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# Fibrous Histiocytoma Simulating Congenital Fibromatosis

## A Light-, Electron Microscopic and Tissue Culture Study

H. Joachim Wigger and Sumi M. Mitsudo

Departments of Pathology, College of Physicians and Surgeons
of Columbia University and Montefiore Hospital Medical Center, New York

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*Summary.* The unusual occurrence of a fibrous histiocytoma of subcutaneous soft tissues, bones, and viscera is described in a newborn infant. The clinical and radiologic picture simulated a congenital fibromatosis, but histologic, electronmicroscopic and tissue culture studies indicated a malignant tumor with a bimodal cell population resembling immature fibroblasts and histiocytes. Although less mature and more uniform, it essentially parallels the findings in the adult malignant fibrous histiocytomas.

*Key words:* Histocytoma — Fibroma, congenital.

*Zusammenfassung.* Ein fibröses Histiocytom in subkutanem Bindegewebe, Knochen und parenchymatösen Organen eines neugeborenen Säuglings wurde morphologisch untersucht. Die klinischen und röntgenologischen Befunde waren identisch mit denen einer kongenitalen Fibromatose. Die Ergebnisse der histologischen, elektronenoptischen und gewebekulturellen Untersuchungen deuteten jedoch auf eine maligne Geschwulst, die aus zwei Zelltypen bestand. Diese ähnelten Fibroblasten und Histiozyten und, obwohl weniger differenziert, entsprachen im wesentlichen den Zellen der malignen fibrösen Histiozytome der Erwachsenen.

## Introduction

Fibrous histiocytoma is a term applied to a group of benign and malignant lesions believed to be of common histogenesis, although their histologic appearance may vary considerably. Previously used synonyms include fibrous xanthoma and sclerosing hemangioma, xanthosarcoma, and malignant fibrous xanthoma. This report describes a malignant fibrous histiocytoma in a newborn infant presenting with the clinical and radiologic features of a congenital fibromatosis.

## Clinical Abstract

The patient was a 2-days-old lethargic term infant with symptoms of respiratory distress and a left upper hemiparesis. A $4 \times 5$ cm firm immobile left retroauricular mass encroached upon the adjacent occipital and cervical areas. The neurologic examination suggested a compression of the spinal cord and injury to cranial nerves IX-XII. A skeletal survey revealed a large destructive lesion in the left temporal and occipital bones as well as destruction of the petrous bone and the base of the skull. Other lytic lesions were found in the proximal right humerus, the distal right ulna, both proximal femora, the pelvis, and the calcaneus. The cerebrospinal fluid contained protein in excess of 800 mg/100 ml and some questionable tumor cells. The infant deteriorated rapidly, developed seizures, and died in a decerebrate posture.

## Material and Methods

Biopsy tissue was fixed for light microscopy in Bouin's solution and for electron microscopy by immersion of 1 mm cubes in cold 2.5 % glutaraldehyde for 1-2 h, washed in

0.1M phosphate buffer at pH 7.4 and postfixed for 1 h in Dalton's fixative. Dehydration was carried out in graded concentrations of ethanol following block staining with uranyl acetate for 15 min. The tissue was embedded in Spurr's medium and cut with glass knives on a Porter-Blum microtome, mounted on uncoated copper grids, stained with uranyl acetate and lead citrate and examined under a Siemens Elmiskop 1 A.

For tissue culture some fragments of the tumor were explanted in plastic flasks coated with rat tail collagen and fed with MEM Eagle's nutrient medium to which were added 10 % fetal calf serum, glutamine, bicarbonate, penicillin, streptomycin, and amphotericin B. After 2 weeks, the nutrient medium in one flask was decanted, the monolayer washed with buffer and then coated with cold 2.5 % glutaraldehyde in 0.1M phosphate buffer at a pH of 7.4 for 2 h, washed again with buffer and photographed by interference microscopy. A part of the monolayer was stained with toluidine blue. The remainder was dehydrated in graded concentrations of ethanol and amylacetate in ethanol, submitted to critical point drying, coated with gold palladium in a vacuum unit and examined in a Jeol scanning electron microscope. The remainder of the tissue was maintained in culture for 4 weeks.

## Pathology

At autopsy the main tumor mass measured 4.5 cm in greatest diameter (Fig. 1). It had destroyed the petrous bone and the adjacent areas of the temporal bone as well as the lower lateral aspect of the occipital bone but spared the foramen magnum. The subcutaneous tissue was invaded and the skin appeared thin and stretched. The intracranial extension remained grossly extradural but compressed brain stem, medulla oblongata and cerebellum causing angulation at the level of the medulla oblongata. Small satellite nodules (0.3–1.5 cm) were firmly attached to the dura and may have invaded the leptomeninges but not the neural tissue. The left side of the spinal cord was compressed at its entrance into the foramen magnum. Bone lesions were found where indicated by the roentgenograms (Fig. 2).

