Solitary Infantile Myofibromatosis: Report of Two Cases

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Infantile myofibromatosis (IM) is an unusual tumor of infancy and early childhood. It typically presents as a solitary or multicentric nodular mass involving skin, soft tissue, bone, or viscera. We describe 2 cases of solitary infantile myofibromatosis (IM) of the soft tissue with typical light microscopic features. The first is a 7-month-old boy who had a rapidly growing tumor of the right thigh. The fragile tumor, measuring 7.0 ¡ 6.0 ¡ 3.5 cm was completely removed, but the patient was lost to follow-up after surgery. The second case, a 2-year-old boy, was referred from a local clinic due to a non-tender mass in the left abdominal wall. The tumor, measuring 2.0 ¡ 2.0 ¡ 1.6 cm, was completely excised. No recurrence or malignant transformation was found after 22 months of follow-up. The histopathologic, histochemical, and immunohistochemical features of the tumors were studied. Reticulin preparation showed that the tumor cells were outside the reticulin sheath of the vascular spaces and were individually enclosed by reticulin fibers. Tests for vimentin, anti-α-smooth muscle actin, and myoglobin were positive in the neoplastic spindle cells. IM has a variable appearance on radiologic images and often mimics an aggressive neoplasm. These factors can make a rapid and correct diagnosis difficult. IM must be considered in the differential diagnosis in any child who presents with either solitary or multiple tumors, particularly those occurring in the neonatal period. *(Chang Gung Med J 2002;25:393-8)*

Key words: infantile myofibromatosis.

Infantile myofibromatosis (IM) is an uncommon mesenchymal disorder of early childhood which manifests by the formation of either solitary or multicentric tumors in the skin, soft tissue, muscle, bone, or visceral organs. It is also the most common fibrous tumor in infancy.[1] This disease entity was initially introduced by Stout[2] in 1954 as "congenital generalized fibromatosis". The term "infantile myofibromatosis" was first coined by Chung and Enzinger in 1981 based on the histological and ultrastructural resemblance of the tumor cells to myofibroblasts and the frequent occurrence of the disorder in both newborns and infants.[3]

According to the clinical presentations, 3 forms of IM have been defined: solitary, multicentric, and generalized.[1,3,4] The solitary form is the most common and affects the dermis, subcutis, deep soft tissue, or muscles of the head, nuchal, and truncal regions. In these cases, the clinical course is benign with little morbidity and almost no mortality. Spontaneous regression is not infrequent.[1,3] The multicentric form tends to affect skin, soft tissues, or bone. The generalized form of IM is less common and is distinguished by visceral involvement in addition to skin, bone, and soft tissue sites. The prognosis is much less favorable when visceral lesions are

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Received: May 4, 2001; Accepted: Nov. 14, 2001
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present.[1,3,4] Microscopically, a typical biphasic pattern with central hemangiopericytoma-like and peripheral leiomyoma-like appearance characterizes this entity.[1,3] Herein we report on 2 typical cases of soft tissue IM. The characteristic clinical manifestations, pathologic and immunohistochemical features, and prognosis are reviewed in order to familiarize physicians with this uncommon entity.

CASE REPORTS

Case 1

The first case is a 7-month-old male infant who had a rapidly growing tumor on the right upper thigh noted for a few days. Physical examination showed a mass of about 7 × 6 × 3.5 cm, located in the subcutaneous region of the right upper thigh and extending to the inguinal area. No skin discoloration, ulceration, or bone involvement was noted. The general physical condition of the patient was excellent, and no abnormalities other than the soft tissue tumor were found. There was no family history of soft tissue tumors. No radiologic study was performed. Complete excision of the tumor was performed.

During the operation, a discrete, fragile mass measuring 7 × 6 × 6 cm with a well-demarcated border was noted. The cut surface was hemorrhagic with blood coagulum. The periphery was more fibrous and grayish white, while the center appeared red and had a softer consistency.

