

Giant fibrous hamartoma of infancy: pitfall of CD34 positive dermal mesenchymal tumor

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Abstract

Fibrous hamartoma of infancy (FHI) is a rare benign soft tissue tumor with a triphasic organoid histologic appearance. The authors present a case of a 21-month-old healthy girl with a slowly growing flesh-colored subcutaneous plaque 12cm in size on the lower back, with overlying hypertrichosis. A punch biopsy revealed a proliferation of spindle cells infiltrating the dermis and hypodermis organized in a dense storiform pattern with a strong diffuse positivity for CD34. The diagnosis of congenital dermatofibrosarcoma protuberans (DFSP) was considered and an excision was performed. Histopathologic analysis showed an extensive poorly demarcated mass infiltrating the dermis and hypodermis, composed of different components: a monomorphous fibroblastic/myofibroblastic component, a mature adipose component, and an immature mesenchymal basophilic component. The clinical aspects with the histologic and immunohistochemical features led to the diagnosis of giant fibrous hamartoma of infancy. In our case the strong diffuse CD34 positivity was a diagnostic pitfall leading to an incorrect hypothesis of congenital DFSP. The characteristic triphasic histology of FHI was missed owing to the small size of the punch biopsy. This article highlights the importance of being aware of the CD34+ dermal mesenchymal tumor differential diagnosis and the necessity of appropriate size biopsies to avoid sampling error.

Keywords: fibrous hamartoma of infancy, hypertrichosis, hyperhidrosis, dermatofibrosarcoma protuberans

Introduction

Fibrous hamartoma of infancy (FHI) is a rare benign soft tissue tumor with a triphasic organoid histologic appearance that typically occurs in the first 2 years of life [1]. It is present at birth in 20 to 25% of the cases and has a male predominance [2]. It presents as a solitary, skin colored, asymptomatic, subcutaneous nodule characteristically located on the shoulder, back, or arm [3]. From the histological point of view it is characterized by a proliferation in the deep dermis and hypodermis, consisting of varied proportions of mesenchymal elements — intersecting fascicles of dense fibrocollagenous tissue, adipose tissue, and undifferentiated immature mesenchymal cells. The excision is usually curative, although there are cases of local recurrence [2].

Case Synopsis

A 21-month-old healthy girl was referred to the dermatology clinic because of a slowly growing flesh-colored plaque on her lower back that was present since birth. The lesion was apparently asymptomatic and the parents reported episodes of perspiration on the plaque.

On physical examination the plaque was 12×3cm wide, firm, not fixed to the underlying tissues, with localized hypertrichosis (Figure 1).

The young girl had a monozygotic twin with no cutaneous lesions and there was no family history of dermatologic abnormalities.



Figure 1. Subcutaneous skin color plaque, 12×3 cm wide, with associated hypertrichosis, localized in the lower back.

A punch biopsy was performed and histopathologic examination revealed a proliferation of spindle cells infiltrating the dermis and hypodermis, extending into the subcutaneous fat along the septa (Figure 2A). The spindle cell proliferation was organized in a dense storiform pattern (Figure 2B). Immunohistochemical analysis showed no staining for smooth muscle actin (SMA) and a strong diffuse reactivity for CD34 (Figure 2C).

Among the heterogeneous group of CD34+ spindle cell tumors, four main conditions in the differential diagnosis were considered: fibroblastic connective tissue nevus (FCTN), plaque-like CD34+ dermal fibroma (PDF, medallion-like dermal dendrocyte hamartoma), congenital dermatofibrosarcoma protuberans (DFSP), and fibrous hamartoma of infancy (FHI).

Based on the storiform pattern infiltrating the deep dermis and hypodermis and on the strong positivity for CD34, the concern for congenital dermatofibrosarcoma protuberans (DFSP) was raised. Although a larger biopsy was advised, surgical excision of the whole lesion was performed by the attending pediatric surgeon.

Histopathologic analysis of the resected specimen showed an extensive poorly demarcated mass infiltrating dermis and hypodermis, with adipose tissue in the reticular dermis (Figure 3A).

