Case Report
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Shprintzen-Goldberg syndrome with an oro- facial anomaly: A rare case report

Dr. Deepak Chauhan (MDS) Assistant Professor,
Dr. Seema Thakur (MDS) Professor & HOD,

Dr. Reetica Sharma, PG Student

Dr. Dolly Singh, PG Student.

Dr. Tripti Chauhan (MD) Associate Professor

Deptt. of Community Medicine, IGMC, Shimla Himachal Pradesh, India

Corresponding author

Dr. Deepak Chauhan

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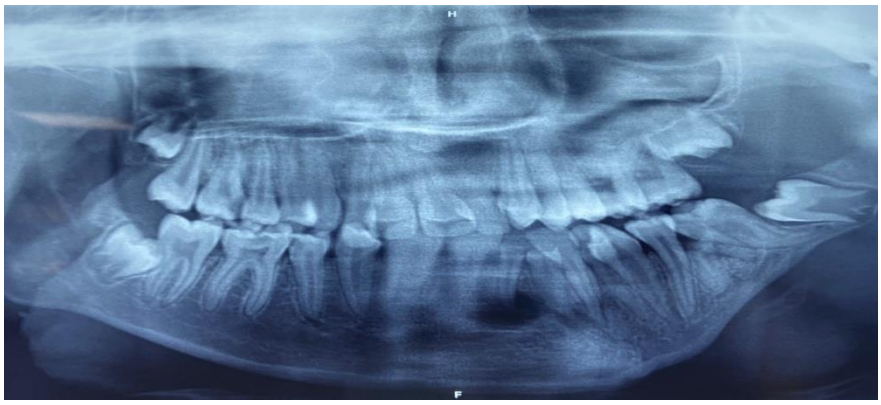


Abstract

The Shprintzen-Goldberg syndrome is an extremely rare syndrome with a characteristic facial and skeletal features. It is one of the group of disorders characterized by craniosynostosis and marfanoid features. This syndrome is an autosomal dominant disorder with multiple congenital abnormalities. It is the result of de novo gene mutations. Recently, mutations in the SKI gene are considered to be related to this rare entity. This gene is responsible for the manufacturing of protein which regulates the transforming growth factor beta (TGF-β) signaling pathway.

There are characteristic craniofacial, skeletal, neurological, and connective tissue abnormalities associated with SGS. This is a case report of an 12 year-old female child who has reported to the Department of Pediatric and preventive Dentistry of HP Government Dental College and Hospital, Shimla Himachal Pradesh, India, with her decayed teeth. She had craniofacial, skeletal, cardiovascular, and other abnormalities suggestive of SGS.

The patient had a tall forehead with plagiocephaly and a high-arched palate with hypoplastic teeth and ears were apparently low-set with posterior rotation and she had eyes with proptosis, myopia, hypertelorism, and down-slanting palpebral fissures. The patient did not show signs of mental retardation but craniofacial features were typical of this syndrome. The Shprintzen-Goldberg syndrome has many similarities with the Marfan syndrome (MFS) or the Loeys-Dietz syndrome (LDS) due to considerable phenotypic overlapping.

The aim of present case report is to highlight the features of this rare syndrome with peculiar findings at the oro- mandibulo-facial region.

Keywords: Shprintzen–Goldberg syndrome; high-arched palate; plagiocephaly; strabismus.

