SURGICAL TREATMENT OF DERMATOFIBROSARCOMA PROTUBERANS USING A REVERSED ADIPOFASCIAL SURAL FLAP – CASE REPORT

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Abstract

Dermatofibrosarcoma protuberans is a rare superficial tumor characterized by high rates of local recurrence and low risk of metastasis. Dermatofibrosarcoma protuberans occurs most commonly on the trunk and proximal extremities, it affects all races, and often develops between the second and the fifth decade of life. The tumor grows slowly, typically over years.

We present a rare case of a young male patient, 21 years old, with an asymptomatic calf tumor which was suspected to be an angioma, but after the initial excision histology and imunohistochemistry proved to be a Dermatofibrosarcoma protuberans without safety limits. After 2 weeks, we excised the remaining scar with 4 cm tissue limit and the defect was covered using an adipofascial reversed sural flap from the posterior part of the left calf and after another 2 weeks we applied a skin graft from the thigh.

The patient had a good evolution, with full recovery, without local recurrences or metastasis, and the histology was within good safety limits.

Keywords: Dermatofibrosarcoma protuberans, adipofascial reversed sural flap

Introduction

Dermatofibrosarcoma protuberans (DFSP) is a dermal or hypodermal mesenchymal tumor, considered to be a low grade sarcoma and by others a borderline fibrous hystiocytoma or a tumor derived from dermal dendritic cells, because of its positivity at CD 34.

DFSP is a rare tumor that constitutes less than 0.1% of all malignancies and 1% of all soft-tissue sarcomas. Nevertheless, DFSP is the most common sarcoma of cutaneous origin.

DFSP is a relatively unusual, locally aggressive cutaneous tumor, characterized by high rates of local recurrence, but low risk of metastasis. DFSP most commonly occurs between 20 and 50 years of age, although it may appear at any age [1].

Immunoreactivity for CD34 in DFSP is the main immunohistochemical marker for the diagnosis of DFSP, particularly when associated with the absence of immunostaining for factor XIIIa. Nevertheless, 10% of DFSP are negative for CD34, and 25% of DFSP may be positive for factor XIIIa.

Histologically, several variants of DFSP have been described and should be well characterized to avoid misdiagnosis with other tumors. These include pigmented

(Bednar tumor), myxoid, myoid, granular cell, sclerotic, atrophic DFSP, giant cell fibroblastoma, and DFSP with fibrosarcomatous areas. Of all these variants, only the

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DFSP with fibrosarcomatous areas is high grade, with a higher rate of local recurrence and distant metastasis.

The standard treatment is wide local excision with at least a 2 cm margin. Nowadays, the usage of adipofascial flaps based on reversed sural flow (RASF), for the reconstruction of soft tissue defects after DFSP excision has good clinical results. When surgery is insufficient, clinical evidence has suggested that Imatinib mesylate or radiotherapy is a safe and effective treatment in DFSP, especially in cases of local advanced or metastatic disease [2].

The aim of the paper is to emphasize that the use of the RASF is a safe option for the coverage of the defects in the distal third of the leg, especially after the excision of a DFSP, being a simple and rapid surgical intervention, using a constant vascularization of the sural region, having a long, thick and good quality pedicle and because the morbidity of the donor area is minimal and with no significant functional loss.

Case report

Patient presentation

We present a rare case of a young male Caucasian patient, 21 years old, without any history of systemic disease or malignancy, who was admitted to our Clinic with an asymptomatic calf tumor.

The laboratory data were all normal and the patient did not have lymph node involvement.

Ultrasound imaging

Previous ultrasound examination described a tumour of 28/14/20 mm on the antero – lateral part of the left calf, very well delimited, depressible, elastic and incapsulated, with a developed arterial vascularization and with perilesional tissue oedema. The conclusion was a subcutaneous hypervascular tumour and an angioma was suspected. After the clinical examination, the first diagnosis considered was angioma or a sebaceous cyst with fibrosis.

