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NIH Fiche to Paper Journal

TITLE:	AMERICAN JOURNAL OF SURGICAL PATHOLOGY
PUBLISHER/PLACE:	Raven Press New York Ny
VOLUME/ISSUE/PAGES:	1993 Sep;17(9):924-30 924-30
DATE:	1993
AUTHOR OF ARTICLE:	Ishida T; Dorfman HD
TITLE OF ARTICLE:	Massive chondroid differentiation in fibrous dyspl
ISSN:	0147-5185
OTHER NOS/LETTERS:	Library reports holding volume or year 7707904 8352377
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The American Journal of Surgical Pathology 17(9): 924–930, 1993

Massive Chondroid Differentiation in Fibrous Dysplasia of Bone (Fibrocartilaginous Dysplasia)

Tsuyoshi Ishida, M.D. and Howard D. Dorfman, M.D.

Eight cases of fibrocartilaginous dysplasia (fibrous dysplasia with massive cartilaginous differentiation) of bone are reported. The age of the patients ranged from 4 to 26 years, with an average of 17.5 years. The male/female ratio was 1:1. In two patients the lesions occurred in a setting of polyostotic fibrous dysplasia. The anatomic sites most frequently affected were the femur and tibia. The proximal femur was the most common site. Roentgenograms showed well-demarcated lucent lesions of ground-glass opacity. In addition, stippled or ring-like calcifications suggesting cartilaginous elements were seen in six cases. Histologically, hyaline cartilage islands were found in juxtaposition to a fibro-osseous lesion characteristic of fibrous dysplasia. Enchondral ossification was commonly seen, frequently showing columnar arrangement of cartilage cells mimicking a growth plate. The cartilage may show moderate atypism. The important thing is to recognize the benign nature of chondroid elements in fibrous dysplasia. Even if cartilage dominates the histologic picture, it is important to identify the fibro-osseous elements and thereby avoid the misdiagnosis of chondrosarcoma.

Key Words: Fibrocartilaginous dysplasia—Fibrous dysplasia with massive cartilaginous differentiation—Fibrochondrodysplasia—Fibrous dysplasia—Cartilaginous tumors.

Am J Surg Pathol 17(9): 924–930, 1993.

Fibrous dysplasia is a relatively common, benign fibro-osseous lesion of bone. It is well known that cartilage islands are sometimes seen in fibrous dysplasia (3,8,13,14,20,21). The cartilage component in fibrous dysplasia is generally rather small, considerably less than 1 cm in diameter (15). On rare occasions, however, it is so prominent a feature that it may be misinterpreted as a cartilage neoplasm (9, 19,22). This condition has been designated as fibrocartilaginous dysplasia (7) or fibrochondrodysplasia (19).

We report herein eight cases of fibrous dysplasia with massive cartilaginous differentiation (fibrocartilaginous dysplasia) of bone and discuss the differential diagnosis from true cartilaginous neoplasms.

MATERIALS AND METHODS

Eight cases of fibrocartilaginous dysplasia of bone were encountered among 144 cases of mono- and polyostotic fibrous dysplasia in the consultation files of one of us (H.D.D.). Hematoxylin and eosin–stained slides were available for review in all cases. Roentgenographs were also available for review in all cases. One case in our series has already been reported previously (19).

Clinical and Roentgenographic Features

The clinical data of these eight cases are summarized in Table 1. The patients ranged in age from 4 to 26 years, with an average age of 17.5 years. Four patients were male and four were female. Two patients had polyostotic involvement of fibrous dys-

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TABLE 1. *Summary of clinical data of fibrocartilaginous dysplasia*

