



A case of split notochord syndrome: a child with a neuroenteric fistula presenting with meningitis

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Abstract The authors describe a case of split notochord syndrome with a neuroenteric fistula in a newborn presenting with meningitis. Associated anomalies included agenesis of the corpus callosum, short colon, malrotation, epispadias, and an abnormally high bifurcation of the abdominal aorta and inferior vena cava. The embryological mechanisms and etiologic theories are discussed in short.

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Split notochord syndrome (SNS) describes congenital spinal anomalies, associated with anomalies of the vertebrae, central nervous system, and gastrointestinal tract. The anomalies arise from a persistent connection between endoderm and dorsal ectoderm. Depending on its size, site, and point in time, abnormal splitting of the notochord can result in a wide variety of malformations and clinical symptomatology.

1. Case report

A 4-day-old boy was referred to our hospital on suspicion of meningitis with secondary dehydration and for evaluation of vertebral anomalies. He was born at 37 weeks of gestation through normal vaginal delivery as the third child of a 26-year-old mother. Birth weight was 3010 g. Physical examination revealed normal tonus, minor

facial dysmorphic signs (eg, broad mouth and dysmorphic, normally placed ears with a thin helix), left-sided congenital hip dysplasia, sacral dimple, and rocker bottom feet. The penis showed a mild epispadias, whereas anus, scrotum, and testes were normal. The mother had smoked during pregnancy and had not used supplementary folic acid. Besides local treatment of a vaginal yeast infection, no other medication had been used during pregnancy. The day before, the patient had been brought in at the referring hospital with a 2-day history of poor feeding and fever. He was jaundiced and showed a tachycardia at a body temperature of 39°C. Neurologic examination revealed high tonus and a bulging anterior fontanel. The abdomen was distended. Abdominal x-ray showed a spinal cleft of the vertebrae of Th 12 and L1 (Fig. 1). The kidneys were normal on ultrasound. Blood tests showed elevated C-reactive protein (109 mg/L) and white blood cell count (25,500 cells per cubic millimeter). No lumbar puncture was attempted because of the vertebral anomalies. Blood cultures showed growth of *Escherichia coli* bacteria, after which, antibiotic treatment was switched from amoxicillin/cefotaxim to meropenem.

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Fig. 1 Plain x-ray of the spine: showing spinal cleft of the vertebrae of Th 12 and L1.

Magnetic resonance imaging studies (including non-contrast T1- and T2-weighted images) of the brain, abdomen, and spine displayed a wide variety of congenital malformations (Figs. 2 and 3). The brain scan revealed complete agenesis of the corpus callosum with small periventricular calcifications. The abdominal scan showed a left-sided colon. A neuroenteric fistula was suspected at the splenic flexure. Bifurcations of the abdominal aorta and inferior vena cava were located immediately distal to the renal arteries.

Laparotomy by transverse incision, performed on day 16 of life, confirmed intestinal malrotation. A colonic stenosis was present. Proximal to the stenosis, a fistula of approximately 1 cm in diameter was found, leading into the vertebral cleft (Fig. 4). The fistula was resected and the stenosis was treated by enteroplasty. Postoperative recovery, with reintroduction of enteral feeding, was uneventful.

At the age of 5 months, the patient was readmitted with a mechanical ileus. At laparotomy, a restenosis seemed to be the causal factor. Resection and reanastomosis followed. Pathological examination of the resected bowel section showed presence of ciliary pseudolayered epithelia and ectopic tissue derivative of the stomach, esophagus, and pancreas.

At the age of 10 months, head circumference was found to grow steadily along the 99th percentile growth line. Magnetic resonance imaging studies of the brain clearly showed ventricular distension, but there were no signs of elevated intracranial pressure. Fundoscopy showed a