The microscopic examination of both the surgical biopsy and the autopsy tumor tissue revealed two patterns of growth, a spindle cell pattern, and a histiocytelike pattern with prominent giant cell formation especially in the deeper portions of the main tumor. The spindle cells were arranged in a storiform fashion (Fig. 3) or formed interlacing bundles. Many of the spindle cells were quite plump and there was either transition to or intermingling with histiocytelike cells (Fig. 4a, b). The histiocytelike pattern was the predominant one, judging from the multiple sections taken at autopsy. Its components consisted of large cells with round-to-oval nuclei, distinct nuclear membranes, prominent nucleoli and ample eosinophilic cytoplasm as well as of many giant cells with nuclei varying in number from 2 to 20. Collagen was irregularly and sparsely distributed in both patterns. These features were found in the bony as well as the solitary visceral lesions of the liver and of one adrenal. The adrenal tumor was associated with thrombosis of an adrenal vein.

Tumor necrosis was present only in the main mass. Several foci of questionable vascular invasion or embolization of tumor were noted in meningeal and dural veins. There was considerable variation in the degree of hypercellularity, the distribution of bizarre giant cells and the number of mitoses from area to area (average: 8 per 50 h.p.f.). Collagen production appeared sparse. Reticulin fibers were short and haphazardly distributed between the tumor cells. Foamy xanthomatous cells were absent.

