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HIRSCHSPRUNG DISEASE, AN OVERVIEW WITH DIAGNOSIS AND CURRENT TREATMENT SCENARIO

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ABSTRACT

Hirschsprung disease, an common disease, as the enteric nervous system develops, its function is affected by the lack of ganglion cells in the submucosal and myenteric plexuses of the distal intestine. To diagnose Hirschsprung's disease, histological examination of surgical specimens or colonic biopsies found no ganglion cells. An additional technique that can aid in the diagnosis, particularly in challenging instances, is acetylcholinesterase (AChE) staining, which identifies the enhancementin the muscular mucosa and lamina propria of parasympathetic nerve fibers. Surgical intervention is typically required following a diagnosis of Hirschsprung's illness. A range of complications, from 4% to 16%, have been reported with various pull-through surgery procedures for Hirschprung's disease.

KEYWORDS: Hirschsprung disease, ganglion cells, colonic biopsies, pull-through surgery.

INTRODUCTION

One out of every five thousand live-born newborns is born with Hirschsprung disease. In this disorder, As the enteric nervous system develops, its function is affected by the lack of ganglion cells in the submucosal and myenteric plexuses of the distal intestine. The afflicted gut stops peristalsizing, and a functional intestinal blockage forms as a consequence.

The earliest documented case of Hirschsprung illness was a 5-year-old boy who died of an intestinal blockage in the 17th century, according to Frederick Ruysch. Publication of

Domenico Battini's narrative of a kid born with a congenital megacolon occurred after he died in 1800Pathologist Harald Hirschsprung of Copenhagen's Queen Louise Children's Hospital recorded the patient's condition twice in 1887.;[3] The disease would subsequently be named after its discoverer. two, three, four The enterocolitis ultimately proved fatal for these children, aged 8 and 11.[4]

ETIOLOGY

Hirschsprung disease is characterized by an imbalance between RET and its ligands causing neural crest cells to migrate and differentiate uncontrollably inside the enteric nervous system. Because of this disruption, the nerve plexuses have zero GC. Constant secretion of acetylcholine causes the intestines to become overactive. Afterwards, the healthy proximal colon gradually enlarges, while the constricted (affected) colonic section continuously contracts.[5]

Multigenic inheritance complicates the complicated process of HD transmission. Its penetration is not very strong, and it varies between the sexes. About one-third of random cases and nearly half of all familial occurrences are caused by the proto-oncogene RET.[6] There are 21 exons in the RET gene, and mutations can happen in any one of them. There have been over a hundred distinct mutations found. Nonsense, missense, deletions, and insertions are all part of this category.[7][8] Among the many genes that contribute to HD etiopathogenesis, only 5–10% of patients contain these genes. Several components make up this complex, including endothelin-3, GDNF, SOX10, the PHOX2B gene, and EDNRB.

EPIDEMIOLOGY

The prevalence of Hirschsprung's disease was determined by analyzing hospital data from over 1.5 million live births in Denmark. To diagnose Hirschsprung's disease, histological examination of surgical specimens or colonic biopsies found no ganglion cells. There were 4.11 males for every female in the short segment and 2.41 in the long segment; there was a rate of 0.140 cases of Hirschsprung's disease per 1000 live births (1:7,165; $p = 0.36$). The sequence of birth and the mother's age had no bearing on the results. Although there is some evidence linking the Possible link between Hirschsprung's disease and congenital cardiac abnormalities; 9 out of 207 individuals with the condition also had Down syndrome problems in 2% of patients (not counting those with Down syndrome) is less convincing. The critical need for prompt diagnosis is highlighted by the 16% death rate observed in Hirschsprung's disease patients.[9]

PATHOPHYSIOLOGY

As a result of a constricted colon that blocks the passage of peristaltic waves, because parasympathetic intrinsic ganglion cells are absent, functional obstruction is the fundamental pathophysiological hallmark of HSCR. Extensive studieshave not fully resolved the reason why the aganglionic gut contracts tonicly. Nitric oxide synthase (NOS) distribution abnormalities, aganglionosis, cholinergic hyperinnervation, and other related conditions.[10]

