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Case Study

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THE BREAST DERMATOFIBROSARCOMA OF DARIER AND FERRAND

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ABSTRACT

Dermatofibrosarcoma of Darier and Ferrand (DFSDF) is a rare cutaneous sarcoma of low to intermediate grade characterized by a slow evolution with a major risk of local recurrence in case of insufficient excision. We describe a case of DFSDF of the breast in a 16-year-old girl with a lesion on the left breast in the form of a painless, more or less clear-cut, raised, flesh-colored plaque. She underwent a biopsy confirming DFSDF and underwent a wide surgical excision with healthy margins of the tumor and oncoplasty of the operated breast with a very satisfactory result.

KEYWORDS: Dermatofibrosarcoma of darier and ferrand; skin tumor; histopathology; CD4 antibody immunostaining; partial mastectomy; resection with wide safety margins; imatinib; oncoplasty; recurrence.

INTRODUCTION

DFSDF is a locally aggressive cutaneous mesenchymal tumor of intermediate malignancy. It is a rare but not exceptional tumor, representing 0.1% of cutaneous malignancies.

The trunk is the preferential location. Most often the skin lesion presents as a flesh-colored plaque with nodules. Its diagnosis of certainty is histological facilitated by immunohistochemistry. Cytogenetics allows the formal diagnosis in doubtful cases. Wide surgical excision is the reference treatment. Oncoplasty with breast reconstruction provides comfort to the patient in case of breast involvement.

CASE REPORT

A 16 year old female patient, with no previous history of local trauma, who consulted for the management of a skin lesion in the superolateral quadrant of the left breast that had been evolving for 5 years. In view of the increase in size, the patient consulted and was referred to our hospital.

Examination of the breasts revealed a tumourous placard in the super-internal quadrant of the left breast, about 4 cm long, hard to palpate, with a bumpy surface and two nodules, flesh-coloured, with more or less clear boundaries, painless, and without inflammatory signs.

The breast ultrasound showed breasts with a discreetly heterogeneous glandular echostructure with no visible nodular or cystic lesion, a small palpable swelling on the left super-internal quadrant corresponded sonographically to a small hypoechoic avascular skin thickening with respect for the subcutaneous fatty plane without any sign of retraction and absence of axillary adenopathies.

Pathological examination of the biopsy of the lesion shows a skin covering largely infiltrated by a tumor proliferation made of short intertwined bundles and shows in the periphery a storiform architecture. The cells have oval nuclei with fine chromatin and inconspicuous nucleoli and an eosinophilic cytoplasm. Cytoplasmic boundaries are not very visible. Mitosis figures are rare and estimated at 2 mitoses per 10 fields at high magnification.

The immunohistochemical study shows:

- Anti-CD34 antibody: positive
- Anti-SMA (smooth muscle actin) antibody: negative.
- Anti-DESMINE antibody: negative.
- Anti-H-CALDESMONE antibody: negative.
- Anti-SOX10 antibody: negative.
- Anti-PS100 antibody: negative.
- Anti-EMA(epithelial membrane antigen) antibody: negative.
- The mitotic index is Ki67% estimated at 10%.

This anatomopathological study concludes to a cutaneous localization of a DFSDF.

The decision was made to perform a partial mastectomy with wide tumor resection and adequate safety margins. An omega skin incision was made. A partial mastectomy was performed with a wide excision of the lesion with a safety margin of 2 cm, including part of the gland. It was decided to perform an oncoplasty of the left breast with glandulocutaneous and glandulothoracic detachment allowing remodeling of the gland and recentering of the nipple. A redon drain was placed in an aspirator. A subcutaneous approximation was made with vicryl 0 thread and dermal suture by intradermal overjet with vicryl 3/0. The operation lasted one hour.

The surgical specimen was located with two threads on the upper side and one thread on the inner side. It was sent to the pathology laboratory for cytological study and histological confirmation.

Anatomopathology Shows

- In the dermis and hypodermis: a massive spindle cell tumor infiltration made of short intertwined bundles and shows in places a storiform architecture. The cells show an oval nucleus with fine chromatin, inconspicuous nucleoli and eosinophilic cytoplasm with invisible cytoplasmic boundaries. Rare figures of mitosis are found.

On the surface, the epidermis is of preserved morphology, separated from the tumor proliferation by a band of healthy dermis (grenz zone).

