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CASE REPORT

Benign fibrous hamartoma of infancy: a case of MR imaging paralleling histologic findings

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Abstract Fibrous hamartoma of infancy is a rare fibrous tumor of the subcutaneous tissue in infants. While most case reports focus on the unique histologic appearance, which has traditionally been relied upon for diagnosis, there are few reports in the radiology literature of its appearance at MR imaging. In this report, the authors present the case of a 9-month-old male who presented with a soft tissue mass on the shoulder. The MRI findings in benign fibrous hamartoma of infancy parallel the three components of the lesion seen histologically, with an organized arrangement of fat interspersed among heterogeneous soft tissue bands composed of mesenchymal and fibrous tissue. When present, this characteristic appearance may allow the diagnosis to be suggested preoperatively.

Keywords Benign fibrous hamartoma of infancy · Magnetic resonance imaging · Pediatric fibrous tumors

Introduction

Fibrous tumors represent 12 % of the soft tissue tumors in the pediatric population, fourth in frequency following tumors of vascular, neural, and rhabdomyomatous origin [4]. Fibrous hamartoma of infancy accounts for 5 % of the fibrous soft tissue tumors in the pediatric age group, 0.5–0.6 % of overall soft tissue tumors, and was initially described in a 1956 case series by Reye [4, 11, 20]. The clinical description and the histologic characteristics were later refined in a larger case series by Enzinger, in which the name fibrous hamartoma of infancy was coined [8]. In these initial case series, as well as in subsequent ones, these tumors most frequently occur in otherwise healthy males under 1 year old [2, 5, 6, 8, 18]. The majority of lesions occur above the waist with a predilection for the shoulder girdle. No familial cases have been reported. While the etiology was initially theorized to be a reparative process [8], the results of more recent cytogenetic analyses, identifying genetic translocations, point to a true neoplasm arising from a monoclonal cell origin [21].

In the initial report of six cases, Reye described the characteristic histologic appearance and came to the conclusion that "one good-sized section from any one of them represents the histologic structure of them all [8]." The MRI findings in our case, as well as those presented in the literature, correlate with the pathology findings, showing a characteristic imaging appearance, which may suggest the diagnosis preoperatively.

Case report

An infant male presented at 9 months of age with a mass on his right shoulder. The mother initially noticed the mass at 7.5 months, at which point it was described as the size of a marble. The patient was brought to medical attention as the mass had been slowly enlarging, but did not seem to be painful. The child had a history of pneumonia at 7 months of age but was otherwise healthy, without a history of trauma. At the child's initial clinical visit the mobile mass was 5 × 3 cm with overlying skin hyperpigmentation. An MRI was ordered for further characterization.

The MRI demonstrated a non-encapsulated complex mass in the superficial soft tissues of the dorsal shoulder measuring 4.5 cm in maximal dimension (Fig. 1). T1-weighted images

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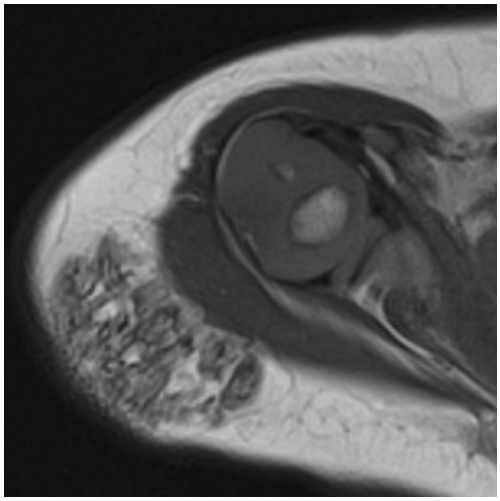

