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Case report

Orthognathic treatment in Greig cephalopolysyndactyly syndrome: A case report

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ABSTRACT

Typical Greig cephalopolysyndactyly syndrome (GCPS) is characterized by preaxial polydactyly or mixed pre- and postaxial polydactyly, true widely spaced eyes, macrocephaly. Individuals with mild GCPS may have subtle craniofacial findings. The diagnosis of GCPS is based on clinical findings and family history. *GLI3* is the only gene known to be associated with GCPS. It has an autosomal dominant inheritance. The literature fails in documentations of any treatment protocol for defective jaw relationship in these patients. Therefore, we report on a patient with GCPS presenting polysyndactyly, frontal bossing, high forehead, skeletal Class III deformity due to maxillary retrognathism and mandibular prognathism, treated with orthognathic surgery by means of double jaw surgery and orthodontic treatment with fixed appliances.

Introduction

Greig cephalopolysyndactyly (GCPS) syndrome is named after David Middleton Greig for his 1926 manuscript describing a patient with this disorder [1]. Greig cephalopolysyndactyly syndrome (GCPS) is an uncommon congenital disorder that affects development of the limbs, head, and face with an estimated incidence range of 1–9 per 1,000,000. The primary clinical triad of GCPS is polysyndactyly, macrocephaly, and hypertelorism (increased interpapillary distance) [2–4] The most common finding is postaxial polydactyly of the hands and preaxial polydactyly of the feet [4]. Some craniofacial abnormalities can be seen in GCPS rather than macrocephaly and hypertelrosim are high forehead, frontal bossing, telecanthus and broad nasal root [4].

GCPS is caused by mutations in the GLI3 gene located on chromosome 7p13. This condition is inherited in an autosomal dominant pattern. Translocations that interrupt the gene, microdeletion and large cytogenetically detectable deletions have also been described in addition to mutations. [5].

Pallister-Hell syndrome and at least one case of acrocallosal syndrome are also consequence of GL13 mutations. As diagnostic methods, sequencing of the GLI3 coding exons or scanning with denaturing high performance liquid chromatography (DHPLC), single-strand conformation polymorphism (SSCP), or other conformation detection methods is an appropriate first screen for patients with typical GCPS [6].

The purpose of this paper is to report a Greig cephalopolysyndactyly syndrome case which has dentofacial deformities treated with bimaxillary surgery emphasizing the good and stable results obtained in terms of facial aesthetics and occlusion.

Case presentation

A 20 year old female patient complaining of occlusal alterations of her jaws referred to oral and maxillofacial surgery department. The patient presented with obvious dysmorphic facial features. Extra oral examination revealed a long face, maxillary hypoplasia and mandibular prognathism (Fig. 1). On further examination partially cutaneous syndactyly of 2nd, 3rd and 4th and 5th fingers of both hands, and 2nd and 3rd toes on both feet were observed (Fig. 2). On intra oral examination V-shaped and narrow maxillary arch, Class III molar and canine relationship on both sides, severe crowding, permanent dentition and multiple decay teeth were present (Fig. 3). Preoperative

