Hirschsprung's Disease: a Clinical and Pathologic Study in Iranian Constipated Children

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Abstract

Objective: Hirschsprung’s disease (HD) is a complex disorder resulting from absence of ganglion cells in the bowel wall leading to functional obstruction and bowel dilatation proximal to the affected segment. The aim of our study was to evaluate rectal biopsies from constipated children in different age groups to see in which age it is more likely to encounter HD to avoid unnecessary rectal biopsy.

Methods: Records of all children with chronic constipation undergoing a rectal biopsy to exclude HD were obtained from the files of Children’s Medical Center in Tehran, Iran. A detailed retrospective demographic review, including age of beginning of signs and symptoms was made of all cases.

Findings: Totally, 172 biopsies were taken from 168 children in a five year period, of which 127 cases (75%) had HD. The mean age of constipated patients at biopsy was 39 months and the mean age of patients with proven HD was 18 months. Males were affected more than females. Congenital anomalies associated with HD were found in 9.6%. In 85 (91%) cases constipation had begun in neonatal period.

Conclusion: Our data supports previous studies that if constipation begins after the neonatal period, the child is unlikely to have HD. In neonates delay in meconium passage is the most important clinical sign of HD.

Key Words: Hirschsprung’s Disease; Functional Gastrointestinal Disorders; Constipation; Biopsy; Intestinal Obstruction
Introduction

Functional obstruction and bowel dilatation proximal to the affected segment, first described by Harald Hirschsprung in 1888, is a complex disorder resulting from absence of ganglion cells in the bowel wall leading to functional obstruction and bowel dilatation proximal to the affected segment [1,2,3]. It may present in neonatal period as intestinal obstruction. It is usually diagnosed in infants but Hirschsprung’s disease (HD) may be diagnosed in the older children presenting with chronic constipation, which is unresponsive to conventional treatment.

As constipation is a common problem among children and only small minority of patients have an organic cause for their constipation, it is necessary to distinguish between these two conditions. Constipation is defined in neonates as failure to pass meconium within the first 48 hours of life and in the older children as the infrequent passage of stool of increased consistency. Only a small percentage of children with constipation have HD [4]. A number of constipated children are referred for rectal biopsy to exclude a possible HD [1].

The diagnosis of HD is based on a combination of symptoms, radiological study, rectal manometry, and histological features of rectal biopsy. The histological features of HD include the absence of ganglion cells of the myenteric (Auerbach’s) and submucosal (Meissner’s) plexuses, and increased number of hypertrophic nerves [2,3]. Rectal biopsy with histopathologic examination can reliably exclude HD and it is the gold standard for the definitive diagnosis of aganglionosis [4].

It is said that 12% to 17% of children undergoing rectal biopsy are found to have HD [4-6] and so about 80% of patients receive an unnecessary surgical procedure. Lewis et al hypothesized that key features in the history, physical examination, and radiographic evaluation would allow us to avoid unnecessary rectal biopsies. In a retrospective study they found that a history of delayed passage of meconium, abdominal distension, vomiting or the results of a contrast enema identified all patients with HD and excluded HD in approximately 36% of patients with idiopathic constipation; in a child presenting only with constipation and none of the above features, it is not necessary to perform a rectal biopsy [4].

Ghosh and Griffiths in a retrospective study in 186 children concluded that if the age at onset of constipation is after the neonatal period, rectal biopsy is unnecessary and it is unlikely that the child has HD [6].

The aim of our study was to evaluate rectal biopsies from constipated children of different age groups to see in which age HD is more likely in order to avoid unnecessary rectal biopsy and on the other hand in which age group we need to pay more attention to avoid missing HD.

Subjects and Methods

The names and record numbers of children with chronic unremitting constipation undergoing a rectal biopsy to exclude HD were obtained from the histopathology department of Children’s Medical Center. Children with previous diagnosis of HD or incomplete data were excluded.

Cases were divided into 4 groups according to their age: a) neonatal period: the first 4 weeks of life, b) between 5 to 12 weeks old, c) 13 weeks to 1 year old, and d) above 1 year old.

A detailed retrospective demographic review, including age of beginning of signs and symptoms, gender, family history of disease, signs and symptoms, paraclinical data and congenital anomalies, was made in all cases.

Rectal biopsies are preformed at least 1 cm above the pectinate line and types of biopsies were submucosal biopsies and full thickness muscle coat stained with hematoxilin and eosin. In aganglionic biopsies at least 30-50 sections were examined to make the diagnosis of HD. Aganglionic cases less than 0.5 cm in diameter, presence of squamous epithelium or striated muscle fibers or submucosal biopsies in which the amount of submucosa was less than mucosa were excluded as the signs of inadequacy or inappropriateness.

