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Jaffe-Campanacci Syndrome
Report of a Case

I am reporting a 7-year old boy presenting with multiple non-ossifying fibromas and associated extraskeletal congenital anomalies. such as cataract-café - au- lait spots. hypogonadism, cataract and cardiovascular malformation. Review of the clinical features and correlation with pathologic and radiologic data support a diagnosis Jaffe-Campanacci syndrome; a rare malformation syndrome, possibly related to neurofibromatosis.

Index Terms: skeletal anomalies, Non ossifying fibroma, (nof), fibrous cortical defect (FCD) ,

Keywords: non ossifying fibroma, neurofibromatosis,

Introduction

Non ossifying fibroma (NOF) and the related fibrous cortical defect (FCD)are the most common benign lesions of the skeletal system.[2] Small cortical fibrous lesions in the tubular bones are encountered regularly during radiographic examination of healthy children. It has been estimated that one or more cortical defects are apparent in more than 50 percent of boys and 20 percent of girls who are older than 2 years of age.(1.8) Both (NOF) and (FCD) refer to the same histopathologic process in bone and are differentiated only by the larger size and extension from the cortex into the medullary cavity in the non-ossifying fibroma.[12] Generally, the lesions are silent clinically, being discovered on roentgenograms obtained for incidental reasons. In %8 of cases nonossifying fibromata are multiple[13] presenting either as an independent entity or in association with neurofromatosis.[10,15] Association of multiple non- ossifying fibromata with extra-skeletal anomalies diagnosed as Jaffe-Campanacci syndrome has rarely been reported.[3,4,9,11,16] In this report, we present an additional case of patient with features of this syndrome and some not previously described lesions.

Case report

A 7 year-old boy was admitted to Chamran hospital because pain and swelling in his right leg after a fall. He had been the product of an uncomplicated pregnancy and weighed three kilograms at birth. His development was appropriate for his age. Family history was negative for neurofibromatosis or any related disorders.

Physical examination was remarkable for tenderness and swelling around the proximal part of right leg. There were multiple “Coast of California” cafe-au-lait spots on the right side of trunk (Fig 1).

The skull was abnormal in shape with patchy hair loss on the right occiput. The right auricle was larger than the left. A mass with wormy appearance was noticed in the right upper lid, with extension to conjunctiva, consisted with neurofibromatosis. Examination of the eyes demonstrated right eye amblyopia with scleroma and optic nerve hypoplasia.

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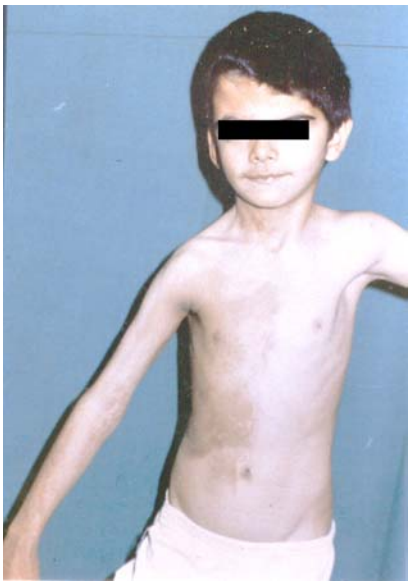


Figure1: Café-au-leit spots are visible on right side of the trunk.

Electrocardiographic findings and results of cardiac examination revealed mild cardiomegaly, ASD (Atrial Septal Defect) and coartation of aorta.

His intelligence was normal. The remainder of the physical examination was non-contributory.

Lab studies revealed no abnormal findings.

Radiologic examination revealed multiple multiloculated radiolucent areas with well-defined sclerotic margins located eccentrically in metaphyseal cortices of both proximal and distal tibia and femur and also humeral diaphysis, all on the right side. The proximal tibial lesion revealed the fracture causing the patients symptoms. All lesions showed characteristic features of nonossifying fimromata. (Figure 2, 3, 4).

Three months later the patient underwent intralesional excision, curettage, and allograft strut grafting of the proximal tibial lesion.

Curetted material from the lesion consisted of multiple fragments of tan, fleshy tissue, which showed numerous, plump, collagen producing spindle cells, among which were osteoclast-like giant cells. They contained from tree to 15 nuclei per cross section.

The spindle cel1s had ovoid to spindle shaped nuclei with rounded ends. The chromatin was finely and evenly dispersed. Nucleoli were inconspicuous and mitosis sparse. In some fields, the spindle cel1s were arranged in a storiform pattern (fig 5).

