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Case and Review

Down Syndrome Patients with Congenital Portosystemic Shunts: A Case Report and Review

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Keywords
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Abstract
Introduction: Down syndrome is due to trisomy 21 and is characterized by intellectual disability, dysmorphic facial features, congenital malformations, and gastrointestinal abnormalities. There is an increased appreciation of congenital portosystemic shunts in Down syndrome patients. Congenital portosystemic shunts have been associated with many defects in body systems, including cardiac, metabolic, and neurological. ***Case Presentation:*** Herein, we describe a portosystemic shunt in a Down syndrome patient that resulted in hyperammonemia with altered mental status and choreiform movements. Computed tomography angiography of the abdomen and pelvis identified a connection between the right portal vein and inferior vena cava. An 18 mm Amplatzer PFO closure device was placed within the congenital shunt, significantly improving symptoms. The patient has no sequelae from the related shunt or the device at the 2-year follow-up. We extensively reviewed the literature and identified cases of portosystemic shunts in Down syndrome patients. Shunts can either be extrahepatic or intrahepatic and are classified by vasculature connections. ***Conclusion:*** From our literature review and case presentation, we identify other conditions in patients, including cardiac and gastrointestinal defects. We then review the available treatment options, whether observation or surgical, depending on the patient's clinical picture.

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Introduction

Down syndrome (DS) is liveborn infants' most common chromosomal abnormality. Trisomy 21 is associated with characteristic dysmorphic features, intellectual disability, and congenital malformations. Children with trisomy 21 are at increased risk for gastrointestinal tract anomalies and cardiovascular abnormalities [1, 2]. Congenital portosystemic shunts (CPSSs) are rare anomalies that allow venous outflow from the intestines and spleen to bypass the liver and enter the systemic circulation. Reports of patients with CPSS are increasing, with DS being the most frequently reported genetic disorder associated with CPSS [3]. CPSS is associated with various systems involving cardiac, hepatic, neurological, and metabolic [4]. Herein, we present a DS patient with hyperammonemia due to CPSS and review the literature on CPSS in DS.

Historical Review

Portal system development occurs between week 4 and week 10 of embryonic development. The two vitelline veins give rise to the systemic and portal venous systems. The vitelline venous system involutes during embryonic development by 12 weeks. Incomplete involution of the vitelline venous system likely gives rise to portosystemic shunt formation depending on where the vitelline vein failed to differentiate [5]. The first reported case of a congenital portocaval shunt was a termination of the portal vein in the inferior vena cava [6]. CPSSs are rare and occur in 1:30,000 births [7]. An infant with DS was first described as having a right portal vein to inferior vena cava shunt [8]. A shunt involving the portal sinus system was described shortly after [9]. Advances in imaging technology and understanding pathophysiology have clarified portosystemic shunts. Classification of portosystemic shunts has been challenging given the variety in complexity, size, variable vessel involvement, and localization. Improved imaging techniques have refined the classifications that we use today. There have been several proposed classification methods. One classification system was based on the severity of the intrahepatic portal hypoplasia and portal pressure [10], which may show some benefit in predicting the response to therapy. Other classification systems focused on system site drainage and symptoms [11] or the origin of portal shunt circulation [12]. Intrahepatic shunts seem to be most described with the Park et al. classification [13]. In Park classification, shunts are defined as vascular connections greater than 1 mm in diameter between the hepatic or perihepatic veins and the intrahepatic portal vein. Park identified four types of single vessel communication: portal vein main branch and IVC (type 1), peripherally located segment (type 2), aneurysm involvement (type 3), and multiple communications diffusely across both lobes of the liver (type 4) [13]. A patent ductus venosus (type 5) is considered intrahepatic because its origination is in the left portal vein [14].

Classification of extrahepatic shunts most commonly uses the system defined by Morgan [15]. End-to-side (type 1) directly connects the portal and systemic veins, with no intrahepatic portal vein flow. Type 1 extrahepatic is further divided based on drainage of the superior mesenteric and splenic vein, draining separately (type 1a) to IVC via the common trunk (type 1b) [16]. Side-to-side (type 2) connects the systemic venous and portal systems [15, 16]. Extrahepatic shunts are usually described as single communications, but double communications have been reported [17]. An alternative classification system incorporates the clinical presentation and liver histopathology [18].