Hystology imaging

Macroscopy described a sectioned tumor of 3.5/2/1 cm after the initial excision on local anesthesia Lidocaine 1%, but the histology and imunohistochemistry identified a medium grade dermatofibrosarcoma protuberans without safety limits laterally and on the profound tissues. In order to establish the histopathological diagnosis, several stainings were done (eosin - hematoxylin, imunohistochemistry CD 34 and Ki 67).

Eosin - hematoxylin staining evidenced a part of the tegument partially covered by epidermis, with the presence of a tumor in the dermal layer which infiltrated the hypodermis, keeping the grenz zone. The tumor is composed of homogeneous spindle-like cells, with moderate atypias and with storiform disposition. Tumoral cells have little cytoplasm, hyperchrome nuclei, moderate

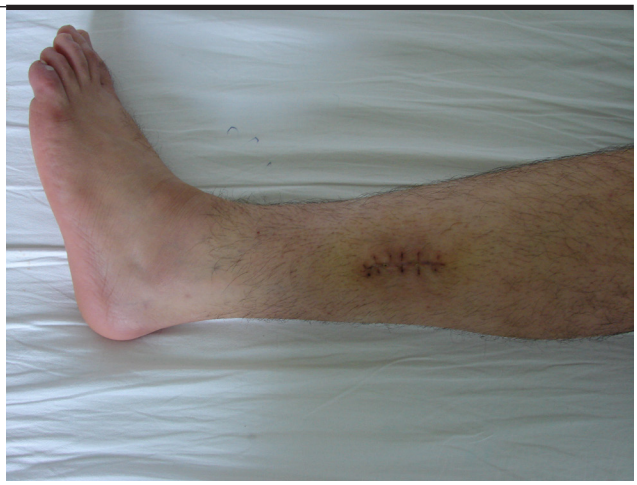

Figure 1. Calf aspect after the initial excision of DFSP.

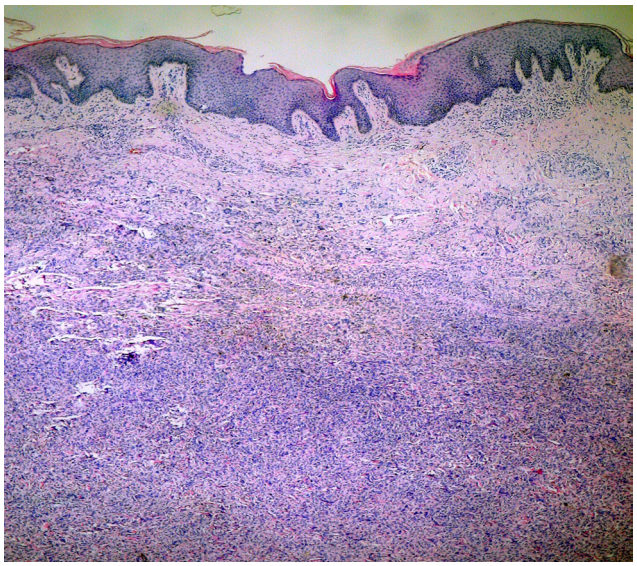

Figure 2. Fragment of tegument partially covered by epidermis, with the presence of a tumor in the dermal layer which infiltrates the hypodermis keeping the grenz zone (Eosin - hematoxylin staining 4x).

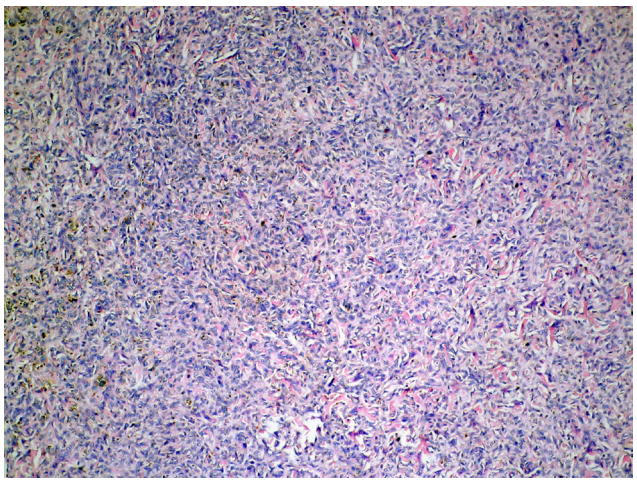

Figure 3. Tumor section with homogeneous fusiform cells, moderate atypias and storiform disposition (Eosin - hematoxylin staining 20x).

