

Benign Fibrous Tumors and Tumorous Lesions of the Bone

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Abstract—We report here 6 cases with classical forms of nonossifying fibroma (NOF) and 1 case of fibrous cortical defect (FCD) which occurred in the metaphysis of the long bones of children along with 2 cases of fibrous histiocytoma (FH) which occurred in the vertebra and femur neck of adults. Their clinical data, radiographs, histopathology, and ultrastructural features are described. Through these series, we concluded that microscopic and ultrastructural findings are not basically different among NOF, FCD, and FH. NOF is different from FCD in the extent of the disease, the latter involving only the cortex, which is best evaluated by radiological examination. The FH cases were located in sites other than the metaphysis of the long bones and were older than FCD or NOF. Our data concurred with the previous notion that the FCD and NOF(MFD) are evolutionary forms of the same process. It is believed that certain lesions that we called fibrous histiocytoma of the bone do exist based on their microscopic similarities to fibrous histiocytoma of the soft tissue, although they can be put into NOF or FCD by the age and site of the involvement.

Key Words: *Benign tumor, Nonossifying fibroma, Fibrous tumor, Metaphyseal fibrous defect, Fibrous cortical defect, Fibrous histiocytoma, Bone, Childhood*

INTRODUCTION

Nonossifying fibroma (non-osteogenic fibroma, NOF), metaphyseal fibrous defect (MFD), and fibrous cortical defect (FCD) have been used synonymously to describe the same basic histopathological process in bone (Jaffe & Lichtenstain, 1942; Steiner, 1974). These benign fibrous lesions are distinctive pathological conditions of the bone that occur in children, most often in the long tubular bones. Clinically, there are few or no symptoms except pain (Cunningham & Ackerman, 1956). They are usually eccentric and show a scalloped sclerotic border (Sontag & Pyle, 1941; Moser *et al.*). Fracture can occur through the thinned cortex (Arata *et al.*). Microscopically, scattered osteoclast-like

giant cells and collections of foamy and hemosiderin-laden macrophages are frequent, and these microscopic features are very reminiscent of a benign fibrous histiocytoma of soft tissue. However, the benign fibrous histiocytoma of the bone is a controversial and not fully established nor generally accepted lesion. Some authors designated it as such, especially when it occurs in adult patients and in a site other than the metaphyses of long bones (Clarke *et al.*; Bertoni *et al.*). However, rare bone tumors do exist that do not appear to fit into any previously described entity, and the designation of benign fibrous histiocytoma seems justified.

We have studied retrospectively 6 cases of NOF, 1 case of FCD, and 2 cases of fibrous histiocytoma in order to elucidate the diagnostic criteria of each tumor and to find any differences among these

3 entities.

MATERIALS AND METHODS

From the files of the Seoul National University Hospital and Children's Hospital from 1985 to 1990 we collected 6 cases of nonossifying fibroma, 1 case of fibrous cortical defect, and 2 cases of fibrous histiocytoma of the bone. These cases were diagnosed under a variety of fibrous lesions of the bone. Clinical data, microscopic slides and radiographs were available for review in all cases. One case of NOF and 1 case of vertebral FH were studied ultrastructurally using fresh tissue fixed in 2.5% glutaraldehyde and postfixed in osmium tetroxide. The specimens for electron microscopic study were processed routinely, embedded in epoxy resin, and stained with uranyl acetate and lead citrate.

RESULTS

Clinical data

Pertinent clinical findings are summarized in Table 1. Among 6 cases of NOF, the male-to-female ratio was 4:2. The ages at the time of diagnosis varied from 8 to 15 years (average: 12.5 years). One case of FCD occurred in an 11-year-old boy. Two cases of fibrous histiocytoma were 32- and 43-year-old females. Out of 6 cases of NOF, the

presenting complaint was pain in 2 cases; 4 cases were found incidentally by X-ray examination taken to evaluate trauma. The one FCD case was also found incidentally during a workup of the pain on the contralateral knee. Three out of 6 cases of NOF showed pathologic fractures on initial X-ray examination. The fractures, managed by cast only, had uneventful healing courses, and the underlying NOF lesions showed no interval changes. Five cases of NOF occurred in the tibia (2 in the distal metaphysis and 3 in the proximal metaphysis) and 1 case in the proximal metaphysis of the fibula. The 1 case of FCD occurred in the distal metaphysis of the tibia. Two cases of fibrous histiocytoma occurred in the T7-8 vertebrae and the left femur neck, respectively.