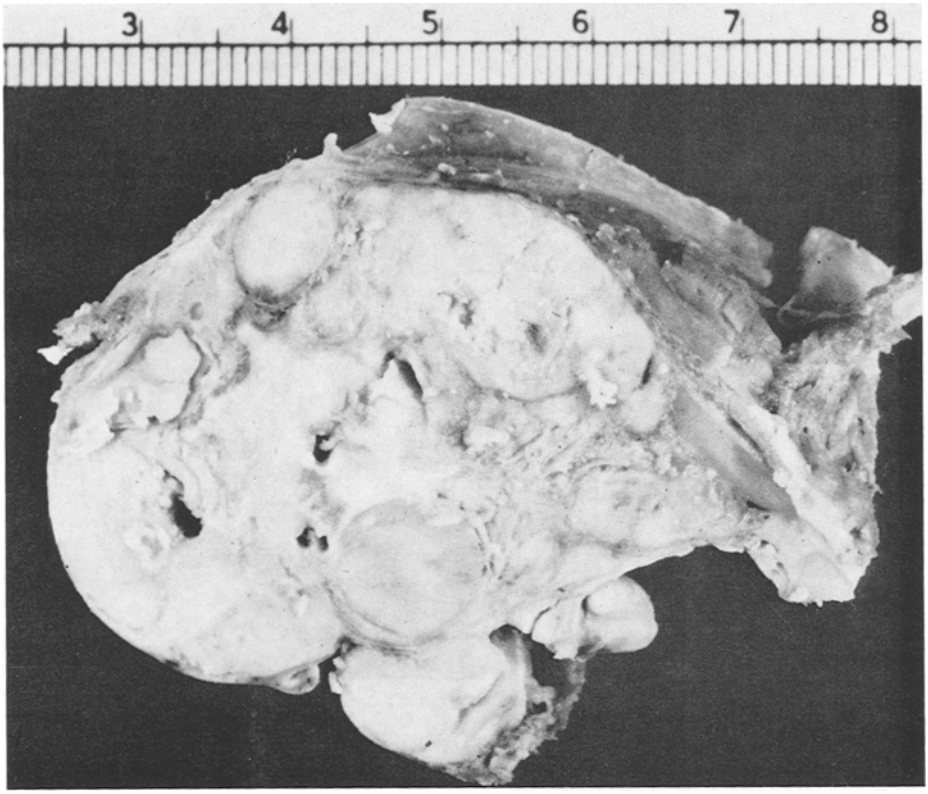


Fig. 1. Cross- section of main tumor abutting on bone

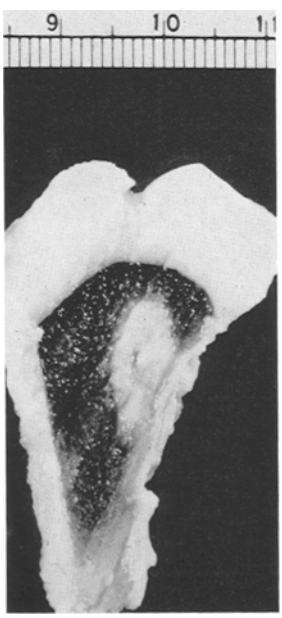


Fig. 2. Cross-section of humeral bone with tumor

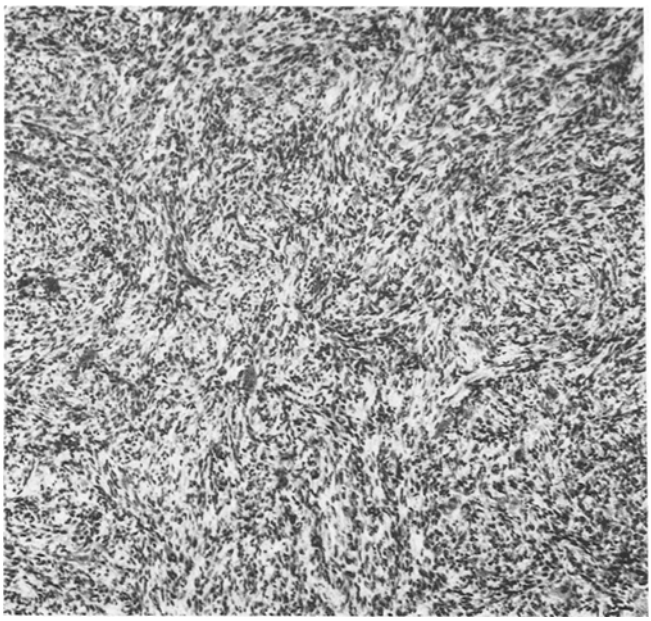

Fig. 3. Fibrous area of tumor showing storiform pattern. Hematoxylin-phloxin-saffron ×88

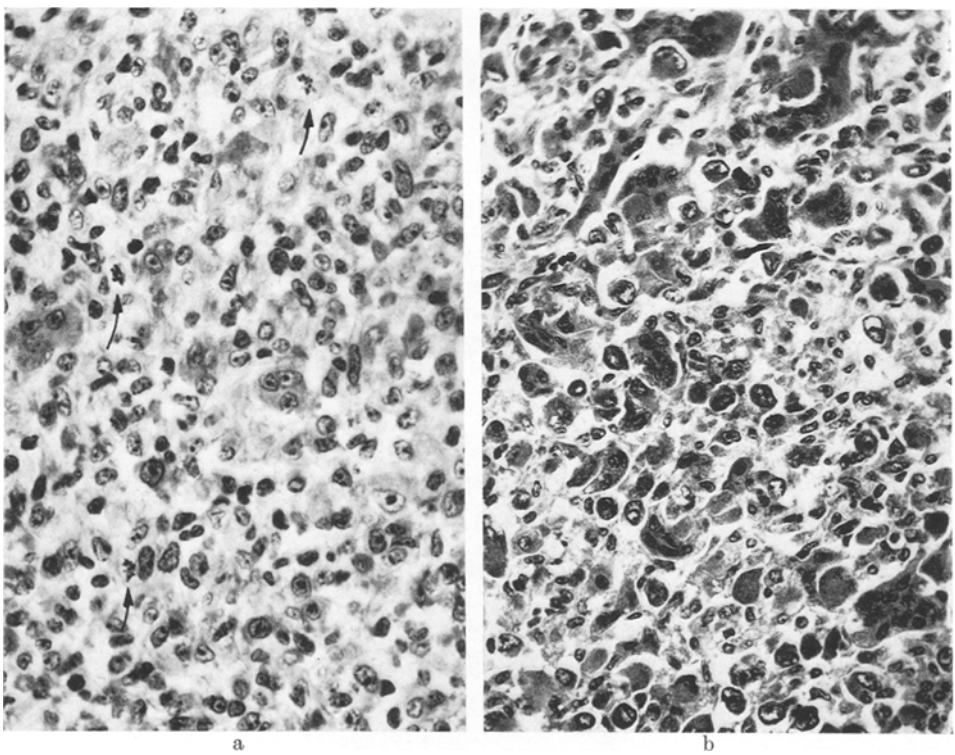

Fig. 4a and b. Mixed population of histiocytelike and fibroblastlike cells with 3 mitoses (a) and areas composed of bizarre nistiocytelike and giant cells (b) indicate malignant nature of tumor. Hematoxylin-phloxin-saffron (a) ×325, (b) ×250

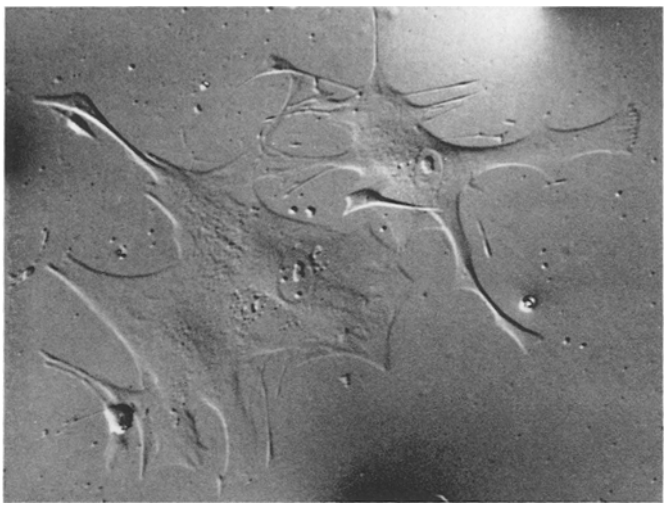

Fig. 5. Outgrowth of histiocytelike cells after 2 weeks in tissue culture. Interference microscopy ×55

The only pertinent finding in the remainder of the autopsy was a bronchopneumonia.

