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Cherubism*

The hereditary form of fibrous dysplasia localized to the jaws

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A previously unrecognized disease of the jaws was described by Jones[1] in 1933. The disease affected four of five siblings and presented with swelling of the jaws. Radiograms showed multilocular cysts in the affected bones. The genetic nature of this disease was confirmed by its transmittence from the eldest sibling in the family Jones followed, to two of his four children.[2]

Through further case reports, mainly in the recent years, there were 91 known patients with this disease in the world literature by 1969.[3] Review of these cases indicates that cherubism is a distinct clinico-pathological entity, consisting of a hereditary form of fibrous dysplasia with a characteristic localisation in the jaws. The disease usually has its onset in children around 2 years of age, and has a benign, self-limited course.[4] Thus its correct diagnosis is important in order to avoid unnecessary surgery and radiation therapy, and in order that the physician be alerted for other possible cases in the family. In this communication we shall discuss the characteristic findings of this disease and add one new case report.

Report of a Case

A. O. (Hosp. No. 288431), a 6 year-old boy, was hospitalized with complaints of swelling of the jaws and difficulty in chewing. Bony-hard bilateral swelling of the lower jaw was first observed by the child's parents two years prior to admission. This was later accompanied

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by some difficulty in breathing and swallowing. There was also a history of occasional discharge of whitish viscous material from fistulous openings on both sides of the neck.

A paternal uncle had died of tuberculous osteomyelitis; Otherwise the family history was unremarkable. Specifically, the parents of the child were not related and there was no history of a similarly affected relative.

Physical examination revealed a well-developed boy with normal vital signs. There was bilaterally symmetric bony-hard swelling of the mandibular rami. The lower molar teeth were missing. Painless and mobile lymph nodes 2x1 cms in diameter were palpable in the submandibular regions. Branchial fistulae openings were present along the anterior margins of the sternocleidomastoid muscles bilaterally. The tonsils were hypertrophied. Bronchial rales were present over both lungfields and a grade II/IV systolic murmur was audible over the cardiac apex.

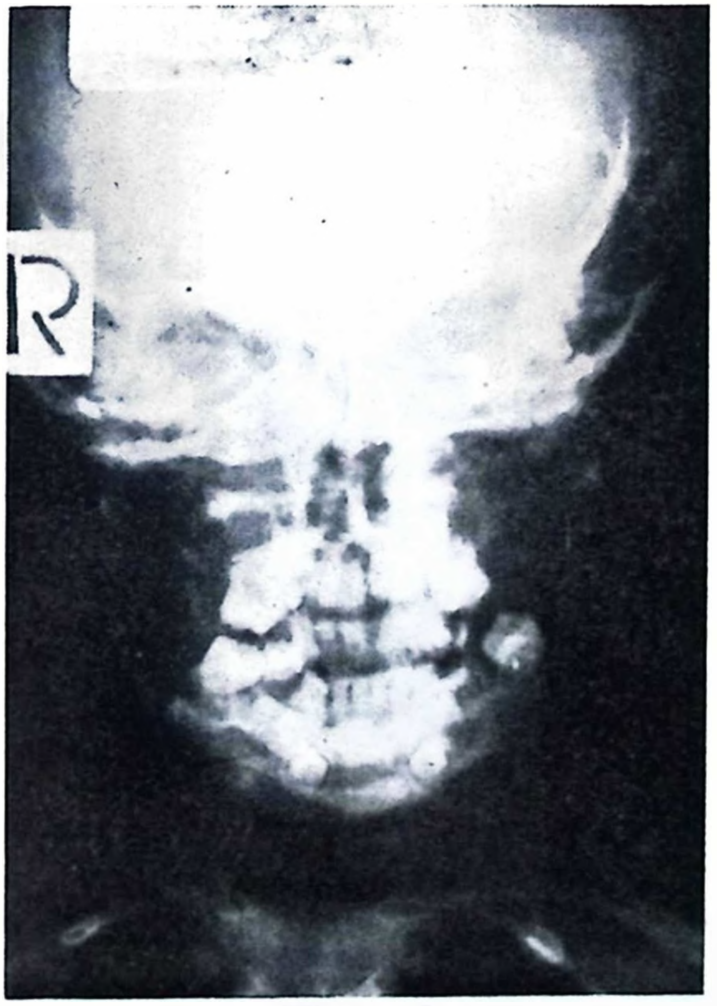

Figure 1

Laboratory tests showed a normal urinalysis and essentially normal hemograms. Various blood chemical analyses including phosphorus, calcium and alkaline phosphatase determinations were also normal.

