

Dermatofibrosarcoma Protuberans  
(DFSP): Case Report and Literature  
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## Article Information

Received date: Jun 14, 2017

Accepted date: Jun 26, 2017

Published date: Jun 28, 2017

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CC-BY 4.0Keywords Dermatofibrosarcoma  
Protuberans; Skin Sarcoma; Imatinib  
Mesylate

## Abstract

Dermatofibrosarcoma Protuberans (DFSP) is a slow-growing, low-grade, malignant fibroblastic mesenchymal tumor that arises from the dermis and invades deeper tissues. The precise origin of DFSP is not well known but evidence hints that the cellular origin is fibroblastic, histiocytic, or neuroectodermal. Cytogenetic abnormalities have been found in patients with DFSP, such as reciprocal translocations of chromosomes 17 and 22, t(17;22), and supernumerary ring chromosomes composed of interspersed sequences from bands 17 (17q22) and 22 (22q12). It is a relatively uncommon soft tissue neoplasm with an estimated incidence of 4.2 to 4.5 cases per million persons per year in the United States. DFSP may present as an asymptomatic, skin-colored plaque with possible dark red or blue discoloration. Clinical suspicion is confirmed by biopsy. Histologically, DFSP shows a storiform or fascicular proliferation of bland spindled cells that extend from the dermis into the subcutaneous tissues. Almost all cases of DFSP are CD34-positive (Figure 1) and factor XIIIa- negative. The treatment of choice for a DFSP is wide local excision. Every effort should be made to completely remove the tumor at the time of initial operation, considering the proclivity that DFSP has for irregular and frequently deep subclinical extensions. The margins of resection vary in the medical literature anywhere between with 2 to 4 cm. Imatinib mesylate was approved by the FDA for the treatment of unresectable, recurrent, and/or metastatic DFSP. We are reporting a case of a 28-year old male patient with a DFSP treated by our multidisciplinary team.

## Introduction

Dermatofibrosarcoma Protuberans (DFSP) is a malignant skin tumor which represents less than 0.1% of all malignant neoplasms and 1% of all soft tissue sarcomas [1]. It is a relatively uncommon, low-grade, soft tissue neoplasm, of fibroblast origin with an estimated incidence of 4.2 to 4.5 cases per million persons per year in the United States [2,3]. Incidence rates among women are higher compared to men (4.4 vs. 4.2 cases per million per year), with the exception of the elderly [2]. DFSP is a disease that affects mostly adults between 20 to 50 years [4]. It is a locally aggressive tumor with a very high recurrence rate, between 10-60 % of the cases. This is due to its highly irregular shape and frequent finger-like extensions [5,6], but it rarely produces regional or distant metastasis [7].

DFSP is located in the trunk (42% to 72 % of the cases) followed by the extremities (20% to 30 % of the cases), and the head and neck region (10% to 16 % of the cases) [8]. Locations for DFSP include surgical scars, old burn sites, regions of the body exposed to trauma, central venous line puncture sites, vaccination sites, insect bites, and radiation dermatitis [8-10]. We report on a case of a 28-year old patient with DFSP that had an 8-month delay in seeking medical attention.

## Case report

A 28-year old previously healthy male patient noted a very small, firm reddish to brown plaque / nodule at the junction of the left shoulder girdle with the pectoral is mayor muscle approximately two-years before been referred to our surgical oncology clinic (Figure 2). He referred no pain and observed that the lesion had been growing slowly and changing in form.

The patient took approximately 12 months to seek medical attention because initially he thought it was an insect bite with the resultant scar. A dermatologist performed an incisional biopsy that was read as DFSP that was CD-34 positive and Ki-67 10%. The dermatologist referred the patient to our clinic where we performed a thorough evaluation and a pathology review that confirmed the diagnosis (Figures 2 and 3). A CT of the neck and chest was performed for staging.

The case was presented at our multidisciplinary tumor board and it was agreed to perform a wide local excision with 2cm margins, place a wound VAC and wait for final pathology review to confirm negative margins. The plastic reconstructive team would perform a free flap reconstruction from the left lower extremity due to de size of the defect and inability to adequately rotate tissue to cover the defect (Figure 4). No further adjuvant therapy was required.



