Case Report

Greig Cephalopolysyndactyly Syndrome with Oral Manifestations: A Rare Case Report

Abstract

Greig cephalopolysyndactyly syndrome (GCPS) is one of the autosomal dominant-inherited syndromes, caused by haploinsufficiency of the GLI3 gene. It is a rare, multiple congenital syndrome with an estimated rate of 0.009%. With the classic clinical triad of preaxial polydactyly with cutaneous syndactyly of at least one limb, hypertelorism, and macrocephaly, presumptive diagnosis of GCPS is made. The purpose of this article is to report a case of GCPS with emphasis on craniofacial and oral features.

Keywords: *Greig cephalopolysyndactyly syndrome, hypertelorism, macrocephaly, polydactyly*

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Introduction

Greig cephalopolysyndactyly syndrome (GCPS) was first documented by David Middleton Greig in 1926.[1]

This is characterized by the clinical triad of polysyndactyly, macrocephaly, and hypertelorism – a rare, pleiotropic, multiple congenital anomaly syndrome.[2] It was found that, more than 75% of patients have mutations in GLI3 gene leading to haploinsufficiency for GLI3 which is the mode of pathogenesis.[3] This protein plays a role in the normal shaping of many organs and tissues before birth by interacting with certain genes during development.[4] GCPS with oral manifestations is not reported yet to the best of our knowledge.

Case Report

A 26-year-old male patient presented with the complaints of malaligned and missing teeth in the upper front region, associated with difficulty in chewing food, and also facial deformity. His past medical and dental history revealed that his hand and feet had exhibited abnormalities since birth. He underwent orthognathic surgery from Mangalore 4 years ago due to excess maxilla and mandible, along with extraction of the upper front tooth.

He was the first child born to nonconsanguineous parents. Pregnancy and labor were uneventful, but there was a history of abortion pills taken during the pregnancy. The delivery was full term and uneventful. Postnatally, he had experienced no serious illnesses or hospitalization. The developmental milestones were delayed, he started walking at the age of 3, and a slight delay in the eruption of both dentitions was reported. His siblings (brother and sister) had fused toes in both legs.

Extraoral examination revealed a dolichocephalic skull with a leptoprosopic face. Lateral profile of the patient showed midface deficiency, the patient also exhibited a depressed nasal bridge with septal deviation, which gave a parrot's nose appearance. Face was mildly flattened, with hypertelorism, exotrophia, downward slanting palpebral fissures, and slightly prognathic mandible. Macrocephaly with head circumference of 58 cm was noticed [Figure 1]. Cutaneous syndactyly is present between the forefinger and middle finger in the right hand, and thumb and forefinger in the left hand. Preaxial polydactyly was noted in the right foot [Figure 2].

Intraoral examination revealed poor oral hygiene with varying degrees of periodontal involvement. Retained deciduous teeth in relation with 52, 53, 55, 63, 65 and a missing right central incisor(extracted 4 years ago) was noticed.

On the basis of clinical examination of the patient, a diagnosis of GCPS was given.

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Radiological investigations were carried out which included panoramic, posteroanterior views, and hand wrist radiographs. Panoramic radiograph revealed elongation of styloid process on the right side, multiple mini plates in the maxilla and mandible, retained 52, 53, 55, 63, 64, 65 with their missing permanent successors (12, 13, 15, 22, 24, 25) [Figure 3]. Lateral cephalogram showed a concave facial outline with deficiency in the midfacial bones, leading to a mandibular prognathism, and high, prominent frontal bone with presence of flat posterior skull. Radiograph of the left hand was taken which showed the presence of soft tissue syndactyly of thumb and forefinger.

Deciduous teeth were extracted that showed resorbed roots. Patient was then advised for the prosthetic rehabilitation. Opinion of orthopedic and plastic surgery services was sought, and the patient agreed for the conservative management of his acral defects. Genetic counseling of the patient and family members were done.

Discussion

Typical GCPS is manifested by preaxial polydactyly or mixed pre- and post-axial polydactyly, hypertelorism, and macrocephaly.[4] Craniofacial findings are found in mild conditions and those with severe condition can have seizures, hydrocephalus, and intellectual disability.[1] Leukemia and gliomas have been noted in case reports of patients with GCPS and tumors.[5]

Based on clinical findings and family history, the diagnosis of GCPS is made. A proband with preaxial polydactyly, cutaneous syndactyly of toes or fingers, widely spaced eyes, and macrocephaly gives the presumptive diagnosis.[6] The diagnosis can be established, if[7] the close blood relative (firstdegree relative) of proband that includes the individual's parents, full siblings, or children, for whom the diagnosis has been independently established.

Furthermore, the close blood relative of a proband may be diagnosed as affected if he/she has pre- or post-axial polydactyly with or without syndactyly or the craniofacial features. A proband should present with the features of GCPS and a pathogenic variant in GLI3 gene.[1]

Major findings of GCPS are – macrocephaly: occipitofrontal (head) circumference is >97th centile compared to age- and sex-matched normal standards; widely spaced eyes: interpupillary distance is more than 2 standard deviation above the mean or a subjectively increased interpupillary distance; and limb anomalies.