Different components were present: a monomorphous fibroblastic/myofibroblastic component, a mature adipose component, and an immature mesenchymal basophilic component. An increased number of eccrine glands was associated (Figure 3B). Mitoses were rare (Figure 3C).

The immunohistochemistry showed focal reactivity for SMA in the fibroblastic-myofibroblastic component; the mature adipose tissue stained with S100. There was a strong positivity for CD34, staining the immature mesenchymal tissue and the fibroblastic component. Expression of the collagen type 1 alpha 1f-platelet-derived growth factor beta chain COL1A1-PDGFB fusion protein was not detected by fluorescence in-situ hybridization. The clinical presentation associated with the histologic and immunohistochemical features of the excised specimen led to the diagnosis of giant fibrous hamartoma of infancy.

Case Discussion

FHI is a rare benign soft tissue tumor. It was initially termed subdermal fibrous tumor of infancy by Reye in 1956, and renamed as fibrous tumor of infancy by Enzinger, in 1965 [4, 5].

FHI usually is a slow-growing tumor, mostly solitary, with an onset in the first 2 years of life. It is usually asymptomatic and mobile [6]. The usual anatomic locations include the back, axilla, upper extremities, and scrotum. Most tumors range in size from 0.5 to **4.5 cm**. **Our patient's lesion represents one** of the largest reported FHI, exactly the same size as the tumor reported by Melnick et al., which also exhibited associated hypertrichosis and hyperhidrosis [7]. In fact, overlying skin changes such as hypertrichosis, hyperhidrosis, and hyperpigmentation have been described [2].

FHI is recognized by its typical triphasic histology composed of fibrous, mesenchymal, and adipous elements present in variable proportions. Intersecting fascicles of mature fibroblastic-myofibroblastic tissue intermingle with areas of immature basophilic or myxoid mesenchymal tissue, admixed with mature adipose tissue [1]. Salient histologic features may be missed with small biopsies, as happened in our case.

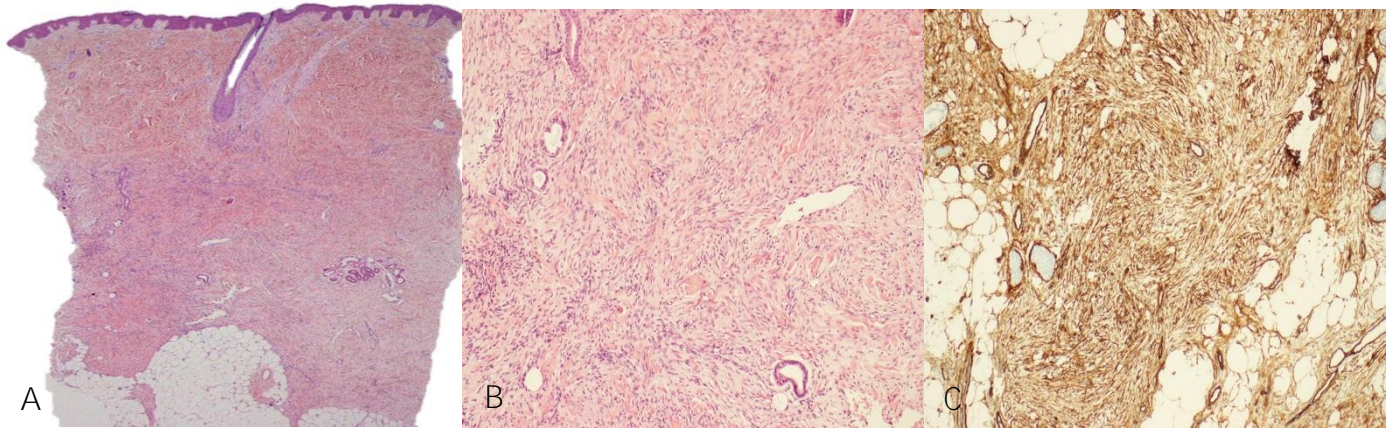


Figure 2. A) Proliferation of spindle cells infiltrating dermis and hypodermis, extending into the subcutaneous fat along the septa. H&E, 40 \times . B) Dense storiform pattern of spindle cell proliferation. H&E, 100 \times . C) Diffuse CD34 reactivity, 100 \times .

