Advances in Management of Dermatofibrosarcoma Protuberans

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KEYWORDS

• Dermatofibrosarcoma protuberans • Skin sarcoma
• Mohs micrographic surgery • Wide local excision
• Complete circumferential peripheral and deep margin assessment • Platelet-derived growth factor
• Targeted therapy

Dermatofibrosarcoma protuberans (DFSP) is an uncommon, low-grade soft tissue neoplasm accounting for less than approximately 0.1% of all cancers and 1% of all soft tissue sarcomas. The overall annual incidence of DFSP is 4.2 per million of all cancers as reported in the Surveillance, Epidemiology, and End Results (SEER) cancer registries. The incidence rate is higher among blacks compared with other groups (6.5 cases per million population), but the incidence among whites has been slowly increasing over the past 30 years, in part due to improved diagnostic immunohistochemical techniques. DFSP develops at approximately equal rates between women and men except in older individuals (>70 years), in whom men have a higher incidence.[1,2]

CLINICAL PRESENTATION

DFSP growth is characteristically indolent. These tumors enlarge gradually over a period of years, but may present with extensive subclinical invasion into underlying subcutaneous tissue, fascia, muscle, or even bone. The broadly infiltrative nature of DFSP contributes to its high rate of local recurrence following treatment with standard surgical excision.

Although DFSP can occur congenitally or in childhood, it most commonly presents in adults between the ages of 30 and 50.[2] Fewer than 10% of DFSPs are diagnosed before the age of 20, and the incidence of this tumor in childhood may in fact be underestimated, since the diagnosis is often delayed. Congenital DFSP can have a variable presentation and may be challenging to definitively remove if the diagnosis is not made early or if scarring from incomplete excision is present.[3]

DFSP classically appears as a violaceous or erythematous nodular plaque (**Fig. 1**) but can also feature skin-colored, erythematous, brown-tinged, or yellow-tinged areas within patches, nodules, or plaques. Areas of induration, telangiectasia, or atrophy may be evident at presentation or may appear over time. Its clinical appearance can vary from indistinct small plaques to large, exophytic tumors that can bleed or ulcerate. Early lesions tend to be asymptomatic but can become painful over months to years due to deeper tissue invasion or accelerated growth.[4] Development of DFSP or acceleration of its growth has been associated with trauma and scars, including sites of vaccination, as well as pregnancy.[5–7] While predominantly located on the trunk (42%) and extremities (34%),[8–10] DFSP may also occur on the head and neck, and in these locations it is associated with a greater risk of morbidity and local recurrence.

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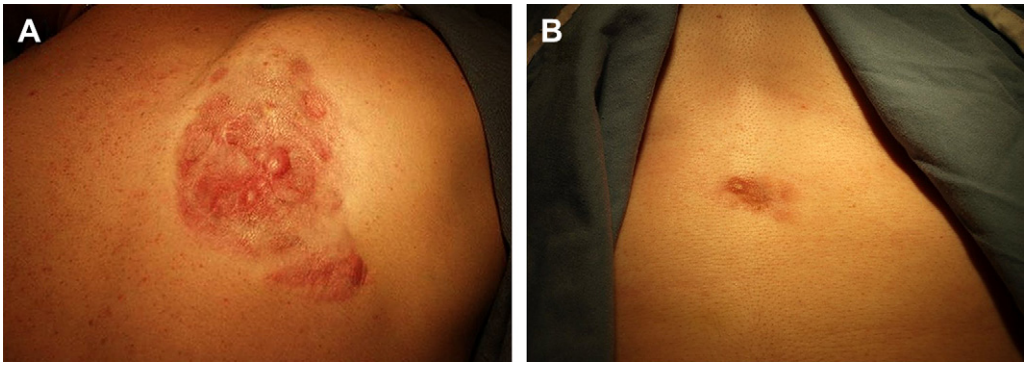

Fig. 1. (*A*) Congenital dermatofibrosarcoma protuberans of the back at presentation in a 16-year-old boy, featuring various morphologic clinical features, including plaques, nodules, atrophy, telangiectasia, and scar-like changes. (*B*) Dermatofibrosarcoma protuberans on the mid-abdomen.

Together with its often-benign clinical appearance, the rare nature of DFSP and its tendency for indolent growth can prompt diagnostic challenges. Clinically, DFSP can be mistaken for hypertrophic or keloidal scarring, morphea, epidermoid cysts, melanoma, or metastatic neoplasms. In congenital DFSP, early lesions may be difficult to distinguish from vascular malformations, infantile fibromatosis or myofibromatosis, fibrosarcoma, or fibrous hamartoma.[3]

STAGING AND PROGNOSIS

A definitive staging system that can assist with prediction of patient outcomes does not yet exist for DFSP. In some cases, the Short German Guidelines or the general American Musculoskeletal Tumor Society Staging System, which take into account high- or low-grade histopathology, local tumor extension, or distant spread, may be helpful,[11,12] but the 5-year survival for classical DFSP is over 99%. Imaging studies for staging purposes are typically not required, since tumor involvement is most frequently limited to local disease. If metastasis occurs, it spreads most frequently to regional lymph nodes. While distant metastasis occurs in less than 5% of cases, it is associated with a poor prognosis, with death from widespread metastatic disease typically occurring within 2 years. In advanced, recurrent, or high-grade variants of DFSP, the risk of hematogenous dissemination is greater and most commonly leads to pulmonary metastases. Imaging of the chest using computed tomography (CT) to evaluate for pulmonary metastasis is therefore indicated in high-risk clinical situations. Other potential sites of hematogenous spread include bone, brain, heart, and other soft tissues.

Distant metastasis and disease-specific mortality are usually consequences of local recurrence after inadequate surgical excision.[2,8,13,14] In some prospective case series, disease-free survival after wide local excision correlated inversely with tumor depth, tumor grade, patient age, positive margin after primary resection, or presence of the high-risk fibrosarcomatous variant on histology.

HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY

Clinical suspicion for DFSP following a complete skin examination typically requires an incisional skin biopsy to help confirm the diagnosis. Histological features suggestive of DFSP typically include a dense collection of monomorphous fusiform cells forming focal storiform or cartwheel configurations as demonstrated in **Fig. 2**A. Early lesions may feature an area of dermal sparing, or a Grenz zone, which is clearly seen just beneath the epidermis.[15] Coursing through the dermis and infiltrating the subcutaneous fat (see **Fig. 2**B), an extensive proliferation of spindle cells disrupts the adipose tissue architecture and creates a honeycomb or lace-like appearance. Deeper projections into fascia or muscle can further complicate demarcation of the tumor border and subsequent surgical management.[16] Determination of the precise surgical margin in DFSP can be challenging owing to the tumor's bland histologic appearance and diffuse infiltration, as well as its similarity to other neoplasms. Occasionally DFSP can be difficult to distinguish from dermatofibroma, dermatomyofibroma, fibrosarcoma, leiomyoscarcoma, malignant fibrous histiocytoma (also called pleomorphic scarcoma), or atypical fibroxanthoma. Dermatofibromas have