

Osteoglophonic dysplasia: a case report

Vemanna Naveen Shankar¹⁾, Vidhya Ajila²⁾ and Gopa Kumar³⁾

¹⁾Department of Oral Medicine and Radiology, Institute of Dental Studies and Technologies, Uttar Pradesh, India

²⁾Department of Oral Medicine and Radiology, A. B. Shetty Memorial Institute of Dental Sciences, Karnataka, India

³⁾Mahatma Gandhi Dental College and Hospital, RIICO Institutional Area Sitapura, Rajasthan, India

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Abstract: We report a rare case of osteoglophonic dysplasia affecting father and daughter. Osteoglophonic dysplasia is a very rare skeletal dysplasia with craniosynostosis, multiple radiolucencies of bone and clinical anodontia. It is an autosomal dominant disorder characterised by short stature. The affected children have normal intelligence. Close association with missense mutation of fibroblast growth factor receptor-1 has been reported. Life expectancy depends on the degree of cranial malformation. In previous reports, bone defects usually resolved by adulthood, but multiple tooth impaction may cause aesthetic and masticatory problems. Cytogenetic studies and routine laboratory tests were all within normal limits. (*J Oral Sci* 52, 167-171, 2010)

Keywords: osteoglophonic dysplasia (OGD); craniosynostosis.

Introduction

Osteoglophonic dysplasia is a very rare genetic disorder, characterised by stunting of stature, craniosynostosis, multiple unerupted teeth and multiple lucent metaphyseal defects (1). This syndrome was first described by Fairbank in 1951 (2,3). The second report was made by Theodore E. Keats, who named the disease 'Craniofacial dysostosis with fibrous metaphyseal defects' (4). Spranger suggested

the term 'Osteoglophonic dwarfism', based on the radiographic changes of the syndrome (5). The name 'osteoglophonic' was derived from the Greek word meaning a 'hollowed-out' appearance of bone. Beighton called this disorder 'Osteoglophonic dysplasia' in his review published in 1989 (6).

Case Report

A 5-year-old girl was referred to A. B. Shetty Memorial Institute of Dental Sciences with delayed tooth eruption, which caused difficulty in feeding and speech. She was the only child born to consanguineous parents, was conscious and responded well to verbal commands. The patient was 38 inches tall and weighed 13 kg (Fig. 1). She



Fig. 1 Height 38"; Weight 13 kg.



Fig. 2 Showing depressed nasal bridge and retarded midfacial growth.



Fig. 3 Showing tower-shaped head, depressed nasal bridge, and relative mandibular prognathism.

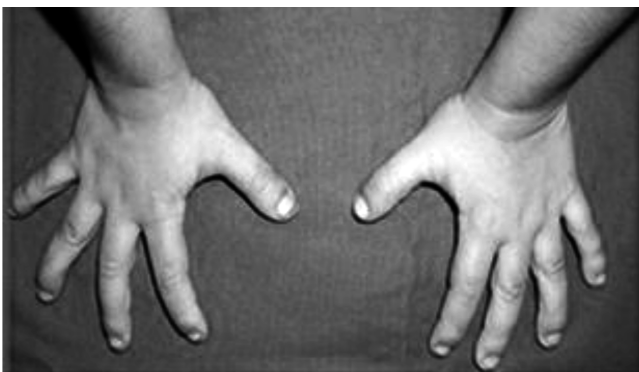


Fig. 4 Short and stubby fingers.

had a tower-shaped head with frontal bossing, depressed nasal bridge and malar prominences (Figs. 2 and 3). Moderate orbital hypertelorism and abnormal protrusion of the mandible were also observed (Figs. 1 and 3). All the fingers were short and stubby (Fig. 4). Oral examination revealed a complete lack of dentition, shallow palate, and thick and bulbous alveolar ridges. There was no morphological abnormality in the tongue (Figs. 5 and 6). Her father also had a short stature with abnormal craniofacial features resembling those of his daughter.

On the orthopantomogram, multiple impacted deciduous teeth and developing permanent tooth buds were noted in both jaws with narrow maxillary sinuses (Fig. 7). Lateral cephalographs showed a typical tower-shaped cranium with a classical beaten metal appearance and cranio-

