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□ Case Report □

Infantile Myofibromatosis

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We report a case of infantile myofibromatosis in a male infant with involvement of the lungs and subcutaneous tissue. We studied our case by light microscopy, immunohistochemistry and electron microscopy. The results reveal that this entity is of a myofibroblastic nature. We reviewed 165 cases including our case. We believe this is the first report in Korea of infantile myofibromatosis with pulmonary involvement.

Key Words: Infantile myofibromatosis, lung, subcutaneous tissue

Infantile myofibromatosis (IF) is a rare mesenchymal disorder, which most often presents before the age of 2 years, shows a male predominance and may be characterized by multiple tumors at a variety of sites in about a quarter of cases. In 1954, Stout reported two fatal cases of congenital generalized fibromatosis in which nodular lesions were seen in the superficial and deep soft tissues, viscera and bone. Since then, 164 cases of this entity have been published in foreign literature but none have been documented in Korean literature. Eighteen of the 86 infants (20.9%) who presented with multiple lesions had lung involvement (Table 1). The prognosis for a solitary lesion is uniformly good, except for possible local recurrence. In the multiple form, the mortality is high when vital internal organs are involved. In fatal cases, death occurs in the first few months of life (Morettin *et al.* 1972; Baer *et al.* 1973; Rosenburg *et al.* 1978). In those infants who survived, spontaneous regression of the masses has been described (Schaffzin *et al.* 1972; Liew *et al.* 1981). The outcome of pulmonary involvement was fatal. Death was due to bronchopneumonia or progressive respiratory distress (Roggli *et al.* 1980).

We report a case of IF with pulmonary involvement in a 10-month-old infant.

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CASE HISTORY

A 10-month-old male infant was admitted to the

Table 1. Clinical features of patients with infantile myofibromatosis.@

Characteristic	Solitary lesion	Mutliple lesions
No. of patients	78	87
Sex		
Male	47	53
Female	29	34
Time of presentation*		
Birth	36	81
<6 mo	12	4
6-12 mo	8	0
>12 mo	17	2
Visceral involvement without lungs affected	0	12
Visceral involvement with lungs affected	0	19
Deaths	0	24

@ Compiled from references; Christensen *et al.* 1961; Kindbloom *et al.* 1977; Kindbloom and Angervall 1978; Rosenburg *et al.* 1978; Briselli *et al.* 1980; Chung and Enzinger 1981; Brill *et al.* 1982; Dimmick and Wood 1983; Katz and Mills 1983; Vangsted and Linpaphayom. 1983; Jenings *et al.* 1984; Nasr *et al.* 1986; Fletcher *et al.* 1987; Wiswell *et al.* 1988 and the current case.

* Time unknown in five patients with solitary lesions.

pediatric department because of a two day history of dyspnea and fever. He weighed 3,500gm at birth and was the product of a full-term, normal pregnancy delivered by cesarean section because of previous cesarean section. At birth, he was found to have three subcutaneous nodules, one in the abdomen, another in the right flank and the other in the occiput. His mother enjoyed excellent health during her pregnancy. The pregnancy was not related with any history of infection, trauma, or drug ingestion. After birth, mild respiratory difficulty was noted. He suffered from a cold frequently. At the age of 10 months, dyspnea and generalized edema gradually developed. One month before admission, he was admitted to another hospital and was given treatment under the impression of pneumonia without any improvement. Two days before admission, a fever and dyspnea developed and were aggravated. His temperature continued to be 39°C, so he was brought to this hospital.

