Congenital Segmental Intestinal Dilatation: A 25-Year Review with Long-Term Follow-up at the Medical University of Innsbruck, Austria

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Abstract

Background and Aim Congenital segmental intestinal dilatation (CSID) is a neonatal condition with unclear etiology and pathogenesis. Typically, the newborn with CSID presents with a limited (circumscribed) bowel dilatation, an abrupt transition between normal and dilated segments, neither intrinsic nor extrinsic perilesional obstruction, and no aganglionosis or neuronal intestinal dysplasia. We aimed to review this disease and the long-term follow-up at the Children’s Hospital of the Medical University of Innsbruck, Tyrol, Austria.

Study Design Retrospective 25-year review of medical charts, electronic files, and histopathology of neonates with CSID.

Results We identified four infants (three girls and one boy) with CSID. The affected areas included duodenum, ileum, ascending colon, and sigmoid colon. Noteworthy, all patients presented with a cardiovascular defect, of which two required multiple cardiac surgical interventions. Three out of the four patients recovered completely. To date, the three infants are alive.

Conclusion This is the first report of patients with CSID and cardiovascular defects. The clinical and surgical intervention for CSID also requires a thorough cardiologic evaluation in these patients. CSID remains an enigmatic entity pointing to the need for joint forces in identifying common loci for genetic investigations.

Keywords
- dilatation
- intestine
- obstruction
- aganglionosis
- Hirschsprung’s disease
- heart defect

Congenital segmental intestinal dilatation (CSID) is a neonatal condition with unclear etiology and pathogenesis. Typically, the newborn with CSID presents with a limited (confined) bowel dilatation with three- to fourfold increase, an abrupt transition between normal and dilated segments, neither intrinsic nor extrinsic perilesional obstruction, and presence of normal ganglionic cells of the gastrointestinal autonomous plexus.1 There is no evidence of Hirschsprung’s disease (aganglionosis) or neuronal intestinal dysplasia.
In some cases, a segmental absence of intestinal musculature may cause spontaneous bowel perforation, intestinal obstruction, or intussusception. The resection of the affected segment usually leads to complete recovery, but the clinical polymorphism and the lack of specificity of diagnostic imaging may point to the difficulty to have a complete preoperative picture of the disease.

We aimed to review this disease and the long-term follow-up at the Children’s Hospital of the Medical University of Innsbruck, Tyrol, Austria.

Materials and Methods

We reviewed the medical charts, electronic medical records, and histopathology at our institution (Children’s Hospital, Innsbruck, Austria) of the Medical University of Innsbruck, Austria.

Results

We found four infants with CSID who underwent surgery at the Innsbruck Department of Pediatric Surgery. The clinical findings of the four infants (three girls and one boy) are shown in Table 1, while the surgical sites and the histopathology findings are illustrated in Figs. 1 and 2, respectively. Briefly, in the first patient, the affected area was the ascending colon. It was reduced by tapering and later used to close the colonic defect caused by atresia of the distal descending colon. The second patient had a dilated duodenum. The infant underwent to open exploratory surgery, and the duodenum was then tapered. The third infant had dilatation of the lower sigmoid colon, which was primarily resected, the rectum was closed, and an artificial anus was created in the sigmoid colon (sigmoidostomy). Six weeks later, a colostomy reversal was performed, and continuity was re-established by an end-to-end anastomosis between the descending colon and rectum. The fourth infant had a dilated segment of the ileum which was resected, and an end-to-end ileoileostomy performed. In our patients, all histological findings showed data like the findings mentioned earlier. We found regular configured bowel wall segments with thin external muscle layers (Fig. 2a-c). The pyloric tumor of patient 2 showed glandular structures lined by cuboidal to columnar epithelium surrounded by hypertrophic smooth muscle bundles, which corresponds to a gastric adenomyoma of the pylorus (Fig. 2d). Ganglia cells were found in all specimens, although occasionally some ganglia cells were reported as immature.