Introduction:

The Shprintzen–Goldberg syndrome (SGS) is a very rare congenital disorder affecting craniofacial, skeletal, neurological, and connective tissues. Craniosynostosis with marfanoid habitus and characteristic facial dysmorphism are the key features of this syndrome.[1–3]

Dolichocephaly, low-set ears, a high prominent forehead, proptosis, hyper-telorism, divergent strabismus, down-slanting eyes, a high-arched narrow palate, and maxillary hypoplasia are the most frequent craniofacial abnormalities in SGS.[1,2]

Arach-nodactyly, flat feet, pectus deformity, scoliosis, and hyper-mobile joints are the skeletal abnormalities.[1] Myopia and telecanthus are some other important ophthalmic features characteristic of SGS.[2] Affected individuals also suffer from hypotonia, cardiac defects and umbilical hernia.[3–5] The Shprintzen–Goldberg syndrome has many simi-larities with the Marfan syndrome (MFS) or the Loeys –Dietz syndrome (LDS) due to considerable phenotypic overlapping.[3–5]

Differential diagnosis includes MFS, LDS, the Idaho syndrome-II, the Antley–Bixler syndrome (ABS), congenital contractural arachnodactyly (CCA), and several other craniosynostotic syndromes.[4,5] There is no male or female predilection. The development of the affected individual is delayed, with mild to moderate intellectual disability.

Here is a case report of an 12 year-old female child who has reported to the Department of Pediatric and preventive Dentistry of HP Government Dental College and Hospital, Shimla Himachal Pradesh, India, with her decayed teeth along with other craniofacial, skeletal, cardiovascular, abnormalities suggestive of SGS.

Some of the traits of Shprintzen-Goldberg syndrome are similar to the traits of Marfan Syndrome and include:

- A tall, lanky body with increased joint mobility, scoliosis, long flat feet, and long fingers.
- Abnormal head shape
- Either a sunken chest or one that bulges outward
- Curvature of the spine
- Long, slender arms, legs and fingers
- One or more permanently bent fingers
- Delayed development
- Mild to moderate intellectual disabilities

(Table1) Characteristic features of the Shprintzen–Goldberg syndrome (SGS) as described by Greally et al.[1]

Features	**Description**	
Craniosynostosis	premature fusion of certain skull bones, involving the coronal, sagittal or lambdoid sutures	
Craniofacial features	Head	dolichocephaly, scaphocephaly, plagiocephaly, prominent forehead
	Palate and jaws	flattening/hypoplasia of the malar bone, high and narrow palate with prominent palatine ridges, micrognathia and/or retrognathia
	Ears	apparently low-set with posterior rotation
	eyes	myopia, proptosis, strabismus, hypertelorism, telecanthus, down-slanting palpebral fissures
Neurological abnormalities	mild to moderate intellectual disability, delayed motor and cognitive milestones	
Brain abnormalities	hydrocephalus, dilatation of the lateral ventricles, Chiari malformation type I	
Cardiovascular abnormalities	prolapsed mitral valve, dilatation of the aortic root, mitral regurgitation/incompetence, aortic regurgitation	
Skeletal anomalies	Joints	hypermobility of joints, osteopenia
	Skull	craniosynostosis, wide anterior fontanel
	Spine and vertebrae	C1–C2 vertebral abnormality (fusion or subluxation), scoliosis (abnormal side-to-side curvature of the spine), square-shaped vertebral bodies
	extremities	dolichostenomelia, arachnodactyly (long, slender fingers), camptodactyly (1 or more fingers permanently bent), metatarsus adductus, talipes equinovarus, flat feet
	Chest	pectus excavatum (sunken chest) or pectus carinatum (protruding chest), thin ribs, 13 pairs of ribs
Genitourinary abnormalities	inguinal hernia, cryptorchidism in males	
Other findings	herniae and abdominal wall defects, loss of subcutaneous fat, arterial tortuosity and aneurysms, broad/bifid uvula, cleft palate, dural ectasia	

Case Report:

A 12 year-old female patient reported to the out patient department (OPD) of Pediatric and preventive Dentistry of HP Govt. dental college, Shimla, HP, with her parents having a chief complaint of decayed teeth **(fig. 1,2).** The patient had defective hearing and speech problem. She was not able to express her problems completely and presented with facial dysmorphism and musculoskeletal abnormalities.