Physical examination disclosed that he was febrile with a respiratory rate of 40/min and pulse of 194/min. The subcutaneous nodules varied from 4 to 7cm in greatest dimension and were uniformly elevated, indurated, movable and apparently nontender. There was no discoloration of the overlying skin. Mild intercostal and subcostal retraction was noted. Auscultation of the chest wall revealed a coarse breathing sound with rales in both lung fields and a regular heart beat with a ejection systolic murmur at the apex. The liver was palpable 5cm below the right costal margin but the spleen was not palpable. Laboratory investigations revealed a hemoglobin level of 12.0gm/dl and a white blood cell count of 25,800/mm with 58% neutrophils and 42% lymphocytes. The chest roentgenogram showed a pattern of diffuse interstitial fibrosis or bronchopneumonia with multiple small linear and nodular masses (Fig. 1). During admission, his clinical course became worse. On the eighth day of admission, an abdominal subcutaneous nodule was excised and an open lung biopsy from the left lower lobe was done. Lesions of the bone and other visceral organs were not found on further evaluation. Despite intensive care, he died on the thirty-third day after admission.

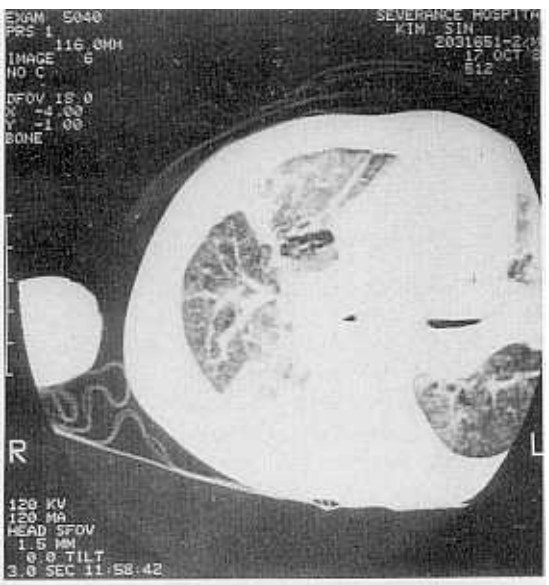

Fig. 1. Chest CT shows multiple, linear or nodular opacities of both lungs.

PATHOLOGIC FINDINGS

Tissues were fixed in phosphate-buffered 10% for-

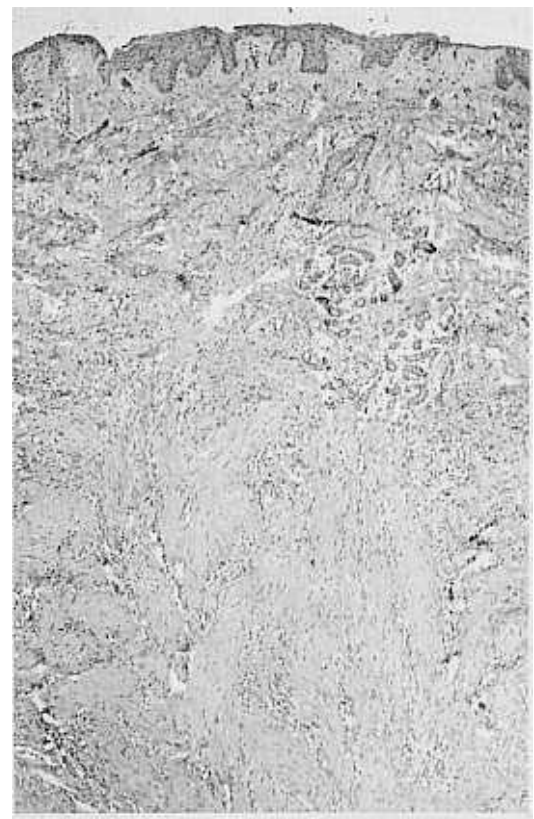

Fig. 2. The cutaneous form of infantile myofibromatosis disclosing bundles or fascicles of spindle cells reminiscent of smooth muscle fibers (Hematoxylin and eosin, ×40).

