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CASE REPORT

Fibrocartilaginous Dysplasia (Fibrous Dysplasia with Extensive Cartilaginous Differentiation)

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Fibrocartilaginous dysplasia is a variant of fibrous dysplasia in which extensive cartilaginous differentiation is identified. The amount of cartilage varies from case to case, however, no percentage has been proposed to consider this diagnosis. We present a 6-year-old girl with a two-year history of hip pain. Initial imaging studies of the right femur revealed a lucent lesion of the proximal shaft that extended into the femoral neck with ill-defined borders but well-maintained cortex. Computed tomography scan demonstrated increased density of the medullary cavity but the cortex appeared intact. Curettage of the lesion was performed and fragments with cartilaginous appearance were obtained, weighing 45 g in total. Microscopically, the tumor revealed a cartilaginous (60%) and a fibro-osseous (40%) component; the former had increased cellularity and some chondrocytes displayed moderate atypia and binucleation, while the latter showed features of fibrous dysplasia. Areas of endochondral ossification and calcification were also identified. After five years of surgery this child is well and without evidence of recurrence. We discuss the differential diagnosis of this variant of fibrous dysplasia in the pediatric group. (Pathology Oncology Research Vol 12, No 2, 111–114)

Key words: Fibrocartilaginous dysplasia, fibrous dysplasia, fibrochondrodysplasia, fibrous dysplasia with cartilaginous differentiation

Introduction

Fibrous dysplasia (FD) represents a dysplastic disorder of bone; the hallmark of this disease is a solitary focal or generalized multifocal inability of bone-forming tissue to produce mature lamellar bone. Genetic studies have shown that FD is a potentially crippling disease caused by postzygotic, activating missense mutations of the GNAS1 gene, which encodes the a subunit of the stimulatory G protein.[1,2] Histologically it is characterized by a benign-appearing spindle cell fibrous stroma containing scattered, irregularly shaped trabeculae of immature bone, lacking osteoblasts, which evolve directly from the stroma.[2,3] The most common locations are the jawbones, the skull, the ribs, and the proximal femur.[4,5] Radiologically, FD is usually a well-delimited lesion whose appearance ranges from lucent to radiodense, depending on the relative proportions of the fibrous and osseous tissue in its composition.[6] Occasionally, nodules of cartilage can be present in cases of polyostotic or monostotic forms of FD.[7-9] The term "fibrocartilaginous dysplasia" has been applied by some authors for cases that exhibit abundant cartilage.[9-12] This variant of FD with extensive cartilaginous differentiation or fibrocartilaginous dysplasia (FCD) occurs in the lower extremities, especially in the proximal portion of the femur, and extensive deformity of the bone may develop. Radiologically, FCD is similar to conventional FD with the addition, in most cases, of ring-like or scattered punctuate to flocculent calcifications that may be so extensive as to simulate a primary cartilaginous lesion.[6,8] The abundant cartilage has occasionally led to a misdiagnosis of chondrosarcoma arising in FD.[9,12,13] The distinction between FCD and other benign and malignant cartilaginous tumors is critical in the management of these patients.

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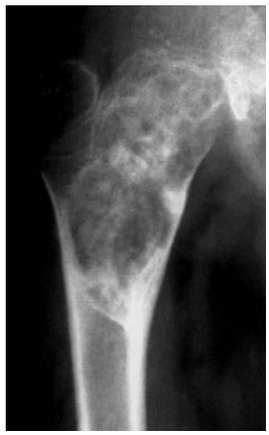

Figure 1. *Radiograph of the femur demonstrating a lucent lesion of the proximal shaft with irregular borders but well-preserved cortex. Notice the fluffy densities.*

