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Complications of Insufficient Dura and Blood Loss During Surgical Intervention in Shprintzen-Goldberg Syndrome: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 9
Final Diagnosis: Mandibular hypoplasia secondary to Shprintzen-Goldberg Syndrome
Symptoms: Difficulty swallowing
Medication: —
Clinical Procedure: Bilateral mandibular osteotomy and distraction for mandibular hypolasia
Specialty: Neurosurgery

Objective: Rare disease

Background: Shprintzen-Goldberg syndrome (SGS) is an extremely rare collagenopathy, most often caused by autosomal-dominant mutations in the SKI proto-oncogene, which is a component of the transforming growth factor beta (TGF-β) signaling pathway. Approximately 50–60 cases of SGS have been recorded in the literature worldwide since its discovery in 1982. This collagen disorder affects bone and vascular development throughout the body, resulting in craniosynostosis, scoliosis, chest deformities, and aortic root dilation. Patients may have problems in the central nervous system, including Chiari 1 malformation, hydrocephalus, and dilation of the lateral ventricles. Unfortunately, the symptoms of SGS closely parallel those of related collagenopathies involving mutations in the TGF-β signaling pathway, which makes accurate diagnosis difficult without genetic testing, especially in cases with complex presentation.

Case Report: In this report we present the unique and complex disease manifestations in a 9-year-old girl with SGS. The patient had severe cervical spinal instability that resolved after surgical occipital-C4 fusion with an autograft from the rib. Midface distraction surgery was used to treat the patient's craniosynostosis and related facial deformities. This surgery was complicated by loss of 750 mL of blood due to insufficient dura and prominent vasculature.

Conclusions: Connective tissue symptoms associated with SGS can involve dural and vascular problems, as seen in this case report. Thus, the risk of extreme blood loss should be anticipated any time midface distraction surgery is performed on an SGS patient. Continued research is needed to define how this case relates to the SGS patient population.

MeSH Keywords: Craniosynostosis • DiGeorge Syndrome • Dura Mater • Osteogenesis, Distraction • Spinal Cord Compression

Abbreviations: **SGS** – Shprintzen-Goldberg Syndrome; **LDS** – Loeys-Dietz Syndrome; **MRI** – magnetic resonance imaging; **CT scan** – computerized axial tomography scan; **CSF** – cerebrospinal fluid

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/914924

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Background

Shprintzen-Goldberg syndrome (OMIM #182212) is an ultra-rare autosomal-dominant genetic collagenopathy. Common characteristics include marfanoid body habitus, characteristic craniofacial abnormalities, craniosynostosis, severe scoliosis, rib abnormalities, intellectual disability, abdominal and umbilical hernias, and aortic dilation. SGS is molecularly heterogeneous, with mutations most often found in the R-SMAD binding region of exon 1 of the SKI (Sloan-Kettering Institute) gene. Mutations in this gene result in an overactive SMAD-dependent pathway of TGF-β signaling.

The proto-oncoprotein SKI normally inhibits SMAD proteins by preventing them from entering the nucleus to transcribe the TGF-β gene. The TGF-β pathway is essential for cell growth, proliferation, and programmed cell death. Its dysregulation results in many of the cardiovascular and connective tissue deformities seen in SGS [1]. Less frequently, SGS patients have mutations in the fibrillin 1 (FBN1) gene, which also codes for a TGF-β regulatory protein. Mutations in other proteins on this pathway can also result in excess activity, leading to similar phenotypic presentations as seen in Marfan and Loeys-Dietz syndromes [2]. There is often an extensive delay preceding SGS diagnosis because it is extremely difficult to distinguish between these related collagenopathies. Delay of diagnosis in SGS can have fatal consequences, as will be discussed later in this report.

Fortunately, the differential expressions of various proteins in the TGF-β pathway lead to slight differences between related collagenopathies. For example, aortic abnormalities are usually milder in SGS than in Loeys-Dietz syndrome because the SKI gene is expressed less pervasively in the aorta than are TGF-β receptor genes[1]. Moreover, intellectual disability appears in SGS patients more often than in Loeys-Dietz patients [1]. The present patient's unique presentation of SGS most notably involves severe cervical spinal cord compression, abnormal facial vasculature, and insufficient dura mater.