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Case Presentation

The authors have completed the CARE Checklist for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000535477). A 30-month-old boy with his adoptive mother presented random, choreiform movements involving the upper and lower extremities and pupil size changes. He has a past medical history of DS, atrial septal defect, gastroesophageal reflux disease status-post Nissen fundoplication, Celiac disease, failure to thrive, and developmental delay (primarily speech and motor). The patient, while nonverbal, appeared confused during these episodes. Verbal and tactile stimulation failed to resolve the movements. His mother denied any recent inciting events, including trauma or changes to prescription medication. No travel history, sick contacts, recent illnesses, or known toxic ingestion was reported. An extensive 14-point review of systems was noncontributory. On the physical exam, the patient appeared lethargic with normal vital signs for his age. Facial dysmorphism is consistent with DS. A grade 2/6 systolic murmur was heard on auscultation. Anisocoria was noted, with the left pupil measuring between 6 and 7 mm and the right pupil at 4–5 mm. Hypotonia of the extremities and trunk was observed beyond his baseline hypotonia. In our differential, we considered hyperammonemia, infectious etiologies, intracranial injury, and toxins based on the presentation. A comprehensive metabolic panel (CMP) showed a bicarbonate level of 15 mmol/L (reference range 23–32), anion gap of 22 mmol/L (reference range 9–18), aspartate aminotransferase of 129 U/L (reference range 8–60), alanine aminotransferase of 62 U/L (reference range 6–45), alkaline phosphatase 378 U/L (reference range 117–390), total bilirubin 0.7 mg/dL (reference range 0.0–1.2), and lactic acid of 10.9 mmol/L (reference range 0.7–2.5). Computerized tomography and magnetic resonance imaging demonstrated no acute intracranial abnormality. After a normal saline bolus, repeat laboratories showed resolution of his elevated anion gap with improved bicarbonate and transaminases. His lactic acid continued a downtrend. Blood cultures and Group A Streptococcus throat culture yielded no growth. Comprehensive saliva toxicology screen, salicylate, and ethanol levels were normal. The serum ammonia level was elevated at 231 mol/L (reference range 12–48), with repeat ammonia at 198 mol/L. Serum ammonia levels remained persistently elevated despite administering sodium phenylacetate and sodium benzoate. The patient was asleep and had minimal oral intake the night before his ammonia levels were drawn. Evaluation for metabolic causes was unrevealing with workup, including serum homocysteine levels, plasma amino acids, plasma acylcarnitine, urine organic acids, and pyruvic acids. Abdominal ultrasound revealed an anomalous course of portal venous flow. A computerized tomography angiography of the abdomen and pelvis demonstrated a connection between the right portal vein and inferior vena cava, consistent with an intrahepatic congenital portocaval shunt shown in Figure 1a. The lower lungs showed dilated pulmonary artery branches of the peripheral system, suggesting hepatopulmonary syndrome, as shown in Figure 1b. A 2D Echocardiogram did not identify pulmonary hypertension and was consistent with previous. There were no diagnostic challenges. The prognosis was guarded until the closure device could be placed. The patient was subsequently transferred to an outside facility because the hospital could not perform the needed intervention. Interventional radiology was consulted at the outside facility, and an 18 mm Amplatzer PFO closure device was placed within the congenital shunt, which showed no residual flow from the portal vein into the inferior vena cava [19]. Following the procedure, his ammonia normalized. His mental status returned to baseline, while his anisocoria was intermittent and eventually resolved. There were no adverse or unexpected events from the device placement. His most recent abdominal ultrasound demonstrated no residual or recurrent portocaval shunt with the septal occluder correctly positioned at the