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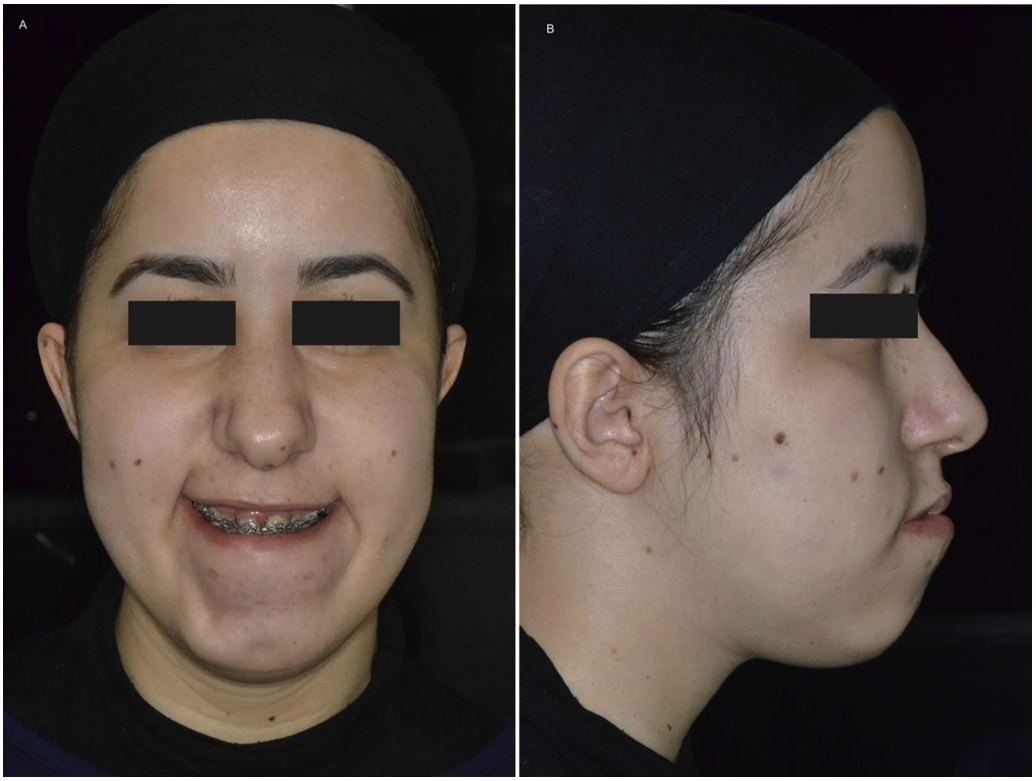

Fig. 1. A. Pre-surgery extra oral photo, frontal view. **B**. Pre-surgery extra oral photo, lateral profile.

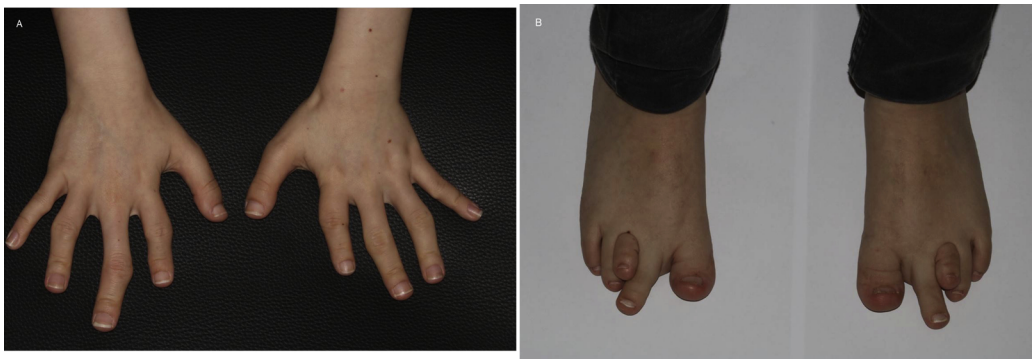

Fig. 2. A. Partially cutaneous syndactyly of fingers. (2^{nd}, 3^{rd} and 4^{th} and 5^{th} fingers of both hands.) **B.** Partially cutaneous syndactyly of toes. (2^{nd} and 3^{rd} toes on both feet.).

