ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 09 | September - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SIMPSON–GOLABI–BEHMEL SYNDROME: AN INTERESTING CASE REPORT

General Medicine

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ABSTRACT

Simpson–Golabi–Behmel syndrome (SGBS) is a rare X.linked disorder characterized by pre & postnatal overgrowth, craniofacial dysmorphism, and a broad spectrum of skeletal and visceral anomalies.[1] The clinical findings that are associated with the disease include supernumerary nipples, hernias, congenital heart defects, genitourinary defects, intellectual disability (mild to severe), vertebral & rib abnormalities, postaxial polydactyly. The affected individuals are at increased risk of developing embryonal tumors. The association between mutations in the glypican-3 gene (GPC3), localized to chromosome Xq26.2, and SGBS was first identified by Pilia et al. in 1996. GPC3 is considered to play a vital role in regulating growth factor activity and is highly expressed in mesodermal embryonic tissues that are prone to overgrowth in SGBS. SGBS is believed to be caused by a nonfunctional GPC3 protein. Here, we report a young male patient who had a clinical picture suggestive of SGBS syndrome.

KEYWORDS

Simpson–Golabi–Behmel syndrome (SGBS), Glypican (GPC), Computed tomography (CT), Positron emission tomography (PET), Generalized tonic clonic seizures (GTCS)

DISCUSSION

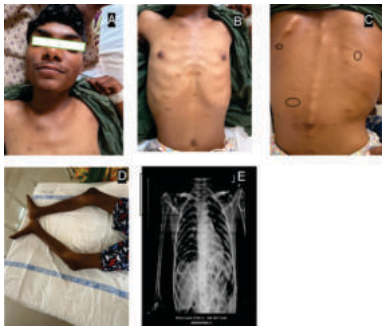
Simpson–Golabi–Behmel syndrome (SGBS) is a rare X-linked, congenital syndrome that can cause craniofacial dysmorphism, skeletal, vascular, cardiac, and renal abnormalities. There is a high prevalence of malignancies such as Wilms tumor, Neuroblastoma, tumors of the Adrenal gland, liver, lungs, and other abdominal organs. The syndrome is inherited in X-linked recessive manner. Females that possess one copy of the mutation are usually carriers of the disease but sometimes may express varying degrees of the phenotype, suffering from mild to severe abnormalities. The males experience a higher likelihood of foetal death.

Here we report a rare case of a 17-year-old male survivor, Mr Balaji, with previous birth history of macrosomia, who presented to the Emergency Room (ER) with involuntary jerky movements of upper & lower limbs suggestive of Generalized tonic clonic seizures (GTCS).

Vital data: Afebrile, Pulse 96/min, BP 100/70 mm of Hg, RR > 20/ min, Sp02 98% @ RA, CVS- S1 S2, RS- VBS heard normally, Abdomen- Soft, no organomegaly

On detailed physical examination: the patient had craniofacial dysmorphism, supernumerary nipples, skeletal anomalies Kyphoscoliosis & Genu varus deformity. Examination of the Nervous system revealed muscle weakness with hypotonia.

All the above-described features clinically fit into Simpson– Golabi–Behmel syndrome (SGBS)



Figures:
A. Dysmorphic facies
B. Supernumerary nipples
C. Winged Scapula
D. Genu varus
E. CXR PA view

Although not all causes of SGBS have been identified, one cause of SGBS type I is a mutation of the glypican-3 gene (GPC3) on the X chromosome locus q26.1. This particular gene is widely expressed, especially in tissues derived from the mesoderm during foetal development. The function of this gene is to produce a protein that acts as a cell surface receptor that binds to transcription factors. Binding of the transcription factors allows regulation of cellular responses to growth factors such as members of the hedgehog protein family. When large or small deletions and missense mutations occur along the GPC3 gene, GPC3 can no longer negatively regulate Hedgehog signalling during development, therefore increasing cell proliferation and the risk of developing cancer.[2] Limb patterning and skeletal development may also go awry when GPC3 mutations inhibit the regulation of responses to bone morphogenetic proteins, another type of growth factor.[3]

