Hirschsprung's Disease

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Background:

Hirschsprung's disease is a developmental disorder of the enteric nervous system and is characterized by an absence of ganglion cells in the distal colon resulting in a functional obstruction. Although this condition was described by Ruysch in 1691 and popularized by Hirschsprung in 1886, the pathophysiology was not clearly determined until the middle of the 20th century when Whitehouse and Kernohan described the aganglionosis of the distal intestine as the cause of obstruction in their series of patients (Whitehouse, 1948). In 1949, Swenson described the first consistent definitive procedure for Hirschsprung's disease, rectosigmoidectomy with coloanal anastomosis. Since then, other operations have been described, including the Duhamel and Soave techniques. More recently, advances in surgical technique, including minimally invasive procedures, and earlier diagnosis have resulted in decreased morbidity and mortality for patients with Hirschsprung's disease.

Pathophysiology:

Congenital aganglionosis of the distal bowel defines Hirschsprung's disease. Aganglionosis begins with the anus, which is always involved, and continues proximally for a variable distance. Both intermuscular (myenteric) (Auerbach) and submucosal (Meissner) plexus are absent, resulting in reduced bowel peristalsis and function. The precise mechanism underlying the development of Hirschsprung's disease is unknown. Enteric ganglion cells are derived from the neural crest. During normal development, neuroblasts will be found in the small intestine by the 7th week of gestation and will reach the colon by the 12th week of gestation (Okamoto, 1967). One possible etiology for Hirschsprung's disease is a defect in the migration of these neuroblasts down their path to the distal intestine. Alternatively, normal migration may occur with a failure of neuroblasts to survive, proliferate, or differentiate in the distal aganglionic segment. Abnormal distribution in affected intestine of components required for neuronal growth and development, such as fibronectin, laminin, neural cell adhesion molecule (NCAM), and neurotrophic factors, may be responsible for this theory (Langer, 1994; Tosney, 1986). Additionally, the observation that the smooth muscle cells of aganglionic colon are electrically inactive when undergoing electrophysiologic studies also points to a myogenic component in the development of Hirschsprung's disease (Kubota, 2002). Finally, abnormalities in the interstitial cells of Cajal, pacemaker cells connecting enteric nerves and intestinal smooth muscle have also been postulated as an important contributing factor (Ward, 2001; Vanderwinden, 1996).

Frequency:

- The exact worldwide frequency is unknown, although international studies have reported rates ranging from approximately 1 case per 1500 newborns to 1 case per 7000 newborns (Meza-Valencia, 2005; Russell, 1994).

Mortality/Morbidity:

- Approximately 20% of infants will have one or more associated abnormality involving the neurological, cardiovascular, urological, or gastrointestinal system (Ryan, 1992). Hirschsprung's disease has been found to be associated with the following:
  Down syndrome.
  Neurocristopathy syndromes.
  Waardenburg-Shah syndrome.
  Yemenite deaf-blind syndrome.
  Piebaldism.
  Goldberg-Shprintzen syndrome.
  Multiple endocrine neoplasia type II.
  Congenital central hypoventilation syndrome.
- Untreated aganglionic megacolon in infancy may result in a mortality rate of as much

as 80%. Operative mortality rates for any of the interventional procedures are very low. Even in cases of treated Hirschsprung disease, the mortality rate may be as high as 30% as a result of enterocolitis.

- Possible complications of surgery include anastomotic leak (5%), anastomotic stricture (5-10%), intestinal obstruction (5%), pelvic abscess (5%), and wound infection (10%). Long-term complications include ongoing obstructive symptoms, incontinence, and enterocolitis. Although many patients will encounter one or more of these problems postoperatively, long-term follow-up studies have shown that most children experience significant improvement and will do relatively well (Yanchar, 1999). Patients with an associated syndrome and those with long-segment disease have been found to have poorer outcomes (Caniano, 1990; Hackam, 2003).

