Hirschsprung’s Disease

Sangeetha Prabhakaran, MD

INTRODUCTION

Hirschsprung’s disease (HD) or congenital aganglionic megacolon is characterized by an absence of ganglion cells in the myenteric Auerbach’s plexus, the deep submucosal Henle’s plexus and the submucosal Meissner’s plexus in the distal colon. The usual presentation of Hirschsprung’s disease can be demonstrated by the following clinical scenario. A 3-day-old male presented with failure to pass meconium within 48 hours of birth and progressive abdominal distension. Barium study showed dilated colon with no specific zone of transition. The newborn was delivered at 40 weeks gestation after an otherwise normal pregnancy. Transanal rectal biopsy demonstrated the absence of ganglion cells on multiple sections and special staining. The patient underwent an exploratory laparotomy, upon which he was found to have markedly dilated small bowel and colon up to the area of sigmoid. A transverse loop colostomy was performed. The patient recovered well from the initial surgery and underwent definitive surgical therapy of the HD at a later time.

Patients with HD lack a functional myenteric nervous system in the aganglionic segment leading to defective propulsion and receptive relaxation. The precise etiology of Hirschsprung’s disease remains unknown. The length of aganglionosis varies but commonly affects the distal rectosigmoid. To date, nine genetic mutations have been associated with HD. These include the RET proto-oncogene, the endothelin B receptor (EDNRB), endothelin 3 gene (EDN3), but also GDNF, NRTN, ECE-I, PHOX2B, SOX10, and ZFHX1B. A loss in the function of any of these genes may lead to a pan-neuronal lesion resulting in aganglionosis. The RET proto-oncogene is the major gene involved in the development of the disease. RET gene mutations were identified in significant proportions of familial (50%) and sporadic (15-20%) Hirschsprung’s disease, while homozogosity for EDNRB or EDN3 mutations accounted for the rare Hirschsprung- Waardenburg syndrome. Most cases of HD are sporadic but long-segment and total colonic aganglionosis, especially in female children are strongly associated with familial inheritance. The familial variant has been associated with RET mutations and thus has a linkage to MEN types II A and II B and familial medullary thyroid carcinoma. Associated cardiac defects are seen in 2-5% of HD cases. Of interest, trisomy 21 is seen in approximately 5-15% of HD cases.

CLINICAL FEATURES

The commonest clinical manifestation in the neonatal period is the failure to pass meconium in first 24-48 hours of life. This might be accompanied by feeding intolerance, abdominal distension and bilious emesis. The clinical spectrum ranges with minimal symptoms developing within the first few weeks or months of life to complete intestinal obstruction. In later childhood, HD tends to present as constipation, may be complicated by enterocolitis, and frequently associated with growth retardation. Enterocolitis is seen in 10-30% of cases and presents with fever, abdominal pain and malodorous diarrhea. Rapid clinical deterioration can lead to death as early as 12-24 hours if prompt treatment is not initiated. Associated mortality may reach 25-50%.

Disease variants include: (a) total colonic aganglionosis (TCA); (b) total intestinal type, which involves the entire bowel; (c) ultra-short segment variant involving the distal rectum below the pelvic floor and the anus; and (d) suspended variant (controversial) where a portion of the colon is aganglionic above a normal distal segment.

In ultra-short segmental Hirschprung disease or internal sphincter achalasia, the aganglionic segment is limited to the internal sphincter. The child presents with symptoms of functional constipation. Ganglion cells are present on rectal suction biopsy, but the rectal motility is abnormal.

Adult onset Hirschprung disease is rare and often undiagnosed or misdiagnosed. It should be considered in adults with longstanding and refractory constipation. Identification on a barium enema of an abrupt, smooth transition zone in the rectum with proximal colonic dilatation, in conjunction with appropriate...
clinical history, should suggest the diagnosis of adult HD.

DIAGNOSIS
A high index of suspicion should be maintained in a newborn infant with abdominal distention and failure to pass meconium in 24 to 48 hours of life. Abdominal plain radiographs are usually non-specific and show distended, air-filled loops of bowel consistent with distal intestinal obstruction. Thickened bowel and pneumatosis intestinalis can be present if enterocolitis is present.