Radiological features

All cases of NOF were located eccentrically in the metaphysis and were seen as lobulated radiolucent lesions with prominent rim of sclerosis (Fig. 1). The base of the lesions paralleled the cortex. FCD showed no evidence of medullary involvement. The pedicles and laminae of the vertebrae involved by fibrous histiocytoma also showed a bubbly appearance with sclerotic rim. There was extradural extension. The left femur neck involved by fibrous histiocytoma revealed the same radiologic appearance as NOF, and the tumor masses were located eccentrically in the epiphyseal

Table 1. Clinical summary of benign fibrous bone lesions in this series

Case	Sex	Age	Site	Chief Complaint	Pathologic Fracture	Operation	Diag.
1	M	12	Rt distal tibia metaphysis	Pain	+	Curettage	NOF
2	M	13	Lt proximal fibula metaphysis	!	+	En bloc	NOF resection
3	F	8	Rt proximal tibia metaphysis	!	-	Curettage	NOF
4	M	12	Rt distal tibia metaphysis	Pain	+	Curettage	NOF
5	M	15	Lt proximal metaphysis	!	-	Curettage	NOF
6	F	15	Rt proximal tibia metaphysis	!	-	Curettage	NOF
7	M	11	Lt distal tibia metaphysis	!	-	Curettage	NOF
8	F	32	Lt neck femur	!	-	Curettage	FH
9	F	43	Vertebra T7-8	spastic paraparesis	-	Curettage	FH

NOF: nonossifying fibroma, FCD: fibrous cortical defect, FH: fibrous histiocytoma, !: incidentally found during trauma evaluation