The dura mater is the outermost layer of the meninges, which provides a protective covering for the brain and spinal cord. The dura mater forms a barrier between cerebrospinal fluid and blood. Thus, cerebrospinal fluid will leak if the dura is compromised. Cerebrospinal fluid leakage is a major neurosurgical complication that can result in pneumocephalus, meningitis, improper wound healing, and infections of the graft-bone or epidural space [3]. Our patient presented with insufficient dura, resulting in CSF leakage during a combination Monobloc advancement and cranial vault remodeling surgery aimed to treat midface hypoplasia. Midface hypoplasia is common among SGS patients and can result in lagophthalmos, obstruction of the upper airway, and obstructive sleep apnea [4]. Midface hypoplasia and its resultant problems are often addressed in SGS patients with surgical treatment involving opening of the skull. However, such surgeries are extremely risky in patients with collagen disorders affecting the dura and surrounding vascularity. Thus, the prevalent connective tissue problems must be assessed prior to surgical intervention in SGS patients.

Case Report

This patient was a full-term baby, birth weight 8 pounds 11 ounces, born to a G5P5 35-year-old mother. The pregnancy was complicated by spotting at 7 weeks, difficulty picking up heartbeat at 19 weeks, and a 2-vessel umbilical cord. Although the vaginal delivery was relatively easy, the baby had a fractured clavicle at birth. The patient's dysmorphic facial features included frontal bossing, low-set ears, hairy ear lobes, and facial features resembling trisomy 21. The patient displayed moderate hypotonia, loose hips, and significant head lag. These concerns led to immediate transfer from the birthing center to the local hospital and subsequent transfer via life-flight to the regional hospital. Karyotype was normal (46XX) and Fluorescence *in situ* hybridization (FISH) assays were negative for all trisomies. Upon discharge, the patient had difficulties feeding and gaining weight, resulting in 3 hospitalizations for failure to thrive during the first year. Facial deformities and hypotonia contributed to her inability to innervate muscles needed for eating and swallowing. After supplementary high-calorie formula and breastfeeding showed limited success, a gastrostomy tube (G-tube) was placed at 4 months. Adequate caloric intake and expected growth for age were attained. G-tube feedings continue to be the primary form of nutrition to date.

Many of the patient's symptoms corresponded with collagen-related disorders. Observed bony abnormalities included cervical spinal instability, 13 pairs of ribs, recurrent left knee subluxation, coxa valga, contractures, joint hyperflexibility, and focal reversal of lordosis at T12–L1. Finger abnormalities included camptodactyly, clinodactyly, hypoplastic thumbs, and arachnodactyly. This patient exhibited an asymmetric chest deformity involving both the pectus excavatum and carinatum. Notable craniofacial abnormalities included craniosynostosis, midface hypoplasia, exophthalmos, hypertelorism, ptosis, lagophthalmos, low-set ears, retrognathia, and a high narrow palate. At 2 years, the patient was diagnosed with obstructive sleep apnea and prescribed continuous positive airway pressure (CPAP), which improved energy and progress with developmental milestones (see Table 1 for a full list of patient symptoms).

This patient was tested for Loeys-Dietz syndrome, otopalatodigital syndrome, Sticklers syndrome, Zellweger syndrome, Marshall-Smith syndrome, and Marshall syndrome prior to

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Table 1. Complete list of symptoms seen in this patient.

Craniofacial abnormalities:
- craniosynostosis with copper beaten appearance
- flat facial features, midface hypoplasia
- oblong, square facial shape
- mildly abnormal calvarial (skull) shape w/mild brachycephaly (short skull)
- frontal bossing/turribrachycephaly/prominent forehead
- large fontanel as an infant
- short and upturned nose with depressed nasal bridge/malar flattening
- long philtrum
- superiorly over-folded/floppy right ear w/crumpled helix
- soft ears with thin cartilage
- low set ears
- soft high narrow palate with extra rugae (ridges)
- broad, long, and bifid uvula
- bilateral torus palatini
- retrognathia/mandibular hypoplasia (class III malocclusion)
- underdeveloped supraorbital ridges
- hypertelorism/telecanthus (widely spaced eyes)

Orthopedic/skeletal abnormalities:
- severe cervical spinal stenosis
- dural ectasia w/Tarlov cysts/syringomyelia
- focal reversal of lordosis at T12–L1/transitional thoracolumbar anatomy/kyphosis
- low bone mineral density
- asymmetric pectus deformity (excavatum and carinatum)
- pes planus (flat feet)
- arachnodactyly (long, slender fingers)
- camptodactyly (bent fingers)
- clinodactyly of little fingers
- hypoplastic digits of hands treated w/safe position thumb spica splints
- joint contractures
- joint hyperflexibility/hypermobility
- joint dislocation and instability (left patella, thumb, foot, and C1–C2 spine)
- bone fracture of right collarbone (birth, fall 2016)
- thin ribs, 13 ribs
- unusual iliac horns (hip joints), coxa valga

Cutaneous symptoms:
- thin to absent dura not adhering to skull
- thin translucent skin
- skin rashes
- widely-spaced, inverted nipples
- easy bruising
- atrophic scars
- delayed wound healing
- sclerodactyly
- thin periosteum w/fat herniation
- widely spaced/elongated pedicles
- recurrent hernias
- recurrent torticollis