pleomorphism, with focal atypias, with medium mitotic activity (<5 mitosis/10 HPF), sometimes elevated (7 mitosis/10 HPF).

In imunohistochemical staining CD 34 a tumoral proliferation with the presence of a positive marker for CD 34 staining could be noticed, which highlights endothelial DFSP where it is diffuse positive, unlike the dermatofibroma where it is focal positive and the myxoid liposarcoma which is CD 34 negative.

In imunohistochemical staining Ki 67 we noticed a tumoral proliferation with immunostaining Ki 67 positive for cells during the mitosis, which highlights a medium mitotic activity.

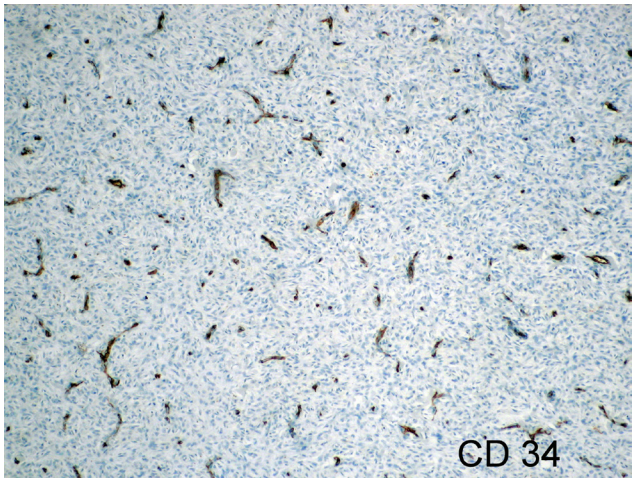

Figure 4. Diffuse positivity of CD 34 staining at the level of vascular endothelial cells (Imunohistochemical staining CD 34 20x).

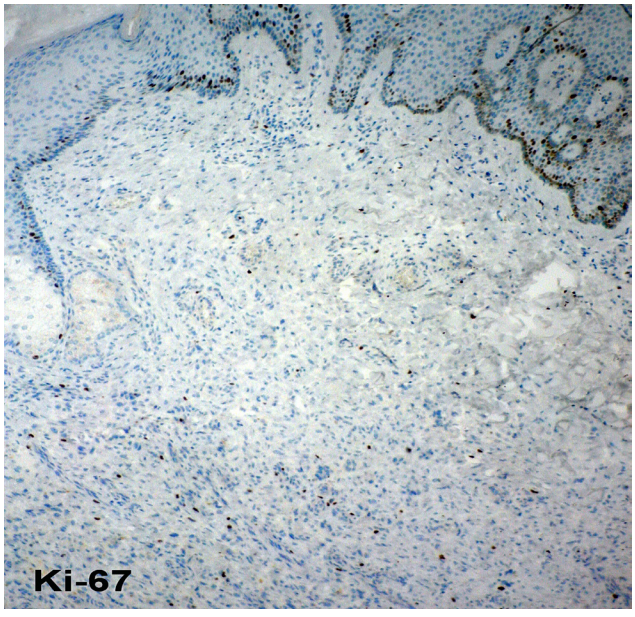

Figure 5. Positive Ki 67 immunostaining for cells during the mitosis (Imunohistochemical staining Ki 67 4x).