The microscopic patterns consisted of interlacing fascicles of spindle-shaped cells giving a leiomyoma-like appearance, with variable central vascular areas resembling a hemangiopericytoma surrounded by tightly packed, immature-appearing neoplastic cells (Fig. 1). Focal coagulative necrosis, infiltration of the surrounding adipose tissue, and mild chronic inflammatory cell infiltration were present. There was mild focal cellular pleomorphism with 1-2 mitoses/10 HPF throughout the sections. Spindle cells immunostained were positive for vimentin (Fig. 2), anti-α-smooth muscle actin (Fig. 3), and myoglo-

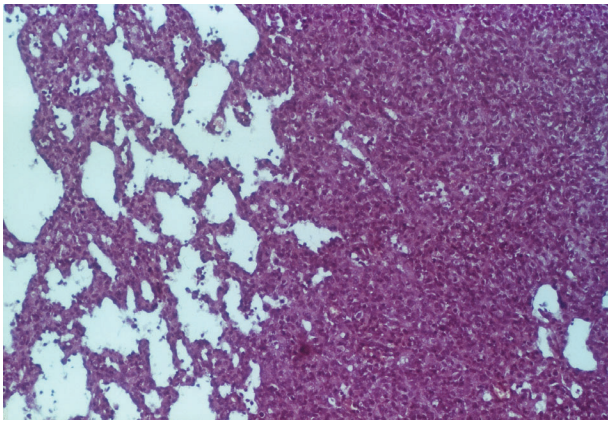

Fig. 1 Central portions of an example of infantile myofibromatosis (case 1) showing a branching hemangiopericytoma-like vascular pattern. The immature perivascular cells have indistinct pale cytoplasm and round, somewhat vesicular nuclei. (H & E, 100 ×)

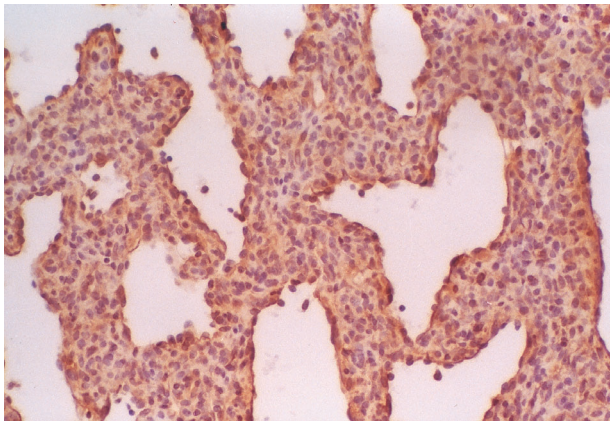

Fig. 2 Majority of the neoplastic cytoplasm positive for vimentin. (paraffin immunohistochemical stain, 200 ×)

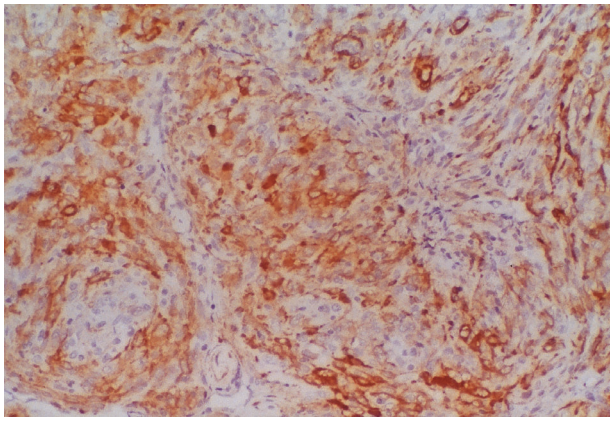

Fig. 3 Neoplastic cytoplasm positive for anti-α-smooth muscle actin. (paraffin immunohistochemical stain, 200 ×)

bin antibodies. Reticulin preparation showed that the tumor cells were outside the reticulin sheath of the vascular spaces and were individually enclosed by reticulin fibers. The patient was not treated further and was eventually lost to follow-up.

