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Case Presentation
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Dermatofibrosarcoma Protuberans: Trauma and Genetics

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Abstract

Dermatofibrosarcoma protuberans (DFSP) is a rare dermal sarcoma which can be misdiagnosed by non-specialists as a keloid, hypertrophic scar, sebaceous cyst or lipoma. It has high local recurrence rates but only metastasizes in 2% to 4% of cases. DFSP presents a challenge for the surgeon, as its delayed diagnosis allows more extensive radial and vertical growth than can be clinically appreciated. Extensive spread in the dermis results in a much larger defect requiring specialized reconstruction. DFSP has been linked with genetic deregulation; however, the literature repeatedly suggests an association with trauma, especially in young patients. We use one of our patients to illustrate a case of dermatofibrosarcoma protuberans of the right hip in a 24-year-old male with a history trauma to the same area 5 years prior to presentation. A thorough literature review is presented with diagnostic and treatment recommendations.

Keywords: Dermatofibrosarcoma protuberans; Lower extremity and trunk sarcoma; History of trauma

Introduction

Dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous sarcoma that exhibits slow progression and spread. Delayed diagnosis often allows for tumor growth radially and vertically, making histological clearance more difficult to achieve. Metastasis occurs in 2% to 4% of the cases; however, local control is often the greatest challenge. Due to lack of pathognomonic clinical findings, DFSP can be mistaken for a keloid, hypertrophic scar, sebaceous cyst or lipoma and is often referred late for specialized evaluation. The delay in diagnosis and insidious proliferation in the dermis allows for tumor growth that is more extensive than clinically appreciated, often leading to large defects requiring specialized reconstruction. Earlier diagnosis is crucial to minimize morbidity. A number of risk factors have been associated with this tumor including accidental and surgical trauma [1-5]. A complete history and physical should be obtained on the initial evaluation. A history of prior trauma associated with an ill-defined cutaneous lesion warrants consideration of DFSP in the differential diagnosis.

A case of DFSP on a patient that had a history of trauma to the same area 5 years prior to presentation prompted us to re-evaluate whether this repeatedly described association of DFSP with trauma is warranted.

Case Presentation

A 24-year-old African American male presented to our dermatology clinic for evaluation of a 'keloid' on the right hip. His pertinent history includes a motorcycle accident at the age of 19 which included skin and soft tissue trauma to the right hip that required surgical removal of debris from the wound. The foreign bodies consisted of cement and gravel. The wound healed by secondary intention with no complications, however, 5 years later, he developed a rapidly growing lesion in the area of the scar.

On exam, the mass was firm, multinodular, erythematous, hyperpigmented, measuring 10 cm × 7 cm (Figure 1). The mass was mildly tender to palpation and demonstrated irregular borders, surrounding skin induration, and a central area of ulceration. The remaining physical exam, including inguinal lymph nodes, was unremarkable. The patient was otherwise healthy with a non-contributory family and social history.

Trauma is a known risk factor in the pathogenesis of keloids and hypertrophic scars. However,

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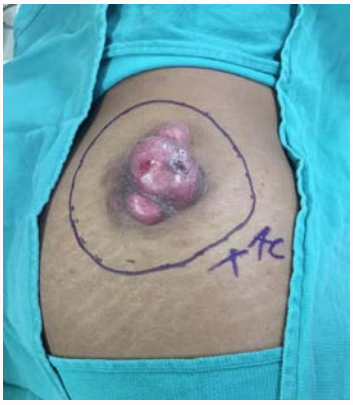

Figure 1: Preoperative image of the tumor with 3 cm margins marked.

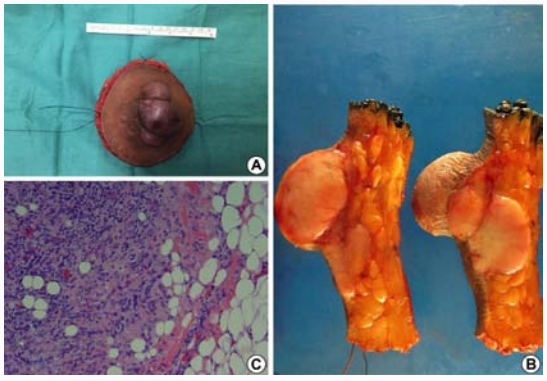

Figure 2: Intraoperative image of the tumor after WLE with defect measuring 16 cm × 10 cm. Nodular appearance of the lesion (A) and the cut surface (B) with infiltrating growth at the periphery (C).