Case	Age (yrs)/ sex	Location	Type of FD	Symptoms	Duration of symptoms	Calcification on radiograph	Preconsultation diagnosis	Other findings
1	20/M	Femur (proximal)	Polyostotic	Mass	15 yrs	+	Chondrosarcoma	—
2	23/F	Tibia (proximal)	Polyostotic	—	—	+	FD with cartilage	Ovarian dysgenesis
3	8/F	Femur (proximal)	Monostotic	Pain	7 mos	+	Cartilage tumor	—
4	20/M	Femur (proximal)	Monostotic	Pain	?	−	FD with cartilage	—
5	26/F	Ischiopubic bone	Monostotic	Mass	8 yrs	+	Chondrosarcoma	—
6	14/F	Femur (proximal)	Monostotic	—	—	+	Cartilage tumor	Wilms' tumor, fibromatosis
7	25/M	Femur (proximal)	Monostotic	Pain, fracture	2 yrs (pain)	+	Enchondroma R/O chondro-sarcoma	—
8	4/M	Femur (shaft)	Monostotic	Limp	?	−[a]	?	—

R/O, rule out; FD, fibrous dysplasia.
[a] Chondroid tumor suggested by magnetic resonance imaging.

plasia. One patient had a history of Wilms' tumor of the right kidney at the age of 4 years and underwent nephrectomy and chemo- and radiotherapy. This patient also had fibromatosis of the buttock at the age of 14.

The symptoms were variable. Two patients had a swelling or mass, two were asymptomatic. Three had pain, and one of them developed a pathological fracture. The duration of the symptoms ranged from a few weeks to 15 years.

Most lesions were located in the femur, especially in the femoral neck, and the tibia. One case involved the ischiopubic bone.

Roentgenographically, the lesions were generally well demarcated and showed ground-glass opacity or were osteolytic in appearance (Figs. 1–5). When the shaft of the femur or tibia was involved, cortical expansion was seen; however, the cortex was always intact (Figs. 1 and 5). In one case, a typical "shepherd's crook" deformity was found in the femoral neck (19). In six cases, stippled or ring-like calcifications suggesting chondroid elements were evident in plain roentgenograms (Figs. 1–4). One case examined by magnetic resonance (MR) imaging showed low intensity in T1-weighted images and high intensity with lobulation in T2-weighted images suggesting chondroid tumors (Fig. 5). All the lesions showed nonaggressive roentgenographic features.

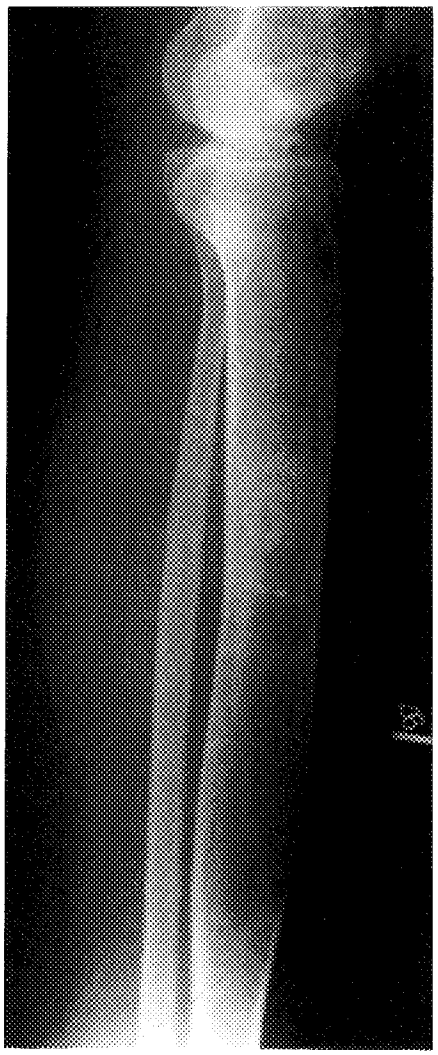

FIG. 1. Case 2. Lateral view of tibia shows stippled calcification in an expansile osteolytic and ground-glass radiolucent lesion of the proximal shaft.