Surgery and follow-up

Preoperatively, intending to perform a RAFS, the lateral leg perforators were marked by Doppler ultrasound and the safety limits of excision were marked at 4 cm around the scar. The distal leg perforators mark the distal extent of the flap elevation. These are usually located 5 to 8 cm above the lateral malleolus.

The site to be covered was initially estimated and this measurement was transferred to the hind zone of the leg. The flap was drawn in the pronounced region of the calf.

With the patient in prone position, the remaining scar was excised with 4 cm tissue through the muscle and tendinous layer, with complete excision of aponeurosis.

The flap was elevated under a tourniquet in a proximal to distal direction. The initial proximal incision was made through the dermis, and the sural nerve and the short saphenous vein were located in the subcutaneous plane.

The pivot of the pedicle was located 6 cm from the medial malleolus. The cutaneous incision was Z-shaped, having its upper boundary 5 cm below the popliteal hollow and 6 cm above the lateral malleolus.

The RASF was then raised from its medial and lateral boundaries altogether with the muscular fascia, keeping fixed only by its superior boundary near the popliteal hollow. The small arteries, which appear near the fascia when it is segmented, were linked and divided so that they could promote the liberation of the flap. As soon as the flap was released in its lateral boundaries, the next step was to perform the incision in its superior boundary.

We performed a tunnel under the skin bride in order for the whole flap to be laid and displayed in the reception site. Keeping the articulation of the ankle at 90°, the flap was fastened with no tension. Inset was performed loosely with resorbable fine sutures.

The donor site was closed primarily and the flap was skin grafted after 2 weeks.

The tourniquet was deflated and hemostasis using bipolar diathermy was achieved. Finally a splint was made and we used the elevation of the limb for a few days.

The patient was nursed postoperatively in a prone position with particular care to prevent compression on the lateral leg.

The patient received intravenous antibiotics for 5 days postoperatively and was continued by oral antibiotics for 2 weeks.

The patient had a good evolution, with full recovery, without local recurrences or metastasis, and the histology was within good safety limits. The patient did not have local recurrences or metastasis at a distance, during the follow-up at 3, 6, 12, 18, 24 and 30 months.

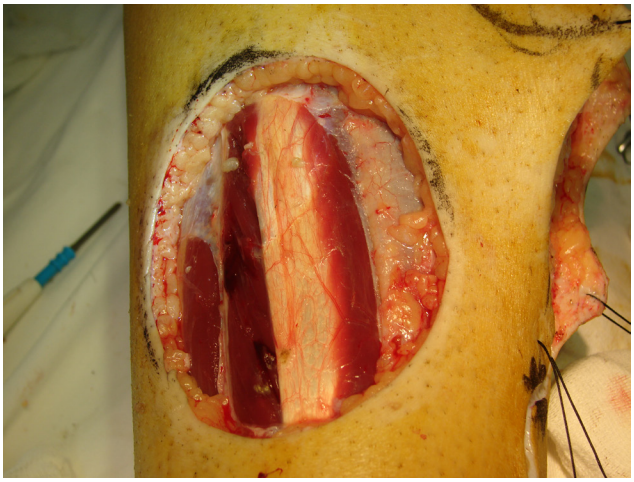

Figure 6. Excison of the DFSP with 4 cm safety limits with completely excision of the aponeurosis.