HISTOPATHOLOGY

Radiographic findings and histological examination of biopsied tissue work together to confirm a diagnosis of HD. By linking the enlargement of nerve fibers in the aganglionic segment with the lack of GC in the submucosal and myenteric plexus, rectal histology supports the illness diagnosis. Polygonal cells (GC) have a lot of fibrillar eosinophilic cytoplasm, a big nucleolus, and an eccentric nucleus. the top tier. The International Gastroenterology Committee announced in 2009 that standards for doing preoperative biopsies that would allow for a good interpretation, to reduce the percentage of ambiguous results caused by insufficient samples.[12]

A minimum of two 3-millimeter-diameter biopsies should be necessary. The amount of submucosa and mucosa in the biopsy should be equal It has to be positioned correctly and integrated into the right axis to avoid tissue loss when cutting levels change. At least two centimeters above the dentine line is the recommended minimum height for preoperative biopsies. This region exhibits nerve fiber hyperplasia and is physiologically free of GC. To diagnose HD, conventional histopathology often uses the hematoxylin-eosin (H and E) stain.[12][13]

An additional technique that can aid in the diagnosis, particularly in challenging instances, is acetylcholinesterase (AChE) staining, which identifies the enhancementin the muscular mucosa and lamina propria of parasympathetic nerve fibers. Staining with AChE is not observed in the normally innervated gut.[14][15] Nevertheless, AChE staining necessitates the expertise of technicians and pathologists and is a tedious and time-consuming process.[15][16] The calretinin antibody-based immunohistochemistry (IHC) method has recently become a gold standard for HD diagnostic confirmation or exclusion.[17][18] in A vitamin D-dependent protein called calretinin attaches to nerve fibers and acts as a calcium buffer. In its absence, hyperexcitability and cell degeneration result from intracytoplasmic calcium buildup.[24]

Several human tissues, including the CNS and peripheral nervous systems, biologically express it.[19]

In 2004, the loss of GC was associated with the characteristic of HD, the lack of calretinin expression, according to Barschak et al.[6] Immunolabelling the submucosa, muscular mucosa, and lamina propria with an anti-calretinin antibody reveals interstitial nerve fibers that are positive for GC. For example, in[20], The lack of calretinin expression was added as a diagnostic criterion for HD in the most recent 2009 guidelines released by the International Gastroenterology Committee.[12] When dealing with HD, a frozen section inspection is crucial. In the first case, it helps confirm HD, and in the second, It locates the ganglionic zone so that endo-anal resection can be performed.[21][22] The diagnostic process relies on biopsies that specifically target the muscles of the colonic wall. Some have proposed circumferential biopsies as the ultimate diagnostic tool.[23]

CLINICAL PRESENTATION

Contrary to long-held beliefs, only 6.5% of HSCR patients manifest within the first week of birth, according to a retrospective study of national inpatient databases. This is not a disease that affects infants. The onset occurred at an average of three years of age and a median of one year.[26] At six months, around 40% are present, at one year, 60% at two years, at seven years, 80%, and at thirteen years, 93%, in that sequence. The clinical symptoms are determined by the size of the aganglionic section and the age of presentation. Neonatal intestinal obstruction signs include bilious emesis, abdominal distention, delayed passage of meconium (>48 hours), trouble feeding, and delayed passage of stool. 25 and 27 Up to 5% of infants with HSCR may first experience bowel rupture of the cecum, ascending colon, or appendix. Infants with intestinal obstruction symptoms are the most prevalent presentation in children with longer segments of aganglionosis (TCA).[27] However, up to 14% of these cases had a delayed presentation of more than 6 months.[28] Infants and toddlers can experience mild to severe constipation that lasts beyond the newborn period. This constipation can be resistant to oral laxatives, requires rectal treatments, and is often accompanied by symptoms including vomiting, abdominal distention, and development failure.[25,27,29] Intestinal blockage, recurring fecal impactions, acute or chronic enterocolitis, and other complications might worsen their course. When you have Hirschsprung-associated enterocolitis (HAEC), you may notice an enlarged abdomen, high body temperature, and severe diarrhea. Which is

frequently bloody. HAEC is detected in 6% to 60% of patients before surgery, 25% to 37% after, and 1% to 10% of those patients die as a result. Pages.[30–34]

Extremely few cases of HSCR persist throughout maturity and beyond infancy. Sections[35,37] According to Doodnath and Puri's[36] comprehensive study and meta-analysis of HSCR in adults, 79.8% of patients had the rectosigmoid disease and 12.5% had rectum sickness. Flatulence, bloating, irregular bowel movements, and pain that did not improve with enemas or laxatives persisted throughout the lifetimes of the majority of patients, who first experienced symptoms during the neonatal era. Thus, any adult or teenager exhibiting signs of chronic constipation that started in infancy should be considered a possible case of HSCR.

