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Dermatofibrosarcoma: a rare form of soft tissue. Management and review of the literature

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Rezumat

Dermatofibrosarcom: o formă rară de tumoră de țesuturi moi

Dermatofibrosarcomul (DFSP) este o tumoră rar întâlnită de țesuturi moi, de origine cutanată cu potențial de malignitate de nivel intermediar. Incidența acestuia este de 0,1% din totalul neoplaziilor și de 1% din sarcoamele de țesuturi moi. Prezentăm cazul unei femei de 65 ani având o masă dureroasă, palpabilă la nivelul coapsei drepte. S-a practicat excizia chirurgicală a leziunii pentru care examenul histopatologic, inclusiv analiza imunohistochimică cu CD-34 confirmă diagnosticul de DFSP. Controlul efectuat la 2 ani de la intervenție atestă absența bolii și lipsa metastazelor sau recurenței locale. Terapia chirurgicală de elecție constă în excizia radicală cu bază largă în cazul DFSP fără metastaze. DFSP este o tumoare rezistentă la chimioterapia și radioterapia convențională, în timp ce în cazul metastazelor, tratamentul depinde de citologia și biologia moleculară a tumorii, astfel încât sunt în cercetare noi strategii terapeutice.

Cuvinte cheie: dermatofibrosarcom protuberans (DFSP), tumoare de țesuturi moi, translocare COL 1A-PDGFB, CD-34

Abstract

Dermatofibrosarcoma protuberans (DFSP) is an uncommon soft tissue tumor of cutaneous origin of intermediate grade malignant potential. The incidence of DFSP is 0.1% of all cancers and 1% of all soft tissue sarcomas. We present the case of a 65years old female with a palpable, painful mass on the right thigh. A surgical excision of the lesion was done and the histopathology, as well as the immunohistochemical analysis with CD-34, confirmed the diagnosis of DFSP. Two years later, the patient is free of disease and no local recurrences or metastases have been found. Wide radical excision is the preferred surgical method for therapy of DFSP without distant metastasis. Furthermore, DFSP resists to conventional chemotherapy and radiation therapy, while, in cases of metastasis, therapy depends on cytogenesis and molecular biology of the tumor, so new therapeutic strategies are under research.

Key words: Dermatofibrosarcoma protuberans (DFSP), soft tissue, tumor, translocation COL1A1-PDGFB, CD-34

Case presentation

A 65 years old female patient with no significant past medical history was presented at the outpatient clinic (of Dept of Surgery) for assessment of a palpable painful mass at the right thigh, over the last year (Fig. 1). There was no history of trauma, fever or weight loss. On physical examination a 7x7 cm well defined mass was revealed on right thigh. The mass had smooth surface, was fixed and attached to the skin. Regional lymph nodes were not enlarged, while the rest clinical examination did not reveal any other abnormality. The laboratory

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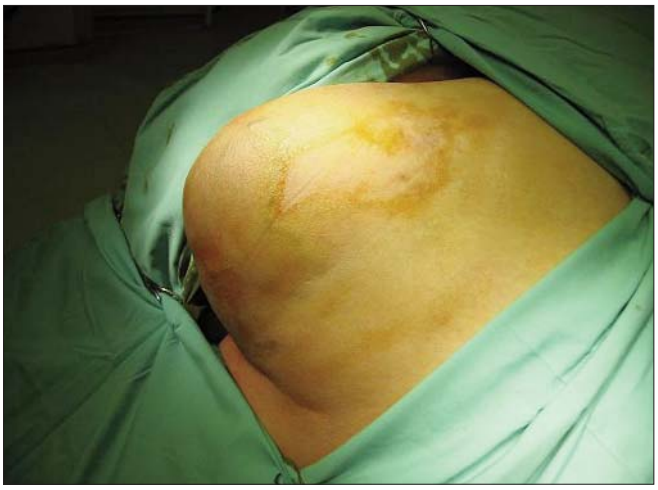

