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FACULTY OF MEDICINE AND BIOMEDICAL SCIENCES

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

PRIMARY BREAST SARCOMA IN A 17-YEAR-OLD FEMALE: CASE REPORT AND LITERATURE REVIEW

Dissertation submitted in partial fulfilment of the requirements for the award of a University Diploma

in

Senology And Breast Pathology by;

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DEDICATION

This work is dedicated to my parents

Mr. SULE GARBA DANLADI

And

Mrs. SODA IDIRISU ZENABU

ACKNOWLEDGEMENTS

TO ALMIGHTY GOD: THANK YOU, ALLAH, FOR EVERYTHING.

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LIST OF TEACHERS OF THE "UD" IN SENOLOGY AND BREAST PATHOLOGIES

Pr MEKA Née NGO UM Esther

Pr NOA NDOUA Claude Cyrille

Pr ESSIBEN Félix

Pr BELINGA Etienne

Pr ZE MINKANDE Jacqueline

Pr ONGOLO ZOGO Pierre

Pr ZEH Odile

Pr TCHENTE NGUEFACK Charlotte

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Dr EYOUM Christian

Dr MAPENYA Ruth

Dr SEME Ambroise

Dr ATENGUENA Etienne

Dr KOUOTOU Née MENDOUGA Coralie

Dr METOGO NTSAMA Junie

Dr ESSON MAPOKO Berthe

Dr MOUELLE Michel

PROGRAM OVERVIEW

The University Diploma (DU) in Senology and Breast Pathology is the fruit of a long struggle and unprecedented hard work by our lecturers at the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I, Professor MEKA Née NGO UM Esther, Senior Lecturer in Obstetrics and Gynaecology, assisted by Professors NOA NDOUA Claude Cyrille and ESSIBEN Félix, both Senior Lecturers in Obstetrics and Gynaecology. The aim of this diploma in senology is not only to popularise medical practice in relation to breast pathologies, but above all to transmit good methodological techniques, rigour and systematisation of work, and to teach obstetrician-gynaecologists good practice in the field of senology. It's a real privilege for us to be among the first group of specialists and residents selected for this training.

t was high time for such an initiative to be launched because, despite all that is at stake, we are all aware that there are many professionals and practitioners who deal with breast pathologies without any minimum training in senology. A few months ago, we were part of this group. However, there are a number of obstacles to this training, but our supervisors were able to spare their busy schedules to complete this DU professional training course in senology and breast pathology. We are very grateful to them.

Our expectations during this DU were high and mainly based on the quality of the training and the acquisition of all possible skills to be a good senologist who knows the obligations of scientific competence and technical efficiency normally expected in order to make my modest contribution to reducing breast cancer mortality. In this report, we invite you to take a look at our training and the clinical case we reported.

PRESENTATION OF THE UNIVERSITY DIPLOMA IN SENOLOGY AND BREAST PATHOLOGY

The University Diploma (DU) in Senology and Breast Pathology is a training diploma organised by the Faculty of Medicine and Biomedical Sciences (FMSB) of the University of Yaoundé I. It covers the fields of gynaecology and obstetrics, general surgery, radiology, Anatomopathology, oncology and psychology. The aim of the course is to acquire knowledge of benign and malignant breast pathology, the various investigations, treatment methods and protocols, indications and side effects, and the psychological impact of breast cancer. The aim is to develop skills in breast surgery, reconstruction surgery, chemotherapy protocols and targeted therapies, hormone therapy, histopathology of breast cancer, radiological and anatomopathological examinations of the breast, radiotherapy protocols, palliative care and management of benign breast conditions. In order to achieve these objectives, our training programme has been structured as follows:

- Four lecture seminars over four months, i.e. one week of lectures per month in the new training block of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I,
- Timetable: 08:00-17:00 Monday to Friday with one hour break
- Organised work placements
- 02 months of practical training in various hospitals, including: HGY, HGOPY and CHRACERH, which consisted of attending, as far as possible, all breast surgery operations scheduled in these different university health facilities.
- culminating in a final examination consisting of multiple-choice questions, open questions and clinical cases.

INTERNSHIP REPORT

Our practical training took place mainly in three health facilities in the city of Yaoundé, namely HGY, CHRACERH and HGOPY. It consisted of attending multidisciplinary consultations and observing various breast surgeries scheduled in the operating theatres of the different training sites. The aim was to acquire practical skills in senology and breast surgery. During our consultations, we had the opportunity to follow several cases, including the one we are going to present.