Pathologic Features

A large amount of hyaline cartilage and a disproportion between cartilage and fibro-osseous elements are troublesome findings histologically. The

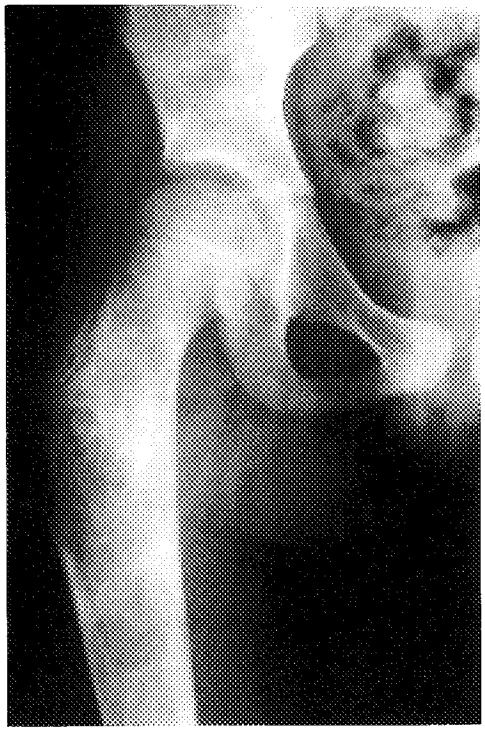

FIG. 2. Case 3. Sharply demarcated lytic lesion with ring-like calcification of the right proximal femur.

cartilage islands are irregularly distributed. Lobulation of the cartilage islands is seen; however, unlike a true cartilage neoplasm, each lobule is surrounded by fibro-osseous tissue typical of fibrous dysplasia, with sharp demarcation (Figs. 6 and 7). The cartilage usually shows relatively low cellularity; however, it may reach moderate cellularity and show some nuclear atypia of the cartilage cells (Fig. 8). Binucleate cells are occasionally found (Fig. 8).

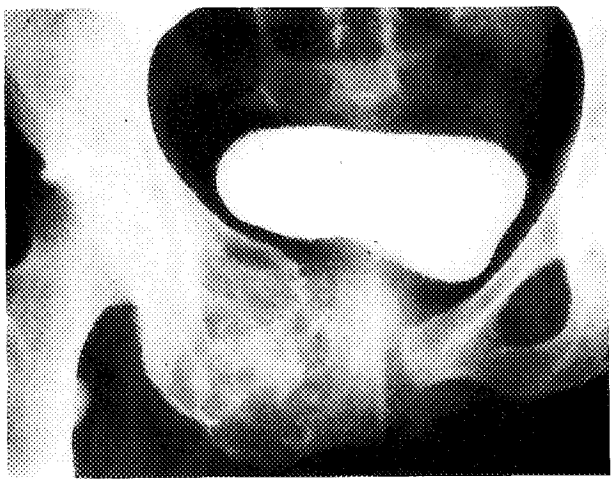

FIG. 3. Case 5. Expansile, well-defined lytic lesion with prominent stippled calcification of the ischiopubic bone, compressing the urinary bladder.

Myxoid change of the cartilaginous matrix was seen in only one case.

Enchondral ossification is commonly seen in the peripheral regions of the cartilage islands (Fig. 7). Hypertrophic chondrocytes tend to be arranged in columns with calcification of the matrix similar to that seen in the epiphyseal growth plate (Fig. 9). There are prominent capillaries between the vertical columns of the primary spongiosa and osteoclastic resorption is also found. Active enchondral ossification was seen in five cases.

Enchondral ossified trabeculae merge into the irregularly shaped bone trabeculae in the surrounding fibro-osseous lesion (Fig. 10). Although the fibro-osseous lesion shows the typical histologic appearance of fibrous dysplasia (Fig. 11), bone trabeculae around the cartilage islands are surrounded by osteoblasts representing the process of enchondral ossification. Prominent immature osteoid formation was seen in one case with a history of Wilms' tumor.

