Original Article

Retrospective Study of Hirschsprung's Disease in Erbil City/Iraq during 2004–2016

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Abstract

Background: Hirschsprung's disease is caused by the failure of ganglion cells to migrate cephalocaudal through the neural crest during 4–12 weeks of gestation, causing an absence of ganglion cells in all or part of the colon. Most patients present in infancy, and the early diagnosis is important to avoid complications. With proper treatment, most patients live normal adult live. **Objectives:** The objective of this study is to investigate the incidence and severity of Hirschsprung's disease in our location (Erbil city/Iraq). **Materials and Methods:** In this prospective study, we collected 150 cases that referred to our private laboratory in Erbil city from January 2004 to December 2016. A total of 108 cases were studied grossly and histopathologically stained by H and E in addition to Phosphotungstic acid-haematoxylin stain (PTAH) special stain for ganglion cells and neural plexuses. **Results:** The results found that Hirschsprung's disease was more common in males than females (male gender 52% and female 48%). The majority of cases were below the age of 1 year (48% of cases). The resected segment is 21–30 cm in about 46% of cases. Regarding the narrowing segment is about 5 cm in most cases (56% of cases). Finally, the number of neural plexuses in the whole narrow segment was five neural plexuses in the majority of cases (found in 24 cases [23%]). **Conclusions:** Hirschsprung's disease is a common disease in this locality (Erbil city/Iraq). All constipated newborn babies should be examined to exclude HD.

Keywords: Ganglion cells, Hirschsprung's disease, neural plexuses, resected segments

Introduction

The cause of Hirschsprung's disease is multifactorial, and the disease can be familial or develop spontaneously. It is more common in boys than that of girls.[1,2] Approximately 3%–5% of male siblings and 1% of female siblings of children with a short-segment disease also have the disease.[3] However, the risk is substantially higher (12.4%–33%) in siblings of children with total colonic involvement.[4] Eight genomes have been associated with Hirschsprung's disease;[1,2] however, most cases are not considered familial. Hirschsprung's disease has been observed from newborn to adolescence ages, although the diagnosis is established in the newborn in 90% of cases.

The chief complaint is the defecation disorder which in newborns is manifested by the delayed passage of meconium for more than 48 h, intestinal obstruction, or even perforation of the colon.[5,6] Intestinal perforation occurs mostly in the cecum and then in the transverse portion of the splenic flexure. In older patients (infants and children), the chief complaint is chronic constipation and its related problems. In some cases with a history of chronic constipation, the patient comes down with severe and explosive diarrhea, abdominal distention, fever, and bad general condition; these symptoms indicate that the worst consequence of the disease enterocolitis has occurred which leads to death in 30%–40% of cases unless the appropriate treatment is performed immediately.[5,7,8] The most prevalent area involved is the rectosigmoid region (75%–80%), although more extensive forms, involving even the entire colon have also been reported.

Between the regions containing ganglions and the aganglionic area, there is an intermediate region of hypoganglionosis

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termed as transitional zone (TZ), determining that TZ is of critical importance for performing colostomy and definitive surgery. The aganglionic region sometimes is very short and includes just the terminal portion of the large intestine.[6,7,9,10] Definitive diagnosis is established by patients' symptoms, plain abdominal film, barium enema, rectal manometry, suction rectal biopsy, full-thickness rectal biopsy 2 cm above the dentate line, and histochemical staining. Once the diagnosis is established, colostomy is performed just proximal to TZ, and then, depending on the growth of the infant, in 6–9 months of age, the definitive operation is performed to eliminate the aganglionic region, with the establishment of anastomosis between the ganglionic colon and the point 1.5–2 cm from the end of colon, the treatment comes to its end.

The aim of this study was to investigate the incidence and severity of Hirschsprung's disease in our location (Erbil city/Iraq).

Materials and Methods

Study design and patients

A total of 200 patients referred to the pediatric surgeons as constipation, of whom 150 rectal biopsy performed by a pediatric surgeon and sent to our laboratory in Erbil city from January 2014 to December 2016. We did routine histopathological examination in addition to PTAH stain for neural plexuses; among these 150 cases, only 108 cases found to be Hirschsprung's disease by identifying the aganglionic areas, and then the surgeon did resection of the narrow segment with the dilated segment. We measured the length of both narrow and dilated segments and we took several full-thickness biopsies (usually three biopsy from each: proximal, middle , and distal parts); even sometimes, we took five pieces from each segment to identify the TZ when the length of the resected segment was more than 10 cm, and then we did histopathological examination using H & E and PTAH stains. All biopsies were examined, and the data collected as a result and statistically analyzed.

