CASE REPORT

A RARE CASE OF SHPRINTZEN-GOLDBERG SYNDROME

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Shprintzen-Goldberg syndrome is a relatively rare congenital connective tissue type of disorder with a constellation of dysmorphic features including craniosynostosis, craniofacial, skeletal, cardiovascular and neurological abnormalities. We present the case-report of a 5-year-old boy with Shprintzen-Goldberg syndrome and a brief review of literature pertaining to this condition. The patients with Shprintzen-Goldberg syndrome show a considerable phenotypic overlap with other craniosynostosis syndromes. So, a meticulous evaluation of these patients should be performed for a prudent diagnosis. Since these patients present with multiple systemic conditions,a multidisciplinary approach should be planned for their management.

Keywords: Brachycephaly; Cleftpalate; Craniosynostosis; Cryptorchidism; Hypertelorism; Uvula

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INTRODUCTION

Shprintzen Goldberg syndrome (SGS) is an extremely rare connective tissue disorder that has a combination of discrete craniofacial, skeletal and neurological abnormalities.[1] In 1981, Sugar man and Vogel reported a case in a 17-year-old boy who presented with multiple craniofacial, skeletal, vertebral anomalies, plagiocephaly, umbilical and inguinal hernia, hypotonia and intellectual disabilities. However, later in 1982, Shprintzen and Goldberg presented this as a separate clinical entity.[2] Since then, fewer than 60 cases have been reported in the medical literature till date presenting with typical features.[1] However, the exact prevalence of this condition is unknown. The diagnosis of Shprintzen Goldberg syndrome relies on comprehensive and meticulous clinical evaluation and the identification of the paradigmatic features of this syndrome.

CASE REPORT

A 5-year-old male patient reported to the OPD of Government Dental College, Kottayam with a complaint of pain in the right upper back tooth region for the last one month. His parents reported about delayed developmental milestones, cognitive disabilities and mild intellectual disability. He was the first child of those non-consanguineously married parents and his birth was by normal delivery with no significant perinatal and family history.

On general examination he appeared thinly built and malnourished. His height, weight and head circumference were less than third centile for his age and sex. The vital signs were within normal limits. General physical examination showed remarkable craniofacial findings like microcephaly, frontal bossing, small triangular shaped face, large protruding eyes with down slanting palpebral fissures, hypertelorism, flattened nasal root, low set and posteriorly rotated ears (Figure-1). The chest examination revealed a barrel shaped chest with a precordial bulge, pectus carinatum. On CVS examination, there was no cardiomegaly. A pan systolic murmur of grade 4 intensity was heard in the second aortic area and along the left heart border. On per abdominal examination, umbilical hernia was noted (Figure-2). Another presenting feature was bilateral cryptorchidism. Neurological examination revealed generalised hypotonia along with muscle wasting. There were no remarkable findings on musculoskeletal examination.

On intraoral examination, hypo plastic maxilla with V-shaped and high arched palate, absence of uvula and cleft palate were observed (Figure-3 and 4). Maxillary right primary first molar was found to be grossly decayed. Multiple carious teeth were present in the maxillary and mandibular arch.

On further medical evaluation, Chest X-ray revealed an abnormal configuration of cardiac shadow with upturned cardiac apex (Figure-5). On echocardiography, he was found to have aortic regurgitation, ventricular septal defect and mitral valve prolapse. Routine blood and urine investigations were within normal limits. MRI scan of brain showed prominence of extra-axial CSF spaces and ventricle on left side. (Figure-6). The skeletal survey did not show any abnormal findings. Based on history and comprehensive clinical evaluation, a diagnosis of Shprintzen Goldberg syndrome was made. Differential diagnosis considered were Loeys-Dietz syndrome, Marfan syndrome and other craniosynostosis syndromes. After obtaining a medical consent, incision and drainage followed by extraction of the offending tooth was performed under antibiotic prophylaxis.

Restoration of the carious teeth was planned. The parents were educated about the necessity of a low sugar diet to arrest the progression of caries and the surgical correction of the cleft palate and umbilical hernia was also advised.

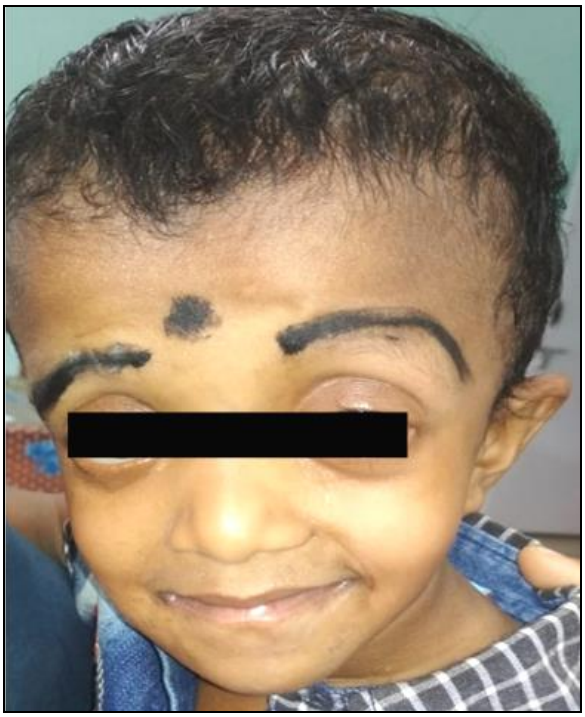

Figure-1: Small triangular face, frontal bossing, large protruding eyes, depressed nasal bridge, low set ears