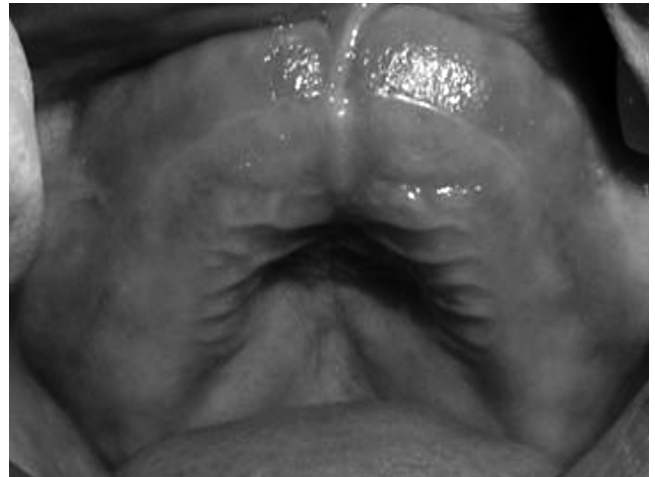


Fig. 5 Clinical anodontia (maxillary).



Fig. 6 Clinical anodontia (mandibular).

synostosis (Figs. 8 and 9).

Multiple well-demarcated cystic radiolucencies at the distal end of both femurs, anterior beaking in the vertebral column, and platyspondylia were revealed on roentgenographic examination of the trunk and extremities (Figs. 10 and 11). Calcium and phosphorus levels in urine and serum, and serum alkaline phosphatase level were all within normal limits. Genetic detection of missense mutation in the fibroblast growth factor receptor-1 (FGFR1) gene was not performed on this patient.

Discussion

Osteoglophonic dysplasia (OGD), also known as Fairbank-Keats syndrome, was first reported by Fairbank in 1951 (1-3). Since then, only 15 cases have been described in the literature. It is a rare disorder characterised by

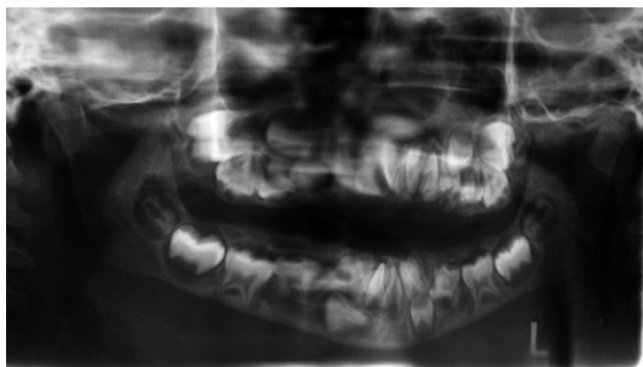


Fig. 7 Multiple unerupted primary teeth and developing permanent tooth buds.



Fig. 8 Tower-shaped skull, beaten copper appearance, and craniosynostosis.

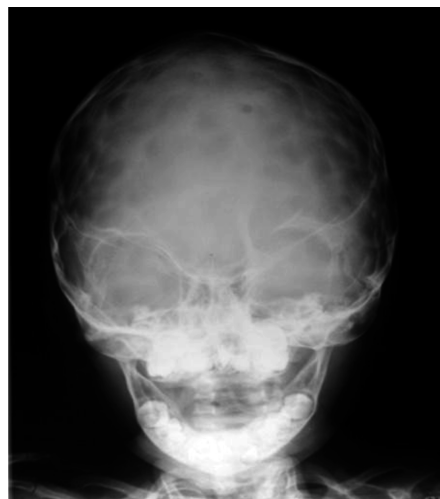


Fig. 9 Beaten copper appearance and midfacial hypoplasia.

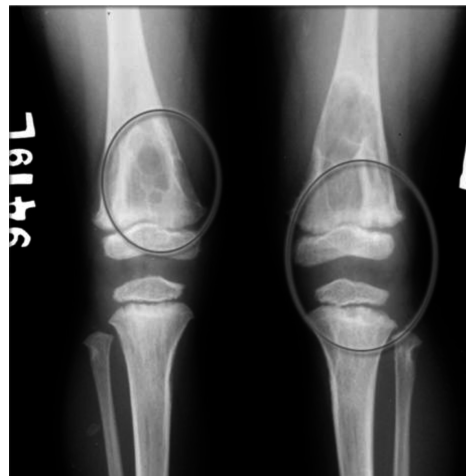


Fig. 10 Multilocular radiolucencies in the distal ends of femur.



Fig. 11 Anterior beaking of vertebrae.

craniosynostosis and short stature. OGD seems to be a familial condition with an autosomal dominant pattern of inheritance, although most of the reported cases are thought to be the result of de novo mutation (6). No clear sex predilection has been reported (7). Recently, White et al. demonstrated that OGD is caused by missense mutations in the FGFR1 gene on chromosome 8p11.2-p11.1 (8). Most mutations observed in major craniosynostosis syndromes are identified in the fibroblast growth factor receptor-2 (FGFR2). Dwarfism is not a symptom in these syndromes. Many other hereditary skeletal disorders associated with dwarfing are closely related to mutations in fibroblast growth factor receptor-3 (FGFR3), including achondroplasia, hypochondroplasia and thanatophoric dysplasia (9). Although, as described above, missense mutations of FGFR2 lead to OGD, further cytogenetic investigations by White et al. and Farrow et al. elucidated a novel role for FGFR1 as a negative regulator of longitudinal growth in long bones (6).