Tumor cells grown in tissue culture and fixed after 2 weeks comprised two cell types, a spindle-shaped cell and a large irregular cell with broad thin cytoplasmic processes (Fig. 5). By interference microscopy and scanning electron microscopy these cells appeared quite flat. Vacuoles and nuclei could be discerned. Continuous growth of tumor cells in culture resulted in conversion to a purely spindle cell pattern.

Electron microscopy of the surgical biopsy of the main mass revealed three main cell types. The spindle-shaped and plump cells resembled fibroblasts (Fig. 6) with their large elongated nuclei, at times folded or invaginated, and ample rough endoplasmic reticulum (RER) in long profiles which occasionally were quite dilated and filled with amorphous electron-dense material. Mitochondria were moderate in number and generally round-to-oval in shape. The Golgi zones appeared well developed. Cytoplasmic filaments were scant.

The cells interpreted by light microscopy as histiocytes and giant cells showed a remarkably similar ultrastructural appearance differing essentially only in the number of nuclei. These were mostly oval-to-kidney-shaped but at times also quite irregular. The bulky cytoplasm contained many ribosomes and mitochondria of variable configuration, some RER, much smooth endoplasmic reticulum, and subplasmalemmal vesicles. Phagocytic vacuoles were relatively sparse and there were also multivesicular bodies. The cell membranes were ruffled and formed pseudopodia and filopodia. Mitotic figures were not uncommon (Figs. 6 and 7). Some histiocytelike cells appeared dark and relatively small, others contained virtually no phagocytic vacuoles but otherwise suggested that they may be immature histiocytes (Fig. 8).