Figure 1. *The mass at the righ thigh*

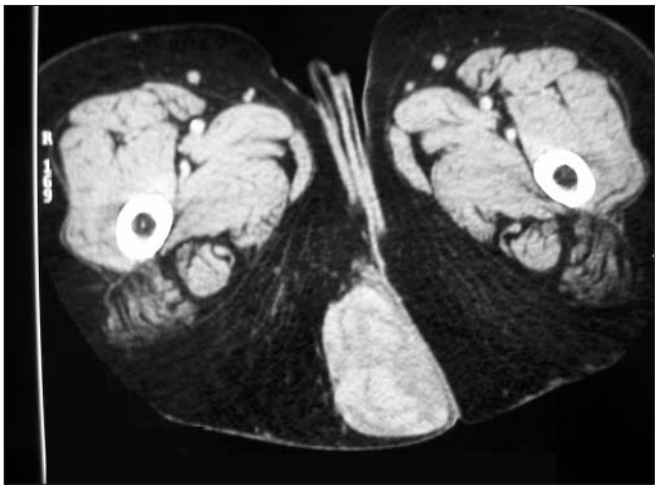

Figure 2. *The CT scan imaging of the mass*

investigation was unremarkable. Full screening test was performed in order to accurately localize the lesion, to evaluate its extension and to rule out distant metastasis. The CT scan (Fig. 2) revealed a well circumscribed, oval shaped, soft tissue attenuation mass in subcutaneous fat of the right thigh. The overlying skin was stretched over the mass and was not separately identifiable from it. The patient underwent a local excision of the mass, with 4 cm safety margin. The relationships of the lesion to adjacent tissues were inspected. The macroscopic examination revealed a mass 7.5 x 7 x 5.5 cm of a solid and elastic texture, with nodal appearance and focal hemorrhages (Fig. 3). The microscopic histological appearance revealed a mesenchymatic neoplasm with characteristics compatible to DFSP. The neoplasm was localized to the subcutaneous fatty tissue and the deep soft tissues. Furthermore, the histopathology revealed a high cellularity neoplastic tissue composed of rather relatively spindle cells with focal storiform pattern. Other features were the low mitotic activity, its reticular pattern of evolution and CD34 were positiveness intensively (Fig. 4). Finally, histopathology confirmed that all the surgical margins are free. After short recover period the patient was discharged. Two years later, the patient is free of disease, while she undergoes a full screening test every 6 months.

