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Concomitant Duodenal Atresia and Hirschsprung disease

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Background	Duodenal atresia (DA) and Hirschsprung disease (HD) are rare congenital anomalies involving the gastrointestinal tract; their co-existence is a diagnostic and management challenge.
Summary	A full-term, three-day old Caucasian male with polyhydramnios was taken to the operating room on the third day of life for an exploratory laparotomy due to persistent bilious emesis. A type 1 duodenal atresia was found and a Kimura-type duodenoduodenostomy was performed. Post-operative recovery was uneventful. At six weeks of age the patient was readmitted for symptoms of bowel obstruction and failure to gain weight and full thickness suction rectal biopsies revealed colonic aganglionosis. A staged Soave endo-rectal pull-through with colostomy reversal was performed at 5 months of age without complications. The child continues to gain weight and has had no complications related to HD or DA.
Conclusion	Although rare, DA and HD may co-exist, even in the absence of trisomy-21. When managing a neonate with small bowel atresia, a concomitant lower gastrointestinal tract anomaly should be included in the differential diagnosis. When managed appropriately, patients with co-existing DA and HD can have excellent long-term outcomes.
Keywords	Duodenal atresia; Hirschsprung disease; colonic aganglionosis; trisomy-21

Case Description

Congenital anomalies of the gastrointestinal tract are uncommon, and are more likely to occur in patients with genetic disorders.[1,2] Duodenal atresia (DA) is a congenital anomaly resulting in proximal intestinal obstruction due to failure of midgut recanalization. DA presents as a proximal bowel obstruction in early neonatal life, requiring definitive surgical repair and has an incidence of one in 10,000 live births with a slight predominance in preterm males.[3,4] DA may be associated with additional anomalies including intestinal malrotation, trisomy-21, or congenital heart disease.3-8 Hirschsprung disease (HD) is a congenital neurenteric abnormality resulting in a failure of cranio-caudal migration of neural crest cells that results in variable lengths of intestinal aganglionosis.5,6 HD has a varied presentation. Failure to pass meconium in the first 24 hours of life may be missed, with a later diagnosis made only after the occurrence of persistent constipation.[6] The incidence of HD is approximately one in 5-10,000

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live births.[5,6] Trisomy 21 is associated with both DA and HD.9 Concomitant DA and HD has been reported, but is extremely rare. We report a patient with coexistent DA and HD, without Trisomy 21, and add an additional previously unreported case to a literature review of similar cases.[1,4,7,8,10-12]

A Caucasian male was born at 39 weeks of gestation to a 20-year-old primipara via elective cesarean section secondary to polyhydramnios. DA was identified on a routine prenatal ultrasound at 31 weeks of gestation. Cell-free DNA testing revealed no fetal aneuploidy. On first day of life (DOL) the neonate developed bilious emesis, and a plain abdominal radiograph demonstrated a double bubble in the mid-abdomen without distal bowel gas (Figure 1a). The neonate was electively taken to the operating room on DOL3 for an exploratory laparotomy. Intra-operatively, a type 1 DA involving the second portion of the duodenum was repaired via a Kimura-type duodenoduodenostomy. The rest of the small bowel was unremarkable. The post-operative course was uneventful, with bowel function on postoperative day 9 and discharge home at 3 weeks of age. The patient was re-admitted 4 days later for constipation and intermittent vomiting and discharged two days later after symptom resolution following non-operative management. At 6-weeks of age, the patient was readmitted for progressive bilious vomiting, abdominal distension,, obstipation and failure to gain weight. Plain abdominal radiograph revealed dilated loops of small bowel with multiple air fluid levels. Upper gastrointestinal imaging revealed no proximal obstruction or malrotation. A lower gastrointestinal study showed a transition point at the proximal-mid sigmoid colon (Figure 1b) and full thickness suction rectal biopsies revealed colonic aganglionosis.

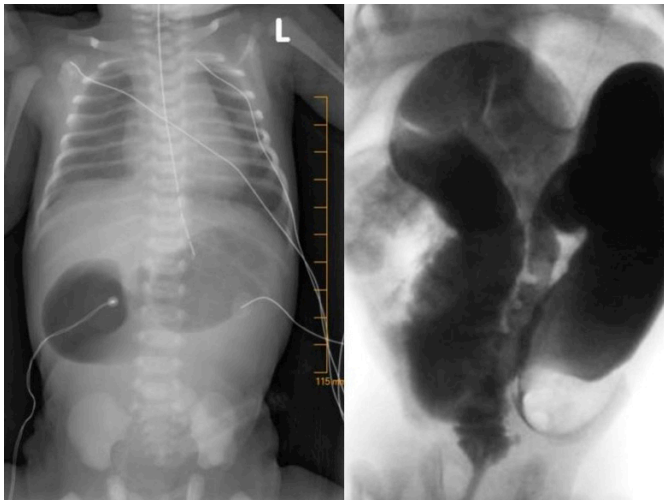

Figure 1a and 1b. Double bubble on KUB and Transition point on contrast enema.