Fig. 1 Axial T1-weighted image (TR 770, TE 25) demonstrates a non-encapsulated mass with interspersed fat and soft tissue strands. The soft tissue strands demonstrate central hyperintensity and peripheral hypointensity relative to skeletal muscle

revealed fat interspersed with strands of soft tissue in an organized fashion. The soft tissue strands had a heterogeneous pattern of signal intensity and enhancement, with a larger central portion and a smaller peripheral portion. The central portion of the soft tissue strands demonstrated T1 hyperintensity, STIR isointensity, and hypoenhancement relative to skeletal muscle (Figs. 2 and 3). In contrast, the thinner peripheral portion was T1 hypointense, STIR hyperintense, and enhancing. The soft tissue strands were oriented in a parallel fashion, perpendicular to the humerus and the skin surface. The mass extended deep to contact the deltoid muscle, which was normal in appearance. There was no cutaneous thickening or edema-like signal in the adjacent subcutaneous fat.

The mass was excised through an 8-cm elliptical incision. The mass was readily removed from the deltoid muscle and

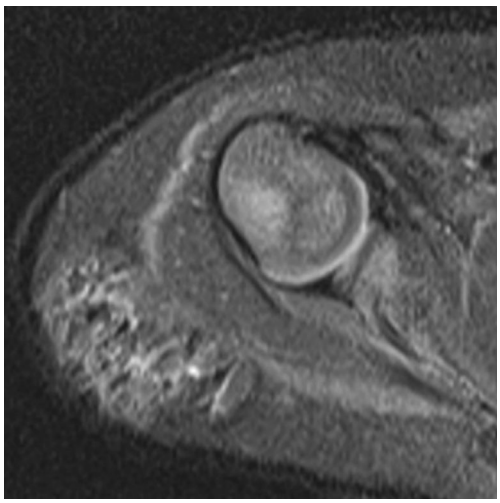

Fig. 2 Axial STIR image (TR 4,480, TE 200, TI 140) demonstrates suppressed signal from the fatty component of the mass along with soft tissue strands that are centrally isointense and peripherally hyperintense

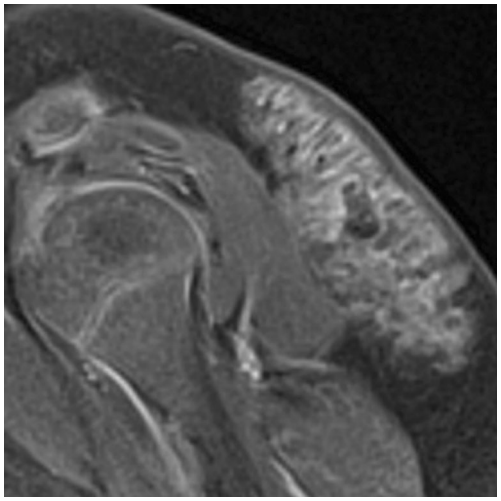

Fig. 3 Oblique sagittal T1-weighted, fat-suppressed post-contrast image (TR 719, TE 9) demonstrates the mass in the subcutaneous tissues abutting the deltoid muscle, with soft tissue strands oriented perpendicular to the long axis of the humerus and the skin surface. The soft tissue strands demonstrate peripheral enhancement with hypoenhancing tissue centrally. The interspersed fat signal is suppressed

sent for pathologic evaluation. On gross sectioning, the mass was poorly demarcated with a yellow coloration and interspersed fibrous bands (Fig. 4). Histologic evaluation confirmed the suspected diagnosis of fibrous hamartoma of infancy with the presence of intersecting fascicles of fibrous tissues, immature mesenchyme, and mature adipose tissue (Fig. 5). Multiple surgical margins were positive. At 1-month follow-up, he was recovering well with a minor defect in the subcutaneous tissues.

