Umbilical fibrous hamartoma of infancy: a case report

Hamartoma fibroso de la infancia umbilical: reporte de un caso

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Received: 7-5-2018; Approved: 15-7-2018

Abstract

Introduction: Fibrous hamartoma of infancy (FHI) is a benign, soft tissue tumor that usually occurs in children and has a characteristic histological morphology. Objective: To describe a case of congenital FHI with atypical histological and clinical characteristics. Clinical case: Full-term male newborn, with no perinatal morbid history was referred to dermatology due to a congenital erythematous plaque in the umbilical region. The histological study showed a fusocellular proliferation in dermis and hypodermis of biphasic distribution, with an infiltrative, swirling pattern and bundles of spindle fibroblast-like and myofibroblast-like cells, associated in depth with a mature adipose tissue component. The immunohistochemical study revealed diffuse positivity for CD34, and focal positivity for FXIIIa, without immunoreactivity for actin, desmin, MyoD1, S100, HMB45, Melan-A, or EMA. Fluorescent in situ hybridization (FISH) was negative for platelet-derived growth factor receptor beta (PDGFR-beta) and for ETV6 gene. PDGFR-beta and ETV6 gene are present in congenital dermatofibrosarcoma protuberans and infantile fibrosarcoma, respectively. This history, in addition to previous histological findings, supported the diagnosis of FHI. Surgical resection was performed, without signs of recurrence during clinical follow-up. Conclusion: It is important to consider the FHI within the differential diagnosis of subcutaneous tumors in children, especially in those under two years of age. Although its behavior is benign, it is similar to multiple benign and malignant lesions, which makes it imperative to perform a histological study in front of suspicious clinical lesions.

Keywords:  
Fibrous hamartoma of infancy; congenital; umbilical; soft tissue tumour

Versión in press ID 735-ing
**Introduction**

Soft tissue tumors in children are diverse and often complex diagnostic entities. Therefore, an exhaustive clinical evaluation with a complete histological study is essential to differentiate the diverse entities and thus to establish an accurate treatment and prognosis.

Fibrous hamartoma of infancy (FHI) is an uncommon benign fibroproliferative tumor with a characteristic three-phase morphology. It was first described by Reye in 1956 as a subdermal fibrous tumor of infancy and was renamed by Enzinger in 1965 with the current name. The WHO classification of soft tissue tumors defines it as a fibroblastic/myofibroblastic tumor poorly defined, with a characteristic histologic pattern.

It usually occurs before the age of two as a single, asymptomatic lesion located in the subcutaneous cellular tissue or in the reticular dermis, and it is difficult to differentiate from adjacent healthy tissue. Due to its similarity with several entities, its diagnosis must be confirmed by a histological and immunohistochemical study. However, these methods may have limitations since their findings are sometimes unspecific.

Although nearly 200 cases have been published in the international literature to date, there are few reports in the Latin American population. The objective of this study is to describe a case of congenital FHI in an infant, with atypical clinical and histological characteristics, where additional molecular studies were needed to differentiate it from other skin conditions.

**Clinical case**

Full-term male newborn, controlled pregnancy, eutocic delivery, with no perinatal morbid history. He was referred to the dermatology department due to a slightly infiltrated erythematous plaque in the peri and infra-umbilical region which was present since birth, with well-defined borders and adherent superficial yellowish peeling at the lower pole, without other local inflammatory signs. A skin ultrasound study revealed homogeneous hypoechoic dermoepidermal lesion, with slight extension to the subcutaneous tissue and few sinuous vessels in its deepest segment.

Given the clinical characteristics, a deep incisional biopsy was performed which showed proliferation of thin fusiform cells in dermis and hypodermis, of biphasic morphology with one segment arranged in a infiltrate swirling pattern and another one with fused cell bands with fibroblastic and myofibroblastic appearance, and with absence of Grenz zone. It presented in depth a component of mature adipose tissue with no signs of atypia (Figure 3). Mature epidermis, partially atrophic. There was no atypical necrosis or mitosis. The immunohistochemical study of the tumor cells showed intense and diffuse positivity for CD34 and focal FXIIIa positivity, with the absence of immunoreactivity for actin, desmin, MyoD1, S100, HMB45, MelanA, and EMA. Moderate Ki-67 proliferation index, with positivity in approximately 20% of cells. The study was complemented with FISH using PDGF beta and ETV6, which were negative, excluding differential diagnoses of congenital dermatofibrosarcoma protuberans and infantile fibrosarcoma, respectively. These antecedents, along with the histological findings, were consistent with the diagnosis of FHI.

