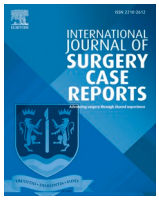
International Journal of Surgery Case Reports 96 (2022) 107325

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr



Case report

Dermatofibrosarcoma protuberans of the hallux: A case report with review of the literature

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ARTICLE INFO

Keywords:
Dermatofibrosarcoma protuberans
Darier–Ferrand dermatofibrosarcoma
Toes
Acral

ABSTRACT

Introduction and importance: Darier-Ferrand dermatofibrosarcoma (DFS) is a rare mesenchymal tumor with an aggressive local behavior, high local recurrence frequency and low metastatic potential. It commonly presents as a raised slowly growing mass. It usually occurs on trunk and proximal extremities but rarely touches distal extremities such as hands, fingers, or foot below knees.

Case presentation: A 15-year-old girl presents with a protuberant painful mass of the right hallux of 2 years. After surgical excision, histological examination revealed a spindle shaped cells with a strong CD34 expression and the diagnosis of Darier-Ferrand dermatofibrosarcoma of the toe was confirmed.

We proceeded to a review of the literature of Dermatofibrosarcoma on the toes with the aim to reveal, its clinical presentations, histopathology, and treatment options.

Clinical discussion: DFS represents 0.1 % of all cancers. It is a low-grade sarcoma with a locally aggressive behavior and a low metastatic potential. Only 11 cases of DFS of the toes have been reported in the literature. It usually occurs in the trunk, and proximal extremities. Histological and immunohistochemical examination are mandatory to confirm the diagnosis with diffuse expression of CD34 by the tumoral cells. Surgery is the standard treatment for localized and resectable lesions.

Conclusion: Darier-Ferrand Dermatofibrosarcoma is an uncommon and recurrent dreadful tumor, that rarely occurs on toes, but should be considered in front of persistent slowly growing foot lesions.

1. Introduction

Darier-Ferrand dermatofibrosarcoma or dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous fibrous tumor with a local aggressive behavior and low metastatic potential. It represents 0.1 % of all cancers and 1.8 % of all soft tissue's sarcomas [1]. The most frequent tumor location is the trunk and the extremities proximally situated but rarely on acral sites and especially on toes [2].

Our review of the literature found 11 cases of DFSP on toes and herein we are reporting a 12th case of a Darier-Ferrand dermatofibrosarcoma of the right Hallux [3]. This case report has been reported in line with the SCARE Criteria [4].

2. Case presentation

We present the case of a 15-year-old Tunisian girl, with no medical history nor allergies, who was sent by her rheumatologist for a protuberant mass of the dorsal side of the right hallux. The mass was evolving for the past 2 years and while it became painful and growing rapidly, the patient decided to seek medical attention without taking any medication so far. No other systemic or local symptoms were reported. Physical examination revealed a 2 cm firm, tender, mass of the dorsal sulcus of the right hallux. There was no sign of ulceration or bleeding. No adenopathy was found. The lesion was fixed to overlying skin but movable over the deeper tissues.

Standard radiographs showed a soft tissue mass with no bony involvement neither erosion nor fracture.

An ultrasound scan was performed and revealed a suspect heterogeneous mass of the right hallux that could refer to a malignant lesion. No distant metastasis was found. After a multidisciplinary reunion, the patient underwent a wide local excision of the mass. The intervention was performed by a senior orthopedic surgeon in an orthopedic surgery department of a university hospital in Tunisia. The surgical site was primarily closed, and good approximation was achieved. Gross pathological examination showed a whitish encapsulated mass of 1.3 × 1.2 × 1 cm. Histopathological examination revealed a malignant

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https://doi.org/10.1016/j.ijscr.2022.107325
Received 13 March 2022; Received in revised form 14 June 2022; Accepted 15 June 2022
Available online 22 June 2022

mesenchymal proliferation, made of spindle cells with little atypia and low mitotic activity arranged in storiform fascicles. No tumoral necrosis was seen. Immunohistochemistry showed a strong expression of CD34. Thus, the anatomopathological examination concluded to a dermatofibrosarcoma with tumor free margins. This way no adjuvant treatment has been recommended. The patient was seen at 4 days and 2 weeks postoperatively, and had recovered well at that point without any significant complications. We are now at 4 years of clinical follow up with no local recurrence nor distant metastasis. The patient is able to walk and do all her usual activities with no pain nor discomfort (Figs. 1-5).