Discussion

Benign fibrous hamartoma of infancy presents as a non-painful, mobile mass that has been noted to be present since birth in 23 % of cases [5]. Skin changes superficial to the mass

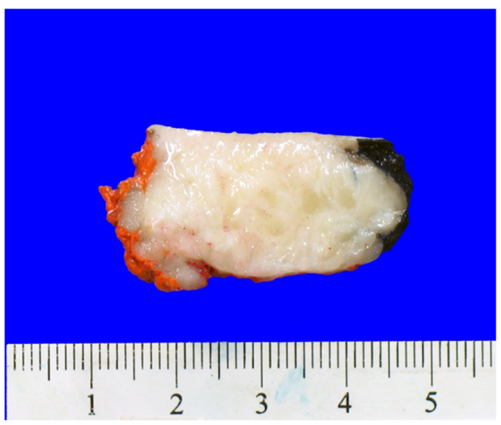

Fig. 4 Fibrous hamartoma of infancy displays white to yellow cut surfaces. The lesion is poorly circumscribed

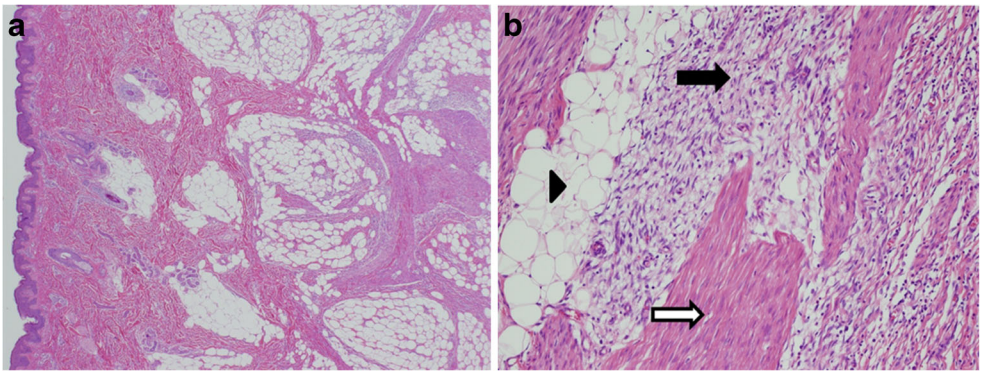

Fig. 5 **a** Fibrous hamartoma of infancy is a subcutaneous lesion that displays a characteristic triphasic appearance with interlacing bands of fibrosis, interspersed mature adipose tissue, and immature mesenchymal tissue (hematoxylin and eosin [H&E] low magnification). **b** Fibrous bands (*open arrow*) are composed of spindle myofibroblasts and fibroblasts. Sheets of small spindle or stellate cells within a loose myxoid stroma are characteristic of the immature mesenchymal component (*closed arrow*). Mature adipose tissue (*arrowhead*) is present (H&E high magnification)

including hyperpigmentation and increased coarse hair may occur [5, 8, 10, 14]. The tumor may have a period of rapid initial growth but if left untreated stops growing by the age of 5 years, without subsequent regression [2, 6, 8]. Lesions up to 20 cm in diameter have been reported [6], however more commonly they range from 1 to 8 cm. The lesion is most frequently singular, however synchronous and metachronous lesions have been reported [8, 10, 15]. Surgical excision is the treatment of choice with cure being achieved by a combination of sub-total and repeat excisions as necessary to avoid disfiguring surgeries [2]. Other sources recommend the use of intra-operative frozen sections to ensure clear margins [10]. The local recurrence rate is low, ranging from 12 to 16 %, with no evidence of metastases [5, 8].

Macroscopically, the lesion is a poorly demarcated superficial soft tissue mass. The cut surfaces are yellow with pale white fibrous bands [3]. Microscopic evaluation consistently reveals a mixture of three tissue types in varying proportions; well-defined bundles of dense fibrous connective tissue, primitive mesenchyme (organized in nests, concentric whorls, or bands), and interposed mature adipose tissue [5]. These findings are well illustrated histologically in the presented case. The immunohistochemical profile of fibrous hamartoma of infancy is relatively nonspecific and does not usually contribute to making the pathologic diagnosis, however it may be helpful in atypical cases. Although a recurrent cytogenetic abnormality has not been identified, there are case reports of several different chromosomal rearrangements [22]. The differential diagnosis based on the dominant histologic feature includes fibrolipoma, lipoblastoma, lipofibromatosis, myofibroma, and cellular schwannoma. Large or rapidly growing lesions may also raise concern for malignant neoplasms such as infantile fibrosarcoma and rhabdomyosarcoma. Careful microscopic examination for the presence of the three different tissue types, as well as consideration of the clinical presentation, differentiates fibrous hamartoma of infancy from the other diagnoses. A recent pathology review reported that fibrous hamartoma occurs in atypical locations in 50 % of cases (outside shoulder girdle or upper back), and also demonstrates a pseudoangiomatous pattern in an additional 50 % of cases [22].