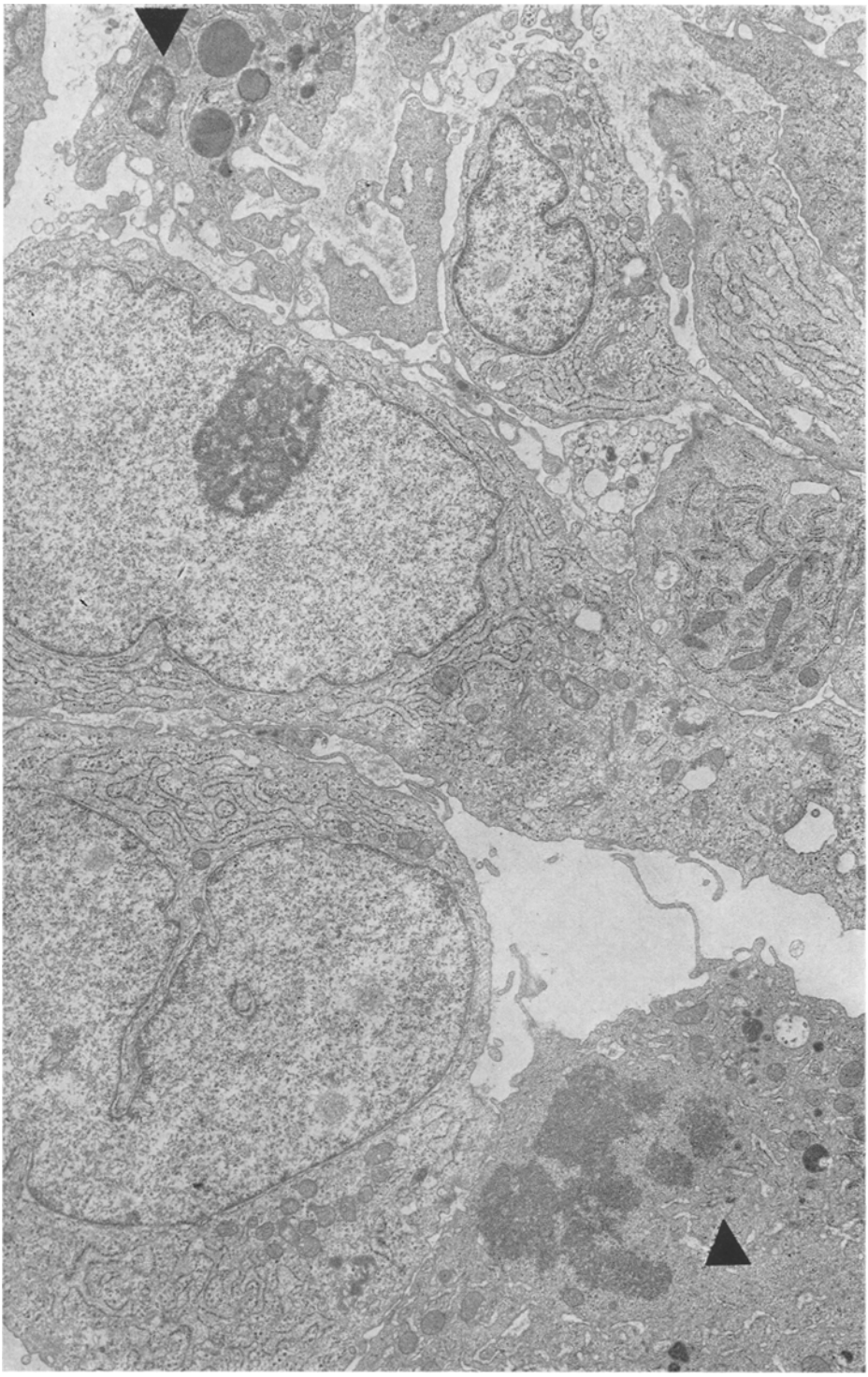

Fig. 6. Histiocytelike cells (▲) and fibroblastlike cells, one in mitosis, intermingled frequently. ×6,300

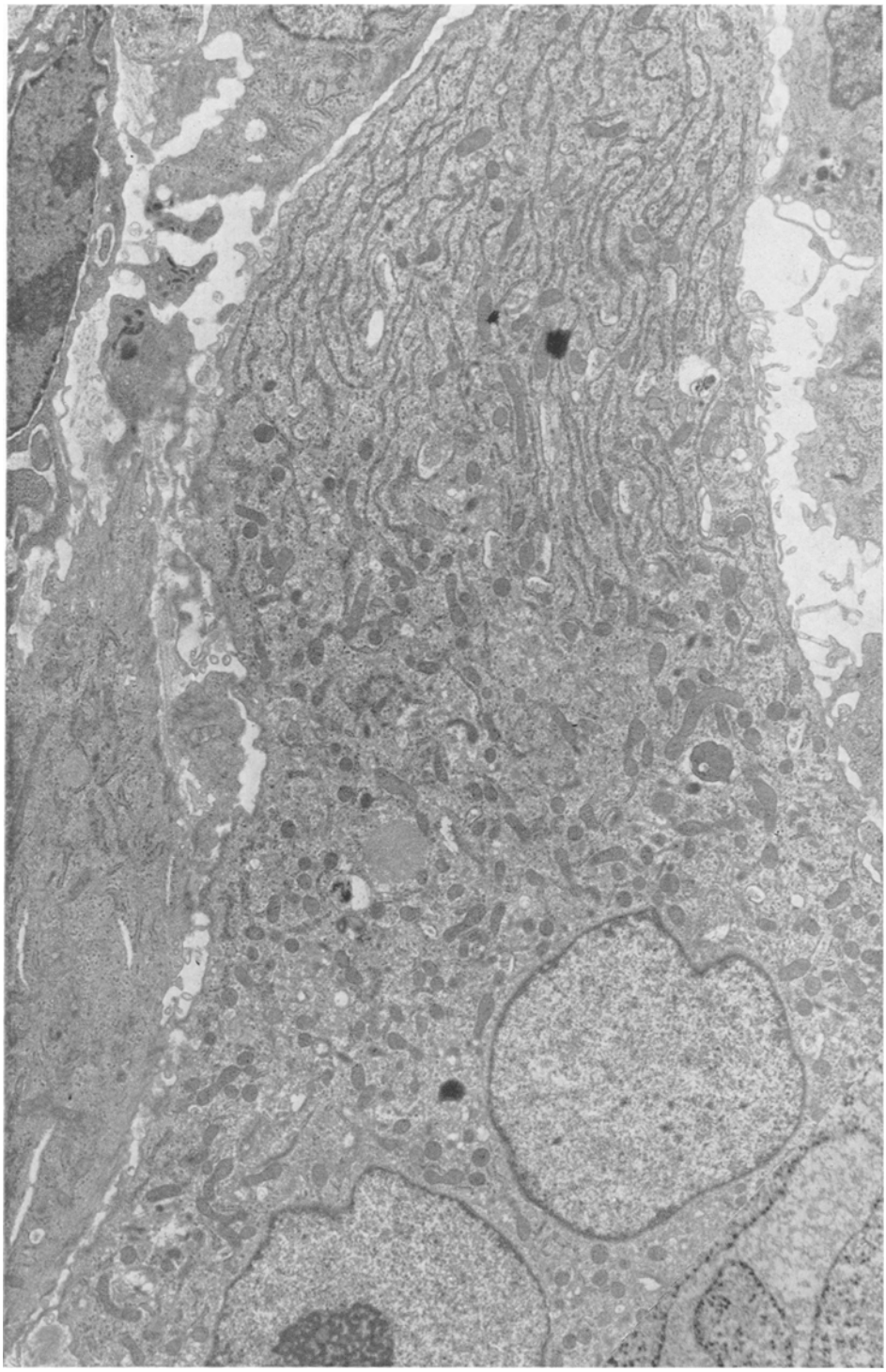

Fig. 7. Multinucleated tumor giant cell with abundant RER and many mitochondria. × 7,250. Insert: Occasional dilated cisternae of RER contain finely granular material. × 24,300

