

Dermatofibrosarcoma Protuberans: One Centre Experience

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Abbreviations:

DFSP - dermatofibrosarcoma

protuberans;

PDGF - platelet derived growth factor;

PDGFRB - platelet derived growth

factor receptor beta;

MMS - Mohs micrographic surgery;

FDA - food and drug administration;

STSG - split-thickness skin graft

RO - microscopically margin-negative

resection;

WLE - wide local excision.

Rezumat

Dermatofibrosarcom protuberans - experiența unui singur centru

Dermatofibrosarcomul protuberans (DFSP) este o tumoră rară a țesuturilor moi, fiind încadrată în categoria neoplasmelor cutanate non-melanocitare. Excizia chirurgicală cu margini largi de siguranță este tratamentul principal, necesitând frecvent metode avansate de reconstrucție pentru închiderea defectului postexcizional. Scopul acestui studiu este de a raporta experiența noastră în gestionarea a șapte pacienți cu dermatofibrosarcom protuberans.

Materiale și Metode: Am efectuat un studiu retrospectiv ce cuprinde 7 pacienți cu diagnostic histopatologic de dermatofibrosarcom protuberans internați în departamentul de chirurgie plastică al Spitalului Clinic de Urgență "Prof. Dr. Agrippa Ionescu", între 12 iulie 2018 și 4 iulie 2022.

Rezultate: Vârsta medie a pacienților a fost de 38.2 ani. Patru dintre pacienți au beneficiat de excizia primară cu margine largă de siguranță, în timp ce 3 pacienți au beneficiat de tratament chirurgical primar în alte centre, prezentându-se pentru re-excizie. Toate cazurile au necesitat metode complexe de reconstrucție, astfel: 3 pacienți au fost tratați prin reconstrucție cu plastie de piele liberă desplicată, un defect post-excizional de dimensiuni superioare a necesitat utilizarea unui lambou local de avansare + plastie de piele liberă desplicată și în alte trei cazuri defectele au fost acoperite folosind lambouri locale. În două cazuri, diagnosticul histopatologic a evidențiat diferențiere fibrosarcomatoasă (cele mai mari dimensiuni ale tumorii primare), într-un caz din acestea fiind identificată și invazia

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fasciei subiacente, iar ambii pacienți au necesitat radioterapie adjuvantă.

Concluzii: În prezența unei tumori cutanate cu aspect clinic sugestiv pentru DFSP, mai ales în cazul unor dimensiuni tumorale crescute, biopsia incizională și abordarea multidisciplinară ulterioară vor conduce către o excizie chirurgicală largă, cu margini histopatologice negative, ca tratament standard, pentru un sarcom de părți moi care rar metastazează.

Cuvinte cheie: dermatofibrosarcom protuberans, excizie, biopsie, diferențiere fibrosarcomatoasă, tumoră Bednar

Abstract

Background: Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue tumor that is classified as a non-melanoma skin cancer. Surgical excision with wide safety margins is the cornerstone treatment and frequently requires advanced reconstruction methods for wound closure. This study aimed to report our experience with the management of seven consecutive patients with dermatofibrosarcoma protuberans.

Materials and Methods: We performed a retrospective study of seven consecutive patients with dermatofibrosarcoma protuberans admitted to our Plastic and Reconstructive Surgery Department of Clinical Emergency Hospital “Prof. Dr. Agrippa Ionescu” Bucharest, Romania, between July 12, 2018, and July 4, 2022.

Results: The mean age of the patients was 38.2 years. In 4 patients, the primary treatment consisted of wide local excision, while 3 presented to our clinic for re-resection. All cases required complex reconstruction methods: 3 patients with a split-thickness skin graft (STSG), 3 patients with local flaps, and in one patient, because of the superior size of the post-excisional defect, we used local advancement flaps and STSG. In two cases, the histopathological diagnosis revealed fibrosarcomatous differentiation (the largest primary tumor dimension), one of which showed fascial invasion, and both of them received adjuvant radiotherapy.

Conclusion: A soft tissue tumor with a clinical appearance suggestive of DFSP, especially in cases of increased tumor sizes, incisional biopsy and subsequent multidisciplinary approach will lead to a wide surgical excision with negative histopathological margins, as a standard treatment, for a low-grade sarcoma, which rarely metastasizes.