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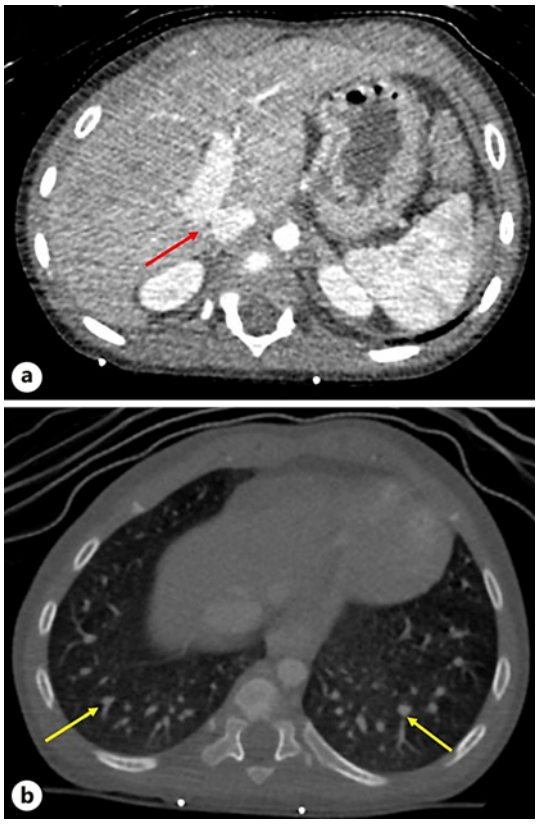

Fig. 1. a A computed tomography of the abdomen and pelvis with contrast shows a connection between the right portal vein and inferior vena cava, consistent with a CPSS (red arrow). **b** Dilated pulmonary artery branches of the peripheral system are seen, suggesting hepatopulmonary syndrome (yellow arrows).

CPSS. On a 2-year follow-up, the patient had no recurring issues related to the shunt or closure device placement. He had no signs of symptoms of chronic pulmonary problems or recurrent symptoms. The caregiver at that time had no issues to address.

Discussion

CPSSs are rare vascular malformations forming connections between a portal vein and one or more systemic vein(s), diverting portal flow from the liver to the systemic venous system [3]. The number of reported cases of CPSS has increased dramatically in recent years, likely due to the improvement in imaging techniques. CPSS manifests primarily neurologic, hepatic, and pulmonary involvement [4]. Laboratory abnormalities, including elevated ammonia, galactose, conjugated bilirubin, bile acids, and transaminases, should raise suspicion of CPSS and prompt liver imaging [20]. CPSS is based on the anatomic location of the shunt and is either extrahepatic or intrahepatic. An extrahepatic shunt is defined based on the absence of the portal vein (extrahepatic type 1) or preservation of portal venous flow (extrahepatic type 2) [15]. Intrahepatic shunts are more variable and involve portosystemic connections or both liver lobes [21]. These shunts carry a risk of severe multisystemic complications.

We conducted our literature review in August 2022, which searched PubMed, Embase, Scopus, and Google Scholar with variations on search terms "*Portosystemic shunt and Down Syndrome*." We performed the literature search in conjunction with our librarian team. We selected case reports involving portosystemic shunts in DS patients, listed in Table 1. We identified various metabolic and anatomic abnormalities across the case reports.

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Table 1. List of reported cases with DS and CPSS

First author, year	Chromosomal abnormality	Age at diagnosis	Shunt description	Cardiovascular malformations	Hyperammonemia	Hyperbilirubinemia	Gastrointestinal malformations
Kieran [14] (1992)	47, XY, 2/21 translocation	Newborn	Right PV to IVC	Complete AVSD with PDA	N	Y	Small right lobe
Kitagawa [15] (1992)	47, XY, +21	Three years old	Portal sinus to IVC branch of the proper hepatic artery	AVSD and heart block	Y	Y	–
Mahony [16] (1992)	Trisomy 21	Fetus	Varix of UV	–	–	–	–
Estroff [17] (1992)	Trisomy 21	Fetus	Varix of UV	–	–	–	–
Challis [18] (1997)	Trisomy 21	Fetus	Varix of UV	–	–	–	–
Hartung [19] (2000)	47, XY, +21	In utero (14 weeks)	Patent ductus venosus	AVSD	–	–	–
Hartung [19] (2000)	47, XY, +21	In utero (31 weeks)	Patent ductus venosus	–	–	–	Duodenal atresia and macroglossia
Courtens [20] (2000)	47, XY, +21	Newborn	Absence of ductus venosus. Portal vein to IVC	VSD	N	–	Hepatosplenomegaly, portal hypertension
Contratti [21] (2001)	Trisomy 21	Fetus	Absence of ductus venosus	–	–	–	Esophageal atresia
Pipitone [9] (2003)	47, XY, +21	Fetus	Absence of the intrahepatic portal vein and ductus venosus. Portal sinus to IVC	VSD	Y	Y	–
Pipitone [9] (2003)	47, XY, +21	Newborn	Absence of the intrahepatic portal vein and ductus venosus. Portal sinus to IVC	VSD and ASD	Y	N	-