DISCUSSION

Although cartilaginous differentiation in fibrous dysplasia is usually inconspicuous, its presence is well known, and all textbook descriptions of fibrous dysplasia include at least a passing reference to the occasional presence of cartilage islands (3,8,13,14, 20). In rare instances, the cartilage elements may be massive in amount and reach several centimeters in diameter (15). In these situations, large dysplastic cartilage islands may be misinterpreted as benign or even malignant cartilaginous neoplasms (8,19,22). It is of the utmost importance to be aware of the possibility of finding cartilaginous predominance in otherwise typical monostotic or polyostotic fibrous dysplasia and to avoid the pitfall of diagnosing cartilage neoplasia.

Radiologically, all the lesions were well demarcated and showed a benign appearance. Six of eight cases had roentgenographically visible calcified areas that might be misinterpreted as enchondroma or chondrosarcoma (22).

The proximal portion of the femur is the most common site of fibrocartilaginous dysplasia (7). Five cases involved the femoral neck or proximal shaft of the femur. Tibial involvement was seen in one case and involvement of the mid- and distal femur was seen in another case. There was no case of fibrocartilaginous dysplasia involving the craniofacial bones or ribs in spite of the fact that these are the most common sites of conventional fibrous dysplasia.

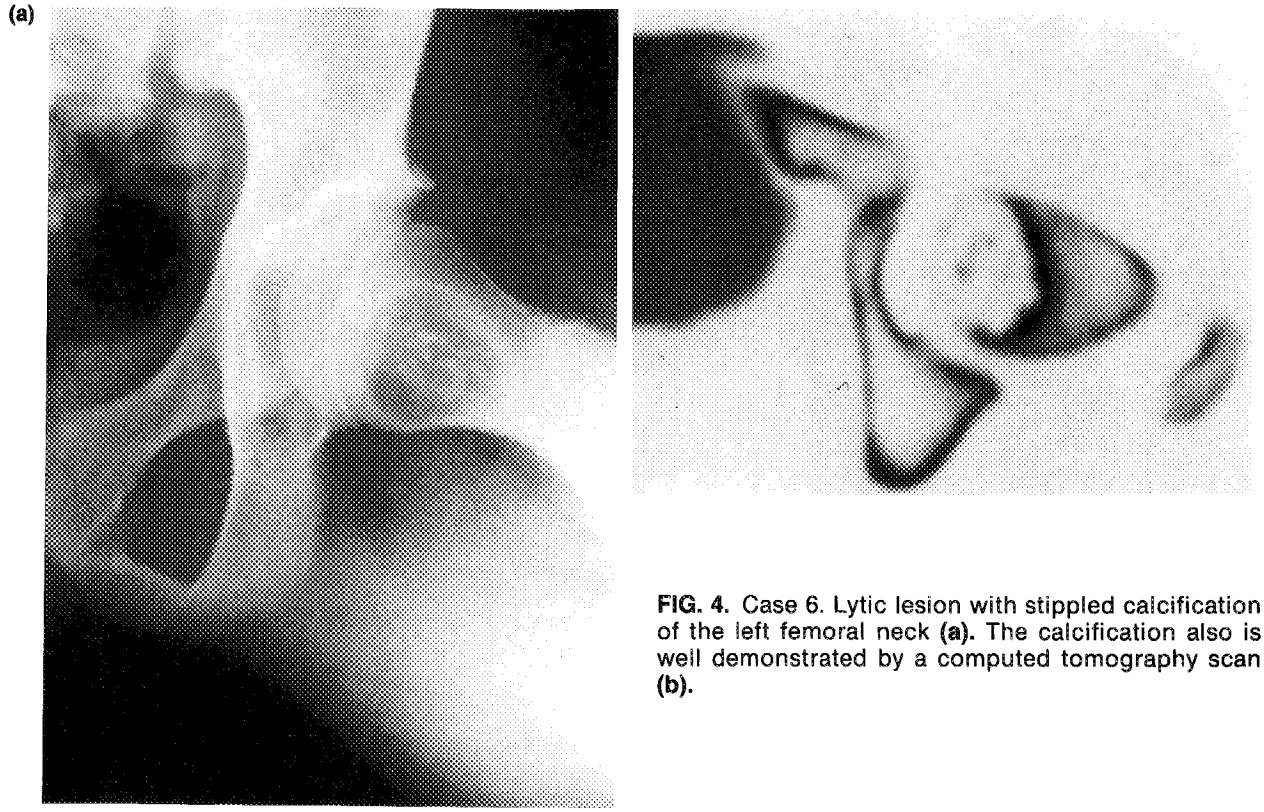

FIG. 4. Case 6. Lytic lesion with stippled calcification of the left femoral neck **(a)**. The calcification also is well demonstrated by a computed tomography scan **(b)**.

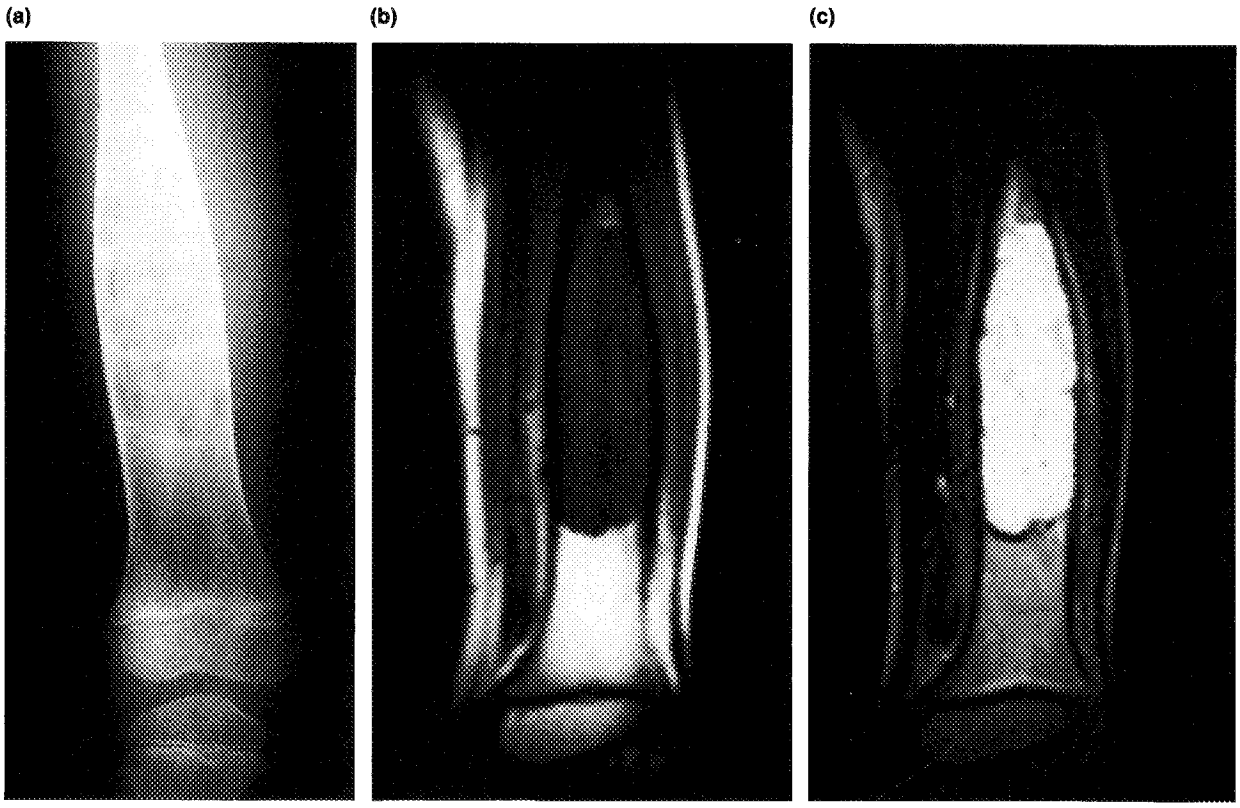

FIG. 5. Case 8. Hazy radiopaque, expanded lesion of the midshaft of the left femur **(a)**. The lesion shows low intensity in T1-weighted magnetic resonance (MR) image **(b)** and high intensity with lobulation in T2-weighted MR image **(c)**.