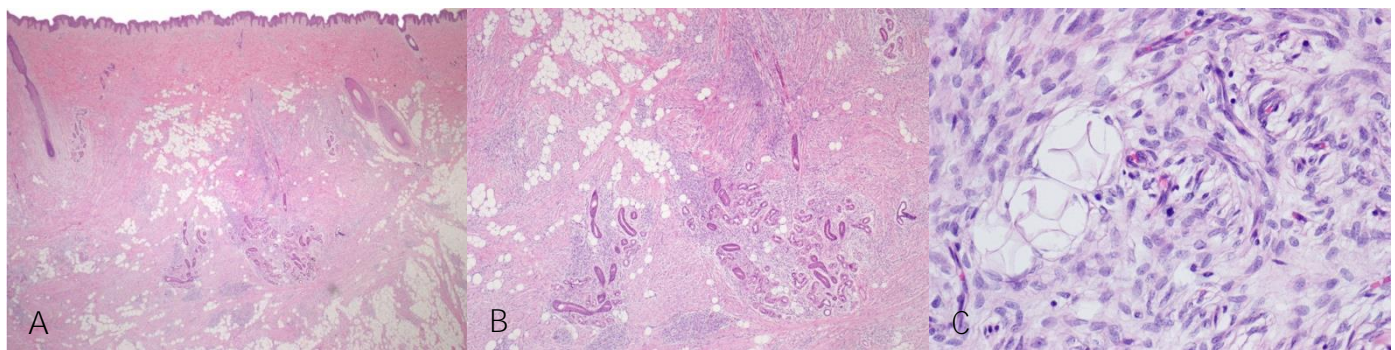


Figure 3. A) Poorly demarcated mass infiltrating dermis and hypodermis, with adipose tissue in the reticular dermis. H&E, 40 \times . B) Presence of an increased number of eccrine glands. H&E, 100 \times . C) Rare mitosis. H&E, 400 \times .

Immunohistochemical stains may be helpful in the diagnosis of FHI: the fibroblastic-myofibroblastic component typically stains for vimentin and SMA; the mature adipose tissue stains for S100 protein; and the mesenchymal tissue is diffusely reactive for vimentin. CD34 stains the immature mesenchymal tissue and has been reported by Saab et al. to stain pseudo-angiomatous foci described by them in half of a series of 60 cases of FHI [1]. Four main conditions in the differential diagnosis were considered between the heterogeneous group of CD34+ spindle cell tumors: FCTN, PDF, DFSP, and FHI.

Dermatofibrosarcoma protuberans is a fibrohistiocytic tumor of intermediate malignancy, that appears as a slow-growing violaceous to reddish macule or papule that may progress to a nodular stage. Most often it is observed between the second and fifth decades, but it may be congenital or appear early in childhood. The size normally ranges from 1 to 5 cm. The most frequent locations are the trunk

and proximal extremities; recurrence is frequent and metastases are rare. Histologically, DFSP involves the deep dermis and hypodermis and is characterized by a storiform pattern of elongated spindle cells. The tumor extends into the subcutaneous fat **surrounding adipocytes in a 'honeycomb' configuration**. It expresses diffuse CD34 positivity in the majority of the cases and is factor XIIIa and S-100 negative. Genetically is described by a translocation that results in COL1A1-PDGFB fusion protein [8-10].

Fibroblastic connective tissue nevus is a rare, distinct, and benign dermal CD34-positive mesenchymal proliferation. The nevus most often affects children and presents as a tan-brown to tan-white, solitary, painless plaque of 0.3 to 2 cm on the trunk, neck, or limbs. There is no associated hypertrichosis. In addition, recurrence after surgical excision and metastases are not seen. FCTN is composed of spindle-shaped fibroblastic/myofibroblastic cells that involve primarily the reticular dermis and

extends into superior hypodermis in half of the cases. In the majority of the cases the growth is CD34-positive with multifocal distribution; half of the cases are SMA positive and do not express FXIIIa [11].