3. Discussion

Dermatofibrosarcoma protuberans (DFSP) was first described by Taylor in 1890, then by Darier and Ferrand in 1924, named progressive and recurring dermatofibroma or fibrosarcoma of the skin, and then by Hoffmann in 1925 named dermatofibrosarcoma protuberans [5]. DFSP is a rare mesenchymal tumor which has been clarified by WHO as a low-grade sarcoma as it is locally aggressive and has a low metastatic potential [6]. It represents 1.8 % of all the soft tissue's sarcomas and only 0.1 % of all cancers [1].The incidence is higher in women and in black population [7,8]. It occurs most commonly in patients aged between 20 and 50 years [1,9,10]. The most usual anatomical tumor locations are trunk and proximal extremities especially inferior extremities but rarely below the knees [5,11,12]. Dermatofibrosarcoma protuberans on the toes is extremely rare, our literature review showed only 11 cases reported [2,3,9,13–16]. The mean age was 45.6 years, with a predominance in men. The clinicopathological features of the found cases are gathered in Table I, other reports of dermatofibrosarcoma protuberans of the toes without enough details were excluded from analysis.

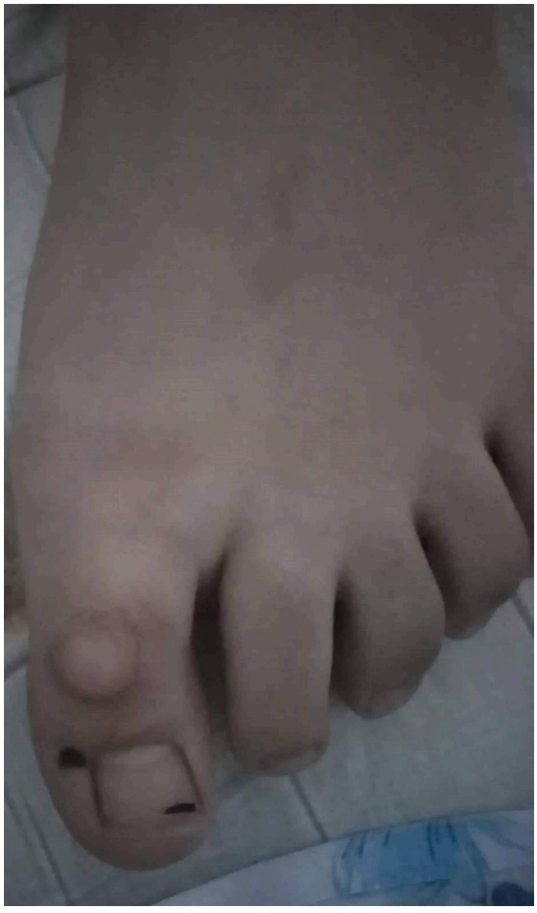

Fig. 1. Clinical photo.

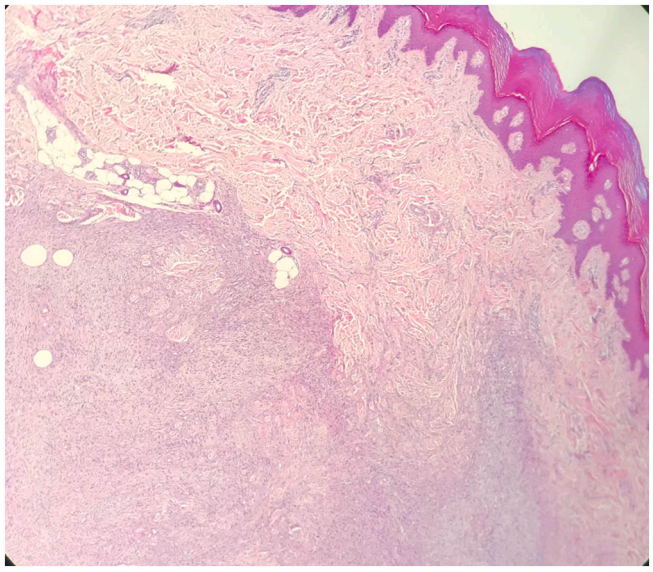

Fig. 2. HEX 40 mesenchymal proliferation occupying the deep dermis and hypodermis.

