Hirschsprung’s Disease

by Lakshmi Pasumarthy, James W. Srour

Hirschsprung’s disease is an unusual, but well-recognized cause of chronic constipation in young children. It is suspected in cases of low gastrointestinal obstruction in the neonatal period, or in cases of chronic severe constipation in childhood. It is characterized by an absence of ganglion cells in the distal bowel beginning at the internal sphincter and extending proximally for varying distances, and diagnosed by pathological examination of rectal biopsies. Early recognition of Hirschsprung’s disease before the onset of complications is essential in reducing morbidity and mortality. There are multiple genetic abnormalities associated with the disorder, Down’s syndrome being the most common.

Hirschsprung’s disease is caused by failure of ganglion cells to migrate completely through the neural crest during the first trimester of gestation. This causes an absence of ganglion cells in all or part of the colon. The result is functional obstruction, because the affected segment of bowel fails to relax. Ultra-short-segment Hirschsprung’s disease involves only a few centimeters proximal to the dentate line. Short segment disease is defined as absence of ganglion cells in the rectosigmoid area—this is the most common form. Long segment can involve the entire colon. Very rarely it can involve the small intestine, as well.

EPIDEMIOLOGY

Hirschsprung’s disease occurs about 1 in 5,000 births and affects males more frequently than females. Siblings of patients are also at risk with males being more commonly affected than females (4% as opposed to 1%), with the rates increasing substantially if the patient has total colonic involvement (13%–33%).

GENETICS

Current research interest is focused on RET proto-oncogene on 10q11.2 which accounts for 50% of familial and 20% of sporadic cases and is especially seen in patients with long segment disease. RET proto-oncogene is associated with multiple endocrine neoplasia, type IIA in which increased incidence of medullary carcinoma of the thyroid and adrenal tumors are noted. Defects in SOX10 (22q13) have been associated with Hirschsprung’s disease and Waardenburg syndrome.

There are eight genomes associated with the disorder. Down syndrome is the most common chromosomal abnormality associated with the disease, accounting for 10% of the cases (1) Hirschsprung’s disease may be associated with other congenital defects, including Smith-Lemli-Opitz, Waardenburg, cartilage-hair hypoplasia, and congenital hypoventilation (“Ondine curse”) syndromes and urogenital or cardiovascular abnormalities (2).

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ETIOPATHOLOGY

Hirschsprung’s disease is the result of an absence of ganglion cells in the bowel wall, extending proximally and continuously from the anus for a variable distance. The aganglionic segment is limited to the rectosigmoid in 75% of patients; in 10% the entire colon lacks ganglion cells. Total bowel aganglionosis is rare. Histological specimens are noteworthy for absence of Meissner and Auerbach plexus and hypertrophied nerve bundles with high concentrations of acetylcholinesterase between the muscular layers and in the submucosa. Failure to pass stool leads to dilatation of the proximal bowel and abdominal distention. As the bowel dilates, intraluminal pressure increases, resulting in decreased blood flow and deterioration of the mucosal barrier. Stasis allows proliferation of bacteria within the colon, which may lead to enterocolitis with associated sepsis and signs of bowel obstruction. Early recognition of Hirschsprung disease before the onset of enterocolitis is essential in reducing morbidity and mortality. Hirschsprung’s disease—associated enterocolitis occurs more frequently in the first three months of life, in patients with delayed diagnosis, in trisomy 21, and with long-segment involvement; females and patients with a positive familial history also are more frequently affected.

SYMPTOMS

1. Inability to pass meconium in the first 24 hours in a full term infant—seen in 90% of cases. Hirschsprung’s disease should strongly be considered in an infant who has not passed meconium in first 24–48 hours. Breast fed infants manifest symptoms less often and the constipation is less severe because the high concentration of lactose in breast milk produces watery stools that are passed more easily. Once weaned off, the symptoms become more apparent.
2. Poor feeding, often associated with failure to thrive.
3. Progressive abdominal distention, variable but significant constipation.
4. Bilious vomiting.
5. Blood tinged diarrhea must raise the suspicion of enterocolitis—this complication is associated with 30% mortality.

SIGNS

1. Anemia and evidence of malnutrition are common.
2. The abdomen may be distended due to retention of feces, and peristaltic waves may be visible.
3. Rectal examination demonstrates tight anal sphincter and is usually followed by an explosive discharge of foul-smelling feces and gas.