Cardiovascular symptoms:
- mild aortic root dilation (sinus of vasalva and ascending aorta)
- vibratory 2/6 murmur at LSB noted once at 3 years

Neurological abnormalities:
- developmental delay
- dural ectasia
- hearing loss possibly sensorineural in nature
- hypotonia in infancy

Ophthalmology features:
- blue sclera
- mild myopia, anisometropia (eyes w/different prescriptions)
- exopthalmia (bulging eyes, proptosis)
- unable to close eyelids (lagophthalmos)
- ptosis rt>left
- astigmatism

Pulmonary:
- obstructive sleep apnea
- left bronchomalacia (weak bronchial cartilage)
- mildly blunt carina
- recurrent pneumonia
- asthma

Gastrointestinal Symptoms:
- failure to thrive/difficulty gaining weight
- GERD
- reflux
- G-tube fed since 5 months

Allergy related symptoms:
- asthma
- allergic rhinitis

diagnosis. Finally, a genetic test at age 4 years revealed a c.104C>A transversion mutation in exon one of the SKI gene, which converts a proline to a glutamine. This mutation causes SGS. Through genetic consult, an official SGS diagnosis was made 2 months later.

Doctors conducted risk assessment tests upon diagnosis, including echocardiogram of heart and imaging of the cervical spinal cord. Imaging of this patient's cervical spine revealed severe stenosis and radiographic evidence of myelomalacia at the craniocervical junction (Figure 1). This prompted surgical decompression of the foramen magnum and an occipital-cervical fusion. Postoperatively, her strength markedly improved and she became ambulatory. The echocardiogram showed mild aortic root dilation in the sinus of Valsalva and the ascending aorta, as well as mild regurgitation in the mitral valve. Losartan was prescribed at age 6 years to prevent further dilation.

The patient's craniosynostosis involved midface hypoplasia (Figure 2), a symptom in which the middle of the face is not fully developed. This was treated at age 5 years with a combination Monobloc osteotomy and LeFort III distraction surgery. Table 2 provides a full description of the preoperative CT scan and surgical procedure. During the surgery, the surgeons