Race : The disease has no racial predilection.

Sex : Hirschsprung's disease occurs more often in males than females, with a male-to-female ratio of approximately 4:1. However, with long-segment disease, the incidence increases in females.

Age : Hirschsprung's disease is uncommon in premature infants.

- The age at which Hirschsprung's disease is diagnosed has progressively decreased over the past century. In the early 1900s, the median age at diagnosis was 2-3 years; from the 1950s to 1970s, the median age was 2-6 months.
- Currently, approximately 90% of patients with Hirschsprung's disease are diagnosed in the newborn period.

Clinical presentation:

History:

- Approximately 10% of patients have a positive family history. This is more common in patients with longer segment disease.
- Hirschsprung's disease should be considered in any newborn with delayed passage of meconium or in any child with a history of chronic constipation since birth. Other symptoms include bowel obstruction with bilious vomiting, abdominal distention, poor feeding, and failure to thrive.
- Prenatal ultrasound demonstrating bowel obstruction is rare except in cases of total colonic involvement (Belin, 1995).
- Older children with Hirschsprung's disease have usually had chronic constipation since birth. They may also show evidence of poor weight gain.
- Older presentation is more common in breastfed infants who will typically develop constipation around the time of weaning.
- Despite significant constipation and abdominal distension, children with Hirschsprung's disease rarely develop encopresis. In contrast, children with functional constipation or stool-withholding behaviours more commonly develop encopresis.
- About 10% of children may present with diarrhea caused by enterocolitis, which is thought to be related to stasis and bacterial overgrowth. This may progress to colonic perforation, causing life-threatening sepsis (Teitelbaum, 2003).

Physical examination:

- Physical examination in the newborn period is usually not diagnostic, but it may reveal a distended abdomen and/or spasm of the anus.
- A low imperforate anus with a perineal opening may have a similar presentation to that of a patient with Hirschsprung's disease. Careful physical examination differentiates the two.
- In older children, however, a distended abdomen resulting from an inability to release flatus is not uncommon (Teitelbaum, 2003).

Investigations:

Lab studies:

- Chemistry panel: For most patients, electrolyte and renal panel findings are within reference ranges. Children presenting with diarrhea may have findings consistent with dehydration. Test results may aid in directing fluid and electrolyte management.
- CBC count: This test is obtained to ensure that the preoperative hematocrit and platelet

count are suitable for surgery. In most cases, values are within reference ranges.

- Coagulation studies: These studies are obtained to ensure that clotting disorders are corrected before surgery. Again, values are expected to be within reference ranges.

Imaging studies:

- Plain abdominal radiographs may show distended bowel loops with a paucity of air in the rectum.
- Barium enema:
  * Avoid washing out the distal colon with enemas before obtaining the contrast enema because this may distort a low transition zone.
  * The catheter is placed just inside the anus, without inflation of the balloon, to avoid distortion of a low transition zone and the risk of perforation.
  * Radiographs are taken immediately after hand injection of contrast and again 24 hours later.
  * A narrowed distal colon with proximal dilatation is the classic finding of Hirschsprung's disease after a barium enema. However, findings in neonates (i.e. babies aged <1 mo) are difficult to interpret and will fail to demonstrate this transition zone approximately 25% of the time (Smith, 1991).
  * Another radiographic finding suggestive of Hirschsprung's disease is the retention of contrast for longer than 24 hours after the barium enema has been performed.

Other tests:

- Anorectal manometry:
  *Anorectal manometry detects the relaxation reflex of the internal sphincter after distension of the rectal lumen. This normal inhibitory reflex is thought to be absent in patients with Hirschsprung's disease (Pensabene, 2003).
  *Swenson initially used this test. In the 1960s, it was refined but has recently fallen into disfavor because of its many limitations. A normal physiological state is required, and sedation is also usually necessary. Although some authors find this test quite useful, false-positive results have been reported in up to 62% of cases, and false-negative results have been reported in up to 24% of cases.
  * Because of these limitations and questionable reliability, anorectal manometry is not commonly used in the United States.
- Because cardiac malformation (2-5%) and trisomy 21 (5-15%) are associated with congenital aganglionosis, cardiac evaluation and genetic testing may be warranted.

