Congenital dermatofibrosarcoma with associated hypertrichosis

Ryan S. Berry[1], Tamara M. Berry[2], Michaela Haney[2], Anil Shetty[3], Limin Yu[1] and Aimee C. Smidt[2,4]

[1]Department of Pathology, University of New Mexico School of Medicine, Albuquerque, NM,
[2]Department of Dermatology, University of New Mexico School of Medicine, Albuquerque, NM,
[3]Department of Surgery, Division of Plastic Surgery, University of New Mexico School of Medicine, Albuquerque, NM, and
[4]Department of Pediatrics, University of New Mexico School of Medicine, Albuquerque, NM

Ryan S. Berry, Department of Pathology, University of New Mexico School of Medicine, MSC08 4640, 1 University of New Mexico, Albuquerque, NM 87131, Tel: (505) 272-4814, Fax: (505) 272-8084, e-mail: rberry@salud.unm.edu

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Dermatofibrosarcoma protuberans (DFSP) represents a fibrohistiocytic tumor of intermediate malignancy that is locally aggressive and has a high propensity for local recurrence.[1] It is the second most frequent cutaneous sarcoma, accounting for approximately 18% of all such tumors, yet it only represents 0.1% of all cutaneous malignancies.[2] The majority of cases are observed between the ages of 20 and 60 years,[2] but DFSP may be congenital or appear in early childhood.[3] Clinically it presents as a slow-growing, violaceous to reddish brown plaque that eventually becomes nodular or protuberant. In infants and children, there is often a delay in diagnosis (5-years average) or misdiagnosis due to variability in presentation. Further, DFSP may share similar characteristics with more common childhood lesions such as vascular birthmarks.[4] DFSP occurs most commonly on the trunk, followed by the distal then proximal extremities, and the head and neck.[2–4]

The illustrations in this report represent a congenital lesion present on the lateral trunk of a 6-month-old female. It was a firm dermal plaque measuring 6×6 cm, and it was composed of coalescing deeply pink to purple papules and nodules with central hypertrichosis (Figure 1). A punch biopsy was performed and showed a partially storiform proliferation of small spindled cells with a honeycomb pattern of infiltration into the subcutaneous fat (Figure 2). Immunohistochemical stains showed the spindled cells to be diffusely reactive for CD34 (Figure 3) and negative for factor XIIIa, CD68, S100 protein, Melan-A, and smooth muscle actin (SMA). A diagnosis of DFSP was rendered and the patient later underwent wide local excision. The resected specimen shared similar histomorphologic features with the original biopsy (Figures 4 and 5). Additionally, it demonstrated focal areas with stromal edema and multinucleated cells, consistent with a giant cell fibroblastoma (GCF) component (Figure 6).

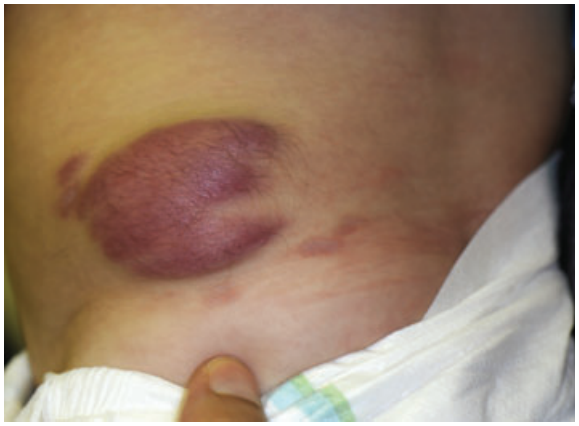

Fig. 1. A violaceous plaque exhibits assocaited central hypertrichosis.

The diagnosis of DFSP is primarily based on histopathologic examination. Classically, DFSP is characterized by a storiform or cartwheel pattern of small, uniform, elongated spindle cells with minimal cytoplasm and indistinct borders. The cells diffusely infiltrate the dermis, trapping adnexal structures, and extend into the subcutaneous

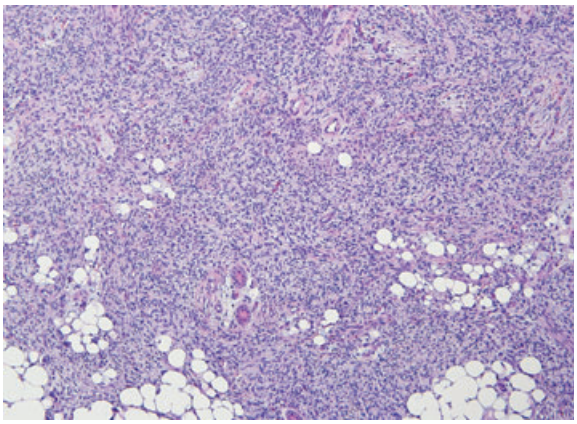

Fig. 2. A punch biopsy demonstrated a spindle cell tumor with a storiform configuration and infiltration of the subcutis.