Focal col1ections of foam cel1s were noticed. Hemosiderin was present within histiocytes, spindle cells fibroblast-like and osteoclast-like giant cells. Mild to moderate focal hemorrhage was noticed and mild to moderate number of lymphocytes were scattered throughout the lesion.

Discussion

Although solitaty non-ossifying fibroma is common in the pediatric population, multiple non-ossifying fibromas are rare. [8, 12, 13] Association of multiple non-ossifying fibromas with extraskeletal anomalies has been reported in only 14 cases.

In 1958, Jaffe was the first to mention a possible relationship between multiple non-ossifying fibromata and cafe-au-Iait spots. [2, 16] Campanacci et al in 1983 reported an association between non-ossifying fibromas and extra skeletal anomalies in 10 cases.[4]

Mirra called this entity Jaffe-Campanacci syndrome, in honor of the two physicians who brought the entity to light.[12] There were seven boys and three girls in Campanacci's series ranging in age from 5 to 18 years. All patients had multiple bone lesions, the most frequent sites being the distal femur and proximal tibia. Six children had cafe-au-Iait spots. Six of the 10 patients were mentally retarded, six had either hypogonadism or cryptorchidism, three had cardiovascular anomalies and three had ocular anomalies such as dermolipoma, colobomata and pigmentary dispersion of the retina and one had malformation of an eyelid. There were single cases of precocious puberty, alopecia, and hyphoscoliosis with epiphysiolysis and mega ureter. Seven patients had experienced one or more fracture.[4]

Mirra et al reported a similar case with disseminated non-ossifying fibromas and cafe-au-lait spots and no other extraskeletal anomalies.[11]

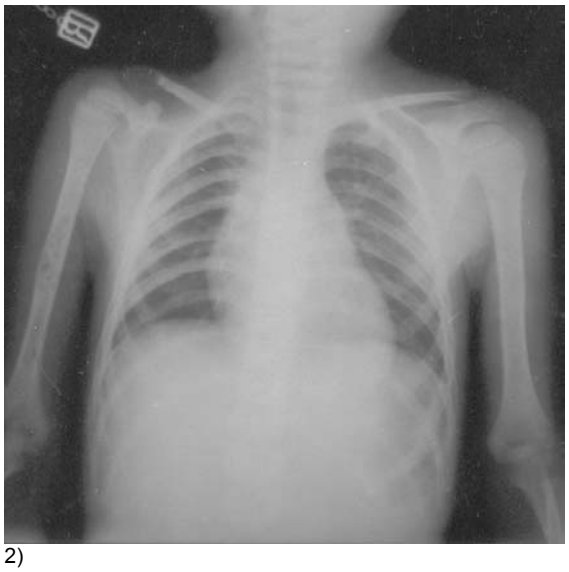
Steinmetz et al published a case with the same kind of disorder and discussed the possible relationship of this syndrome with neurofibromatosis; his patient was also mentally retarded.[16]

Kotzol et al and Boivin et al both in 1994 reported two cases of Campanacci syndrome.[3, 9] Our patient in addition to above-mentioned disorders has questionable neurofibroma of the eyelid, skull deformity and unilateral optic nerve hypoplasia, which have not been reported.

There are severa1 reports of association between multiple non-ossifying fibromas and neurofibromatosis but without extraskeletal anomalies of .Jaffe-Campanacci syndrome.[6, 10, 15]

Neurofibromatosis is thought to be genetically heterogeneous with multiple forms.[16]

Among the different disorders producing café au lait spots and multiple lytic bone lesions in addition to the possible diagnosis of neurofibromatosis and multiple nonossifying fibroma syndrome, the other likely entity to be considered is a polyostotic fibrous dysplasia.[2,4,18,19] Despite skeptical reports on diagnostic value of smoothness of spot edges, the



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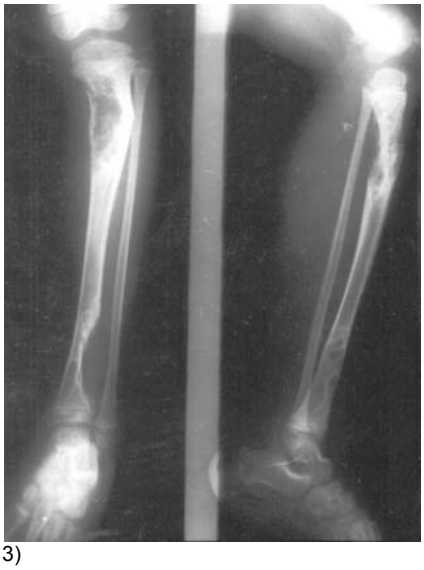