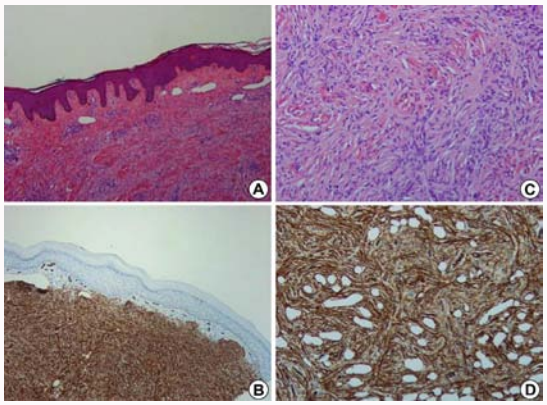

Figure 3: Microscopic analysis shows spindle cell lesion in dermis with focal storiform pattern with monotonous morphology (A). The spindle cells are immunohistochemically positive for CD34 (B), and negative for S100, desmin, CD31 and SMA (not shown). Spindle cells infiltrate the dermal collagen (C) with entrapped fat cells highlighted by CD34 immunohistochemical stain (D).

the rapid growth and irregular contour of the lesion were suspicious for a neoplastic process of soft tissue or vascular origin. Core needle biopsy revealed dermatofibrosarcoma protuberans.

The patient underwent surgical excision with 3 cm margins. The final wound measured 16 cm × 10 cm (Figure 2). The defect was temporarily closed with xenograft, while awaiting final pathology results. Microscopic analysis of specimen showed spindle cell lesion in dermis with focal storiform pattern with monotonous morphology

Figure 4: Intraoperative picture after reconstruction of the defect with a propeller myocutaneous TFL flap and primary closure of the donor site.

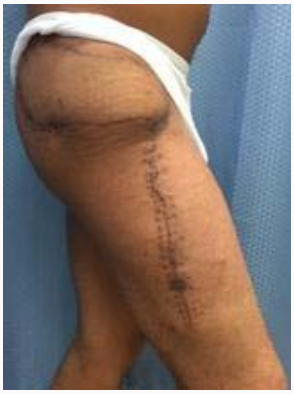

Figure 5: Postoperative image 3 months after excision and reconstruction with no signs of recurrence.

(Figure 3). The lesion had nodular appearance with infiltrating growth at the periphery. The spindle cells were immunohistochemically positive for CD34 and negative for S100, desmin, CD31 and SMA. After clear margins were confirmed, a pedicled tensor fascia lata (TFL) myocutaneous flap was performed for reconstruction (Figure 4). The postoperative course was uncomplicated with excellent functional results and no signs of reoccurrence at 12 months of follow-up (Figure 5).

Discussion

DFSP is a rare monoclonal sarcoma that typically arises from the skin and specifically the dermal layers, but extends to the deeper tissues as it grows. It initially spreads radially and usually exhibits a vertical growth pattern only at later stages [1]. Two types of DFSP have been described in the literature. 85% of all tumors exhibit a more indolent course and have low metastatic potential, representing the classical dermatofibrosarcoma protuberans (DFSP). The remaining 15% can present with a more aggressive behavior, thus described as fibrosarcomatous “high-grade” type (FS-DFSP) [6].

DFSP has been linked to a genetic mutation, a product of the rearrangement of chromosomes 17 and 22. This mutation causes the gene for collagen Type Ia1 (COL1A1) to fuse with the gene coding for the platelet-derived growth factor subunit B (PDGFB). This genetic disorder deregulates the expression of the PDGF-chain, leading to continuous activation of the PDGF receptor (PDGFR) protein tyrosine kinase, which eventually allows for proliferation

of DFSP cells [7-9]. This is a somatic mutation, which means that it is acquired and non-inherited. It is unclear which environmental factors may increase the risk for this genetic deregulation. Identifying the tumorigenesis of DFSP has led to development of potential future medical treatments for patients who may avoid surgery and may help control or treat metastatic spread [10].