Statistical analysis

The categorical and continuous variables were compared using the independent *t*-test and identified standard deviation using Microsoft SPSS version 19 version 21 (SPSS, IBM Company, Chicago, IL, USA) to measure. $P < 0.05$ is regarded as statistically significant, <0.01 highly significant, and above 0.05 was considered as nonsignificant.

Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before the sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee.

Results

Table 1 shows the age distribution of studied cases. The majority of cases (44%) are ≤1 year, the mother complains the constipation of her baby since birth, then followed by 2 years age (22%), and only 5 cases (5%) at late age of 8 years.

The results also revealed that regarding the gender ratio it is more common in males (52%) than that of females (48%), i.e., male:female ratio is 1.1:1.

Table 2 shows the number of cases for each length of resected segments. Regarding the resected segment, in most patients, the length is 21–30 cm that constitutes 50 cases (46%).

Table 3 displays the number of cases for each length of narrowing segments. Corresponding to the narrowing segment, the length mostly is about 5 cm and constitutes about 56%. The maximum narrow segment was 15 cm and constitutes about 7%.

Table 4 shows the frequency of neural plexus in narrowing segments in the studied cases. In majority of cases there were few neural plexuses [Figures 1 and 2], and 5 neural plexuses were found in 24 cases (23%) [Figure 3]. Single ganglion cell was seen in neural plexuses [Figure 4].

Table 1: Age distribution of studied cases

Age (years)	Number of cases (%)
≤1	48 (44)
2	22 (20)
3	16 (15)
4	8 (7)
5	2 (2)
6	4 (4)
7	3 (3)
8	5 (5)

Table 2: Number of cases for each length of resected segments

Length of the resected segment (cm)	Number of cases (%)
≤10	20 (19)
11-20	15 (14)
21-30	50 (46)
31-50	15 (14)
>50	8 (7)

Table 3: Number of cases for each length of narrowing segments

Length of narrowing segment (cm)	Number of cases (%)
≤5	60 (56)
≤10	40 (37)
≤15	8 (7)

Discussion

In this study, the male:female ratio is 1.1:1 which means a little bit more common in males than females, whereas in a study conducted by Abdul-Ghafoor, the male-to-female ratio was 9:2.[11]

Table 4: Frequency of neural plexus of narrowing segments in the studied cases

Frequency of neural plexus	Number of cases (%)
2	8 (7)
3	8 (7)
4	4 (4)
5	24 (23)
6	8 (7)
7	20 (19)
8	8 (7)
9	4 (4)
10	8 (7)
>10	16 (15)

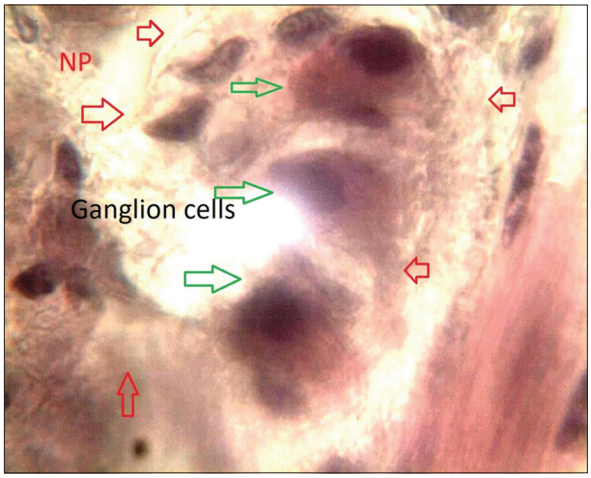

Figure 1: Three ganglion cells and neural plexus in proximal dilated segment (H and E staining ×1000)

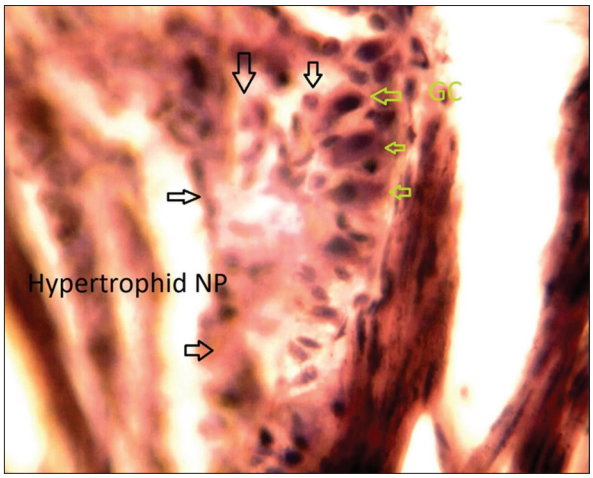

Figure 3: Hypertrophied neural plexus contain four ganglion cells in the proximal segment of the colon (H and E ×1000)

