



# Dermatofibrosarcoma protuberans in pediatric patients: A diagnostic and management challenge

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## INTRODUCTION

Spindle cell tumors occur in the pediatric population and can prove to be aggressive clinically, as in the case with dermatofibrosarcoma protuberans (DFSP). Soft tissue sarcomas represent less than 1% of malignant tumors overall,<sup>1</sup> and the prevalence of DFSP before 20 years of age is 1.0 per million.<sup>2</sup> This malignancy is characterized by invasive growth, low frequency of metastasis, and a tendency to relapse locally, making it a high-morbidity tumor.<sup>3</sup> DFSP has an insidious onset with slow growth,<sup>4</sup> requiring a high index of clinical suspicion and ultimately a biopsy for diagnosis. The heterogeneous presentation of the tumor often leads to a delay in diagnosis, partly because of a differential diagnosis that includes a number of benign entities such as scars, vascular malformations,<sup>5</sup> dermal dendrocyte hamartoma (CD34<sup>+</sup> dermal fibroma), dermatofibroma,<sup>6</sup> and others.

Histologically, DFSP exhibits small, elongated cells arranged in a storiform pattern extending into the subcutaneous fat.<sup>7</sup> The infiltrative pattern of DFSP aids in distinguishing it from benign entities, which can have similar elongated cells in a storiform pattern that lack infiltrative features, but this is often not sufficient for definitive diagnosis. When classification of a spindle cell tumor is not evident through routine histopathology alone, immunohistochemistry studies and fluorescence in situ hybridization (FISH) for the platelet-derived growth factor- $\beta$  (PDGFB) rearrangement can be useful ancillary tests.

### Abbreviations used:

COL1A1:	collagen 1 $\alpha$ 1
DF:	dermatofibroma
DFSP:	dermatofibrosarcoma protuberans
FISH:	fluorescence in situ hybridization
JXG:	juvenile xanthogranuloma
PDGFB:	platelet-derived growth factor- $\beta$

Traditionally, tumor cells of DFSP stain positively for CD34 and negative for factor XIIIa,<sup>3</sup> whereas benign entities such as dermatofibroma (DF) are typically CD34<sup>-</sup> (Table 1). However, there are a small number of DFSPs that are CD34<sup>-</sup>, and conversely some DFs that are CD34<sup>+</sup>. The genetic translocation t(17:22)(q22;q13) has been identified in DFSP, which results in a collagen 1  $\alpha$ 1 (COL1A1)/PDGFB fusion gene.<sup>8</sup> FISH analysis for the PDGFB gene rearrangement has been positive in 89%<sup>12</sup> to 96%<sup>13</sup> of cases felt certain to be DFSP.

We present the cases of 3 pediatric spindle cell tumors, 2 DFSPs, and 1 mimicker exhibiting the importance of clinical judgment and the limitations of current diagnostic tools.

## REPORT OF CASES

### Case 1

A 10-month old boy was seen for evaluation of a firm, pink plaque on his left dorsal forearm noted at 1 month of age. It had grown proportionally with him and appeared asymptomatic. The patient

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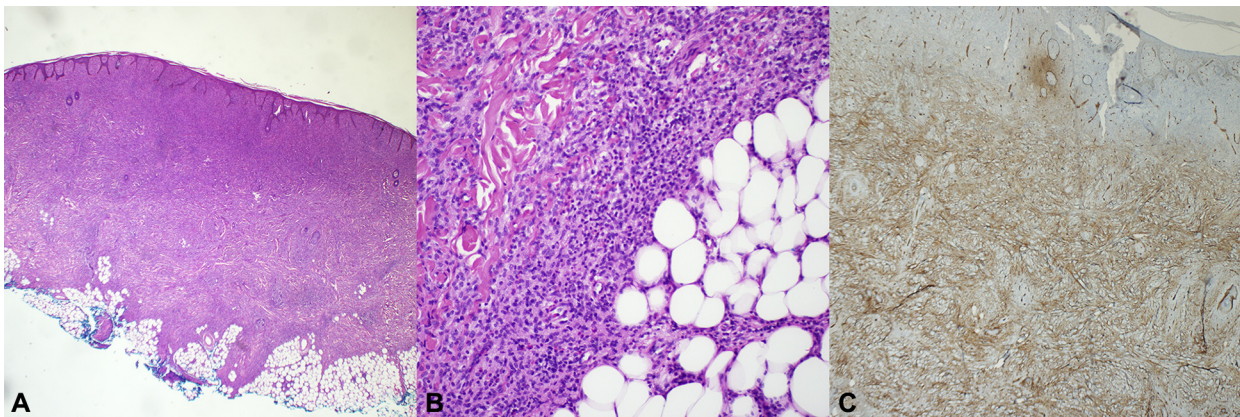
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**Table I.** Differentiating staining characteristics of pediatric spindle tumors<sup>4,8-11</sup>

	CD34	Factor XIIIa	P75	Stromelysin	CD163
DF	Positive up to 40%	Positive up to 100%	Typically negative	Typically positive	Positive 89%
JXG		Positive 93%	—	—	—
DFSP	Positive 80%-100%	Positive 10%-15%	Positive up to 95%	Positive <10%	Positive <17%
Medallionlike dermal dendrocyte hamartoma	Positive 100%	Significant variation	—	—	—



**Fig 1.** Case 1. Foam cell—poor juvenile xanthogranuloma **A** and **B**, Fibrohistiocytic spindle cell lesion extending from the epidermis to superficial subcutis with storiform pattern. **C**, Diffuse expression of CD34. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**,  $\times 2$ ; **B**,  $\times 40$ ; **C**,  $\times 20$ .)

underwent an excision. Histopathologic examination found an unencapsulated, fibrohistiocytic spindle cell tumor extending from the epidermis to superficial subcutis with storiform pattern diffusely expressing CD34 and CD10. CD68 and factor XIIIa showed diffuse staining of the spindle cells, and S100 was negative (Fig 1). FISH analysis for PDGFB was negative. The lesion was initially characterized as a DF, but because of CD34 positivity, outside pathology consultation was sought, and it was ultimately reclassified as a foam cell-poor juvenile xanthogranuloma (JXG). He did well postoperatively without recurrence for 11 months.

