipsilateral lymphadenectomy was indicated and done. Intraoperative findings included palpation of an axillary lymph node under the pectoralis minor muscle with a long axis of approximately 5 cm, attached to the axillary vein. Per-operatively, a lymph node sampling was also performed. The surgical specimen, including the whole right breast, a lymph node picking, and a lower skin re-cut were sent to the pathology department (**Figure 2**).

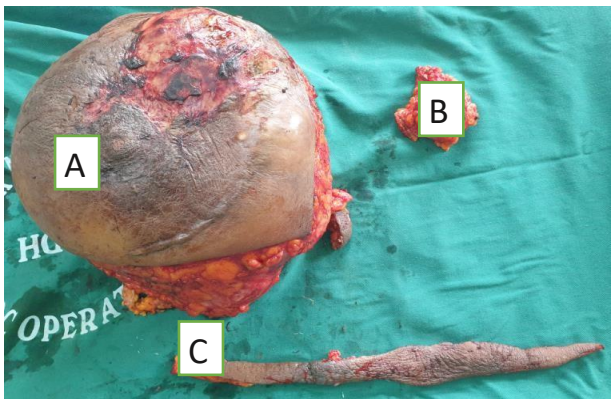

Figure 2: *right total mastectomy specimen including the old lumpectomy scar (A) with lymph node picking (B) and infiltrated lower cutaneous re-cut specimen (C), sent to the pathology department.*

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Macroscopically, the mastectomy specimen measured 22x21.5x14 cm. The skin surface showed an area of irregular ulceration extending to the nipple. On cross-section, the slices showed a fibrous, haemorrhagic tumour with myxoid remodeling, infiltrating the surgical margins.
Microscopic analysis of the samples showed mammary parenchyma dissected by fuso-cellular proliferation in variable clusters (**Figure 3**).

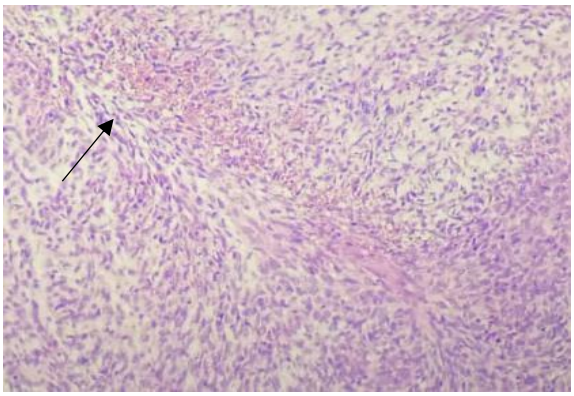

Figure 3: *Haematoxylin-eosin staining at high magnification: spindle cell proliferation forming variable clusters (black arrow) [image from the Pathology Laboratory of the Centre Pasteur in Cameroon]*

Cytonuclear atypia were moderate, chromatin was heterogeneous, and there were 10 to 20 mitoses/HPF (High Power Field). Areas of necrosis represented approximately 50% of the tumour volume. The deep surgical margins and one of the lateral margins were infiltrated by the tumour. These features were consistent with a primary breast sarcoma of the leiomyosarcomatous type and Grade 2 according to the FNCLCC. Following this result, immunohistochemistry was also requested which revealed a periductal stromal sarcoma with intermediate malignancy and with moderate cytoplasmic expression of CD34+ by 70% of tumour cells.

The patient was once more presented at a multidisciplinary consultation meeting following which she was referred to the Cameroon Oncology Centre for radiotherapy, which was not done due to a lack of financial resources. We received her seven months later with a large firm non- tender tumour that covered the entire right anterior chest wall extending to the clavicle and the axilla with a purple discoloration of skin and ulceration at the site of the mastectomy scar (**Figure 4**).

A thoracic-abdominal-pelvic CT Scan was thus requested as extension work-up, which revealed a voluminous, multi-lobed and necrotic right chest mass with infiltration of the pectoral muscles and axilla, measuring 212x118mm. There were no axillary and mediastinal adenopathy nor secondary metastases (**Figure 5**).