lateral cephalometric evaluation of the patient revealed a retrognathic hypoplastic maxilla, mid face retrusion and prognathic mandible (Fig. 4 and Table 1). Posteroanterior radiograph showed high forehead, frontal bossing and broad nasal root (Fig. 5). Other systemic evaluation was found to be normal. According to these findings initial diagnosis of GCPS was given and the patient was sent to perform differential genetic testing. Genetic testing results supported our diagnosis. Our patient had the disorder as the result of a de novo GLI3 pathogenic variant. Parents of the patient didn't show any clinical symptoms of the disorder. The proportion of cases caused by de novo pathogenic variants is unknown, as the frequency of subtle signs of the disorder in parents has not been thoroughly evaluated and molecular genetic data are insufficient. Before starting orthodontic treatment, the patient was sent to the conservative department for restoring the cavities. Initial panoramic radiograph evaluation revealed impacted third molars in all four segments (Fig. 6). Surgically extraction was performed to remove all four third molars at the beginning of dental treatment prior to orthodontic treatment. First step of orthodontic treatment was performed with a rapid palatal expansion device (bonded hyrax appliance with occlusal coverage) to increase the transversal width of maxilla. After removing the expansion device fixed orthodontic mechanics (22 slots edgewise stainless steel brackets) were bonded on all teeth and alignment was started with a 0.14 inch dimensional nickel titanium arch wire. Alignment of both

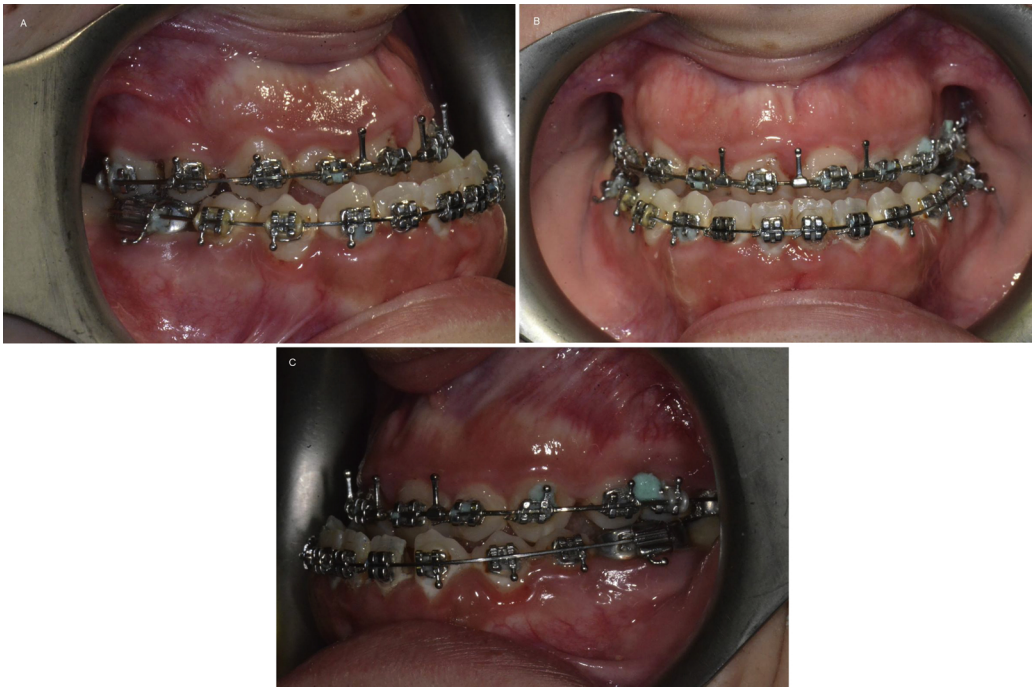

Fig. 3. A. Pre-surgery intra oral photo, right side occlusion. **B.** Pre-surgery intra oral photo, frontal occlusion. **C.** Pre-surgery intra oral photo, left side occlusion.

