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Case Report

Shprintzen Goldberg syndrome: a classic case

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ABSTRACT

Shprintzen Goldberg syndrome (SGS) is an uncommon genetic condition marked by a mix of craniofacial, skeletal, and cardiovascular abnormalities. This syndrome was initially detailed in 1984 by Dr. Shprintzen and Dr. Goldberg, as a distinct clinical condition. Since then, only a small number of cases have been reported in literature. A total of just 50 instances of SGS have been documented globally. A 6 months old male child presented with Acute respiratory illness. On examination child had marked failure to thrive features with Marfaniod habitus along with craniosynostosis, low set ears, prominent eyes, small lower jaw, long, slender fingers, joint hypermobility, high arched palate, flat feet and developmental delay. Supportive management of active complaints was done given but patient has poor prognosis. Our patient came as a case of acute respiratory infection but on examination had typical features consistent with SGS and on further investigations Genotype was found to have SKI mutation and on ECHO patient had Mitral valve involvement. All this led us to the rare diagnosis of SGS.

Keywords: Craniosyanostosis, Marfanoid features, Arachnodactly, Pectus excavatum, Mitral valve involvement, Septal defects

INTRODUCTION

Shprintzen Goldberg syndrome (SGS) is an uncommon genetic condition marked by a mix of craniofacial, skeletal, and cardiovascular abnormalities.[1] This syndrome was initially detailed in 1984 by Dr. Shprintzen and Dr. Goldberg, as a distinct clinical condition. Since then, only a small number of cases have been reported in literature. A total of just 50 instances of SGS have been documented globally.[2]

CASE REPORT

A 6-month-old male child presented with chief complaints of fever and cough for the past two days. There was no history of seizures, vomiting, cyanosis, or feeding intolerance. On general examination, the child appeared thin and lean with marked failure to thrive, suggestive of poor nutritional and developmental status for age. The child was alert but showed features suggestive of global developmental delay.

Detailed physical examination revealed multiple dysmorphic features. The child demonstrated a Marfanoid habitus, characterized by a slender body build and disproportionately long extremities. Craniofacial examination showed craniosynostosis (Figure 1), with abnormal skull shape due to premature fusion of cranial sutures. Additional facial dysmorphic features included low-set ears, prominent eyes (proptosis), and micrognathia. Oral examination revealed a high-arched palate (Figure 3).

Examination of the extremities showed long, slender fingers (arachnodactyly) (Figure 2) along with joint hypermobility, suggestive of connective tissue involvement. The child also had flat feet (pes planus) (Figure 4). These skeletal and craniofacial abnormalities,

along with developmental delay and marfanoid habitus, were consistent with the phenotypic features seen in SGS.

Overall, the clinical presentation of craniosynostosis, marfanoid body habitus, craniofacial dysmorphism, skeletal abnormalities, and developmental delay raised a strong clinical suspicion of SGS in this child.

Management and outcome

Investigations

ECHO showed Flail anterior mitral leaflet without mitral regurgitation.

Whole genome sequencing showed mutation in SKI gene on Exon 1 consistent with findings of Shpintzen Goldberg autosomal dominant syndrome (Figure 5).

Treatment

Symptomatic treatment with multidisciplinary approach and yearly ophthalmological examination for myopia.

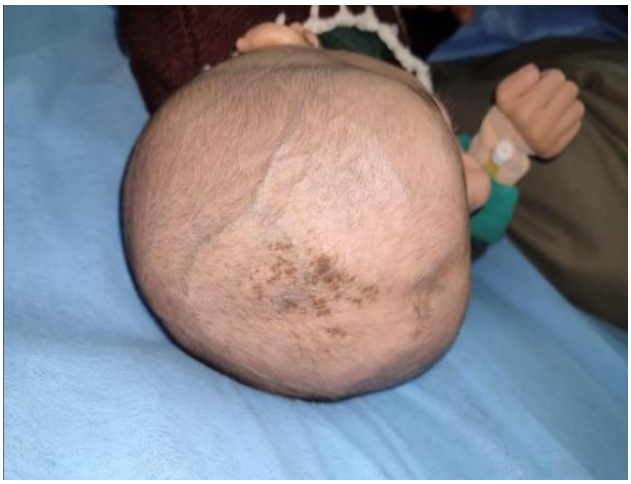


Figure 1: Craniosynostosis in the patient.