Key words: dermatofibrosarcoma protuberans, surgical management, fibrosarcomatous, Bednar tumor, wide local excision

Introduction

Dermatofibrosarcoma protuberans (DFSP) is a rare and uncommon soft tissue tumor with an incidence rate of 0.8 to 4.5 cases per million persons per year and is classified as a non-melanoma skin cancer (1). With its origin in the dermis and slow development, it is a malignant pathology considered an intermediate tumor between dermatofibroma (benign tumor) and fibrosarcoma (malignant tumor). The

malignant characteristic consists of a local invasion of the subcutaneous fat and very rare in the underlying fascia or muscle, with a low likelihood of metastasis (2). The most common sites of metastasis are the lungs and bones, and are very rare in the locoregional lymph nodes (3).

Tumorigenesis is unclear, but a translocation involving chromosomes 17 and 22 was found, leading to a fusion protein causing continuous activation of the receptor PDGF receptor beta

(PDGFRB) tyrosine kinase, promoting cell growth (4). This mechanism justifies the use of tyrosine kinase inhibitors in the treatment of advanced DFSP (5).

The clinical presentation may initially appear as bruises or scars. It has also been reported the predominant location on areas of the skin with injury history, even tattoos, and preexisting scars (6). With local evolution, it may have the characteristics of a painless plaque and/or nodule (protuberans) on the trunk of young adults, with decreased mobility due to infiltration of the surrounding tissue (7). Bednar tumor are pigmented variants of DFSP and accounts for less than 5% of all DFSP cases (8). A more aggressive form that needs careful attention because of the higher recurrence and metastatic rates is fibrosarcomatous dermatofibrosarcoma (9).

The diagnosis should be made via incisional or excisional skin biopsy (10). Differential diagnosis includes cutaneous melanoma, dermatofibroma, dermatologic manifestations of metastatic carcinomas, keloid and hypertrophic scars, and morphea (11-13). Given the fact that it is a poorly circumscribed tumor, Mohs micrographic surgery (MMS) is a surgical technique that ensures complete histopathologic margin control with lower recurrence rates. However, wide local excision with 2-5 cm margins is the most commonly used treatment option (14). Regional lymph node dissection is not recommended given the lower lymphatic metastatic rates.

For recurrent, unresectable, and metastatic DFSP, an oral tyrosine kinase inhibitor, imatinib mesylate, was approved by the FDA, with 65% response rates and a duration of 6 months; however, this may be extended if needed (15). Radiation therapy may represent another option for unresectable and metastatic DFSP, or it can be used for local control after surgery (16).

This study aimed to report our experience with the management of seven consecutive patients with dermatofibrosarcoma protuberans.

Material and Method

The current article presents a retrospective series of seven cases treated in our clinic, at the Clinical Emergency Hospital "Prof. Dr. Agrippa Ionescu", from July 12, 2018, to July 4, 2022. We analyzed the age, sex, location of the primary tumor, primary or secondary intervention, tumor dimensions, oncological safety margins used, reconstruction methods of the post-excisional defect, presence or absence of metastasis, post-interventional complications, histopathological characteristics, and need for adjuvant therapy. Local ethical agreement and informed consent were obtained from all patients. The number of documents from the Ethical Commission of Clinical Emergency Hospital "Prof. Dr. Agrippa Ionescu" was 1736615, 05.08.2014.

Results

Of the seven patients analyzed, four were male and three were female, with a mean age of 38.2 years.

Four patients underwent primary excision at our clinic. Two patients benefited from primary intralesional excision in other surgical centers; the histopathological result led to the recommendation of wide local re-resection, and one patient presented with clinical suspicion of recurrence 5 years after the first resection performed in another center.

The primary locations were on the trunk in five cases (3, anterior thorax; 1, lower abdomen; 1, right lumbar area). One patient had a tumor in the upper right arm and the last in the antero-lateral part of the left calf.

The initial size of the tumor was in the range – 3-5 cm in 5 cases and > 5 cm in the other two.