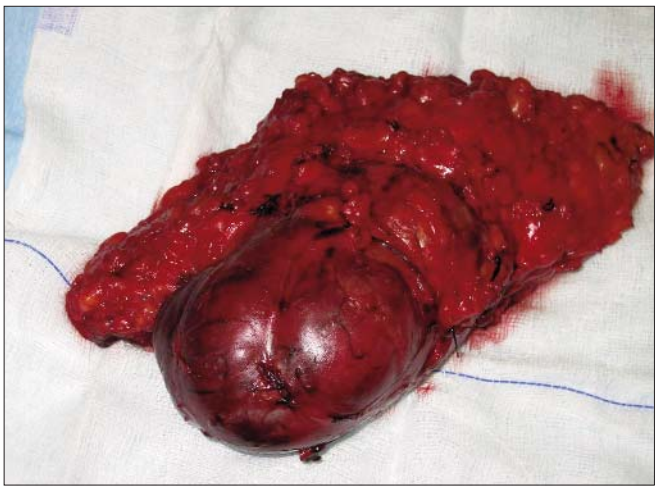

Figure 3. *The surgical speciment of the mass*

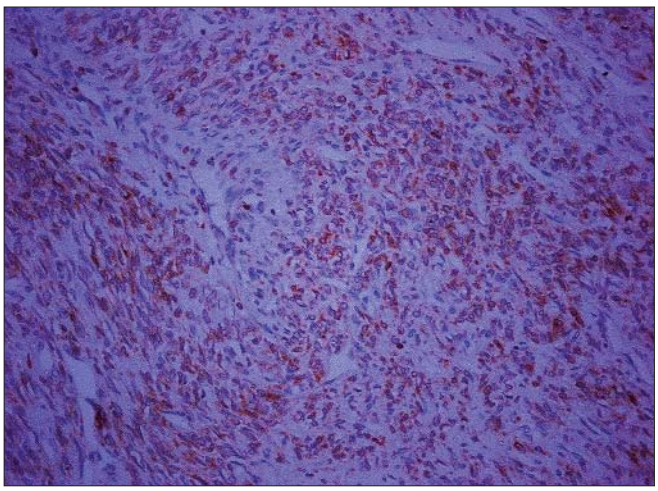

Figure 4. *Tumour cells showing immunoreactivity for CD34*

Discussion

Dermatofibrosarcoma protuberans (DFSP) is an uncommon slow – growing soft tissue tumor of cutaneous origin with an intermediate grade malignant potential (1). It is believed that the cell of origin is a dermal stem cell or an undifferentiated mesenchymal cell with fibroblastic, muscular and neuronic features (1,2). Although it rarely metastasizes, it is characterized by a high morbidity due to its locally aggressive invasion and a high rate of recurrence following surgical removal (3). The incidence of DFSP has been estimated between 0.8 – 4.5 cases per million in general population, per year in the USA (3). It represents 0.1% of all cancers and 1% of all soft tissue

sarcomas (3,4). Furthermore, DFSP is the most common sarcoma of cutaneous origin (3).

A wide range of studies have shown that DFSP can appear at any age. However, it is most common in individuals aged between 20 and 50 years (3,5). It must have been noticed that few cases of DFSP have been reported in children, though there is a delay to their diagnosis, due to its slow growth (3,6). Recently, giant cell fibrosarcoma (GCF) is considered as the juvenile form of DFSP (3).

The incidence of DFSP reported in the literature has not shown any preference in sex distribution. However, the National Cancer Institute has recently reported a higher incidence in women (3).

Finally, it has to be noticed that DFSP is been reported in all races, though the incidence is higher in black race (2:1), while there is no pathophysiological mechanism which explains such preference.

A number of authors have reported cases of DFSP of varying etiology. In a recent review a history of trauma is reported in 10% - 20% of cases (3,5). In many cases, tumors have been found on surgical, trauma or vaccination scars or even on burns or radiodermatitis.

The most common location of DFSP is the trunk. In 40% - 50% of all cases it is found in this area and mainly to the chest and shoulder. Other less usual locations of DFSP are the limbs (30% - 40%) and head and neck (10% -15%). It has to be mentioned the fact that treatment is less effective in cases of DFSP on the head and neck, as the possibility of invasion is higher there (3,7,8).

The tumor first appears as a single, red to bluish, blanchable, rigid, cutaneous nodule. As the nodule grows, ulcerations develop on the surface. During the late stage, the rate of growth accelerates and fixation to the deep structures become more intense (3,4,8). Its growth rate varies. Lesions may remain stable for many years or they may grow slowly with periods of accelerated growth (9-11). The tumor invades laterally through the fascias of the dermis over a period of many years, which may vary from half a year to 30 years, local recurrences occur in 20-55% of cases (12-14). The tumor invades laterally through the fascia of the dermis over a period of many years, which may vary from half a year to 30 years. Metastases may occur mainly to lungs, followed by the regional lymph node. The visceral organs and bones are rarely affected (10). Generally, distant metastases are seen after recurrent local relapses. The tumor is initially localized to the dermis. Macroscopically, the tumor is composed of a dense growth of monomorphous fusiform cells with a large elongated nucleus and generally with low pleomorphism and a low mitotic rate. There is generally very little stroma, with intercellular deposits of collagen and small capillaries. The spindle cells are organized in irregularly linked fascicles with a storiform arrangement. The main histological characteristic of DFSP is its capacity to invade surrounding tissues to a considerable distance from the main focus of the tumor. The cellularity is greater in the central region than in the peripheral part of the tumor, where the edges invade the surrounding dermis and subcutis (12).