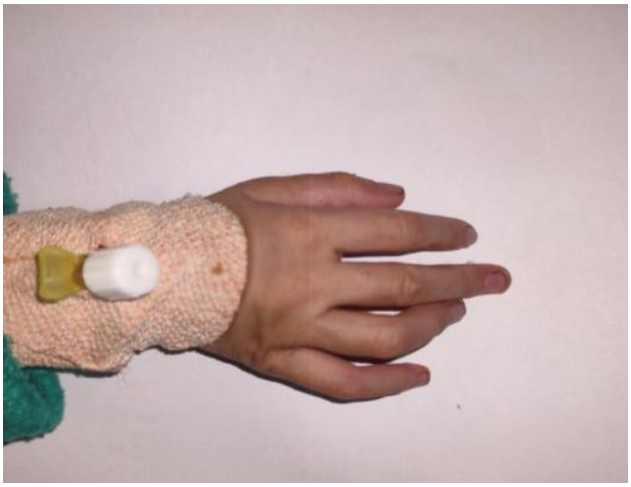


Figure 2: Long slender fingers.

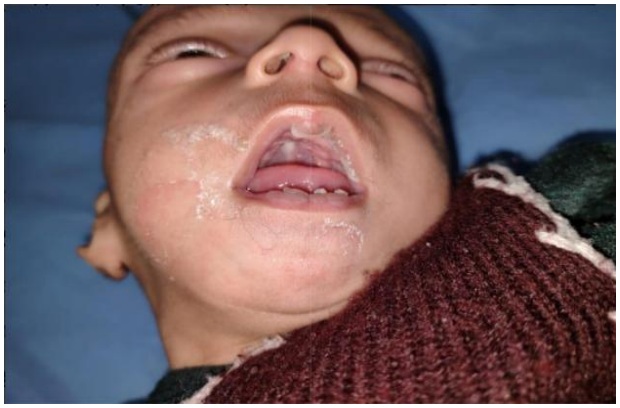


Figure 3: High arched palate.

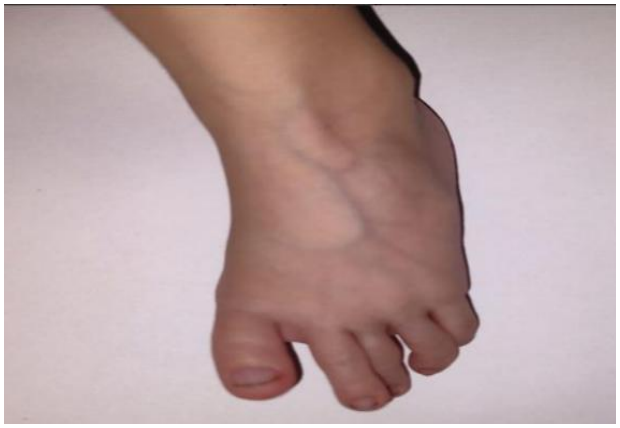
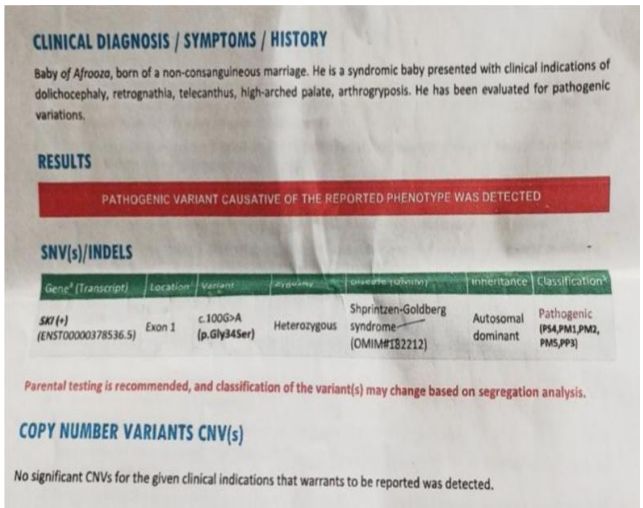


Figure 4: Flat feet in the patient.


CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

Baby of Afrooza, born of a non-consanguineous marriage. He is a syndromic baby presented with clinical indications of dolichocephaly, retrognathia, telecanthus, high-arched palate, arthrogryposis. He has been evaluated for pathogenic variations.

RESULTS

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

SNV(s)/INDELS

Gene[a] (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification[b]
SKI (+) (ENST00000378536.5)	Exon 1	c.100G>A (p.Gly34Ser)	Heterozygous	Shprintzen-Goldberg syndrome (OMIM#182212)	Autosomal dominant	Pathogenic (PS4,PM1,PM2, PM5,PP3)

Parental testing is recommended, and classification of the variant(s) may change based on segregation analysis.

COPY NUMBER VARIANTS CNV(s)

No significant CNVs for the given clinical indications that warrants to be reported was detected.

Figure 5: Whole genome sequencing showed mutation in SKI gene on Exon 1 consistent with findings of Shpintzen-Goldberg autosomal dominant syndrome.