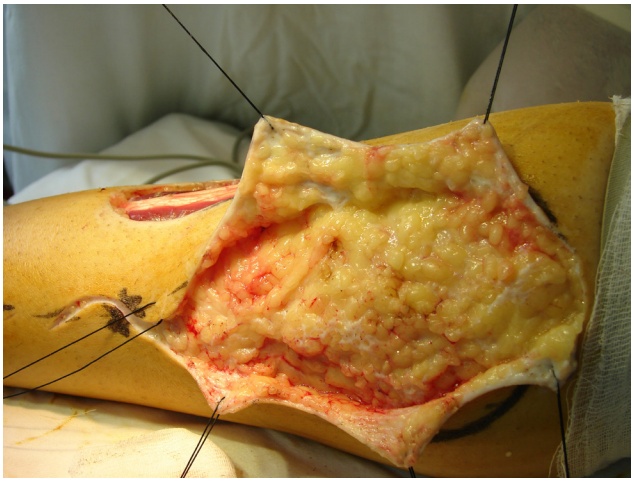

Figure 7. Posterior Z-shaped incision

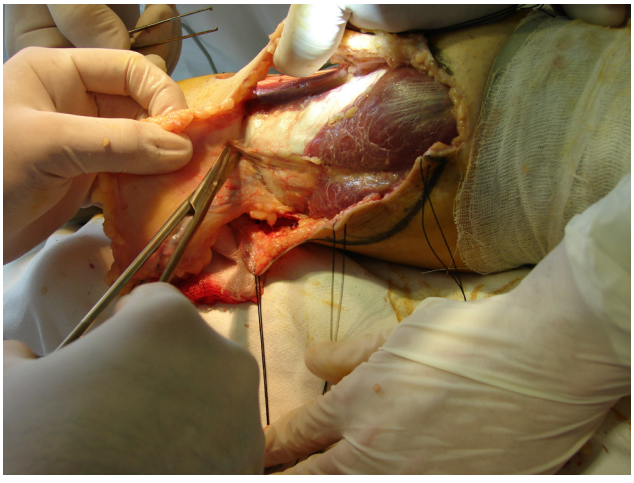

Figure 8. Preparing of the reversed adipofascial sural flap.

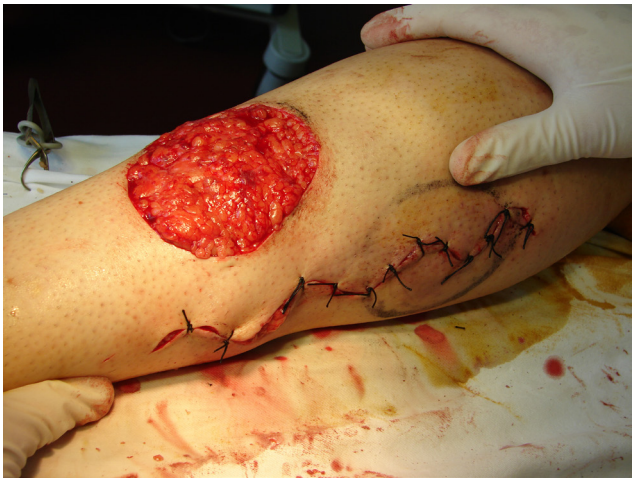

Figure 9. Final aspect after the excision of DFSP.

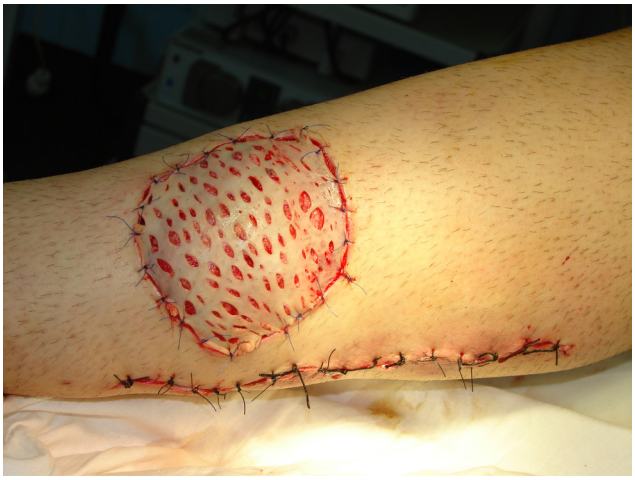

Figure 10. The aspect after skin grafting.