### Case 2

A 9-month-old boy presented for evaluation of lesions on his genitalia noted at 1 month of age. The patient's parents reported that the lesions had grown proportionately with him since they were first noted. On examination, there were smooth papules and plaques seen on the suprapubic and proximal penile shaft, extending inferiorly onto the left aspect of the scrotum (Fig 2). A punch biopsy found a dermal and subcutaneous spindle cell tumor with storiform

growth pattern. Tumor cells expressed diffuse CD34. Factor XIIIa, smooth muscle actin, desmin, S100, and SOX10 were negative. FISH analysis for PDGFB rearrangement was also negative. Based on clinical behavior, location, and immunohistochemistry studies, the lesion was presumed to be DFSP, excised with narrow surgical margins and closed primarily. One margin was positive for tumor and was subsequently re-excised with a 2-mm margin. The defect was covered with a full-thickness skin graft. The patient did well postoperatively without recurrence for 21 months.

### Case 3

A 7-year-old boy presented for evaluation of a lesion on his left leg that had slowly and steadily grown since it was noticed 3 years ago. On examination there was a 2.5-cm by 15-cm oval atrophic plaque with an overlying nodule on the anterior left leg. Separate biopsies were taken of the atrophic and nodular areas, which showed spindle cell proliferation extending into the dermis consistent with DFSP. Immunohistochemistry was positive for CD34 and vimentin and negative for epithelial membrane



**Fig 2.** Case 2. DFSP: smooth papules and plaques on suprapubic skin and penile shaft.

antigen, desmin, S100, and factor XIIIa. The lesion was excised with 3 cm margins and covered with a full-thickness skin graft. The patient has remained tumor free for more than 4 years.

## DISCUSSION

Firm plaques and nodules on a pediatric patient present the clinician with a broad differential diagnosis. The decision to biopsy will be driven by the evolution of the tumor and the location. Even more challenging is reconciling clinical presentation with a potentially ambiguous histologic picture to determine the best treatment. Standard excision of DFSPs traditionally requires 3-cm surgical margins because of poorly circumscribed clinical margins, as illustrated by case 2. However, such large surgical defects can be disfiguring in an infant or child. DFSP can be excised with Mohs micrographic surgery (MMS) but must be done in a modified multiday approach because of the challenge of keeping a child anesthetized for multiple stages in a single day. DFSPs may also require adjuvant treatment such as radiation, chemotherapy, or imatinib, all of which have their own respective morbidities that can be accentuated in children. Undertreating a DFSP is even more problematic, as the tumor is locally destructive, can metastasize, and can prove fatal without treatment.

Further, although some cases of DFSP are straightforward histologic diagnoses, such as case 3 presented above, it is occasionally a very challenging histopathologic diagnosis. Other spindle cell tumors, such as the benign medallionlike dermal dendrocyte hamartoma, also stain with CD34<sup>9</sup> and exhibit a similar histologic pattern: epidermal atrophy and a spindle cell proliferation infiltrating the dermis and subcutaneous fat.<sup>14</sup> In some cases, DFs will stain with CD34, and a small percentage of DFSPs paradoxically do not stain with CD34.<sup>10</sup> JXG is a dendritic cell–related disorder<sup>15</sup> histologically characterized

by a dermal lymphohistiocytic infiltrate with foamy macrophages.<sup>11</sup> The first case was classified as foam cell poor, making it difficult to distinguish from DFSP. As with our patient, JXG typically stains positive for factor XIIIa, although not in every case (Table I).<sup>11</sup>

In these equivocal cases, FISH for the PDGFB gene rearrangement can be a useful test. Various studies report positivity of this fusion gene in 89%<sup>12</sup> to 96%<sup>13</sup> of DFSP cases. The challenge for the clinician is how to proceed for the cases with mixed histologic, immunohistochemical, and FISH results.

## CONCLUSION

The diagnosis of DFSP in children is often delayed because of either a general hesitancy to biopsy in the pediatric population or as a result of an unclear pathologic diagnosis. The 3 aforementioned cases illustrate that the clinician must consider the histology, immunohistochemistry, and FISH results and whether they fit the clinical picture to determine the best course of treatment. Some spindle cell tumors, such as medallionlike dermal dendrocyte hamartoma and JXG, are benign and do not require intervention. Other entities such as DFSP are much more aggressive, requiring surgical intervention and, in some instances, adjuvant therapies with their own respective morbidities. Although immunohistochemistry for CD34, factor XIIIa, and FISH analysis for the PDGFB gene rearrangement can be helpful in distinguishing these tumors from each other, some cases remain agonizingly ambiguous. This variability makes DFSP a diagnostic challenge, and, consequently, both patient presentation and clinical judgment are critical in guiding appropriate treatment.

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