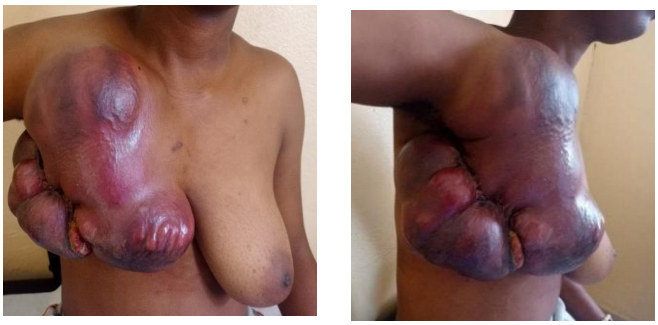

Figure 4: *clinical appearance of the recurrent right chest tumour seven months after right total mastectomy and no radiotherapy*

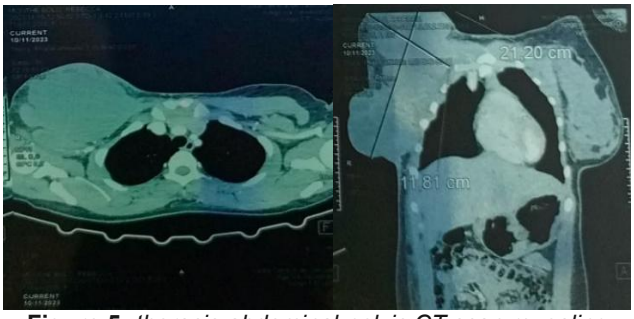

Figure 5: *thoracic-abdominal-pelvic CT scan revealing absence of secondary lesions*

After seeing the results of the CT Scan, the patient was once more referred to the Cameroon Oncology Centre for radiotherapy which was done. Following radiotherapy, she had a favourable evolution, with marked regression of the right chest wall mass.

Discussion

Breast sarcomas are rare, histologically heterogeneous non-epithelial malignancies that arise from the connective tissue within the breast [1]. They account for less than 1% of all breast malignancies and less than 5% of all soft tissue sarcomas [2-4]. This tumor occurs usually in postmenopausal women, with most of the reported cases being between 45 to 50 years (range 17 to 89 years) [5-10]. Men account for 1.5% of cases of breast sarcoma [11]. Its occurrence in very young girls is extremely rare and may be clinically mistaken for fibro-adenoma [12], as seen in the case of our patient. They can be sub-classified as primary breast sarcomas, which arise de novo and are histologically diverse, and secondary breast sarcomas, which arise because of radiation or lymphedema and are most commonly angiosarcomas [6,7]. Our patient had no history of past radiation exposure. There are no known risk

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factors specifically associated with primary breast sarcomas, but certain genetic syndromes, such as Li-Fraumeni syndrome, hereditary retinoblastoma, familial adenomatous polyposis and neurofibromatosis type 1 as well as environmental exposures to arsenic compounds, vinyl chloride, herbicides and immunosuppressive agents have been linked to sarcomas in general [6,11,13]. We could not identify any risk factors in our case, and she was not eligible for oncogenetic screening according to the Chompret diagnostic criteria.

Primary breast sarcomas are histologically heterogeneous with several subtypes, including angiosarcoma, undifferentiated pleomorphic sarcoma, stromal sarcoma, fibro-sarcoma, liposarcoma, leiomyosarcoma, spindle-cell sarcoma and rhabdomyosarcoma [1,5]. Angiosarcoma, undifferentiated pleomorphic sarcoma and stromal sarcoma are the most common subtypes [1,2]. Histologic review by an experienced soft tissue pathologist is critical in making the diagnosis [1]. In our case, the diagnosis of primary breast sarcoma was made after three histological readings which delayed management. Histology of our patient revealed a primary breast sarcoma primarily of leiomyosarcomatous type. It is recommended that a core needle biopsy be performed, to provide a greater amount of material for histological analysis [7]. Instead, a fine needle aspiration was done for our patient, which has a very low accuracy rate with false negative results and this delayed diagnosis and management.