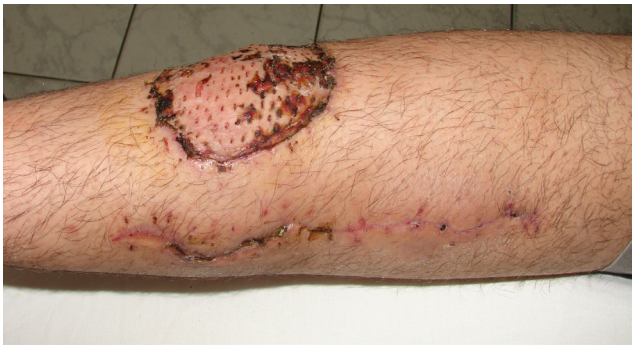

Figure 11. Local aspect after 1 month.

Discussion

This particular case is important because DFSP is a rare dermal or hypodermal mesenchymal tumor, locally very aggressive, characterized by high rates of local recurrence, but low risk of metastasis. The use of the RASF was a safe option for the coverage of the defect in the distal third of the leg after the excision of the DFSP, with a long,

thick and good quality pedicle, without morbidity of the donor area and with no significant functional loss.

The current literature related to our case reports the DFSP incidence in the United States which has been calculated to be between 0.8 and 4.5 cases per million population per year. Although the proportion of pediatric cases in published series of DFSP ranges between 6% and 20%, DFSP is an asymptomatic tumor with a slow growth, and we believe, as other authors, that many cases diagnosed in adults begin during childhood.

In a recent epidemiologic study of 2885 cases, the incidence of DFSP in black individuals was observed to be approximately twice that of whites. Literature reveals an equal sex distribution, with a slight male predominance in some series and slight female predominance in others [3].

DFSP is preferentially located on the trunk, accounting for 40%-50% of cases, generally on the chest and shoulders; in 30%-40% of cases, the tumor is located in the proximal portion of the limbs (more often on the arms than the legs); and in 10%-15% of cases, DFSP affects the head and neck, generally the scalp, cheek, and the supraclavicular area [4].

A history of trauma as a possible etiologic factor in DFSP has been debated. Such events might favor the development of the tumor, as a history of trauma is reported in 10%-20% of cases. Likewise, cases of DFSP have been described in which tumors are located on the sites of surgical scars, burns, radiodermatitis, vaccination scars, and sites of central venous lines.

The appearance of the tumor depends on the stage of disease, as the tumor progresses slowly over a long period before entering a rapid growth phase. DFSP initially appears as an asymptomatic, indurate plaque that may have a violaceous, red-blue, or brown appearance, with a hard consistency and fixed to the skin but not the deep layers. Over a period, which may vary from a few months to decades, the DFSP grows developing multiple nodules within the plaque, from which its name protuberans is derived [5].

Less commonly, DFSP presents initially as a unique firm cutaneous nodule. In the initial stages of DFSP, diagnostic errors are common, with the lesion being interpreted as a scar, morphea, morpheaform basal cell carcinoma, atrophoderma, or vascular malformations [6].

When the tumor progresses or starts as a protruding mass, DFSP may be confused with another tumor type. The more frequent mistaken diagnoses are sebaceous cyst, lipoma, dermatofibroma, hypertrophic scars and keloid. DFSP typically ranges in size from 2 to 5 cm, though in some cases, these lesions may grow as large as 20 cm in diameter and have multiple satellite nodules, especially if not treated earlier.

The tumor is usually fixed to overlying skin, but not to deeper structures. However, recurrent or long-standing tumors may invade fascia, striated muscle, periosteum, and bone [7].

Regarding the histology, DFSP appears as a poorly circumscribed tumor that infiltrates the whole dermis destroying the preexisting structures and spreading into the cellular subcutaneous tissue. The tumor is composed predominantly of a dense, uniform array of cells with spindle-shaped nuclei embedded in varying amounts of collagen. This fibroblast-like proliferation is typically arranged into irregular, interwoven fascicles, resulting in a storiform pattern, as is seen in many other fibrous proliferations [8].