Radiograms of the mandible showed bilateral multilocular areas of radiolucency with marked expansion of the bone. There was marked thinning of the expanded cortical bone (Figures 1 and 2). Maxillae appeared normal. Skeletal survey failed to show any other lesions.

The patient was submitted to a biopsy removal from the mandibular lesion. When the frozen section examination led to the diagnosis of cherubism, complete surgical curettage of the lesion was performed in the same session. Patient has done well postoperatively.

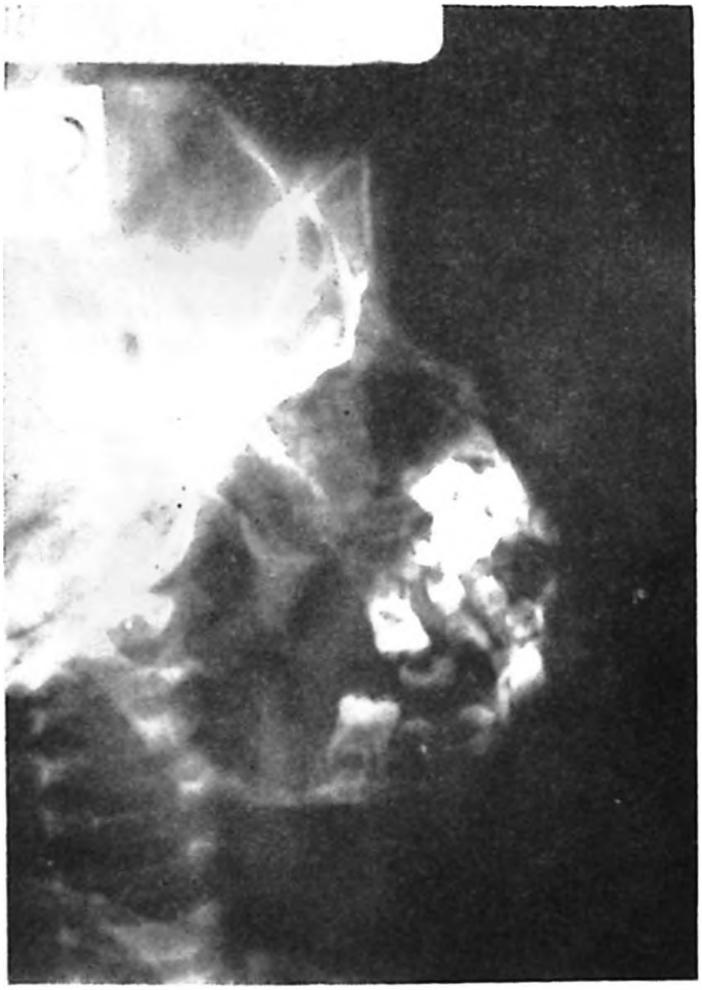

Figure 2

Discussion

Cherubism varies in its severity and in its distribution. Review of the families affected with this disease shows that the mode of inheritance is autosomal dominant with only a variable penetrance in females[4]

The disease occurs more frequently in males. No ethnic predilection has been observed.[5] Most of the cases are recognized clinically and roentgenographically during childhood from the second to the fifth years of life. The earliest age at which the disease has been diagnosed is 18 months.[6] Facial swelling is the initial abnormality most often noticed. The disease has been called Cherubism by Jones because the fullness of the cheek gives a cherubic appearance in a classical case.[1] Other patients may come to the attention of the physician because of loss of teeth or noneruption of permanent molars. The facial swelling is painless and is typically symmetrical. Rarely only one side may be involved. There are only 3 such cases with radiological proof reported in the literature.[7 8 9] The diagnosis in these cases depended on the demonstration of bilateral involvement in the relatives. The mandible is always involved but maxillary involvement is less frequent and does not occur in the absence of mandibular disease. Maxillary disease itself varies in its severity from slight expansion of the maxillary tuberosity to gross expansion and deformity of the entire bone. With advanced maxillary disease, there is complete obliteration of the maxillary sinuses.

The greatest expansion of the jawbones occurs within the first few years after the onset of the disease. This is followed by a spontaneous arrest in this growth and then regression in the swelling which begins in late childhood and continues after puberty. By middle age, there are a few radiographically detectable residual changes in the mandible but the patients have no striking clinical abnormality.