Procedures:

- Rectal biopsy:
  * The definitive diagnosis of Hirschsprung's disease is confirmed by rectal biopsy, i.e. findings that indicate an absence of ganglion cells.
  * The definitive method for obtaining tissue for pathologic examination is by a full-thickness rectal biopsy.
  * The specimen must be obtained at least 1.5 cm above the dentate line because aganglionosis may normally be present below this level.
  * Disadvantages include the potential for bleeding and scarring and the usual need for general anesthesia during full-thickness biopsy procedures.
  * Simple suction rectal biopsy:
  * More recently, simple suction rectal biopsy has been used to obtain tissue for histologic examination.
  * Rectal mucosa and submucosa are sucked into the suction device, and a self-contained cylindrical knife cuts off the tissue.
  * The distinct advantage of the suction biopsy is that it can be easily performed at the bedside.
  * However, pathologically diagnosing Hirschsprung's disease from samples obtained by suction biopsies is considerably more difficult than pathologically diagnosing Hirschsprung's disease from samples obtained by a full-thickness biopsy.
  * Ease of diagnosis has been improved with the use of acetylcholinesterase staining, which intensely stains the hypertrophied nerve fibres throughout the lamina propria and muscularis propria.

Histologic Findings: Both the myenteric (Auerbach) and submucosal (Meissner) plexuses are absent from the bowel wall. Hypertrophied nerve trunks enhanced with acetylcholinesterase stain are also observed throughout the lamina propria and muscularis propria.

A barium enema showing a rectosigmoid Hirschsprung's disease.

A barium enema showing a "long segment" HSD. The transition zone is in the transverse colon. The arrow demonstrates the area of the transition zone between the enlarged area which has ganglion cells (normal) and the small area which does not.

Medical Care: The general goals of medical care are 3-fold: (1) to treat the complications of unrecognized or untreated Hirschsprung's disease, (2) to institute temporary measures until definitive reconstructive surgery can take place, and (3) to manage bowel function after reconstructive surgery.

- Management of complications of recognized aganglionosis is directed toward reestablishing normal fluid and electrolyte balance, preventing bowel overdistension (with possible perforation), and managing complications such as sepsis. Thus, intravenous hydration, nasogastric decompression, and, as indicated, administration of intravenous antibiotics remain the cornerstones of initial medical management.
- Colonic lavage, consisting of mechanical irrigation with a large-bore rectal tube and large volumes of irrigant, may be required.
- Balanced salt solutions may help prevent electrolyte imbalances.
- Nasogastric decompression, intravenous fluids, antibiotics, and colonic lavage may also need to be used in postoperative patients who develop enterocolitis as a complication. Sodium cromoglycate, a mast cell stabilizer, has been reported to be of benefit in these patients as well (Rintala, 2001).
- Routine colonic irrigation and prophylactic antibiotic therapy have been proposed as a means of decreasing the risk of enterocolitis (Marty, 1995; Elhalaby, 1995).
- Injecting the nonrelaxing internal sphincter mechanism with botulinum toxin (BOTOXÆ) has recently been shown to induce more normal patterns of bowel movements in postoperative patients with enterocolitis.

Surgical care:

* Surgical management of Hirschsprung's disease begins with the initial diagnosis, which often requires a full-thickness rectal biopsy. Traditionally, treatment also includes creating a diverting colostomy at the time of diagnosis, and, once the child grows and weighs more than 10 kg, the definitive repair is performed.
* This standard of treatment was developed in the 1950s after reports of relatively high leak and stricture rates with the

single stage procedure were initially described by Swenson. However, with the advent of safer anesthesia and more advanced hemodynamic monitoring, a primary pull-through procedure without a diverting colostomy is increasingly being performed. 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.