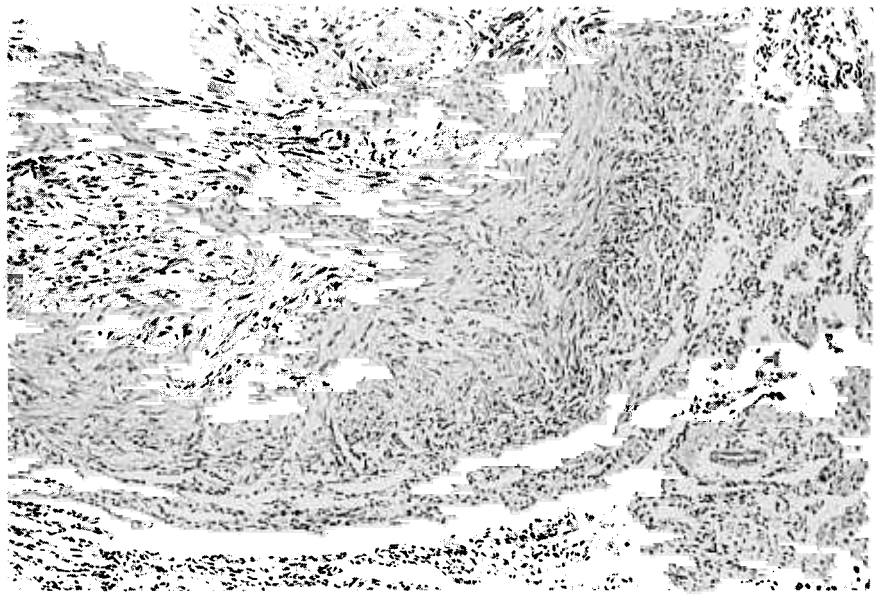

Fig. 3. infantile myofibromatosis involving the lung, displaying a circumscribed nodule of pale-staining spindle cells and a more vascular and less differentiated cellular area (Hematoxylin and eosin, ×100).

malin solution. Formalin-fixed tissues were stained with hematoxylin and eosin, and also by the following techniques: periodic acid Schiff (with and without prior diastase digestion), Masson's trichrome, and alcian blue. Further sections from the lung tissue were examined immunohistochemically using desmin (Dako Ltd; dilution 1/500), S-100 protein (Dako Ltd; dilution 1/1000) and vimentin (Dako Ltd; dilution 1/20). All histochemical stains were performed according to the peroxidase-antiperoxidase method. The tissue from the cutaneous lesion was available for electron microscopy. this tissue was fixed in 2% glutaraldehyde in cacodylate buffer, postfixed in 1% osmium tetroxide, dehydrated in graded ethanol solutions, and embedded in Epon mixture. The sections were stained with uranyl acetate and lead citrate and examined by a Hitachi S-500 transmission electron microscope.

Light Microscopy

Histologic findings of the lung and skin were similar. A discrete, well circumscribed and lobulated nodule with a whorled appearance was located in the dermis and subcutaneous area of the skin (Fig. 2). Nodules of varying size with a histology similar to that of skin lesions occupied a wide range of locations within the pulmonary parenchyma (Fig. 3). They were associated with bronchioles or pulmonary vessels. The tumor nodules characteristically showed zoning phenomena, particularly in nodules of larger size. At the periphery, the tumor showed an admixture of fibroblast-like spindle cells and plump fusiform cells arranged in short fascicles or bundles. A richly vascular pattern was centrally located. Delicate wavy bundles of collagen fibers separated or enclosed the cellular aggregates. Polypoid growth of the tumor cells into the vascular spaces was observed in pulmonary parenchyma, giving an impression of vascular invasion (Fig. 4).