Contrast enema (performed without a rectal balloon in neonates) shows zone of transition distally. This may not always be present in neonates because proximal bowel dilatation takes some time to develop. Contrast remaining in the rectum for ≥24 hours following a study is also suggestive of diagnosis. A digital rectal exam or a rectal irrigation should be withheld before the contrast enema, as these maneuvers might lead to a false-negative radiologic result.

Anorectal manometry shows increased response of the internal sphincter to balloon-induced rectal distention. In Hirschsprung disease there is a characteristic absence of sphincter relaxation in response to rectal dilatation. This diagnostic modality is not primarily used in the United States for diagnosis of Hirschsprung disease. Diagnostic accuracy of anorectal manometry for Hirschsprung’s disease in most cases is 85% to 90%.

Rectal biopsy is the diagnostic standard of choice. Using the rectal suction biopsy technique, a biopsy of the mucosa and submucosa is obtained. This must be taken at least 1.5 cm proximal to the dentate line since normal infants have lack of ganglion cells just proximal to the dentate line. Full-thickness rectal biopsy under general anesthesia is performed in older children and in infants in whom suction biopsy has been inadequate. Diagnostic accuracy is excellent with a correctly obtained rectal suction biopsy and an experienced pediatric pathologist. The characteristic appearance includes an absence of ganglion cells in the myenteric and submucosal plexuses as well as the presence of hypertrophied nerve trunks in the space normally occupied by the ganglion cells. Adjunctive techniques utilized diagnostically include histochemical staining for acetylcholinesterase or nitric oxide synthase.

TREATMENT
Traditionally, the surgical treatment for Hirschsprung’s disease relies on two- or three-stage procedures. The first stage is a leveling colostomy or ileostomy, with intraoperative biopsies performed to determine the level of the transition zone. The second stage is performed between 3 to 12 months of age. At this operation, the ganglionated bowel is anastomosed to the anus. In older children, this definitive procedure is performed after colonic decompression to relatively normal caliber. If a diverting proximal ostomy is performed, then a third stage is planned to close the ostomy.

Recently, many surgeons favor performing a single-stage pull-through procedure. This single-stage procedure is contraindicated in patients with associated life-threatening anomalies, an overall deterioration of general health, severe enterocolitis, or severe dilation of the proximal bowel. Diverting colostomy is still the initial procedure of choice in these cases.

The three definitive surgical procedures commonly performed for HD include: (a) Swenson procedure (removal of aganglionic portion of colon); (b) Duhamel procedure (retro-rectal anastomosis); and (c) Soave procedure (endorectal pull through). The subsequent paragraphs will briefly discuss these three procedures.

In the Swenson procedure, the aganglionic segment of colon is resected and careful extramural dissection of the distal rectum is performed. The dissected rectum is everted through the anus and perineum and excised. The normal proximal bowel is pulled through and colorectal anastomosis is performed. Possible complications of this procedure include injury to vas deferens, seminal vesicles, ureters and pelvic splanchnic nerves. Among long-term complications, significant fecal soiling can affect as many as 32% to 80% of patients. Some of the prognostic determinants of long-term functional outcome following the Swenson procedure include the length of the residual aganglionic colon, pre-existing dysmotility of the gut, and poor rectal conformability resulting from infection or fibrosis.

The Duhamel procedure consists of the resection of the aganglionic colon above the peritoneal reflection, retrorectal pull-through of the gangionated colon and partial distal side-to-side anastomosis between the pulled-through gangionated colon and the remaining distal aganglionic rectum. The neorectum created during this procedure has an anterior aganglionic portion with normal sensation and a posterior ganglionic portion with normal propulsion. A laparoscopic-assisted version of the technique was also described.

The Soave procedure consists of resection of the rectal mucosa and submucosa and pulling the ganglionic bowel through the aganglionic muscular cuff of the rectum. 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.

