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Fibrous hamartoma of the thigh in a neonate

Elizabeth A. Waldrop, MD a,*, Heather Von Bevern, MD b, Anders Meyer, MD c

ABSTRACT

Fibrous hamartoma of infancy (FHI) is a rare, benign lesion characterized as a tumor of myofibroblastic origin that has characteristic features of triphasic histology. FHI was first described in 1956 by Rey and formally named by Enzinger in 1965 [1-2]. The lesion is defined as a hamartoma due to the histologic presentation of disorganized mesenchymal, fibrous, and adipose tissue with absence of mitotic figures; this combination of derived tissue without evidence of anaplasia is diagnostic for FHI. These lesions typically arise as a single, solitary mass, are most commonly located on the extremities, trunk, sacrum, or scrotum and are typically 0.5 to 9.0 centimeters in size [3-4]. Only roughly 200 cases have been reported in the literature [3]. The majority of cases occur in young children; 91% of cases arise within the first year of life [4]. Males are more often affected in a ratio of 2.4:1 [4]. Roughly 20% of cases have been documented as congenital (3). Treatment is surgical excision, which is often curative; local recurrence is rare and incidence decreased by obtaining negative margins (8). We present a case of congenital FHI identified at birth.

1. Case report

Patient is a female infant born to an experienced mother via repeat C-section. There was no significant family past medical history including no history of childhood tumors or genetic syndromes. Newborn course was complicated by neonatal hyperbilirubinemia which resolved after phototherapy. She received hepatitis B vaccine and vitamin K in left thigh. On initial assessment, prior to vaccination, she was noted to have a non-tender anterior left thigh mass without overlying skin changes with an otherwise benign exam. On subsequent exams, the thigh mass was noted to be more localized and firm and it did not appear to cause any distress to the patient. She was neurovasculally intact distal to the lesion and she moved all extremities spontaneously and equally. Due to low concern for immediate intervention of the mass, the patient was discharged with routine newborn follow up. Newborn state screen returned negative.

During a visit on day of life 11, the provider noted that the mass appeared more condensed and was firm to touch. Concern arose about the origin of the mass from a skeletal vs. muscular vs. adipose origin. Left femur x-ray was obtained and radiology report demonstrated no bony involvement and the mass most likely originates from soft tissue. Left lower extremity ultrasound was obtained to evaluate the mass in more detail (Fig. 1-A, 1-B). The mass was found to be muscular in origin but etiology remained unclear. Referral to pediatric surgery was made for evaluation of the left soft tissue lesion.

Pediatric surgery evaluated the patient on day of life 14. The provider identified the left anterior thigh mass on exam, which measured 3 cm in diameter, and palpated the lesion intramuscularly. The patient was noted to be neurovascularily intact with full painless range of motion and there was no evidence of overlying skin changes. Pediatric surgery recommended left thigh MRI to better evaluate the mass. MRI was obtained due to potential of neoplastic lesion. Pediatric surgery and pediatric hematology/oncology both recommended tissue biopsy for histopathologic evaluation of the lesion.

Biopsies were obtained from the overlying skin, medial, anterior, and lateral aspects of the lesion. She was discharged after short admission for the procedure. Biopsy results were confirmed 1 month after specimens were obtained. Surgical pathology report indicated the lesion to be low grade, benign appearing myofibroblastic and fibroblastic neoplasm. Immunostains were performed which showed positive staining for SMA...
and negative for desmin, CD34, S-100, and SOX10 (see Fig. 3-A, 3-B, 3-C, 3-D). Some cases have extensive pseudoangiomatous morphology with accompanying CD34-positivity which may raise the differential diagnosis of giant-cell fibroblastoma and dermatofibrosarcoma protuberans. These features were not present in this case. The differential diagnosis in this case was chiefly limited to lipofibromatosis, lipofibromatosis-like neural tumor and other TRK-associated tumors, and infantile fibrosarcoma. An anchored multiplex PCR based NGS gene fusion assay covering the NTRK genes was performed and was negative, excluding, in conjunction with the morphology, infantile fibrosarcoma, lipofibromatosis-like neural tumor, and the remaining TRK-associated tumors. The triphasic morphology, more slender spindle cells, and lack of myxoid stroma favor fibrous hamartoma of infancy over lipofibromatosis.

Plan of care for this patient includes routine monitoring of the unresected mass at well child checks with primary pediatrician as well as surveillance by pediatric oncology prior to 1 year of life. Discussions for resection continue with initial plan to resect when she grows larger unless complications such as musculoskeletal, neurovascular, or oncologic complications arise.

2. Discussion

Fibrous hamartoma of infancy commonly presents as a slow-growing and asymptomatic subcutaneous mass classically located in the axilla, abdomen, extremities, or genitalia however approximately half of cases present at unusual sites, as in this case [5]. Most tumors are freely mobile, nontender, and well circumscribed; it is rare that lesions are encapsulated and some may exclude the diagnosis of FHI if encapsulation is present on histologic assessment [6]. However, case reports have documented FHI lesions with rapid growth and those associated with overlying warmth, pain, and/or tenderness as well as hyperpigmentation, hypertrichosis, and hyperhidrosis [7–9]. These lesions are largely benign and are inherently defined by the absence of mitotic figures and anaplasia.