(Continued on following page)

Table 1 (continued)

First author, year	Chromosomal abnormality	Age at diagnosis	Shunt description	Cardiovascular malformations	Hyperammonemia	Hyperbilirubinemia	Gastrointestinal malformations
Saxena [22] (2004)	Trisomy 21	1 month	Left portal and left hepatic veins	–	–	Y	Hepatomegaly
Franchi-Abella [3] (2010)	Trisomy 21	35 weeks	L PV and IVC, intrahepatic	–	N	N	–
Golewale [23] (2010)	Trisomy 21	4 months	Complex Nidus-type shunt the portal vein that, in turn, drained via a PDV into IVC	ASD, large VSD, large PDA, PDV	–	–	Hepatosplenomegaly with ascites
Golewale [23] (2010)	Trisomy 21	Newborn	Shunt into a phrenic vein. Patent ductus venosus to IVC	PFO, PDA, RVH	–	–	-
Golewale [23] (2010)	Trisomy 21	Newborn	Intrahepatic shunt L PV to L hepatic vein. Patent ductus venosus to IVC	ASD, VSD, RVH	–	–	–
Sokollik [6] (2013)	Trisomy 21	Newborn	Portal vein to IVC	N	–	–	–
Sokollik [6] (2013)	Trisomy 21	Five months old	Portal vein to IVC	AVSD	Y	N	–
Timpanaro [4] (2015)	Trisomy 21	2 years old	Side-to-side shunt Portal vein to IVC	PDA, coarctation of the aorta	–	–	–
Losa [24] (2015)	Trisomy 21	22 days old	Middle hepatic vein and intra-hepatic portal vein. Left portal and left hepatic vein	–	–	Y	Hepatitis
Yamaguchi [25] (2016)	47, XX, +21	Newborn	Patent ductus venosus anomalous connection. Portal vein to IVC	N	Y	Y	Pancreaticobiliary maljunction (B-P type)
Schnayder [5] (2021)	Trisomy 21	Two years old	Right PV to IVC	ASD	Y	Y	–

ASD, atrial septal defect; AVSD, atrioventricular septal defect; IVC, inferior vena cava; L, left; PDV, patent ductus venosus; PFO, patent foramen ovale; PV, portal vein; VSD, ventricular septal defect; UV, umbilical vein; N, No; Y, Yes; -, not reported.

Hyperammonemia was present 6 out of 9 times, and hyperbilirubinemia was present in 7 of 10 cases. CPSS is associated with congenital heart disease, heterotaxia, Turner syndrome, and Noonan syndrome. A wide range of cardiac defects was present in 12 out of 14 cases that reported a cardiac assessment. Ventricular and atrial septal defects were the most common, as shown in Table 1. Gastrointestinal pathology is reported in eight cases as predominately hepatomegaly, likely due to portal hypertension. Direct causes for portosystemic shunts are poorly understood. Dysfunction in angiogenic factors may play a role, as seen in other phenotypic traits in individuals with DS, including placental hypervascularity, fetal thickened nuchal folds, and a tendency to develop pulmonary hypertension [22]. Associated morbidities include focal nodular hyperplasia, nodular regenerative hyperplasia, hepatocellular adenoma, hepatoblastoma, hepatocellular carcinoma, and hepatopulmonary syndrome [4]. Patients should be followed closely for these conditions, with some studies suggesting yearly imaging [23]. Spontaneous closure may be seen in patients with intrahepatic shunts, mainly within the first year of life [24]. Symptoms may manifest early in childhood, requiring obliterative treatment. For the above reasons, surgical procedures for intrahepatic CPSS should be postponed in asymptomatic infants younger than 1 year [20]. Treatment options include surgical or radiologic guided shunt closures for patients with significant shunting [25, 26]. Liver transplants are necessary for patients with extrahepatic type 1 shunts as the shunts are the only drainage route for mesenteric and splenic blood [4, 27].