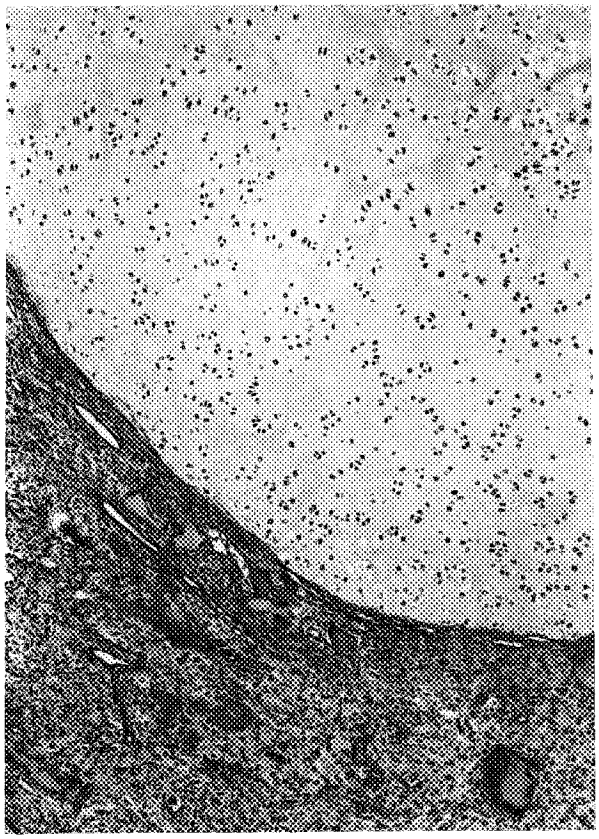

FIG. 6. Case 1. Cartilage island in juxtaposition to the fibro-osseous lesion with sharp demarcation.

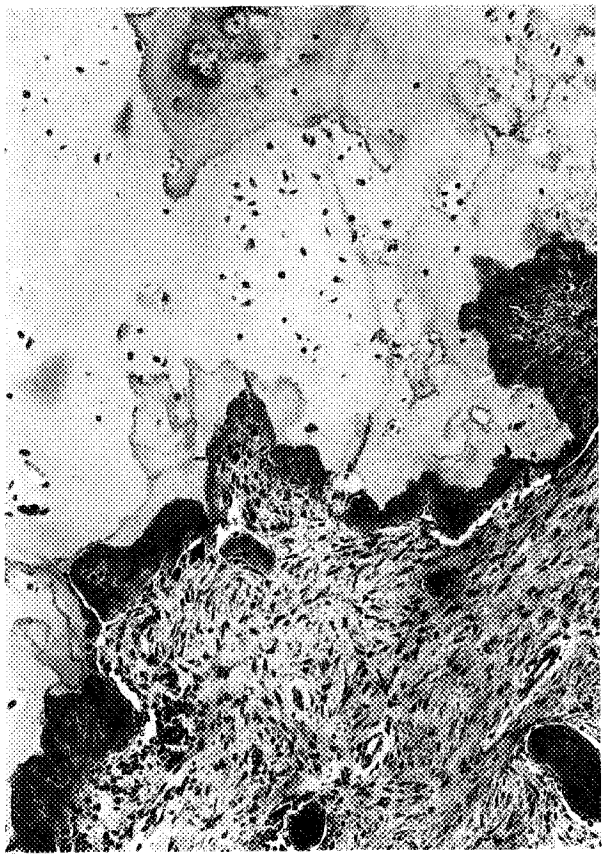

FIG. 7. Case 4. Cartilage island surrounded by ossified rim.