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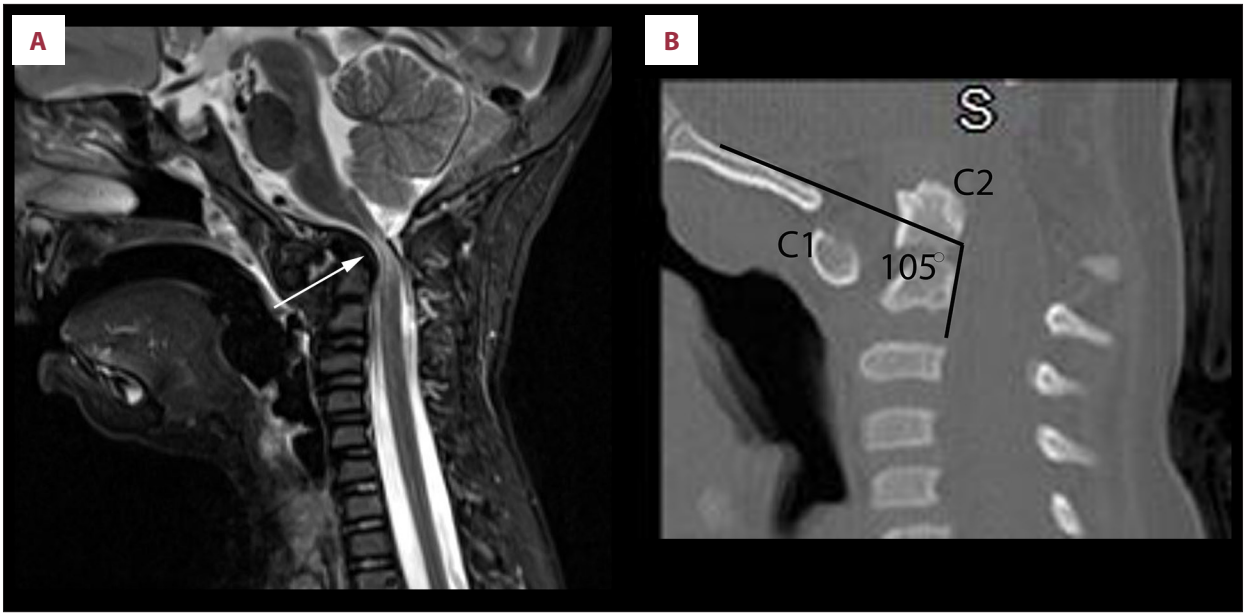
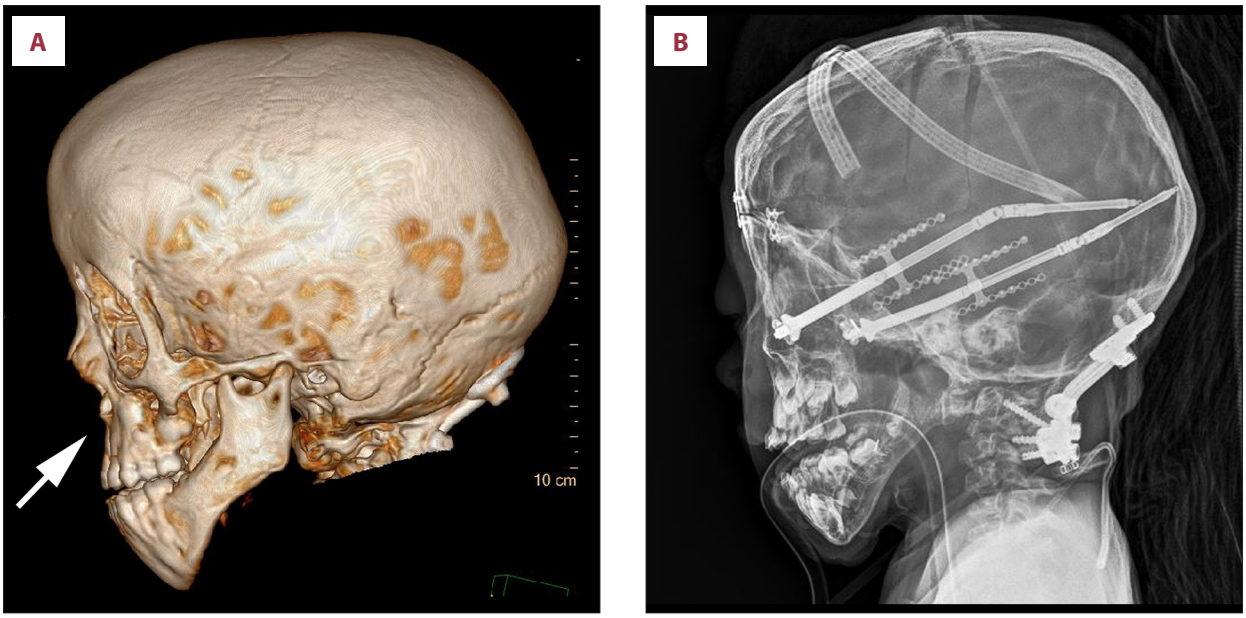


Figure 1. (**A, B**) Radiological findings of craniocervical compression (**A**) A sagittal, T2-Stir-weighted magnetic resonance imaging (MRI) of cervical spine (**A**) shows severe stenosis at the craniocervical junction with evidence of spinal cord myelomalacia (arrow). (**B**) A sagittal computed tomography (CT) reconstruction demonstrates platybasia (PB) with a clival-cervical angle of 105°. Dynamic imaging revealed gross instability. High-resolution CT scanning showed a clival-cervical angle of 105 degrees with anterior and inferior displacement of the C1 ring. A clival-cervical angle of less than 125 degrees indicates severe platybasia and is a marker for craniocervical instability. The Pb-C2 line, a measurement of retroflexion of the odontoid as defined by Grabb and Oakes, measured 15 mm, well above the critical value of 9 mm. A value above 9 mm generally indicates severe compression of the spinal canal; her canal width measured 3 mm. The patient underwent a decompression of the foramen magnum and an occipital-cervical fusion. Postoperatively, strength markedly improved and the patient became ambulatory.



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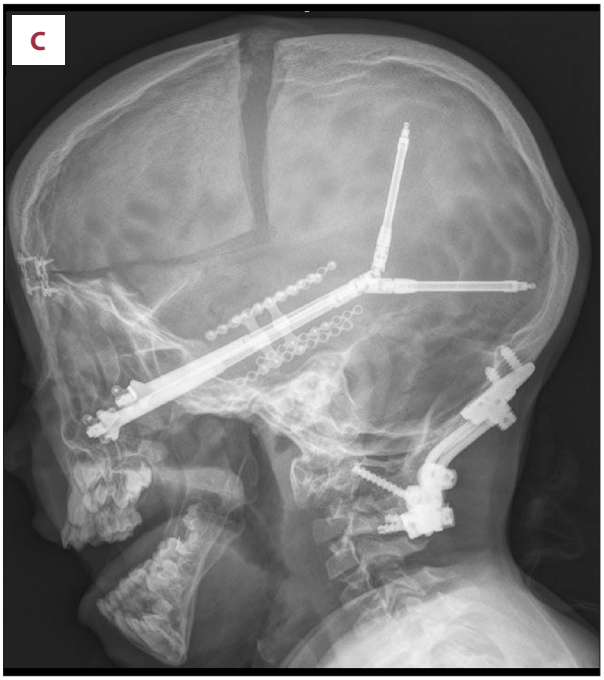