- Morphological aspect compatible with a dermatofibrosarcoma of Darier-Ferrand.
- Non-tumoral surgical borders.

The anatomopathology report was presented to the committee of the multidisciplinary consultation meeting of our hospital bringing together surgeons, oncologists and radiotherapists, concluding that the patient should undergo radiotherapy.

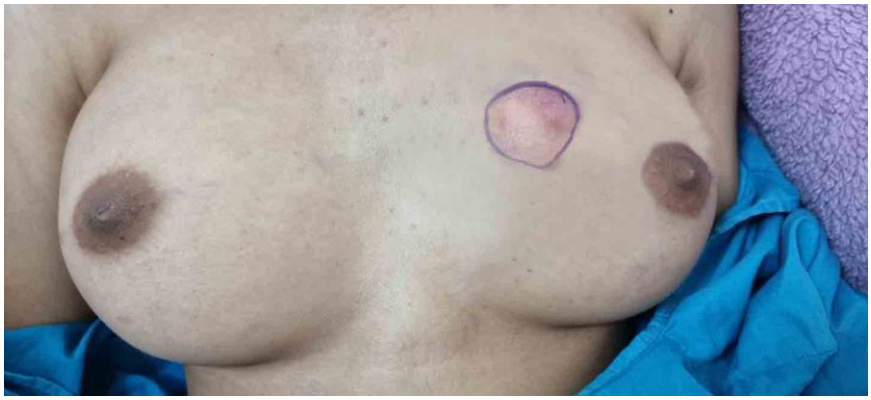
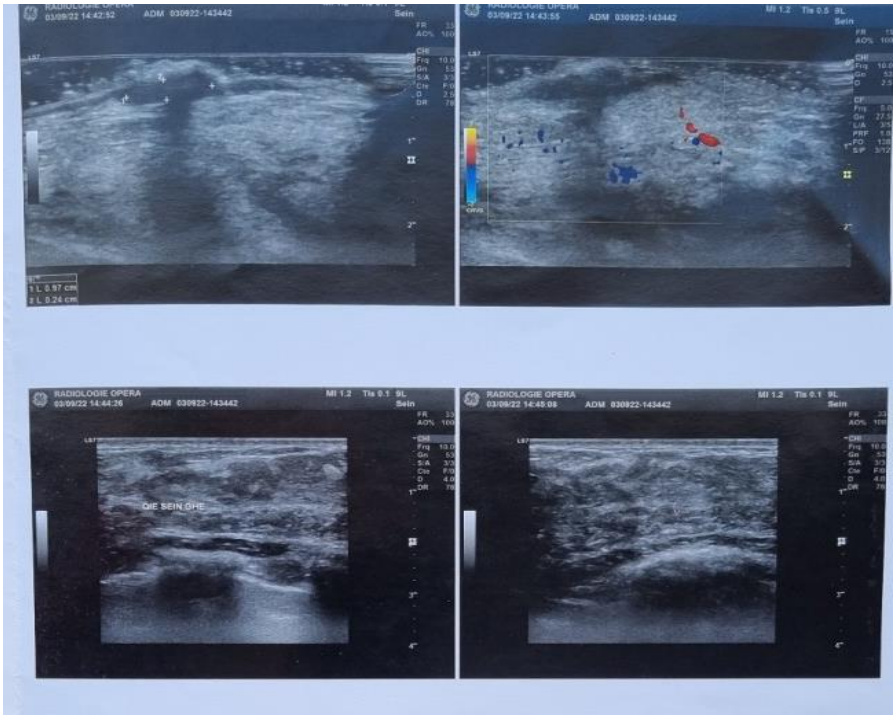


Figure 1: Left Breast Dermatofibrosarcoma, Flesh-Colored Plaque With Two Nodules.