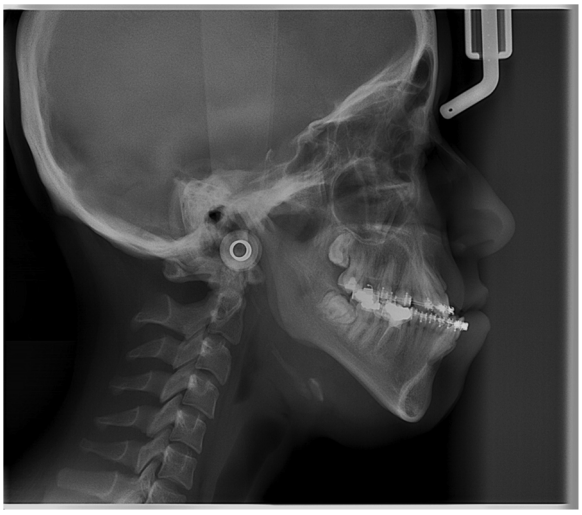

Fig. 4. Pre-surgery lateral chepalogram.

arches was achieved after 16 months. After placing 17 × 25 stainless steel arch wires for upper and lower arches orthognathic surgery planning was performed. Model surgery was planned to achieve 8 mm advancement and 4 mm anterior impaction for the maxilla, 9.1 mm set back followed by counter clockwise rotation for the mandible and genioplasty for 7.9 mm advancement and 3.1 mm impaction of the chin. The surgical procedure was performed in the standard fashion. Under hypotensive general anesthesia conditions, Le fort 1 osteotomy for the maxilla and bilateral sagittal split osteotomies for the mandible were performed. The osteotomy sites were fixed by KLS Martin orthognathic plates and screws (Fig. 9 and Fig. 10). Finally, wing osteotomy was performed for genioplasty and fixed by screws.

Table 1
Normal, Pre-treatment (T0) and Post-treatment (T1) cephalometric values.

	Normal	T0	T1
Vertical Skeletal			
S-N-Ar (º)	123˚ ± 5˚	128˚	126˚
S-Ar-Go (º)	143˚ ± 6˚	147˚	143˚
Ar-Go-Me (º)	130˚ ± 7˚	137˚	137˚
Sum of angles (º)	396˚ ± 5˚	412˚	406˚
Jarabak (%)	62%-65%	55%	59%
ANSMe/Nme(%)	60%	58%	62%
FMA (º)	16˚-35˚	44˚	39˚
Occlusal plane-SN (º)	140˚	266˚	25˚
Mandibular plane-PNS-ANS (º)	25˚ ± 5˚	30˚	34˚
SN-GoMe	36˚	52˚	46˚
Sagittal Skeletal			
SNA (º)	800˚-89,0˚	754˚	842˚
SNB (º)	750˚-82,0˚	75˚	767˚
ANB (º)	2,0˚-4,0˚	0,3˚	7,5˚
Maxillary depth (PoOr / NA) (º)	900˚ ± 3˚	815˚	913˚
Mandibular corpus length (mm)	71 mm ± 3 mm	64mm	65mm
Dental			
U1 / L1 (º)	1300˚-150,0˚	1206˚	1292˚
U1 / FH (º)	90˚ ± 3˚	108˚	105˚
U1 / NA (º)	220˚	214˚	134˚
U1 / NA (mm)	4mm	6mm	4mm
IMPA (º)	84˚-92˚	90˚	87˚
L1 / NB (º)	250˚	377˚	298˚
L1 / NB (mm)	4mm	10mm	9mm
Holdaway ratio	0mm-2mm	13mm	6mm
Overjet (mm)	2,5mm ± 2,5mm	−7,1mm	3,2mm
Overbite (mm)	2,5 mm ± 2 mm	2,7mm	1,9mm
Soft Tissue			
Upper Lip-E Line	−4mm	−2mm	0mm
Lower Lip- E Line	−2mm	3mm	−1mm
Naso-Labial	90˚-110˚	98˚	106˚
Soft tissue convexity	161˚	157˚	153˚
T0: Pre-operation			
T1: Follow-up			