The three different tissue types seen at histology contribute to the MRI appearance. The interspersed fatty components are easily decipherable on T1-weighted images. In our case, the soft tissue strands were heterogeneous and demonstrated two dominant zones based on signal and enhancement characteristics; areas of central T1 hyperintense, STIR isointense, and hypoenhancing tissue as well as a smaller area of peripheral T1 hypointense, STIR hyperintense, enhancing tissue. These soft tissue strands consist of a mixture of the mesenchymal and fibrous components as demonstrated pathologically. Fibrous lesions demonstrate variable signal intensity and enhancement depending on the level of cellularity within the fibrous component, although the presence of STIR hypointense or isointense signal can be helpful in distinguishing fibrous tissue from other types of tissue [17]. Immature mesenchyme has no particular MR signature regarding its signal characteristics and enhancement. However, the mesenchymal cells are embedded within a myxoid stroma, and as such STIR hyperintensity within the mesenchymal component is likely. The source of the enhancing tissue in fibrous hamartoma is not entirely clear as fibrous and mesenchymal tissue can both enhance, as can pseudoangiomatous tissue. It should be noted that no pseudoangiomatous tissue was identified pathologically in this case. The variable appearance of the mesenchymal and fibrous tissue, as well as their interspersed nature potentially allowing both to be present within a single imaging voxel, may limit the ability of MRI to discretely pinpoint the two different components. However, the heterogeneous appearance of the soft tissue strands, particularly on STIR sequences, along with the presence of fat in the lesion, can be helpful for suggesting the diagnosis.

The morphology of fibrous hamartoma, with multiple parallel soft tissue strands oriented perpendicular to the skin surface, is also suggestive of the diagnosis. Small skin ligaments, also known as retinacula cutis, are located throughout the superficial fat. These skin ligaments are small fibrous septa that serve to connect the dermis with the underlying deep fascia at the surface of the muscle [16]. They are thus oriented in a parallel fashion to each other, perpendicular to the skin surface. Given the noninvasive nature of fibrous hamartoma, the lesion may respect the boundaries of these small fibrous septa and thus grow in the same orientation, perpendicular to the skin surface. Skin ligaments function to provide anchorage of the skin and are thus in higher abundance in areas subjected to higher forces such as the upper and lower extremities, with few skin ligaments in the abdominal wall and buttocks and an increased number in the hand and foot. This variable distribution of the skin ligaments throughout the body could lead to the different appearances of fibrous hamartoma of infancy.

While many pediatric soft tissue tumors have a nonspecific imaging appearance, identification of fat within a soft tissue mass allows the radiologist to significantly narrow the differential diagnosis. The interspersed fibrous and fatty components of fibrous hamartoma of infancy distinguish it from other fibrous lesions common in the pediatric population such as nodular fasciitis, myofibroma, superficial fibromatosis, or fibrosarcoma [11, 19, 24]. In a pediatric population the differential diagnosis of fat-containing masses includes hemangioma, lipoblastoma, lipoblastomatosis, liposarcoma, lipomatosis of nerve, and fat necrosis [11, 24]. Hemangiomas have a heterogeneous imaging presentation and may be poorly marginated or well circumscribed with high T2 signal in the vascular components, an infiltrative growth pattern, prompt enhancement, and interspersed fat [11]. The T2 hyperintensity of hemangioma differentiates it from the foci of T2 hypointense fibrous tissue in fibrous hamartoma of infancy. Lipoblastoma, and more rarely pediatric liposarcoma, present as encapsulated masses with enhancing components in contrast to the nonencapsulated appearance of fibrous hamartoma of infancy [11]. While lipoblastomatosis is generally nonencapsulated, the STIR hypointense fibrous components and organized pattern with strands perpendicular to the skin surface would be atypical for lipoblastomatosis. Lipomatosis of nerve occurs in the expected locations of major nerves and demonstrates fascicles and supporting tissues within a fatty mass, which would not be expected for fibrous hamartoma of infancy [11]. Imaging features of fat necrosis are heterogeneous but typical features include a non-mass-like subcutaneous lesion overlying a bony prominence, potentially with a fatty component [24]. These lesions tend to be smaller than fibrous hamartoma of infancy and are directly under the skin; they are most commonly seen in the pretibial and gluteal regions.

