Congenital Localized Multiple Fibromatosis: A Case Report

PITI PALUNGWACHIRA, M.D.*, MASAKO SHIRAI, M.D.**,
KUNIO IWAHARA, M.D.**, HIDEOKI OGAWA, M.D.**

Abstract

Clinical, histopathologic and electronmicroscopic findings in a case of congenital localized multiple fibromatosis of interscapular region are presented. This 10 year-old Japanese girl developed this lesion since she was 3 weeks old, metastases have never been observed. The histological and electron-microscopic features point to the hamartomous origin of this tumor with partial differentiation of its cells towards myofibroblasts and atypical fibroblasts. The differential diagnosis from other soft tissue tumors in infancy and early childhood is discussed.

There are still numerous unresolved conflicts in the literature regarding the nomenclature, behavior, and clinical management of tumors composed predominantly of fibrous tissue in childhood. As defined by Stout and Lattes,(1) the term "fibromatosis" is applied to a group of benign fibroblastic proliferative lesions that are distinguished from the self-limiting scar, and have a propensity to invade locally and recur but not to metastasize(2). Mackenzie,(3,4) has been established with the recognition of two principle subcategories of fibromatoses, those occurring as congenital lesions or diagnosed mainly in childhood and a second group, those that may present at any time during life but are found mainly in adults.

Following is a summary of fibrous proliferations of infancy and childhood.

Classification of fibrous tumors of infancy and childhood.

1. Fibrous hamartoma of infancy
2. Infantile digital fibromatosis
3. Fibromatosis colli
4. Congenital fibromatosis
   a. localized - solitary
      - multiple
   b. generalized
5. Infantile (desmoid-type) fibromatosis
6. Hyaline fibromatosis
7. gingival fibromatosis
8. Calcifying aponeurotic fibroma

* Srinakharinwirot Skin Center, Srinakharinwirot University, Bangkok 10110, Thailand.
** Department of Dermatology, Juntendo University School of Medicine, 1-1, Hongo 2-Chome, Bunkyo-ku, Tokyo 113 Japan.

A fibrous tumor recognized at or soon after birth is properly designed as a congenital fibromatosis. It is a group of connective tissue proliferation which does not fulfil the clinical and pathologic criteria for benign and malignant neoplasias. It was subdivided into localized or generalized form[5-8]. Kindblom et al first described the term congenital localized fibromatosis[9]. Clinically, these lesions may appear as indurated nodules and plaques localized in the dermis or in the subcutaneous tissue. Since there have been only few reports on congenital localized fibromatosis in the dermatologic literature, we would like to describe another one patient whose ultrastructural feature was studied and differential diagnosis from other soft tissue tumors in infancy and early childhood is discussed.

REPORT OF A CASE

A healthy 10-year-old Japanese girl had cutaneous lesions over the left interscapular region. These lesions were asymptomatic and had been present since 3 weeks old without any recongnizable change in appearance. There was no family history of congenital tumors in the rest of her family. There was no signs of other tumors recurrence or metastasis. There was no history of trauma.

On physical examination there was a fibrotic plaque about 5 cm in diameter and also characterized by varying combinations of papules without inflammatory changes (Fig. 1). No similar lesion was found elsewhere on the body.

The general medical examination was otherwise normal. Routine laboratory studies and X-ray examination were normal.

Pathological Investigation

Skin specimens were taken from the papular lesions. They were fixed in 10 per cent neutral-buffered formalin and embedded into paraffin for light microscopy. Tissue sections were stained with hematoxylin and eosin, PAS with or without prior diastase digestion, alcian blue, bodian stain, Verhoeff-Van gieson, Masson's trichome. Some of the specimens were processed for electron microscopy. They were fixed in 2.5 per cent phosphate-buffered glutaraldehyde for 24 hours, post fixed in 2 per cent osmium tetroxide for 2 hours, dehydrated in ascending series of ethanol and embedded in Epon. Thin sections were stained with uranyl acetate and lead citrate. They were examined with a Hitachi. H-500 Electron microscope.