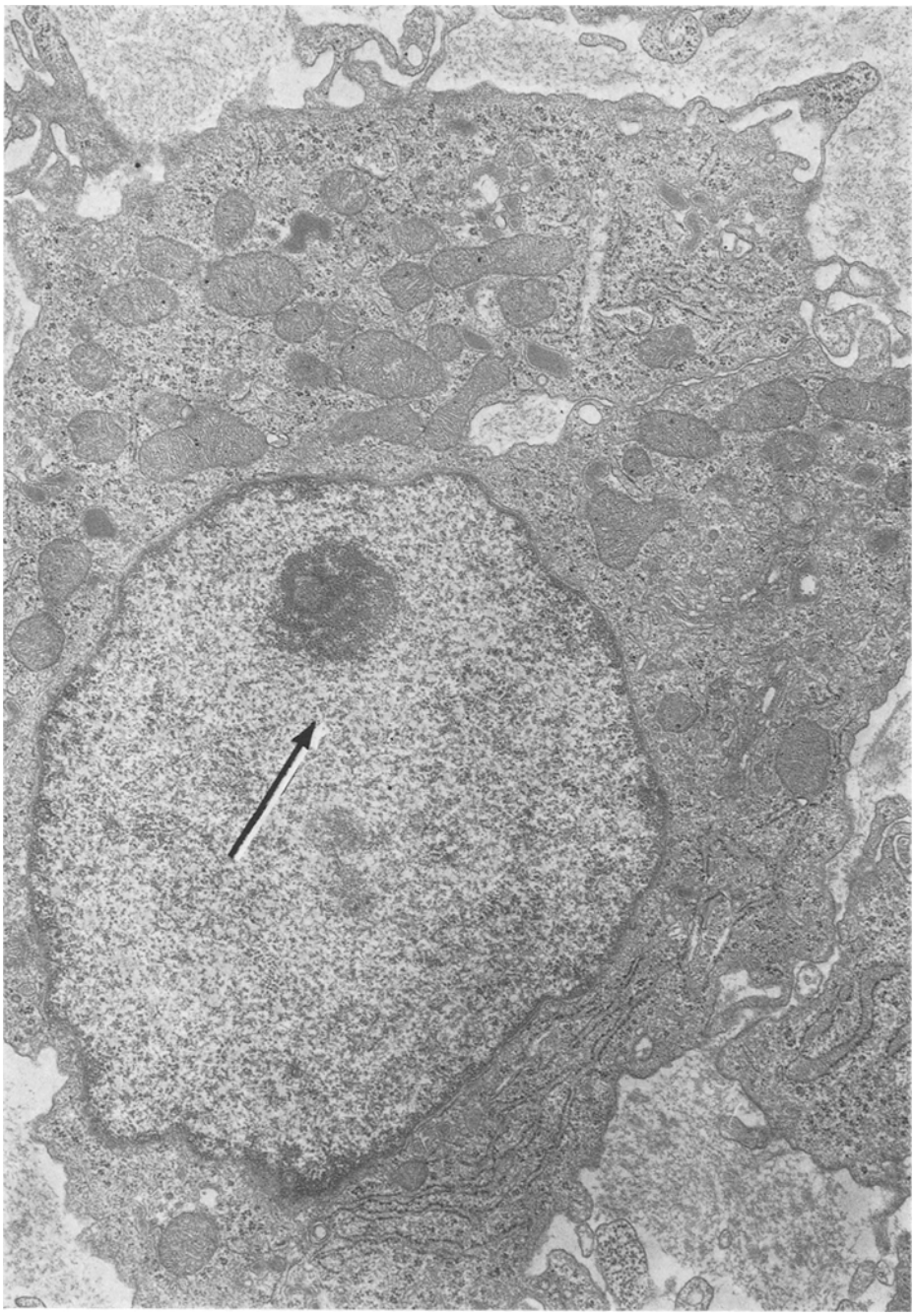

Fig. 8. Many plump and irregular cells with ample cytoplasm and cribriform nucleoli (arrow) suggested a histiocytic character by light microscopy, but their ultrastructure failed to reveal phagosomes and there was ample RER. Their ruffled plasma membranes and filopodia, their size and shape indicate, however, that they are probably immature histiocytes. ×13,500