Case report

A six-year-old girl with a two-year history of hip pain presented to the Hospital para el Niño Poblano. Radiographs of the right femur revealed a lucent lesion with fluffy "popcorn" densities of the proximal shaft that extended into the femoral neck with ill-defined borders but well-maintained cortex (*Figure 1*). Computed tomography scan (CT) demonstrated increased density of the medullary cavity but the cortex appeared intact. Radiological survey revealed no other lesion. The pre-operative diagnosis was fibrous dysplasia vs. enchondroma. Curettage with spongiosa-plasty of the lesion was performed and fragments with a cartilaginous appearance were obtained, weighing 45 g in total. Histologically, the lesion contained zones of conventional FD with trabeculae of bone within a fibrous stroma (*Figure 2a*). The trabeculae were irregularly shaped and consisted of immature (woven) bone lacking osteoblastic rimming; no lamellar transformation was evident. The stroma was composed of benign-appearing spindle-shaped fibroblasts loosely arranged in a whorled, storiform pattern or dispersed within a dense collagenized matrix. There was no fascicular arrangement, nuclear atypia, abnormal mitotic activity or necrosis. The areas of conventional FD were in continuity with similar regions that contained nodules of hyaline cartilage that varied from microscopic islands to large nodular masses (*Figure 2b*). Increased cellularity was found in the cartilaginous areas (*Figure 2c*), and some chondrocytes displayed moderate atypia and binucleation (*Figure 2d*). Areas of endochondral ossification and calcification were also identified. After reviewing eleven slides and several re-cuts of the lesion, the tumor revealed a cartilaginous component (60%) and a fibro-osseous component (40%) with histological features consistent with the diagnosis of fibrous dysplasia with extensive cartilaginous differentiation. After five years of follow-up, radiographic films show no evidence of recurrence and the patient is asymptomatic and well.

Discussion

It is well recognized that FD may contain cartilage, the amount of which, however, is quite variable. Lichtenstein and Jaffe[3] in their original article of fibrous dysplasia recognized that cartilage was "an integral part of the dysplastic process." Despite cases of FD detailing the occurrence of cartilage have been reported since 1930,[7,14] the first description of FCD as a variant of fibrous dysplasia was made by Pelzmann et al.[9] in a 20-year-old man with well documented history of polyostotic fibrous dysplasia. The term used by Pelzmann was fibro-chondrodysplasia, pointing out that documentation of malignant behavior was lacking in the scattered reports of chondrosarcomas complicating fibrous dysplasia and suggested that many of those cases represent examples of FCD.

In an excellent review of the English literature, Kyriakos et al.[15] found forty-one cases of FD in which cartilaginous differentiation was indicated radiographically, grossly or histologically. Kyriakos maintains that since foci of cartilage are well recognized as part of fibrous dysplasia and occur along a quantitative spectrum, FCD represents the extreme end of cartilaginous differentiation in fibrous dysplasia.

Under the title "fibrocartilaginous dysplasia" or "fibrochondrodysplasia", we found 11 cases reported in the literature to date (*Table 1*).[9-12,15] No gender dominance has been found, and the age of presentation ranged from 4 to 53 years. The proximal portion of the femur is the most common site of FCD, although tibial and ischion involvement was seen in one case respectively, and involvement of the femoral shaft was seen in another case. The presenting symptom is pain, deformity or a mass. However, patients can also be asymptomatic. Three patients had an associated polyostotic form of fibrous dysplasia.

Radiologically, the lesion is generally well-demarcated and shows ground-glass opacity. Cortical expansion can be seen, however, the cortex is always intact. Stippled or ring-like calcifications suggesting chondroid elements can also be present.[11,12]

Macroscopically, the appearance of the lesion is similar to that of enchondroma or low-grade chondrosarcomas, and consists of fragments or irregular masses with an obvious cartilaginous appearance. The histological appearance of FCD consists of large lobules of cartilage surrounded by fibro-osseous tissue with features typical of fibrous dysplasia. The cartilaginous component may be massive. In these cases, large dysplastic cartilaginous islands may be misinterpreted as benign or even malignant cartilaginous