Plaque-like CD34-positive dermal fibroma is a rare benign spindle cell neoplasm, usually congenital, that presents as solitary, asymptomatic plaque of 1 to 2 cm localized on the neck or trunk. Histologically, there is a band-like proliferation of CD34-positive spindle cells in the upper dermis. SMA and FXIIIa positivity is variable [12]. In our case the strong diffuse CD34 positivity was a diagnostic pitfall leading to an incorrect hypothesis of congenital DFSP. The characteristic triphasic histology of FHI was missed owing to the small size of the punch biopsy.

Our case clearly shows the need for large biopsies for the definitive diagnosis of CD34+ dermal mesenchymal tumors. When these entities exhibit unusual clinical behavior it is important to

distinguish them histologically and to classify them accurately to avoid inappropriate treatment. Considering the location of **our patient's lesion, its** total surgical excision was fortunately not too aggressive. However, in other body sites it could have been unnecessarily mutilating. Since the prognosis of FHI is excellent and recurrence rates are low, aggressive, mutilating resections are to be avoided [6]. Nonetheless, because of its progressive growth and unlikelihood of regression, local excision is the treatment of choice. In large lesions repeated serial surgical approaches are advised.

Conclusion

This article highlights the importance of being aware of the CD34-reactive dermal mesenchymal tumor differential diagnosis and the necessity of appropriate size biopsies to avoid sampling errors leading to inappropriate treatments.

References

1. Saab ST, McClain CM, Coffin CM. Fibrous hamartoma of infancy: a clinicopathologic analysis of 60 cases. *Am J Surg Pathol*. 2014;38(3):394-401. [PMID: 24525510].
2. Dickey GE, Sotelo-Avila C. Fibrous hamartoma of infancy: current review. *Pediatr Dev Pathol*. 1999;2(3):236-43. [PMID: 10191347].
3. Kang G, Suh YL, Han J, Kwon GY, Lee SK, Seo JM. Fibrous hamartoma of infancy: an experience of a single institute. *J Korean Surg Soc*. 2011;81(1):61-5. [PMID: 22066102]
4. Reye RD. A consideration of certain subdermal fibromatous tumours of infancy. *J Pathol Bacteriol*. 1956;72(1):149-54. [PMID: 13367990].
5. Enzinger FM. Fibrous hamartoma of infancy. *Cancer*. 1965;18:241-8. [PMID: 14254080].
6. McGowan Jt, Smith CD, Maize J, Jr., Cook J. Giant fibrous hamartoma of infancy: a report of two cases and review of the literature. *J Am Acad Dermatol*. 2011;64(3):579-86. [PMID: 20598395].
7. Melnick L, Berger EM, Elenitsas R, Chachkin S, Treat JR. Fibrous hamartoma of infancy: a firm plaque presenting with hypertrichosis and hyperhidrosis. *Pediatr Dermatol*. 2015;32(4):533-5. [PMID: 25660371].
8. Checketts SR, Hamilton TK, Baughman RD. Congenital and childhood dermatofibrosarcoma protuberans: a case report and review of the literature. *J Am Acad Dermatol*. 2000;42(5 Pt 2):907-13. [PMID: 10767703].
9. Berry RS, Berry TM, Haney M, Shetty A, Yu L, Smidt AC. Congenital dermatofibrosarcoma with associated hypertrichosis. *J Cutan Pathol*. 2013;40(12):990-2, quiz 89. [PMID: 24274422].
10. Maire G, Fraitag S, Galmiche L, Keslair F, Ebran N, Terrier-Lacombe MJ, et al. A clinical, histologic, and molecular study of 9 cases of congenital dermatofibrosarcoma protuberans. *Arch Dermatol*. 2007;143(2):203-10. [PMID: 17310000].
11. de Feraudy S, Fletcher CD. Fibroblastic connective tissue nevus: a rare cutaneous lesion analyzed in a series of 25 cases. *Am J Surg Pathol*. 2012;36(10):1509-15. [PMID: 22892597].
12. Stuart LN, Hiatt KM, Zaki Z, Gardner JM, Shalin SC. Plaque-like CD34-positive dermal fibroma/medallion-like dermal dendrocyte hamartoma: an unusual spindle cell neoplasm. *J Cutan Pathol*. 2014;41(8):625-9. [PMID: 25065391].