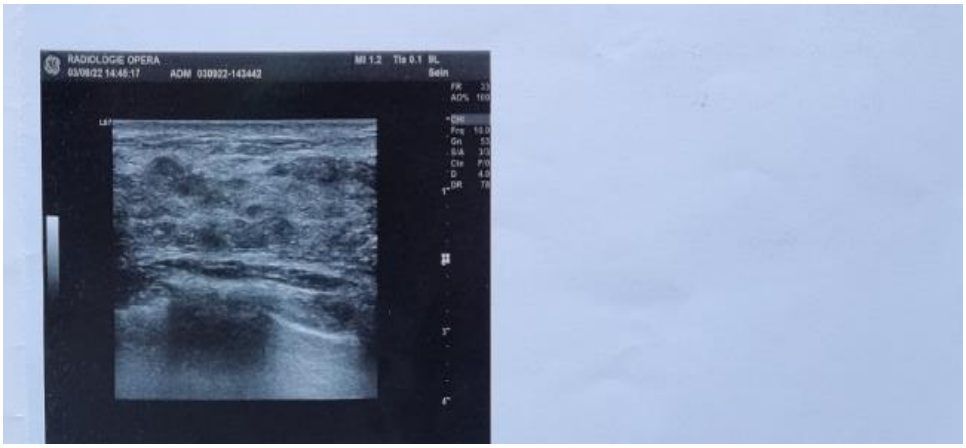


Figure 2: Ultrasound of the left breast showing a swelling of the superior-internal quadrant with avascular hypoechoic skin thickening with respect of the subcutaneous fatty plane without sign of retraction and absence of axillary adenopathy.

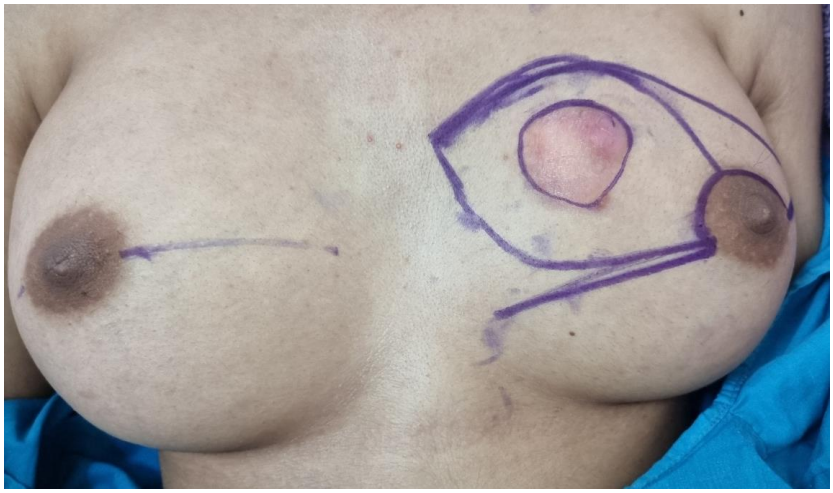


Figure 3: Wide Exeresis Margin of 2cm Minimum.

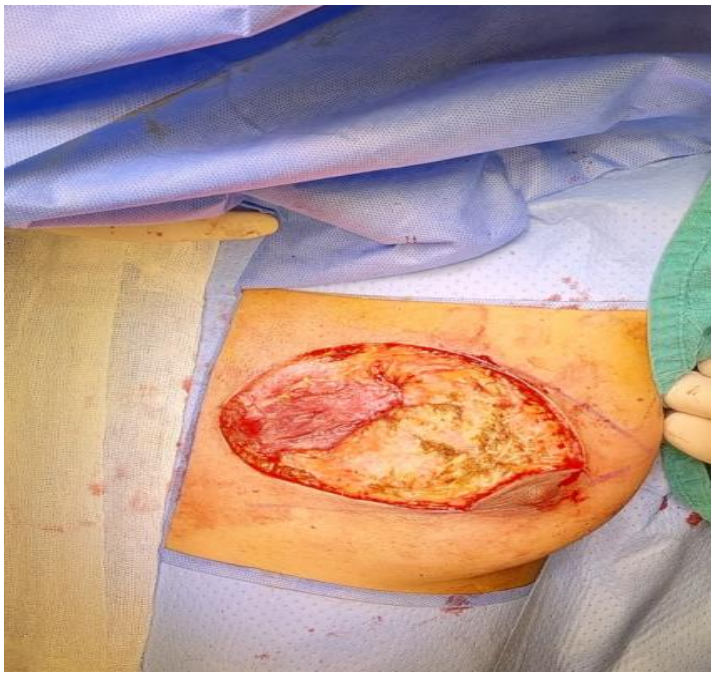


Figure 4: Surgical Removal of The Tumor With A Wide Safety Margin of 2 Cm.

