Fibrous hamartoma of infancy: An Italian multi-institutional experience

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Background: Fibrous hamartoma (FH) of infancy is a benign mesenchymal tumor, occurring as a superficial mass. Complete excision is curative.

Objective and Methods: The clinical features and treatment results of 18 children with FH are described.

Results: Local excision was the most common procedure. Surgery was radical in 10 patients, with microscopic residual disease in 6; all of them are alive with no evidence of disease 2 to 49 months after diagnosis. One patient, treated with a local reexcision for macroscopic residual disease (and chemotherapy for a synchronous desmoid fibromatosis) is well 83 months after diagnosis; the last patient, with a lesion of the labia majora, only underwent biopsy and is doing well, awaiting plastic surgery.

Limitations: The results did not reach statistical significance due to difficulties in collecting cases.

Conclusions: FH should be treated by complete excision; in our experience a nonradical excision was also able to achieve the cure. An aggressive approach should be avoided, as the overall prognosis is excellent. (J Am Acad Dermatol 2006;54:800-3.)

Fibrous hamartoma (FH) of infancy is a mesenchymal tumor of myofibroblastic derivation; it was first described by Reye[1] in 1956 as a subdermal fibromatous tumor of infancy and by Enzinger[2] in 1965 as "fibrous hamartoma of infancy." It is an uncommon, benign, subcutaneous fibrous proliferation, usually detected during the first 2 years of life. Approximately 15% to 20% of FH cases are present at birth.[3] Male infants are more frequently affected than female infants. FH is usually solitary; limbs, trunk, the sacral region, and scrotum are the most common sites. The lesion is characterized by rapid initial growth,[4] but generally it does not cause any symptoms. The clinical and radiologic features are quite similar to those of malignant soft tissue sarcomas, and the definitive diagnosis may be achieved only by histologic evaluation. Complete local excision is curative and the recurrence rate is less than 15%.

We evaluated a group of patients whose data were collected from 6 centers of pediatric surgery and pediatric oncology, with the aim of obtaining information on their tumor characteristics, treatment, and outcome.

PATIENTS AND METHODS

The patients were 14 male and 4 female children, whose age at the time when the lesion was first noticed ranged from birth to 11 years (median, 12.5 months). All the FH cases were solitary; they were located on limbs (9 patients), sacral region (2), scrotum (2), trunk (3), head and neck (1), and vulva (1). Seventeen children were healthy at the moment of diagnosis, whereas one patient was affected by desmoid fibromatosis of the hand. The clinical features of the patients as well as treatment results are summarized in Table I.

The lesion was characterized by rapid initial growth, and its appearance was that of a solid mass, strictly adherent to subcutaneous tissue. The size

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Table I. Clinical features and treatment results

Patient no.	Sex	Site	Time between onset and treatment	FNAB	Size (cm)	Presence of capsule	Age at surgery (mo)	Type of surgery	LR	Further treatments	Outcome	FU (mo)
1	M	Trunk		No			14	Radical	No	No	RC (1°)	
2	F	Sacral region		No			16	Radical	No	No	RC (1°)	
3	M	R arm	2 y	No	2.5 × 2.5 × 1.2	Yes	32	Radical	No	No	RC (1°)	38
4	M	R hemiscrotum	1 y	No	3.5 × 3.5	Yes	26	Radical (partial right hemiscro-tectomy)	Yes (after 12 mo)	Excision of residual scrotum	RC (2°)	66
5	F	L arm	20 days	No	3.5 × 1.5 × 2.5	Yes	8	Radical	Yes (after 18 mo)	Reexcision	RC (2°)	115
6	M	L leg	1 y	No	3		121	Microscopic residual	No	No	RC (1°)	49
7	M	Sacral region	1 day	No	5.5 × 3	No	Birth	Radical	No	No	RC (1°)	79
8	M	H-N		No	4 × 3	No	52	Radical	No	No	RC (1°)	118
9	M	L arm		No	7 × 3		6	Microscopic residual	Yes (after 2 mo)	Reexcision with microscopic residual	RC (2°)	2
10	M	L arm	3 mo	Yes	4.5 × 2.5		11	Microscopic residual	No	No	RC (1°)	4
11	M	L arm		No			17	Radical	No	No	RC (1°)	
12	F	Labia majora		No			136	Macroscopic residual (biopsy)	Yes	No	AWD	38
13	M	R arm		No		No	9	Microscopic residual	No	No	RC (1°)	33
14	M	L hemiscrotum	8 mo	No	2	No	9	Radical (left hemiscro-tectomy)	No	No	RC (1°)	92
15	M	Trunk	4 mo	No	2.5 × 1.5	No	24	Macroscopic residual	Yes (after 3 mo)	Reexcision and CT	AWD	83
16	M	L arm	1 mo	Yes	2.4 × 1.6 × 1	No	8	Microscopic residual	No	No	RC (1°)	4
17	F	R arm		No			4	Radical	No	No	RC (1°)	
18	M	Trunk	5 mo	No	3.0 × 1.8 × 1		11	Microscopic residual	No	No	RC (1°)	