It has been suggested that SGBS type II may be caused by duplication of the GPC4 gene, which helps to regulate cell division & growth.[4]

Also, some patients diagnosed with SGBS do not have any GPC3 or GPC4 deletions or mutations. The possible explanations include promoter mutation or silencing of the GPC3 gene, causing reduced expression in these patients.[5]

The other signs & symptoms that can be found be in SGBS are Neonatal hypoglycemia, cutaneous syndactyly, polydactyly, pectus excavatum, structural & conductive cardiac defects, hernia of the diaphragm, and extra ribs.

Diagnosis

The detection of SGBS usually begins with routine antenatal doctor visit when the fundal height is being measured or during an ultrasound examination. When large for gestational age foetuses (LGA) are identified, there are two common causes: maternal diabetes or incorrect dates. However, if these two causes can be ruled out, an ultrasound is performed to detect overgrowth and other abnormalities.

At this point, the clinical geneticist plays a key role in appropriate selection of tests and aiding towards possible diagnosis. [6]

The first signs of SGBS may be observed as early as 16 weeks of gestational period. The aids to diagnosing might include the presence of macrosomia, polyhydramnios, elevated maternal serum-α-fetoprotein, cystic hygroma, hydrops fetalis, increased nuchal translucency, craniofacial abnormalities, visceromegaly, renal abnormalities, congenital diaphragmatic hernia, polydactyly, and a single umbilical artery. [4]

If there is a known mutation in the family, prenatal testing is the best option. Prenatal testing is also possible by looking for evidence of the SGBS phenotype in the mother and the positive SGBS phenotype in male family members. The family members who are positive for SGBS may undergo mutational analysis of genes GPC3, GPC4, and CXORF5. Genomic balance in Xp22 and Xq26 may also be analysed through array comparative genomic hybridization. The evaluation by a medical geneticist is recommended for those with strong indications or likelihood of SGBS and for immediate relatives of those genetically confirmed to have SGBS. [4]

Due to the high percentage of male deaths during the neonatal period, early detection of the tumours is crucial. To detect these tumours, screening in SGBS patients should include abdominal ultrasonogram, urinalysis, and biochemical markers that screen for embryonic tumours. [4]

The PET scan with CT is recommended for an accurate diagnostic procedure in adult SGBS patients who have manifested tumours and or cysts, especially those of the kidneys, lungs, and or patients who express atypical lesions of the liver or who may be suspected of neuroblastoma.

Once the infant is born, the possibility of hypoglycaemia must be assessed along with cardiac, genitalia, liver, and adrenal evaluations. Such tests include chest radiographs, electrocardiogram, echocardiogram, renal sonography, abdominal sonography, and CT to test for possible abnormalities. [7]

Depending on the severity, surgery, special education, occupational therapy, speech therapy, and physical rehabilitation are some of the available options in managing the patients. (8) SGBS is analogous to another overgrowth pattern called the Beckwith–Wiedemann pattern. SGBS cells are a unique tool to study the function of mortal adipocyte biology. These cells are analogous to mortal primary preadipocytes, and may or may not become a popular model rather of Mouse 3T3- L1 cells to study the storage and adipokine profile in the future. This cellular tool has been described and developed by Dr. Martin Wabitsch, University of Ulm, Germany. (9)

Treatment

Since the pattern is caused by an inheritable mutation in the existing DNA, definitive treatment is unavailable; however symptomatic management & surgical intervention based on the clinical presentation are recommended in SGBS patients.

Due to the liability of cases developing complications, full-body CT imaging & PET scans are important tools for assessment of the disease pattern & detecting malignancies.

As discussed, based on the severity of the disease, the management of the SGBS patients include special education, occupational therapy, speech remedy, physical rehabilitation, and surgeries.