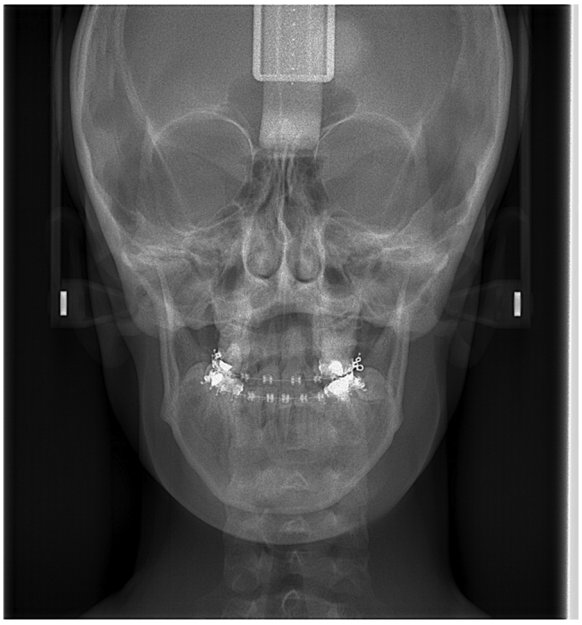

Fig. 5. Pre-surgery posteroanterior radiograph.

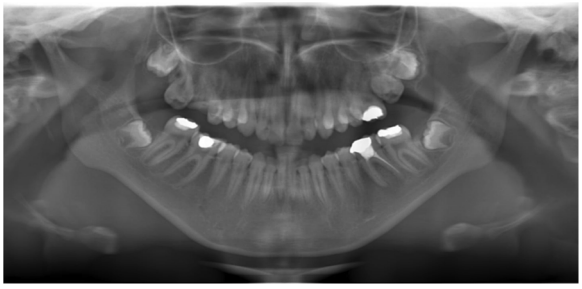

Fig. 6. Pre-treatment panoramic radiograph.

Postoperative recovery was uneventful. Both early and late complications were not observed. Postoperative finishing orthodontic treatment continued for another four months before bracket removal.

The post-treatment extraoral photographs and lateral cephalometric radiograph evaluation shows that the goals of corrective orthognathic surgery were reached with success. 30 months after surgery, the patient still presents stable results. (Figs. 6 and 7, and Table 1). Intra oral photographs reveal that malocclusion was eliminated and Class I molar and canine relationship on both sides were achieved with a good overjet and overbite (Fig. 8 and Fig. 10).

Discussion

Greig cephalopolysyndactyly is a rare multiple congenital anomaly characterized by clinical triad of polysyndactyly, macrocephalia and hypertelorism [7]. As molecular diagnosis methods are not widely used, it is difficult to definitely estimate incidence. At least 75% of cases with clinical diagnosis of cephalopolysyndactyly had GL13 gene mutation. GL13 mutation has a wide spectrum. In general, although it is characterized with autosomal dominant inheritance, there is also autosomal recessive inheritance pattern [7,8]. Many families with Greig polysyndactyly syndrome were reported. Risk of non-GCPS individuals within involved families to have child with GCPS is less than 1% per each conception [9,10]. In our case, there was no other individual with GCPS in the family therefore in this case the first suggestion was a genetic mutation. Genetic tests performed showed proved that the etiology in our case was genetic mutation. When neither parent of a proband with GCPS has clinical evidence of the disorder, the GLI3 pathogenic variant is likely de novo [5].

Polydactyly and cutaneous syndactyly in hands and feet are the most common clinical symptom in GCPS [2–4]. Our case had partial cutaneous syndactyly bilaterally in both hands and feet but no polydactyly.

The craniofacial manifestations for GCPS are also highly variable. Some patients have significant hypertelorism with or without telecanthus and macrocephaly. In our case none of these craniofacial abnormalities was detected. However high forehead, frontal bossing,

Fig. 7. A. Post- treatment extra oral photo, frontal view. **B.** Post-treatment extra oral photo, lateral profile.