Figure 1: Immunohistochemistry showing CD34 positivity.

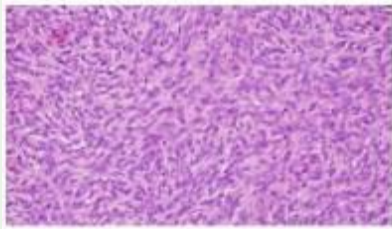


Figure 2: Characteristic storiform pattern seen in patient with DFSP.



Figure 3: DFSP of the chest.



Figure 4: Image of the wound four months after reconstructive surgery.

The patient has been following-up at our clinic for the past two years without any evidence of local recurrence.

## Discussion

Darier and Ferrand described DFSP in 1924 as a cutaneous disease called progressive and recurring dermatofibroma [11], and in 1925 Hoffman officially coined the term DFSP [12]. DFSP is a slow-growing, low-grade, malignant fibroblastic mesenchymal tumor that arises from the dermis and invades deeper tissues (fat, fascia, muscle, and bone). The precise origin of DFSP is not well known but evidence hints that the cellular origin is fibroblastic [13,14], histiocytic [14], or neuroectodermal [15-18]. Experts propose a pluripotent progenitor

cell (undifferentiated mesenchymal cell), as the origin of DFSP, because these tumors demonstrate some features of each cellular type [15].

The growth rate of DFSP tumor cells is increased by the activation of the Platelet-Derived Growth Factor (PDGF)-beta-receptor [19]. Cytogenetic abnormalities have been found in patients with DFSP, such as reciprocal translocations of chromosomes 17 and 22, t(17;22), and supernumerary ring chromosomes composed of interspersed sequences from bands 17(17q22) and 22(22q12) [20,21]. These chromosomal rearrangements fuse the collagen type I alpha 1 (COL1A1) and the PDGF-beta chain genes. The product of this is a COL1A1 and PDGFB fusion protein [22] that is processed into a functional PDGF-B and later interacts with the PDGF receptor on the cell surface of DFSP tumor cells. The activation of the PDGF receptor tyrosine kinase prompts the proliferation of DFSP tumor cells [23].

DFSP tend to grow slowly and because of this the diagnosis is often delayed for months to years as is the case with our patient. DFSP may present as an asymptomatic, skin-colored plaque with possible dark red or blue discoloration [24]. As the disease advances, it may develop irregular nodules that can increase in size and become protuberant or ulcerative [25]. Telangiectasia may be apparent on the surface or at the periphery. With time these nodules can infiltrate the subcutaneous tissue, fascia, muscles and even the bone [8,9].

In the early stages of the disease, DFSP should be differentiated from hypertrophic scars, keloids, lipomas, epidermal cysts, dermatofibroma. Our patient thought that the lesion was a scar from an insect bite which led to the delay in seeking medical attention. As the disease advances, the differential diagnosis should consider cutaneous melanoma, pyogenic granuloma, Kaposi sarcoma, and other soft tissue sarcomas [26].

Clinical suspicion is confirmed by biopsy. The superficial characteristics of a DFSP may appear similar to other benign skin lesions, so it is recommended that a deep subcutaneous punch biopsy or incisional biopsy be performed in all cases [27]. When the suspicion for DFSP is high, but the initial biopsy is unequivocal, re-biopsy is recommended [27]. Wide undermining of the skin is discouraged during the biopsy procedure, because it may potentially result in tumor-seeding [27].

No laboratory tests are available to help diagnose DFSP. In most cases, no imaging studies are needed unless metastatic disease is suspected. Chest imaging may be ordered for baseline screening for pulmonary metastasis in high-risk cases [28-30]. Computed Tomography (CT) may be used if bone involvement or metastasis is suspected [12]. Magnetic Resonance Imaging (MRI) for preoperative assessment can be used in larger or atypical lesions and in recurrent disease [30-32]. Fluorodeoxyglucose (FDG) positron emission tomography scanning is used to monitor metastatic disease [33].