Following the initial description by Loyer et al., follow-up case reports in the radiology literature focused on rare locations such as the wrist and knee, but in both of these cases, the MR appearance was less characteristic [1, 23]. There have been brief descriptions of fibrous hamartoma of infancy in the radiology review literature although many of these imaging examples are from older MRI equipment, which does not characterize the typical tissue variation of the lesion as well as is seen in the current case [11, 12, 19]. Some of these older examples utilized conventional non-fat-saturated T2 images, making it difficult to separate fat from a T2 hyperintense soft tissue component as seen in the current case on STIR images, thus making the heterogeneity of the soft tissue component less apparent. Of the eight additional cases with MR imaging in the radiology literature, macroscopic fat has been identifiable in all cases, narrowing the differential diagnosis. With the inclusion of the presented case, five of the nine cases have soft tissue bands oriented perpendicular to the skin surface. These cases all occurred in the typical locations of the shoulder and upper back [7, 12, 14, 19] where there is a regular pattern of the skin ligaments. All of the cases without an organizational pattern perpendicular to the skin surface occurred in atypical locations such as the wrist, prepatellar region of the knee, lower back, or abdominal wall [1, 9, 13, 23] where skin ligament anatomy is more variable. Enhancement characteristics were not described for the majority of the lesions. In cases with available post-contrast images, the enhancement pattern was heterogeneous in three [1, 13, 23], and minimal or absent in one [9]. There was particularly marked enhancement of the knee prepatellar lesion [1], although this lesion was atypical as it had eosinophilic infiltrate seen histologically that had not been previously reported.

In a recent retrospective review on the ultrasound appearance of fibrous hamartoma of infancy in 13 patients, all patients had masses with a heterogeneously hyperechoic appearance and what was described as a “serpentine pattern”. However, the authors note that in a review of other cases compiled from the literature, a homogeneously hyperechoic pattern was seen in four cases, and the authors also stated that MRI could potentially be needed to further evaluate the lesion in unclear cases [13]. The findings of Lee et al. are helpful in documenting the ultrasound characteristics of the lesion, as this is often the first test ordered in pediatric soft tissue masses. However, while the sensitivity and specificity of MRI are unknown, the currently presented case and the rare earlier MRI cases in the literature demonstrate that MRI likely remains the imaging modality of choice for suggesting the diagnosis. Ultrasound may be able to distinguish the fatty from soft tissue components in some cases, but would have difficulty distinguishing the fibrous and mesenchymal components of the lesion.

The imaging features of fibrous hamartoma of infancy mirror the histologic findings, with discrimination of fatty,

fibrous, and mesenchymal elements by MRI imaging. These characteristic imaging findings and the knowledge of the clinical characteristics may allow the radiologist to suggest the diagnosis in the pre-operative setting. While the diagnosis is ultimately made following surgical excision, the ability to suggest the diagnosis based on the imaging characteristics adds value by allowing the clinicians to reassure the family of the benign nature of the tumor and prevents aggressive and potentially disfiguring wide resection.

Conflict of interest The authors declare that they have no conflicts of interest.

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