Figure 2. (**A–C**) Radiological Visualization of Midface Distraction. (**A**) 3D CT reconstruction shows pronounced midface hypoplasia (arrow). (**B**). Lateral x-ray shows the immediate postoperative anatomy after a midface distraction procedure. (**C**) Lateral x-ray after distraction demonstrates advancement of midface and frontal calvarium.

Table 2. Description of preoperative CT scan and midface distraction surgery as found in the medical record.

Preoperative CT scan: 1. Copper beaten appearance 2. Midface hypoplasia 3. Nasal septum deviated to the right 4. Bony stenosis of the foramen magnum 5. Mild kinking in the cervicomedullary junction 6. Partial dislocation of C1 with respect to C2
Reconstructive surgery: 1. Monobloc osteotomies with bone graft 2. Periosteal flap 3. Insertion left cranial distractor 4. Insertion right cranial distractor
Neurosurgery: 1. Bilateral frontotemporoparietal craniectomy for multiple cranial suture synostosis due to diagnosis of Shprintzen-Goldberg syndrome. 2. Takedown of the intact dura from the skull and skull base for subsequent anterior vault reconstruction and monobloc advancement for cranial vault remodeling.
Blood transfusions 1. 6 Plasma transfusions 2. 2 Platelet transfusions 3. 9 RBC transfusions
Postoperative observations: Resulted in more normal midface/jaw relationship, improved exophthalmia, slightly improved sleep apnea, improved hypertelorism, open bite from midface advancement, velopharyngeal insufficiency(VPI) that limited speech, mild prominence of bilateral orbital rims that was shaved down upon distraction removal.

discovered dura that was "less than toilet paper thin" adjacent to the sinus bilaterally and nonexistent over multiple brain sections, including about 4 cm of the sagittal sinus. The dura was also not sticking to the skull. This was not identified on the preoperative CT scan. DuraGen was applied to partially seal the dura. In spite of this insufficiency, there was enough dura at the skull base for removal for subsequent anterior vault reconstruction. The patient experienced a surgical blood loss of

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approximately 750 ml requiring a total of 17 blood transfusions. Blood flow was stopped with light pressure and application of Tisseel sealant. The surgeons also noted very thin periorbital tissue with pervasive fat herniation and a thin periosteal flap manifesting in adjacent connective tissue problems.

The patient was placed in a medically induced sedation for 72 hours postoperatively to aid in recovery from the blood loss and difficult surgery. The patient was discharged after 7 days, without complications. Distractors were advanced 1 mm per day for 3 weeks and removed after 9 weeks (Figure 2B, 2C). This surgery normalized the midface-to-jaw relationship, improved exophthalmos and hypertelorism, and slightly improved sleep apnea.

Discussion

This case relates to many other SGS cases presented in the literature, and the present report improves understanding of this disease. A comprehensive summary of SGS cases is shown in Tables 3–5. Notably, this patient's scoliosis was mild relative to other patients in the literature. This patient's focal reversal of lordosis at T12–L1 does not currently require surgery. A previous report presented 4 SGS patients requiring surgical scoliosis repair [5]. These surgeries involved numerous bone density-related complications during the operation and in the years following the procedure. Our patient's cardiac symptoms were also milder than some of those seen in the literature. In contrast, SGS patients may display severe aortic dilation resulting in aneurysm [6,7]. Moreover, 1 patient required mitral valve replacement to treat severe regurgitation. Our patient presented with mild aortic root dilation and mitral valve regurgitation, suggesting that the cardiac symptoms were relatively mild. Our patient presented with a c.104C>A in exon 1 of the SKI gene, which is considered the genetic hotspot for SGS mutations.

Our patient's combination Monobloc osteotomy and LeFort III distraction surgery has not been previously recorded anywhere in the literature, as they are rarely performed concurrently. The procedural method for Monobloc osteotomy is described in Dr. Laure's 2014 surgical case study [4,8], while the procedure for LeFort III distraction id presented in Ianetti et al's 2012 meta-analysis on this procedure [9]. Any midface distraction surgery comes with a high risk of blood loss. However, our patient's extreme intraoperative blood loss of 750 mL had syndromic causes. The patient had significant holes and paucity in the dura mater that were not observable on preoperative CT scans and could not be completely sealed using DuraGen. This represents an unprecedented symptom of SGS.