Surgical extirpation was performed by the pediatric surgery team, with umbilical readjustment through lateral rotation flaps. The histological and immunohistochemical study supported the previously described findings, compromising margins of surgical resection. The patient evolved without signs of recurrence at seven months of follow-up (Figure 5).
Discussion

FHI most frequently affect males, generally occurring during the first two years of life, with an average age ranging from 15 and 18 months. Although congenital lesions have been described as in our case, they represent between 4-23% of the total according to various reports. It does not show family history and it is not related to other neoplasms or congenital disorders.

Currently, there are controversies regarding the origin of this entity. Cytogenetic abnormalities involving different chromosomes have recently been identified, supporting the theory that FHI is a neoplastic rather than a hamartomatous process.

Classically, it is presented as a single, mobile, small, poorly limited, asymptomatic, skin-colored, firm nodule with no associated epidermal changes. It is located mainly in armpits, back, and upper extremities. Although most patients share the described characteristics, multiple lesions and changes in adjacent skin have been reported, such as alteration in pigmentation, hyperplasia of eccrine glands, and hypertrichosis. It is interesting in our case the observed epidermal changes, as well as the anatomical location. Generally, the FHI increases in size up to five years and then slows its growth, but without stopping or regressing. On the other hand, there are reports of accelerated growth during childhood. However, it is important to note that in most of the published series a smaller percentage of patients have completed clinical follow-up.

Histologically, the tumor may be subcutaneous or adhered to the dermis. It is characterized by a variable three-phase component of mature fibroblastic-myofibroblastic tissues, immature mesenchymal and mature adipose tissues, frequently associated with chronic inflammatory infiltrate. These components vary in proportion but maintain a uniform general morphology. It
has no mitosis or necrosis. It is important to highlight the existence of areas of dense collagen, fissures, and pseudoangiomatosis in a significant percentage of FHI, typically positive for CD34, which may simulate other soft tissue tumors and need the use of complementary examinations. Immunohistochemistry allows the identification of antigens in a particular tissue through the use of specific antibodies, which are then visible under the microscope due to chemical reactions. The FHI has non-specific immunohistochemical characteristics and is similar to other fibroblastic-myofibroblastic tumors. This component shows positivity for vimentin and smooth muscle actin, being able to show focal CD68 reactivity, desmin and Factor XIIIa. Mature adipose tissue may show positivity for S100 protein, whereas primitive mesenchymal tissue is hardly reactive for vimentin, showing occasional focal staining for actin and desmin. The presence of pseudoangiomatous foci typically CD34 reactive is also described, but they are negative for more specific endothelial markers such as CD31 and podoplanin. On the other hand, the presence of CD34 correlates with well-vascularized tumors, while Ki-67 shows variable reactivity in the immature mesenchymal component and pseudoangiomatous.

The FISH technique is a cytogenetic study that allows the evaluation of chromosomes through fluorescence emission. In our case, given the histological similarity with congenital dermatofibrosarcoma protuberans, FISH was requested for PDGF beta-receptor, which reinforced the diagnosis of FHI, as well as in the literature. In addition, the study was complemented with FISH for ETV6 present in infantile fibrosarcoma, which was also negative.

The use of nuclear magnetic resonance as a complementary diagnostic element has recently been reported, showing an organized fat-like structure with heterogeneous soft tissue interleave bands.

The differential diagnosis depends on the dominant tissue component, which includes benign tumors such as lipomas, neurofibromas, dermatofibromas, lymphadenopathies, and vascular malformations, as well as malignant tumors such as lymphomas or sarcomas.

The treatment of choice is a surgical removal, although sometimes it is not possible due to cosmetic and/or functional implications. A recurrence rate of approximately 15% has been reported secondary to incomplete resections. Although it does not remit spontaneously, there are no cases of malignancy described.

Conclusions

As physicians, it is important to consider FHI within the differential clinical and histological diagnosis of childhood subcutaneous tumors, especially in patients under two years of age and those located in the armpit, the back, and the upper extremities.

Although its behavior is benign, its location, size, and similarity with malignant lesions generate anxiety in the family group, which makes it necessary to maintain a good therapeutic link, always highlighting the need for histological, immunohistochemical, and molecular biological studies to differentiate it from other entities.

Despite the fact that surgical extirpation is the treatment of choice, we must consider the functional and/or cosmetic implications involved, which may require a therapeutic approach along with surgeons, pediatricians, and dermatopathologists, which was our case.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.
Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure
Authors state that no economic support has been associated with the present study.

Conflicts of Interest
Authors declare no conflict of interest regarding the present study.

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