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A case report

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Breast sarcoma in a pregnant patient. A case report

Sarcoma of the breast is a rare and heterogeneous lesion. We describe a case of a patient surgically treated for a breast lesion during pregnancy. The lesion resulted in a concentric neoplasia with the histological features of high grade sarcoma growing in a phyllodes tumor which was at the time grown in a fibroadenoma.

KEY WORDS: Breast sarcoma, Non-epithelial breast tumour, Phyllode, Pregnancy.

Introduction

Sarcoma of the breast is a rare and heterogeneous lesion, it represents less than 1% of breast neoplasias and less than 5% of all sarcomas in soft tissues^{1,2}.

The annual rate of incidence is of 44.8 new cases per 10 million women³.

On mammary level, as found in other parts of the body, the tumours in soft tissues include benign and malignant lesions; a sarcomatoid (thus, malign) differentiation has been described both in fibroepithelial and in pure epithelial tumors (metaplastic carcinomas)⁴. Benign fibroepithelial breast tumors are mainly represented by fibroadenoma and phyllodes tumor.

The phyllodes tumor is a breast neoplasia, with a double, connectival and epithelial, component, histological-

ly classifiable as benign, border-line and low malignancy grade neoplasia; on the base of stromal component's histological aspects, whose proliferation represents the neoplasia's origin, the malignancy, primitive or developed from dedifferentiation of the originary benign form, can assume the aspect of fibrosarcoma, liposarcoma, osteogenic sarcoma, chondrosarcoma, malign istiocitoma, leiomyosarcoma^{5,6}.

Breast fibrosarcoma is a very rare kind of breast sarcoma, it represents the most common malign evolution of the phyllodes tumor arising from mesenchymal component.

Most frequently diagnosed in the V-VI decade of life, sarcomas appear usually as unilateral voluminous masses with rapid growth, often well defined and palpable, mobile non hurting or painful; lymphatic spread is uncommon, more common is the hematogenous spread, typically to the lungs, bones and liver^{1,7}.

The signs and symptoms are similar to those of a typical fibroadenoma, even though a more rapid growth should arouse suspect of a malignant evolution.

According to previous reports⁸, mammography and ultrasounds scan exam are useful to document the presence and the characteristics of a solid lesion of connective mammary derivation however they do not result very useful in distinguishing it from other benign or malign lesions of epithelial origin; it typically presents itself as

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a dense mass, occasionally indistinct margins, rarely associated to calcifications; it never presents spiculated aspect. (1-7) The breast MRI can evidence a rapid increase in signal intensity on dynamic contrast material-enhanced images as useful findings to indicate malignant breast tissue⁸.

The rarity of breast sarcoma limits most studies to little retrospectives of single case reports and it makes difficult clinic-pathologic studies on the subject³.

The observation and related treatment of a pregnant patient has imposed us a different diagnostic and therapeutic procedure and brings to a series of considerations subject of the present writing.

Case report

A woman of 43 years has reached to our observation at the 21st week of pregnancy (first pregnancy after hormonal stimulation); the assisted referred n°6 hormonal stimulations in 2 years with “follicle-stimulating hormone (FSH) human recombinant + urofollitropin”, corresponding to FSH human highly purified urinary hormone; each stimulation was carried out by Intracytoplasmic Sperm Injection (ICSI).

The pregnancy occurred long after the sixth ICSI. Familiar medical history was negative for mammary neoplasia.

The patient referred a swelling of the external quadrants of the right side breast, strongly painful and hurting, of approximately 1,5cm diameter, non responsive to antibiotic therapy (ampixillin tablets) and to analgesic-antiaedemous therapy (paracetamol + bromelin), without fever.

The patient brought a precedent breast ultrasound (of approximately 12 months before) which described in that area a mass of approximately 7mm with a solid slightly non homogeneous echo structure and distinct regular margins, but without signs of intralesional vascularisation.

As recommended in the approach for evaluation of a palpable breast neoplasia in a pregnant patient⁹⁻¹⁰, initially an ultrasound investigation has been performed which documented in that site a polilobated area of maximum 20mm diameter of non homogeneous echo structure composed of several converging nodal areas; at Doppler ultrasound, an intense intra and perilesional vascularisation of the described area has been observed.

The radiologist posed the diagnostic doubt (on the base of the painful symptoms) of an inflammatory lymphadenopathy in other words fibroadenoma (but the pain would have been inexplicable), and the patient was therefore suggested to undergo a day surgery procedure of removal of the breast neoplasia, in local anaesthesia considering pregnancy.