Our patient's insufficient dura mater is likely syndromic. Collagen disorders, including SGS, may affect all connective tissues, including the dura mater. Furthermore, dural issues have been identified in other heritable connective tissue disorders. In a study by Dr. E. Reinstein, 9 patients with hereditary connective tissue disorders experienced CSF leakage due to dural fragility, 7 of whom had Ehlers-Danlos or Marfan syndromes. All these cases resolved with epidural blood patching [10]. Our case was more severe, with pervasively thin dura and gaps as large as 4 cm. DuraGen could not seal the gaps and epidural blood patching would not have resolved this case. Thus, the dural problems presented in this SGS case are more severe than those recorded in related connective tissue disorders.

Unfortunately, it is difficult to detect dural insufficiencies preoperatively. CSF leakage may be indicative of compromised dura because the dura mater holds in the CSF [11]. CT and MRI scans do not allow for proper examination of the dura unless it is inflamed.

Once detected, dural deficiency can be treated in several ways. In our case, patches of DuraGen, a dural-sealing adhesion barrier matrix, were placed. Additional dural supplements have been used to treat CSF leakage. A 2014 paper by Goldschmidt provided evidence that growth factors, including insulin, FGF-2, and human serum, can aid in dural closure by facilitating cell migration [12]. Epidural blood patches can be used to noninvasively treat symptoms of CSF leakage and perforated dura. This method exerts the "mass effect", which is when injection of the patient's own blood propels CSF into the cranium and increases intracranial pressure [13]. In a 2011 study by Burkett, patients who received dural sealants had shorter average hospital stays and time in intensive care units, decreased need for additional incisions, and decreased lumbar CSF drainage than those treated with autologous fat graft and lumbar drain replacement [14]. This indicates that application of dural sealants may be the most effective treatment for compromised dura.

Collagen is a crucial part of the cardiovascular system because it is a protein in the matrix that supports the shape of blood vessels [15]. Thus, collagenopathies are linked to aortic and peripheral aneurysms [16].

In our patient, surgery was used as treatment for midface hypoplasia, which was caused by craniosynostosis [17,18]. This symptom spurred surgical intervention because it hindered quality of life. In our patient, midface hypoplasia caused lagophthalmos and airway obstruction, which contributed to breathing difficulties and obstructive sleep apnea. The severity of these symptoms should be weighed against the risk of this type of surgery, considering the findings in the present report. Posterior distraction may be a safer alternative to the external methods used here. Dural issues and consequent blood

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Table 3. Shprintzen-Goldberg syndrome symptoms, a literature review 2010–2019.

2010-2019	[44] O'Dougherty	[43] Zhang 2019	[7] Kimura 2018	[42] Saito2017	[40] Minocha2016	[6] Poninska 2016	[39] Ingle2016	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[37] Schepers 2015	[35] Shah2014	[31] Zhu, 2013	29] Shanske 2012	[29] Shanske 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[1] Doyle 2012	[28] Watanabe 2011	[28] Watanabe 2009	[28] Watanabe 2010	[28] Watanabe 2011	[27] Gupta 2010
Age (years)	12	10		7	3	26	12	50	44	5	4	10	10	12	16	9	13	22	5	2	9	5	43	6	16	12	22	21	2	6	5	4	8	4	11	12	5
Sex	F	F		M	F		M	M	F	M	F	M	F	F	M	M	M	F	F	M	M	F	F	M	M	M	F	M	F	M	M	F	F	M	F	M	F
Craniofacial																																					
Lack of dura mater	++	–																				**															
Craniosynostosis	++	–	+	+			+	–	–	+	+	+		–	+		+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Dolico-/scaphocephaly		–		+	+	+		+	+	+	+	+	+	–		+			+				+	+	+	+	+	+	–	+	+	+					+
Brachiocephaly																						+															
Hypertelorism	+	–		+			+	+	+	+	+	+		–	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Downslanting palpebral fissures	+	–		+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Proptosis	+	–						+	+	+	+	+	+	+	+	+	–	–	+		+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+
Low set ears	+	+																			+	+	+	+	+	+	+	+	+	+	+	+					
High/narrow palate	+	–			+	+	+	+	+	+	+	+	+	+		+	+	+	+		+	+	+	+	+	+	+*	+	+	+	+	+			+	+
Chiari malformation	+	–			+																+	+															
Micro/retrognathia	++	–		+		+	+	+	+	+	+	+		–	+	+				+	+	+	+	+	+	+	+	+	+	+	+		+	+		+
Skeletal																																					
Cervical spine abnormalities	++			++																	+	+		–	–		+	+			+	+					
Arachnodactlyly	+	+		++	+	+	+	+	+	+	+	+	+	+	+	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Camptodactyly	+	–			+			+	+	–	+		+	–		+							+	+	+	+	+	+	–	–	+	+	+	+	+		+
Scoliosis/kyphosis	+	+	+		+	+	++	+	+			–		–		+	–	–			+		+	+	+	+	+	+	+	–	–	+	+	+	++	++	+
Pectus deformiity	+	+	+		+	+	+	+	+	+	+			+	+	+	–	–			+	+	+	+	+	+	+	+	+	–	+	+			+		
Joint hypermobility	+	–				+		–	–	–	–	+	+	+	+	+	+		+				+	+	+	+	+	+	–	+	+	+	+	+	+		+
Foot malposition	+	–		+		+	+												+				–	–	+	–	–		+	+	–	–	+		+	+	+
Joint contracture		–						+	+	+	+	+		+							+		+	+	+	+	+	+	–	+	+	+					
Neurological																																					
Developmental delay								+	+	+	+	+	+	+	+	+	+	–		+	+	+	+	+	+	+	+	+	+	+							+
Intellectual disability	+	–	+	+	+	+	+												+		+	+											+	+	+	+	+
Cardiovascular																																					
Mitral valve prolapse		–		–		+		–			–	–	–	–	+	–	–	–			–		+	+	+	–	–		–	+	+	+		+			
Aortic dilatation	+	–	++	–		+		–			–	–	–	–	–	+	+	–			–		+	+	+	+	+	+	+	–	–	+					+
Obstructive apnea	+	–		+			+														+																
Other																																					
Hearing loss	+	–					+																														
Inguinal hernia	+	–		+			+																														+
Umbilical hernia	+	–		+	+														+																		+
Hypotonia	+	–	+	+		+																	+	+	+	+	+	+	+	+	+	+					
Dural ectasia																								+							+						
Malrotation of intestines																						+															