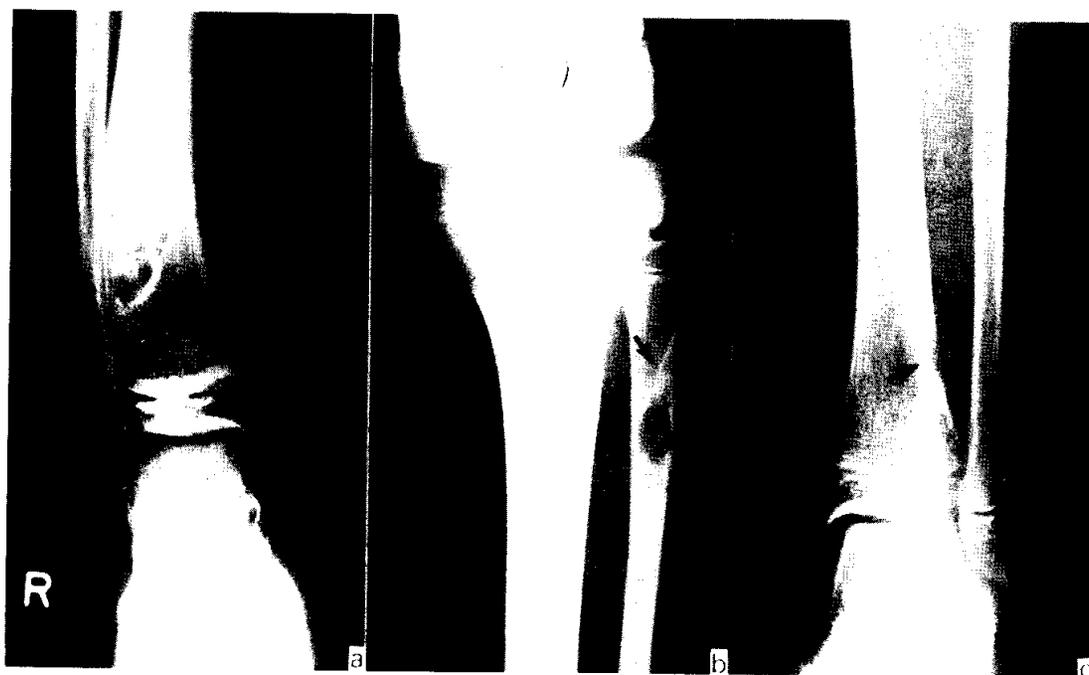


Fig. 1. Radiographic findings of Case 1(a) and Case 2(b) of NOF and Case 7(c) of FCD: a) a lobulated bubbly radiolucent lesion with prominent rim of sclerosis and underlying healed fracture are seen in the distal metaphysis of the tibia which is eccentric; b) a rather centrally located radiolucent lesion with prominent rim and fracture line (arrow) is seen in the metaphysis of the proximal fibula; c) distal metaphysis of the tibia shows an intracortical small lytic lesion with sclerotic rim (arrow).

plate instead of the metaphysis.

Histopathological findings

Since the tumors of the present series were thought benign before the operation, the submitted specimens were curettage material except one that was an en bloc segmental resection fragment. The histologic features of NOFs, FCD, and FHs were similar, although the relative proportions of the various elements differed. The lesions consisted of very cellular spindle cells in a pattern of storiforms or sheets (Fig. 2) with varying numbers of multinucleated giant cells and xanthoma cells which were unevenly scattered areas of fewer cells were present in some cases. The nuclear form of the spindle cells was generally regular-oval to elongated and was bland-looking. Although a few mitoses could be detected in some cases, no atypical mitoses were found. The multinucleated cells were of osteoclast-like giant cells, the size of which

varied by the number of nuclei that ranged from several to 30. In Case 7, fibular NOF involved nearly the entire medulla on cross section (Fig. 3a). At the thinnest portion of the cortex, the cortical bone was still intact. Microscopically, it showed a similar histology with NOF (Fig. 3b). In the fibrous histiocytoma of the vertebra, clusters of foam cells and occasional Touton-type giant cells were seen (Fig. 4). Mononuclear inflammatory cells were seen in varying numbers in all cases. Varying amounts of hemosiderin deposit were seen in some cases. Reactive or reparative new bone formation with osteoblastic and osteoclastic rimming was found focally only in vertebral fibrous histiocytoma (Fig. 5).

Electron microscopic findings

One case of nonossifying fibroma consisted mainly of myofibroblasts and a fewer number of fibroblasts that were elongated (Fig. 6). Their

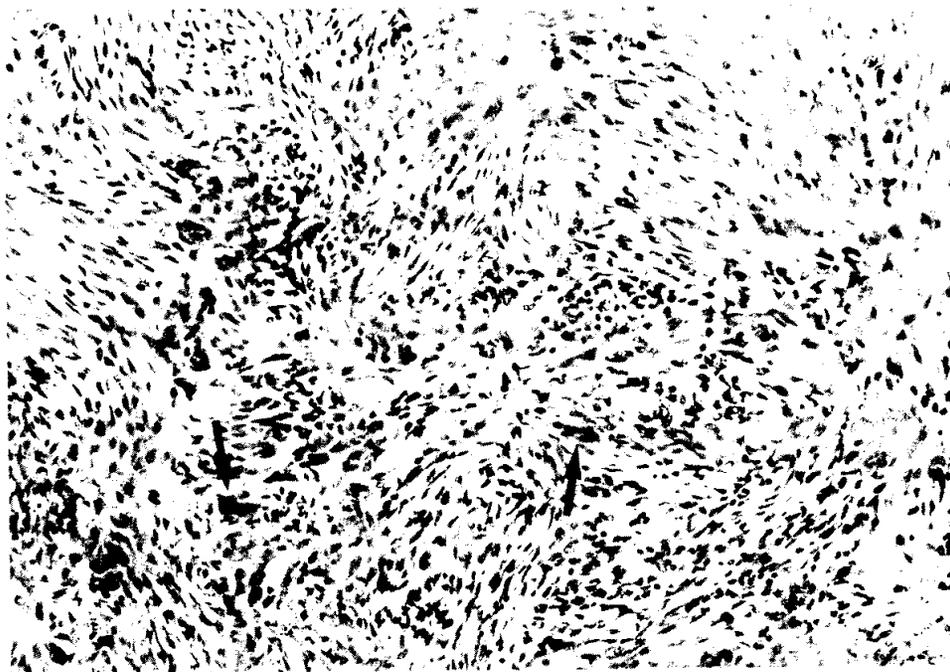


Fig. 2. Cellular spindle cells in storiform pattern with small osteoclast-type giant cells (arrows) are seen. (H&E, X200)

