

Cherubism in sub-Saharan Africa: a first case-report in a child

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Abstract

Cherubism is rare disease and has been rarely reported in African pediatric population. We report here the case of a 10-year-old child who was referred to our hospital for bilateral jaws swelling. Physical examination revealed bilateral swelling symmetry of the face. Histopathological examination of the biopsy specimen showed loose fibrous stroma, proliferating fibrous connective with tissue interspersed with multinucleated giant cells, small thin walled blood vessels and scattered sparse mononuclear inflammatory infiltrate. Our patient presented cherubism. Cherubism is rarely described in children living in sub-Saharan Africa. Genetic and molecular investigations plays an important role in diagnosis but were not available in poor resources settings in developing countries such as the Democratic Republic of Congo.

Introduction

Cherubism is a familial multilocular cystic disease of jaw that was described as a distinct clinicopathologic entity by William Jones in 1933.¹ The term *Cherubism* is related to the particular morphology of full round cheeks and upward cast of the eyes to the angelic look of the cherubs immortalized by renaissance art. It is characterized by progressive painless

bilateral swelling of jaws involving either maxilla or mandible producing chubby face. It is classified as quiescent, non-aggressive and aggressive on the basis of clinical behavior and radiographic findings.²

Cherubism has been mainly reported in all races and ethnic groups.^{2,3} However, data in Africa is rare. A first case of a child seen in our institution (University Hospital of Kinshasa, Kinshasa, the Democratic Republic of Congo) was described.

Case Report

A 10-year-old boy child was referred for assessment of bilateral swelling. He is the fourth in a family of eight children. His previous medical history were uneventful. The parents gave no history of febrile illness, drug utilization or herbal plant. No findings suggest a particular risk period or an environment exposure. There was no history of similar complaint in any of the siblings and parents of affected child. No findings suggest a particular risk period or an environment exposure.

The history of present illness dates back about 6 years by gingival bleeding treated successfully by traditional healers in his village. One year after this episode, swelling started initially as smaller in size in left side of the face which gradually increases in left side of face following by right side.

At presentation in our center, physical examination revealed bilateral symmetric swelling of the face without pain (Figure 1). On palpation, temperature of the overlying skin was normal and no tenderness was elicited. There was no lymphadenopathy. No abnormality was found on clinical examination of the chest, abdomen, cardiovascular system. Neurologic exam was normal. It reveals an active and alert child with normal interests and social curiosity. No extra-gnathic skeletal involvement was observed. No cutaneous pigmentation or congenital abnormality was associated. The intra-oral examination shows backward displacement of the tongue, dental eruption abnormalities with absence and displaced teeth, the rudimentary development of molars, abnormally shaped teeth, partially resorbed roots or delayed and ectopically erupting teeth.

Hematological and biochemical investigations for serum calcium, phosphorous, hepatic and renal tests were found to be within normal limits. In contrast, there was an elevation of the Serum alkaline phosphatase levels for age at 984 U/L. HIV and hepatitis serology were negative. No plasmodium was found.

X-ray shows that the bones were involved with a multilocular radiolucency with thin and expanded cortices, including the inferior border. The

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condyle and the condylar neck were normal.

A computed tomography (CT) scan revealed honeycomb-like lesions of the mandibular cortical bone with further progression in the size of the lesion.

Histopathological examination of the biopsy specimen from the central area of both right and left rami shows loose fibrous stroma, proliferating fibrous connective with tissue interspersed with multinucleated giant cells, small thin walled blood vessels and scattered sparse mononuclear inflammatory infiltrate. The process is highly vascularized and hemorrhagic. No atypical or evidence of malignancy (Figure 2). This description is suggestive of giant cell lesions of bone including cherubism.

Clinical feature, radiographic feature, histopathological examinations are suggestive of cherubism.

No genetic and molecular tests were made because of their unavailability.

During his hospitalization, the child did not receive specific chemotherapy and was kept under follow up with no further surgical intervention and we prefer waiting until the end of puberty before performing a surgical intervention.

Death occurred 4 months after admission by

a sudden cardio-respiratory arrest probably due to obstructive sleep apnea. Autopsy was refused by the family.

Discussion

Cherubism a very rare disorder with only an estimated 300 cases reported in the literature has been reported in patients of all racial and ethnic backgrounds.² However, in Africa, the description of the disease is scarce. Only description in African population in Maghreb could be found with the use of available computer-assisted medical literature search programs.^{4,5} In sub-Saharan Africa, this affection was not previously noted.

Cherubism is a familial disease in which the trait is transmitted in an autosomal dominant fashion with 100% penetrance in males and 50-70% penetrance in females.^{2,6}

Affected children appear normal at birth. Swelling of the jaws usually appears between 2 years and 7 years of age, with a peak at the age of five, after which, lesions proliferate and increase in size until his admission in our institution as described in previous report.^{2,7} This description is in accordance with the present case.

Clinical and radiologic features of our patient were similar of those described in the literature.^{2,4,8} Swelling of the jaws was explained by the expansion of cortical bone by fibrous tissue masses invasion. The painless of the mass could be due to the high osteoclastic activity.⁹

The radiologic characteristics of cherubism are not pathognomonic.^{2,10} The diagnosis is strongly suggested by bilateral relatively symmetric jaw involvement that is limited to the maxilla and mandible as show in Figure 2.