Noteworthy, all patients presented with a cardiac/vascular defect. Two of the four defects required multiple cardiac surgical interventions. Two patients had each an atrial septum defect and a ventricular septal defect (VSD), while the other two patients had complex congenital heart disease. Three patients recovered completely. To date, these

Table 1 Data of patients with CSID, associated anomalies, surgical interventions, and outcome

| Case | Sex | Year | Birth | BW | CSID | MCA | Surgery | Outcome |
|------|-----|------|-------|----|------|-----|---------|---------|
| 1    | F   | 1994 | Term, VD | 2,410 | Ascending colon | High anal atresia and atresia of the descending colon, VUR III, ASD | (1) Tapering of ascending colon, double-barreled transverse loop colostomy (2) Resection of the residual descending colon, ascending colon pull-through operation (Soave) with the construction of a neoanus | Alive, uneventful, apart from pubertas praecox |
| 2    | M   | 1996 | Term, VD | 2,360 | Duodenum | Pyloric “tumor,” aortic arch hypoplasia (isthmus), IM | Excision of the tumor, tapering of the dilated duodenal segment after explorative duodenotomy | Death after cardiac surgery |
| 3    | F   | 1997 | Term, VD | 2,660 | Lower sigma | Trisomy 21 syndrome, VSD | (1) Resection of the dilated segment, blind rectum closure, and terminal sigmoidostomy (2) End-to-end anastomosis between descending colon and rectum | Alive, frequent mechanical dilatation of the anastomosis during the first 2 years of life, growth delay |
| 4    | F   | 2008 | 39th, CS | 3,700 | Ileum | AVC, unroofed CS, AAD, AL, LCVP, left liver, IM | Resection of dilated ileum segment, end-to-end ileoileostomy | Alive, uneventful, apart from multiple (7) CV operations |

Abbreviations: AAD, arcus aortae dexter (right aortic arch); AL, arteria lusoria; ASD, atrial septal defect; AVC, atrioventricular channel; BW, birth weight (g); CS, cesarean section; CSID, congenital segmental intestinal dilatation; CV, cardiovascular; IM, intestinal malrotation; LCVP, persistence of the left caval vein; VD, vaginal delivery; VSD, ventricular septal defect; VUR III, third degree of vesical-urethral reflux.

Notes: Ileoileostomy is a surgical anastomosis between two segments of the ileum. The pyloric “tumor” was a gastric adenomyoma of the pylorus. Pathological examination revealed glandular structures lined by cuboidal to columnar epithelium surrounded by hypertrophic smooth muscle bundles. Gastric adenomyoma should be considered a differential diagnosis of hypertrophic pyloric stenosis and gastric duplication in newborns and children.
Fig. 1 (a) Patient 1: Scheme of the operation site with the malformations of the lower gastrointestinal tract (dilatation of the ascending colon, atresia of the descending colon, blindly closed rest of the sigmoid colon and the rectum, as well as anal atresia) after a double-barreled colostomy at the transverse colon. (b) Patient 1: Operative site of the CSID of the ascending colon. (c) Patient 2: Plain abdominal X-ray showing a sizeable gas-filled bowel loop in right upper abdominal quadrant. (d) Patient 2: Operative site of the mobile dilated duodenum. (e) Patient 3: Scheme of the circumscribed dilatation of the lowest part of the sigmoid colon. (f) Patient 3: Operative site of the dilated segment of the sigmoid colon (diameter of 10 cm), the oral colon with standard configuration. (g) Patient 4: Upper gastrointestinal X-ray series showing pooling of the contrast media in a dilated loop of the ileum in the right hemiabdomen. (h) Patient 4: Intraoperative photograph of an 18-cm-long segmental dilatation of the middle ileum. The arrow in (h) points to the segmental dilatation of the portion of the intestine. The transition of normal bowel on both ends did not show any sign of mechanical obstruction. CSID, congenital segmental intestinal dilatation.
three infants are alive. One patient died of cardiac surgery complications.