RESULTS

Light Microscopy

Histological sections showed normal epidermis with loss of rete ridge contour. Tumor cells located only in the subepidermal area (Fig. 2). They formed well-circumscribed nodules consisting of elongated or oval fibroblast-like nuclei within a fusiform, faintly eosinophilic, poorly-outlined cytoplasm. Some cells at the periphery of the tumour were immature-looking and a weakly eosinophilic

Fig. 1. Congenital localized fibromatosis on the back of a patient. (Interscapular region)

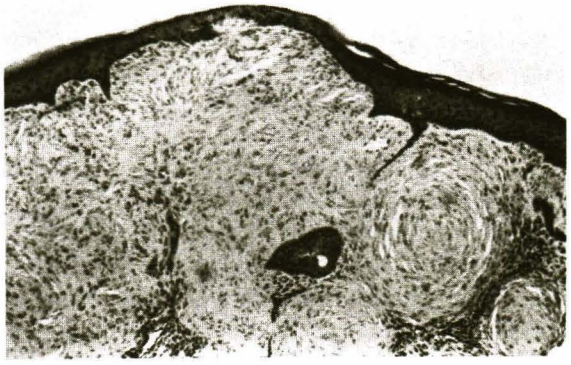

Fig. 2. Fibroblast and collagen bundles arranged in well-circumscribed appearance but not encapsulated in the subepidermal region. (Hematoxylin-eosin x 40)

cytoplasm. Mitotic figures were exceedingly rare. Neither axon nor myelin sheaths suggestive of a neurogenic origin was found, nor was significant amounts of glycogen or intracytoplasmic fibrils, suggestive of a muscle tumour, observed. Elastic tissue stains revealed an absence of fibers in the subepidermal area. Masson's trichome demonstrated the presence of collagen and staining them green. Alcian blue demonstrated substantial amounts of acid mucopolysaccharides in the tumor area corresponding to the areas of cellular hyperplasia.

Electron microscopy

Under comparatively low magnification, in the overlying epidermis, keratinocyte, melanocytes, merkel cells appeared normal. The basal lamina of the epidermis was almost intact.

In the dermis, the collagen bundles, elastic fibers appeared normal in size, appearance and orientations. Proliferation of normal fibrous tissue was generally observed. The cell membranes were smooth, the cytoplasm of these normal fibroblasts contained variable development of cell organelles, including ribosomes, rough endoplasmic reticulum (RER), pinocytic vesicles, microfilaments, golgi apparatus. In some cells, numerous parallel-arranged tubules of the rough endoplasmic reticulum are ascertained. The endoplasmic reticulum of some of the fibroblasts were severely changed, displaying large round lamellar figures. A basal lamina was discernible in some areas (Fig. 3).

Some fibroblasts showed dense aggregation of microfilaments. Bundles of these fine filaments and fibrils with irregularly interspersed dense bodies were seen in all the cells (Fig. 4). These were usually oriented parallel to the long axis of the cells and sometimes were seen in the cytoplasm of the fine cell processes.

Depending on the plane of the section, the cell nuclei are either oval or round present in lightly-stained chromatin with a narrow rim of marginal condensation. The nuclei are of moderate to large size (Fig. 5). Nuclei were oval, usually with a smooth outline, but often showing both shallow and deep indentations.

In some areas, a neoplastic fibroblast with irregular lobulated nuclei has also been seen. Meandering invagination of the nuclear envelop has produced small to large pseudoinclusions (P) which give the nucleus a lobulated appearance.