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACR: American College of Radiology

BI-RADS: Breast imaging-reporting and data system

FNA: Fine needle aspiration

HPF: High power field

MRI: Magnetic resonance imaging

TAP: Thoraco-abdomino-pelvic

ABSTRACT

This study presents a rare case of primary breast sarcoma in a 17-year-old female, detailing her clinical presentation, diagnostic challenges and treatment outcome. Although breast masses in children and adolescents are predominantly benign, this case highlights the potential for malignancy, particularly primary breast sarcomas, which account for only 1% of all breast malignancies but are associated with aggressive behaviour and a poor prognosis.

The patient initially presented with a painless, rapidly enlarging breast mass that was misdiagnosed as a fibroadenoma. Subsequent investigations revealed a primary sarcoma of the leiomyosarcomatous type with cutaneous and axillary extension following surgical intervention. The study highlights the importance of prompt and accurate diagnosis, emphasising core needle biopsy over fine needle aspiration due to its poor diagnostic accuracy. It also discusses the critical role of multidisciplinary management in the management of breast sarcoma, where complete surgical resection with negative margins is paramount, while the role of adjuvant radiotherapy and chemotherapy remains controversial.

This case serves as a reminder of the need for vigilance in the evaluation of breast masses in young patients and highlights the need for further education and training in the diagnosis and management of such rare entities.

RESUME

Cette étude présente un cas rare de sarcome primaire du sein chez une jeune femme de 17 ans, en détaillant sa présentation clinique, les difficultés diagnostiques et le résultat du traitement. Bien que les masses mammaires chez les enfants et les adolescents soient principalement bénignes, ce cas met en évidence le potentiel de malignité, en particulier les sarcomes mammaires primaires, qui ne représentent que 1 % de toutes les tumeurs malignes du sein, mais sont associés à un comportement agressif et à un mauvais pronostic.

La patiente s'est d'abord présentée avec une masse mammaire indolore, qui a été diagnostiquée à tort comme un fibroadénome. Les examens ultérieurs ont révélé un sarcome primaire de type léïomyosarcome avec une extension cutanée et axillaire, suite à une intervention chirurgicale. L'étude souligne l'importance d'un diagnostic rapide et précis, en privilégiant la biopsie à l'aiguille centrale plutôt que la ponction à l'aiguille fine en raison de sa faible précision diagnostique. Elle discute également du rôle critique de la prise en charge multidisciplinaire dans le traitement des sarcomes du sein, pour lesquels une résection chirurgicale complète avec des marges négatives est primordiale, tandis que le rôle de la radiothérapie et de la chimiothérapie adjuvantes reste controversé.

Ce cas rappelle la nécessité d'être vigilant dans l'évaluation des masses mammaires chez les jeunes patientes et souligne le besoin d'un enseignement et d'une formation plus poussés en matière de diagnostic et de prise en charge de ces entités rares.

INTRODUCTION

Breast masses in children and adolescents are generally of a benign nature [1]. The most common mass is fibroadenoma which constitutes 30–50% of breast masses [1, 2]. Malignant tumours are extremely rare in this age group, with phyllodes tumour being the most common. Primary breast sarcoma was first described by Chelius in 1828, and this rare entity constitutes 1% of all breast malignancies [3]. We present the clinical features of a 17 years old with primary breast sarcoma, its pathological features, and an up-to-date review of literature on the topic.

CASE PRESENTATION

17yrs old G0 With no family history of breast cancer or any other comorbidity, presented with a rapidly growing, painless mass in the right breast of 4 months duration. Physical examination revealed a firm, non-tender, mobile mass of about 9cm on both right external quadrants with a normal overlying skin and nipple-areola complex with no axillary lymphadenopathy. The left breast was normal. Breast ultrasound revealed two hypoechogenic heterogenous masses of 75x65x58 mm and 38x25x20mm with regular borders classified ACR IV. A fine niddle aspiration showed cytopathological aspects in a fibroadenoma. A lumpectomy was done with findings; a poorly defined mass of about 10cm. Histology of the mass confirmed a periductal fibroadenoma with no malignant lesions. progress was marked 4 months later by an asymmetrically enlarged ulcerative right breast which was fixed to the chest wall, non-tender, with peri-areolar hyperpigmentation and peau d'orange aspect (figure 1).

