An extreme case of cherubism

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SUMMARY. We describe an 8-year-old boy who presented with severe facial swelling. This progressed rapidly and 17 months later he died of gastrointestinal and pulmonary infections. The diagnosis was initially brown tumour associated with hyperparathyroidism, but this was revised in the light of laboratory investigations that were within the reference ranges, and normal appearance of the parathyroids on exploration to that of an extreme case of cherubism that behaved in a locally aggressive manner. © 2002 The British Association of Oral and Maxillofacial Surgeons

INTRODUCTION

Many different pathological conditions may show histologically multinucleated giant cells in a background of ovoid to spindle-shaped mesenchymal cells. The range of these diseases includes giant cell tumour, central and peripheral giant cell granuloma, cherubism, and the brown tumour of hyperparathyroidism.

The giant cell tumour is a benign, locally aggressive neoplasm of long bones. Radiographically, it presents as a radiolucent lesion with well-defined borders involving the epiphyses. Its course is unpredictable, almost half the lesions recur if treated by curettage only, and metastases have been reported.1

Peripheral and central giant cell lesions are reactive lesions of the jaws. Peripheral lesions are usually related to local factors and are supposed to arise from the connective tissue of the gingiva or the periosteum of the alveolar ridge,2 and central lesions tend to develop in the anterior portion of the mandible of young female patients.3 Some lesions grow slowly and do not recur, while others grow rapidly and the cortex perforates, and these often recur after excision.3

Diffuse or focal bone lesions may be a consequence of hyperparathyroidism.4 The increased production of parathyroid hormone initiates fibroblastic proliferation and osteoclastic activity that mimic the histological picture seen in other giant cell lesions.

Cherubism is a genetic disorder that affects children. The lesion is usually symmetrical and is characterized by bilateral expansion of the mandible or the maxilla, or both, that becomes noticeable within the first few years of life. It enlarges progressively until puberty, and gradually resolves by middle age.5 Although it is often familial, many sporadic cases have been reported. The lesions vary greatly in size, ranging from minor lesions to large, deforming, destructive ones with massive involvement of both jaws.5,7

Although locally aggressive cherubism has been reported,7–9 we do not know of any patients who have died of the disease. The purpose of the present paper is to describe an aggressive, multiple, and fatal case of atypical cherubism.

CASE REPORT

An 8-year-old boy was referred to the Oral Diagnosis Service at the Universidade Federal de Minas Gerais in August 1969 for evaluation of a facial swelling (Fig. 1). Clinical examination showed a well-developed, cooperative boy with enlargement of the jaws and cheeks, and displacement of the eyes (Fig. 1). Intraoral examination showed generalized alveolar swelling and mobility of most teeth (Fig. 2). Radiograph examination showed multiple extensive radiolucent areas in the maxilla, body, and ramus of the mandible. Past medical and familial histories were unremarkable. Haematological and biochemical evaluation, including serum calcium and phosphorus concentrations and alkaline phosphatase activity, were within the reference ranges.

Histopathological evaluation of an incisional biopsy specimen showed multiple multinucleated giant cells together with ovoid to spindle-shaped cells within a fine fibrillar collagenous stroma (Fig. 3). There were deposits of haemosiderin and a few mitotic figures. In addition, no perivascular cuffing was noted. The diagnosis was cherubism. One month later he returned with a deforming swelling and was admitted to the Hospital das Clinicas, Universidade Federal de Minas Gerais (Fig. 4). Laboratory investigations had not changed. Endocrinological evaluation at that time included measurement of serum calcium and phosphorus concentrations and alkaline phosphatase activity, calculation of the renal tubular resorption of phosphorus index, and exploration of the parathyroid glands; but no abnormality was detected. Because of the provisional diagnosis of cherubism, it was decided at that time to follow up the patient.
Eight months later, he presented with massively increased orofacial enlargement (Fig. 5), and that time found it difficult to feed. Nine months later he presented with aberrant symmetrical orofacial swelling, together with appreciable loss of weight (Fig. 6). A further incisional biopsy specimen showed the same histological picture as previously described. Two months later he died of pulmonary and gastrointestinal infections, according to the clinical records available. No other member of the family evaluated at that time had a similar condition.

**DISCUSSION**

The medical and dental team initially considered a diagnosis of brown tumour of hyperparathyroidism. Hyperparathyroidism is a primary disorder of the parathyroid tissue, secondary to hypocalcaemic states such as osteomalacia, malabsorption syndromes, renal tubular...
disorders, and chronic renal failure, and as tertiary hyperparathyroidism when a true adenoma arises after long-term hypocalcaemic stimulation. Concentrations of calcium and phosphorus, and alkaline phosphatase activity, together with a renal tubular phosphorus reabsorption, index all within the reference ranges, and no abnormality on exploration of the neck and mediastinum excluded any category of hyperparathyroidism and osteomalacia in this case. At the time (1969), parathormone measurements were not available. There was no evidence of chronic hypocalcaemia. In the primary and secondary hyperparathyroidism the concentrations of calcium and phosphorus, and tubular resorption of phosphorus, are altered.

Some cases of tumour-induced osteomalacia associated with giant cell lesions of the jaws have been reported. This clinical syndrome is characterized by generalized severe bone pain, muscular weakness, multiple pathological fractures, normocalcaemia, hypophosphataemia, increased serum alkaline phosphatase activity, hyperphosphaturia, and low tubular resorption of phosphorus induced by a peripheral tumour. Its pathogenesis may be associated with the secretion of a hormone-like substance by the tumour that increases the renal clearance of phosphorus. The blood values of calcium, phosphorus, alkaline phosphatase, and tubular resorption of phosphorus all within the reference ranges, together with the normal appearance of the parathyroid glands at the time of exploration, are not consistent with the diagnosis of osteomalacia associated with a giant cell lesion or brown tumour of hyperparathyroidism.

Other differential diagnoses raised included multiple low-grade osteosarcoma, central giant cell lesion, or an atypical case of cherubism. The fatal course of the case may indicate the diagnosis of low-grade osteosarcoma, but the histological picture did not support it.

The biological behaviour of a central giant cell lesion ranges from quiescent to aggressive, with root resorption and a tendency to recur after excision. Some cases of multiple central giant cell lesions of the jaws have been reported in English, but none of them followed the aggressive course of the present case.

The multiple involvement of jawbones with eyes being pushed upward suggested the diagnosis of cherubism. Although unusually extensive cases of cherubism have been reported, to the best of our knowledge, none have died. In the present case, the immediate cause of death was related to pulmonary and gastrointestinal
infection as a result of aspiration given the gross deformity of the child. In conclusion, although cherubism is normally a self-limiting condition, clinicians must be aware of the early diagnosis and treatment of atypical presentations.

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REFERENCES

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