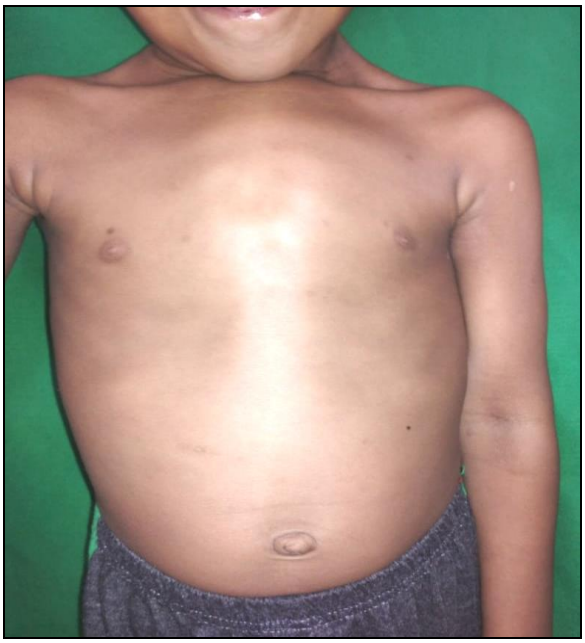

Figure-2: Pectus carinatum and umbilical hernia

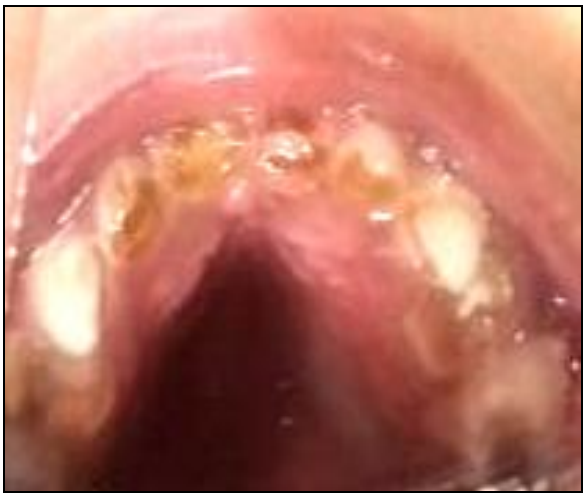

Figure-3: V-shaped and high arched palate

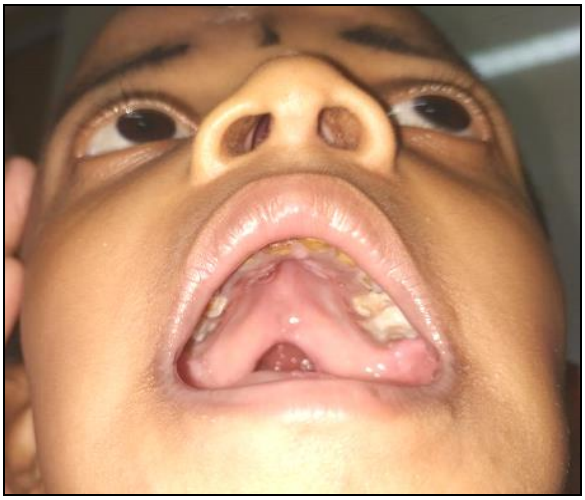

Figure-4: Absent uvula and cleft palate

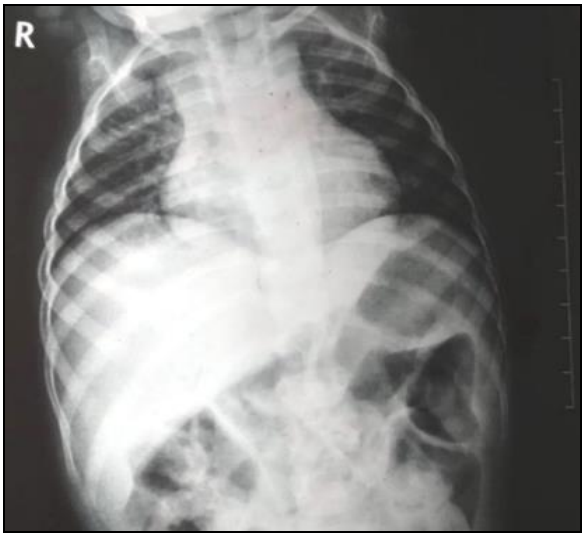

Figure-5: Abnormal configuration of cardiac shadow

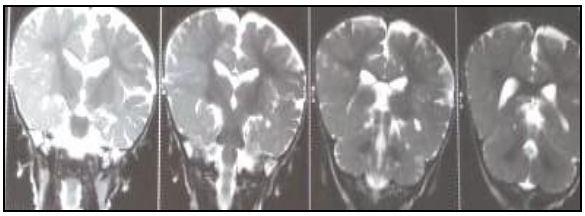

Figure-6: Mild atrophy of left cerebral hemisphere

DISCUSSION

Shprintzen Goldberg syndrome is a very rare congenital connective tissue disorder characterised by premature fusion of skull bones, craniofacial, neurological, cardiovascular, skeletal, and other abnormalities.[1] It is an autosomal dominant disorder which affects both sexes with a female to male ratio of 10:5.[4] Mostof them may have dysmorphic features at birth. The most common presenting feature is early closure of skull sutures (craniosynostosis).[3] Other craniofacial abnormalities include dolicocephaly, prominent forehead, hypertelorism, large protruding eyes, strabismus, down slanting palpebral fissures, high and narrow palatal arch, wide or split uvula, cleft palate, micrognathia, low set and posteriorly rotated ears. The skeletal anomalies include arachnodactyly, campylodactyly abnormalities of cervical spine, scoliosis, square shaped vertebral bodies, flat feet, pectus excavatum or carinatum and hypermobility of joints.[4] Mitral valve prolapse, mitral or aortic regurgitation are the usually reported cardiovascular complications.[3] Neurological manifestations like hypotonia, delayed motor and cognitive abilities may also accompany. Abdominal wall defects, minimal increase of adipose tissue and cryptorchidism are some of the rare features of this syndrome.[1]

The patient in this report exhibited most of the above mentioned craniofacial, cardiovascular and neurologic manifestations innate to this syndrome. Absence of uvula is usually not reported in SGS, but was observed in our case which may be considered as a variation and needs a special mention. However, we could not find any skeletal manifestations other than pectus carinatum. Umbilical hernia was yet another presenting feature in our patient. This is consistent with the findings of Shah *et al*. who reported umbilical hernia in an Indian child with SGS[1]. Medical evaluation of this case reported aortic regurgitation, mitral valve prolapses, ventricular septal defect and generalised hypotonia. This is in line with the report of Topouzelis *et al*. who found out mitral valve prolapse, skin hyper elasticity and hypotonia in an 8-year-old girl with Shprintzen Goldberg syndrome.