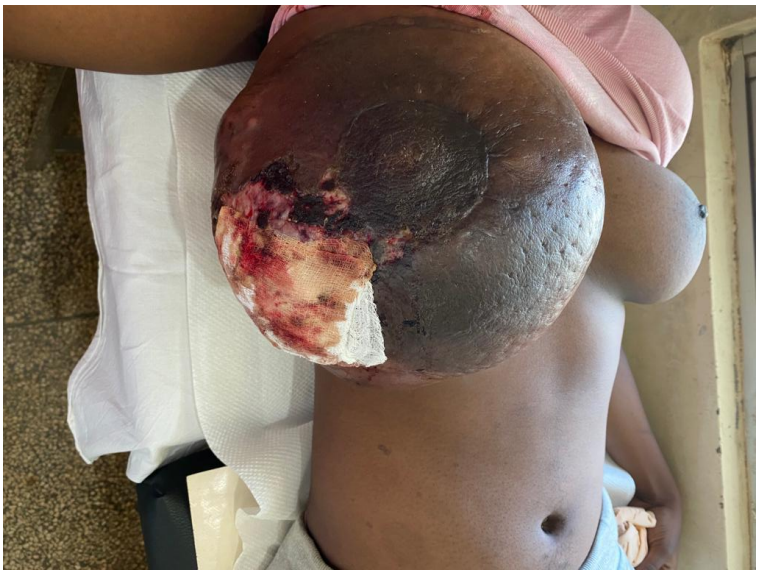

Figure 1 : Evolution of tumour 4 months after lumpectomy

This time, breast ultrasound revealed an oval hypoechogenic heterogeneous mass of 107x105x81mm with irregular borders, posterior acoustic shadowing, long axis oblique to the cutaneous plane, mixed vascularization on doppler, infiltration of overlying fatty tissue and skin with modification of breast architecture and no lymphadenopathy classified ACR V. A second histological reading of the mass post lumpectomy was requested which revealed a benign phyllode tumour. Due to the tumour growing exponentially, a right total mastectomy + ipsilateral lymphadenectomy was done. Histology revealed a primary breast sarcoma primarily of the leiomyosarcomatous type FNCLCC (2+2+1) =5 GRADE II (INTERMEDIATE) with cutaneous and axillary extension, infiltration of deep and lateral limits. Immunohistochemistry revealed a periductal stromal sarcoma with intermediate malignity and with moderate cytoplasmic expression of CD34+ by 70% of tumoral cells. She was referred to the Cameroon Oncology Centre for radiotherapy, but patient did not go.

We received her 7 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 (figures 3,4).