Physical examination revealed that the limbs were weak and she had difficulty in walking and had a tall forehead with plagiocephaly, ears were apparently low-set with posterior rotation. The child had eyes with proptosis, myopia, hypertelorism, and down-slanting palpebral fissures **(fig,3).** She was suffering from strabismus and nasal bridge was broad and somewhat flattened. The facial profile was convex with marked facial asymmetry and lips were potentially in- competent (fig 4). The skeletal findings included pectus carinatum and flat feet. The intraoral examination revealed that the patient was having permanent dentition with multiple carious and crowded teeth and a huge periapical pathology was evident in an OPG **(fig.4).** Her maxillary arch was high with a narrow and deep palate.

Crowding was present in the mandibular arch and her 31, 41 were carious exposed and were associated with huge periapical pathology. Firstly consideration was given to preserve these teeth, but later on keeping in view the prognosis of these teeth and archform of of the patient, these teeth were extracted and curettage and debridement of the socket was done by shoe lace technique to remove the granulation tissue with the help of gauge piece **(fig.5,6).** finally a remarkable improvement was seen in an extraoral wound healing **(fig. 7).**

So based on the unusual and atypical clinical findings, the patient was subsequently diagnosed to be a possible case of SGS. The development of many bodily systems, including the bones and cranium, were disturbed, producing a wide range of signs and symptoms of SGS [4,7]

A defect in the gene pre-sent on chromosome 15 is also considered to be respon-sible for this syndrome.[8] Germline mosaicism with mutation in 3 genomic loci have been linked to SGS, thereby making it a molecularly heterogeneous disorder.[9]

Most investigators believe that multiple genes are responsible for a single phenotype. Thus, mutations in other genes may also be related to SGS. The differential diagnosis of SGS should embrace LDS, MFS, CCA, fronto metaphyseal dysplasia, the Melnick –Needles syndrome (MNS), the Idaho syndrome-II, and ABS.[10–21] The occurrence of SGS is very rare. As of 2016, approx. 60 cases of SGS have been described in the medical literature since the first case was reported in the original publication by Sugarman and Vogel in 1981.6,[22] In present case, the majority of the characteristic features of SGS as described by Greally et al (table 1).[1] The child had moderate mental retardation and craniofacial features typical of this syndrome. Her skeletal, cardiovascular and neurological features could also be associated with SGS.

There was no positive family history in present case. The parents and siblings of the patient were without any abnormalities. The Shprintzen–Goldberg syndrome is mostly the result of de novo gene mutations. In very rare cases, this syndrome may be inherited from normal parents with defective or altered genes.[23]

Discussion:

The Shprintzen Goldberg syndrome is sometimes called as marfanoid craniosynostosis syndrome, the Shprintzen–Goldberg craniosynostosis syndrome, cra-niosynostosis with arachnodactyly and abdominal her-niae, marfanoid disorder with craniosynostosis, or type I marfanoid-craniosynostosis syndrome. Shprintzen and Goldberg described this syndrome in 1982.[3] Sugarman and Vogel were the first to report this condition in 1981, in a 17-year-old male with plagiocephaly, multiple cra-niofacial, vertebral and skeletal anomalies, umbilical and inguinal herniae, hypotonia, and mental retardation.[6]

This syndrome has a variable phenotypic expression, as it involves the abnormalities of skeletal, connective, cra-niofacial, cardiovascular, and neurological tissues. Greally et al. gave a thorough review of the clinical features of SGS (Table 1).[1] Mutations in the SKI gene are considered to be the most common etiology. This gene is responsible for the manufacturing of protein which regulates the transform-ing growth factor beta (TGF-β) signaling pathway.

The TGF-β signaling pathway is responsible for the regulation of cellular proliferation, differentiation, apoptosis, and motility. The SKI protein plays a crucial role in the development of the tissues of the skull, bones, skin, and brain. In this syndrome, a mutation in the SKI gene al-ters the SKI protein. This altered protein is not able to attach to proteins in the TGF-β pathway and to block signaling. This results in an abnormally active TGF-β path-way. Excess signaling of TGF-β affects the gene activity.