It can be difficult to accurately diagnose FHI as the differential diagnosis is wide for a soft tissue lesion. Differential diagnosis includes hemangioma, myofibroma, fibrous hamartoma, infantile fibrosarcoma, infantile myofibromatosis, rhabdomyosarcoma, and non-rhabdomyosarcoma soft tissue tumors.

Initial workup of a soft tissue lesion typically begins with radiologic evaluation to distinguish location of lesion as well as estimated size and preliminary composition assessment. In a review by Ji et al., x-ray has little diagnostic value as lesions do not have characteristic appearance, however cross-sectional imaging modalities such as CT and MR can be useful in determining histological origins and ruling out challenging differential diagnoses [10]. On CT and MR imaging, lesions consistent with FHI present as soft tissue mass with oval shape (balanced type) or irregular shape (non-balanced type) [10]. The latter, non-balanced type, has a greater tendency to invade deep fascia and can make surgical resection with negative margins more challenging. Ji et al. suggests that MR imaging is useful diagnostically due to the ability to differentiate between tissue types; fat-containing FHI lesions demonstrate adipose signal intensity, ruling out dominantly low signal fibrous tissue tumors including infantile fibromatosis, myofibromatosis, and congenital fibrosarcomas [10]. Other adipose-containing tumors may be more difficult to distinguish. There is no role for ultrasound in the diagnosis of FHI.

Histopathologic features and immunostaining techniques aid in diagnosis to differentiate FHI from other cancerous lesions and rich

![Fig. 1. (A–B) demonstrates ultrasound findings of the thigh mass on day of life 11. Fig. 1-A is the transverse view and Fig. 1-B, the longitudinal view. Ultrasound demonstrates the heterogenous nature of the mass with presumptive origin from the musculature however unable to be confirmed without more detailed imaging.](image-url)
adipose tumors. A careful histopathologic examination meeting criteria is diagnostic. The characteristic microscopic histologic features of FHI include triphasic hamartomatous components: (i) primitive undifferentiated spindle cells and mesenchymal tissue organized in whorls, bands, or nests, (ii) well-defined fibroblastic to myofibroblastic bundles and (iii) intimate admixture of mature adipose tissue [11]. The proportion of these elements are variable in reported cases but all contained this classical triphasic morphology [5]. Immunostaining can support diagnosis but is not specific for FHI. In the large clinicopathologic study by Al-Ibraheemi, immunostaining was positive in all cases for S100 protein, expressed by adipocytes, and CD34, expressed by primitive mesenchyme [5]. Immunostaining for desmin was negative in all tested cases [5]. Presence of smooth muscle action (SMA) expressed by myofibroblasts is also consistent with a diagnosis of FHI [12]. FISH analysis on biopsied material can aid in ruling out particular diagnoses if histologic examination is inconclusive; absence of PDGFB (positive in giant cell fibroblastoma), absence of ETV6 (positive in infantile fibrosarcoma), and absence of NTRK (positive in soft tissue sarcomas) is support diagnosis of FHI. In our case, histopathologic examination of biopsied material demonstrated positive classical triphasic morphology, immunopositivity for SMA, and absence of ETV6 and NTRK on FISH analysis, suggestive of a diagnosis of FHI.
The treatment of choice is local excision, unless excision will be mutilating or result in significant poor cosmetic outcome. Current surgical recommendation includes obtaining 1.0 cm surgical margin; the majority of cases with local recurrence occurred in those that did not or were not able to obtain adequate negative margin [3,13]. In cases which resection is difficult or incompletely performed, tyrosine kinase inhibitors may be used as adjunct therapy [14]. In the large case review by Al-Ibraheemi of 145 cases, follow up information was available for 52 patients; local recurrences after resection were seen in 2 patients, or 1%, and no cases of metastasis were documented [5]. With low risk of spread without surgical removal, low risk of local recurrence, and no documentation of metastasis in the literature, the diagnosis of FHI carries an excellent prognosis.

3. Conclusion

FHI is a benign, soft tissue lesion presenting in early infancy and even the neonatal period that carries diagnostic histopathology and supportive MR imaging and immunostaining that can differentiate this tumor from other pediatric soft tissue masses. However, due to its rarity, it is important to recognize its characteristic diagnostic criteria and ensure its place on the differential diagnosis because it is largely benign and does not warrant aggressive therapy.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

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<tr>
<th>Abbreviation</th>
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<tr>
<td>FHI</td>
<td>Fibrous hamartoma of infancy</td>
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<tr>
<td>CT</td>
<td>Computed tomography</td>
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<tr>
<td>MR</td>
<td>Magnetic resonance</td>
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<tr>
<td>FISH</td>
<td>Fluorescence in situ hybridization</td>
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<tr>
<td>PDGFβ</td>
<td>Platelet Derived Growth Factor Subunit B</td>
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<tr>
<td>ETV6</td>
<td>ETS Variant Transcription Factor 6</td>
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<tr>
<td>NTRK</td>
<td>Neurotrophic Tyrosine Kinase</td>
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Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

References