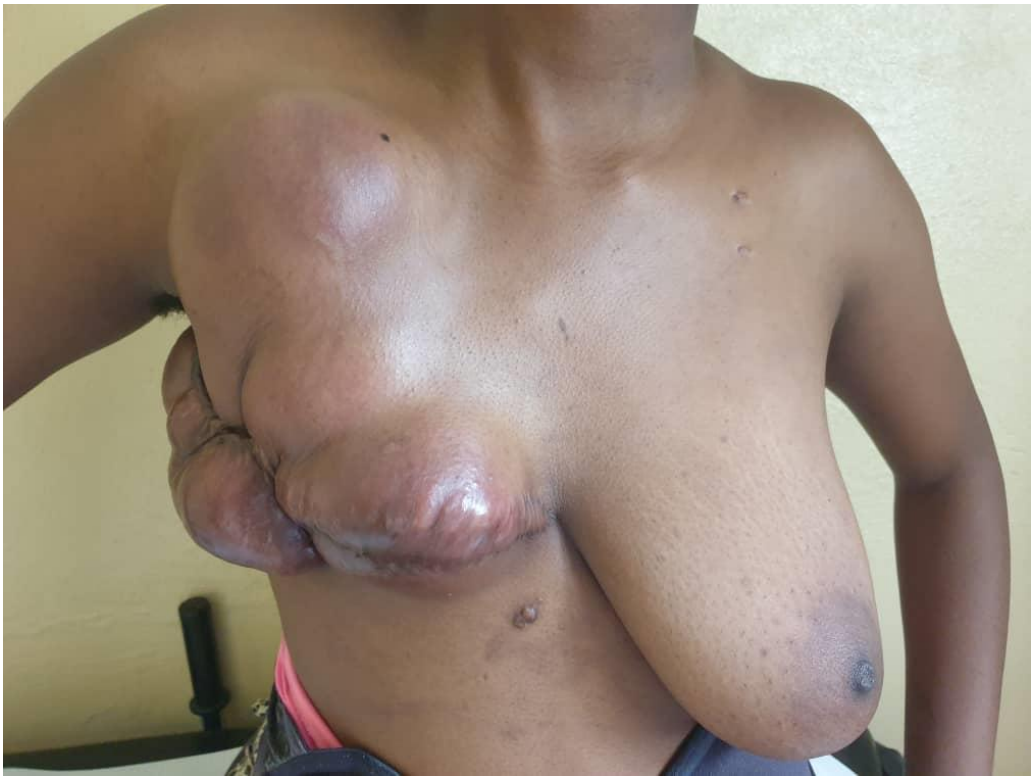

Figure 2 : Evolution of tumour 4 months after radical mastectomy

Figure 3 : Anterior view of evolution of tumour 7 months after radical mastectomy

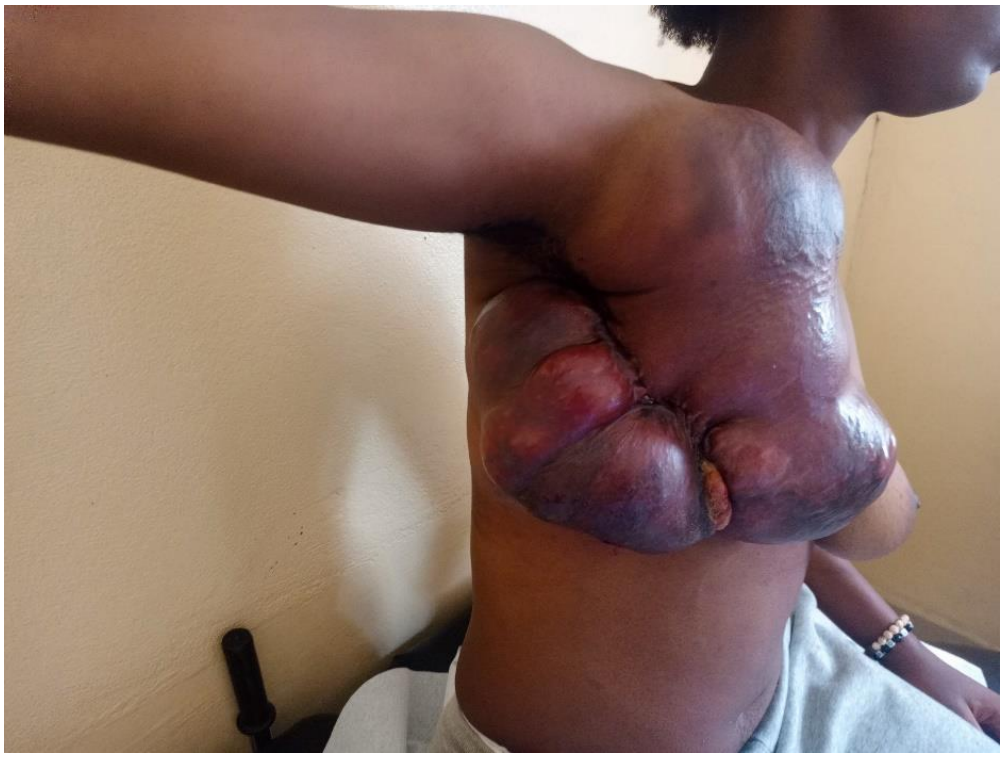

Figure 4 : Lateral view of evolution of tumour 7 months after radical mastectomy

TAP scan revealed a voluminous breast mass, multilobed, necrotic with infiltration of the pectoral muscles and axilla measuring 212x118mm with no axillary and mediastinal adenopathy and secondary metastases.