The histological differential diagnosis should be carried out from other tumors with a fibrohistiocytic appearance, such as fibrosarcoma, malignant fibrous histiocytoma, dermatofibroma, infantile myofibromatosis, nodular fasciitis, keloid, and hypertrophic cicatrix, all of which may have similar pathologic findings.

DFSP is a locally aggressive tumor and rarely metastasizes; however, the recurrence potential of DFSP is directly relative to the extent of the resection. The indicated (gold standard) treatment is radical surgical excision of the lesion. The technique should include resection of a 3 cm margin of skin beyond the borders of the tumor and should include the fascia and even muscle tissue if necessary to attain negative intact borders histopathologically. On microscopic examination the tumor displays a low degree of malignancy (85% -90% of all cases) (7,9,12). However, in 10-15% of cases fibrosarcomatous transformation may be present. Excision with wide margins leads to a notable reduction in the rate of recurrence. Thus, when the surgical margins are at least 3 cm, the rate of recurrence is 20%, whereas if they are less than 2 cm, the rate increases to 40%. Those series in which margins of 5 cm were used reported rates of recurrence of less than 5%. DFSP is a tumor that rarely gives distant metastases, and when metastasis does occur, it does so only after many years of tumor progression. The rate of metastasis is 1% to 3%, with a mean DF interval from the first excision of 6 years (12).

Excision by means of Mohs Micrographic Surgery (MMS), with continuous histological margin control, is an attractive surgical option because it is potentially tissue-sparing. Furthermore, MMS is an effective surgical tool for body regions where wide excision is not feasible or desirable. However, MMS may have utility only for local limited disease, because recurrent DFSPs have a tendency to grow deeper, so MMS will probably not be as useful for advanced DFSP. Experience, though, with MMS in the treatment of DFSP is relatively limited; although in several series have been reported recurrence rates as low as 0% to 6.6% (4,10).

The use of fluorescence in situ hybridization revealed that the ring chromosome in DFSP contains sequences from chromosome 17 and revealed involvement of chromosome 22, with low levels of amplification of the 17q22 and 22q10-q13.1 regions. In recent studies it has been found that more than 90% of cases DFSP carry the t (17;22) translocation (11,13). This leads to a constitutive activation of the platelet-derived growth factor receptor (PDGFR) followed by continuous stimulation of the tumor cell growth, while it has been found that the translocation COL1A1-PDGFB in DFSP has an ongogenic power. The use of targeted inhibitors of PDGFR could be a good therapeutic option in the treatment strategy of unresectable locally advanced, recurrent or metastatic disease. With Imatinib, a selective PDGFR tyrosin kinase inhibitor, partial and complete remissions of DFSP could be achieved (8,12,14).

As previously discussed, recent evidence indicates that the constitutive activation of the PDGFB-PDGFR signaling pathway has a central role in the pathogenesis of DFSP. Imatinib is a potent, selective inhibitor of PDGFRb and PDGFRa with demonstrated activity against DFSP cells in vitro and in vivo. Guidelines for DFSP released in 2006 by the U.S. National

Comprehensive Cancer Network state that Imatinib has shown clinical activity against localized and metastatic DFSP containing the t(17:22) and it has been established for the treatment of adult patients with unresectable, recurrent and/or metastatic DFSP who are not eligible for surgery (15,16).

In our case, the patient underwent a local excision with clear 3-cm margins. We did prescribed neither further chemotherapy and/or radiation therapy nor biological treatment, since the incision borders were negative on histopathology, while it was revealed a low degree of malignancy. Two years later, the follow up revealed that there is no evidence of regional or distant metastases and the patient lives a normal life.

Reviewing the Literature and to our knowledge, the average size of these tumors is reported as being under 5 cm. In our patient the tumor was 7.5x7x5.5 cm in size, which is exceptional; despite the large size there were no metastases.

In conclusion, dermatofibrosarcoma protuberance is an uncommon soft tissue tumor of cutaneous origin with an intermediate grade of malignant potential. In agreement with modern literature, our case report shows that local excision with 3 cm margins of intact tissue, which also included normal underlying muscle, is adequate therapy for local DFSP without metastasis and a favorable outcome can be expected with minimal trauma.

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