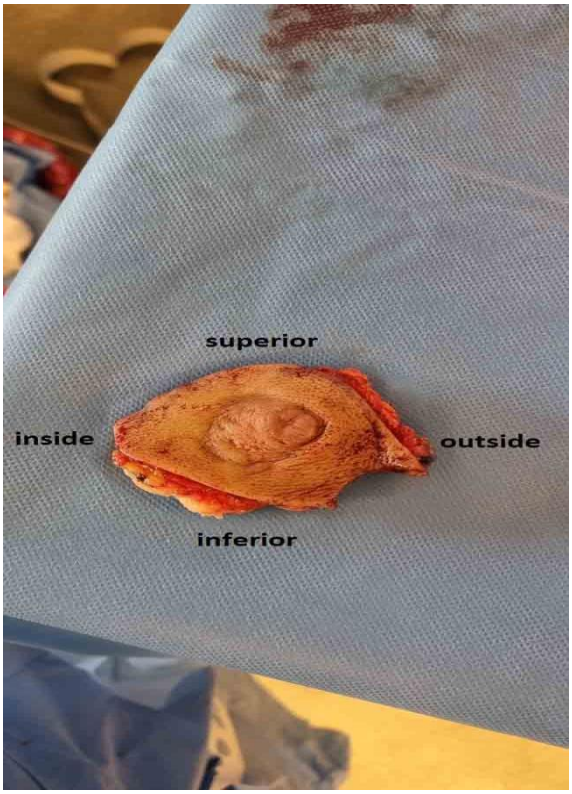


Figure 5: The Exeresis Piece.

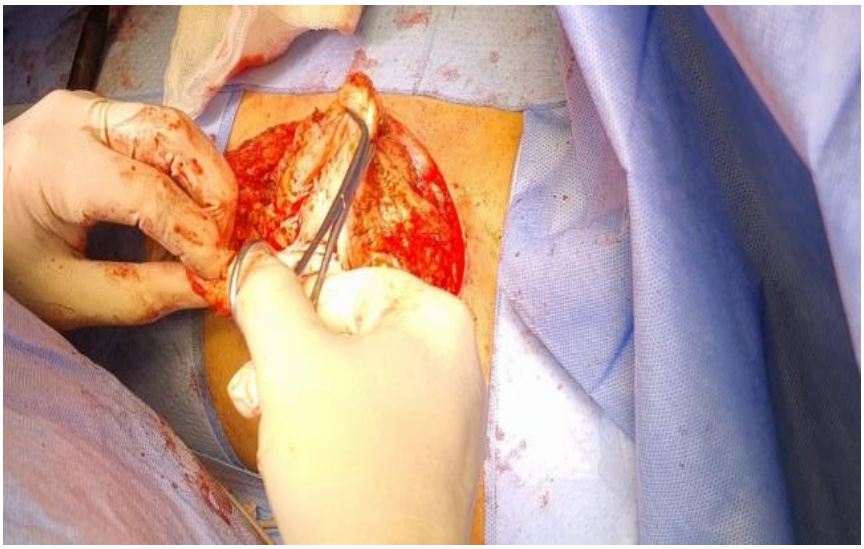


Figure 6: Large Surgical Removal of The Tumor.

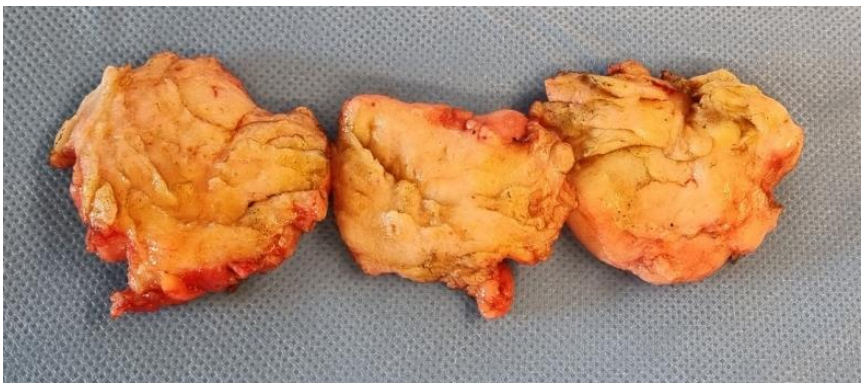


Figure 7: Glandular Reduction For Oncoplasty.

