Familial Congenital Short Small Bowel with Associated Defects

A Long-term Survival

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In 1974, Royer *et al.* described a familial syndrome consisting of a short and sluggish small bowel, malrotation of the gut, and pyloric stenosis. These authors stressed the uniformly fatal outcome of their four cases, as well as other possibly unrecognized cases previously described in the literature. The present report deals with two more familial cases, of which one represents a long-term survivor of the syndrome. The intensive work of maintaining nutrition, controlling infection, and managing the complications of associated defects are described.

A FAMILIAL SYNDROME consisting of a short small intestine, malrotation of the gut, and pyloric stenosis was first described in four infants by Royer *et al.* in 1974.[1] Intestinal dilation, poor motility, and episodes of obstruction also were features of this syndrome, which was uniformly fatal. It is the purpose of this communication to report two new cases in one family, one of whom survived. We believe this to be the first long-term survival of an infant with the complete syndrome.

Case Reports

Case 1

This infant was admitted to another hospital at 18 days of age with fecal vomiting and diarrhea. He was the product of a full-term pregnancy complicated by polyhydramnios and a breech presentation, and delivered by cesarean section. Severe dehydration and marked abdominal distension were present on admission. Laparotomy revealed duodenal bands, mesenteric adhesions, and malrotation of the colon with normal common mesentery; the thickened dyskinetic small intestine was only 65 cm long.

The infant underwent three more laparotomies for what appeared clinically to be necrotizing enterocolitis, but this was not confirmed. He died at 9 weeks of age with *Klebsiella* peritonitis and sepsis, complicated by gram-negative shock and renal failure.

Autopsy revealed extensive acute and chronic peritonitis with dense fibrous adhesions and thickened, leathery walls of the gastrointestinal tract. Mixed flora were recovered from multiple loculated collections of cloudy peritoneal fluid. Normal appearing ganglion cells were present in the gastrointestinal tract. There was ischemic necrosis of the kidney, centrilobular necrosis of the liver, and hemorrhage into the lung, liver, and adrenals. A patent ductus arteriosus and a single mesenteric artery also were found.

Case 2

The brother of case 1 was admitted to the New York University Hospital at 6 weeks of age because of failure to thrive, vomiting, and frequent mucoid, watery stools. He was a full-term infant, whose birth weight was 3.29 kg. His parents are not related but are from the same small town in Yugoslavia. The family history is relevant and is documented in Figure 1.

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On admission, temperature, pulse, and respiration were normal; weight 3.55 kg; length 53 cm. The infant was pale, listless, and emaciated. A faint systolic thrill was palpated at the precordium, and a crescendo systolic murmur with a slight spill into early diastole was present at the left base.

The abdomen was distended, and bowel sounds were diminished. An ECG revealed left ventricular hypertrophy; the findings on chest x-ray were compatible with a diagnosis of patent ductus arteriosus. X-rays of the abdomen demonstrated distention of the small intestine and air fluid levels. The upper gastrointestinal series demonstrated a peculiar pattern of scattered barium, which persisted for 5 days. The colon was of normal size. All other laboratory investigations, including serum gastrin levels and chromosomal studies, were normal. Serum norepinephrine was 779 pg/ml (nl 256 ± 84), epinephrine 324 pg/ml (nl 97 ± 50), dopamine 17 (nl 27 ± 12).

The infant became obstructed on the sixth day of hospitalization, and laparotomy was performed after hydration and decompression. Operative findings included malrotation of the gut and the common mesentery, normally present in the 7- to 10-week fetus; numerous mesenteric membranes; duodenal bands; and pyloric stenosis. The small bowel was adynamic and distended, with a diameter equal to that of the colon; it was 72 cm long (normal 200 to 300 cm with a mean of 250 cm). The pyloric stenosis was repaired, the bands and membranes lysed, and an appendectomy performed. Normal ganglion cells were present in the appendix. Total parenteral alimentation (TPN) was started, and although bowel contractions returned in 1 week, the patient continued to vomit. An upper gastrointestinal series performed 3 weeks later demonstrated a sharp arrest of the barium at the third portion of the greatly dilated duodenum. A second laparotomy confirmed these findings but did not reveal any mechanical obstruction. Hence, serial full-thickness mucosal biopsies were taken from the duodenum to the rectum; normal ganglion cells were found in all specimens.

Although bowel sounds returned slowly, the infant continued to vomit. Cinefluoroscopic examination of the intestine, performed with barium, demonstrated that the contrast medium went past the duodenum only when the patient was placed in the prone position; this suggested the diagnosis of a superior mesenteric artery syndrome. Very active peristalsis was seen when repeated subcutaneous injections of urecholine 1.5 mg were given. Therapy with urecholine and maintenance in the prone position after feeding allowed him to tolerate larger volumes of formula, but it was still impossible to maintain his nutrition without intravenous supplementation. Attempts to reach the jejunum with various types of feeding tubes also were unsuccessful. A proximal feeding jejunostomy at 5 months of age and a side-to-side jejunostomy performed a month later, in an effort to bypass the site of obstruction, were unsuccessful in reducing the vomiting to a point at which nutrition could be maintained solely with oral feeding. Intravenous alimentation was continued until 22 months of age.