Dental abnormalities are frequently seen and are secondary to the bone lesions. These abnormalities are delayed eruption, missing or displaced teeth and sometimes the absence of permanent molars.[10 11]

Enlarged submaxillary lymph nodes are present in most of the patients first seen at 6 years of age or younger as is the case with our patient. Histologic examination of these nodes have revealed nonspecific changes such as reticuloendothelial hyperplasia, prominence of germinal centers and fibrosis.[1 12 13] These changes may be secondary to gingival inflammation due to malposition of the teeth.[6 7] There is probably no direct relationship between the osseous disease and the lymphadenopathy, especially since the latter does not always accompany cherubism.

Routine blood and urine examinations and serum calcium and phosphorus levels have always been normal in cases of cherubism. Alkaline phosphatase level has been observed to be elevated in some

cases. This is not surprising since elevation of the alkaline phosphatase is a well-known finding in fibrous dysplasia.[14]

Roentgenographically, the mandible typically shows bilaterally symmetric, well-defined, multilocular areas of radiolucency extending from the molar region to the notch. There is expansion of the bone with extreme thinning of the cortex in places. The molar and retromolar regions are usually the initial sites of involvement.[3] From there the lesions expand into the body and ramus of the mandible, at times involving the entire bone. The condyles are the only portions of the mandible which are not involved.[3 4]

Initially the radiographic findings are those of pure bony destruction and expansion. With regression of the disease beginning at age 8 to 12 years, new bony septa are formed with an increase in bone density. New cortical bone is laid down and the margins of the mandible become more regular. In adults the multilocular pattern is usually poorly defined or absent, and the entire mandible may appear sclerotic.[4]

When the maxilla is involved, the maxillary tuberosity and the adjoining molar regions are the initial sites of involvement.[3] From there the expanding lesions spread into the alveolar processes. Since the volume of spongy bone is limited in the maxilla, there may be early break through the cortical bone with soft tissue tumors extending into the maxillary antrum or the oral cavity. Since the dental follicles in the molar region are usually absent or displaced in the presence of a soft tissue mass, the posterior portion of the hard palate becomes readily discernable in lateral radiograms of the skull. This abnormal appearance has been called "the hard palate sign" by Cornelius and Clendon, and is thought to be diagnostic of the disease by these authors.[3] We have already mentioned obliteration of the sinuses by these masses. Again with reggression of the disease following puberty, the sinuses become normally aerated and the maxillae resume a normal appearance: There may be residual calcification in the regions of the previous soft tissue masses.[15]

Histopathologically the lesions of cherubism display a nonspecific picture of vascular fibrous tissue containing numerous multinucleated giant cells (Figure 3). Since this histologic picture cannot always be differentiated with certainty from that seen in fibrous dysplasia, giant cell reperative granuloma, giant cell tumour, and the localized bone lesions of hyperparathyroidism, the above described roentgenographic findings of a typical case are crucial in the diagnosis.[16]