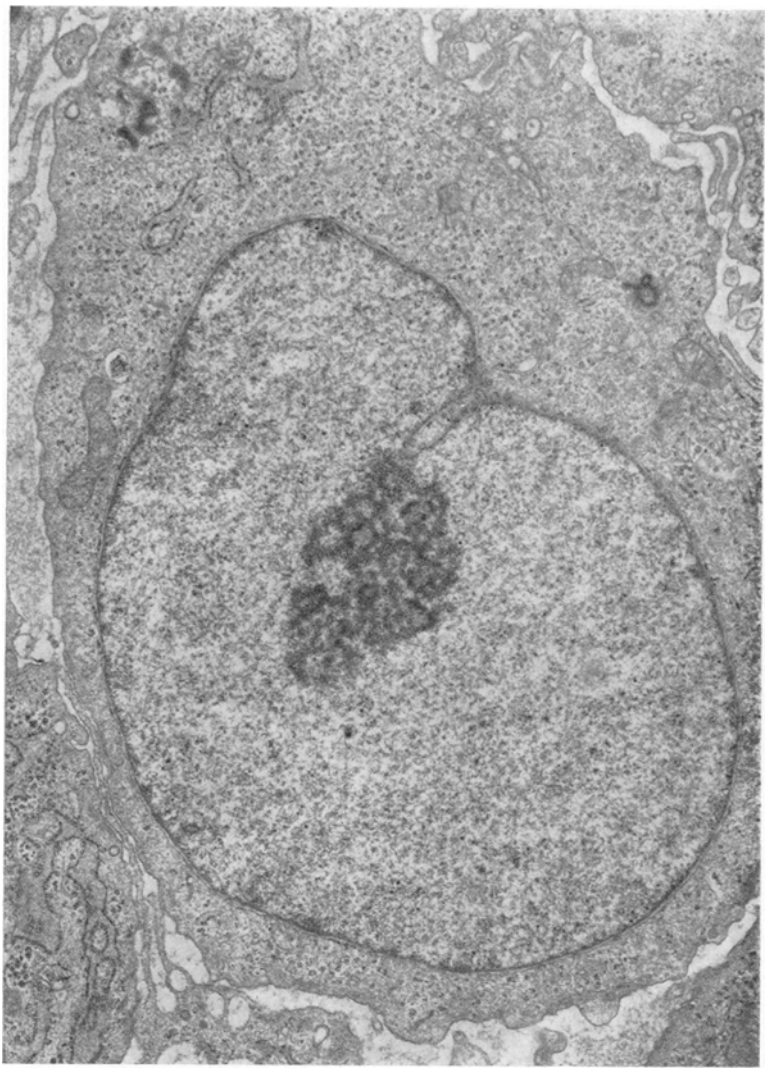

Fig. 9. Immature cells, possibly stem cells, were not often encountered. ×10,500

Even more immature cells were not recognized as a separate group by light microscopy, but the ultrastructure of these small-to-medium-sized ovoid cells showed a smooth cell membrane and a marked paucity of cytoplasmic organelles; instead they displayed masses of ribosomes and occasional localized accumulations of glycogen (Fig. 9).

Junctional complexes between any of the cells were not observed, only points of close approximation of cell membranes. The intercellular interstitium consisted mostly of flocculent amorphous material. Long-spaced collagen and mature collagen were extremely sparse (Fig. 10).

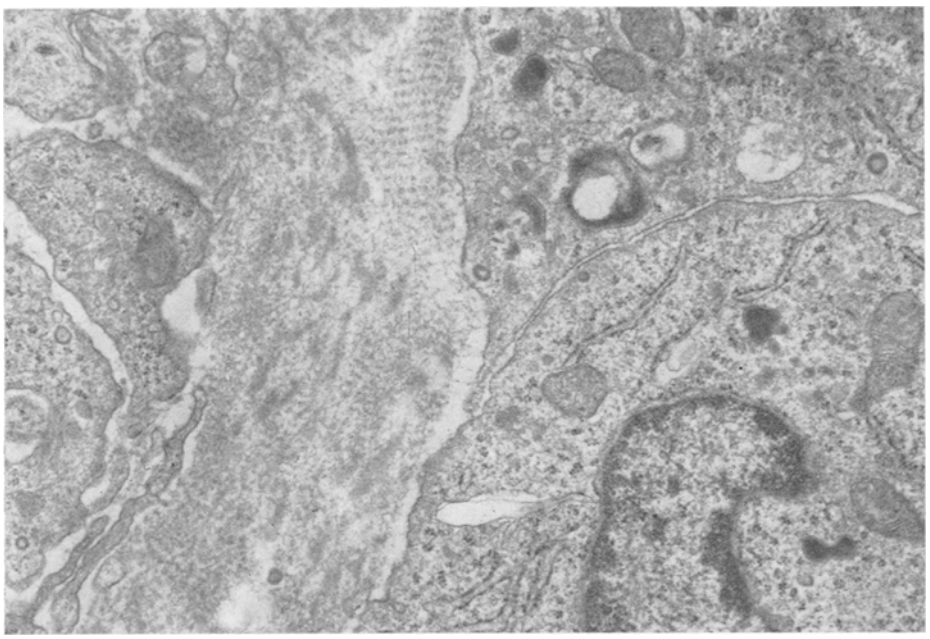

Fig. 10. Most of the intercellular material was amorphous or finely fibrillar, but scant long-spaced collagen was observed. ×10,500