EVALUATION

The lack of ganglion cells can be confirmed by pathological evidence, which is often used to diagnose HD. The journey to a conclusive pathology diagnosis has its challenges, though. Among these are the following: normal, immature ganglion cells in infants; poor and undesirable quality; tissue disorientation on the way to the pathology ward; and pathologists' lack of experience with the samples.[17]

The examination of the rectal tissue using specialized staining procedures, such as acetylcholinesterase (AChE), is an essential part of the evaluation process in HD. But regular staining procedures, such as H and E, play an important but often-overlooked function. It is possible to use ACE staining to evaluate tissues from fresh frozen sections.[38] Additional tests that can be used to diagnose Hirschsprung disease include contrast enema and anorectal manometry. Anorectal manometry is based on the recto-anal inhibitory reflex (RAIR), which is present in all healthy infants. Failure to perform RAIR during manometry may indicate HD.[39]

In a contrast enema, HD manifests as the transition zone, irregularities in the mucosa, unequal contraction, and chronic retention of contrast (lasting more than 24 hours).[40]

TREATMENT AND MANAGEMENT

Surgical intervention is typically required following a diagnosis of Hirschsprung's illness. To better communicate with the surgeon and the patient's family, it is recommended that physicians possess a general understanding of typical operations. To avoid enterocolitis and relieve bowel compression before surgery, rectal irrigations are carried out. When newborns

with short-segment Hirschsprung's disease do not exhibit colon distention, the definitive ileoanal pull-through anastomosis can be done.[42] quotations from[42–47] The recommended interval between the colostomy set-up and the pull-through therapy is four to six months. although it can be extended for many months if the kid develops Hirschsprung-associated enterocolitis or a substantially dilated colon.[45]

A range of complications, from 4% to 16%, have been reported with various pull-through procedures. According to Swenson, the anus is attached to the healthy ganglionated colon that is pushed through after removing the rectum.[41] Modern methods (such as the Duhamel or Soave operations) aid in maintaining the complex nerve supply to the bladder and rectum.[48] For a few months after the Soave surgery, the patient's parents can keep the anastomosis from getting too tight by performing the necessary dilations at home. The success rate and morbidity associated with these treatments are both very high.[42,49] To save babies with short-segment illnesses the agony of an abdominal incision and colostomy, some surgeons opt for a one-stage transanal Soave procedure.[50] Though outcome studies of this method have been restricted The risk of complications is comparable to the more invasive Soave procedure, as a result of brief follow-up periods.[43–49]