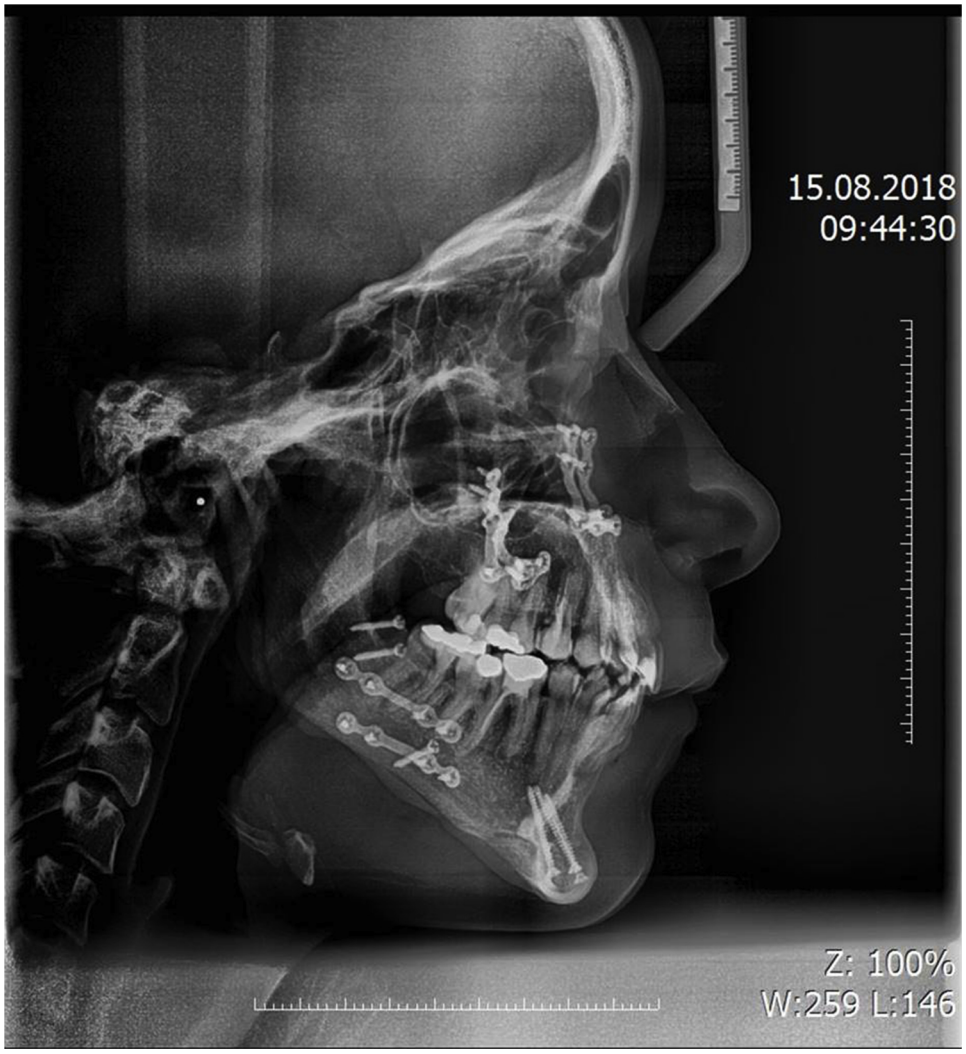

Fig. 8. Post-treatment lateral chepalogram.