Results of Special Staining and Immunohistochemistry

With the Masson's trichrome stain, the cytoplasm of the tumor cells stained variably and was partly fuchsinophilic. Most of the fusiform or spindle-shaped cells were intimately associated with a varying amount of reticulum or collagen (Fig. 5). Extracellular mucinous material was present around some of the tumor cells in the alcian blue stain. With the PAS preparation, intracellular glycogen was mostly absent in the spindle cells in the dermis but pulmonary nodules showed focally PAS-positive, diastase-sensitive glycogen within spindle cells. The tumor cells reacted positively for vimentin and negatively for S-100 protein. However, the spindle cell component showed focal cytoplasmic

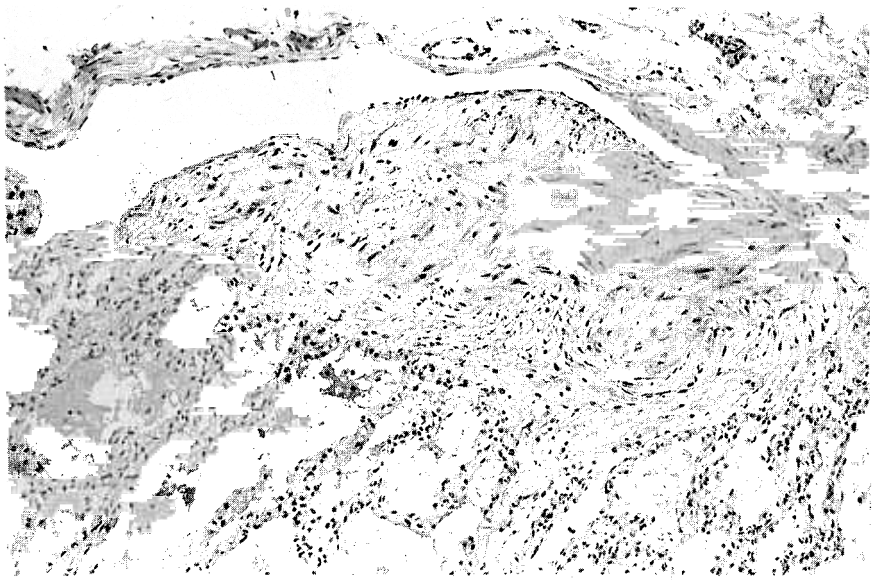

Fig. 4. Intravascular extension of the tumor in the pulmonary lesion (Hematoxylin and eosin, ×200).

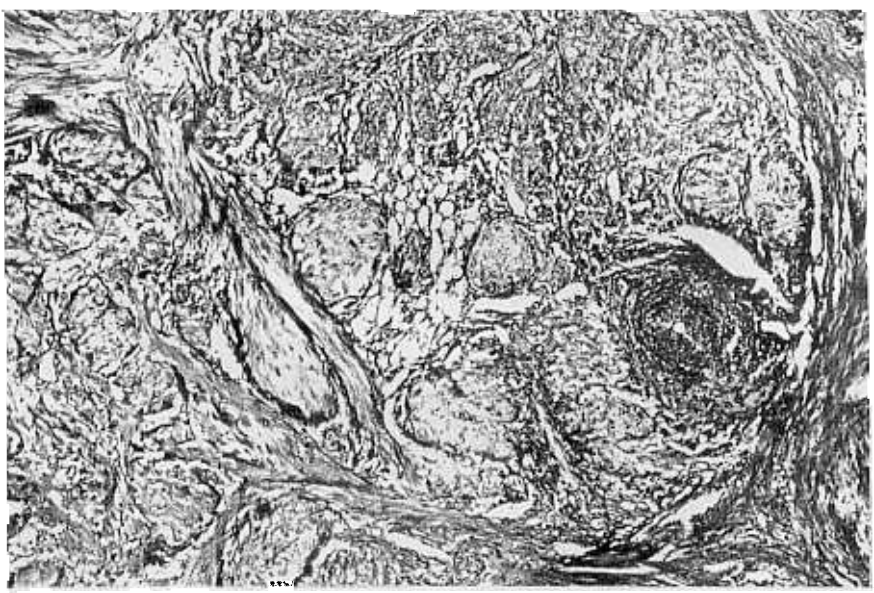

Fig. 5. Infantile myofibromatosis showing variable staining characteristics with Masson's trichrome stain; the tumor cells are fuchsinophilic and are intimately associated with varying amounts of collagen (Masson's trichrome, ×200).

positivity for desmin.