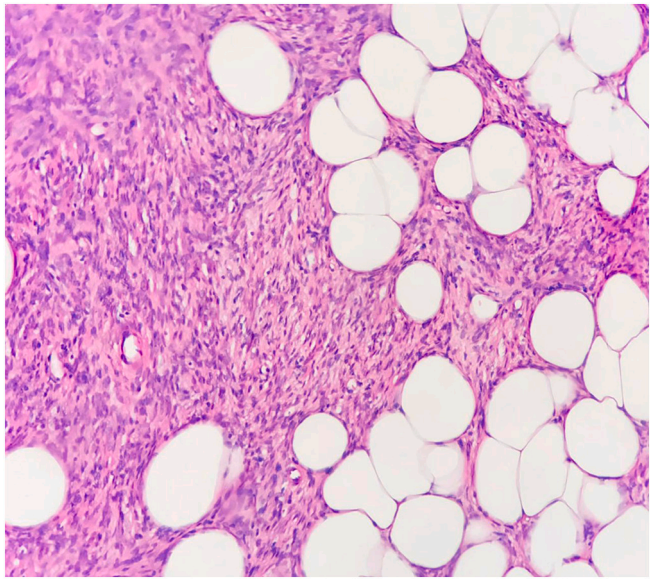

Fig. 3. HEX 200 infiltration of subcutaneous adipose tissue.

Dermatofibrosarcoma protuberans, while an uncommon malignancy in adults, is even less common in the pediatric population [17]. Although childhood DFSP has been reported in the literature, its prevalence in this age group is low with an estimated incidence thought to be one per million in patients less than 20 years old [18,19]. There is a variant of congenital DFSP; an even rarer entity; which often goes unnoticed and is diagnosed months or years after birth [20]. The usual sites of occurrence of skin lesions in children are similar to those found in adults; with the majority affecting the trunk and proximal extremities [18,21,22]. Clinically, this kind of tumor begins as a single brownish or purplish plaque-like area of cutaneous thickening, or as a small, raised, nipple-like projection usually asymptomatic. The development to a noticeable lesion or multinodular mass usually takes several years, initially slow or stationary for a considerable period before a more rapid evolution ensued [23]. The primary lesion may be taken by patients as benign lesion such as keloid or scars. Its evolution is progressive and extensive, and it is refractory to usual local symptomatic treatment, the

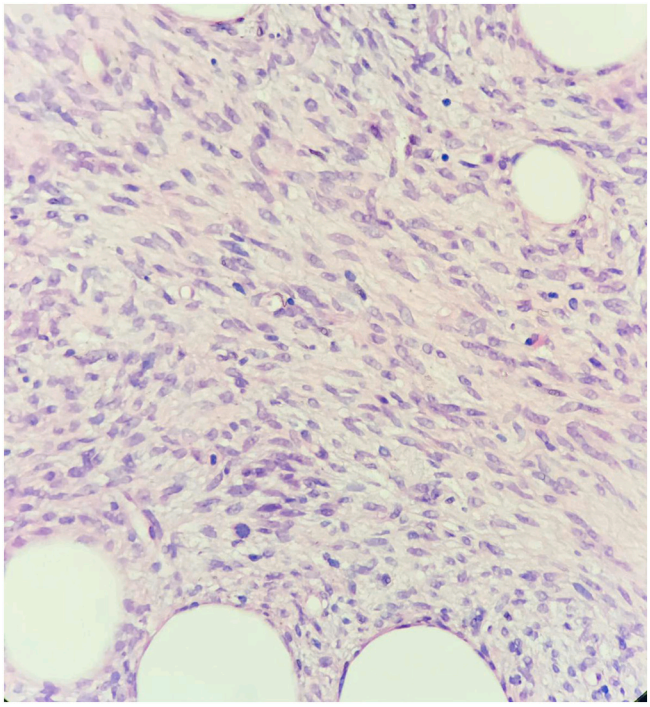

Fig. 4. HEX 400 At high magnification: the tumor cells are spindle-shaped with a fibroblastic appearance and discrete anisokaryosis, arranged in short intersecting bundles.