**Discussion**

CSID has been defined as a circumscribed dilatation of the lumen with an abrupt transition between normal and dilated bowel and neither intrinsic nor extrinsic barrier distal of the dilatation. There is a sharply defined and markedly enlarged segment of the intestine flanked by normal caliber afferent and efferent bowel segments.\(^7\) CSID can involve the gastrointestinal tract anywhere from duodenum to the distal colon. The ileum and colon are the most commonly affected sites, while duodenum and jejunum are less frequently involved (Swenson and Rathauer [1959] [colon], Rossi and Giacomoni [1973] [jejunum], Sjölin and Thoren [1962] [ileum], Ueda and Okamoto [1972] [ileum], Irving and Lister [1977] [ileum], and Rovira et al [1989] [duodenum]).\(^7,9-13\) Since the entity may be described differently, the precise number of all published cases of CSID may be challenging to identify. In consideration of it, Ben Brahim et al reported 125 literature cases of CSID published up to 2006\(^6\) and added eight of their own, of which seven were newborn. However, Elemen et al\(^14\) indicated 2 years later that “slightly more than 100 cases” have been reported up to 2008. It seems that there are ~110 to 120 cases adequately reported in around 50 years of reviewed literature. In consideration of the number of cases reported in the literature, two to three cases may present to the clinical attention yearly. In the last couple of decades, the criteria became stricter and, since 2008, to the best of our knowledge, 20 adequately described cases have been reported in the English literature.\(^14-32\) Here, we report on four infants with CSID with segmental dilatation located in the duodenum, ileum, ascending colon, and sigmoid colon. Two of our infants showed additional intestinal anomalies, but remarkably, all four patients had cardiovascular defects, and this is the first report demonstrating such a consistent association in four consecutive cases. In the review of the CSID cases, it is manifest that the associated malformations, which are found in more than 50% of the cases, are quite

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**Fig. 2** (a, b) Microphotograph of CSID (Patient 4) with thin external muscle layer (hematoxylin and eosin ×40) and dilated lymphatic vessels of the submucosa (hematoxylin and eosin staining, ×40 original magnification); (c) microphotograph of CSID (Patient 3) showing sclerosis of the submucosa (hematoxylin and eosin staining, ×20 original magnification); and (d) microphotograph of the “pyloric tumor” showing hypertrophic muscle layers with some scattered glandular proliferations corresponding to a gastric adenomyoma of the pyloric region (hematoxylin and eosin staining, ×100 original magnification). The yellow arrows in (a) and (b) point to the very thin muscularis propria, while the yellow arrows in (c) and (d) point to the sclerosis of the submucosa and to the gastric adenomyoma of the pylorus, respectively. The gastric adenomyoma of the pylorus is characterized by glandular structures lined by cuboidal to columnar epithelium surrounded by hypertrophic smooth muscle bundles by histological examination. CSID, congenital segmental intestinal dilatation.
distinguish, although the gastrointestinal tract and the omphalomesenteric duct are mostly involved.\

Histopathological findings of cases described in the literature range from partial or complete absence of lamina propria in the affected segment to partial hypertrophy of muscle layers with or without an irregular muscular network, minimal thinning of the external muscle layer, degenerated myocytes filled with vacuoles, and distended submucosal vessels up to angiodysplasia.\textsuperscript{1,12,13,28,40–45} In most cases, the histology of the resected segment is normal. Occasionally, a supernumerary intestinal muscle coat in the dilated segment, without any evidence of neurological abnormality, was observed. Histopathological findings of the resected ileal portion are reported to discuss the role of developmental malformation of muscularis propria as a cause of CSID.\textsuperscript{46} The presence of ganglion cells was reported in all cases of CSID as part of the criteria. Cheng et al performed an extended histochemical and immunohistochemical analyses of one instance of a jejunal CSID and postulated that segmental dilatations of the small bowel might not be in origin of the enteric nervous system but accuse a localized myopathy of the smooth muscle of being at least part of the sources of this entity.\textsuperscript{40} A differential diagnosis may reside in a segmental aganglionosis, an entity which is controversially discussed in the literature.\textsuperscript{47–49} In the case reported by Soyer et al,\textsuperscript{46} a 3-day-old male neonate presenting with clinical findings of intestinal obstruction was diagnosed to have CSID and had supernumerary intestinal muscle coat in the dilated segment, without any evidence of neurological abnormality. Histopathological findings identify a striking similarity to our cases with duodenum dilatation or colon dilatation with anal atresia.