fat along the fibrous septa. This pattern of infiltration results in the characteristic 'honeycomb' configuration classically associated with DFSP. In addition to this conventional morphology, several variants of DFSP have been described including myxoid, pigmented (Bednar tumor), and GCF.[1] These are not considered distinct entities but rather represent a spectrum of DFSP, and in some instances, the histopathologic findings of a variant form may constitute a small or moderate proportion of a given tumor. Histopathologically, areas of GCF are typically hypocellular and are composed of spindled cells with scattered mono- and multinucleated giant cells. The background stroma is collagenous to myxoid and well vascularized. Areas with variant histopathology may be intermixed or may show an abrupt transition from areas with classic DFSP morphology. Rarely, DFSP can undergo fibrosarcomatous transformation, which is characterized by increased cellularity and mitotic activity. When this occurs, the architecture typically transitions from storiform to fascicular or 'herring-bone' in configuration, although pleomorphic areas resembling pleomorphic sarcoma may also occur.[1,5]

Often, initial histopathologic evaluation is based on small punch biopsies that may not represent the overall composition of the entire tumor, thereby making an accurate diagnosis difficult. Superficial samples may be confused with benign entities like dermatofibroma, neurofibroma, fibromatosis, or fibrous hamartoma of infancy. Conversely, partial biopsies of hypercellular areas could be mistaken for fibrosarcoma or liposarcoma.[6] Immunohistochemical markers can aid in differentiating DFSP from other fibrohistiocytic tumors. DFSP expresses CD34 in up to 90% of cases; this serves as a sensitive but non-specific marker.[7] Similarly, apolipoprotein D and CD63 (NKI/C3) have been shown to be sensitive but not specific markers for DFSP.[8,9] Immunostains such as factor XIIIa, D2-40, stromelysin III, CD68, and CD163 are most often positive in dermatofibroma and negative in DFSP.[1,10–13] In tumors with areas of GCF, the spindled and giant cells usually express CD34.

Genetically, DFSP is typically characterized by a translocation between chromosomes 17 and 22: t(17;22)(q22;q13). More commonly in adults, a supernumerary ring chromosome containing genomic material from 17q22 and 22q13 is present. This translocation results in the fusion of the collagen type I alpha 1 gene (*COL1A1*) on chromosome 17 and the platelet-derived growth factor β gene (*PDGFB*) on chromosome 22. Several other fusion variants of *COL1A1* and *PDGFB* have been described and can be detected by fluorescence in situ hybridization (FISH) or reverse transcription polymerase chain reaction (RT-PCR).[14]

We posit that the hypertrichosis is an unusual feature that can occur in DFSP, although it has not been previously reported in the literature. Generally speaking, hypertrichosis can be classified as congenital or acquired and can be further divided into localized or generalized depending on its extent. Congenital localized hypertrichosis may be associated with infantile tumors or hamartomas such as plaque-type blue nevus, fibrous hamartoma of infancy, dermal dendrocytic hamartoma, eccrine angiomatous hamartoma, tufted angioma, congenital melanocytic nevus, plexiform neurofibroma, or, as we now document, DFSP. Acquired localized hypertrichosis can be seen in areas of friction, inflammation, or trauma.[15,16] The mechanism by which localized hypertrichosis occurs is not well established, but it is likely due to a complex interplay between epithelial and mesenchymal components of the cutaneous microenvironment.[17] We believe that the localized hypertrichosis in this patient was congenital rather than acquired given her age, her clinical presentation, and the location of the tumor, which would not prone to habitual trauma or irritation. It is plausible that DFSP can alter the cutaneous microenvironment, resulting in upregulation of signal pathways involved in hair follicle cycling, thereby producing localized hypertrichosis.

Fig. 3. The spindled cells express CD34.

Figs. 4-5. An excisional specimen demonstrates residual spindle cell tumor with infiltration of the subcutis, similar to what was seen in the initial biopsy.

Fig. 6. An area of the excised tumor demonstrates giant cell fibroblastoma-like morphology.

Cover Quizlet

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