Case 2

The second case, a 2-year-old boy, was referred from a local clinic to our pediatric surgical service because he had a non-tender mass in the left aspect of the abdominal wall. According to the patient's medical history, the mass had been noted for several days. The family history was unremarkable. Physical examination showed a firm, well-circumscribed, and freely movable mass with dark red discoloration of the overlying skin. The excised tumor specimen revealed an intramuscular nodular lesion measuring 2 × 2 × 1.6 cm. It was non-encapsulated and relatively well circumscribed. Microscopically, it was composed of whorled fascicles of spindle cells having elongated or cigar-shaped nuclei, and abundant pale eosinophilic cytoplasm. The spindle cells were arranged in interlacing fascicles with scattered collagen bundles and poorly defined boundaries, giving a leiomyoma-like appearance. The central portion of the tumor showed numerous tiny elongated capillaries between the dense bulk of the tumor cells. Mitotic figures were hard to find. Results of the immunohistochemical profile were similar to those of the previous case. He has remained free from tumor recurrence for 22 months after tumor removal.

DISCUSSION

Infantile myofibromatosis is one of the most-common fibrous tumors of infancy and is usually found in the first decade of life with 88% of cases detected before the age of 2 years and 60% at or shortly after birth.[3] Many authors have confirmed the multivariant nature of the disease as lesions have been found in nearly all kinds of tissues, including the bone, lip, oral cavity, central nervous system, gastrointestinal tract, lungs, myocardium, liver, and biliary tree.[3-6] The most common clinical manifestation of IM is the presence of discrete nodules in the skin, muscle, or subcutaneous tissues.[1,3,6] In the skin and soft tissue, they most commonly involve the head and neck region, followed by the trunk and extremities.[3] Due to prominent tumor vascularity, superficial skin lesions may resemble hemangiomas.[3] In its multicentric form, the number of lesions varies from 2 to 100, and they may be mistaken for a metastatic lesion.[1,7] Bone and soft tissue lesions may undergo rapid growth in the early weeks after birth but then regress spontaneously during the first few years of life.[3,8] Although there has been no documentation describing the mechanism of the spontaneous regression of IM, Fukasawa et al.[8] postulated that massive apoptosis was responsible.

Microscopically, both the solitary and multicentric forms have similar characteristic appearances with a distinct zoning pattern.[1,3,6,7] The peripheral areas of nodular lesions are composed of spindle cells arranged in whorled or interlacing fascicles, giving a leiomyoma-like appearance. The constitutive spindle cells demonstrate staining characteristics of both myoblasts and fibroblasts, and frequently contain a large quantity of collagen within the surrounding matrix. In the central areas, a hemangiopericytoma-like pattern consisting of cells with less differentiation is usually found. A high mitotic rate with the presence of up to as many as 3 mitotic figures per 10 high-power field and infiltration of adjacent adipose tissue and skeletal muscle are not unusual but have no adverse prognostic significance. As in our case 1, the hemangiopericytoma-like pattern was more prominent, while in case 2, typical intertwining fascicles of spindle cells were the main feature.

The pathogenesis of these tumors remains unknown, but its association with estrogen receptors has been postulated. Familial occurrence has been reported in all 3 forms of IM in siblings, cousins, and successive generations. Most cases are sporadic, but autosomal recessive, dominant, and polygenic modes of inheritance have been postulated.[9-12] These indicate a need for taking a complete family history in cases with IM. Cytogenetic and florescence in situ hybridization analyses revealed a pseudodiploid karyotype with an interstitial deletion of the long arm of chromosome 6, del[6] (12q15q), which has been the sole anomaly found thus far.[13]