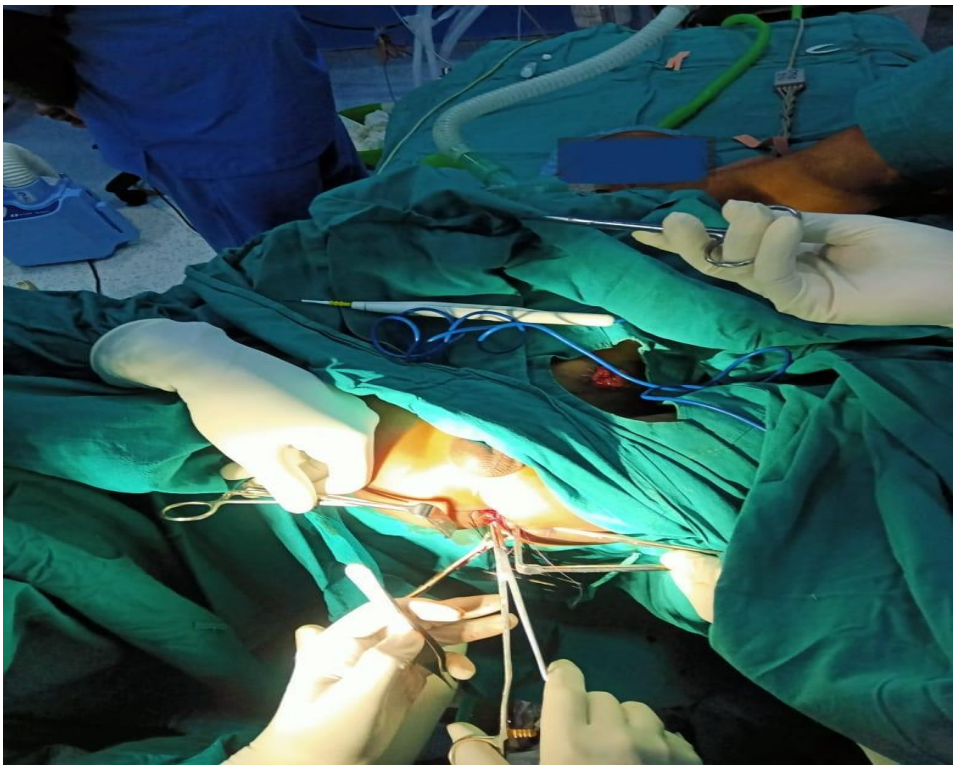

Fig. 1:- Pull Through Surgery for Hirschprung Disease.

DIAGNOSIS

When diagnosing Hirschsprung's illness, imaging might be helpful. A proximal colon or enlarged small bowel could be revealed by an ordinary abdominal radiograph. Contrast enema radiographs of the colon usually do not reveal any abnormalities in persons with full colonic disease throughout the first three months of life and forever thereafter. As the dilatation starts, the portion of the colon closest to the location will grow, making the affected area appear normal. Radiographs taken after a contrast enema may reveal a "transition zone"—the spot where the normally ganglionic bowel becomes abnormally shaped but in around 10% of cases, the aganglionic colon will continue beyond this area. contains radiographs of a baby with Hirschsprung's illness taken with a contrast enema.[41,53] Patients with enterocolitis should not have contrast enemas because of the significant danger of perforation. According to anal manometry (rectum balloon dilatation), Following rectal dilation, the internal anal sphincter remains rigid.[53][54] The specificity and sensitivity of contrast enema and anal manometry are comparable.

PROGNOSIS

Among the many indicators of HD patients' well-being, fecal continence stands out. Life quality in long-term HD is still under-discussed in the research. A modified questionnaire was used to assess almost 3,000 adult patients with Hirschprung disease in one of the rare and extensive surveys conducted by a French researcher that covered the whole country.[55] In 2001, a group from the Netherlands detailed the initial questionnaire, which pointed to a variety of anorectal abnormalities and HD in particular.[56]

COMPLICATIONS

Hirschsprung disease can cause long-term difficulties in children, such as incontinence, enterocolitis, and constant obstructive symptoms. Many times, a single child may be juggling several problems. The prevalence of these difficulties varies greatly across the literature; yet, in several series, it can reach 50%. Public awareness of these issues has undoubtedly grown because more recent publications have reported greater figures.[57]

ENHANCING HEALTHCARE TEAM OUTCOMES

Most children with operated HD will have far fewer postoperative chronic bowel difficulties if their care is based on an interprofessional team approach that takes a bio-psychosocial perspective. A child's ability to deliberately and routinely defecate sufficient volumes of waste will determine how much medicine he needs and how much autonomy he will have

from the therapist and his parents. Learning self-control is the primary goal. Given the potential harm that intrusive operations may do in such a delicate area, particularly during the early stages of a child's development, it is crucial to address defecation problems as soon as possible to avoid them from the beginning of therapy.

The amount of long-term care that children with HD may need depends on the length of the intestinal tubes that were removed. Poops that aren't contained, incontinence, or issues with peristalsis due to a constricted anal opening are all symptoms of a more transient or intermittent condition. Nutritionally speaking, a kid may not obtain enough fluids and nutrients after having a long section of their intestine removed.

Infection, stunted development, and gastrointestinal issues are all possible side effects for children. To make sure the kid grows and develops appropriately, nutritionists will help reach nutrition objectives and provide advice on how to meet nutrition requirements. Pediatric radiologists, a pediatric gastroenterologist, and an expert in bowel management protocols should be part of the interdisciplinary team that works with the pediatric surgeon to care for children with HD. Important members of the team include seasoned nurses who will keep an eye on the patient's vitals and warn of any potentially fatal complications, such as HAEC, while also helping to educate the family and patient. The chemist's role is to monitor the patient's antibiotic, antiemetic, and analgesic regimen in the postoperative phase.[58]

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