A leveling descending loop colostomy was performed at age 2 months and additional biopsies were taken at the pathologic transition point determined at the level of proximal sigmoid colon (Figure 2a, 2b). A Soave endo-rectal pull-through with colostomy reversal was performed at 5 months of age. Post-operative course was uneventful and the patient was most recently seen in clinic at eight months of age, weighing 7.4 kg (between the 9th and 10th percentile for his age). He has had no complications related to HD or DA to-date.

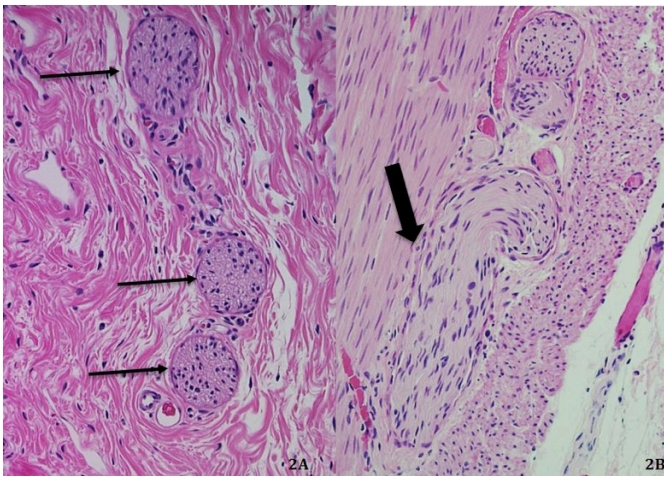

Figure 2a and 2b. Rectosigmoid aganglionosis (Hirschsprung disease)- Hypertrophic nerves are present in the submucosa (thin arrows, fig 2A, HE stain, x200) and muscularis propria (bold arrow, 2B, HE stain, x200). NO submucosal or myenteric ganglion cells are seen (2A and 2B, HE stain, x200).

Discussion

DA is often diagnosed by prenatal ultrasonography with close to half of affected pregnancies demonstrating polyhydramnios.[3,13] The incidence of additional congenital anomalies in newborns with DA is high (55-78 percent), and 24-31 percent of DA cases occur in the presence of Down syndrome.[1-3,7,14] A number of co-existing proximal gastrointestinal anomalies, including tracheo-esophageal fistulas, intestinal atresias, malrotation, midgut volvulus, enteric duplication cysts, annular pancreas, and biliary tract anomalies have been reported in babies with DA.[3,7] The true incidence of various combinations of these anomalies is unknown. Extrapolation from the incidence of the isolated abnormalities probably underreports the true incidence in those patients with a common genetic predisposition. Newborns with DA usually present with bilious emesis, however as many as 20% demonstrate non-bilious vomiting due to preampullary obstruction.[1,15] Abdominal radiography typically demonstrates the classic double

bubble sign and absence of distal bowel gas.[3] To identify any associated anomalies, an echocardiogram, plain chest radiograph, and renal and bladder ultrasound are recommended.[7]

Neonates with HD usually present with failure to pass meconium in the first 24 hours of life. Severe constipation, abdominal distension, and vomiting may be recognized in the first days of life, or much later.[16] A minority of newborns with HD present with either a colonic atresia or bowel perforation.[17,18] A variety of congenital anomalies have been associated with HD, and approximately 12% of cases are associated with Trisomy-21.[16] Most patients have standard-segment HD, with aganglionosis confined to the rectosigmoid colon, as was present in our patient.[5,6] A water-soluble contrast enema is often useful in preoperative planning and may offer osmotic relief of inspissated stool burden.[19] Full-thickness suction rectal biopsy demonstrating absence of ganglion cells in the myenteric and submucosal plexuses confirms the diagnosis.[20] Surgical correction includes resection of the aganglionic segment and anastomosis of the normally invervated bowel to the anus using various methods. Persistent growth and developmental compromise, and Hirschsprung associated enterocolitis have been reported after surgical reconstruction.[21] Approximately half of individuals with standard-segment disease are reported to experience enterocolitis, constipation, or incontinence following definitive surgery.[22-24]

The co-existence of DA and HD is exceedingly rare.[7] We have found 11 previously reported cases all of which occurred in the setting of a chromosomal abnormality, commonly trisomy-21 (Table 1). One of the senior authors (MRL) had a previous patient with trisomy 21 that is included in the table, but has not otherwise been reported.