Other than hypertrophic or very thin muscle layers in the involved segment, ectopic tissue, such as the gastric or pancreatic tissue, was demonstrated.\textsuperscript{8,27,50} Gastric adenomyoma of the pyloric region should be considered a differential diagnosis of hypertrophic pyloric stenosis and gastric duplication in newborns and children.\textsuperscript{51,52}

Non specific inflammatory or erosive changes as well as nonspecific inflammation of the lamina propria were also found.\textsuperscript{14}

In consideration of the clinical and histological presentations, it is unlikely to have only one pathogenesis for this condition. Three theories are frequently postulated, including the theory of Irving and Lister (1977),\textsuperscript{12} the theory of Mathé et al (1982),\textsuperscript{53} and the theory of Heller and Waag (1987).\textsuperscript{54} Irving and Lister suggested embryological damages implicate an extrinsic intrauterine intestinal compression with the intestine being strangulated by an umbilical ring, vitelline blood vessels, or omphalomesenteric bands.\textsuperscript{12} Mathé et al suggested a primitive (embryonic) neuromuscular dysfunction of the intestine,\textsuperscript{53} while Heller and Waag focused on an early disturbance during splitting of the notochord from the entoderm.\textsuperscript{54} These last authors pointed out that parts of the entoderm remain adherent to the ectoderm with the organization of cysts and/or tubes impairing the healthy development of the spine and eliciting other associated defects.\textsuperscript{54}

In consideration of the cardiovascular anomalies encountered in our patients, we may consider our CSID infants to be a part of combined developmental disorders rather than a separate entity. In consideration of the development of the gut muscle layers and identification of pancreatic islets at 12 weeks of embryonal age (crown-rump length of 8.8 cm), we may expect that a developmental disorder limited to the gut may involve these infants at this age. In case of an associated cardiovascular defect, the time of embryonic damage should be located earlier. The time of susceptibility for the development of atrial septal defect, VSD, aortic arch hypoplasia/coarctation of the aorta, and atrioventricular septal defects occurs between 6- and 8-week postfertilization. Thus, the insult should be prolonged enough to reach the 12th week of postfertilization age.\textsuperscript{55} Congenital defects of the cardiovascular system are among the most common congenital birth defects estimated to occur in \(\sim 1\) in 100 living births.\textsuperscript{56} Congenital malformations of the gut, urinary, and musculoskeletal systems are the most frequently seen extracardiac defects in patients with congenital defects of the cardiovascular system.\textsuperscript{57} Intestinal malrotation has been observed in 2.8 to 4.1\% of all the patients with congenital defects of the cardiovascular system.\textsuperscript{58,59} In embryogenesis, the gut is developed at a later stage than the cardiovascular system. Changes in intra-abdominal space caused by congenital heart defects might also increase the risk of abnormal gut development during embryogenesis.\textsuperscript{60,61} A common genetic cause might be another explanation in our patients. The left-right asymmetry is present in both the gut and the heart, and a specific biochemical cascade during embryogenesis has been demonstrated.\textsuperscript{62} Nodal growth differentiation factor (\textit{NODAL}) and paired-like homeodomain 2 transcription factor 2 isoform c (\textit{PITX2c}) are two signaling molecules derived from \textit{NODAL} and \textit{PITX2c} genes. Both \textit{NODAL} and \textit{PITX2c} are inevitable for this cardiac and gastrointestinal asymmetry and hypertrophy of the cardiomyocytes.\textsuperscript{63} In animal studies, an abnormal (reduced, diffuse, or absent) expression of \textit{PITX2c} in the embryo causes abnormal looping from both heart and gut,\textsuperscript{64–67} resulting mainly in abnormal outflow tract orientation (e.g., unseparated or misaligned great artery trunks, double outlet right ventricle, symmetrical outflow tract cushions, and common atrioventricular trunk).\textsuperscript{65,66} The disturbance of the expression of \textit{PITX2c} could cause a spectrum of isomerisms.\textsuperscript{68}