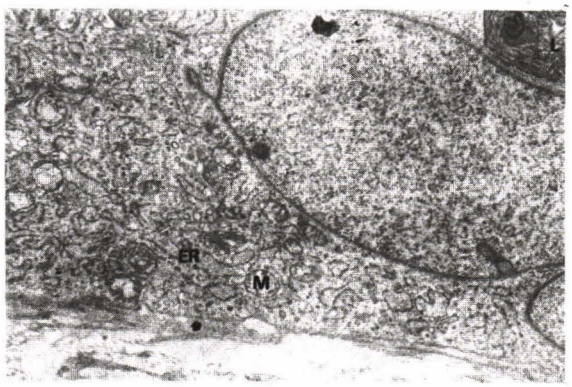

Fig. 3. Electron micrograph, showing major portions of fibroblasts and abundant collagen. Large fibroblast shows well-developed endoplasmic reticulum (ER), numerous mitochondria (M),. Severely changed endoplasmic reticulum appearing as a large, round, lamellar figure (L) inside a fibroblast. Note basal lamina material (*) subjacent to plasma membrane of this cell. (x 12,000)

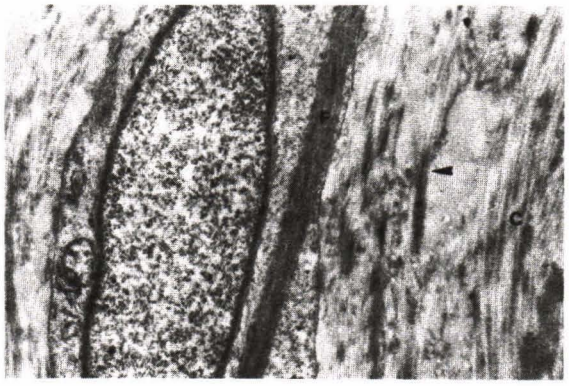

Fig. 4. Ultrastructurally, cell has features of fibroblasts plus large bundle of thick and thin filament at the periphery of the cytoplasm (F), characterizing cell as myofibroblast. Note abundant microfilamentous substance (arrowhead) was also found between collogen fibers (c). (x 20,000)

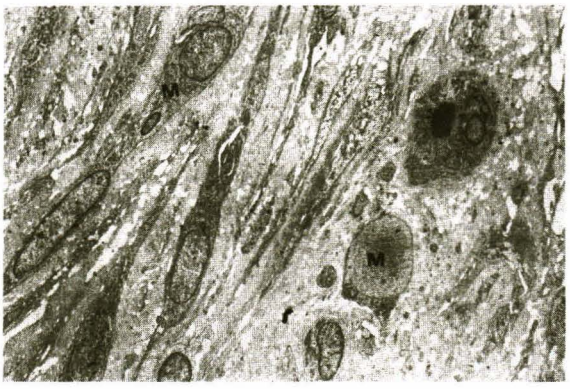

Fig. 5. The mesenchymal cells (M) usually show moderately developed organelles with moderate to large size nuclei surrounded by collagen fibers. (x 1,200)

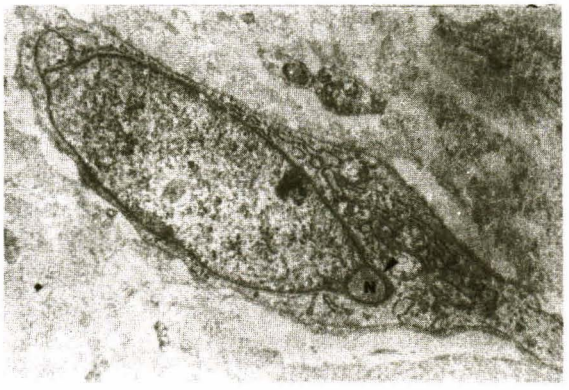

Fig. 7. A fibroblast show pockets containing nuclear material (N). Note also the chromatin bands (arrow head) which demarcate the pocket. (x 1,400)

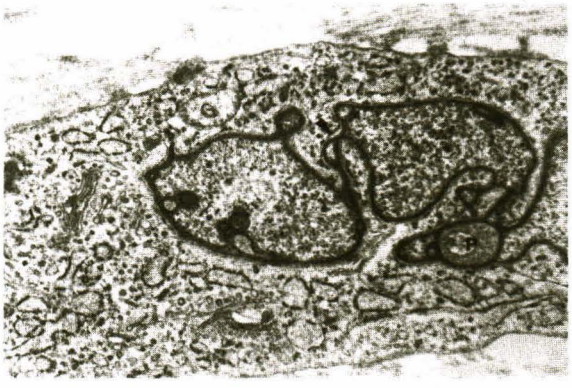

Fig. 6. A neoplastic fibroblast from the fibrous component of the tomour showing meandering invaginations (arrow-head) which give the nucleus a lobulated appearance and pseudoinclusions (P). (x 18,000)