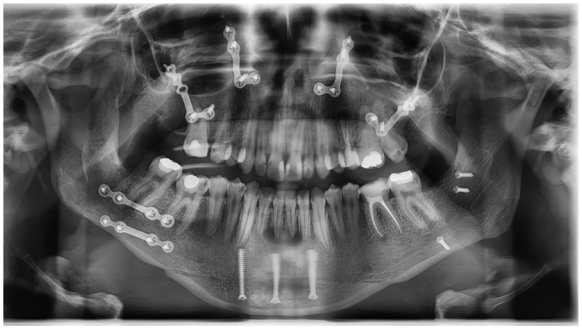

Fig. 9. Post-treatment panoramic radiograph.

broad nasal root and another abnormality which is not a characteristic symptom of the Greig syndrome, a hypoplastic maxilla was present. Although rare, craniosynostosis mental retardation, corpus callosum agenesis, umbilical and diaphragmatic hernia may also be present in Greig syndrome. Our case manifested none of above mentioned findings.

There are few associated medical complications of GCPS. Generally, the patients are healthy and have a normal lifespan [5]. No complications regarding general anesthesia or surgical procedures including healing were observed during or after treatment of the presented case. Good functional and esthetic results were achieved after treatment with orthognathic surgery.

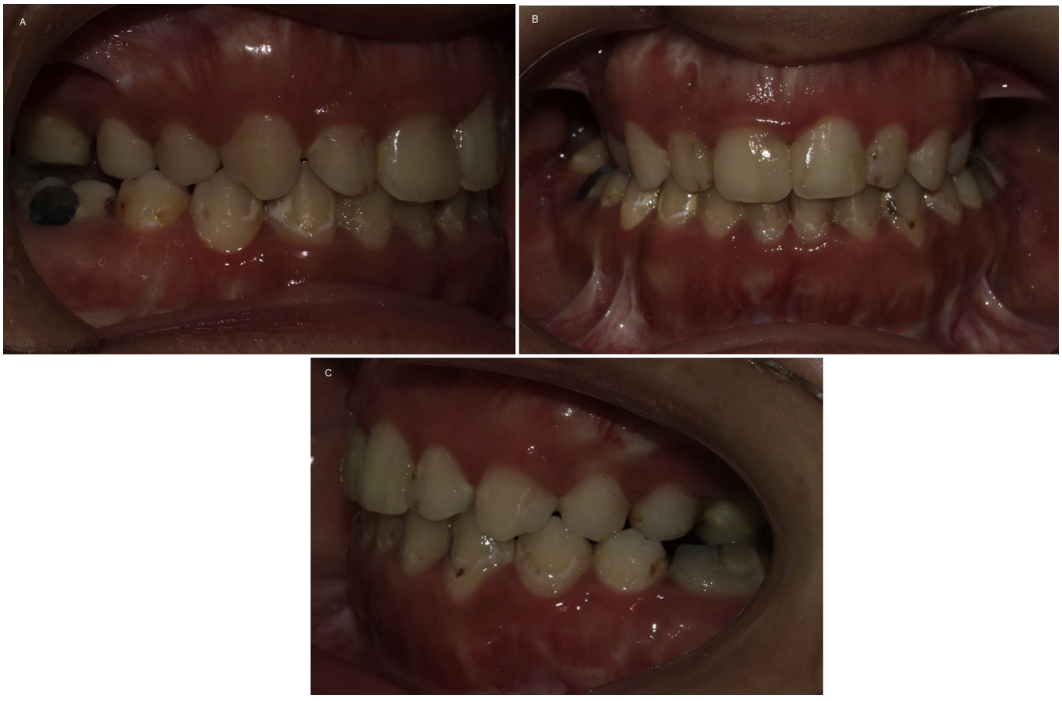

Fig. 10. A. Post-treatment intra oral photo, right side occlusion. **B**. Post-treatment intra oral photos, frontal occlusion. **C.** Post-treatment intra oral photos, left side occlusion.

Conclusion

Greig cephalopolysyndactyly is a rare syndrome and has craniofacial symptoms which should be treated by dental professionals. Therefore it is important that dental professionals should have sufficient knowledge of syndromes associated with dysmorphic faces to detect and effectively treat patients with this syndrome. This is the first case reported in the literature of a Greig syndrome treated with orthognathic surgery.

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