The histological exam set up for a macroscopically nodal neoplasia as a “concentric lesion” of whitish colour 18mm diameter, in which context there was a little round lesion of similar cartilaginous aspect of 10mm; the histological

diagnosis referred it was a highly malignant sarcoma set in the context of a biphasic neoplasia with phyllodes tumour and fibroadenoma characteristics (Fig. 1, 2); the hystological diagnosis was “high grade phyllodes sarcoma”; high mitotic rate (over 10 per 10 at elevated enlargement), frequent atypical mitosis; proliferating rate, evaluated through Ki-67 index, was high (50%); neoplastic cells spread and strongly positive to immuno histochemical coloration for vimentin, locally positive for desmina and actin smooth muscle, weakly positive for S-100; negative colorations for cytokeratin, oestrogens and progesterone : these results confirmed not only the mesenchimal origin of the neoplasia, but in addition they suggest a epithelial-mesenchimal transition has took place in previously highly-proliferating epithelial-derived cells. Furthermore, a completely excised neoplasia with a min-

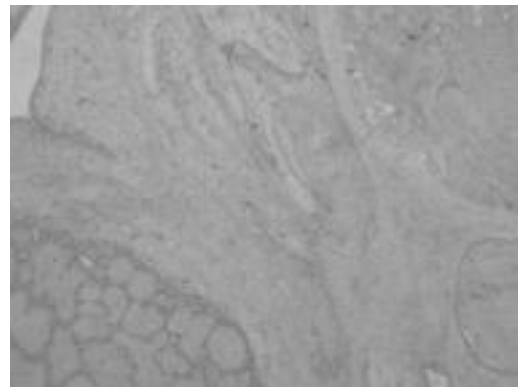


Fig. 1: On the left, high grade malignant sarcoma: proliferation of pleomorphic and atypical cells, often multinucleated, with large and irregular nuclei, prominent nucleoli and abundant eosinophilic cytoplasm; small foci of necrosis are also present. On the right, phyllodes tumor: proliferation of hypercellular, spindled mesenchimal cells, sometimes with nuclear atypia, arranged to form leaf-like protrusions covered by epithelial/myoepithelial cell layers (hematoxylin-eosin, original magnification 10x).

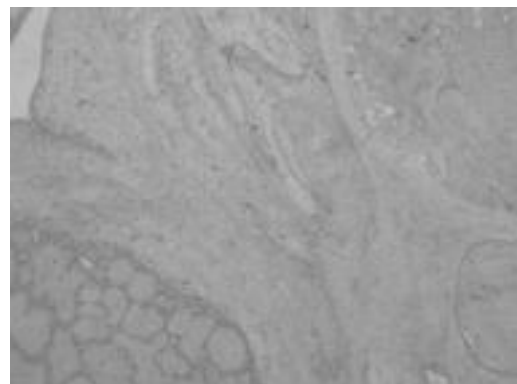


Fig. 2: On the bottom left, phyllodes tumor: note the abundance of leaf-like protrusions of stromal elements covered by epithelial/myoepithelial cell layers; on the top and on the right, fibroadenoma: proliferation of hypocellular stroma around relatively sparse epithelial/myoepithelial-lined spaces (hematoxylin-eosin, original magnification 10x).

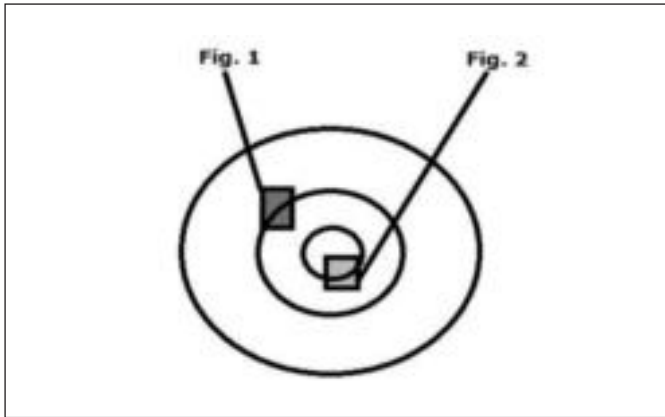


Fig. 3: Schematic drawing.

imum distance of approximately 2mm from the resection borders was documented.

Thus, the patient subsequently underwent (approximately 15 days after the first surgery) to an extension of the precedent simple surgical removal of the neoplasia with involvement of the entire breast quadrant.

In this case the histological examination presented a glandular breast parenchyma free from neoplastic alterations or of relevance aspects.

The patient carried out pregnancy, and a month after breast feeding of maternal breast, she underwent breast x-ray, breast ultrasound scan exam and breast MRI of follow up and TC total-body of staging, exams which resulted negative for pathological reports.

The oncologic evaluation of the case, already carried out in a first moment, in the immediate post surgical and then post staging, confirmed the indication to periodic instrumental follow up exams.

One year after surgery, the patient, checked with follow up instrumental exams, resulted free from disease.

