Giant dermatofibrosarcoma protuberans – rare form of mesenchymal tissue neoplasm: case presentation

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Abstract
Dermatofibrosarcoma protuberans (DFSP), a rare type of mesenchymal neoplasm, is defined by the WHO as a superficial sarcoma with low-grade malignancy that develops in the cutaneous and subcutaneous tissues. The purpose of this paper is to present a case of a giant DFSP, with post-traumatic onset in childhood and a very long evolution. Clinical data: 51-year-old Caucasian patient presents for 41 years a presternal neoplastic lesion, with onset at 10-year-old, a few months after a strong trauma. The patient addressed for a clinic examination, secondary to a spontaneous hemorrhage of the lesion. The local examination reveals the presence of a red-purple polynodular neoplastic lesion of 180×110×30 mm, of firm consistency, adherent to the subcutaneous tissue, painless, with lateral extension at 8 o’clock with an erythematous infiltrated atrophic plaque appearance. One of these nodular masses presents surface ulceration and areas of necrosis. The CT scan did not detect any infiltration into the pectoral muscle or loco-regional metastasis. Under general anesthesia a wide surgical excision with free macroscopic margins of 3 cm was performed. Histopathological diagnosis was DFSP, with evidence of tumoral spindle cells disposed in storiform pattern, embedding small adipocyte panicles, creating a lace-like or honeycomb appearance. Immunohistochemically, the tumor cells express an intense and diffuse CD34 and they are negative for S-100 and SMA. The Ki-67 is focal positive in almost 2–4%. Clinical and paraclinical monitoring at 18 months follow-up does not detect any local recurrences or metastases, and an excellent quality of life.

Keywords: giant dermatofibrosarcoma protuberans (DFSP), post-traumatic, CD34, keloid.

Introduction
Dermatofibrosarcoma protuberans (DFSP), a rare mesenchymal neoplasm, accounts for <0.01% of all malignancies and <0.1% of all the cutaneous neoplasms [1, 2], is defined by the WHO (World Health Organization) as a superficial sarcoma with low-grade malignancy, that develops in the cutaneous and subcutaneous tissues. DFSP was described for the first time in 1924 by F.J. Darier and M. Ferrand, as a progressive and relapsing dermatofibroma. Also, they highlighted the evolving and recurrent nature of the tumor [3]. In 1925, Hoffman associated the term “protuberans” with the clinical prominent aspect of the lesion [4]. The metastases rarely occur and especially in cases of repeated skin relapses.

The DFSP is mainly located on the trunk, thorax or abdomen and more rarely on the lower limbs. Other described locations are head and neck. The palms and the plantar surfaces are not affected.

The onset can be correlated with a local trauma or scar, initially as an atrophic plaque similar to morphea and subsequently taking a protuberant multinodular aspect [5–7].

The case presented in this study overlaps the classic aspect of a DFSP, adding some particular aspects regarding the giant clinical aspect, simultaneously nodular, erythematos infiltrated atrophic plaque and the 41 years evolution.

Patient, Methods and Results
We report a case of a 51-year-old Caucasian woman from the rural area that presents for 41 years a pre sternal neoplastic lesion, with onset at the age of 10 years, a few months away from a strong trauma. The patient addressed for a clinic examination, secondary to a spontaneous hemorrhage of the lesion.

The local examination reveals the presence of a red-purple polynodular neoplastic lesion of 180×110×30 mm, of firm consistency, adherent to the subcutaneous tissue, painless, with lateral extension at 8 o’clock with an erythematous infiltrated plaque appearance. One of the central nodular lesions, of 50×25×20 mm, presents ulceration and necrosis.

The lesion evolved according to the anamnesis, in two stages, initially as an erythematous or purple plaque, slightly infiltrated, subsequently followed by nodular mass, slowly growing in size. Simultaneously, it shows a lateral expansion similar to the initial erythematous infiltrated lesion (Figure 1, a and b).
Figure 1 – (a and b) Clinical aspects.

The paraclinical tests do not evidentiate significant abnormalities. The CT scan evidentiate the existence of the cleavage plane with the sternal manubrium, without lymph node metastases, intrathoracic evolution of the tumor, or invasion of the pectoral muscle.