DISCUSSION

SGS is a rare connective tissue disorder characterized by craniosynostosis, craniofacial dysmorphism, marfanoid habitus, skeletal abnormalities, developmental delay, and cardiovascular involvement including aortic dilatation.[1,2]

The condition shares several clinical features with other heritable connective tissue disorders such as Marfan syndrome and Loeys-Dietz syndrome, particularly with regard to skeletal manifestations and vascular abnormalities.[3,4]

SGS was first described by Shprintzen and Goldberg in 1982 as a syndrome involving craniosynostosis and marfanoid habitus with multiple craniofacial and skeletal abnormalities.[1] The disorder follows an autosomal dominant pattern of inheritance, although a significant proportion of cases occur due to de novo mutations.[5] The clinical phenotype is variable but typically includes craniosynostosis, intellectual disability, hypotonia, joint hypermobility, arachnodactyly, and characteristic craniofacial features such as micrognathia, proptosis, and low-set ears.[2,6]

Molecular genetic studies have identified heterozygous mutations in the SKI proto-oncogene as the primary cause of SGS.[7] The SKI gene encodes a transcriptional co-repressor that plays an important role in regulating the transforming growth factor-beta (TGF-β) signalling pathway, which is essential for normal connective tissue development and vascular integrity.[7,8]

Under normal physiological conditions, SKI functions as a negative regulator of TGF-β signalling and is rapidly degraded following ligand stimulation.[8] Mutations in SKI disrupt this regulatory mechanism, leading to abnormal interactions with SMAD proteins and dysregulation of downstream transcriptional activity.[9] In particular, pathogenic variants affecting the SMAD-binding domain impair the interaction between SKI and phosphorylated SMAD proteins, resulting in stabilization of the SKI protein and altered transcriptional responses.[9,10]

Studies using dermal fibroblasts derived from affected individuals have demonstrated abnormal activation of TGF-β signalling cascades and increased expression of TGF-β-responsive genes, suggesting that dysregulation of this pathway plays a central role in disease pathogenesis.[7,10]

Alterations in TGF-β signalling also contribute to the development of vascular abnormalities such as aortic root dilatation and aneurysm formation, which are important clinical features of SGS.[3,11] Similar mechanisms have been described in other connective tissue disorders including Marfan syndrome and Loeys-Dietz syndrome, further highlighting the role of TGF-β pathway dysregulation in these conditions.[3,4]

Because of the overlapping phenotypic features with other connective tissue disorders, clinical diagnosis may be challenging, and molecular genetic testing for SKI mutations plays a crucial role in confirming the diagnosis.[6,7] Early identification of SGS is important to allow appropriate monitoring and management, particularly for potential cardiovascular complications.

CONCLUSION

Our patient came as a case of acute respiratory infection but on examination had typical features consistent with SGS and on further investigations genotype was found to have SKI mutation and on ECHO patient had Mitral valve involvement. All this led us to the rare diagnosis of SGS.

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Ethical approval: Not required

REFERENCES

1. Shprintzen RJ, Goldberg RB. A recurrent pattern syndrome involving craniosynostosis and marfanoid habitus. Am J Med Genet. 1982;13:101-12.
2. Glesby MJ, Pyeritz RE. Association of craniosynostosis with marfanoid habitus. J Med Genet. 1989;26:41-4.
3. Loeys BL, Dietz HC, Braverman AC, Callewaert BL, De Backer J, Devereux RB, et al. The revised Ghent nosology for the Marfan syndrome. J Med Genet. 2010;47(7):476-85.
4. MacCarrick G, Black JH, Bowdin S, El-Hamamsy I, Frischmeyer-Guerrerio PA, Guerrerio AL, et al. Loeys-Dietz syndrome: a primer for diagnosis and management. Genet Med. 2014;16(8):576-87.
5. Verstraeten A, et al. Clinical spectrum of Shprintzen–Goldberg syndrome. Genet Med. 2016;18:1-9.
6. Greally MT. Shprintzen-Goldberg syndrome. Orphanet J Rare Dis. 2017;12:23.
7. Doyle AJ, Doyle JJ, Bessling SL, Maragh S, Lindsay ME, Schepers D, et al. Mutations in the TGF-β repressor SKI cause Shprintzen-Goldberg syndrome. Nat Genet. 2012;44(11):1249-54.
8. Hill CS, et al. Regulation of TGF-β signalling by SKI family proteins. Cell Signal. 2012;24:147-54.
9. Schepers D, et al. Mutational spectrum in SKI in Shprintzen-Goldberg syndrome. Eur J Hum Genet. 2015;23:1302-7.
10. Gori I, George R, Purkiss AG, Strohbuecker S, Randall RA, Ogrodowicz R, et al. Mutations in SKI in Shprintzen-Goldberg syndrome lead to attenuated TGF-β responses through SKI stabilization. eLife. 2021;10:e63545.
11. Cook JR, et al. TGF-β signalling in heritable aortic disease. Nat Rev Cardiol. 2014;11:13-23.

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