Electron microscopy

The main part of the proliferation was made of fibroblastic cells with elongated or oval-shaped nuclei and elongated cytoplasm with well developed endoplasmic reticulum. In some cells inside the cytoplasm, more often close to the cytoplasmic mem-

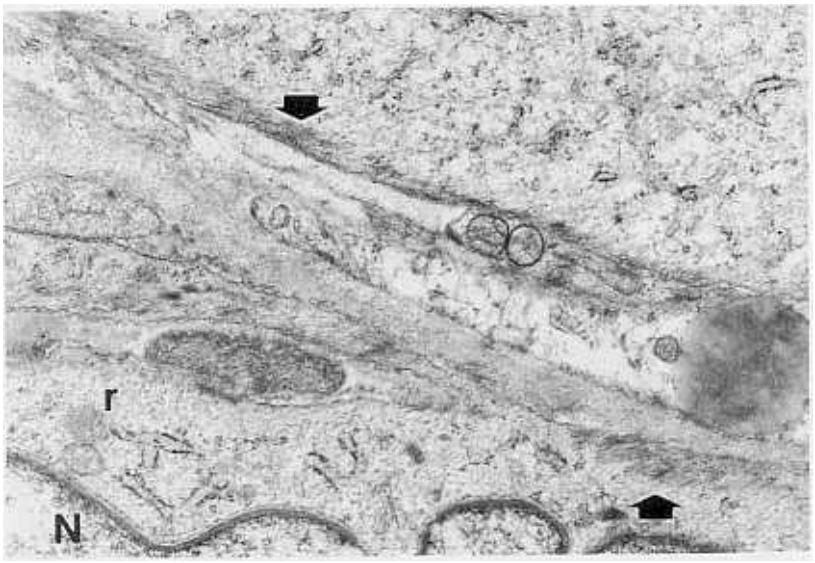

Fig. 6. Electron micrograph of a myofibroblast with prominent nuclear infolding(N), abundant rough endoplasmic reticulum(r) and peripheral myofilaments with focal densities (arrow head) (original magnificance, ×375,000).

brane, bundles of myfilaments that are characteristic of myofibroblasts were observed (Fig. 6).

DISCUSSION

A rare but distinct childhood form of fibromatosis is an entity known as "congenital generalized fibromatosis" (CGF), a term first coined by Stout in 1954. The different terms used in the literature for CGF include congenital fibromatosis, multiple congenital mesenchymal tumors, multiple congenital neoplasms, generalized hamartomatosis, multiple mesenchymal hamartomas, multiple vascular leiomyomas, diffuse congenital fibromatosis, and congenital fibrosarcoma (Chung and Enzinger 1976). The term "infantile myofibromatosis" (IF) was introduced because of clinical and histochemical findings coupled with ultrastructural evidence and the need to clearly distinguish this process from the more locally aggressive infantile fibromatosis of the desmoid type (Benjamin *et al.* 1977; Chung and enzinger 1981).

IF is a rare neoplasm which most often appears before the age of two years and shows a male predominance. These lesions clinically present two major types: (1) as a solitary lesion, most commonly in the skin, muscle, or subcutaneous tissues; and (2) as multiple lesions usually confined to the soft tissue and bone (Chung and Enzinger 1981). The clinical

Table 2. Infantile myofibromatosis: Anatomic distribution of lesions.*

Characteristic	No.	% Affected
Solitary lesions (78 patients)		
Skin, muscle or subcutaneous tissue	72	92.3
Bone	6	7.7
Multicentric lesions (86 patients)		
Skin, muscle or subcutaneous tissue	85	97.7
Bone	48	55.8
Lung	19	21.8
Heart	12	13.0
Gastrointestinal tract	11	12.8
Pancreas	8	9.3
Upper respiratory tract	7	8.1
Liver	6	6.9
Tongue	6	6.9
Serosa	6	6.9
Lymph nodes	4	4.7
Kidney	3	3.5
Adrenal	3	3.5
CNS	3	3.5
Dura	2	2.3
Peripheral nerves	2	2.3
Spleen	1	1.2
Thyroid	1	1.2
orbit	1	1.2