Immunohistochemistry is useful to distinguish primary breast sarcomas from non-mesenchymal malignant tumors and to delineate the level of differentiation of primary breast sarcomas [7,14]. In our patient, immunohistochemistry revealed a periductal stromal sarcoma with intermediate malignity and with moderate cytoplasmic expression of CD34+ by 70% of tumor cells. This is contradictory to the histological findings of leiomyosarcoma which express smooth muscle actin and desmin. However, CD34 reactivity is well described in the stromal cells of phyllodes tumours. It is of diagnostic value in differentiating high-grade spindle-shaped lesions of the breast, such as breast-type Darier Ferrand dermatofibrosarcoma [15].

Breast sarcoma most often present as a unilateral (rarely bilateral), well-defined, large, painless, firm mass within the breast, and often characterized by a rapid increase in size [6, 11, 14] as in the case of our patient. Breast skin and the nipple-areola complex are only rarely involved by breast sarcomas [2]. However, angiosarcomas are the exception; they may be associated with skin thickening, erythema, or skin discoloration with an overlying bluish tint [3,4] as in our case. These findings are sometimes mistaken for cellulitis or a hematoma.

The finding on mammography is a single oval hyper-dense mass with indistinct or circumscribed margins without calcifications [6]. A mammography was not done in our patient due to her age and dense breasts. Ultrasound is better than mammography for evaluating the margins of the mass, for differentiating between solid and complex masses, for identifying and characterizing internal vascularization, and for guiding percutaneous procedures [6,16]. On ultrasound, a primary breast sarcoma typically presents as an oval mass, with indistinct margins, a hypoechoic or complex echotexture, posterior acoustic shadowing and internal vascularization (on Doppler assessment) [16] as in the case of our patient. Magnetic resonance imaging (MRI) of a primary breast sarcoma usually shows an oval mass, with irregular margins, a hypo-intense signal on T1-weighted imaging, and a hyper-intense signal on T2-weighted imaging [14]. MRI can also provide information on skin infiltration, as well as the degree of involvement of the deep fascia and pectoralis muscle, which is important in planning the surgical approach [7,17]. MRI was not done by our patient due to financial constraints.

The treatment for breast sarcomas is planned by a multidisciplinary team following the treatment model of sarcomas in other locations [5]. However, there is still no definitive consensus regarding the treatment of primary breast sarcomas [16]. Surgery represents the only potentially curative modality [11]. Mastectomy without axillary lymph node dissection is the treatment of choice for primary breast sarcoma. Wide excision can be done if negative surgical margins can be achieved [16]. Axillary lymph node dissection should be avoided unless they are clinically positive nodes [14]. In our patient a right mastectomy with ipsilateral lymph node dissection was done. Negative surgical margin is the most important determinant of local recurrence [4] which was not achieved in our case. Adjuvant and neo-adjuvant chemotherapy and radiotherapy should be considered in high-risk cases [5]. Adjuvant radiotherapy has been recommended especially for large or high-grade tumours [16].

Overall, the prognosis of primary breast sarcoma is poor with a high recurrence rate [8]. Tumours typically spread through local invasion or haematogenous spread, and the lungs, bone marrow, and liver are common metastasis sites [7]. The prognosis dependents on tumour size, histopathological type, histopathologic grading, the

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presence of positive margins, and local recurrence [9]. Tumours larger than 5 cm are associated with worse outcomes [12] as in our case. Delay in its diagnosis has important clinical and treatment implications [2]. The median overall survival for breast sarcoma is 108 months, and the 5-year survival rate varies, ranging from 14% to 90% [4].

Conclusion

Breast sarcomas are rare and associated with a poor prognosis. The early and correct diagnosis of primary breast sarcoma is extremely relevant because of its aggressive behavior. Core biopsy is necessary for the definitive diagnosis of primary breast sarcoma because findings on imaging are not pathognomonic, and well marginated masses are generally interpreted as benign in young females. A rapidly growing breast mass should alert the clinician to investigate for malignancy.

Informed consent: The patient's informed consent was obtained for the publication of information in this clinical case.

Declaration of interests: The authors declare no conflicts of interest regarding the publication of this paper.

Author's contribution:
Mouelle MA: conception, writing of the article, review of literature Meka EJ: approval of the final version, Tompeen, Mbia CH, Esson Mapoko, Adiang SG, Litingui, Ngo Tega N, Mbenoun LF: writing of the article, created figures, final proofreading, review of literature, traduction Sando Z: approval of the final version

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