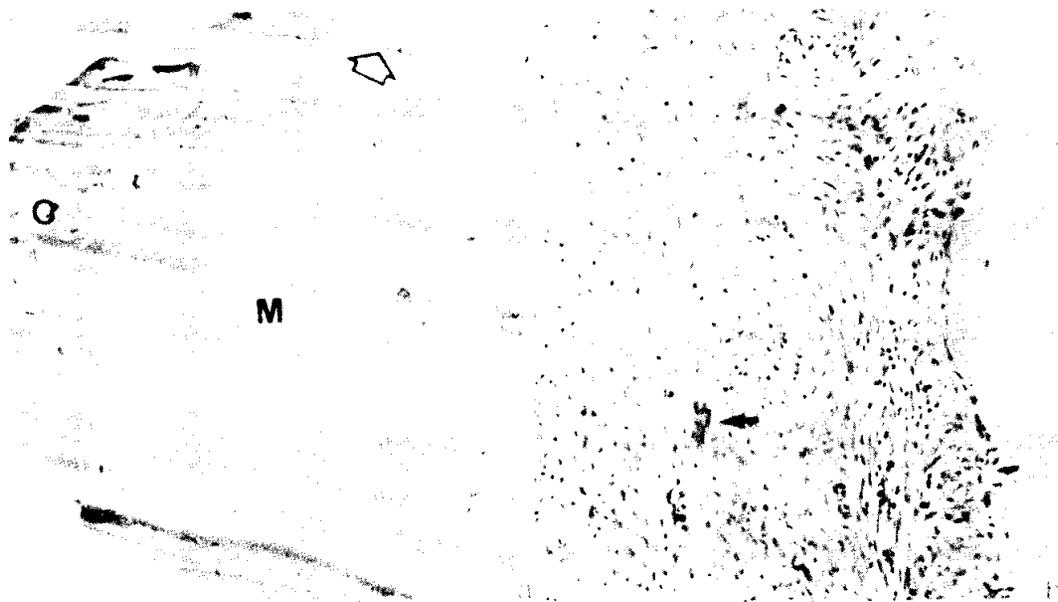


Fig. 3. a) Low-power view of cross sectioned fibula shows that the fibrous lesion nearly replaced the entire medulla, and the cortex is intact with eccentric thinness of the cortex (open arrow). c: cortex, M: medulla with tumor (H&E, X1) b) A high-power view of a) shows well preserved cortical bone and sheets of spindle cells with osteoclast-type giant cells (arrow). (H&E, X200)