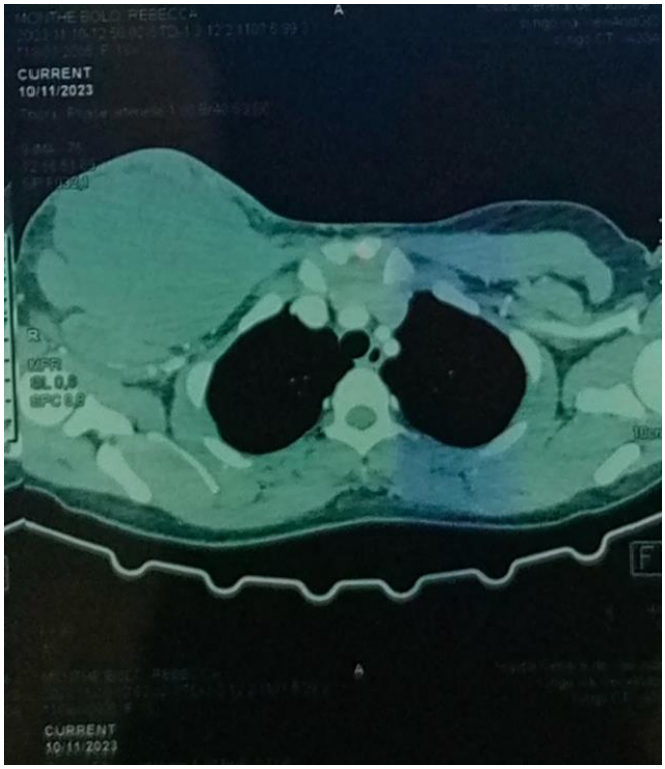

Figure 5 : Crossectional view of TAP SCAN showing no axillary and mediastinal adenopathy and secondary metastases

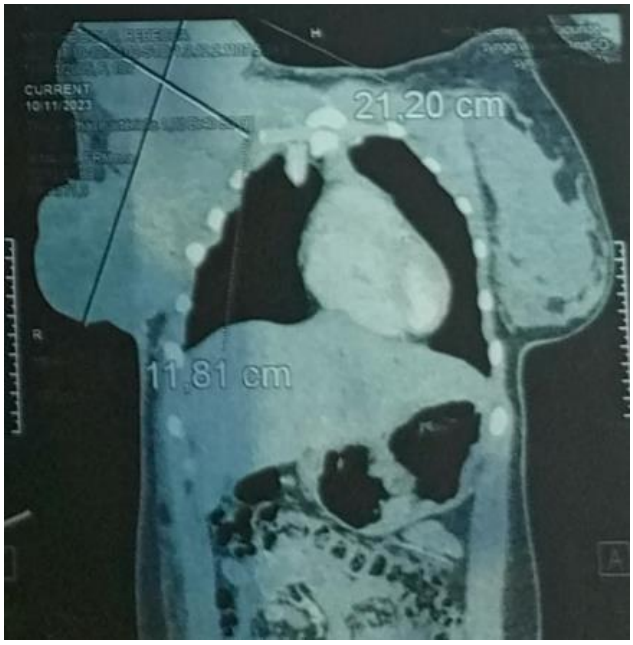

Figure 6 : Craniocaudal view of TAP SCAN showing no secondary metastases

Patient was referred to Cameroon Oncology Centre for radiotherapy.

DISCUSSION

EPIDEMIOLOGY

Breast sarcomas are rare, histologically heterogeneous nonepithelial 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]. There are approximately 4.6 new cases per million women per year [1, 2]. This tumour occurs usually in postmenopausal women, with most of the reported cases being between 45 to 50 years (range 17 to 89) [7,9,12-15]. Men accounted for 1.5 percent of cases of breast sarcoma [17]. Its occurrence in very young girls is extremely rare and may be clinically mistaken for fibroadenoma [8] as seen in the case of our patient. They can be subclassified 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. The reported incidences of angiosarcoma following breast cancer treatment varies between 0.01 and 1% [2]. Radiation-induced breast angiosarcoma has also been associated with a worse prognosis than primary angiosarcoma [3]

There are no known risk 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 [9] as well as environmental exposures to arsenic compounds, vinyl chloride, herbicides and immunosuppressive agents have been linked to sarcomas in general. We could not identify any risk factors in our case, and she was not eligible for oncogenetic screening according to the champret diagnostic criteria. Secondary breast sarcomas occur after breast or chest wall radiation or in the setting of chronic lymphedema. As such, they most commonly occur in women who have been treated for invasive or in situ breast cancer. To be considered radiation associated, a secondary breast sarcoma must occur within the irradiated field, be of a different histology than the initial tumour, and occur after a prolonged latency period (more than 4 years by Cahan's initial definition [12] or more than 2 years by other modified definitions [13]). Our patient had no history of radiation exposure.