This study was approved by the ethics committee of Tehran University of Medical Sciences. No extra sampling was imposed to individuals and no extra the parents were not charged.
Findings

With exclusion of inadequate biopsies (6% of all biopsies), 172 biopsies were available from 168 children with constipation, 127 (75%) had HD and 41 cases had normal biopsies with normal ganglion cells in appearance and distribution. The mean age of constipated patients at the time of biopsy was 39 months and the mean age of patients with proven HD was 18 months.

Males were affected more than females (male to female ratio: 4/1). Positive Family history was present in only one case. Table 1 shows frequency of HD among patients in different age groups based on the time of diagnosis.

In 93 children with HD, the parents could remember the beginning time of constipation, in 85 (91%) cases it was in neonatal period \( (P<0.005) \) although the time of taking biopsy was later in many. In 8 cases the beginning of clinical manifestation was beyond neonatal period. In the remaining children (28 cases) the parents could not remember the time they noticed constipation (at or beyond neonatal period).

From 27 cases without HD, 5 cases had constipation from neonatal period. In 22 cases the beginning of clinical manifestation was beyond neonatal period and in the remainder (14 children) the beginning of clinical manifestation was not clear. Frequencies of different clinical manifestations in patients with HD are listed in Table 2.

Congenital anomalies associated with HD were found in 9.6% and included 4 cases with CNS malformation, 3 cases with congenital heart disease, 2 cases with anatomical gastrointestinal malformation, 2 cases with genitourinary malformation, 1 case with congenital dislocation of hip, 1 case with polydactyly and one case with Down syndrome.

Barium enema was done in 103 children and there were false positive and false negative results in 7 and 3 cases, respectively, the diagnostic sensitivity was 91.3%.

Discussion

Constipation accounts for nearly 3% of visits to a general pediatric office and 25% of visits to a pediatric gastroenterologist\(^{[7,1]}\). 95% of children with chronic constipation have functional

<table>
<thead>
<tr>
<th>clinical manifestation</th>
<th>In neonates</th>
<th>In remaining patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed passage</td>
<td>64.8%</td>
<td>15.8%</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>64.8%</td>
<td>58.3%</td>
</tr>
<tr>
<td>Constipation</td>
<td>54.7%</td>
<td>84%</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>18.5%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Enterocolitis</td>
<td>9.3%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16.7%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>40.7%</td>
<td>24.1%</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>3.7%</td>
<td>14.1%</td>
</tr>
<tr>
<td>Bowel perforation</td>
<td>3.7%</td>
<td>0%</td>
</tr>
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</table>
constipation while only 5% have an organic cause for their symptoms, and a rectal biopsy, the goldstandard for the diagnosis of HD, is necessary to exclude this condition[1,8]. Some authors are of opinion that if the onset of constipation is beyond neonatal period, the child is unlikely to have HD [6]. The indications for rectal biopsy in children before 6 months of age: (a) delayed meconium passage; (b) low intestinal obstruction of unknown cause; (c) severe constipation; (d) chronic abdominal distention and (e) failure to thrive [9,10,11].

Our results show that males were affected 4 times more than females and it is parallel to those of other studies like results reported by Amiel[3] and Halevy [12]. In a study in Korea HD male to female ratio was 3.6:1 [13].

The most frequent sign of disease in neonates in our study was abdominal distension and delay in meconium passage which is the same as in other studies [1,2].

Most cases with HD were diagnosed in neonatal period (1.8% of patients without and 30% of patients with HD were neonates, \( P<0.004 \)).

In 85 (91%) cases the beginning of constipation was in neonatal period and in five non-HD cases the constipation was present in newborn infant (\( P<0.008 \)). Our data supports Griffith’s results suggesting that if the onset of constipation occurs after the neonatal period, it is unlikely that the child has HD and therefore a rectal biopsy is unnecessary [6]. Also Nicola in showed that in sixty percent of patients with HD and 15% of patients without HD the onset of symptoms was in the first week of life [4].

In our study, a large number of suspected children had HD. This may be because our hospital as a referral one is usually attended by cases with prolonged or complicated diseases; also the reason may be the good selection of patients for taking biopsy since in suspicious cases anorectal manometry and/or a barium enema is undertaken as screening methods before undergoing rectal biopsy.

In 9.6% of our cases HD was associated with other congenital anomalies. This is lower than in Australian and Boston studies which show 16% (Australia) and 22% (Boston) of children with associated anomalies [13,14]. These findings plus the fact that 9% of these children had also Down’s syndrome, is evidence for the assumption that the etiology of HD may be partially genetic.

The diagnostic sensitivity of barium enema in our study was about 91.3% and was close to Amsterdam study in 2005 [15].

Conclusion

According to our data and those of Griffith and also Nicola studies it can be concluded that delay in meconium passage is the most important clinical sign of HD and it should be emphasized in the patients history if noticed. Furthermore, radiologic findings in older cases that are unresponsive to medical therapy are other means to select correct patients for biopsy.

Acknowledgment

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Conflict of Interest: None

References


4. Lewis NA, Levitt MA, Zallen GS, et al. Diagnosing Hirschsprung’s disease: increasing the odds of a