## Discussion

Fibrous histiocytomas have been reported uncommonly in the pediatric age group. The largest series is still that of Stout with 27 cases (Kauffman and Stout, 1961; O'Brien and Stout, 1964). Eight of these were considered to be malignant or questionably malignant and were 10 years of age or older. Two tumors recurred locally and one patient died because the growth could not be controlled by surgery or radiation. Except for one pulmonary tumor, all other primary sites were in the subcutaneous tissues or the skeletal muscle. Kempson and Kyriakos (1972) included two teen-aged girls in their group of fibroxanthosarcomas, both tumors being solitary and subcutaneous. Soule and Enriquez (1972) did not have any malignant fibrous histiocytoma before the fourth decade among their 33 patients from the Mayo Clinic. Eleven fibrous histiocytomas were primary in bone but no patient was younger than 18 years (Spanier et al., 1975). Probably the earliest fibrous histiocytoma occurred at the age of 2 months (Kauffman and Stout, 1961).

Kauffman and Stout commented on the difficulty in establishing criteria which would separate the benign from the potentially malignant fibrous histiocytomas. Other authors have agreed that the mitotic rate alone is not a reliable indicator of malignancy (Soule and Enriquez, 1972; Kempson and Gavran, 1964). Fibroblasts with irregular, hyperchromatic nuclei and large nucleoli as well as many benign and atypical giant cells in conjunction with mitoses may be considered safe criteria of malignancy in these tumors (Soule and Enriquez, 1972; Fu et al., 1975).

The presentation of a fibrous histiocytoma with malignant histologic features in a newborn infant is quite unusual. Furthermore, the clinical and radiologic picture and the distribution of the lesions in the subcutaneous tissues, bones, and viscera resemble a congenital fibromatosis more than a fibrous histiocytoma. Congenital fibromatosis is generally conidered multifocal rather than metastatic because of its histologic composition of mature, thin fibroblasts without mitoses and of many instances of spontaneous regression when the tumor involved only musculoskeletal sites (Schaffzin et al., 1972; Heiple et al., 1972). In addition, familial multicentric fibromatosis has been reported in older children (Zayid and Dihmis, 1969; Enjoji et al., 1968; Woyke et al., 1970). The malignant histologic characteristics would, therefore, indicate that this congenital fibrous histiocytoma is a metastasizing malignant tumor, unusual as it may be. At the present state of our knowledge, it is, however, impossible to predict whether the tumor cells might have followed the pattern of conversion that they showed in tissue culture or would have behaved more benignly than their histology indicated, a trait that is not without precedent in congenital tumors (Wigger, 1975).

Both the congenital and the adult fibrous histiocytomas demonstrate the same mixed microscopic pattern, i.e. fibrous and histiocytic, but ultrastructurally the congenital tumor displayed some difference. There was less variation from the two basic cell types and less maturity of both cell structure and function (Fu et al., 1975; Merkow et al., 1971). Most fibroblasts and histiocytes were relatively immature and showed little evidence of phagocytosis and no production of typical collagen fibers. There was also less variety in cytoplasmic organelles; giant mitochondria with rodlike inclusions were absent and so were whorled membranes, lamellated inclusions, appreciable amounts of microfilaments and annulate lamellae. Junctional complexes, erythrophagocytosis, and complex reduplication of the capillary basal lamina were not encountered (Fu et al., 1975; Merkow et al., 1971). Histiocytes and giant cells were very much alike aside from the expected difference in cell size and the number of nuclei and cytoplasmic organelles. Xanthoma cells were absent.

The cell population of the congenital fibrous histiocytoma may therefore be considered even more clearly bimodal than that of its adult counterpart. In principle, it parallels the findings and supports the conclusions of the ultrastructural and tissue culture studies in the malignant adult tumors. Still unresolved remains the question whether or not there are "two pathways of differentiation of a single mesenchymal cell line which has been transformed by the neoplastic stimulus" (Fu et al., 1975).

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Dr. H. J. Wigger
Department of Pathology
College of Physicians and Surgeons
of Columbia University and Montefiore
Hospital Medical Center
630 West 168th Street
New York, N. Y. 10032, USA