After the informed consent was sign, wide surgical excision was perform under general anesthesia with free macroscopic margins of 3 cm (Figures 2 and 3).

Figure 2 – Surgical intervention.

Figure 3 – Post-surgical appearance.

Tissue fragments were processed by standard histological techniques: fixing in 10% formalin, pH 7.2 for 24 hours, paraffin embedding, sectioning at 4–5 μm thickness, staining with Hematoxylin–Eosin (HE) and van Gieson. For immunohistochemical examination were selected the most representative paraffin blocks. After dewaxing and hydration, endogenous peroxidase blocking was performed with 3% hydrogen peroxide. Incubation with the primary antigen was done for 30 minutes. Working method used was Streptavidin–Biotin complex system, the final result was revealed with DAB (3,3’-Diaminobenzidine) in brown color. The panel of primary antibodies included: CD34 (Clone QBEnd/10; 1:200 dilution; Lab Vision), CD68 (Clone KP-1; 1:600 dilution; Dako), SMA (Clone 1A4; 1:500 dilution; Dako) and S-100 (Polyclonal Rabbit; 1:6000 dilution; Dako) and Ki-67 proliferation index (MIB-1; 1:200 dilution; Dako).

The microscopic examination reveals a tumor proliferation in the middle and deep dermis, and hypoderm, consisting of spindle cells, with storiform pattern, monotonous, in a fibrous stroma. No cyto-nuclear atypia was observed. In some areas, rare mitosis can be observed (3–4/10 HPF). In the deep dermis, near the hypoderm, the tumoral cells surround small islands of adipocytes, observing the classic lace-like or honeycomb appearance: small adipose lobules between spindle cells. We did not observe the areas of sarcomatoid transformation in fibrosarcoma (Figure 4).

The immunohistochemical profile: tumor cells are strongly positive for CD34 and negative for SMA and S-100. Rare macrophages CD68 positive were observed, especially at the periphery of the lesion in surrounding dermis. The Ki-67 was focal positive in almost 2–4% of the tumor cells (Figure 5).

Figure 4 – Microscopic aspects, excisional skin biopsy. HE staining, 20×, 40× and 100×.
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The surgical lateral and profound margins were tumor-free, even through free margins measure microscopically only 1 cm in some areas.

The clinical and paraclinical (CT scan) follow-up at 18 months after the surgical excision did not detect any local recurrences or metastases. In the present, the patient is in a very good state of health, with a quality of life identical to the one of a healthy person. Clinical and paraclinical follow-up will be continued because of the high risk of local relapses in the first five years after surgical excision. Although rare, metastases can present in lymph nodes and lungs, therefore further investigation is needed.

Discussion

DFSP is a mesenchymal tumor with low-grade malignancy, rarely seen in practice. Criscione and Weinstock, in an epidemiological study [8] conducted by analysis of several Cancer Registries in USA, over a 30 years period, highlights an annual incidence of 4.2 cases per million, with a 1.6 times higher frequency in African-American population, without any explanation of this prevalence. DFSP affects both sexes, with a slightly higher prevalence for females, of 1.04 times in some studies [8] opposite to others, in which males prevail with a 1.1 times higher frequency [9, 10].

The presented case has some particularities. Firstly, giant aspect of the lesion 180×110×30 mm, rarely mentioned in the specialized literature [11, 12], and the slow constantly progressive evolution in over 41 years. The case enrolls in one of the 10% up to 20% of the cases that recognize a traumatic etiology [13, 14]. The relatively short period of time elapsed between the trauma and the onset of the lesion according to the anamnesis must be mentioned. However, the real onset of the DFSP is difficult to determine in case of a post-traumatic debut, because the erythematous plaque, atrophic and infiltrated, can be easily confused with post-traumatic lesions in case of severe trauma.

The post-traumatic debut took place in childhood, at the age of 10 years, a few months after a strong trauma. In generally, the time between the trauma and the debut of the lesion varies between two and four years, but in our case was a few months [13, 14]. Usually, is difficult to establish with precision, because of the long period of disease and no clinical typical characteristic. The erythematous plaque can be easily confused with a post-traumatic scar [15, 16].