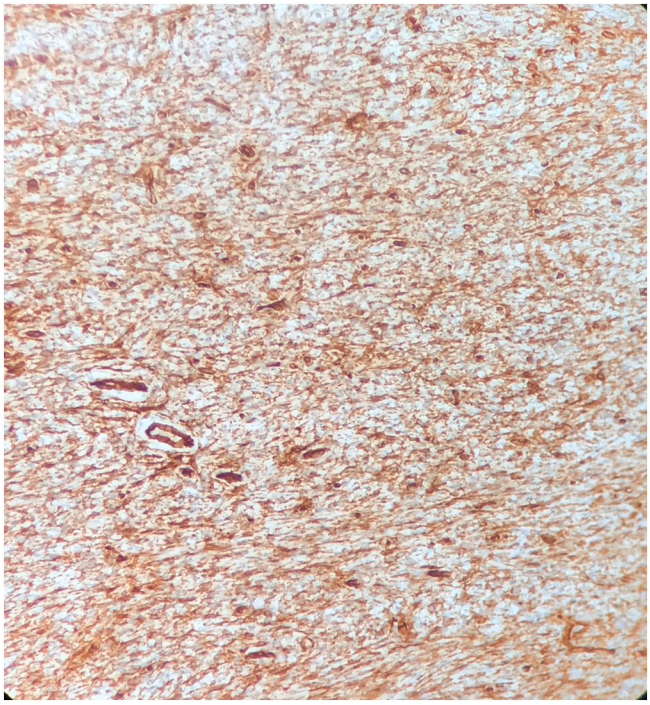

Fig. 5. HEX 200 CD34 immunoexpression: cytoplasmic (vascular control).

change in the appearance of the tumor or of the symptoms such as ulceration with infection or bleeding prompts the patients to seek medical attention [23,24]. There are no known predisposition conditions to develop a DFSP, but there may be a history of a trauma. DFSP has also reportedly arisen in old burn wounds, surgical scars, and sites of multiple immunizations [8,25]. Histologically, DFSP in an acral location exhibits similar features as DFSP in other sites: monomorphous spindle shaped cells in a storiform or tight cartwheel pattern with little atypia and low mitotic activity. The neoplastic cells often infiltrate the surrounding adipose tissue in a honeycomb pattern [1,11,25]. Immunohistochemically, DFSP show diffuse and strong expression of CD34 but negative expression for other biomarkers such as protein S100, Factor XIIIa, alpha smooth muscle actin and melanA [26,27]. Beyond this classical form (representing 90 % of cases), many morphological variants have been described including: myxoid, myofibroblastic, pigmented (Bednar's tumor) or fibrosarcomatous variants [19,28]. The latter of which is characterized by a high cellularity and nuclear grade and an elevated mitotic activity which makes it associated with worse prognosis [29]. Cytogenetic and molecular studies showed that approximately 90 % of DFSPs expressed chromosomal translocation t (17;22) (q22;q13), leading to the fusion of collagen type 1-alpha 1 (*COL1A1* at 17q22) and platelet-derived growth factor beta (*PDGFB* at 22q13) genes. The product of this fusion causes dysregulation of PDGFB with subsequent activation of PDGF receptor β protein tyrosine kinase, resulting in tumorigenesis. This gene alteration can be demonstrated by FISH (fluorescence in situ hybridization) targeting the PDGFB gene, revealing a rearrangement/amplification [23,30]. This fusion gene was expressed in 86 % of the cases in the Krewer et al. study [31]. Dermatofibrosarcoma's Imaging characteristics are variable, and no specific ones were reported. Radiographs may show an infiltration of the subcutaneous tissue, fascia, muscles, and even bone, on ultrasound scan DFS is mostly hypoechoic or mixed hyperechoic, with well-defined or irregular margins. Vascularity of DFS, which is a marker of malignancy, varies as well [26,32]. The most common differential diagnosis of DFS, are neurofibroma, dermofibroma, haemangioma (in children), giant-cell fibroblastoma, pilomatrixoma and malignant melanoma [17,21,28]. Histologically the tumor cells often extend several centimeters beyond the obvious clinical margins the latter of which are usually underestimated, that's why the reference treatment of DFS is wide local excision (WLE), with safety margins ranging from 3 to 5 cm [33,34]. The excision should go beyond the limits of the neoplasm and attain the macroscopic healthy tissues which was achieved with our patient. The risk of local recurrency is related to the quality of the excision and the status of the margins. Re-excision is recommended if surgical margin is positive. Mohs Micrographic Surgery (MMS) is an alternative to wide local excision that is considered by some surgery teams as the preferred treatment for DFS especially for the tumors located in delicate areas such as head and neck or toes to avoid an amputation [24]. It consists in removing a thin margin of tissue circumferentially around and deep to the clinical tumor that is immediately examined under a microscope. The process is repeated until the tumor has negative histologic margins. Thus the MMS offers precise microscopic control of the entire tumor margin while maximizing the conservation of healthy tissue [34,35]. Distant metastases are seen in about in 6% of patients often with multiple failed attempts at local surgery [5]. All the patients whose cases were reported in our literature review underwent wide local excision and 7 of them had clear margins, only 4 of them had positive margins and developed a local recurrency within 15 to 300 months [3,13–16]. As for adjuvant treatment, Imatinib mesylate, an inhibitor of protein tyrosine kinase, has been approved for adults in unresectable, recurrent and/or metastatic DFS that shows the t(17, 22) (q22,q13) translocation [30,33]. If this translocation is absent in the tumor, it is unresponsive to imatinib treatment. Also in these cases (recurrent/unresectable or metastatic tumor) radiotherapy can be combined to surgery, this combination was reported to reduce local recurrence by ≃5% [36,37].