Cherubism cannot be diagnosed by histology alone because they are not distinguishable from other giant cell lesions of bone because they contain many giant-cells and mononuclear or stromal cells. The same difficulties are described in the literature.² In our case, the typical finding of multinucleated osteoclast-like giant cells (arrows) near bone and within soft fibrous stroma in microscopic examination is suggestive of cherubism. Hemorrhage observed in endothelial cells is probably due to hemosiderin, a breakdown product of hemoglobin as described by Chormette *et al.*¹¹

Gene testing confirms the diagnosis. These investigations were not performed because of technical reasons in our institution. Recent studies shows that mutation in the gene encoding SH3-binding protein 2 (*SH3BP2*) plays a role in the disease.¹² There are indications that the gene *SH3BP2* plays a role in regulating the increased osteoblast and osteoclast activities. *SH3BP2* gene mutations cause dys-

regulation of the *Msx-1* gene, which is involved in regulating mesenchymal interaction in craniofacial morphogenesis. Increased bone activity in children affected, occurs between age 2.5 and 10-12 years, due to the up-regulation of *Msx-1*. Dysfunction of *Msx-1* stops at the end of molar development, leading to remineralization of lesions.¹³

To confirm this finding, cytogenetic and molecular abnormalities were reported in most patients by the SH3-binding protein 2 (*SH3BP2*) gene on chromosome 4p band 16.3 dominant mutation.^{12,14,15} This discovery was an important step in knowledge about the pathogenesis of the disease.

Detection of *SH3BP2* gene mutation in exon 9 is the molecular marker of cherubism.^{12,16} In our conditions of poor resources settings, the diagnosis is essentially a clinical diagnosis in combination with clinical and morphologic features. The diagnosis of cherubism is based on patient age, medical history, clinical examination, radiographic findings, biochemical analyses and histologic analysis.

There was no familial history of cherubism in our case. The absence of a positive family history does not rule out the possibility of cherubism. Previous studies have described sporadic cases of cherubism.^{8,17} In the present case, we have evoked the possibility of *de novo* mutation or incomplete penetrance as reported in previous studies.^{8,12,18} In USA, a recent study shows that approximately 50% of all cases of cherubism with mutations in *SH3BP2* identified had no family history.¹²

Surgical removal should be exclusively restricted to specific indications. Excision of tissue is suggested in aggressive cases to reduce maxillofacial deformity after puberty and to ensure a successful outcome without the risk of progression requiring additional resection.

Lesions in the aggressive form of cherubism occur in young children and are large, rapidly growing and may cause tooth displacement, root resorption, thinning and perforation of cortical bone. Cherubism in our child would be finding aggressive. Death occurred four months after admission. Previous studies showed that cherubism can be associated with aggressive form of the disease in young child.^{2,19}

Future perspective

Facilities for genetic and molecular studies are not readily available in Democratic Republic of Congo, this limits understanding of the genetic disorder underlining this first description cherubism.

An implementation of molecular and genetic laboratories is advocacy in tertiary institutions of the Democratic Republic of Congo to elucidate particular cases for a contribution to knowledge and progress of science in tropical environment. Health determinants were differ-

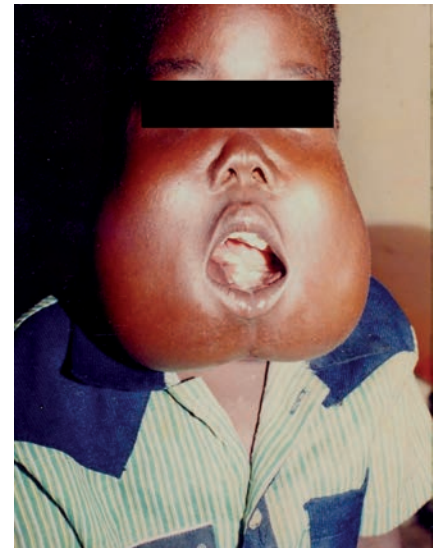


Figure 1. Facial appearance of the patient revealed bilateral swelling symmetry of the face.

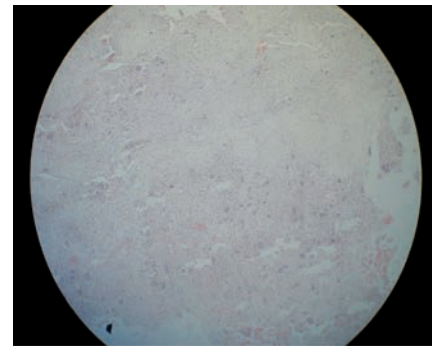


Figure 2. Histopathological examination of the biopsy specimen from the central area of rami shows loose fibrous stroma, proliferating fibrous connective tissue interspersed with multinucleated giant cells, small thin walled blood vessels and scattered sparse mononuclear inflammatory infiltrate.

ent with geographical area. Physicians need to rise up to the challenges in management of children with rare pathologies such as cherubism and be equipped to answer without unnecessary delay the usually burning questions in the minds of the parents.

Conclusions

Cherubism is rarely described in sub-Saharan children. Genetic and molecular

investigations plays an important role in diagnosis but were not available in poor resources settings in developing countries such as the Democratic Republic of Congo.

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