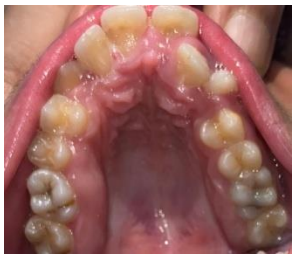
Conclusion:

Patients with SGS can have variable phenotypes and ab-normalities. A thorough and meticulous clinical examination along with a detailed history are required to diagnose this entity. This syndrome is not a life-threatening situation, but the patient can suffer from the complications arising from cardiac, respiratory or skeletal abnormalities. A disciplinary team including a pediatrician, cardiologist, ophthalmologist, radiolo-gist, speech pathologist, physical therapist, a surgeon, a pedodontist and an orthodontist are required to treat and manage such patients effectively. Now this case will be referred to an orthodontist for more comprehensive treatment.

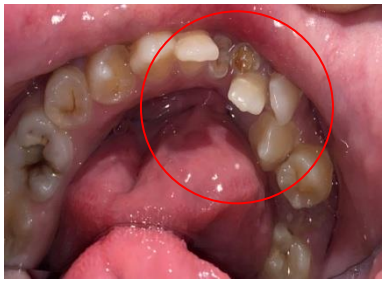
Standard therapies are limited to symptom management, such as the re-pair of aneurysms and heart valves as well as spinal and chest malformations, and the operation of craniosyno-stosis, which has to be done in the early infancy.

(fig.3) Patient showing down-slanting palpebral fissures and unilateral deviation of the face with cataract on left eye wall

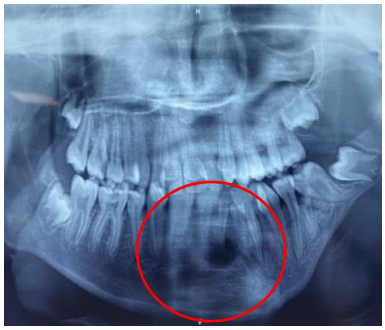
(Fig.4) lateral view of the patient showing convex profile of the patient



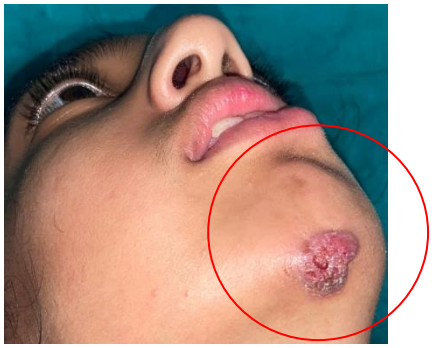
(Fig.1) Pre treatment photograph of maxillary arch of the patient



(Fig. 2) Pre treatment photograph of mandibular arch of the patient

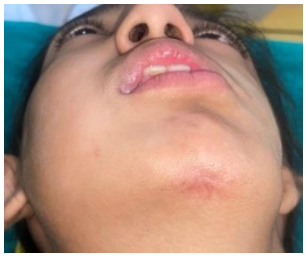


(Fig.4) OPG of the patient showing periapical pathology with respect to 31,41



(Fig. 5) Extra-oral photograph showing draining sinus tract

(Fig.6) Showing treatment of extraoral cutanious tract



(Fig.7) post treatment photograph of the patient showing remarkable improvement in extraoral scaring tissue

References:

1. Greally MT, Carey JC, Milewicz DM, et al. Shprintzen– Goldberg syn-drome: A clinical analysis. Am J Med Genet.1998;76(3):202–212.

2. Topouzelis N, Markovitsi E, Antoniades K. Shprintzen–Goldberg syndrome: Case report. Cleft Palate Craniofac J. 2003;4 0(4):433–436.

3. Shprintzen RJ, Goldberg RB. A recurrent pattern syndrome of cra-niosynostosis associated with arachnodactyly and abdominal her-nias. J Craniofac Genet Dev Biol. 1982 ;2(1): 65–74.