* 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.
* A number of definitive procedures have been used, all of which have demonstrated excellent results in experienced hands. The 3 most commonly performed repairs are the Swenson, Duhamel, and Soave procedures. Regardless of the pull-through procedure chosen, cleaning the colon prior to definitive repair is necessary.

- Swenson procedure:
  * The Swenson procedure was the original pull-through procedure used to treat Hirschsprung's disease.
  * The aganglionic segment is resected down to the sigmoid colon and the remaining rectum, and an oblique anastomosis is performed between the normal colon and the low rectum.
- Duhamel procedure:
  * The Duhamel procedure was first described in 1956 as a modification to the Swenson procedure.
  * Key points are that a retrorectal approach is used and a significant portion of aganglionic rectum is retained.
  * The aganglionic bowel is resected down to the rectum, and the rectum is oversewn. The proximal bowel is then brought through the retrorectal space (between the rectum and sacrum), and an end-to-side anastomosis is performed on the remaining rectum.
- Soave (endorectal) procedure:
  * The Soave procedure was introduced in the 1960s and consists of removing the mucosa and submucosa of the rectum and pulling the ganglionic bowel through the aganglionic muscular cuff of the rectum.

Diagram showing rectosigmoidectomy (Swenson procedure).

Diagram showing Retrorectal pull-through (Duhamel procedure).

  * The original operation did not include a formal anastomosis, relying on scar tissue formation between the pull-through segment and the surrounding aganglionic bowel. The procedure has since been modified by Boley to include a primary anastomosis at the anus.

Diagram showing Endorectal pull-through (Soave Procedure).

Anorectal myomectomy:

* For children (and occasionally adults) with ultrashort-segment Hirschsprung's disease, removing a strip of posterior midline rectal wall is an alternative surgical option.
* The procedure removes a 1-cm wide strip of extramucosal rectal wall beginning immediately proximal to the dentate line and extending to the normal ganglionic rectum proximally.
* The mucosa and submucosa are preserved and closed.

- Procedures for long-segment Hirschsprung's disease:
  * Patients with total colonic involvement require modified procedures to bypass the aganglionic colon yet preserve the absorptive surface area and allow for proper growth and nutritional support.
  * Most procedures include a side-to-side anastomosis of the ganglionic/propulsive small bowel to a short segment of the aganglionic/absorptive colon.
  * Whether a short right colonic patch or a small bowel-to-rectal wall Duhamel anastomosis is created is perhaps less important than maintaining a short patch length (<10 cm).
  * Long-segment anastomoses, such as the Martin procedure, are no longer advocated.
- A laparoscopic approach to the surgical treatment of Hirschsprung's disease was first described in 1999 by Georgeson. The transition zone is first identified laparoscopically, followed by mobilization of the rectum below the peritoneal reflection. A transanal mucosal dissection is performed, followed by prolapsing of the rectum through the anus and anastomosis. Functional outcomes appear to be equivalent to open techniques based on short-term results (Georgeson, 1999; de Lagausie, 1999; Curran, 1996).
- Transanal pull-through in which no intra-abdominal dissection is performed has also been described (Langer, 1999; De La Torre-Mondregan, 1998). The entire procedure is performed from below in a manner similar to perineal rectosigmoidectomy. The transition zone is identified and anastomosis is performed. Similar to the laparoscopic approach, outcomes have been similar to open single stage approaches with the benefits of minimal analgesia and shortened hospital stays (Langer, 1999; De La Torre, 2000).