HISTOLOGY

Primary breast sarcomas are histologically heterogeneous with several subtypes originating from the supporting stroma (1,7). Histologic review by an experienced soft tissue pathologist is critical in making the diagnosis. A diagnosis of primary breast sarcoma was posed after three histological readings which delayed management. The various subtypes include angiosarcoma, undifferentiated pleomorphic sarcoma, stromal sarcoma, fibrosarcoma,

liposarcoma, leiomyosarcoma, spindle-cell sarcoma and rhabdomyosarcoma. Angiosarcoma, undifferentiated pleomorphic sarcoma and stromal sarcoma are the most common subtypes (2). In our case histology 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. In our patient a fine niddle aspiration was done instead of a core biopsy which has a very low accuracy rate with false negative results which delayed diagnosis and management.

STAGING

Breast sarcomas are staged according to the combined American Joint Committee on Cancer/Union for International Cancer Control system, which takes into consideration the primary tumour characteristics, regional lymph node involvement, presence or absence of distant metastases, and histologic grade. Primary tumour stage is based solely on tumour size. Unlike carcinomas, sarcomas rarely spread to regional lymph nodes, and the presence of regional lymph node metastases is considered stage IV disease. Histologic grade is based on the degree of differentiation, mitotic rate, and degree of necrosis.

T (primary tumour)

- Tx = Cannot be assessed
- T0 = No evidence of primary tumour
- T1 = Tumour ≤ 5 cm in greatest dimension
- T2 = Tumour > 5 cm and ≤ 10 cm in greatest dimension
- T3 = Tumour > 10 cm and ≤ 15 cm in greatest dimension
- T4 = Tumour > 15 cm in greatest dimension

N (regional lymph nodes)

- N0 = No regional lymph node metastasis or unknown lymph node status
- N1 = Regional lymph node metastasis

M (distant metastasis)

- M0 = No distant metastasis
- M1 = Distant metastasis

G (grade)

•GX = Cannot be assessed

•G1 = Total grade score of 2–3

•G2 = Total grade score of 4–5

•G3 = Total grade score of 6–8

Grade Scoring

Differentiation

•1: Sarcomas closely resembling normal adult mesenchymal tissue

•2: Sarcomas for which histologic typing is certain

•3: Embryonal and undifferentiated sarcomas, sarcomas of doubtful type, synovial sarcomas, soft tissue osteosarcoma, Ewing sarcoma/primitive neuroectodermal tumours of soft tissue.

Mitotic count

•1: 0–9 mitoses per 10 HPF

•2: 10–19 mitoses per 10 HPF

•3: ≥ 20 mitoses per 10 HPF

Necrosis

•0: No necrosis

•1: < 50% tumour necrosis

•2: ≥ 50% tumour necrosis

Staging

•IA = T1, N0, M0, GX or G1

•IB = T2-4, N0, M0, GX or G1

•II = T1, N0, M0, G2–3

•IIIA = T2, N0, M0, G2–3

•IIIB = T3-4, N0, M0, G2–3

•IV = Any T, N1 or M1

Abbreviation: HPF, high-powered field.

In our patient she was initially classified stage IB (cT2N0M0, GX)

CLINICAL FEATURES AND DIAGNOSIS

Breast sarcomas most often present as a unilateral, well-defined, large, painless, firm mass within the breast; they are rarely bilateral. They are usually larger in size than epithelial breast cancers (median size 5 to 6 cm) and are often characterized by a rapid increase in size [5,9,10] 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 the case of our patient. These findings are sometimes mistaken for cellulitis or a hematoma.

IMAGING FINDINGS

Finding on mammography is a single oval hyperdense mass with indistinct or circumscribed margins and no calcifications. Spiculated margins are rarely seen [9]. A mammography was not done in our patient due to her age and dense breast.

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. On sonography, 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) [6] as in the case of our patient. It is uncommon to see skin thickening or suspicious axillary lymph nodes [10].