At least one limb should manifest any of these features – Preaxial polydactyly, a markedly broad hallux, and a markedly broad thumb. Cutaneous syndactyly. May be partial or complete.[4]

Differential diagnosis for polydactyly comprise more than 100 disorders, but those that overlap with other features include the following: acrocallosal syndrome – preaxial polysyndactyly, macrocephaly, agenesis of the corpus callosum, mental retardation, seizures and hernias are seen and is inherited in an autosomal recessive pattern.[8] Teebi hypertelorism syndrome – the polydactyly is not preaxial but shares same craniofacial manifestations with GCPS.[9] Carpenter syndrome – polysyndactyly and craniosynostosis, with mental retardation is present and caused by mutations in the*RAB23* gene.[6] Gorlin syndrome (nevoid basal cell

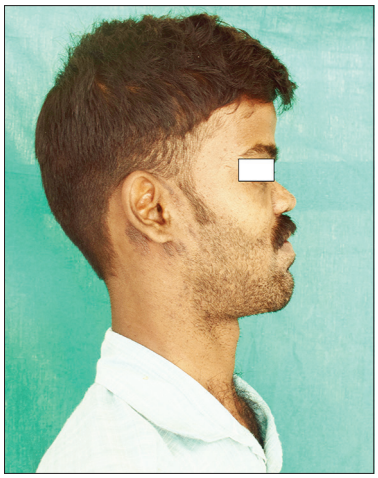

Figure 1: Lateral view

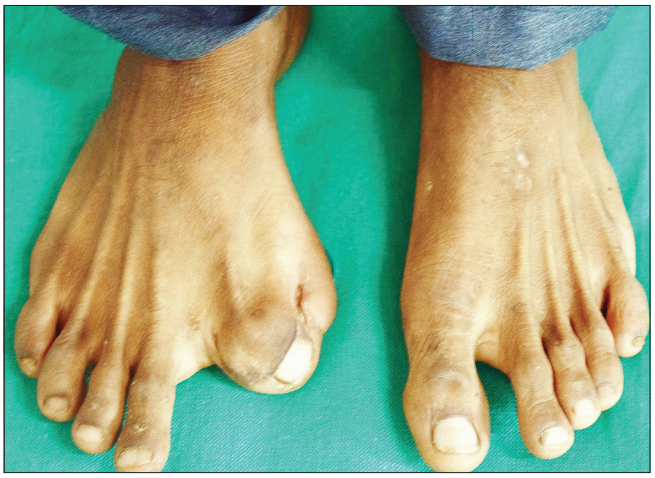

Figure 2: Preaxial polydactyly in the right foot

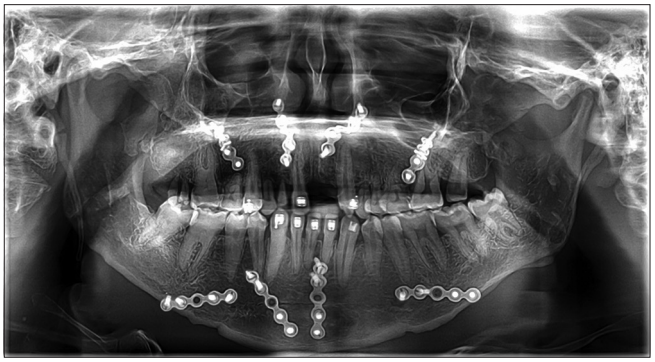

Figure 3: Orthopantomograph showing retained deciduous teeth and missing successors

syndrome) - macrocephaly, and sometimes hypertelorism and polydactyly is seen, which is caused by mutations in PTCH1.[10] Pallister–Hall syndrome also has some phenotypic overlap with GCPS but is clinically distinct.[2]

Conclusion

Greig syndrome is a rare genetic disorder. Patients with this syndrome have a triad of hypertelorism, macrocephaly, syndactyly and polydactyly. It is caused by a mutation in the GLI3 gene, which is a gene located on chromosome 7p13. The prenatal diagnosis and the genetic counseling are recommended in choosing a responsible management of Greig syndrome cases. This case report attempts to throw some light on this rare syndrome with its oral manifestations such as hypodontia and pathologic root resorption of retained deciduous teeth.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Balk K, Biesecker LG. The clinical atlas of Greig cephalopolysyndactyly syndrome. Am J Med Genet A 2008;146A: 548-57.
2. Gorlin RJ, Cohen MM Jr., Hennekam RC, editors. Greig cephalopolysyndactyly syndrome. Syndromes of the Head and Neck. 4th ed. New York: Oxford University Press; 2001. p. 995-6.
3. Johnston JJ, Olivos-Glander I, Killoran C, Elson E, Turner JT, Peters KF, *et al*. Molecular and clinical analyses of Greig cephalopolysyndactyly and pallister-hall syndromes: Robust phenotype prediction from the type and position of GLI3 mutations. Am J Hum Genet 2005;76:609-22.
4. Greig Cephalopolysyndactyly Syndrome. Genetics Home Reference (GHR); 2006.
5. Biesecker LG. The Greig cephalopolysyndactyly syndrome. Orphanet J Rare Dis 2008;3:10.
6. Jenkins D, Seelow D, Jehee FS, Perlyn CA, Alonso LG, Bueno DF, *et al*. RAB23 mutations in carpenter syndrome imply an unexpected role for hedgehog signaling in cranial-suture development and obesity. Am J Hum Genet 2007;80:1162-70.
7. Biesecker LG. The Greig cephalopolysyndactyly syndrome. Orphanet Journal of Rare Diseases 20081;3:10.
8. Gorlin RJ, Cohen MM Jr., Hennekam RCM, editors. Acrocallosal syndrome. Syndromes of the Head and Neck. Oxford: Oxford University Press; 2001. p. 996-8.
9. Teebi AS. New autosomal dominant syndrome resembling craniofrontonasal dysplasia. Am J Med Genet 1987;28:581-91.
10. Gorlin RJ, Cohen MM Jr., Hennekam RC, editors. Gorlin (nevoid basal cell carcinoma) syndrome. In: Syndromes of the Head and Neck. Oxford: Oxford University Press; 2001. p. 444-53.