Complications:

- Potential complications for the complex operations associated with Hirschsprung's disease encompass the entire spectrum of GI surgical complications.
- Complications may include an increased incidence of postoperative enterocolitis with the Swenson procedure, constipation following the Duhamel repair, and diarrhea and incontinence with the Soave pull-through procedure.
- In general, the complications are anastomotic leak (5%), anastomotic stricture (5-10%), intestinal obstruction (5%), pelvic abscess (5%), and wound infection (10%).
- Later complications associated with surgical management of Hirschsprung's disease include enterocolitis, continued obstructive symptoms, and incontinence.
- Enterocolitis accounts for significant morbidity and mortality in patients with Hirschsprung's disease.
- Enterocolitis results from an inflammatory process of the mucosa of the colon or small intestine. As the disease progresses, the lumen of the intestine becomes filled with fibrinous exudate and is at increased risk

for perforation. This process may occur in both the aganglionic and ganglionic portion of the bowel.

- Patients typically present with explosive diarrhea, abdominal distention, fever, vomiting, and lethargy.
- Approximately 10-30% of patients with Hirschsprung's disease develop enterocolitis. Long-segment disease is associated with an increased incidence of enterocolitis. Moreover, the risk of developing enterocolitis remains despite surgical correction.
- Treatment consists of intravenous antibiotics and aggressive colonic irrigations. Some authorities advocate decompression of the bowel, especially in patients with long-segment disease, with an enterostomy placed proximally to the transition zone.
- Patients may present postoperatively with abdominal distension, vomiting, or constipation indicative of ongoing obstruction (Dasgupta, 2004).

Special concerns:

- Ultrashort-segment Hirschsprung's disease:
  * Ultrashort-segment Hirschsprung's disease is characterized by a few centimeters of aganglionic bowel in the rectum, adjacent to the anus.
  * Recognizing this condition can be very difficult. These patients are not typically diagnosed with Hirschsprung's disease until they are older.
  * The principal symptom is severe constipation that usually begins between the ages of 6-12 months (Angerpointner, 2005).
  * Barium enemas tend not to demonstrate a transition zone.
  * Anorectal manometry is useful in the workup of these patients and demonstrates an absent anorectal reflex, but the definitive diagnosis is made by rectal biopsy.
  * A definitive pull-through procedure is usually unnecessary because most patients with ultrashort-segment disease can be satisfactorily treated with a surgical myomectomy. This involves resecting a longitudinal strip of the posterior muscular wall of the rectum.
- Total colonic aganglionosis:
  * Total colonic aganglionosis is a more severe form of Hirschsprung's disease in which the entire colon and even some of the small intestine is aganglionic. It occurs in 3-12% of cases and extends to the terminal ileum in about 75% of cases, to the mid-ileum in about 20% of cases, and to the jejunum in 5% of cases (Bickler, 1992).
  * These patients tend to have more severe signs and symptoms than those who have other forms of Hirschsprung's disease and have been found to have increased morbidity and mortality (Anderson, 1986; Bickler, 1992; Ikeda, 1986).
  * Diagnosis may prove to be difficult with radiographic studies being diagnostic in only 20-30% of cases. In general, diagnosis is made at the time of laparotomy or leveling colostomy. Frozen section of the appendix confirms the diagnosis (Coran, 2000).
  * Any of the 3 standard repairs may be used to treat patients with total colonic aganglionosis, although primary pull-through in the newborn period is controversial since results in this subgroup of patients is poorer than in those with rectosigmoid disease (Coran, 2000).
  * Specific modifications have been made to these repairs, with the goal of increased fluid and electrolyte absorption.

Prognosis:

- The long-term outcome after definitive repair of Hirschsprung's disease is difficult to determine because of conflicting reports in the literature. Some investigators report a high degree of satisfaction, while others report a significant incidence of constipation and incontinence.
- Unfortunately, approximately 1% of patients with Hirschsprung's disease require a permanent colostomy to correct incontinence.
- As expected, patients with associated trisomy 21 tend to have poorer clinical outcomes.
- In general, more than 90% of patients with Hirschsprung's disease have satisfactory outcomes.

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