** Prominent venous structure in posterior Fossa. '+' – present; '++' – severe; '–' – not present; blank – no information.

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Table 4. Shprintzen-Goldberg Syndrome Symptoms, a literature review 1981–2008.

1981–2008	[26] Stheneur 2008	[25] Kosaki 2006	[25] Kosaki 2007	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[24] Robinson 2005	[23] Greally 1998	[23] Greally 1998	[23] Greally 1998	[23] Greally 1998	[23] Greally 1998	[21] Shprinzten and Goldberg 1991	[21] Shprinzten and Goldberg 1991	[20] Sugarman, Vogel 1981
Age (years)	17			17	21	6	4	2	17	10	6	2	7	25	16	17	16	12	12	12	5	~6			17
Sex	M	M	M	M	M	M	M	F	M	M	M	M	M	M	M	M	M	F	M	M	M	F	M	M	M
Craniofacial																									
Lack of dura mater																									
Craniosynostosis	+	+	+						+	–	–	+	–		+		+	+	–	+	+		+	+	+
Dolicocephaly		+	+	+	+	+	+	+	–	+	+	+	+	+	–	–	+	+	+		+				
Scaphocephaly																									
Hypertelorism	+	+	+	+		+	–	+	+	+	+	–	+	+	–	–	–				+	+	+	+	
Downslanting palpebral fissures		+	+	–	–	+	+	+	–	+	+	+	+	+	+	+	+	+			+		+	+	
Proptosis		+	+	+	+	+	–		+	+	+	+	+		+	+	+				+	+	+	+	
Low set ears		+	+																+		+	+	+	+	
High/narrow palate		+	+	+*	+	+*	+	+	+	+	+	+	+	+	+	+	+	+			+	+	+	+	
Chiari malformation																									
Micro/retrognathia	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	
Skeletal																									
Cervical spine abnormalities																		+		+					
Arachnodactlyly		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+		+	+	+	
Camptodactyly				–	–	+	–	–	+		+	+	–	+	–	+	–		+	+		+	+	+	
Scoliosis/kyphosis		+	+	+	+	+	+		+	–	+	+	–	+	+	+	+	+	+	+		–	+	+	
Pectus deformiity		+	+	+	+	+	+	+	+	+	+	+		+	+	+	+			+	+	+	+	+	
Joint hypermobility			+	+	+	+	+	+	+		+	+			+		+								
Foot malposition		+	+															+	+	+	+				
Joint contracture		+	+															–	+	+	+				
Neurological																									
Developmental delay	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+		+	+	–	+	+	+	+
Intellectual disability				+	+	+	–			+	++			+					+	+	–		+	+	+
Cardiovascular																									
Mitral valve prolapse				–	+	+	–		+	–	+	–		–	–		–		–			+		+	
Aortic dilatation		+	+	–	–	+	+		+	–	+	–		–	–		–		–						
Obstructive apnea					–	–	–	–	+		+	+					–						+		
Other																				+					
Hearing loss									+	+	+														
Inguinal hernia			+	+	+	–	+	–	+		+	–		–	+	+	+					+	+	+	+
Umbilical hernia				+	–	–	+	–	–		+	–					–						+	+	+
Hypotonia				++	–	+			+	+	++	+	+	+	+	+	+			+					+
Dural ectasia																									

'+' – present; '++' – severe; '–' – absent; blank – no information; '*' – cleft lip.