* Compiled from references from Table 1 and the current case.

features and the anatomical distribution of infantile myofibromatosis in the 164 patients that have been reported to date are presented in Tables 1 and 2, respectively (Christensen *et al.* 1961; Kindbloom *et al.* 1977; Kindbloom and Angervall 1978; Rosenburg *et al.* 1978; Briselli *et al.* 1980; Chung and Enzinger 1981; Brill *et al.* 1982; Dimmick and Woo 1983; Katz and Mills 1983; Vangsted and Linpaphayom 1983; Jennings *et al.* 1984; Nasr *et al.* 1986; Fletcher *et al.* 1987; Wiswell *et al.* 1988). In our case, manifestations of the disease were present at birth. The outcome was fatal and the cause of death was respiratory failure due to progressive respiratory distress (roggli *et al.* 1980).

Microscopically, the solitary and multiple lesions varied little in their appearance. All were composed of short, curving bundles of fusiform, collagen-producing cells, which showed staining characteristics intermediate between fibroblasts and smooth muscle cells. There was been some debate in the literature about the exact nature of the tumor cells. Lin and Svoboda (1971) suggested a smooth muscle origin. Electron microscopic studies performed by Morettin *et al.* (1972) revealed fibroblasts and smooth muscle-like cells that led them to support the concept of hamartomatosis proposed earlier by Shnitka *et al.* (1958), Bartlett *et al.* (1961), and others (Beatty 1962). Benjamin and his associates (1977), however, concluded that the spindle-shaped tumor cells, which showed the ultrastructural features of both fibroblasts and smooth muscle cells, were myofibroblasts. Electron microscopic evaluation of our case revealed a myofibroblastic origin, resembling the features of both fibroblasts and smooth muscle.

Chung and enzinger (1981) were the first to study a large number of cases of IF immunohistochemically. They found a degree of fuchsinophilia using a Masson's trichrome stain, occasional longitudinal fibrils with PTAH, and minimal glycogen, if any, with PAS. In recent years, immunohistochemical and immunofluorescent techniques have been increasingly used to characterize the intermediate filament population of both normal and neoplastic tissue (Lin and Svoboda 1971; Gabbiani *et al.* 1981; Miettinen *et al.* 1982; Denk *et al.* 1983; Osborn and Weber 1983). The fact that our case was desmin- and PAS-positive is suggestive of differentiation toward smooth muscle. The etiology of IF is uncertain. Several lines of evidence have suggested a relationship to estrogenic hormones (Nadel 1950; Schaffzin *et al.* 1972; Liew and Haynes 1981). There has been evidence to support that IF is a heritable condition (Baird and Worth 1976; Rosenburg *et al.* 1978; Brill *et al.* 1982; Jennings *et al.* 984). Some investigators have suggested that IF is hamartomatous in nature (Liew and Haynes 1981).

The clinical course of IF seems to be largely determined by the extent of the disease. When the tumor is solitary, the prognosis is excellent, although the recurrence rate is about 11% (Chung and Enzinger 1981). When the lesion is multicentric, spontaneous regression may occur in nearly one-half of the cases unless the lesion involves visceral organs (Liew and Haymes 1981; Schaffzin *et al.* 1972). Prognosis is less favorable in infants with multiple visceral lesions, and in many of these cases, pulmonary involvement of IF seems to carry a particularly grave prognosis (Roggli *et al.* 1980). Death usually occurs from cardiopulmonary or gastrointestinal problems (Morettin *et al.* 1972; Baer and Radkowski 1973; Rosenburg *et al.* 978). Complete local excision appears to be the treatment of choice for the solitary form, and simple diagnostic biopsy or simple excision of symptomatic lesions for the multicentric type. Genetic counseling should be provided to families regarding the possibility of subsequent children being affected and the possibility of occurrence in successive generations.

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