The typical localization is on the thorax; between 50–60% of the DFSP cases have the same localization on the thorax area [5]. In this case, the localization is presternal, without the invasion of the pectoral muscles on the CT scan, being determined by the strong trauma from childhood that occurred in that area.

The clinical aspect simultaneously combines the erythematous infiltrated form, in plaque that is the debut form, with huge polylobate aspect, typical to the evolution of DFSP. The evolution of the presented case fits the classical described variations, with lack of metastases despite the age of the disease. It generally metastasizes in lymph nodes, lungs and bones. Metastases are generally found after local recurrences of the tumor [13].

The clinical differential diagnosis includes: post-traumatic keloid – especially in DFSP with post-traumatic debut, similar to the presented case, because of the age of the disease and the slow progressive evolution; the
malignant peripheral nerve sheath tumor, morphea, giant dermatofibroma, dermatomyofibroma, neurofibroma or pigmented lesions [17, 18].

The histopathological differential diagnosis includes: dermatofibroma or benign fibrous histiocytoma, especially the cellular version, plaque-like CD34-positive dermal fibroma (medallion-like dermal dendrocytic hamartomas), spindle cell melanoma, leiomyosarcoma and perineurioma [19, 20].

The most frequent and difficult differential diagnosis is with giant dermatofibroma (benign fibrous histiocytoma), hypercellular variant. In case of the histiocytoma, the cells have only a focal storiform pattern, with cyto-nuclear atypia, more polymorphic nuclei, without mitosis. The tumor cells are negative for CD34 and there are numerous macrophages positive to CD68 between the tumor cells. There is no honeycomb appearance and the surface epithelium presents characteristic changes (overlying hyperplasia).

The neurofibroma presents positivity for CD34, and especially for S-100, which is negative in DFSP. Pigmented DFSP (Bednar tumor) is S-100 positive in melanin-containing dendritic cells.

In myxoid variants of DFSP, in the differential diagnosis we should include the pleomorphic sarcoma, myxoid liposarcoma, and myxofibrosarcoma.

Immunohistochemical, the tumor cells can also present positivity for CD99, and general negativity for S-100, desmin, SMA, factor XIIIa and CD117.

Cytogenetics can detect in many cases (especially in cases with family aggregation) specific modifications: translocation t(17;22)(q11.2;q13) or ring chromosome 22. These genetic modifications will lead to combining of two genes: PDGF B-chain gene (PDFGB) and collagen gene (COL1A1) [21–23].

The macroscopic free margins were estimated at 3 cm by the surgeon, but do not totally overlap with the histopathological results, where the thinner free margins were reduced at 1 cm. These findings require, in case of the surgical treatment, the application of the gold standard of 3 cm free margins at excision [14, 24, 25].

There are notable differences between the macroscopic dimensions of the tumor and the microscopic dimensions established at the examination in light microscopy. The excision with free margins of 1 cm revealed the presence of residual tumor lesions in 70.7%, at 2 cm in 39.7%, at 3 cm in 15.5% and at 5 cm in 5.2% [24, 26].

The majority of the relapses occur in the first three years, half of them in the first year, but there are described even relapses after five years [25, 10]. The relapse rate is reported to be of 20% in the cases of 3 cm free margins [25].

Large excision in this case, with 3 cm free margins alongside with relatively short time, 18 months, could explain the lack of relapses [27, 28].

Tyrosine-kinase inhibitors, like Imatinib, can be used in the treatment of these tumors in adults, especially in case of metastases or local relapses, using doses of 800 mg/day, with a response rate of 46% [5]. Others therapies include Sorafenib, molecular targeted therapy, radiotherapy or electro-chemotherapy [29–32].

Conclusions

We presented this rare case of giant dermatofibrosarcoma protuberans, the particularity of the case consisted in post-traumatic onset in childhood, dramatically clinical appearance and slow progressive evolution in over 41 years. Immunohistochemical investigations were essential for final histopathological diagnosis and establishing therapeutic management.

References


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