The current case presented with concomitant DA and HD without trisomy-21. This has not been previously reported. It is important to note that HD and other distal obstructive anomalies of the gastrointestinal tract may be clinically masked by proximal obstruction from DA. Indeed, HD discovered intra-operatively at the time of DA repair has been reported only once. All other cases, including our two were diagnosed after repair of the DA, due to constipation and abdominal distension. These findings should alert the surgeon to the possibility of HD. Kimble et al advocate obtaining a lower gastrointestinal series and suction rectal biopsies when DA and trisomy-21 are encountered together.[7] It may be reasonable to obtain a contrast enema on patients with duodenal atresia due to the co-existence of malrotation in babies with DA with incidence as high as 53%.[25,26] Other option is to look specifically for rotational abnormalities at the time of duodenal repair. Whether a contrast enema would show findings of HD in a baby with a DA is unknown. To date a preoperative diagnosis based on this study has not been reported. Since trisomy 21 is associated with many problems of surgical importance a careful evaluation for these anomalies should occur before repair of the DA.9,25,27 Our case demonstrates the importance of close clinical follow-up after repair of DA. Timely recognition of HD allows prompt surgical management resulting in good long-term outcomes in neonates with DA who also have HD.

Conclusion

Although rare, DA and HD may co-exist, even in the absence of trisomy-21. When managing a neonate with small bowel atresia, a concomitant lower gastrointestinal tract anomaly should be included in the differential diagnosis. When managed appropriately, patients with co-existing DA and HD can have excellent long-term outcomes.

Lessons Learned

Neonates with clinical features of duodenal atresia, with or without trisomy-21, may have additional gastrointestinal anomalies including Hirschsprung disease, which should be included in the differential diagnosis of infants who are constipated following DA repair. Close clinical follow-up and staged operative management can result in good long-term outcome.

Author / Year / Demographics	Case Presentation	Other Associated Anomalies
Ikeda K (1986), case 1a		Trisomy-21
Ikeda K (1986), case 2a		Trisomy-21
Akhtar J (1992)a		Trisomy-21
Coppens B (1992), 2070-g infanta	Patient died from meningitis following repair of duodenal atresia.	Trisomy-21
Touloukian RJ (1993), case 1a	DOL 10: HD diagnosed.	Trisomy-21
Touloukian RJ (1993), case 2a	DOL 10: HD diagnosed.	Trisomy-21
Khong TY (1994), 1630-g preterm male	32 weeks GA: Polyhydraminos and fetal double bubble on prenatal ultrasound. DOL 2: Multuple atretic segments of duodenum and jejunum, duodenal diverticulum, accessory spleniculi, and small distal colon with inspissated meconium on laparotomy. Rectal biopsy deferred due to prematurity. DOL 26: Abdominal mass, distension, and feeding intolerance resolved with conservative management. DOL 48: Diverting ileostomy performed for biopsy-proven total colonic aganglionosis. 10 months' age: Patient died from recurrent aspiration pneumonia.	Interstitial del 13q, optic nerve hypoplasia, polysplenia, jejunal atresia, bilateral cerebral atrophy, umbilical cord ulceration.
Kimble RM (1997)a		Trisomy-21
Piper HG (2008), case 1a		Trisomy-21
Piper HG (2008), case 2a		Trisomy-21
Sekmenli T (2011) 2500-g female	DOL 2: Vomiting, abdominal distension, and double bubble. Proximal diverting colostomy performed for intraoperative appearance of rectosigmoid transition point and full-thickness biopsy c/w HD. 1 year-of-age: Patient died from HAEC-related sepsis.	Trisomy-21, congenital hypothyroidism
Previously unreported (MRL, 1994), 2100-g full-term male	DOL 1: Abdominal distension, diffuse air filled, dilated, small bowel. Laparotomy for suspected ileal atresia revealed DA and duplication cyst treated with extended Jaboulay-type gastroduodenostomy. Serosal injury to transverse colon repaired with Lembert suture. DOL 6: Peritonitis led to laparotomy with finding of transverse colon perforation at previous site treated with closure and proximal diverting colostomy. 5 months of age: Colostomy closed with postoperative abdominal distension, and constipation. Work up with contrast enema and biopsy reveals HD. 6 months of age: Endo-rectal pull-through for HD with 3 episodes of HAEC in first year post pull through. Alive and well at 22 years of age without subsequent HAEC.	Trisomy-21, left renal agenesis, duodenal duplication cyst, cryptorchidism, micropenis, patent ductus arteriosus
Current case, (2015), 2780-g full-term male	31 weeks GA: Polyhydraminos and DA on prenatal ultrasound. DOL 1: Bilious emesis and double bubble on plain radiograph. DOL 25: New-onset constipation and vomiting resolved with conservative management. 6 weeks age: Progressive bilious emesis, abdominal distension, obstipation, and failure to gain weight. Dilated loops of bowel on plain film, sigmoid colon transition point on lower GI series. 2 months' age: Leveling colostomy performed for biopsy-proven HD. 5 months' age: Definitive endo-rectal pull-through	No anomalies detected on genetic testing.

Table 1. Reported cases of duodenal atresia combined with Hirschsprung disease. aNo further case details or patient characteristics provided in the literature.

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