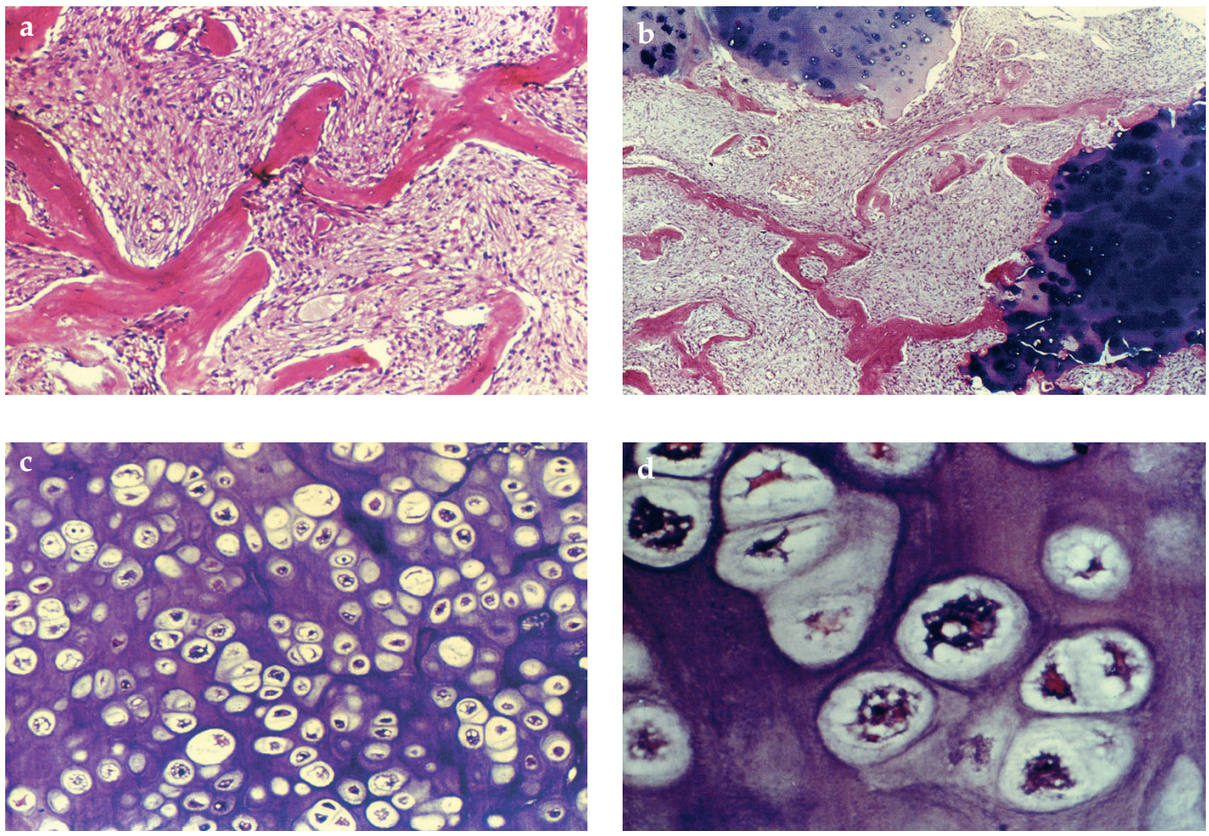

Figure 2. ***(a)*** *Typical "Chinese characters" of fibrous dysplasia.* ***(b)*** *Well-demarcated islands of cartilage surrounded by extensive fibro-osseous tissue.* ***(c)*** *Cartilaginous areas showing increased cellularity.* ***(d)*** *Nucleoli, binucleation and moderate atypia were identified in some chondrocytes.*

neoplasms. Increased cellularity and atypical chondrocytes may be present, and focal enchondral ossification is usually seen in the majority of cases. However, the key to a correct diagnosis is the identification of the classical component of fibrous dysplasia.

The differential diagnosis of FCD includes: enchondroma, chondrosarcoma, well-differentiated intramedullary osteosarcoma and fibrocartilaginous mesenchymoma. Enchondroma is a common benign cartilaginous tumor that occurs most frequently in small bones of the hands and feet, particularly the proximal phalanges. Histologically, it is composed of mature lobules of hyaline cartilage. Foci of myxoid degeneration, calcification, and endochondral ossification are common. Chondrosarcoma in childhood is distinctly uncommon. The risk of chondrosarcoma is increased in children with enchondromatosis syndromes (e.g. Ollier`s disease, Maffucci`s syndrome, metachondromatosis) and in those with hereditary multiple exostosis. Most malignant bone tumors in this age group exhibiting cartilage formation actually correspond to osteosarcomas with predominant cartilaginous component. Chondrosarcoma comprises 5% or fewer of all primary malignant skeletal tumors in the first two decades of life. Three variants of chondrosarcoma are recognized in children: mesenchymal, clear cell, and myxoid. Histologically, these variants of chondrosarcoma lack the fibroosseous component characteristic of fibrous dysplasia. In the case of well-differentiated intramedullary osteosarcoma most patients are adults, the femur and tibia being the most commonly affected sites. Histological features simulating fibrous dysplasia and small foci of atypical cartilage may be present. However, areas of high-grade pleomorphic osteosarcoma can be found.