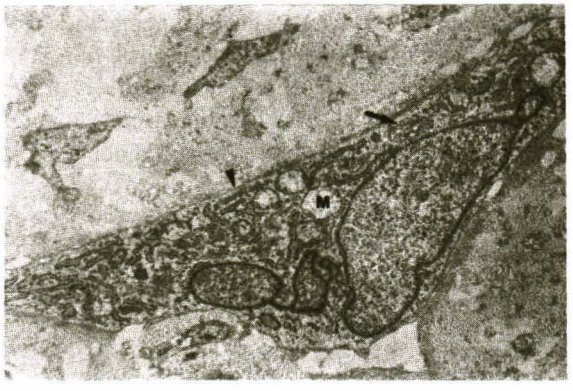

Fig. 8. This electron micrograph shows neoplastic fibroblasts with much enlarged irregular nuclei, golgi apparatus (arrow) and bizarre mitochondria (M) are evident. There are interrupted basal lamina (arrow heads) surround this cell. (x 9,600)

When such invaginations are transected they present as pseudoinclusions in the nucleus (Fig. 6). Other nuclear configurations seen in this patient were due to the presence of nuclear pockets. Such pockets demarcated by a band of chromatin, may contain cytoplasmic or nuclear material (Fig. 7). In some areas, neoplastic fibroblasts contained numerous golgi apparatus, rough endoplasmic reticulum and bizarre mitochonodria have seen (Fig. 8).

The stroma is composed of densely arranged delicate fibrils whose diameter is about 70 A^{o}. The fibrils are parallel arranged in undefined, often wavy, bands running in various directions. Single band of fibrils show the presence of subtle cross-striation with about 1000 A^{o} periodicity. Among these delicate fibrils there are sparsely disseminated collagen fibrils exhibiting the characteristic 640 A^{o} periodicity.

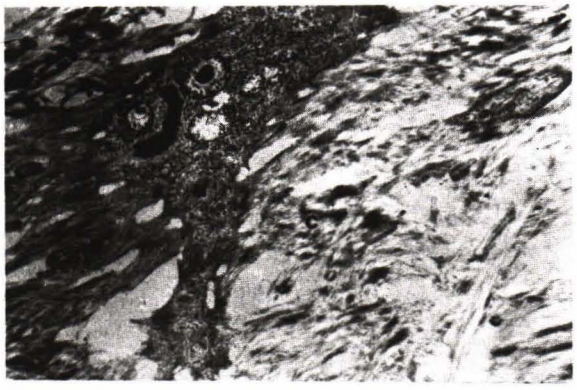

Fig. 9. Branching cell process of myofibroblast cell (M) is seen extending into the collagen-rich stroma (c). (x 7,200)

DISCUSSION

Congenital localized multiple fibromatosis designates a disease process consisting of multiple nodular lesions largely composed of collagen-forming spindle cells and involving variously in the skin and/or the subcutis[10], muscle, aponeurosis or bone. Our case reported posed considerable diagnostic difficulties, there are no deep intra or intermuscular location but there are nodular and some infiltrative growth patterns (Fig. 9) with predominantly, or partly immature fibroblast-like cell population[8,11-13].

It is impossible to distinguish histologically between solitary and generalized fibromatosis, but the clinical picture of congenital fibromatosis varies widely and ranges from a fatal generalized form to a solitary form with benign course. The histological and electron microscopic figures which sometimes show atypical fibroblast may lead to misinterpretation of the tumor as a sarcoma. In our case, where the lesion was present since 3 weeks, the following diagnosis were entertained, such as infantile fibrosarcoma, Juvenile hyaline fibromatosis, extra-abdominal desmoid, fibrous hamartoma of infancy, juvenile aponeurotic fibroma.