Patients treated in our department were discussed on the tumor board before the surgical plan. Five patients benefited from wide local excision with a 3 cm margin, while for the other two, we opted for a 2 cm margin. All surgeries were performed under general anesthesia. Preoperative MRI was performed in all cases to determine the depth of invasion

and area of extension for better design of the surgical plan. Our surgical approach regarding the extent of the excision was determined by considering the guidelines for DFSP – wide local excision for oncologic margin safety and the optimal reconstruction methods to ensure the functionality of the implied anatomical region. The depth of excision was subfascial for all patients, including deep re-excisions whenever the tumor was in proximity to the underlying fascia or invading the fascia.

Immediate reconstruction was performed after WLE in all cases requiring complex methods: 3 patients with split-thickness skin graft (STSG) and 1 patient with advancement pectoral flap and STSG (*Fig. 1*), and three with local flaps—one patient with a rotational flap (*Fig. 2*), and the other two with transposition flaps.

Post-interventional complications were detected in two out of four flap procedures, represented by 5×5 cm wound dehiscence after lower abdominal defect coverage with rotational flap, suture granuloma, and cellulite when the combination of pectoral advancement + STSG was used. The three skin-grafted cases did not present post-interventional complications.

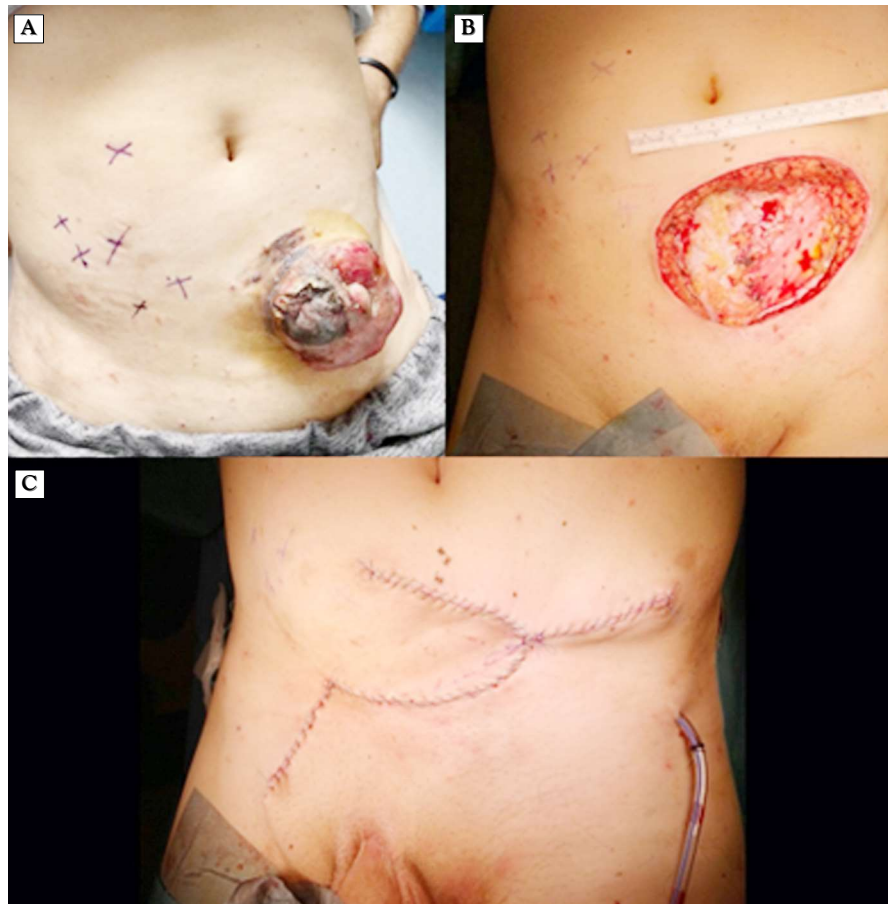
In two cases, the histopathological diagnosis revealed fibrosarcomatous differentiation (the largest primary tumor dimensions), one of which showed fascial invasion. Three of seven patients had deep fascial invasion. All patients treated in our facility had R0 excisions, and 3 cases presented the nearest edge of the tumor at < 1 cm, which was always the deep edge.

Adjuvant radiation therapy was indicated in 3 cases, which presented with deep fascial invasion after deep margin assessment, of



Figure 1. Dermatofibrosarcoma Protuberans; (A) Macroscopic appearance of an erythematous plaque with nodules “Protuberans”; (B) post-excisional defect after 3 cm macroscopic safety margins resection; (C) Final appearance after reconstruction with advancement flaps and split-thickness skin graft.