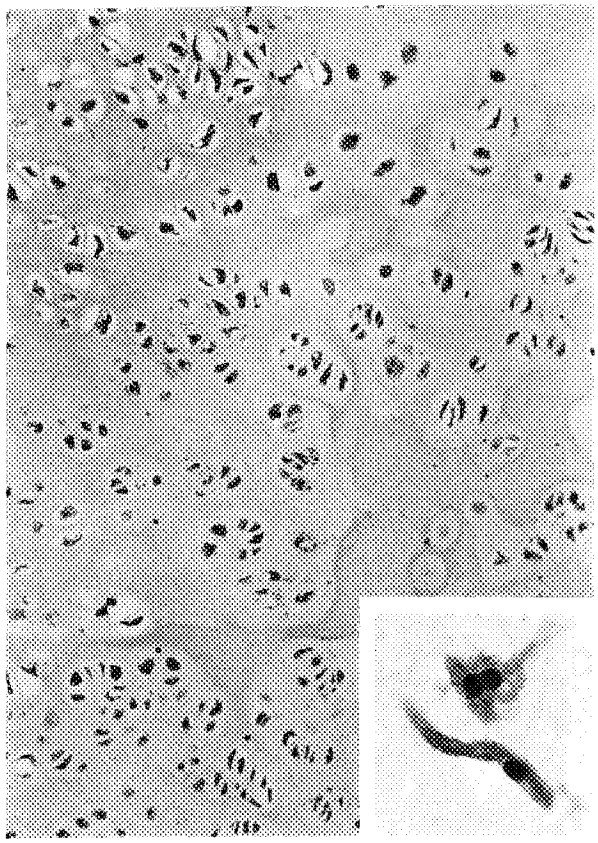

FIG. 8. Case 1. Cartilage component shows moderate hypercellularity. **Inset:** Case 8. A binucleate cell and a chondrocyte with elongated cytoplasmic processes are found.

Although the chondrocytes in fibrocartilaginous dysplasia are generally small with condensed nuclei, they may also show atypical findings such as hypercellularity, binucleate cells, and enlargement of chondrocytes in focal areas (19). The presence of large amounts of cartilage and its atypism are diagnostic pitfalls in the histologic diagnosis. The fibro-osseous lesion (typical of fibrous dysplasia) adjacent to the cartilage islands is the most important diagnostic clue to differentiate this entity from other cartilaginous neoplasms such as enchondroma and chondrosarcoma (7,22).

The cartilage islands tend to become calcified peripherally and show enchondral ossification merging with the surrounding fibro-osseous lesion. Enchondral ossification is frequently seen at the periphery of the cartilage islands resembling the epiphyseal growth plate. Such prominent enchondral ossification is not usually found in conventional chondroid neoplasms. This is another characteristic finding of fibrocartilaginous dysplasia, and is helpful in distinguishing these lesions from true cartilage neoplasms.

The differential diagnosis other than enchondroma and conventional chondrosarcoma includes dedifferentiated chondrosarcoma (5,17,18) and fi-

FIG. 9. Case 3. Columnar arrangement of hypertrophied chondrocytes and endochondral ossification mimicking the epiphyseal growth plate.

brocartilaginous mesenchymoma (2,6). Fibrous areas in fibrous dysplasia sometimes show high cellularity, and in such cases dedifferentiated chondrosarcoma would have to be considered. However, careful microscopic examination easily revealed malignant cartilage and anaplastic dedifferentiated sarcomatous elements. It is not difficult to distinguish dedifferentiated chondrosarcoma from fibrocartilaginous dysplasia when attention is paid to the absence of nuclear anaplasia.