In some areas, the tumor cells appear to be arranged radially about a central "hub," producing a pattern resembling the spikes of a wheel or whirligig. This pattern is most readily observed in the more cellular areas and was reported in 1962 by Taylor and Helwig as being of great diagnostic value. Tumor cells have large nuclei with low pleomorphism, and mitotic figures are infrequent, even in cellular areas. Inflammatory infiltrates, hemosiderin deposits, multinucleated giant cells, and foamy histiocytes are uncommon [9].

DFSP may contain small amounts of stromal mucin, which is often seen just below the epidermis. Cystic changes, dilated vascular spaces, and hemorrhage are sometimes present, but necrosis and lymphovascular invasion are rare. The epidermis over the tumors is usually thin, with flattened rete ridges. Less often, there is a slight-to-moderate acanthosis, although not to the extent that can be seen in dermatofibromas [10].

The main histological characteristic of DFSP is its capacity to invade surrounding tissues to a considerable distance from the central focus of the tumor. The cellularity is greater in the central zone than in the peripheral part of the tumor, where the edges invade the surrounding dermis and subcutis. The tumor cells invade the subcutaneous tissue in the form of tentacle-like projections through the septa and fat lobules. These tumor extensions contain few cells and, at first sight, can appear similar to normal fibrous tracts. This makes it difficult to determine the true extent of the lesion and may be why recurrences appear after excision with apparently wide margins. DFSP invades the fat with a particular "honeycomb" pattern or, more frequently, with a multilayered pattern or "sandwich" involving spindle cell layers oriented parallel to the skin surface [11]. Involvement of the fascia, underlying muscles, periosteum, and bone is a late event.

The definitive diagnosis of DFSP is usually established on the basis of routine histopathological and immunohistochemical features. Immunohistochemical expression of CD34 has been considered characteristic for the diagnosis of DFSP.

Approximately 80%-100% of DFSP express this marker, although between 10% and 20% are negative, most commonly, the fibrosarcomatous variant. Nonetheless, CD34 expression has been increasingly reported in other

sarcomas, such as inflammatory myofibroblastic tumor, myofibrosarcoma, epithelioid sarcoma, or angiosarcoma, and even in some benign fibrohistiocytic lesions, such as solitary fibrous tumor, sclerotic fibroma, cellular digital fibromas, nuchal-type fibroma, superficial acral fibromyxomas, and dermatofibromas [12].

Consequently, this marker should now be considered less specific for DFSP. Factor XIIIa is very useful in the differential diagnosis between DFSP and cellular fibrous histiocytomas, as it is usually negative in DFSP. However, a fraction of between 10% and 15% of cutaneous fibrous histiocytomas are negative for this marker, and, approximately the same proportion of DFSP show some level of expression. As a consequence, in recent years, new immunohistochemical markers have been described for the differential diagnosis between these 2 entities, including stromelysin III, nestin, CD163 and apolipoprotein D, though most of these are still under discussion [13].

Lower limb reconstruction, especially the calf, aquilian and calcaneal regions, after the excision of the DFSP, represents a therapeutic problem for the surgeon.

Appropriate protection to the mobility and vascular structures causing minimum sequelae in the donor site and promoting constant vascular activity are some of the desired factors in an ideal coverage. The quantity of transferred tissue must allow plantar stay for mobility support. The main limiting factors are the dimensions and depth of the lesion. The single skin grafting is used only when there is no bone, nervous, tendinous or vascular exposure. However, in many cases the flaps are the best alternative and adipofascial and adipofascio-cutaneous flaps are commonly used [14].

Complete surgical resection is accepted as the optimal treatment for local DFSP. However, the minimum resection margin needed to achieve local control remains undefined. The high recurrence rate can be explained by the eccentric growth of the tumor when it invades the subcutaneous cellular tissue. At this level, the tumor invades in the form of tentacle-like projections at a distance from the initial focus. In contrast, after wide local excision (2-3 cm), the reported total local recurrence rate is much lower and varies from 0% to 30%. Series in which margins of 5 cm were used reported rates of recurrence below 5%. Therefore, increasingly wider margins have resulted in lower recurrence rates. Nevertheless, obtaining generous margins is not always possible in patients when the tumors involve the face or neck or in pediatric cases. In addition, as the surgical margins are extended, the risk of complications after surgery increases (infection, or bleeding), the closing of the resultant wound is more complex and may leave an important cosmetic defect [15].