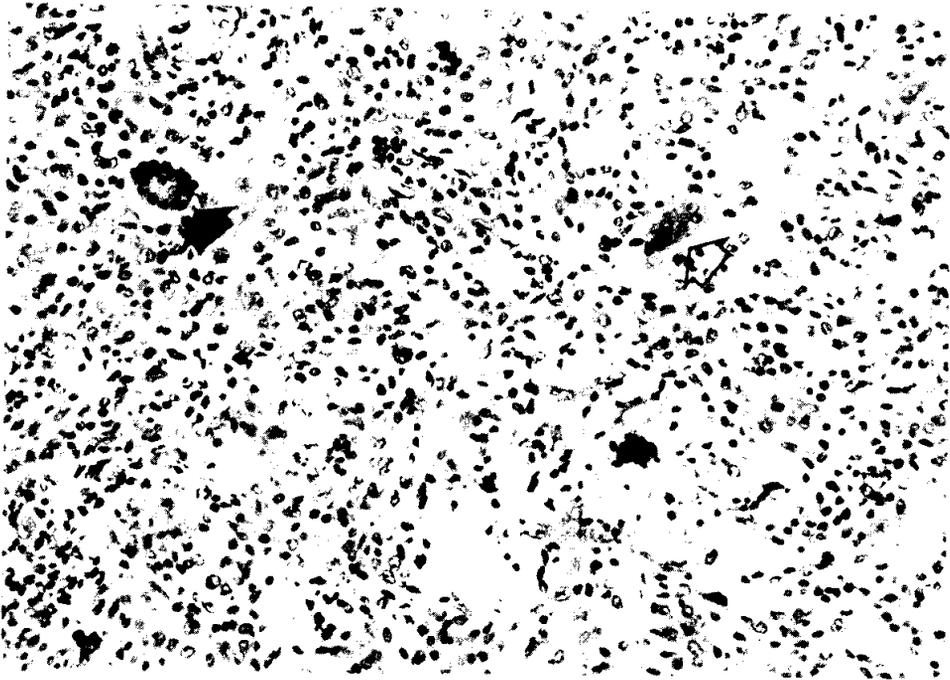


Fig. 4. Microscopic view of Case 9 shows clusters of foam cells and Touton-type (solid arrow) and osteoclast-type giant cells (open arrow). (H&E, X200)

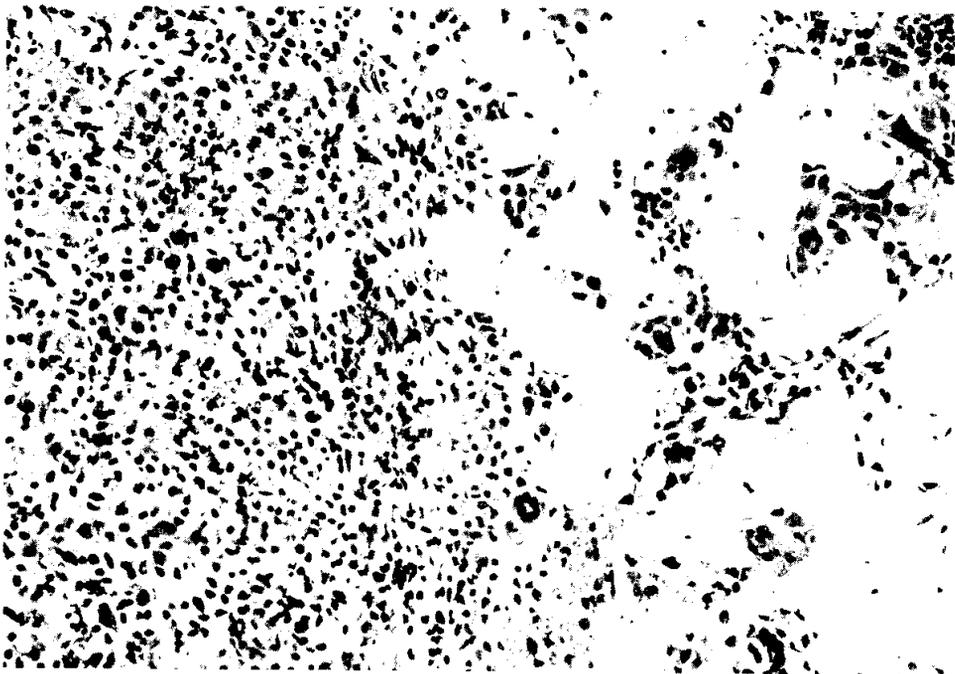


Fig. 5. Focal area of Case 9 shows reactive bone formation with osteoblastic and osteoclastic giant cell rimming. (H&E, X100)