Figure 2. Fibrosarcomatous dermatofibrosarcoma on lower abdomen;
(A) "X" - perforators detected via hand held Doppler for rotational flap design;
(B) postexcisional defect after 2 cm macroscopic safety margins resection;
(C) Final appearance on the surgical table.



which two had fibrosarcomatous differentiation. The latter was treated with 60 Gy / 30 fractions and the other with 50 Gy / 25 fractions. Radiation therapy was delivered within a month of surgery.

Discussions

The average age of the studied patients was in accordance with the literature and near the upper limit of the interval, as stipulated in the largest retrospective study conducted on DFSP, in which the highest incidence was in the age group 20-39 years (42%). Our results regarding sex predominance were consistent with those in the literature, with a slight male predominance (17).

A tumor with a macroscopic appearance suggestive of DFSP should be treated using a multistep approach and a multidisciplinary team to lower the intralesional excision rate.

The initial approach should be a biopsy of the lesion in order to have a correct diagnosis, leading to the selection of adequate treatment (18). Surgery is the cornerstone treatment for DFSP, including MMS or WLE. Preoperative MRI imaging is mandatory to evaluate the extent (peripheral and deep tissue involvement) (19).

The location of the primary tumors is also consistent with the literature, where most of them (41.7%) were described on the trunk, followed by the upper and lower limbs (17).

Patients with histopathological fibrosarcomatous differentiation of DFSP, a much more aggressive and faster-growing form, had the largest tumor size (> 5 cm). This histological subtype is also associated with higher rates of local recurrence, requiring larger excisional margins with minimal undermining of the surrounding tissue. The latest guidelines recommend delayed reconstruction until

negative histologic margins are confirmed, and do not recommend the use of flaps in this subtype (20).

DFSP has a high rate of local recurrence (up to 25%), and the main negative prognostic factors are age > 50 years, fibrosarcomatous variant, high mitotic rates, increased cellularity, and the number of previous recurrences (20).

The wider the excisional margin, the lower is the probability that the tumor will relapse, which is the main predisposing factor for recurrence (21). Wider margins decrease the risk of recurrence, but also unnecessarily remove healthy tissue, increasing the risk of complications affecting functional and cosmetic results (22). We encountered these aspects in our patients, all of whom required complex reconstruction methods (STSG and local flaps). The patient with the largest tumor dimensions benefited from excision with a margin of 2 cm and coverage of the post-excision defect using a local rotation flap, thus respecting the principles of functionality and aesthetics, without neglecting oncological safety (*Fig. 2*). This patient presented with a 5x5 cm wound dehiscence that required longer local wound management, with a good final outcome.

No patient presented preoperatively with locoregional or systemic metastasis, supporting the low dissemination rates specified in the literature (23). Follow-up at 1 one year revealed no secondary lesions. Further follow-up time frames could not be included in this study due to the lack of patient's compliance.

The use of 2-5 cm safety margins proved to be suitable to ensure an R0 wide lateral excision in all cases, but it was observed that the edges closest to the tumor were deep (<1 cm), a fact also found in the literature, emphasizing the need to perform a wide excision, including the underlying tissues and deep fascia (24).

Dermal finger-like extensions are those that accompany an increased risk of recurrence and dictate the need for wide resection (24). In the case of intralesional resections,

recurrences, unresectable tumors, or selected cases with more aggressive subtypes, patients may require complementary treatments (radiotherapy and imatinib) (16). 3 patients in our group received adjuvant RT (25).

The limitations of this study are represented by the small group of patients in line with the reduced incidence and retrospective nature of the analysis, but it opens the way for further research.

Conclusions

Dermatofibrosarcoma protuberans is a low-grade sarcoma that rarely metastasizes to other organs. A multidisciplinary approach is recommended to coordinate treatment given the high recurrence rates. The Mohs technique or wide excision, including the underlying fascia, is the initial treatment. For positive margins or recurrences, re-resection is recommended whenever possible to achieve oncological clearance. Patients with metastatic, unresectable, or recurrent DFSP, when additional resection leads to unacceptable functional or cosmetic outcomes, are candidates for imatinib mesylate or radiation therapy.

Conflicts of Interests

The authors have declared that no competing interests exist.

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