The differential diagnosis for IM includes other types of fibromatosis, congenital infantile fibrosarcoma, infantile hemangiopericytoma, inflammatory myofibroblastic tumors, fibrohistiocytic tumors with

a predominantly fibrous pattern, smooth muscle tumors such as leiomyomas and leiomyosarcomas, neurogenic tumors such as neurofibromas and low-grade malignant peripheral nerve sheath tumors, and nodular fasciitis.[7,14] Most of the other forms of fibromatosis and congenital-infantile fibrosarcomas have distinct clinical and pathologic features. The reported cases of infantile hemangiopericytoma share many clinical and histologic features with IM.[3,6,14,15] Generally, the pericytoma-like element of IM is only present in the center of the tumor nodule and is rarely prominent in the peripheral region.[3] We propose that the purported differences between IM and infantile hemangiopericytoma simply reflect the result of maturation in a single group of myofibroblastic lesions in infancy. Therefore, distinction of IM from infantile hemangiopericytoma is unnecessary and infantile hemangiopericytomas may be best regarded as the more primitive examples of IM.[15]

If there is no visceral involvement, solitary lesions or multiple lesions in infants usually have a benign and self-limited course. The typical course usually ends with spontaneous regression. In the solitary form, the recurrence rate after excision is less than 10%.[1,7] In the multicentric form, when lesions are limited to the skin and bones, the prognosis is excellent; 60% of cases spontaneously regressed during follow-up periods of 1 - 2 years. In a series of 170 patients reviewed by Wiswell et al.,[1] the overall mortality rate for these patients was less than 15%. However, 24 of 33 patients (73%) with the multicentric form of the disorder and visceral involvement died. Death from IM usually occurs as a result of complications, mostly cardiopulmonary or gastrointestinal, and of visceral involvement.[3,6]

Modalities of treatment other than surgery include radiation therapy with limited success, and local glucocorticosteroid injections and chemotherapy, which has been used with some success when all other modalities failed. Surgery is recommended only if vital structures are affected or if tissue is needed for diagnosis. A few patients with recurrent or nonresectable tumors have been treated with some success with a combination of vincristine, actinomycin-D, and cyclophosphamide with or without radiation.[16]

In general, the prognosis of solitary infantile myofibromatosis without visceral involvement is excellent, and spontaneous regression is commonly reported.[1,3,4] It should be considered in the evaluation of newborns or young infants presenting with solitary or multiple tumors. Since visceral involvement has been documented in 25%-37% of patients with multicentric IM,[3,4] careful and complete evaluation of these patients is necessary. The diagnosis should be confirmed histologically, and continuing observation is pertinent, because recurrence has been reported in the literature.[17]

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單發多樣性嬰孩型肌肉纖維瘤：二例報告

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嬰孩型肌肉纖維瘤是一個在嬰兒及兒童早期很罕見的腫瘤。這種個案典型的就是會在皮膚、軟組織、骨頭或內臟形成單一或多發性的腫塊。本報告描述二例軟組織單發多樣性嬰孩型肌肉纖維瘤患者。第一個病例爲一爲7個月大的男孩，其主訴爲右側大腿快速生長的腫瘤，這個大小爲7 ×6 ×3.5 cm的易碎腫瘤，經由手術作完全的切除。第二個病例爲一位兩歲大的男孩，其主訴爲左側腹壁無壓痛性腫瘤，這個腫瘤的大小爲2 ×2 ×1.6 cm，它經由手術作完全的切除。第一位病人在手術之後並沒有追蹤資料，而第二位病人手術之後追蹤二十二個月後並沒有復發或惡性化轉變的情形。這個腫瘤在影像學上有不同的型態，常常酷似一個具侵襲性的腫瘤，這些因素容易造成快速及正確診斷上的困難。因此，我們建議在嬰幼兒時期，無論是單一或多發性的腫瘤，必須考慮嬰孩型肌肉纖維瘤的可能性。(長庚醫誌 2002;25;393-8)

關鍵字：多樣性嬰兒型肌肉纖維瘤。

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