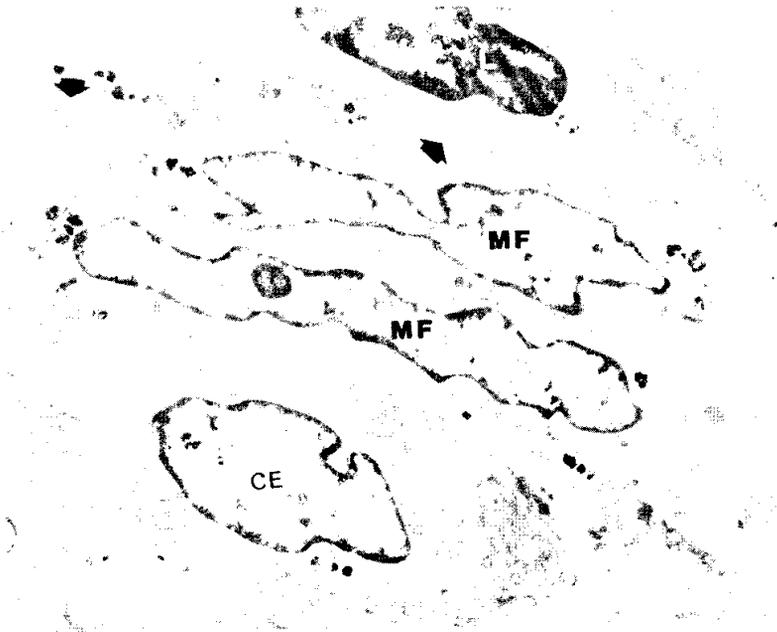


Fig. 6. Ultrastructural finding of Case 4 (NOF) reveals myofibroblasts. Their nuclei show elongation with chromatin condensation along the nuclear membrane. The cytoplasm contains rough endoplasmic reticulum, mitochondria, and microfilaments with focal densities beneath the cytoplasmic membrane (arrows). MF: myofibroblast, CE: capillary endothelial cell, L: lymphocyte. (Uranyl acetate and lead citrate, X7,500)



Fig. 7. A multinucleated giant cell in Case 4 (NOF) has several nuclei with prominent nucleoli. The cytoplasm contains plentiful rough endoplasmic reticulum, mitochondria, and small Golgi apparatus. The remaining cytoplasm is filled with filamentous material. (Uranyl acetate and lead citrate, X10,000)

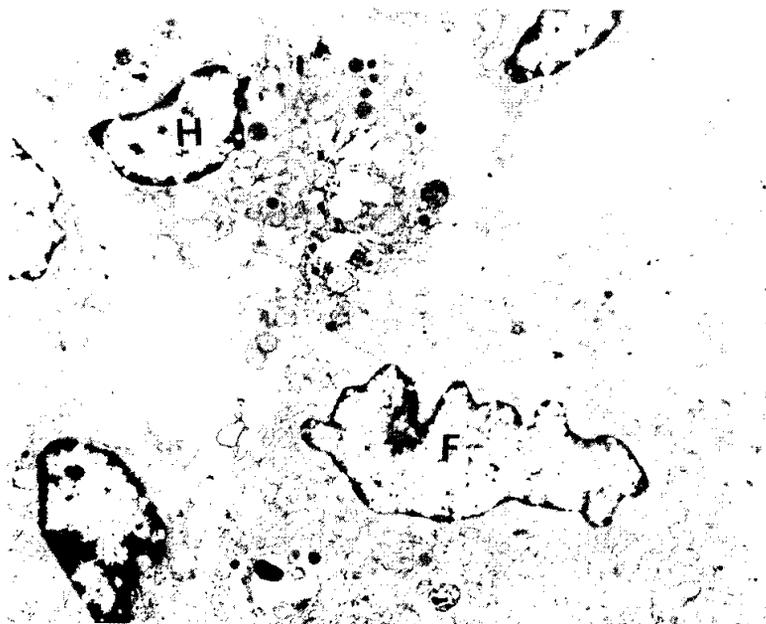


Fig. 8. Ultrastructure of vertebral fibrous histiocytoma (Case 9) consists of histiocytes (H) and fibroblast (F). The histiocytes contain a fair amount of lysosomes, mitochondria, and lipid droplets. The fibroblasts show eccentric nuclei and plump cytoplasm containing abundant rough endoplasmic reticulum with dilated cisternae. (Uranyl acetate and lead citrate, X8,800)