Infantile fibrosarcoma may resemble congenital solitary fibromatosis, both tumors are predominantly composed of immature, spindle shaped, fibroblast like cells. However, infantile fibrosarcoma differs histologically in its greater cellularity, higher mitotic activity, cellular atypia, and also clinical appearance[14,15]. The lesion of this patient was asymptomatic and had been present since 3 weeks old without any recognizable changes in appearance.

Juvenile hyaline fibromatosis is another rare hereditary disease that bears a superficial resemblance to congenital fibromatosis but differs by the cutaneous distribution of the tumor nodules and their histological picture, which show complete absence of mature collagen. Clinical findings, in contrast to the fibromatosis, the condition rarely occurs before the second month of life and is usually first noticed in children between 1 and 5 years of age. Typically it consists of multiple cutaneous tumors, in some of the cases there is marked thickening of the gums, flexural contractures of multiple joints, or mental retardation.

Dermatofibrosarcoma protuberans was carefully considered as a possible diagnosis. This tumor usually affects adults, although Taylor and Helwig[16] claimed that the lesion had been present since birth. The initial lesion is usually either a plaque or a small protruding nodule. There were some histologic features in our cases that made the diagnosis of Dermatofibrosarcoma protuberans unlikely, namely the absence of definitive cartwheel or storiform arrangement of fibroblasts in the dermis.

Extra-abdominal desmoid, occurring in adults, affecting fascia and muscle, sparing the dermis and subcutaneous tissue, should be included in the differential diagnosis of intramuscular fibrous lesions[17]. Usually, however, extra-abdominal desmoid can be clearly distinguished from solitary congenital multiple fibromatoses by its monotonous desmoplastic appearance, with evenly distributed collagen and elongated slender cells forming interlacing bundles of fascicles.

Fibrous hamartoma of Infancy may be present at birth, rarely affects the trunk, and involves the subcutaneous tissue and lower dermis and clearly distinguished from congenital solitary fibromatoses by the characteristic organoid arrangement of traversing bundles of dense fibrocollagenous tissue, immature-appearing mucoid loose-textured cellular areas and mature fat[18,19].

Juvenile aponeurotic fibroma may have some features similar to those seen in our cases, because of its infiltrative growth pattern of a cellular fibrous tissue, because of its infiltrative growth pattern of a cellular fibous tissue. Histolo-

gically, juvenile aponeurotic fibroma contains, however, calcified foci surrounded by radiating column of cells in a chondroid matrix and multinucleated giant cells adjacent to calcium deposits (20,21). Juvenile aponeurotic fibroma is located in the hand, wrist, or sole of the foot; which is very useful in differential diagnosis.

Our case differed from each other, first in the age of onset of the patient at discovery, secondly benign clinical and histological appearance. Therefore, our case have been described as being of "Congenital localized multiple fibromatosis".

However, these ultrastructural observations reveal that these tumors have ultrastructural features of fibroblasts, atypical fibroblasts and myofibroblasts. Three ultrastructures of the tumors presented by us should be emphasized. The first one is the presence of large amount of fibroblasts with abundant rough endoplasmic reticulum. The second feature is the presence of oriented microfibrils fitting the cytoplasm of the fibroblasts which are remarkable : One might think that these were collagen microfibrils, since the fibroblast is the source of collagen. However, this product is never evident intracellularly. To us, these cells appear to be myofibroblasts, which are specialized, contractile fibroblasts containing bundles of actin(22).

Bundles of smooth muscle myofilaments occupy the peripheral cytoplasm of myofibroblasts, and anchoring filaments extend from the outer aspect of cell to attach to adjacent collagen providing a fulcrum for contraction. Myofibroblast and basal lamina identified in our cases were quite similar to multiple subcutaneous nodules from a newborn reported by Benjamin et al(23) and 3 cases reported from Shin-Hoe liew et al(24). Myofibroblasts have been described in several apparently unrelated conditions, suggesting that the acquisition of smooth muscle-like features is one of a limited number of ways in which fibroblasts may react to an abnormal environment.