4. Conclusion

Darier-Ferrand dermatofibrosarcoma in an uncommon recurrent tumor, that could stay longtime unknown by the patients for its very slowly growth period. The most important clinical aspect is that typical lesions of DFS may occur in sites other than the trunk and proximal extremities. So that, location per se should not influence the diagnosis of

Table I
Clinicopathological features of the reported cases diagnosed with DFSP of the toes.

Authors	Gender	Age (years)	Site	Size (mm)	CD34	Treatment	Margin status	Recurrence (months)
Kraemer and Fremling [13]	M	37	Right second toe	25	+	Amputation of the right second toe	Negative	No recurrence (120)
Assassa et al. [14]	F	28	Right dorsal toes	80	+	CT followed by WLE	N/A	N/A
Behfar et al. [15]	M	91	Left hallux	35	+	Distal Syme's amputation	The tumor was noted to invade the deep soft tissue and distal phalanx	N/A
Leblanc et al. [9]	M	41	Left hallux	35	+	Excisional biopsy followed by an amputation of the left hallux	Positive on biopsy and negative on amputation	Lost to follow - up
Shah et al. [16]	F	72	Dorsal toes	N/A	+	Primary excision and amputation	Unknown on excision negative on amputation	Yes (300)
	M	45	Dorsal toes	N/A	+	Biopsy	Positive	Lost to follow-up
	M	64	Toe	N/A	+	WLE	Negative	No recurrence
	F	21	Dorsal toes	N/A	+	Primary excision and amputation	Positive on excision negative on amputation	Yes (9)
	M	57	Toe	N/A	+	Biopsy and amputation	Positive on biopsy negative on amputation	No
	M	38	Dorsal toes	N/A	+	Biopsy and amputation	Positive on biopsy negative on amputation	No
Madden et al. [3]	M	39	Right hallux	35	+	Excisional biopsy	Tumor cells in peripheral and bottom margins	Lost to follow-up
Study case	F	15	Right hallux	20	+	WLE	Negative	No (48)

M: male, F: female, N/A: not available, WLE: wide local excision, CT: chemotherapy.

lesions occurring on unusual anatomical sites.

Patient consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Sources of funding

None.

Ethical approval

N/A.

Author contribution

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Research registration number

Not applicable.

Guarantor

Rafik Elafram, MD.

Declaration of competing interest

None.

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