Fibrocartilaginous mesenchymoma is an exceedingly rare bone tumor consisting of benign cartilaginous elements and a low-grade fibrosarcomatous component (2,6). In contrast to fibrocartilaginous dysplasia, a prominent component of fibrocartilaginous mesenchymoma is a low-grade fibrosarcoma, and the cartilage areas show organoid, hamartomatous features mimicking an epiphyseal growth plate.

Several cases of chondrosarcoma arising in fibrous dysplasia have been reported (1,4,8–13,16). Well-documented cases among these reports did not show the actual malignant behavior, with the exception of a case reported by Feintuch (10) that had undergone radiation therapy 30 years earlier and a case reported by De Smet et al. (9) that had not had radiation therapy. The tumors in these two cases showed cortical destruction and soft-tissue invasion. The latter case also showed metastasis to the sacral epidural space and lungs. The case reported Maeyama et al. (16) could be another example of chondrosarcoma arising in polyostotic fibrous dysplasia, because of its late onset of age (60 years old) and progressive course with soft-tissue involvement; however, follow-up data were not available. The other cases of chondrosarcoma complicating fibrous dysplasia with follow-up study could represent examples of fibrocartilaginous dysplasia, in view of their benign subsequent course (4,12,13). Although chondrosarcoma may develop in an area of fibrous dysplasia, it is distinctly unusual.

In general, fibrous dysplasia shows metaplastic bone formation in which spindle stromal cells directly form osteoid or bone similar to the process of membranous bone formation. In fibrocartilaginous dysplasia, another bone-forming process—that of enchondral bone formation—in which bone trabeculae form through the cartilage pathway, is found. □

FIG. 10. Case 2. Irregularly shaped, endochondrally ossified trabeculae found in a fibrous background.

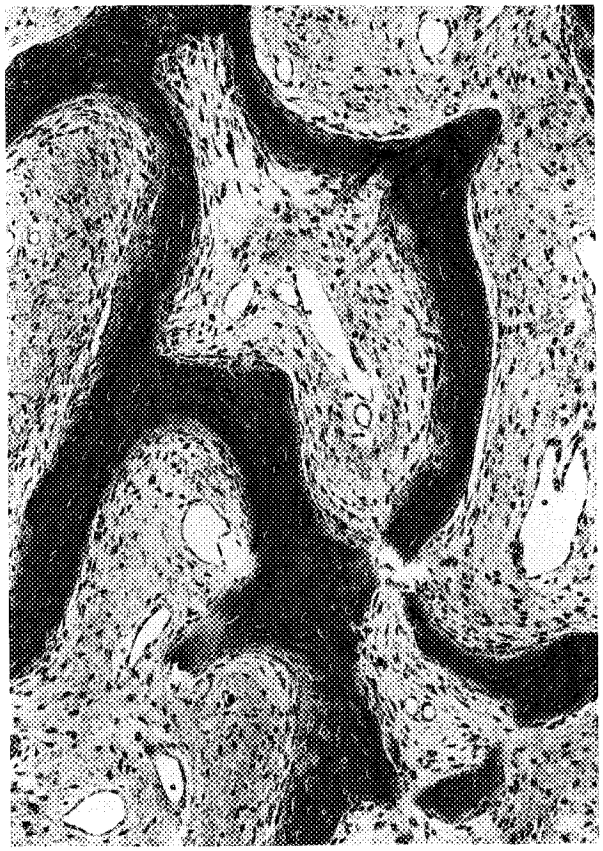

FIG. 11. Case 4. Typical fibro-osseous lesion characteristic of fibrous dysplasia.

Acknowledgement: We wish to thank the following for referring cases for this study: K. Pelzmann, M.D. and W. Salyer, M.D. (case 1), G. Mendelsohn, M.D. (case 2), A. Gamez, M.D. (cases 3 and 4), A. Michelena, M.D. (case 5), F.B. Askin, M.D. (case 6), B. Bennett, M.D. (case 7), and S.E. Crawford, M.D. (case 8). We also wish to thank Ms. D. Crawley for typing the manuscript.

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