The third feature is related to neoplastic fibroblasts. Because of this occurrence of atypical fibroblasts some doubt has been expressed as to whether a true tumour of congenital localized multiple fibromatosis infact exists or not. Neoplastic fibroblasts occur not only in fibroma, fibrosarcoma, but also in various other benign and malignant tumours such as: fibroadenoma, elastofibroma, neurofibroma, neurofibrosarcoma, fibrous histiocytoma, synovioma, synovial sarcoma, benign and malignant mesenchymoma, osteosarcoma and chondrosarcoma(25). Thus, the finding of few atypical fibroblasts in our cases is not diagnostic; nevertheless it is important to recognize this cell type. The other changes in atypical fibroblasts oberved in our case are "nuclear pocket". The presence of "nuclear pocket" in large quantities has been observed in rapid growing or synthesising cells(26,27). This phenomenon may be related to enhancement of the nucleolo-cytoplasmic interactions(26).

We have reached the conclusion that the exact cause of this condition is not clear, with most suggestions focusing on trauma or a congenital malformation(28). The resemblance to a scar or keloid suggests a reparative process, but physical trauma has not been specifically incriminated as a cause in many cases and also in our case. Most fibromatoses appear sporadically, without a recognized antecedent event. In our case, some areas, and electron microscopic appearance had shown the characteristics of myofibroblasts and we believed in the concept that myofibroblasts indicate an early phase of fibroblastic differentiation associated with cellular motility and play a role in the shrinkage and eventual disappearance of the lesions. We don't belive in the concept of transition between fibroblasts and smooth muscle cells because no reported cases that the tumor nodules ever into leiomyomas. The last point which we want to conclude is "the presence of atypical fibroblast". It is perhaps worth pointing out that the presence of neoplastic fibroblasts in our tumour is not diagnostic, as we have seen that atypical fibroblasts are found in a variety of benign tumours and they have also seen in some carcinomas.

SUMMARY

Congenital localized multiple fibromatosis is clearly a benign self-limiting localized process probably of hamartomous origin. The exact cause of this condition is not clear, with most suggestions focusing on trauma or a congenital malformation. The histologic and electron microscopic appearance had shown the characteristics of fibroblasts, atypical fibroblasts and myofibroblasts.

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มัลติเปิล ไฟโบรมาโตสิสเฉพาะที่ชนิดเป็นแต่กำเนิด

ปิติ พลังวชิรา, พ.บ., มาซาโกะ ชิราอิ, พ.บ.**,*
*คูนิโอ อิวาฮารา, พ.บ.**, ฮิเดโอกิ โอกาวา, พ.บ.***

ผู้ป่วยเด็กหญิงชาวญี่ปุ่น อายุ 10 ปี ได้รับการวินิจฉัยเป็น congenital localized multiple fibromatosis บริเวณ interscapular ลักษณะเนื้องอกได้เริ่มเกิดขึ้นตั้งแต่ผู้ป่วยอายุได้ 3 เดือน โดยไม่มีการกระจายของเนื้องอกไปยังบริเวณอื่น ได้ทำการศึกษาทางพยาธิวิทยาและจุลทรรศน์อีเล็คตรอนพบว่าเนื้องอกมีต้นกำเนิดเป็นแบบ hamartoma และมีการวิวัฒนาการของเซลล์เป็นแบบ myofibroblast fibroblast และ atypical fibroblast การวินิจฉัยผู้ป่วยรายนี้ต้องอาศัยจุลทรรศน์อิเล็คตรอนช่วยแยกจาก soft tissue tumor อื่น ๆ

* ศูนย์ผิวหนัง, คณะแพทยศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ ประสานมิตร, กรุงเทพ ฯ 10110
** ภาควิชาตจวิทยา, คณะแพทยศาสตร์ มหาวิทยาลัยจุนเท็นโด, 1-1 ฮองโกะ นิ โจเมะ, บุงเกียว-กุ, โตเกียว 113, ประเทศญี่ปุ่น