Figure 8: Oncoplasty With Breast Reconstruction And Recentering of The Nipple.

DISCUSSION

DFSDF is a cutaneous sarcoma of low malignancy first described in 1890 by Taylor[1] as a sarcomatous tumor resembling a keloid scar. dermatofibrosarcoma was later reported by Kuznitzky and Grabish in 1921, Darier and Ferrand in 1924[2], and Hoffman in 1925[3] who entitled it "dermatofibrosarcoma protuberans". In 1951, Pack and Tabah published the first important serie[4] and In 1962, Taylor and Helwig established the histological characteristics of this entity.[5,6]

It is a rare tumor representing 0.1% of malignant skin tumors[7] and 6% of soft tissue sarcomas.[8] It can occur at any age but most often in young adults between 20 and 50 years of age[9] with a slight male predominance.[6,7,10,11] It is rare in elderly people and children under 15 years of age. The congenital form is exceptional.[12] However, a few congenital cases have been reported.

DFSDF can affect any part of the body.[7] The preferred sites are the trunk, followed by the proximal extremities and then the head and neck.[13]

Breast localization remains exceptional with less than 50 cases reported in the literature.[14,15]

Some authors have mentioned the occurrence of DFSDF after local trauma.[16] This notion is found in 10 to 20% of cases.[11,17,18] Taylor and Helwig, in a serie including 115 cases, found a history of trauma in 16.5% of cases.[11] Other authors mention various exogenous factors in the occurrence of the condition, such as burn scars[19], vaccination scars[19], radiotherapy scars[19], traumatized nevi[20], syphilitic lesions[20], and iatrogenic or professional keratosis arsenica lesions.[7]

It has been noted that during pregnancy, the DFSDF shows a rapid extension, suggesting the presence of endocrine stimuli.[5]

According to some authors, this tumor is more frequent in Africans and the black race in general.[7,21]

The delay between the appearance of the lesion and the first request for care is on average 5 years. This delay is explained by the slow evolution of the lesion and the absence of functional signs and general disorders.[7]

The revealing clinical signs are poor like mild pruritus or moderate localized pain. The tumor usually occurs on healthy skin, on trauma or burn scars. It initially presents as a firm indurated sclerodermic plaque, red-brown purplish or normal skin color; rarely the lesion takes the aspect of a uninodular or polylobed painless mass with slow growth.

Over several years, one or more embedded and prominent nodules may ulcerate the skin. The tumor size varies from 1 to 5 cm with extremes of more than 20 cm.[8,14,22,23]

The general condition of the patients is generally preserved for a long time.[7]

Histological examination is essential for diagnosis. The tumor is made of a dense cellular proliferation, badly limited, not encapsulated, occupying the dermis most often in its entirety. It sends fine extensions sometimes very deep in the hypodermis, which would explain the occurrence of recurrences even with wide resection margins. The epidermis is respected. The cells are elongated, spindle-shaped, with more or less abundant cytoplasm with regular oval nuclei. Mitoses are variable with rare atypia. The stroma is variable from one area to another.

Architecturally, the cells are grouped in small radiating flexuous bundles entangled in nodular areas of high cell density realizing a storiform "wheel spoke" or "woven cart" appearance.[8,24] Necrotic areas are rarely seen.[7,11,25,26,27]

DFSDF is considered a low-grade sarcoma of malignancy.[7] Bendix-Hansen and al, using the Myhre-Jensen grading system, found that, of the 19 cases studied, 15 are grade I, 4 are grade II, and no cases are grade III.[4]

In general, the histological appearance helps to guide the diagnosis. In doubtful cases, immunohistochemistry facilitates the diagnosis. It can distinguish DFSDF from other spindle cell tumors. It shows intense and diffuse positivity of CD34, focal positivity of smooth muscle actin and vimentin, constant negativity of PS100 desmin[5] and HMB-45 proteins. PS-100 positivity points more toward a nerve tumor and actin positivity points toward a dermatomyofibroma.[8,14,24]

The CD34 marker is not very specific but very fiable when confronted with the morphological appearance.[8,24]

Areas undergoing sarcomatous transformation only exceptionally and very weakly express CD34.[7]