DFSP usually presents as pink or violet-red plaques, often with surrounding telangiectasias [11]. Due to the superficial location of DFSP, pain does not present until later in the course when the tumor invades deeper tissue. This tumor is often mistaken for a keloid scar because of its slow growing course and clinical picture. The median age of presentation is 38.5 years old with roughly equal distribution between males and females [5].

DFSP has been reported to arise in areas with history of prior trauma, including tattoos, vaccination sites, burn scars, surgical scars and radiation treatment [1-5]. The exact mechanism in which trauma may predispose for development of DFSP is unknown, but it seems intuitive that chronic inflammation and stimulation of the immune system at a local level may trigger the immunopathologic changes that could lead to the malignant transformation of dermal cells. In the case we presented, the patient had an open, contaminated wound with dermal debris that healed by secondary intention, causing significant prolonged inflammatory and immune response in the area. Additionally, our patient presented 10 years prior to the median onset of DFSP as recorded in the literature, suggesting that early onset may be seen with a "trigger", such as trauma, causing continuous low grade infection and inflammation.

A similar mechanism has been described in the pathogenesis of Marjolin ulcers after trauma or skin injury [12,13]. Literature highlights the presence of 2 distinct types: acute Marjolin ulcers that develop within 12 months after injury, and chronic Marjolin ulcers that develop later. We suggest that similarly, trauma and dermal debris causing chronic low grade infection and inflammation, may trigger the molecular changes that lead to development of DFSP.

Current literature proposes treatment with wide local excision (WLE) or Mohs microscopic surgery (MMS). One to three centimeters margins of excision have been presented by different surgeons; however, there is no consensus in the literature. Monnier et al. [2] conducted a retrospective review of patients with DFSP and investigated the margins of excision. A total of 66 patients were included in the studies that were followed up for a mean of 9.6 years. The rates of recurrence were significantly different, depending on the extent of margins. Patients with surgical margins less than 3 cm had a local recurrence rate of 47%, compared to patients with margins from 3 cm to 5 cm, which demonstrated a recurrence rate of 7%. Khatri et al. [14] reported a 0% reoccurrence rate in 24 patients that were treated with surgical excision and margins of 2.5 cm to 3.3 cm.

Radiation therapy (RT) has been shown to be an effective adjuvant treatment along with WLE. Sun et al. [15] performed a retrospective review of the recurrence rates of patients that had surgical excision only and patients that underwent surgical excision with additional adjuvant RT. The margins of surgical excision were 1.5 cm in this study. They demonstrated that patients treated with surgery alone with close margins, had a 66% chance of local recurrence, compared to 33% in patients with negative margins. When RT was performed in conjunction with surgery, recurrence rates decreased significantly to 16.6% in patients with close margins and to 0% in patients with negative margins [15]. Chen et al. [16] reported recurrence rates of 14.23% in patients treated with surgery combined with adjuvant RT that had positive or close margins, compared to 0% in patients that received the same treatment but had negative margins. The above studies also highlight the importance of negative surgical margins in the treatment of this tumor.

The prognosis of DFSP after adequate excision with clear margins is generally good. Kreicher et al. [5] collected data from 18 registries from 2000 to 2010 and concluded that the ten-year survival rate of DFSP was 99.1%. Furthermore, it was found that older, male and black patients, with tumors located on the limbs and head, had an overall higher mortality rate [5]. In a different study, Liang et al. [17] found a 0.8% mortality rate in 1,422 patients with DFSP.

Conclusion

The plastic surgeon should be aware of this rare entity given the often indolent course and diagnostic uncertainty. While there is no clear evidence of association with trauma, similar to the pathogenesis of Marjolin ulcers, we suggest that dermal injury and chronic low grade infection and inflammation may be a trigger for development of early onset DFSP. We recommend including DFSP in the differential diagnosis of soft tissue mass with a history of previous local trauma. Once a biopsy confirms the diagnosis, excision with 3 cm margins achieves acceptable local recurrence rates and usually mandates plastic surgery reconstruction, given the size of the resultant defect. Radiotherapy can be a useful adjunct to surgical treatment and should be considered in select patients with aggressive pathology, close margins or recurrent disease.

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