Discussion

Phyllodes tumor was described for the first time by Johannes Müller, in 1838⁹, who initially named it *cystosarcoma phylloides*, choosing the name of sarcoma because of tumor's macroscopic appearance.

Phyllodes tumors are fibroepithelial neoplasms with epithelial and cellular stromal components, the latter of which represents the neoplastic process⁹. The presence of an epithelial component differentiates the phyllodes tumor from other stromal sarcomas.

Usually neoplastic breast sarcomas are diagnosed once they reach important sizes (which often occurs in little time) with a range between 4 and 10 cm maximum of diameter, because they are often initially confused with breast lesion of benign origin according to the radiologic similar benign characteristics they present¹⁻³.

A certain number of connective malign neoplasias have been described during pregnancy.

The patient we treated has received a precise diagnosis of a well capsulated sarcomatoid lesion of 1 cm, probably because it was very painful for the strong swelling oedematous component and non responding to practiced medical therapy compatible with pregnancy as solution of the local situation; the pre-surgical diagnostic tru-cut breast biopsy has been avoided. The correct diagnostic procedure should have included ultrasound-guided core biopsy and subsequent surgery¹².

The report of solid neoplasia from ultrasound exam often represents an indication to breast biopsy; however core needle biopsy (and even less the fine needle breast biopsy which in this sense has low diagnostic value) cannot be indicative of a correct diagnosis of sarcomatoid breast lesions, so the removal biopsy is indicated as the most accurate method for the diagnosis of phyllodes neoplasia³.

The histological grading and size are highly predictive of the results (local relapse and at distance), even if such results are not universally approved. The possibility of a local relapse seems to increase

with the increasing of the size of the neoplasia, anyhow the cellular pleomorphism, number of mitosis, untypical stromal and infiltration of the margins of surgical section result as important prognostic factors^{2,4}.

Surgical treatment is the gold standard in sarcoma's management; there is a general consent that surgical removal always represents the primary modality of treatment in breast sarcoma^{2,14}.

The indication for conservative surgery against mastectomy has been very disputed.

Several Authors have documented how a conservative surgery of the breast with clean resection margins represents the appropriate treatment for phyllodes malign neoplasias (sarcomas) and that, thus mastectomy, often considered as best treatment for the control of local relapses, does not bring to significant benefits in terms of survival compared to the large local resection^{3,14}.

Asoglu O. and coll. (2004) have documented how the type of surgery does not influence the rate of local relapses in neoplasia, which results, on the contrary, strongly associated to the presence of positive surgical resection's margins¹⁵.

The rapid growth of phyllodes neoplasias in pregnancy poses a limit to conservative surgery of the breast, which in our case has been overcome thanks to a rapid and precocious diagnosis¹².

The hazards and causes of the development of breast sarcoma are largely unknown; some Authors have documented a significant relation between external breast or thoracic wall irradiation and the development of a sarcomatoid lesion³.

There is the suspect that hormonal stimulation, which our patient has undergone in the past, and the pregnancy's hormones later, might have had a role in the

development of the sarcoma even if in literature there is nothing in regards; the pregnancy can influence diagnosis, prognosis and treatment of breast tumours. Few cases of phyllodes tumour have been described during pregnancy and it has been documented that there is a rapid growth in pregnant women¹².

In our report, the specific tissue architecture unveiled by histological analysis evidenced the sarcoma process at the core of the breast tumour development. Meanwhile more superficial layer are occupied by non-malignant neoplastic tumour cells of both stromal (phyllode) and epithelial origin, the centre of the lesion is occupied by sarcomatous cells. Thus, from the centre to the periphery of the lesion, sarcoma, phyllode and eventually fibroadenoma cells can be easily identified. Such a structure suggests a diachronic evolution of the tumour. So far, it is tempting to speculate that sarcomatous transformation took place later in the context of a primitive benign mixed lesion. As it is well recognized, cells at the inner core of a mass are more likely to be exposed to an anaerobic and acidic milieu. Therefore, their glucose utilization is frequently shifted toward a Warburg-like metabolism¹⁶. It is tempting to speculate that such rewiring of the cell metabolism might play a causative role in favouring the epithelial-mesenchymal transition as well as the transformation of benign mesenchymal tumours into malignant sarcomas¹⁷.

Acknowledgments

The observation of a particular case of a patient at the 21st week of pregnancy and the subsequent surgical treatment for a lesion apparently benign, but with a rapid growth and particularly painful, have permitted us to individuate a sarcoma probably at the beginning phase of his development.

The particularity of the described concentric lesion (Fig. 3), sarcoma in the context of a biphasic neoplasia fibroadenoma-phyllodes tumor, induces us to suspect more hypothesis related to the origin, the timing and the progression of the neoplasia.

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