HIRSCHSPRUNG'S DISEASE

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INTRODUCTION

Hirschsprung's disease (HD) is a congenital illness in which there is a lack of intrinsic nerves (ganglion cells) in the distal segments of the intestinal tract. These abnormal segments produce mechanical obstruction because of failure to relax during peristalsis. Hirschsprung's disease always starts in the anal verge, but the length of the segment without ganglion cells (aganglionic) varies: it is limited to the rectum and sigmoid in 75% of patients; involves the whole colon in 8%; and rarely involves the small bowel.

The incidence of Hirschsprung's disease varies from 1 in 5,000 to 1 in 10,000 live births. There appears to be a male preponderance with a ratio of 3:1 to 5:1, particularly in those with short segments. However, the incidence in both sexes seems to be the same in those with long segment disease.

The average age at the time of diagnosis has been decreasing over the years. The diagnosis is established in 15% within the first month of life, in 40-50% in the first 3 months, in 60% at the end of the first year of age, and in 85% by 4 years. Occasionally, the diagnosis of Hirschsprung's disease is not made until adulthood. In a study of 29 patients in which the diagnosis was made after 10 years of age, the mean age at the time of diagnosis was 26 years (range 11-73 years). Most of these adults reported symptoms from an early age, but others reported the onset during adulthood. Adults report constipation as the predominant symptom,

and most evacuate the bowel only with enemas. The presentation in the adult may also be atypical, and there are at least two reports of patients presenting with chronic colitis and pseudopolyps.

The symptoms vary with the age of the patient and the extent of the disease. In the newborn period, bilious emesis, abdominal distention, and failure to pass meconium or abnormal stool frequency are common. Complete intestinal obstruction and perforation of the cecum or the appendix may occur. If the diagnosis is not established in the newborn, the infant may present with mild constipation that may be followed with acute obstruction, frequent episodes of fecal impaction or with the development of acute life threatening enterocolitis. The latter develops in from 15% to 50% of cases, and may be the presenting feature of Hirschsprung's disease in up to 12% of patients. It remains the main cause of death, and the mortality rate can reach 20 to 50%. From infancy until adulthood, mild to severe constipation may be the only symptom, so Hirschsprung's disease must be differentiated from functional constipation. Because clinical features do not allow a complete differentiation between these problems, the diagnosis of Hirschsprung's disease must always be considered in any child, adolescent or adult with severe intractable constipation.

DIAGNOSIS

Once the diagnosis is suspected, confirmation of the disorder is necessary. The final diagnosis needs to be based on the pathologic demonstration of aganglionosis with the use of rectal biopsies.

Biopsies

Confirming the absence of ganglion cells in the diseased segment is a crucial step in the diagnosis of Hirschsprung's disease. There are different techniques to obtain small amounts of tissue from the rectum, and the test can usually be performed in an outpatient setting, although at times they may need to be performed in the operating room. Accuracy is excellent if the specimen is adequate, and if there is a trained pathologist. When ganglion cells are present, the diagnosis of Hirschsprung's disease is excluded.

Because obtaining biopsies involves risks, other less invasive techniques such as anorectal manometry or a barium enema can be used to select those patients that require a biopsy.

Anorectal manometry

In normal individuals distention of the rectal ampulla causes relaxation of the internal anal sphincter, the involuntary high pressure zone at the anal canal. This effect is mediated by the intrinsic nerves of the intestine, and it is absent in patients with Hirschsprung's disease. This relaxation can be duplicated in the motility laboratory with the use of a procedure called anorectal manometry. During anorectal manometry, a flexible balloon is introduced into the rectum, and the pressures are measured. When the balloon is inflated, the sphincter relaxes, mimicking the effect of stool. If the patient has HD, there is no sphincteric relaxation after the distention of the balloon. After the newborn period, manometry has been shown to accurately exclude or diagnose Hirschsprung's disease in 90 to 100% of the patients, with a specificity of 97% and sensitivity of 79%. Therefore in this age group, anorectal manometry is the diagnostic study of choice to exclude HD. If the study is abnormal the diagnosis needs to be confirmed by

biopsy. In newborns and prematures the diagnostic accuracy is less (from 70 to 90%).

Barium Enema

The barium enema (BE), a procedure in which barium is instilled in the rectum, and x-ray pictures are taken, while not diagnostic, can be strongly suggestive and supportive. Barium enema is widely available, as opposed as the anorectal manometry that is performed only in specialized centers. Single contrast barium enemas are used, and the colon is not prepared. In infants with Hirschsprung's disease, a transition zone from the distal nondilated colon is usually easily detected. The absence of a transition zone however does not exclude the diagnosis, as it may be absent in up to 20% of patients. In patients with total colonic aganglionsis the entire colon may appear normal. A barium enema may be less helpful in the newborn because a visible transition zone is often not present. However, even if there is a normal barium enema, further work up may be indicated in those patients that continue to be intractable.

TREATMENT

The treatment of Hirschsprung's disease is surgical. Initial medical management is important, however, in stabilizing the patient before surgical therapy is undertaken. This includes the correction of fluid and electrolyte imbalances, antibiotic therapy if enterocolitis is present and rectal decompression with the use of rectal irrigations and rectal tubes until the time of surgery.

The basic principle for the definitive surgical therapy is resection of the aganglionic segment followed by a pull-through of ganglionic bowel down to the anus. There are different procedures that have been used, but the three most common ones are: Swenson pull-through

(rectosigmoidectomy), Duhamel pull-through (retrorectal transanal pullthrough) and Soave pull-through (endorectal pull-through). Recently the surgery is being performed in the newborn period using minimally invasive surgical techniques, like laparoscopy.