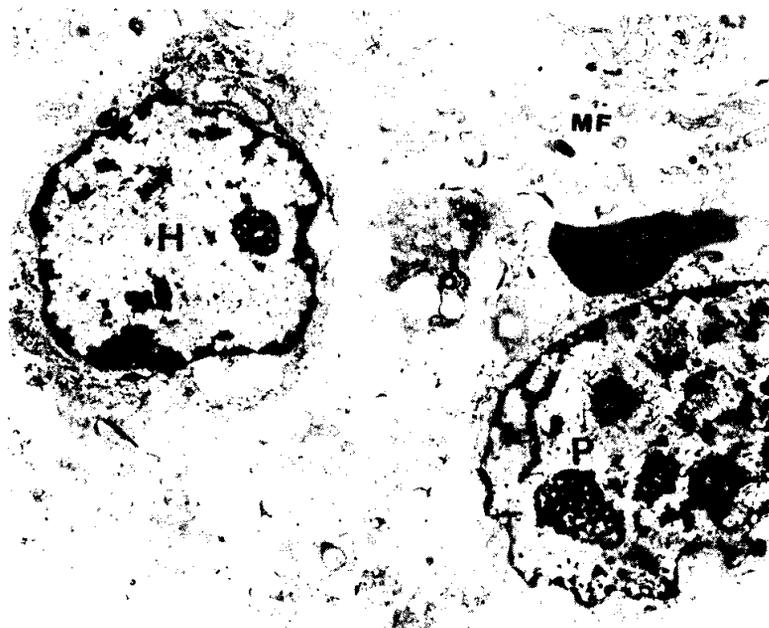


Fig. 9. A few primitive cells, found in a case of fibrous histiocytoma (Case 9), are seen and show large nuclei with heterochromatin and prominent nucleoli and rather sparse cytoplasmic organelles. P: primitive cell, H: histiocytic cell, MF: myofibroblast. (Uranyl acetate and lead citrate, X11,000)

nuclei were elliptical-to-cigar shaped with chromatin condensation along the nuclear membrane. The cytoplasm contained abundant rough endoplasmic reticulum and microfilaments with focal density beneath the cytoplasmic membrane. Some of the tumor cells were surrounded by external lamina. In the intercellular area, collagen fibers were deposited. There were also oval-to-elongated undifferentiated mesenchymal cells with a few cytoplasmic organelles. A few inflammatory cells and cells with fat vacuoles were interspersed. The multinucleated giant cells showed ruffled cytoplasmic membranes. Their cytoplasm contained plentiful rough endoplasmic reticulum, mitochondria, Golgi apparatus, and vacuoles (Fig. 7). The remaining cytoplasm was filled with fine filamentous structures that made the cytoplasm look dark. One case of vertebral FH consisted of almost equal mixtures of fibroblastic, histiocytic, and primitive cells. The fibroblastic cells showed eccentric nuclei and abundant dilated rough endoplasmic reticulum. The histiocytic cells contained a fair amount of lysosomes, mitochondria, and lipid droplets (Fig. 8). The primitive cells had large nuclei with heterochromatin and prominent nucleoli and rather sparse cytoplasmic organelles (Fig. 9).

DISCUSSION

Benign fibrous histiocytoma is a well-recognized tumor of the soft tissue. Histologically identical lesions, composed of fibroblastic and histiocytic cells arranged in a storiform pattern, occur in the bone, and these tumors have been known as fibrous cortical defect or nonossifying fibroma, or even fibrous histiocytoma (Steiner, 1974; Clarke *et al*). All of our 6 cases of NOF were found in children from 8 to 15 years of age. The male-to-female ratio was 2:1. All were located in the metaphysis of the tibia or fibula. Four (67%) were found incidentally, and the remaining 2 (33%) presented with local pain. A pathologic fracture was found in 3 (50%) of the 6 NOFs. during follow-up, it was noted the pathologic fractures healed naturally by palliative management, i.e., by application of a cast. The underlying lesions, NOF, showed minimal progression or a slight increase or no interval change at all. The cases

of NOF without fracture also showed a slight increase of tumor size in about 1-year intervals. Since the clinical and radiological courses in all cases were benign, each patient had undertaken curettage except for the one of en bloc resection. Radiologically, in all cases, the curettage sites were completely replaced by new bone without evidence of recurrence during the postcurettage follow-up period of 5 months to 4 years. The one case of FCD incidentally found in an 11-year-old boy involved the superficial cortex but only at the time of diagnosis, suggesting that FCD is only the smaller lesion of the larger NOF as Jaffe's (1958) concept alludes. Therefore we concur with the notion that the term FCD refers to those small purely intracortical, lucent lesions that occur in young children rather than NOF (Steiner, 1974). Jaffe (1958) noted that most FCD are eventually obliterated by either reparative ossification or gradual extrusion from the cortex by remodeling and tubulation at the metaphyseal growing end of the bone. In a small percentage of cases, however, FCD persists and proliferates into the medullary cavity, can render symptomatic, and even lead to pathologic fracture. Jaffe considered this process to be the tumorous evolving form of FCD, for which he introduced the term nonossifying or non-osteogenic fibroma. Later, Hatcher (1945) preferred the term metaphyseal fibrous defect, because these lesions eventually are obliterated by bone. The term NOF and MFD appear to be equally used, and FCD and NOF (MFD) are considered to be different evolutionary forms of the same process.