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Table 5. Imaging results and treatment interventions for Shprintzen-Goldberg syndrome patients, a literature review 1981–2019.

Test Performed	Results	[44] O'Dougherty 2019	[43] Zhang2019	[7] Kimura2018	[42] Saito 2017	[40] Minocha 2016	[6] Poninska 2016	[39] Ingle 2016	[31] Zhu 2013	[29] Shanske 2012	[29] Shanske 2012	[1] Doyle 2012 case 1of10	[1] Doyle2012 8 of 10	[28] Watanabe 2011	[28] Watanabe 2011	[28] Watanabe 2011	[27] Gupta 2012	[26] Stheneur	[25] Kosaki 2006	[25] Kosaki 2006	[24] Robinson 2005(1)	[24] Robinson 2005(3)	[24] Robinson 2005(4)	[24] Robinson 2005(7)	[24] Robinson 2005(8)	[24] Robinson 2005(9)	[24] Robinson 2005(11)	[24] Robinson 2005(12)	[24] Robinson 2005(14)	[23] Greally Case 3 of 5	[23] Greally 5 of 5	[21] Shprintzen 1982	[21] Shprintzen 1982	[20] Sugarman 1981
* Spinal MRI	Cervical spine instability	+			+					+	+						+																
	*Dural ectasia	+TL						+L																										
	Severe spondylolysis						+																											
	*Spinal cord impingement	+C			+MO																									+C				
Brain MRI	Small pituitary gland										+																							
	Enlarged ventricles									+											+		+	+	+								+	
EEG	Seizure activity					+			+	–																								
Spine Xray	Scoliosis	+	+	+		+	+	+			+			+	+	+	+	+	+	+														
	Spina bifuda occulta		+																					+										
Skull Xray	Midface hypoplasia	+						+		+							+		+	+														
	Craniosynostosis	+	–	+	+			+		+	+			+	+	+	+		+	+				+	+							+	+	
Echo-cardiogram	Atrial septal defect								+		–			+													+							
	Mitral valce prolapse					+	+				–																							+	
	Aortic root dilatation	+	–	+	–		+			+	–				+		+	+	+	+		+	+											
CT chest	Recurrent pneumonia							+																							+			
	*** Aneurysm			ThAAA			TAA					SAA	SAA																					
Ultrasound	Undescended testes																										+		+					
Surgery/ treatment	Gastrostomy tube placed	+									+										+													
	Tracheostomy										+																				+			
	Tonsillo-adenoidectony	+					+																		+									
	Mandibular osteotomy and distraction	+																																
	Cranioplasty/craniectomy	+									+										+													
	Cervical spine surgery	+									+																							
	***Hernia	+UI	–		+UI	+U		+										+U			+I	+U		+I		+	+	I		+I	+			+
	Mitral valve prolapse repair					+																												
	Aortic valve repair																				+													
	***TAA, ThAAA, SAA repair			+								SAA	SAA																					
	Atrial septal defect repair								+																									
	Scoliosis surgery										+			+	+	+	+				+													
	Metatarsus adductus surgery																				+										+			
	Knee surgery																			+														
	Genu recurvatum repair										+										+										+			
	Cleft palate repair																				+												+	+
	Continuous positive airway pressure (CPAP)	+																									+		+					
	Orchidoplexy																										+		+					
	Seizure meds					+																												

'+' – present; '–' – not present; blank – no information. * C – cervical; T – thoracic; L – lumbar; MO – medulla oblongata.
** Thoracic, Abdominal Aortic (ThAAA); Thoracic Aortic (TAA); Splenic Aortic (SAA). *** Umbilical (U) or Inguinal (I) Hernia; UI – both.

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loss may be avoided in this procedure because the dura remains attached to the "endocranial surface of the vault bone." This surgery was successful in treating midface hypoplasia in an Antley-Bixler Syndrome patient, but further investigation is needed regarding application to SGS [19].

Conclusions

This case report presents dural insufficiency as a previously unreported symptom of SGS. We also discussed the risk of major blood loss in combination Monobloc osteotomy and LeFort III distraction surgery for treatment of symptoms stemming from craniosynostosis. Our literature review assessed how this case relates to previous findings in SGS.

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Conflict of interest

None.

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