Fibrocartilaginous mesenchymoma is an extremely rare lesion that tends to affect the metaphyseal region of bones, particularly the proximal fibula. The lesion contains fibrous areas and islands of cartilage that show a pattern of organization reminiscent of epiphyseal growth plates. It is locally aggressive with a high frequency of recurrence, especially when resection is incomplete.[16]

Finally, no percentage of cartilage in FD has mentioned by other authors in order to consider the diagnosis of FCD, but in our case 60% of the lesion was composed by hyaline

Table 1. **Reported cases of FD under the title "fibrocartilaginous dysplasia" or "fibrochondrodysplasia"**

Case	*Age*	*Location*	*Symptoms*	*Type of FD*	*Treatment*	*Follow-up*	*Reference*
1	20	PF	Mass	Polyostotic	Multiple osteotomies	15 years	Pelzmann et al.[9]
2	23	Tibia (proximal)	NS	Polyostotic	NS	NS	Ishida et al.[12]
3	8	PF	Pain	Monostotic	NS	NS	Ishida et al.[12]
4	20	PF	Pain	Monostotic	NS	NS	Ishida et al.[12]
5	26	Ischion	Mass	Monostotic	NS	NS	Ishida et al.[12]
6	14	PF	NS	Monostotic	NS	NS	Ishida et al.[12]
7	25	PF	Pain, fracture	Monostotic	NS	NS	Ishida et al.[12]
8	4	FS	Limp	Monostotic	NS	NS	Ishida et al.[12]
9	15	PF	Pain	Polyostotic	Tumor excision	NS	Drolshagen et al.[10]
10	53	PF	Pain	Monostotic	NS	NS	Hermann et al.[11]
11	21	PF	Progressive deformity	Monostotic	Amputation	18 years	Kyriakos et al.[15]
12	6	PF	Pain	Monostotic	Curettage	5 years	Current case

PF: proximal femur, FS: femur shaft, NS: not specified

cartilage. The important thing is to be aware of the possibility of finding extensive cartilaginous areas in an otherwise typical lesion of monostotic or polyostotic fibrous dysplasia and thus avoiding misdiagnosing it as a cartilaginous neoplasia.

References

1. *Alman BA, Greel DA, Wolfe HJ:* Activating mutations of Gs protein in monostotic fibrous lesions of bone. J Orthop Res 14: 311-315, 1996
2. *Bianco P, Riminucci M, Majolagbe A, et al:* Mutations of the GNAS1 gene, stromal cell dysfunction, and osteomalacic changes in non-McCune-Albright fibrous dysplasia of bone. J Bone Miner Res 15:120-128, 2000
3. *Lichtenstein L, Jaffe HL:* Fibrous dysplasia of bone. Arch Pathol 33: 777-816, 1942
4. *Dorfman HD, Czeniak B:* Bone Tumors. Mosby, St. Louis, 1998, pp. 441-481
5. *Forest M, Tomeno B, Vanel D:* Orthopedic surgical pathology: diagnosis of tumors and pseudotumoral lesions of bone and joints. Churchill Livingstone, Edinbourgh, 1998, pp. 595-612
6. *Kransdorf MJ, Moser RP, Gilkey FW:* Fibrous dysplasia. Radiographics 10: 519-537, 1990
7. *Harris WH, Dudley HR Jr, Barry RJ:* The natural history of fibrous dysplasia. J Bone Joint Surg Am 44:207-233, 1962
8. *Sanerkin NG, Watt I:* Enchondromata with annular calcification in association with fibrous dysplasia. B J Radiol 54: 1027-1033, 1981
9. *Pelzmann KS, Nagel DZ, Salyer WR:* Case report 114. Skeletal Radiol 5:116-118, 1980
10. *Drolshagen LF, Reynolds WA, Marcus NW*: Fibrocartilaginous dysplasia of bone. Radiology 156: 32, 1985
11. *Hermann G, Klein M, Abdelwahab IF, Kenan S:* Fibrocartilaginous dysplasia. Skeletal Radiol 25: 509-511, 1996
12. *Ishida T, Dorfman HD:* Massive chondroid differentiation in fibrous dysplasia of bone (fibrocartilaginous dysplasia). Am J Surg Pathol 17: 924-930, 1993
13. *De Smet AA, Travers H, Neff JR:* Chondrosarcoma occurring in a patient with polyostotic fibrous dysplasia. Skeletal Radiol 7: 197-201, 1981
14. *Teldorf ED:* A case of osteitis fibrosa (with formation of hyaline cartilage). Br J Surg 18:409-414, 1930
15. *Kyriakos M, Mc Donald DJ, Sundaram M:* Fibrous dysplasia with extensive cartilaginous differentiation ("fibrocartilaginous dysplasia"): a review, with an illustrative case followed for 18 years. Skeletal Radiol 33: 51-62, 2004
16. *Bulychova IV, Unni KK, Bertoni F, Beabout JW:* Fibrocartilaginous mesenchymoma of bone. Am J Surg Pathol 17: 830-836, 1993