Two of our cases of FH occurred in adults (32 and 43 years old) at sites other than the metaphysis. They were located in the vertebral bone or the femur neck, with characteristic bubbly radiological features.

In reviewing the histological features of these tumors that were described, it was our conclusion that there were no distinctive microscopic findings that were significant among FCD, NOF, and FH. NOF was different from FCD only by radiological findings. FCD involved only the cortex and did not extend into the medullary cavity. However, FH was different in site and age from NOF or FCD. FHs were located at sites other than the meta-

physis of the long bones and involved those older in age than FCD or NOF. Among the 8 cases, one was an atypical case of NOF involving the femoral neck. The patient was a 7-year-old boy (Klein *et al*). In addition, our vertebral FH revealed more inflammatory cell infiltration and Touton-type giant cells, and reactive bone formations were found only in this lesion.

There has been the still unresolved problem of whether these tumorous conditions represent a developmental aberration or a disturbance in ossification (Ponsetti & Friedman, 1949; Hatcher, 1945; Dorfman, 1989). Recently, these entities are thought not to represent true neoplasms, since they are self-limited processes and have not been shown to undergo malignant change (Spjut *et al*). Malignant transformation of NOF has been reported (Bhagwandeem, 1966). Jaffe noted that FCD arise from the proliferation of fibrous tissue of the periosteum that subsequently invades the bone. Because these lesions apparently begin in a juxtacortical area, they have an eccentric radiographic appearance. Because these lesions begin in youth and because the extensive growth of the long bones in this direction, the lesion within the long bones generally assumes a longitudinal axis.

Among our cases, all fit these descriptions. However, Case 7, fibular NOF, involved nearly the entire medulla with an intact cortex. The X-ray of Case 7 showed no evidence of cortical bulging or cortical bone change. On cross section, it was apparent that the lesion was confined to the medulla. Therefore, one could surmise that NOF may not arise from the periosteum but from the marrow itself.

Histologically, the presence of multinucleated giant cells in a cellular spindle-cell background may cause some diagnostic problems with giant cell tumors. However, this interpretation should never be made, since giant cell tumors affect the ends of the bone in skeletally mature individuals (Dorfman, 1989). Yet occasionally, a giant cell tumor can be seen in a child (Picci, 1983) and may even be located in the metaphysis or diaphysis (Peison, 1976).

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==국 문 초 복==

골의 양성 섬유성 종양 및 증양성 병변

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어린이에 주로 발생하는 양성 골 증양종 섬유성 조직의 증식이 추가되는 병변들이 있는데 이들은 워낙 드물어서 그 정확한 병태를 파악하기가 쉽지 않다. 또다른 이름을 가진 비슷한 종양들이 어린이 및 어른에서 기술되어 있어, 병리의가 이런 병변을 만날때 마다 그 진단에 어려움을 겪고 있다.

본 논문에서 저자들은 본 병원에서 1985년부터 5년간 경험한 환자들을 통하여 비슷한 조직학적 특성을 가지는 섬유종성 병변을 증례별로 검색하였다. 여기에는 6예의 비골화 섬유종과 1예의 섬유성 피질결손 그리고 2예의 섬유성 조직구종이 포함되었다.

6예의 비골화 섬유종과 1예의 섬유성 피질결손은 모두 소아연령이었으며 장골의 골간단에 발생하였고 2예의 섬유성 조직구종은 성인의 척추 및 대퇴골에 각각 발생하였다. 병리조직학적으로 또 전자현미경적으로 이들 세가지 종양을 비교 검색한 결과 이들사이에는 근본적으로 차이가 없음을 알았다. 다만 그 발생부위, 육안적 소견, 나이 등으로 감별될 수는 있으나 이들은 기본적 병리에서 공통성이 있다고 판단되었다.