Concerning the diagnosis, there are challenges both during pregnancy and in the postpartum. CSID can either become symptomatic during the intrauterine life or after birth. However, the opinion that a CSID in the newborn is associated with subileus or ileus is not always correct. Depending on the extent of the enlargement, the intestinal transit is more or less affected, which means that a CSID can be entirely asymptomatic explaining the report of cases in older children. CSID is a malformation that becomes symptomatic at any age or even is an incidental finding at laparotomy.\textsuperscript{10,14,69} As a CSID can already become symptomatic in a fetus and/or in a newborn, a wide range of possibilities arises regarding diagnostics. To date, prenatal diagnosis has also increasingly diagnosed minor cystic changes in the
abdomen of fetuses, for example, duodenal atresia, meconium ileus, intestinal duplication, and mesenteric cyst. The problem that arises is that while these structures are usually easy to recognize, they often cause diagnostic challenges when associated with CSID. Apart from a single case diagnosed prenatally, CSID is most commonly identified after birth because of the inaccuracy of the fetal intestinal echography. Paradiso et al. found that two of their patients had a prenatal ultrasonographic suspicion of intestinal abnormality, which was confirmed in postpartum surgery.

However, the diagnosis of a CSID is not easy even postpartum, mainly if other intestinal malformations are associated. The clinical polymorphism and the glazing nonspecificity of radiological investigations complicate the diagnostic procedure. This entity remains enigmatic and challenging because of the ambiguous clinical findings, nonspecific radiological examinations, and mimickers of the urinary tract.

In our four patients, two patients had ileal symptoms, and an exploratory laparotomy was scheduled on the second postpartum day (after deriving the gastric contents via a nasogastric tube). In the third patient, a cystic structure was detected in the fetus in the pelvis as part of sonographic pregnancy monitoring, but an assignment was not made. In the postnatal period, Hirschsprung’s disease was suspected, although the megacolon appeared “spherical.” Only in the fourth newborn could the prenatal diagnosis of a presumed cystic duplication be preoperatively revised in the direction of a CSID. Noteworthy, all four patients had congenital heart disease.

The relationship between CSID and heart failure remains to be questioned, although the occurrence of a heart defect in a child with trisomy 21 or with a high level of anal atresia is well known in the literature. Probably, the use of trisomy 16 mice, the animal model for human trisomy 21, may be useful in the future.

The surgical procedure for correcting a CSID depends on its position. Most often, a segment resection in the sense of a one-step procedure with end-to-end anastomosis is possible. In our four patients, however, this was only possible in the third and fourth patients. In the third patient, because of the macroscopically unclear findings with suspicion of aganglionosis or neuronal intestinal dysplasia, such an approach was only feasible in two phases. Postoperative courses and outcomes, although dependent on the associated malformations, are mostly reported to be without complaints. Regarding therapy, low-dose vasopressin may improve cardiac function as identified in previous experiments in newborn piglets with acute hypoxia–reoxygenation.

In conclusion, CSID is a rare intestinal malformation, which can be associated with other anomalies, mostly of intestinal type. An association with cardiovascular defects should be considered an extreme rarity and may suggest that genetic counseling may be appropriate. The final diagnosis relies on the intraoperative picture and the exclusion of a segmental aganglionosis. Standard therapy is the total resection of the affected segment and end-to-end anastomosis or, depending on the position of the intestinal malformation, using specific surgical procedures. Postoperative course and outcome depend on the associated defects, but CSID itself is a condition which is mostly free of complications.

Conflict of Interest
None.

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