The endorectal pull-through procedure described by Boley involves stripping the mucosa from the aganglionic rectum and bringing innervated normal colon through the residual muscular cuff, thus bypassing the abnormal bowel from within. The advantages include absence of any pelvic dissection, the presence of normal propulsive colon all the way down to the anus, the preservation of the rectal muscular cuff and its sensory receptors, fewer Anastomotic problems, as well as the preservation of all sphincters and relatively simple postoperative care. Subsequent technical advances have led to successful laparoscopic endorectal pull-through procedures.

The Duhamel and Soave procedures theoretically offer less risk to the neurovascular plexus surrounding the rectum. In a study of reoperations performed in children who previously underwent Soave and Duhamel procedures, there was no significant difference in the rates of reoperation; however, the patients with Soave pull-through required more complex procedures, with several requiring more than one procedure. Some authors advocate that aggressive reoperation is justified in patients with Hirschsprung’s disease and suggest that further modification to reduce the length of the aganglionic segment may decrease the need for such secondary procedures in the future.

Laparoscopic approaches have been performed for all of the above three procedures. The endorectal dissection has become the most popular minimally invasive pull-through technique and has proven to be a versatile and effective technique for all left and transverse colon aganglionic segments. Some authors prefer laparoscopic-assisted Duhamel procedure for ascending colon...
and total colon aganglionosis. Here, the most important steps include confirmation of the proximal margin of the transitional zone before committing to any mesenteric or mesocolonic dissection, careful attention to prevent any twisting of the neorectum prior to creating the anastomosis, and closure of any window under the colonic pedicle to prevent future internal bowel herniation. Primary transanal pull-through without laparoscopic assist has also been performed and omits the laparoscopic biopsies and preparation of distal mesocolon before transanal dissection. Advantages of the laparoscopic-assisted method includes confirmation of the ganglionated zone prior to starting dissection, its versatility in performing all surgical techniques for Hirschsprung’s disease and helping to create a tension-free anastomosis. In addition, laparoscopic assisted proximal rectal dissection makes the transanal resection both quicker and safer. Early complications of the laparoscopic-assisted pull through techniques include open conversion (2.5%); enterocolitis/chronic diarrhea (7.5% each); anastomatic leak (2.5%); bleeding and recurrent constipation (1% each).

Total colonic aganglionosis accounts for up to 5-15% of Hirschsprung’s disease. Sandegard first described successful treatment of long-segment Hirschsprung’s disease by a pull-through procedure in 1953. Swenson in 1955 advocated total colectomy with ileoproctostomy for this disease. Also, the pull-through techniques described by Duhamel and Soave have been used as well. Other techniques include: (a) Martin's modification using the absorptive capacity of retained ganglionic segment combined with a side-to-side stapled ileocolostomy between the descending and sigmoid colon; (b) Boley's technique of ascending colon patch where a 15-20 cm segment of the ascending colon is anastomosed to the distal ganglionated ileum; and (c) selective use of the J-pouch technique used in ulcerative colitis. In a meta-analysis performed to evaluate the operative methods used to treat total colonic aganglionosis, no single technique has been proven to be superior in terms of operative mortality, morbidity, enterocolitis and functional outcomes.

Management of ultra-short Hirschsprung’s disease. Anorectal myectomy is performed that involves excision of 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.

CONCLUSIONS

Hirschsprung’s disease is the most common cause of lower intestinal obstruction in neonates. It has an overall incidence of approximately 1 in 5,000 live births. Male to female ratio is approximately 4:1. Hirschsprung’s disease is characterized by distal colonic aganglionosis with resultant dysfunctional myenteric plexus. The RET oncogene is the major genetic factor in HD and is involved in familial syndromes, including MEN types II A and II B and familial medullary thyroid carcinoma. Trisomy 21 is present in 5–15% of cases. In the neonatal period, HD presents as failure to pass meconium in first 24–48 hours of life. The presence of pneumatosis intestinalis is associated with high mortality rates. Diagnostic gold standard for HD is rectal biopsy. Surgical treatment is shifting from the traditional three-stage procedures to one-staged and laparoscopic assisted techniques. The three definitive surgical techniques include the Swenson, the Duhamel and the Soave procedures and their modifications. No single technique has been proven clearly superior and further long-term studies are needed in this regard.

SUGGESTED READINGS