AWD, alive with disease; *CT,* chemotherapy; *FNAB,* fine-needle aspiration biopsy; *FU,* follow-up; *H-N,* head and neck; *L,* left; *LR,* local relapse; *L,* left. *R.* right; *RC (1°),* first complete remission; *RC (2°),* second complete remission.

ranged between 2 and 7 cm, and in none of the cases was there a tendency to spontaneously regress.

Clinical examination showed a tender, nonpainful mass, sometimes difficult to distinguish from deeper fascial tissues. Overhanging skin was normal. Ultrasonography showed that the mass was characterized by undefined margins and a heterogeneous echogenicity. No other radiologic investigations were considered useful.

In 2 patients diagnosis was obtained by a fine-needle aspiration biopsy: the examination yielded moderate cellularity, loosely lying and clustered fibroblastic-appearing cells, fatty tissue, and collagenous material without evidence of significant nuclear atypia or mitoses. All histologic specimens were reviewed by the national panel for soft tissue sarcomas. Hematoxylin-eosin–stained sections were reevaluated and a complete immunohistochemical

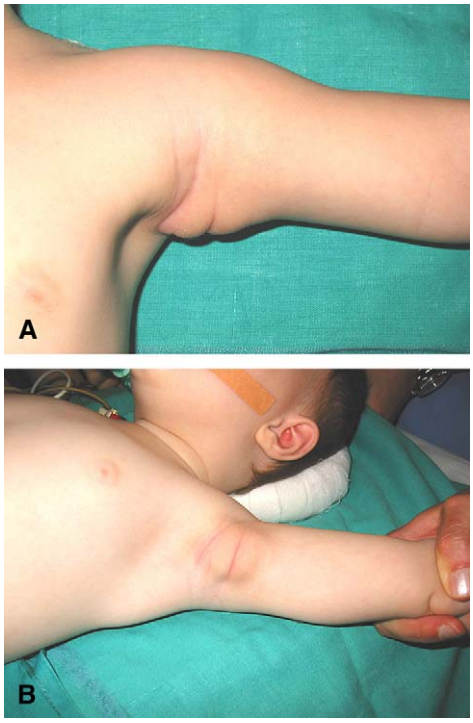

Fig 1. **A** and **B**, Case 16. Clinical appearance of FH.

panel (including smooth muscle actin, desmin, S-100 protein, and CD34) was performed.

RESULTS

All patients underwent surgery. The operation was complete in 10 patients; two of them, one of whom had a local relapse after 12 months and the other after 18 months, underwent local reexcision, and radicality was achieved. All the patients subsequently maintained complete remission with a follow-up period of 38 to 118 months (median, 85.5 months) from diagnosis. In 6 cases the resection was macroscopically radical but microscopic residuals were found at histologic examination; one patient underwent a reexcision after 2 months because of local relapse, without achieving radicality. No relapse was observed either in this or in the other 5 cases at follow-up (range, 2-49 months; median, 4 months). In one patient, who was also affected by desmoid fibromatosis of the right hand, macroscopic residuals were left after the first surgical operation on an FH of the trunk; the patient was treated 3 months later with a local reexcision (which left microscopic residual disease); he also had chemotherapy (vincristine, doxorubicin [Adriamycin], dactinomycin, cyclophosphamide, and methotrexate) for the desmoid fibromatosis; he is alive with disease 83 months after diagnosis. Finally, a large biopsy was performed in one girl with a lesion in the labia majora. At present the patient has stable disease and is waiting for definitive plastic surgery (follow-up, 38 months).