Histologically, DFSP shows a storiform or fascicular proliferation of bland spindle cells that extend from the dermis into the subcutaneous tissues (Figure 2) [34, 35]. Almost all cases of DFSP are CD34-positive (Figure 3) and factor XIIIa- negative [36, 37]. When the diagnosis of DFSP is difficult to make with regular pathologic techniques immunostaining with CD34, factor XIIIa, apolipo-protein D, nestin, and cathepsin K may be useful to differentiate from its benign counterpart (dermatofibroma) [38-40].

The American Joint Committee on Cancer has not developed a TNM staging system for DFSP. Ugurel, S. et al. [30], published a staging system: stage-I - localized disease, stage-II - lymph node metastasis, stage-III - distal metastasis. Our patient had a stage-I disease because it was localized with no clinical or radiographic evidence of regional or distant metastasis.

The treatment of choice for a DFSP is wide local excision [27]. When planning the operative approach the size, the location of the tumor and the cosmetic issues need to be considered for obtaining good oncologic results. Wide radical excision [41] and Mohs micrographic surgery [5,6,42-44] are the most frequently used surgical techniques. Every effort should be made to completely remove the tumor at the time of initial operation taking into account the proclivity that DFSP has for irregular and frequently deep subclinical extensions [45]. Complete pathologic assessment of all the surgical margins is required before any plastic reconstructive surgery is carryout [27]. Extensive undermining or tissue movement should be delayed until negative histologic margins are confirmed to prevent possible tumor seeding with positive margins [27]. In the meantime, the wound could be left open with daily wet to dry dressing changes or a Vacuum Assisted Wound Device (VAC) can be placed as it was done with our patient. An alternative is the use of a split-thickness skin graft if definitive reconstructive plastic surgery is not possible. This will allow the surgical oncologist to monitor for recurrence more easily.

The margins of resection vary in the medical literature between with 2 to 4 cm [41,44,46,47]. In a series of 204 patients with DFSP, Farma J.M., et al. [46], showed a very low local recurrence rate (1%) using wide excision (median 2 cm margin) with a standardized surgical approach, highlighting the importance of a thorough pathologic evaluation of the margins. If the final pathology report shows positive margins, re-resection is recommended whenever possible, with the goal of achieving clear margins.

A substitute to wide local resection is Mohs micrographic surgery which is considered by some as the treatment of choice for DFSP [24,48]. The technique consists of sequential horizontal sectioning (5 to 7  $\mu$ m) and immediate frozen microscopic examination until a tumor-free margin is obtained [8]. The local cure rates with Mohs surgery range from 93% to 100 % [49,50].

Standard chemotherapy is not used in the treatment of DFSP [51]. Imatinib mesylate was approved by the FDA for the treatment of unresectable, recurrent, and/or metastatic DFSP [33]. This targeted therapy is based on the finding of a translocation between chromosomes 17 and 22 [t(17;22)(q22;q13)] resulting in the overexpression of PDGF receptor  $\beta$  [30,52-55]. The recommended oral dose is 800 mg/day [33,56]. Tumors lacking the t(17;22) translocation do not respond to imatinibmesylate [12]. Neoadjuvant imatinib mesylate therapy for DFSP is been studied [57,58]. Imatinib mesylate as a neo-adjuvant therapy in locally advanced or recurrent DFSP may reduce the tumor load, promote tumor cell apoptosis, and therefore may reduce the extent of surgery [58].

When the margins of resection are positive or in circumstances in which adequate wide local excision may result in a major cosmetic or functional deficit Radiation Therapy (RT) may be used [8]. Adjuvant postoperative RT may reduce the risk of recurrence when clear surgical margins are not obtained [8]. The radiation dose used

in patients DFSP ranges from 50 to 70 Gy [12,30,59]. Close follow-up care after radiation therapy is needed because some DFSP tumors become more aggressive [30,59].

The NCCN guidelines recommend due to the high local recurrence rates for DFSP, ongoing follow-up with focus on the primary site every 6 to 12 months, with re-biopsy of any suspicious regions [27] and that is the protocol we are following with our patient. The recurrences usually occur within the first three-years after the surgery [30]. The medium time to the development of a local recurrence is around 32 months [29]. Due to the indolent course of DFSP lifelong surveillance for recurrence is recommended.

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