Our case adds to a growing body of evidence suggesting a rare correlation between DS and CPSSs. In clinical practice, when a DS patient presents with atypical neurological findings, elevated total bilirubin, ammonia, or elevated liver enzymes on blood tests, CPSS should be considered in the differential with careful consideration for abdominal imaging. Treatment should be individualized and guided by the clinical presentation for patients and further explored after the first year of life.

There is no question that over time, there will continue to be newer cases of CPSS that arise. We expect continued improvement in imaging modality and familiarity with the disease process. Detection of CPSS may be faster, allowing for earlier intervention and clinical improvement. Further investigation into the pathogenesis and characteristics of these shunts may allow for better noninvasive treatment options or the potential to prevent their formation.

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Statement of Ethics

Ethical approval is not required for this study in accordance with local and national guidelines. Written informed consent was obtained from the patient's legal guardian to publish the details of their medical care, including accompanying images and laboratories.

Conflict of Interest Statement

There are no conflicts of interest by any authors. There are no financial or nonfinancial relationships or activities to disclose that could be perceived as a conflict of interest.

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Author Contributions

B.N. is the corresponding and lead author in this work. B.N. was involved in the manuscript's conception, research, drafting, and editing. M.H.N.N. was involved in the manuscript's conception, research, drafting, and editing. J.F. was directly involved in patient care and drafting and editing the manuscript. R.C.C. was directly involved in patient care and participated in editing the manuscript. T.G. was involved in the drafting and final editing of the manuscript. All authors agreed to the final approval of this manuscript. All authors agree to be held accountable for all aspects of this work.

Data Availability Statement

All data generated or analyzed during the study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

References

1 Fabia J, Drolette M. Malformations and leukemia in children with Down's syndrome. Pediatrics. 1970;45(1):60–70.
2 Vis JC, Duffels MGJ, Winter MM, Weijerman ME, Cobben JM, Huisman SA, et al. Down syndrome: a cardiovascular perspective. J Intellect Disabil Res. 2009;53(5):419–25.
3 Franchi-Abella S, Branchereau S, Lambert V, Fabre M, Steimberg C, Losay J, et al. Complications of congenital portosystemic shunts in children: therapeutic options and outcomes. J Pediatr Gastroenterol Nutr. 2010;51(3):322–30.
4 Timpanaro T, Passanisi S, Sauna A, Trombatore C, Pennisi M, Petrillo G, et al. Congenital portosystemic shunt: our experience. Case Rep Pediatr. 2015;2015:691618–5.
5 Papamichail M, Pizanias M, Heaton N. Congenital portosystemic venous shunt. Eur J Pediatr. 2018;177(3):285–94.
6 Abernethy J. Account of two instances of uncommon formation, in the viscera of the human body. Philos Trans R Soc Lond. 1793;83:59–66.
7 Bernard O, Franchi-Abella S, Branchereau S, Pariente D, Gauthier F, Jacquemin E. Congenital portosystemic shunts in children: recognition, evaluation, and management. Semin Liver Dis. 2012;32(4):273–87.
8 Kieran MW, Vekemans M, Robb LJ, Sinsky A, Outerbridge EW, Der Kaloustian VM. Portohepatic shunt in a down syndrome patient with an interchange trisomy 47,XY,−2,+der(2),+der(21)t(2;21)(p13;q22.1)mat. Am J Med Genet. 1992;44(3):288–92.
9 Kitagawa S, Gleason WA, Northrup H, Middlebrook MR, Ueberschar E. Symptomatic hyperammonemia caused by a congenital portosystemic shunt. J Pediatr. 1992;121(6):917–9.
10 Kanazawa H, Nosaka S, Miyazaki O, Sakamoto S, Fukuda A, Shigeta T, et al. The classification based on intrahepatic portal system for congenital portosystemic shunts. J Pediatr Surg. 2015;50(4):688–95.
11 Kobayashi N, Niwa T, Kirikoshi H, Fujita K, Yoneda M, Saito S, et al. Clinical classification of congenital extrahepatic portosystemic shunts. Hepatol Res. 2010;40(6):585–93.
12 Lautz TB, Tantemsapya N, Rowell E, Superina RA. Management and classification of type II congenital portosystemic shunts. J Pediatr Surg. 2011;46(2):308–14.
13 Park JH, Cha SH, Han K, Han MC. Intrahepatic portosystemic venous shunt. AJR Am J Roentgenol. 1990;155(3):527–8. Available from: www.ajronline.org.
14 Şenocak E, Oğuz B, Edgüer T, Cila A. Congenital intrahepatic portosystemic shunt with variant inferior right hepatic vein. Diagn Interv Radiol. 2008;14(2):97–9.
15 Morgan G, Superina R. Congenital absence of the portal vein: two cases and a proposed classification system for portasystemic vascular anomalies. J Pediatr Surg. 1994;29(9):1239–41.
16 Howard ER, Davenport M. Congenital extrahepatic portocaval shunts: the Abernethy malformation. J Pediatr Surg. 1997;32(3):494–7.