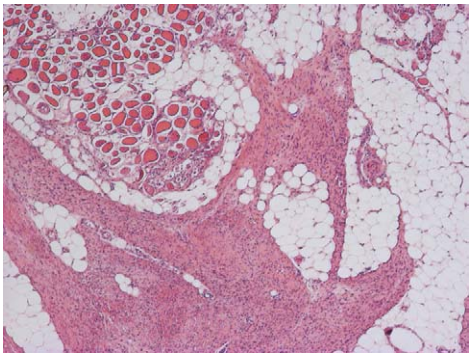

Fig 2. Case 16. Histologic appearance of hamartoma. Typical organoid pattern with adipose component, dissecting striated muscle, and fibroblastic proliferation in fascicles. (Hematoxylin-eosin stain; original magnification: ×80.)

The histologic examinations demonstrated a typical organoid lesion, with a mixture of fat, mature myofibroblasts arranged in fascicles, and immature mesenchymal cells, sometimes forming highly cellular nodules. The proportion of the single components was variable in the different cases, generally with a predominance of fat and myofibroblasts. The diagnosis was generally not difficult with hematoxylin-eosin staining, in the cases in which a wide surgical biopsy was provided. In one case, a previous diagnosis of fibromatosis was given; the biopsy specimen was small, represented only by a myofibroblastic component with an infiltrative growth pattern in the fat tissue at the periphery. The histologic examination of the additional surgical specimen showed the typical triphasic pattern of FH. In all cases a focal positivity for smooth muscle actin was demonstrated at immunohistochemistry. Desmin and S-100 stains were consistently negative.

DISCUSSION

FH of infancy is an uncommon benign lesion with a characteristic histologic appearance; it usually occurs as a small, rapidly growing, superficial soft tissue swelling, developing in the first 2 years of life. The majority of our patients were infants, as described in the literature. The affected children are generally healthy and association with other neoplasms or congenital malformations has not been reported.[5] Although the shoulder girdle area and upper arm are the favored locations, FH may occur anywhere in the body.[6-8] The most common site of the lesion in our series, as in others[5,9] was the upper arm (Fig 1). Most of the lesions are usually small, although masses as large as 10 cm have been

reported.[1,4,9,10] A published clinical photograph of one case showed multiple coarse hair over the surface of the lesion, which had been previously unreported.[11]

Ultrasonography reveals a mixed echogenicity that may be suggestive of hemangioma, lymphangioma, or lipoma. Generally no other radiologic investigations are recommended.[8]

The main diagnostic problem for these lesions concerns the differential diagnosis with other soft tissue masses, which require a different clinical and therapeutic approach. Fine-needle aspiration biopsy may be an useful tool in recognizing the myofibroblastic nature of the lesion,[12] but only histology can disclose the typical organoid pattern that is a clue to the diagnosis, together with the immature mesenchymal component (Fig 2). The most important differential diagnosis is represented by infantile fibromatosis, a locally aggressive lesion, characterized by a myofibroblastic proliferation, sometimes with features of immaturity and devoid of the organoid pattern.

The treatment of choice for FH of infancy is local excision[2,3,13,14] with an envelope of normal tissue because of its deep spread and occasional presence of nearby lesions. The rationale for surgery is the progressive growth of this lesion and the necessity to obtain a diagnosis. FH can mimic a soft-tissue sarcoma, and diagnosis might be misinterpreted when the typical organoid and triphasic patterns are not recognized in the small fragments of tissue obtained through a single biopsy.

A radical excision is mandatory to avoid local relapses, which may occur in 12% to 15% of cases, generally within a few months after primary surgery. However, since FH is a benign lesion, minimal residual disease may be accepted in those cases in which complete surgery would imply serious anatomic and functional impairment for the patient.

In our series 2 of 10 patients had a local relapse 12 and 18 months after primary surgery, despite the initial radical excision. On the other hand, 5 of 6 patients with microscopic residuals after the first operation suffered no relapse.

In conclusion, even if a subcutaneous solid, tender mass in a child usually suggests a malignant tumor, physicians need to be aware of the existence of some benign conditions, such as FH of infancy. Diagnosis is easily made because of its characteristic histologic features. FH of infancy should be treated by a local, complete excision. Since recurrence is rare and the overall prognosis is excellent, aggressive, mutilating procedures are discouraged, and repeated, nondestructive resections should be performed. If a conservative re-excision of an FH is not feasible, a strict "wait and see" strategy should be preferred.

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