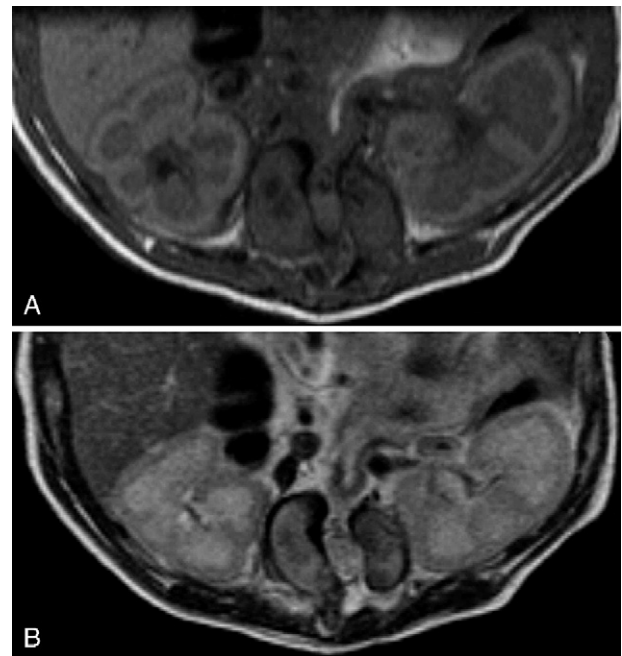


Fig. 2 Magnetic resonance imaging—vertebral column axial T1- and T2-weighted images: The magnetic resonance imaging study of the spine shows a ventral cleft of vertebral bodies Th 12 and L1. A bowel loop projects into this ventral cleft, and may have a connection with the dura. There is a broadened spinal canal.

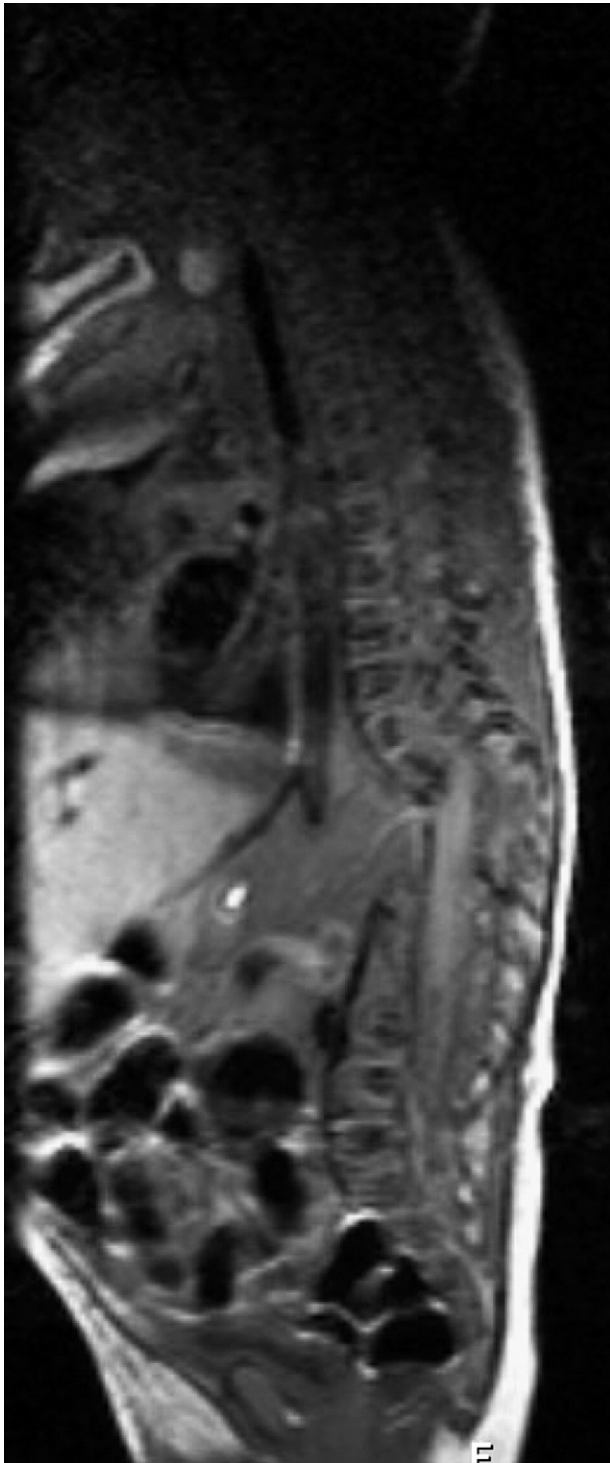


Fig. 3 Magnetic resonance imaging—vertebral column sagittal image: a bowel loop is visible, projecting into the vertebral column. There is a marked kyphoscoliosis. The sacral dimple, more caudally, is not connected to the spine or the spinal cleft.

normal papilla. Ventriculoperitoneal drainage was therefore not initiated.

Presently, at the age of 4 years, the patient's psychomotoric development shows impairment of gait with high deep-tendon reflexes and Babinski sign. Speech and mental



Fig. 4 Peroperative photograph showing a fistula, indicated by the arrow, leading from the colon into the vertebral cleft. The proximal colon is distended, and is indicated by "x."

development are age-adequate. He is macrocephalic with an occipital-frontal circumference (OFC) higher than 2.5 SD and has a marked kyphoscoliosis. Contrast study of the intestine showed no abnormalities except for malrotation of the colon.