The pathogenesis of DFSDF points towards genetic abnormalities present in 90% of cases with a true molecular signature offering a possibility of molecular diagnosis. An unbalanced chromosomal translocation between chromosomes 17 and 22 will lead to fusion of the PDGFB (Platelet-derived growth factor group B) gene on chromosome 22 with the COL1A1 (collagen, type I, alpha 1) gene on chromosome 17 and thus to overexpression of the PDGFB-COL1A1 fusion oncogene leading to uncontrolled cell division by autocrine stimulation and tumor development.[28]

Cytogenetic analysis shows the presence of supernumerary ring chromosomes composed of sequences from chromosomes 17 and 22, or more rarely t(17;22) translocations.[26]

The differential diagnosis is mainly on biopsies with a benign histiocytofibroma, a neurofibroma, or a dermatomyofibroma.[8,14]

Treatment is essentially surgical. The standard of care is a wide excision of the lesions with margins of 5 cm.[29] The latest guidelines of the National Comprehensive Cancer Network (NCCN) recommend margins of 3 to 5 cm.[30]

Currently, the preferred method of removal is with narrower margins of 2 cm, with rigorous control of the margins by anatomical-pathological study.

Oncoplastic breast surgery would be the preferred type of surgery given the large surface area of tissue resected. However, Mohs micrographic or "slow-Mohs" surgery allows these margins to be reduced to less than 2 cm without compromising carcinological safety.[31,32,33] It is based essentially on microscopic and topographic analysis of the entire excisional specimen and offers the benefit of reduced excisional margins while ensuring complete excision of the lesion.[34] This technique performed on paraffine sections allows tissue sparing with extensive analysis of the excisional margins, as distant hypodermic infiltration sites can be detected and removed. Removal of the deep fascial plane is always recommended.[25,26,27]

Due to its low mitotic activity, DFSDF is not radiosensitive.[7,19,35] Postoperative radiotherapy is indicated in case of non-healthy margins after re-excision or in case of recurrence.[27]

Systemic chemotherapy is not recommended[5] and is reserved for metastatic stages.[30]

Immunotherapy is based on a tyrosine kinase inhibitor: Imatinib mesylate, which primarily targets the PDGFB receptor (PDGFRB), is indicated for unresectable tumors, recurrence and metastases.[29,30]

The prognosis depends essentially on the margins of excision, the tumor size, the mitotic activity and the presence of necrosis. Death is exceptional and occurs late due to local complications.[7]

A rigorous clinical surveillance must be maintained, because of the slow evolution and the high recurrence rate of this tumor.[27] This follow-up is based on local clinical examination, general examination and lymph nodes with chest radiography, on a regular basis with quarterly control during the first year, then semi-annual control for 2 years and annual control for life.

If the tumor has already recurred, the recurrence potential of this secondary or tertiary tumor appears to be significantly increased compared to a primary, untreated tumor. The margin of excision is the second most important risk factor for recurrence. However, the risk of histologically incomplete resection and thus of clinical recurrence can only be reduced by increasing the resection margins. The larger the margins, the lower the risk, becoming very low from 5 cm.[36] Several publications report the low rate of recurrence after wide surgery compared to cases seen as second-line surgery.[19,37,38] For many authors, the tendency to local recurrence is estimated to be 20-40% of cases.[39] The frequency of recurrence is 40% for 2 cm margins, 20% for 3 cm margins and 1.75% for 4 cm margins.[14,40]

DFSDF, between the harmless fibroma and the dreaded sarcoma, is a rare fibrous tumor of the skin with local aggressiveness. Frankly malignant metastasizing sarcomatous transformation is exceptional and is seen at a very late stage.[7] The metastases are rare (5%) and are mainly pulmonary.[14] In the serie of Mentzel and al[9], 1.5% of patients who developed metastases had fibrosarcomatous foci on the resection specimens.

CONCLUSION

DFSDF is a rare cutaneous fibrous tumor with intradermal development of low malignancy, essentially local evolution, slow growth and low metastatic potential. Its misleading clinical appearance, which is mostly reminiscent of a keloid scar, is often responsible for a delay in diagnosis. Histology, easily assisted by

immunohistochemistry and cytogenetic study, confirms the diagnosis. Breast localization is rare, requiring surgical removal with a wide margin, which has so far proven to be indisputably effective. An oncoplasty aiming at breast reconstruction and nipple re-centering perfects the management of the patient by the surgeon. Regular clinical monitoring is required after removal because of the very high risk of local recurrence.

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