4. Doyle AJ, Doyle JJ, Bessling SL, et al. Mutations in the TGF-β repressor SKI cause Shprintzen–Goldberg syndrome with aortic aneu-rysm. Nat Genet. 2012;44 (11):1249 –1254 .

5. Robinson PN, Neumann LM, Demuth S, et al. Shprintzen–Goldberg syndrome: Fourteen new patients and a clinical analysis. Am J Med Genet. 2005;135(3):251–262.

6. Sugarman G, Vogel MW. Craniofacial and musculoskeletal abnor-malities. A questionable connective tissue disease. Synd Iden. 1981;7:16–17.

7. Carmignac V, Thevenon J, Ades L, et al. In-frame mutations in exon 1 of SKI cause dominant Shprintzen–Goldberg syndrome. Am J Hum Genet. 2012;91(5):950–957.

8. Sood S, Eldadah ZA, Krause WL, McIntosh I, Dietz HC. Mutation in fibrillin-1 and the Marfanoid-craniosynostosis (Shprintzen–Gold-berg) syndrome. Nat Genet. 1996;12(2):209–211.

9. Paulik S LB, Chan KC, Lorts A, Elias ER, Cayre RO, Valdes-Cruz LM. Shprintzen–Goldberg syndrome with tetralogy of Fallot and sub-valvar aortic stenosis. J Ultrasound Med. 2005;24(5):703–706.

10. Loeys BL, Chen J, Neptune ER, et al. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal deve-lopment caused by mutations in TG FBR1 or TGFBR2. Nat Genet. 2005;37(3):275–281.

11. Loeys BL, Schwarze U, Holm T, et al. Aneurysm syndromes caused by mutations in the TGF- beta receptor. N Engl J Med. 200 6;355(8):788–798.

12. Diet z HC. Marfan syndrome. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 1993–2014; 2001 [updated 2017]..

13. Godfrey M. Congenital contractural arachnodactyly. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 1993–2014; 2001 [updated 2012]..

14. Godfrey M. Fibrillin-2 mutations in congenital contractural arachno-dactyly. In: Robinson PN, Godfrey M, eds. Marfan Syndrome: A Primer for Clinicians and Scientists. New York, NY: Plenum; 2004:123–129.

15. Gorlin RJ, Cohen MM Jr. Frontometaphyseal dysplasia. A new syn-drome. Am J Dis Child. 1969;118(3):487–494.

16. Danks DM, Mayne V. Frontometaphyseal dysplasia: A progressive disease of bone and connective tissue. Birth Defects Orig Artic Ser. 1974;10(12):57–60.

17. Holt JF, Thompson GR, Arenberg IK . Frontometaphyseal dysplasia. Radiol Clin North Am. 1972;10(2): 225–243.

18. Melnick JC , Needles CF. An undiagnose d bone dysplasia. A 2-family study of 4 generations and 3 generations. Am J Roentgenol Radium Ther Nucl Med. 1966; 97(1):39–48.

19. LaMontagne AE. Urological manifestations of the Melnick–Needles syndrome: A case report and review of the literature. J Urol. 1991;14 5(5):1020–1021.

20. Stoll C. Shprintzen–Goldberg mar fanoid syndrome: A case followed up for 21 years. Clin Dysmorphol. 2002;11(1):1–7.

22. Antley R, Bixler D. Trapezoidocephaly, midfacial hypoplasia and cartilage abnormalities with multiple synostoses and skeletal frac-tures. Birth Defects Orig Artic Ser. 1975;11(2):397–401.

23. Greally MT. Shprintzen–Goldberg syndrome. In: Adam MP, Arding-er HH, Pagon RA , et al., eds. GeneReviews® [Internet]. Seattle, WA: University of Washington, Seattle; 1993–2014; 2006 [updated 2013]. http://www.ncbi.nlm.nih.gov/books/NBK1277.