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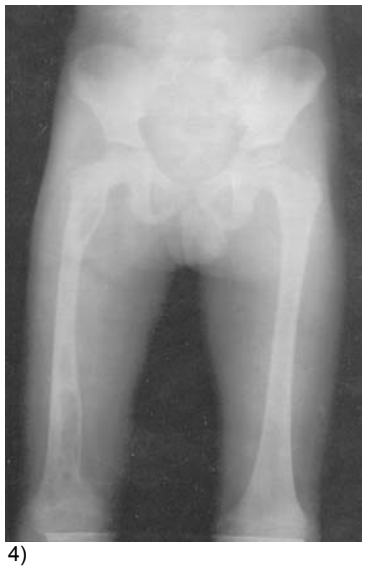

4)

Figures: 2, 3, 4: Right humerus, femur and tibia showing osteolytic lesions rendering a loculated appearance

borders are predominantly irregular (Coast of Maine) in fibrous dysplasia and smooth (coast of Calofornia) in neurofibromatosis and Jaffe-Campanacci syndrome.[19] Histologic differentiation between fibrous dysplasia and nonossifying fibromata is also relatively simple. The clinical finding of smooth bordered café au lait spots and axillary freckeling in association with multiple nonossifying fibromas and without accompanying skin subcutaneous or deeply placed neurofibromas is considered to be characteristic of the Jaffe-Campanacci Syndrome [4,11,20]; However, as Steinmetz et al suggest, the relationship between the two entities is still unclear. Presence of a possible plexiform neurofibroma which with the cafe au lait spots is enough to label the patient as neurofibromatosis type 1. In this patient with multiple features of Jaffe-Campanacci Syndrome, once again the necessity for genetic studies in such patients is highlighted.[19] Since genetic errors responsible for both fibrous dysplasia and neurofibromatosis type 1 have been extensiovely studied, it looks no longer appropriate to speculate on the nature of the Syndrome and its possible relationship with the above-mentioned entities.

Some relationship between multiple non-ossifying fibromas, neurofibromatosis and Jaffe-Campanacci syndrome seems plausible.

The radiographic picture in our patient was fairly typical, they compressed radiolucent lesions with well-defined sclerotic margins, the larger one showing a loculated appearance. They were located in metaphysis , except the one in humerus which extended to diaphysis and also reported in identical cases before.[4]

The radiological differential diagnosis of the lesion include polyostotic fibrous dysplasia and neurofibromatosis. In polyostotic fibrous dysplasia the skeletal lesions tend to be unilateral, more central and more ossified (having a ground glass appearance) than in non-ossifying fibroma.

Although in our patient the lesions were unilateral but they did not meet other criteria and also histologically there was not a definite pattern of interspersed bone among the fibrous stroma, which are seen in polyostotic fibrous dysplasia.

Neurofibromatosis can also mimic non-ossifying fibromas in radiological appearance, but we excluded this by histological exam: which did not show any neural tissue.

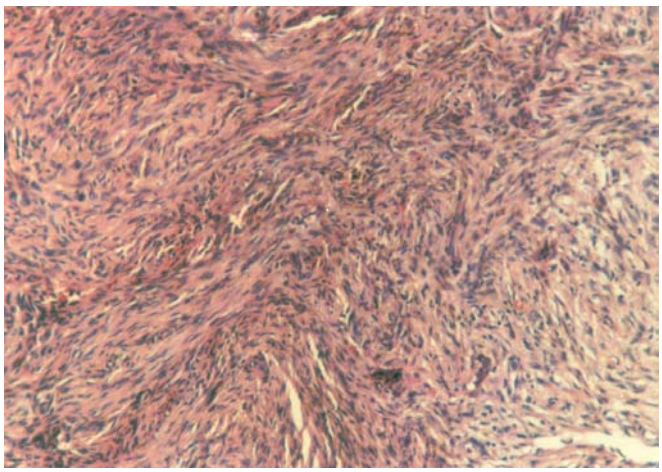

Figure 5: In some areas a prominent storiform pattern was noticed (H&E 125)

We must also excluded multiple giant cell tumor which can also resemble non-ossifying fibroma, however skin lesions are not present and giant cell tumor are seldom seen before the age of twenty.[2]

In this syndrome the skeletal lesions tend to stop growing and to undergo spontaneous repair after skeletal maturation is complete as with solitary non-ossifying fibroma.[4]

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