In this study the majority of cases were presented clinically as constipation in 1st year of life (although 5% of cases were presented at age of 8 years); while in other studies the majority of cases were presented in first 24–48 hrs and their symptoms range from neonatal intestinal obstruction to chronic progressive constipation.[6,11] Approximately 80% of patients present in the first few months of life with difficult bowel movements, poor feeding, and progressive abdominal distention.[11] Up to 90% of infants with Hirschsprung's disease fail to pass meconium in the first 24 h of life,[11] because in this locality, there is some ignorance regarding the passing of meconium which is very important should be within 24–48 h. Otherwise, the baby should be examined to exclude Hirschsprung's disease, for diagnosis imaging can help diagnose Hirschsprung's disease. A plain abdominal radiograph may show a dilated small bowel or proximal colon.

Contrast enema radiographs of the colon commonly are normal for the first 3 months of life and indefinitely in patients with total colonic disease. After the dilation process begins, the diseased portion of the colon will

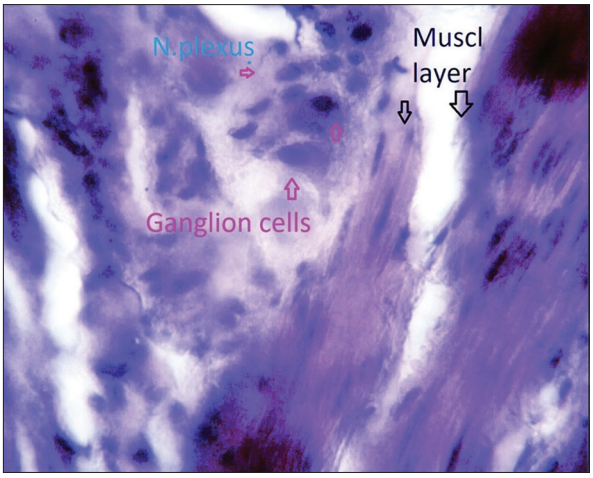

Figure 2: Two ganglion cells light blue in color (PTAH stain ×1000)

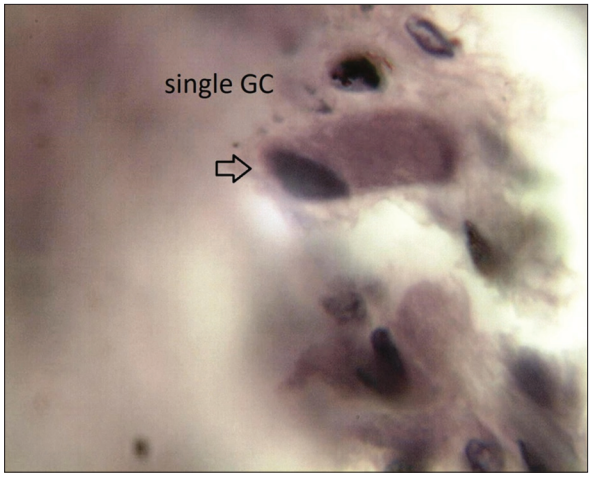

Figure 4: Neural plexus contain single ganglion cell (H and E ×1000)

appear normal, and the more proximal colon will be dilated. A "TZ" (the point where the normal bowel becomes aganglionic) may be visible on a contrast enema radiograph; however, the aganglionic colon will extend beyond this point in about 10% of patients.[12,13]

Contrast enemas should be avoided in patients with enterocolitis because of the risk of perforation.[6] Anal manometry (balloon distention of the rectum) demonstrates the absence of internal anal sphincter relaxation upon rectal distention.[3] Contrast enema and anal manometry are similar in the sensitivity and specificity. The diagnosis can be confirmed with a rectal suction biopsy which should show the absence of ganglion cells and the presence of hypertrophic nerve trunks.[9,14]

Patients are typically referred to a pediatric surgeon or gastroenterologist for biopsy; however, family physicians should be familiar with the procedure to evaluate the outcome of surgery and determine appropriate follow-up. The biopsy site should at least be 0.6″ (1.5 cm) above the dentate line because the distal rectum normally does not have ganglion cells.[15] If no hypertrophic nerve trunks are found, a full-thickness biopsy may be indicated.

Conclusions

All babies should be examined for Hirschsprung's disease monitoring the passing of meconium after delivery within the first 24–48 h. A biopsy is essential for the diagnosis of Hirschsprung's disease. Proper identification of the aganglionic segment is very important for the management. Before resection, the identification of TZ is mandatory to prevent repeated operations and decrease the chance of operational failures.

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Conflicts of interest

There are no conflicts of interest.

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