Magnetic resonance imaging (MRI) of a primary breast sarcoma usually shows an oval mass, with irregular margins, a hypointense signal on T1-weighted imaging, a hyperintense signal on T2-weighted imaging [10]. 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 [11,12]. MRI was not done.

DIAGNOSIS

A breast sarcoma may be suspected based on physical examination and/or imaging. However, the findings may be likely to breast cancer of epithelial origin or a benign entity [5] as in our case where the initial diagnosis was a fibroadenoma, hence definitive diagnosis is

based on histology. Core biopsy is considered the procedure of choice. Fine needle aspiration (FNA) is strongly discouraged as it has a low diagnostic accuracy (23%), and a false negative result may lead to a delay in diagnosis [13] as in the case of our patient. In addition, determination of histologic type and grade is seldom possible with FNA.

Immunohistochemistry is useful to distinguish primary breast sarcomas from non-mesenchymal malignant tumours and to delineate the level of differentiation of primary breast sarcomas [10, 12]. In our patient immunohistochemistry revealed a periductal stromal sarcoma with intermediate malignity and with moderate cytoplasmic expression of CD34+ by 70% of tumoral cells which was contradictory to the histological findings of leiomyosarcoma which express smooth muscle actin (SMA) and desmin.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a primary breast sarcoma includes other primary breast tumours, including inflammatory breast cancer; ductal adenocarcinoma; phyllodes tumour of the breast; breast lymphoma; metastases to the breast from other primary sites; and other benign breast disorders, such as fibroadenoma.

TREATMENT PRINCIPLES AND PROGNOSIS

The treatment for breast sarcomas is planned by a multidisciplinary team following the treatment model of sarcomas in other locations [7]. However, there is still no definitive consensus regarding the treatment of primary breast sarcomas (PBS) [6]. Surgery represents the only potentially curative modality (5). 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 [6]. Axillary lymph node dissection should be avoided unless they are clinically positive nodes [10]. 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 neoadjuvant chemotherapy and radiotherapy should be considered in high-risk cases [7]. Adjuvant radiotherapy has been recommended especially for large or high-grade tumours. The role of chemotherapy, however, is unclear [10] and can be proposed to patients with the worst prognosis [6]. Recommended regimens of chemotherapy are vincristine, doxorubicin and cyclophosphamide (VAC), or vincristine, doxorubicin and ifosfamide (VAI).[9]

Overall, the prognosis of primary breast sarcoma is poor with a high recurrence rate [13]. Tumours typically spread through local invasion or hematogenous spread, and the lungs, bone marrow, and liver are common metastasis sites [12]. The prognosis dependents on tumour size,

histopathological type, histopathologic grading, the presence of positive margins, local recurrence [14]. Tumours larger than 5 cm are associated with worse outcomes [8] as in our case. Delay in its diagnosis has important clinical and treatment implications [2]. The median overall survival for breast sarcoma was 108 months, and the 5-year survival rate varies, ranging from 14% to 90% [4].

CONCLUSION

The correct diagnosis of primary breast sarcoma is extremely relevant, because of its aggressive behaviour and poor prognosis. The findings on imaging are not pathognomonic, as well marginated masses are generally interpreted as benign in young females. A rapidly growing breast mass should alert the clinician to investigate for malignancy. Core biopsy is the gold standard for the definitive diagnosis of primary breast sarcoma. Fine needle aspiration is strongly discouraged as it has low diagnostic accuracy. False negative result may lead to a delay in diagnosis. Immunohistochemistry is useful to distinguish primary breast sarcomas from non-mesenchymal malignant tumours and to help determine the histological subtype. MRI provides information on the extent of skin infiltration, as well as the degree of involvement of the deep fascia and pectoralis muscle, which is important in planning the surgical approach. Management is multidisciplinary and complete surgical resection with negative margins remains the mainstay of the treatment. The role of adjuvant radiotherapy and chemotherapy remains controversial. But is recommended for large and high-grade tumours and positive surgical margins.

RECOMMENDATION

To health care personnel:

- Rapidly growing breast mass should alert the clinician to investigate malignancy.
- Core biopsy and immunohistochemistry should be requested for a definitive diagnosis.
- Multidisciplinary consultation meeting should be held to discuss management of breast tumours.

To the patients:

- Any breast mass should motivate a consultation.

To the faculty of medicine and biomedical sciences:

- Seminars should be organized on the diagnosis and management of breast tumours.

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