There are current reports praising the use of Mohs micrographic surgery as a first-line therapeutic measure in cases of limited tumors for tissue preservation and reduction of recurrence rates.

Regarding our patient, with the localization of DFSP at the calf, it is important to understand the arterial and venous anatomy of the distally based sural artery flap. The arterial supply of RASF is from the distal leg cutaneous perforators from the major lower limb vessels. In the majority of cases, these perforators are septocutaneous perforators from the peroneal artery. These perforators give off branches to supply the vasa nervorum and vasa vasorum of the sural nerve and short saphenous vein, respectively, once it comes above the deep fascia of the leg. It is this intricate arterial network running along the sural nerve and the short saphenous vein that defines the axiality of the flap. At intervals, this vascular network along the nerve and vein gives off cutaneous branches to supply the flap. To maximize flap reliability, it is therefore important that not only both the sural nerve and the short saphenous vein be included with the flap, but both these structures must be included along the entire extent of the flap [16].

Imatinib therapy almost always reduces the clinical appearance and histological cellularity of tumor, but the clinical use of neoadjuvant therapy before complete excision remains to be determined. Several questions remain regarding the action mechanism of imatinib and possible resistance to this target therapy in DFSP. However, imatinib is currently the gold standard in the treatment of local advanced or metastatic DFSP. Another consideration to remember is the fact that tumors lacking the t(17;22) translocation may not respond to imatinib; thus, molecular analysis of the tumor using RT-PCR or FISH may be useful before the administration of an imatinib-based therapy [17].

DFSP is considered to be radiosensitive, although the role of radiotherapy in treating this neoplasm remains uncertain. Radiation has been used as an adjuvant therapy after surgery, and may be considered in cases where there is a concern about the adequacy of surgical margins, when positive surgical margins are found after resection and further surgery is not feasible, or for negative surgical margins for large lesions. Radiation has occasionally been used as a primary treatment.

After surgery, patients should be examined every 6 months for the first 3 years and annually for the rest of the life. Physical examination should pay particular attention to careful inspection and palpation of the scar because DFSP is characterized by its capacity for local recurrence. In this context, most local recurrences appear within 3 years of surgery, although later recurrences can also occur [18].

As DFSP metastasizes in only 2%-5% of cases, extensive evaluations with CT scans, blood cell counts, and liver function tests are not indicated. DFSP most commonly disseminates hematogenously to the lungs, particularly if the lesion is advanced or recurrent. Therefore, a chest x-ray should be performed for all patients, and chest CT should be performed only for patients with suspicion of pulmonary metastases.

Metastases preferentially localize to the lung, but

have also been reported in the brain, bone, and heart. Although it is difficult to determine which cases are at risk of metastasis, they generally involve recurrent lesions that have progressed for many years and when a fibrosarcomatous component is seen by histology [19].

Conclusions

The older age, tumor size >5 cm, head or neck location, high mitotic index, p53 mutations, and increased cellularity are predictors of poor clinical outcome in DFSP.

The main histological characteristic of DFSP is its capacity to invade surrounding tissues to a considerable distance from the central focus of the tumor, so wider margins of resection have resulted in lower recurrence rates.

Imatinib is currently the gold standard in the treatment of local advanced or metastatic DFSP but the role of radiotherapy in treating this neoplasm remains uncertain.

The use of the RASF it is a safe option for the coverage of the defects in the distal third of the leg, being a simple and rapid surgical intervention, using a constant vascularization of the sural region, having a long, thick and good quality pedicle, and because the morbidity of the donor area is minimal with no significant functional loss.

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