17 Winkler JT, Bohling MW, Tillson DM, Wright JC, Ballagas AJ. Portosystemic shunts: diagnosis, prognosis, and treatment of 64 cases (1993-2001). J Am Anim Hosp Assoc. 2003;39(2):169–85.
18 Papamichail M, Ali A, Quaglia A, Karani J, Heaton N. Liver resection for the treatment of a congenital intrahepatic portosystemic venous shunt. Hepatobiliary Pancreat Dis Int. 2016;15(3):329–33.
19 Shnayder MM, Dervishi M, Jo A, Pomerantz B. Congenital portosystemic shunt occlusion with an Amplatzer PFO occlusion device: a case report. CVIR Endovasc. 2021;4(1):14.
20 Sokollik C, Bandsma RHJ, Gana JC, van den Heuvel M, Ling SC. Congenital portosystemic shunt: characterization of a multisystem disease. J Pediatr Gastroenterol Nutr. 2013;56(6):675–81.
21 Park JH, Cha SH, Han JK, Han MC. Intrahepatic portosystemic venous shunt. AJR Am J Roentgenol. 1990;155(3):527–8.
22 Pipitone S, Garofalo C, Corsello G, Mongiovì M, Piccione M, Maresi E, et al. Abnormalities of the umbilico-portal venous system in Down syndrome: a report of two new patients. Am J Med Genet. 2003;120A(4):528–32.
23 DiPaola F, Trout AT, Walther AE, Gupta A, Sheridan R, Campbell KM, et al. Congenital portosystemic shunts in children: associations, complications, and outcomes. Dig Dis Sci. 2020;65(4):1239–51.
24 Plut D, Gorjanc T. A case of a newborn with an intrahepatic congenital portosystemic venous shunt with concurrent congenital duodenal web. Acta Radiol Open. 2019;8(6):2058460119854173.
25 Hu GH, Shen LG, Yang J, Mei JH, Zhu YF. Insight into congenital absence of the portal vein: is it rare? World J Gastroenterol. 2008;14(39):5969–79.
26 Kim MJ, Ko JS, Seo JK, Yang HR, Chang JY, Kim GB, et al. Clinical features of congenital portosystemic shunt in children. Eur J Pediatr. 2012;171(2):395–400.
27 Woodle ES, Thistlethwaite JR, Emond JC, Whitington PF, Vogelbach P, Yousefzadeh DK, et al. Successful hepatic transplantation in congenital absence of recipient portal vein. Surgery. 1990;107(4):475–9.