CONCLUSION

Simpson-Golabi-Behmel (SGBS), an X-linked disorder caused by mutations in the GPC3 gene, is associated with overgrowth, congenital anomalies, and a higher risk of tumors like Wilms tumor and hepatoblastoma.

The case report highlights the importance of reporting a 17-year-old SGBS male survivor who normally has high mortality including foetal death.

It also emphasizes the importance of a good history & thorough clinical examination can aid in making a clinical diagnosis of even rare syndromes such as SGBS despite the unavailability of advanced & specific investigative tools.

A syndromic approach will help in suspecting, diagnosing, and management of systemic anomalies associated with the disease.

Genetic counselling is strongly recommended for Simpson-Golabi-Behmel syndrome (SGBS) due to its increased risk of morbidity & mortality. It helps families understand the genetic basis, recurrence risks (especially for carrier mothers), and also supports informed decision-making for prenatal testing/family planning.

REFERENCES

1. Tenorio, J. , Arias P., Martinez.Glez V., Santos F., Garcia.Minaur S., Nevado J., et al. 2014. Simpson.Golabi.Behmel syndrome types I and II. Orphanet. J. Rare. Dis. 9:138. [PMC free article] [PubMed] [Google Scholar]
2. Debaun, Michael R.; Ess, Jennifer; Saunders, Scott (2001). "Simpson Golabi Behmel Syndrome: Progress toward Understanding the Molecular Basis for Overgrowth, Malformation, and Cancer Predisposition". Molecular Genetics and Metabolism. 72 (4): 279–86. doi:10.1006/mgme.2001.3150. PMID 11286501.
3. Chen, Chih-Ping (1 June 2012). "Prenatal findings and the genetic diagnosis of fetal overgrowth disorders: Simpson-Golabi-Behmel syndrome, Sotos syndrome, and Beckwith-Wiedemann syndrome". Taiwanese Journal of Obstetrics and Gynecology. 51 (2): 186–191. doi:10.1016/j.tjog.2012.04.004. PMID22795092.
4. Veugelers, M.4; Cat, BD; Muyldermans, SY; Reekmans, G; Delande, N; Frints, S; Legius, E; Fryns, JP; Schrander-Stumpel, C (22 May 2000). "Mutational analysis of the GPC3/GPC4 glypican gene cluster on Xq26 in patients with Simpson-Golabi-Behmel syndrome: identification of loss-of-function mutations in the GPC3 gene". Human Molecular Genetics. 9 (9): 1321–1328. doi:10.1093/hmg/9.9.1321.PMID10814714.
5. Garganta CL, Bodurtha JN (1992). "Report of another family with Simpson–Golabi–Behmel syndrome and a review of the literature". Am J Med Genet. 44 (2): 129–135. doi:10.1002/ajmg.1320440202. PMID 1456279.
6. Vora, Neeta; Bianchi, Diana W. (1 October 2009). "Genetic considerations in the prenatal diagnosis of overgrowth syndromes". Prenatal Diagnosis. 29 (10): 923–929. doi:10.1002/pd. 2319. PMC 4426974.PMID19609940.
7. DeBaun, Michael R.; Ess, Jennifer; Saunders, Scott (1 April 2001). "Simpson Golabi Behmel Syndrome: Progress toward Understanding the Molecular Basis for Overgrowth, Malformation, and Cancer Predisposition". Molecular Genetics and Metabolism. 72 (4): 279–286. doi:10.1006/mgme.2001.3150.PMID11286501.
8. Golabi, Mahin (1993). "Simpson-Golabi-Behmel Syndrome Type 1". U.S. National Library of Medicine.PMID20301398.
9. Wabitsch, Martin (January 2001). "Characterization of a human preadipocyte cell strain with high capacity for adipose differentiation". International Journal of Obesity and Related Metabolic Disorders. 25 (1): 8–15. doi:10.1038/sj.ijo.0801520. PMID 11244 452.