Several different types of missense mutations have been detected in FGFR2, but they are all located within or close to the ligand-binding and transmembrane domains of FGFR1 (8). These mutations cause a base change or substitution in a codon of FGFR1, resulting in insertion of a different amino acid into the forming polypeptide chain and constitutive receptor activation. Some patients with OGD show elevated levels of serum FGF2 and FGF3. This may indicate that increased secretion of FGF 2 and FGF 3 in the metaphyseal growth plate of long bones caused by constitutive activation of FGFR1 leads to removal of phosphate from the kidney and development of skeletal lesions. This hypothesis explains the fact that more serious hypophosphatemia is associated with more prominent bone lesions in patients with OGD (10).

Major craniofacial manifestations of OGD, which are evident at birth, are clover leaf- or tower-shaped cranium,

frontal bossing, mandibular prognathism and exophthalmos. Anteverted nostrils, low set and protruding ears, macroglossia and hypertrophy of the gingiva are also reported as early findings of OGD. Gross dwarfism is not apparent during infancy, although the patient's height is always below the 3rd percentile with proximal shortening of limbs and stubby fingers. Serious problems occurring during infancy include feeding difficulty, nasal obstruction and respiratory disturbance. Some patients with OGD die of these complications at this stage (7).

In childhood, dwarfism and morphological abnormalities of bone become prominent with contraction of elbow and knee joints, and uneruption of teeth is noted as the developmental disturbance progresses. Inguinal hernia and hyperplastic pyloric stenosis have also been reported in a few cases. Despite remarkable psychomotor retardation, most patients have average intelligence (3). Life expectancy depends mainly on the severity of craniofacial malformations, which may cause fatal respiratory and/or feeding disturbances (7).

Among the radiographic features of OGD (Table 1), the so-called 'beaten copper' appearance of the calvaria, although prominent in childhood, usually regresses by adulthood. Multilocular metaphyseal radiolucent change is most prominent in the distal part of the femur but may be seen in the iliac bone, the proximal part of the femur, the distal part of the tibia, the distal part of the fibula, the proximal humerus and the distal part of the radius and the ulna. Abnormalities may be seen in the external configuration and internal architecture of the affected bones. The tubular bones of hand and foot are broad and short with cone-shaped phalangeal epiphyses. The carpal and tarsal bones are very dysplastic.

On follow-up, these radiolucent lesions, namely 'holes in the bones', tend to resolve with ossification by adulthood, although they may increase in both size and number during

Table 1 Features of osteoglyphonic dysplasia

Anatomic location	Clinical feature
Skull	Craniosynostosis with oxycephaly, enlargement of the sella turcica, 'beaten copper' appearance of calvarium, frontal bossing, hypertelorism, proptosis and midfacial hypoplasia.
Spine	Vertebral bodies are flattened with anterior beaking and posterior scalloping. The vertebral canal is narrow and discrepancy in the size of the thoracic and lumbar vertebrae.
Limbs and extremities	Multiple cystic radiolucencies of long bone, short and broad tubular bones, spontaneous fractures and pseudoarthrosis.
Dental	Multiple impacted teeth, mandibular prognathism, cystic lucencies of mandible.

childhood. As described above, patients with OGD with multiple non-ossifying bone lesions often show hypophosphatemia due to removal of phosphate from kidney with normal levels of serum 1,25(OH)₂ vitamin D (10,11).

Oral manifestations

The most striking of the oral symptoms of OGD is clinical anodontia, complete lack of dentition, with gingival hypertrophy and a high palate. Macroglossia and cystic changes in the mandibular bone are also reported. Various craniofacial malformations of OGD may cause aesthetic problems and functional disturbances including difficulty in mastication and swallowing and nasal discharge. Although the aetiology of total impaction of teeth in OGD remains unknown, some authors suggest that cystic lesions of the jaw and inverted teeth may inhibit normal dentition (1,12). In the present case, histopathological examination revealed that the gingival swelling lesion of the mandible was consistent with giant cell granuloma. Cytogenetic studies and routine laboratory tests, including serum calcium, phosphorus, alkaline phosphatase, lysosomal hydrolases and urine mucopolysaccharides, were all within normal limits.

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