A number of acute episodes of temperature elevation, increased abdominal distention, and generalized abdominal tenderness characterized by guarding and flexion of the thighs on the abdomen occurred between 6 and 18 months of age. Leukocytosis was a constant feature, and in addition, the

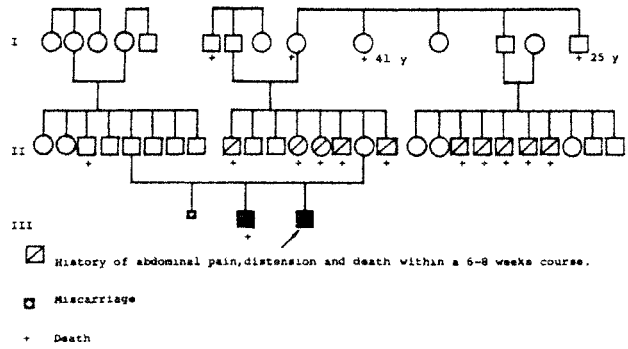

FIG. 1. Family tree of Cases 1 and 2.

spleen became enlarged on a number of occasions. On the basis of past experience with his older brother, these episodes were considered to be peritonitis and were treated with various combinations of antibiotics. They were complicated on 10 occasions by disseminated intravascular coagulation (DIC), which readily responded to heparin, antibiotic therapy, and witholding of the TPN. Seven positive blood cultures were obtained; *Candida* was found on five occasions, and in addition, various types of bacteria were cultured. The patient was placed on oral nystatin therapy at 17 months of age in an attempt to prevent a recurrence of the *Candida* septicemia seeding from the gut. From then on, there were no recurrences in spite of continued TPN. Parenteral antifungal agents were not used.

Other complications included the onset of cardiac failure at 6½ months of age. This was treated with digitalis until surgical correction of his patent ductus arteriosus (PDA) could be performed at 20 months of age. There was also an episode of pneumonia and pulmonary hemorrhage that resulted in a short period of respiratory arrest. Following the PDA ligation, the patient was able to tolerate gradually larger amounts of oral feeding. Five months later, it was possible to discharge him from the hospital. At this time he weighed 8.6 kg, his length was 84 cm, and he was unable to stand or walk alone. The Denver Developmental Test disclosed a delay of approximately 1 year. He was on a lactose-free, but otherwise normal, diet.

At 5½ years of age, he weighed 20 kg (25th percentile) and his height was 102 cm (third percentile). He was symptom-free, but his abdomen remained distended and the bowel sounds were hypoactive.

Discussion

Only four other familial cases[2–5] with all the features of the syndrome described by Royer *et al.* have been reported since the original description in 1974. A single case, reported by Kern and Harris in 1973,[6] also seems to fit into this syndrome. All nine cases died early in infancy despite various trials of supportive therapy; the longest survival was 160 days. The long survival in the present case may have been due to the prolonged intravenous alimentation, control of infection, and the

management of numerous other life-threatening complications.

The familial incidence of all the reported cases suggests a genetic origin.[1-3,5] Here the history is suggestive of a sex-linked transmission, although an autosomal recessive mode cannot be ruled out. This syndrome probably represents a deviation in development occurring between the 7th and 10th weeks of embryonal life, since lengthening of the small gut and fixation of the cecum take place at that time.[7-9] Since atresia of the bowel has not been an associated feature, this syndrome would not seem to be the result of infection or of thrombosis of a major vessel.[3] In case 1, only one mesenteric artery was found at autopsy, but in Case 2, angiography of the abdominal aorta failed to demonstrate this. Again, an anomaly of the vessels supplying the gut is an unlikely explanation for the malformation.

The cause of the *motility disturbance* has not been adequately explained either. Although Royer believed that this is due to an absence or a decreased number of argyrophil ganglion cells, other investigators have not been able to confirm this finding. The ganglia were anatomically normal in our present case. Some aberration in catecholamine metabolism might be a contributing factor; plasma norepinephrine and epinephrine were found to be elevated while dopamine was normal. This may have been fortuitous, but the latter hormones have been known to be inhibitory to gut peristalsis. Our patient's response to urecholine also can be considered suggestive of an abnormality at this level. It is possible that the hypomotility is simply the end result of lack of synthesis of neurotransmitters. The dilation that occurs whenever there is marked shortening of the small bowel is a compensatory mechanism, attempting to enhance the absorptive capacity of the gut. In addition, hyperplasia with mucosal redundancy has been observed.

Additional malformations also may be associated with the syndrome. A PDA was present in our two cases and also in one of the original patients.[1] Surgical repair of the latter anomaly should be undertaken early. Our patient dramatically improved after ligation of the PDA. The role of better perfusion of the gut may have been a factor.

The experience with our patient suggests that survival of these children is possible if they can be maintained long enough with supportive therapy, infections controlled or prevented, and associated important malformations corrected. In time, some maturation may occur that can overcome the original deficiencies of gastrointestinal function, so that growth and development may resume. Continued observation of this patient will be maintained to determine if this syndrome is compatible with normal growth and development throughout childhood.

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