DIFFERENTIAL DIAGNOSIS

1. Meconium plug syndrome—Some newborns present with bowel obstruction from plugs of meconium obstructing the colon. Most of these newborns are otherwise healthy babies, but all should undergo a contrast enema—which almost always is diagnostic in that no pathology is found—as well as therapeutic. Conditions predisposing to meconium plug syndrome are maternal preeclampsia, maternal diabetes mellitus, maternal administration of magnesium sulfate, prematurity, sepsis, and hypothyroidism.
2. Meconium ileus—Meconium ileus is the earliest manifestation of cystic fibrosis in the newborn period. In this condition, the distal small-bowel is obstructed from thickened meconium in patients with cystic fibrosis. Prenatal ultrasonography or neonatal plain radiography may identify a soap bubble or ground glass appearance of inspissated meconium. Treatment of meconium ileus involves evacuation of the meconium. In more than 50% of patients, nonsurgical management relieves the obstruction successfully. A contrast enema may be both diagnostic and therapeutic.
3. Anal atresia—Routine inspection of a newborn should note the position and patency of the anus. Anorectal malformations range from slight anterior displacement of the anal opening to a completely imperforate anus. Many children with imperforate anus have internal fistulas between the rectum and the genitourinary structures.
4. Neuronal intestinal dysplasia—Characterized by hyperplasia of submucosal plexus and by increased numbers of acetylcholinesterase positive nerve fibers in the adventitia of submucosal blood vessels.
5. Functional constipation—This entity presents in the older child and is characterized by distended rectal vault with large amount of fecal material.
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IMAGING
1. Plain X-ray of the abdomen shows gaseous distention of the bowel, evidence of obstruction and absence of gas in the pelvis (Figure 1).
2. An unprepped (unprepped prevents transient dilatation of the aganglionic segment) single contrast Barium enema reveals a “transition zone” (Figure 2a)—a funnel shaped area between the narrowed aganglionic distal segment and the dilated ganglionic proximal segment. Twenty-four-hour delayed films are helpful. If significant barium is still present in the colon, it increases the suspicion of Hirschsprung’s disease even if transition zone is not identified (Figure 2b). This study is not diagnostic in the first two-to-three weeks of life; it may also be difficult to interpret the study in cases of short segment or total colonic involvement (3). Contrast enemas should be avoided in patients with enterocolitis because of the risk of perforation (4).

DIAGNOSIS
Early diagnosis is important to prevent complications such as enterocolitis, colonic rupture. Rectal manometry and rectal suction biopsy are often used and are the most reliable indicators of Hirschsprung’s disease. Anorectal manometry measures the pressure of the internal anal sphincter while a balloon is distended in the rectum. In normal individuals, rectal distention initiates a reflex decline in internal sphincter pressure. In patients with Hirschsprung’s disease, the pressure fails to drop or there is a paradoxical rise in pressure with rectal distention. The accuracy of this diagnostic test is more than 90%, but it is technically difficult in young infants (5). A normal response in the course of manometric evaluation excludes a diagnosis of Hirschsprung’s disease.

The diagnosis is confirmed by rectal suction biopsy which should reveal the absence of ganglion cells and the

Figure 1.
Rectal ampulla is enlarged. By history, the physician should be able to elicit withholding pattern, fear of defecation. Barium enema reveals large amount of stool and no evidence of transitional zone.

Figure 2.
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presence of hypertrophied nerve trunks (6). A full-thickness rectal biopsy may be performed at the time of surgery to confirm the diagnosis and level of involvement. It is also indicated if the rectal suction biopsy is inconclusive. Of note, rectal suction biopsies should be performed no closer than 20 cm to the dentate line to avoid the normal area of hypoganglionosis at the anal verge.

TREATMENT

Pre-operative Management

Concomitant with measures to secure a diagnosis, the patient is decompressed with a nasogastric (or orogastric) tube and rectal irrigations. This has been felt to decrease the risk of preoperative Hirschsprung’s enterocolitis. Any fluid or electrolyte imbalances should be corrected. Severe malnutrition is unusual but if identified, should be treated. If successful intestinal decompression has been accomplished, primary pull through may be undertaken in some patients. Some pediatric surgeons have had success in managing patients with Hirschsprung’s with home rectal irrigations for weeks prior to definitive surgery; this prevents enterocolitis and allows for decompression (4). This has been preferred in some cases since it allows small babies the chance to increase in size and weight prior to surgery.

Surgery

If a staged approach is planned, colostomy should be performed as soon as the diagnosis is confirmed by rectal biopsy. Immediate operation should be undertaken if irrigations are ineffective. The occurrence of definite enterocolitis preoperatively is usually considered a contraindication for primary pull-through, and a leveling colostomy should be performed. For neonates who are first treated with a diverting colostomy, the transition zone is identified and the colostomy is placed proximal to this area. The presence of ganglion cells at the colostomy site must be unequivocally confirmed by a frozen-section biopsy. Either a loop- or end-stoma is appropriate, usually based on the surgeon’s preference. Contraindications to a one-stage procedure include massively dilated proximal bowel, severe enterocolitis, perforation, malnutrition, and inability to accurately determine the transition zone by frozen section. The presence of other associated anomalies may also dictate a staged approach. Broad-spectrum antibiotics are given prophylactically. Colostomy allows the colon to return to a more normal size.

There are three procedures described by Swenson, Duhamel and Soave, the common goal of all being to preserve the distal 1 cm of the anorectum. This allows for continence of bowel. Swenson’s operation involves removing the rectum, pulling the healthy ganglionated colon through, and connecting it to the anus. Laparoscopic repairs have been described to achieve the same results (7).

Post operative complications include anastomotic leaks and strictures, and wound infection. Children with involvement of longer segments often have malabsorption, fluid and electrolyte disturbances. Constipation persists in 15%–20% of children either because of residual disease or intestinal neuronal dysplasia. Severe constipation is treated primarily by dietary manipulation, stool softeners, laxatives and occasionally anal dilatation (stretching).

Later complications associated with surgical management of Hirschsprung disease include enterocolitis (8), continued obstructive symptoms, and incontinence. Approximately 70% to 85% of patients eventually achieve excellent results, with normal bowel habits, no soiling and infrequent constipation.

Neurologically impaired children or those with Down syndrome generally do not fare as well as other children. They have a two-to-threefold increase in incontinence or severe constipation.

References