It is difficult to compare the results obtained with the three techniques, because the incidence of complications may be closely related to the skill of the individual surgeon, to the institution or to the year of the study. Nevertheless, the long term outcome of these procedures appears to be similar. Surgery for Hirschsprung's disease generally results in a satisfactory outcome. There are however, some patients that continue to have long term difficulties. A recent review of 45 patients showed that 51% had some type of bowel dysfunction, and 37.5% fecal soiling. The most common symptoms are constipation, diarrhea, and some times intermittent colitis.

Satisfactory school performance was achieved in 74% in one study. Ninety four percent of the patients appeared to be well adjusted, and 5 patients had severe behavioral problems. In another long term study of 19 adolescents it was found that 32% had significant impairment of continence, but no more psychopathology or psychosocial dysfunction when compared with healthy controls. Fecal incontinence was associated with poorer psychosocial functioning and parental criticism and psychosocial functioning was significantly correlated with the degree of fecal incontinence.

COMMON PROBLEMS FOUND AFTER SURGICAL TREATMENT OF HIRSCHSPRUNG'S DISEASE

Obstructive symptoms

Of the postoperative symptoms occurring in children that have undergone surgical treatment for Hirschsprung's disease, recurrent obstruction (manifested as constipation, abdominal distention and difficulty having bowel movements) is one of the most common and difficult to manage.

Obstructive symptoms may be related either to an anatomic problem, or to functional alterations. The most common anatomic problem is that of *anal stenosis*. This complication can usually be managed with dilatation, although a secondary surgical procedure may be rarely necessary. *Strictures* in the pulled-through bowel have also been described, are probably secondary to ischemic damage, and may require surgical correction. Most patients with obstructive symptoms do not have stenosis. A variety of functional problems can be observed. The first consideration must be that the patient has *residual aganglionosis* after an inadequate initial operation. The aganglionosis may also be *acquired or secondary* after a successful initial operation. This is a rare occurrence, but it has been well documented. If aganglionosis is suspected a BE may show a transition zone, and 4 quadrant rectal suction biopsies at different levels will be necessary to confirm it.

Persistent *internal anal sphincter (IAS) dysfunction* is one of the most common causes for obstructive symptoms. This dysfunction is sometimes referred as "internal sphincter achalasia", and is related to specific abnormalities in the innervation of the IAS. It is possible that the IAS pressure produces a functional outflow obstruction, that with time leads to colonic dilatation and less efficient peristalsis to expel stool. The persistent chronic obstruction from the IAS may also lead to recurrent enterocolitis, or bacterial overgrowth with stasis. The injection of intrasphincteric *botulinum* toxin (BoTox) has become the treatment of choice for these patients.

Frequent injections are necessary, and eventually the sphincter may need to be cut. However many children have long term improvement after BoTox alone.

If symptoms persist, or are not related to sphincteric dysfunction, they may be secondary to generalized motility problems. In those patients a colonic manometry may be needed to pinpoint the extent and location of the motility problems. Some authors have also suggested that *neuronal intestinal dysplasia* (NID) type B, which is an abnormality of the intestinal nerves, may be associated with the presence of obstructive symptoms. There is still controversy regarding the significance of NID, or if it truly represents a distinct clinico-pathological entity. Therefore in children with obstructive symptoms it may be necessary to obtain a full thickness rectal biopsy to exclude the diagnosis. In those children conservative management is indicated. However, if symptoms are severe, and clearly associated with the abnormal segment (by colonic motility and/or histology), surgical resection may be necessary.

Occasionally repeat surgery is indicated. This may involve resecting aganglionic areas, cutting the sphincter, redoing the pullthrough or antegrade colonic enemas (ACE). The ACE procedure produces a continent conduit from the skin to the cecum that can be catheterized for self-administration of enemas.

Fecal Incontinence

Fecal incontinence is another frequent occurrence. It has been described in up to 30- 80% of patients. In some it may be significant with constant leaking, and in some less severe. The treatment of the fecal incontinence is complex. It includes treatment of constipation, biofeedback and at times enemas, or more recently, antegrade colonic enemas.

Enterocolitis

Enterocolitis continues to be the major cause of both morbidity and mortality in Hirschsprung's disease. It occurs after surgical treatment in 2 to 33% of patients, with a mortality that ranges from 0 to 30%. The clinical presentation may be more fulminant, with rapid progression, shock and prostration, and eventually death. Enterocolitis may occur many years after surgery. Enterocolitis presents with abdominal distention, explosive diarrhea, vomiting, fever, lethargy, rectal bleeding and may lead to colonic perforation. The occurrence of explosive diarrhea in any patient with Hirschsprung's disease should suggest the diagnosis, even in the absence of systemic symptoms. The presence of postoperative enterocolitis needs to be recognized promptly, as the child can present initially with mild symptoms that are followed by a rapid fulminating course that may lead to death.

Diagnosis is facilitated by clinical exam, abdominal radiographs, and at times endoscopic examination. Non-operative management in the hospital is usually necessary. The treatment of choice includes fluid and electrolyte support, antibiotics and the use of transrectal decompression either by tube or by sphincter dilatation. The rectal decompression may need to be accompanied by saline irrigations to evacuate the retained stool and gas.

CONCLUSIONS

Since the first operative curative technique for Hirschsprung's disease was described in 1948 by Swenson, progress in diagnostic methods and surgical techniques have allowed the survival and successful treatment of most children with Hirschsprung’s Disease. In spite of these

advances, postoperative problems continue to occur. Recently, research has produced a better understanding of the physiopathology of the disease, knowledge that will undoubtedly lead to further refinements of the surgical techniques and better treatment of these children.

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