[2] Pauliks *et al*. reported a case of Shprintzen Goldberg syndrome with complex congenital heart anomalies including tetralogy of Fallot.[5] Pavon *et al*, described the findings in a 16-year-old boy who was followed up for 12 years to evaluate the clinical course and reported the presence of teeth malfformations among various other features of this syndrome.[6]

A genetic defect has been attributed to the pathogenesis of this syndrome. Greally et al. reported that SKI gene mutation is known to cause Shprintzen Goldberg syndrome.[4] However recent reports suggest that mutation in FBN1 gene have also been seen in Shprintzen Goldberg syndrome. FBN1 gene has been implicated in many connective tissue disorders like Marfan syndrome, Loeys-Dietz syndrome.[3] Kosaki *et al* in his report on a Japanese boy pointed out that there is a 3662E-A transition (134797.0045) resulting in cys 1221-to-tyr (C 1221 Y) substitution in the FBN1 gene.[7]

Even though most Shprintzen Goldberg syndrome cases present with distinct features, there is a considerable phenotypic overlap with other similar syndromes. The differential diagnosis includes Marfan syndrome, Loeys-Dietz syndrome and otopalato digital spectrum of disorders. SGS shares many features with Marfan syndrome like arachnodactyly, aortic dilation and scoliosis. However, craniosynostosis, delayed development, mild to moderate intellectual disability, hypotonia, umbilical hernia are consistent with Shprintzen Goldberg syndrome.[1] Though there is an overlap of clinical features with Loeys-Dietz syndrome, intellectual disability is more reported in Shprintzen Goldberg syndrome whereas cardiovascular anomalies are more common in Loeys-Dietz syndrome.[3] SGS must also be differentiated from other syndromes with craniosynostosis and marfanoid habitus like Idaho Syndrome -2 and Antley-Bixner syndrome[3].

The management of SGS is mainly limited to the treatment of the symptoms. The surgical correction of the craniofacial, cardiovascular skeletal and maxillofacial anomalies may be necessary. Considering the possibility of secondary complications like SABE, dental procedures and other procedures which can contaminate the blood stream with bacteria should be carried out only under appropriate prophylaxis.[1,3]Since these patients present with several systemic conditions, a multiholistic therapeutic approach should be planned for the management of such patients.[3]

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