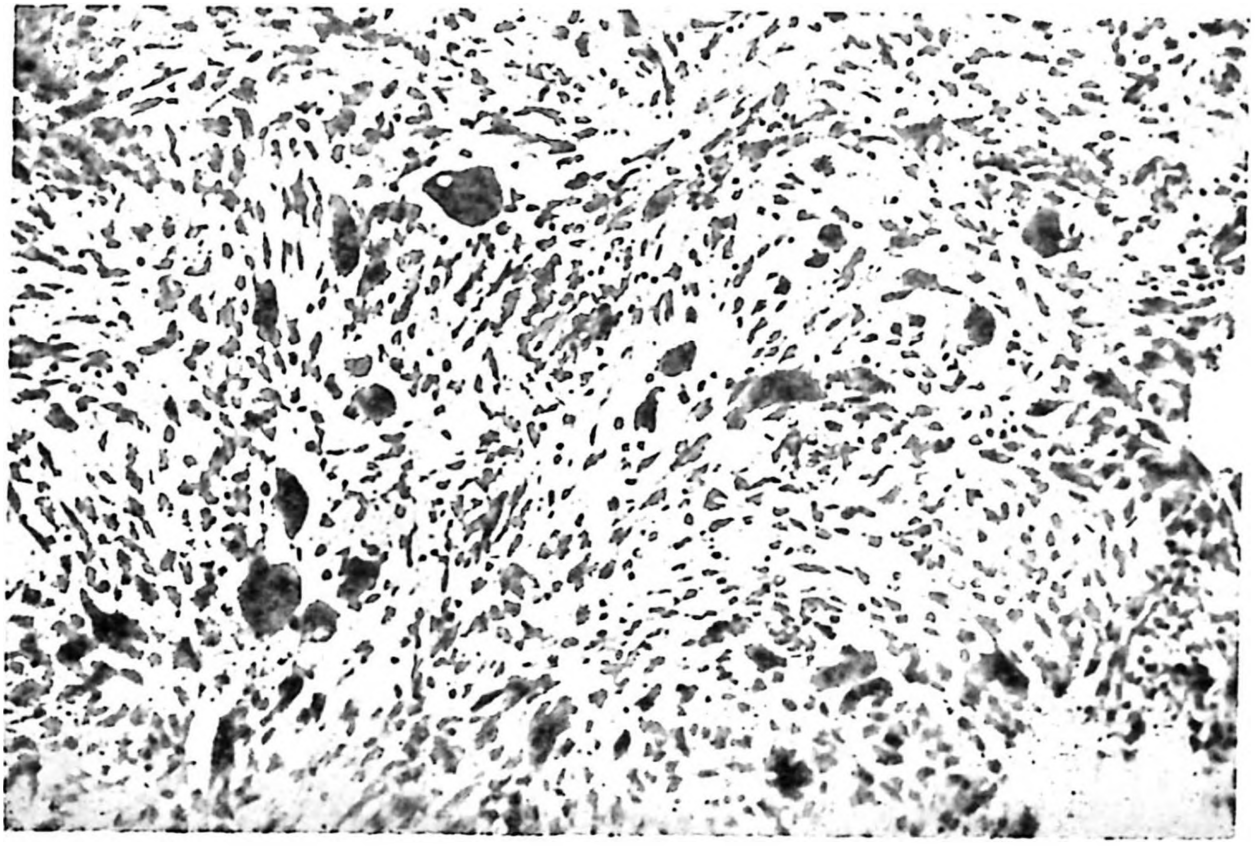

Figure 3
Microscopic sections of lesion showing foreign body giant cells interspersed in a cellular fibroblastic stroma (Haud Estain, x150).

Some conditions which may clinically resemble cherubism, such as bilateral parotid enlargement (mumps, etc.), benign masseteric hypertrophy and fibromatosis gingivae can be easily differentiated by radiological examination since these lesions are outside the bone.[17]

The greatest difficulty arises in differentiating cherubism from fibrous dysplasia, especially since their histopathological appearance is similar. However, there are definite differences between the two diseases which would justify the acceptance of cherubism as a distinct entity. Fibrous dysplasia is not hereditary and affects females more frequently. Sexual precocity is usually present.[14] When it involves the jaws the maxilla is more frequently affected, and the lesions are not bilaterally symmetric.[18] When polyostotic, it tends to be unilateral. It has its onset at an older age than cherubism and facial deformity does not decrease with age, usually is progressive even in old age.[18] On the other hand, the observation of skin pigmentation in 2 cases of cherubism,[3 9] and of bone lesions outside the jaws in four [3 8 19 20] is evidence of the close relationship of the two diseases.

Reticuloendotheliosis may involve the jaws of children, but the lesions are purely destructive.[21] Foci are usually present elsewhere in the skeleton.

True giant cell tumour occurs in an older age group. It is not bilaterally symmetric and is found "extremely rarely in the jawbones".[22] Similarly bilateral odontogenic cysts could theoretically simulate cherubism but they have not been described in patients less than 5 years of age. Infantile cortical hyperostosis may affect siblings, but it usually occurs during the first six months of life and is characterized by cortical thickening of the mandible without any cystic changes in the bone.[23]

Hyperparathyroidism may produce cystic lesions in the mandible but serum calcium and renal phosphate excretion tests together with the typical roentgen signs in the phalanges should establish the diagnosis without any difficulty.[24]

Since cherubism is usually a self-limited disease declining with age, mild lesions which can only be detected roentgenographically do not require any treatment. These patients should be followed for the possibility of any sudden jaw growth that would necessitate surgery. When there is significant enlargement and deformity of the bone, through surgical curettement of the lesion with preservation of the permanent teeth should be performed. Hammer et al. have reported excellent results from this approach.[25] However there are other reports of patients in whom surgical intervention has precipitated the recurrence of the tumor with rapid destruction of the jaws.[11 19] It would be wise to be guarded as to the prognosis following surgery since this apparently varies according to the individual patient. Radiotherapy has been used in some patients with limited success and does not appear to be the treatment of choice in this disease.[3]

Summary

Cherubism is a distinctive hereditary form of fibrous dysplasia which primarily involves the jaws. It has its onset in early childhood and usually reggresses following puberty. Adults who have had this disease during their childhood have little or no sequallae. Pertinent clinical and radiological features of this rare entity are reviewed and a new case report is presented.

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