The karyotype is normal (46,XY). The association of agenesis of corpus callosum with split notochord raised the suspicion of a microdeletion at chromosome 7q36 involving both the Sonic hedgehog (Shh) locus and the HLXB9 locus [1]. Callosal agenesis can be considered as a minimal manifestation of holoprosencephaly. Holoprosencephaly has been described in association with spinal anomalies and tethered cord, with detected deletions at chromosome 1p [2,3]. Fluorescence in situ hybridization studies were initiated. No deletion was detected at 7q36, nor at loci 1p32 or 1p36. Considering the importance of the Shh gene in the embryological development of the notochord and

Table 1 Associated anomalies, also mentioned by other authors of split notochord cases

Agenesis of corpus callosum	Kanmaz et al [11] Razack and Page [12]
Genital deformity	Dindar et al [13] (peniscrotal transposition) Faris and Crowe [14] (epispadias) Rosselet [15] (absent penis)
Kyphoscoliosis	Almog et al [16] Aydin et al [17] Kurisu et al [18] Singh and Singh [8]
Malrotation	Meller et al [20] Alrabeeah et al [9] Kheradpir and Ameri [19] Saunders [21]
Short colon	Kiristioglu et al [22] Pathak et al [23]
Skin dimple	Bentley and Smith [6] (case 3)

floor plate [4], the *Shh* gene was sequenced. No abnormalities could be identified. Multiplex ligation-dependent probe amplification of all chromosomal subtelomeric regions did not reveal any chromosomal aneuploidies [5]. Another emerging technique for detection of submicroscopic chromosome anomalies could be array comparative genomic hybridization. Unfortunately, this technique is not routinely available at our institution.

2. Discussion

The spectrum of SNS includes a wide variety of congenital anomalies of the spine, the nervous system, and the gastrointestinal tract. According to Bentley and Smith [6], visceral malformations can be classified into fistulae, sinuses, posterior enteric diverticula, and posterior enteric cysts. Complicated anomalies may be easy to detect, even antenatally [7]. Clinical presentation of SNS may include gastrointestinal obstruction or meningitis [8-10]. More subtle anomalies, such as spina bifida occulta, may be indicated only by the presence of hypertrichosis, a nevus, angioma, or a sacral dimple. Associated anomalies are diverse, and those present in our case as mentioned by others [6,8,9,11-22] are listed in Table 1. Bentley and Smith stated that malformations of the heart and the great vessels have also been associated with abnormal spinal development, but a ready explanation is not at hand [6].

During the third week of gestation, the human embryo consists of 3 embryological layers: ectoderm, mesoderm, and endoderm. By day 20, the notochordal process has appeared as a tube in the mesodermal layer. The ventral wall of the notochordal process then begins to fuse with the endoderm to form the notochordal plate. During a brief period, an open neuroenteric canal is formed between the yolk sac cavity and the amniotic cavity. The final remnants of this canal are located at the tip of the os coccygis. Then, the notochordal process creates the notochord. Somitomeres appear in the paraxial mesoderm, which form sclerotomes. These eventually give rise to the vertebral bodies, vertebral arches, and part of the back of the skull. Remains of yolk sac origin can differentiate into any tissue resembling a part of the gut or its embryological derivatives (eg, lung tissue). During the fourth week, the neural plate converts into the neural tube. Inadequate closure of the neural tube can result in vertebral anomalies. Fixation of the gut to, for example, the vertebral column, can inhibit adequate rotation [24].

Two main theories explain the etiology of SNS and the presence of neuroenteric fistula. The first, as suggested by Feller and Sternberg [25], stated that the embryological remains of the primitive knot persist and thereby cause the notochord to be cleft. Bremer [26] supported the second theory, which asserts that an accessory or ectopic neuroenteric canal is formed, passing through all the midline

structures of the back. Saunders suggested that this canal is formed within a localized duplication or cleft of the notochord, through which the endoderm (or primitive gut) herniates to adhere to the dorsal ectoderm [21]. Bentley and Smith [6] supported this theory. Beardmore and Wigglesworth suggested that adhesions between ectoderm and endoderm, possibly with an endomesenchymal tract formed around these adhesions (as suggested by Pang and Dias [27]), create an accessory neuroenteric canal, bisecting the developing notochord [28].

The ultimate form of the abnormality depends on the time and location of the split and the degree to which the split or adhesion persists. Because the spectrum of SNS is wide, treatment options should be individualized. In our case, which was the fourth reported case of SNS presenting with meningitis, treatment primarily consisted of identification and resection of the neuroenteric fistula.

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