CHILDREN WITH CLINICAL PRESENTATION OF HIRSCHSPRUNG’S DISEASE – A CLINICOPATHOLOGICAL EXPERIENCE

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ABSTRACT

Background: Enteric neuronal abnormalities include Hirschsprung’s Disease (HD), hypoganglionosis, intestinal neuronal dysplasia (IND Type A & B), and immaturity of ganglion cells. All of these are mostly present with the same clinical features of the HD.

Materials and Methods: A total of 92 patients presented with the clinical features of HD were recruited to this study from two tertiary care Children Hospitals from March 2009 to October 2009. They either had their first presentation or called for definitive surgeries with clinical presentation of HD. After applying exclusion criteria, 84 patients were finally left for the study.

Results: Among 84 patients, 13 (15.5%) proved to be normally ganglionic on rectal biopsies and 71 (84.5%) showed enteric neuronal abnormalities. In these, 51 (71.8%) children had Hirschsprung’s disease, 9 (12.7%) revealed immaturity of ganglion cells (IGC), 9 (12.7%) belonged to isolated hypoganglonic group and 2 (2.8%) showed isolated IND type B. In HD group, M: F ratio was 4:1, mean age at diagnosis was 1.9 years and the presenting complaints were in the descending order i.e., abdominal distention, constipation, vomiting and delayed passage of meconium. Among the group that showed IGC, M : F ratio was 2 : 1, mean age at diagnosis was 12 days of life. The presenting complaints were same as that in HD in a similar order. In isolated hypoganglonic group, M : F ratio was 3.5 : 1, mean age at diagnosis was 2.3 years. The presenting complaints included constipation (88.9%), abdominal distention (77.8 %), vomiting (33.3%) and delayed passage of meconium (33.3%). In isolated IND type B, both patients were males, they came with constipation, abdominal distension and vomiting whereas one of them had history of delayed passage of meconium.

Conclusion: HD was the most common enteric neuronal abnormality. Other neuronal abnormalities included isolated hypoganglionosis, immaturity of ganglion cells and isolated hyperganglionosis (IND Type B). Most common presenting complaints were abdominal distension, constipation, vomiting and delayed passage of meconium in all the groups.

Key words: Hirschsprung’s disease (HD), hypoganglionosis, hyperganglionosis (IND type B) and immaturity of ganglion cells (IGC).

INTRODUCTION

Congenital intestinal neuronal disturbances have been classified as aganglionosis (Hirschsprung’s disease), hyperganglionosis (Intestinal Neuronal Dysplasia), hypoganglionosis, ganglion cell immaturity, combined forms and certain unclassifiable forms.¹ Hirschsprung’s disease (HD) is defined as the absence of ganglion cells in submucosal (Meissner’s) and myenteric (Aurbach’s) plexuses in distal bowel extending proximally from internal anal sphincter for variable distances that result in functional obstruction caused by dysmotility of the diseased segment.² Newborn and infants may present with failure to pass meconium within first 24 hours of life, bilious vomiting, infrequent, explosive bowel movements, difficult bowel movements, jaundice, enterocolitis associated diarrhoea, poor feeding and progressive abdominal distension.³ On the other hand, older children may present with chronic progressive constipation (usually with onset in infancy)³ failure to thrive, malnutrition, faecal impaction and progressive abdominal distension.⁴

IND is a distinct clinical entity that is genetically different from HD,⁵ which is characterized histologically by a total increase in the number of ganglia and ganglion cells per ganglion in the myenteric and submucosal plexuses in the colon.⁶ IND type A presents acutely in the neonatal period with episodes of intestinal obstruction, diarrhoea, and bloody stools; and in IND type B the clinical picture is indistinguishable from HD.⁷ When normal ganglion cells are present in the submucosal and intramuscu-
lar layers, their population is decreased; the disease is referred to as hypoganglionosis. Almost all cases reported in literature occurred relatively late in childhood and the common complaint of the patients with hypoganglionosis is intractable constipation.

Immaturity of ganglion cell group is characterised by the pathological findings that the number of ganglion cells is either normal or slightly increased, whereas the nuclear size is small. It is also interesting that the improvement in the intestinal motility coincides with the maturation of the intestinal ganglia. Therefore, most of the patients with an immaturity of the ganglia are considered to heal spontaneously as time goes on.

MATERIALS AND METHODS
A total of 92 patients were received, 8 were excluded using exclusion criteria (in 2 inadequate tissues and 6 tissues were taken from anorectal transformation zone). Hence, a total of 84 patients were left for the study. All the patients presented between March 2009 and October 2009, with the clinical features of Hirschsprung’s disease, were registered for the study after taking informed consent (from the guardian). All of them presented for the first time or those who were called for definitive surgeries. All the 84 patients belonged to Institute of Child Health and Mayo Hospital, Lahore. Detailed history from the parents or close relatives available at the time of presentation was recorded according to a preplanned proforma. Physical and gastrointestinal (GIT) examination was performed. All the biopsies obtained were processed using automatic tissue processor. This was followed by cutting serial sections (12–15 / biopsy) and stained using H & E staining procedure in the Department of Morbid Anatomy and Histopathology, University of Health Sciences, Lahore.

RESULTS
In a total of 84 patients, 13 (15.5%) proved to be normally ganglionic on rectal biopsies and 71 (84.5%) showed enteric neuronal abnormalities.

Table 1: Shows the mean ± standard deviation age at diagnosis in different groups with minimum and maximum age in patients presenting for the first time in months.

<table>
<thead>
<tr>
<th>Group</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>0.03</td>
<td>156</td>
<td>22.97</td>
<td>3.96</td>
</tr>
<tr>
<td>IGC</td>
<td>0.07</td>
<td>1.32</td>
<td>0.39</td>
<td>0.45</td>
</tr>
<tr>
<td>Hypoganglionic</td>
<td>0.23</td>
<td>77</td>
<td>28.03</td>
<td>2.72</td>
</tr>
</tbody>
</table>

HD: Hirschsprung’s Disease, IGC: Immaturity of Ganglion cells

Among these 71 patients, 51 (71.8%) were diagnosed as Hirschsprung’s disease group, 9 (12.7%) revealed immaturity of ganglion cells (IGC), 9 (12.7%) belonged to isolated hypoganglionic group and 2 (2.8%) showed isolated IND type B. IND type A was not diagnosed in our patients. In HD group, 10 (19.6%) patients were females and 41 (80.4%) were males (M : F = 4.1 : 1). Among the group that showed IGC, 3 (33.3%) were females and 6 (66.7%) were males (M : F = 2 : 1). In hypoganglionic group, 2 (22.2%) were females and 7 (77.8%) were males (M : F = 3.5 : 1) whereas in IND type B, both patients were males. Among the 71 patients having enteric neuronal abnormalities, 23 were re-called for definitive procedure and 48 patients came for the first time. In HD group, 20 patients had planned definitive surgeries and 31 presented for the first time and they had mean age of 22.97 months (1.9 years) (table 1). Maximum number of patients in HD group presented between 0 and 7 days of life followed by 6.1 months to 12 months. In the patients who showed IGC, all of them had their first presentation and the mean age at diagnosis was 0.39 months (12 days) of life (table 1). The maximum (67%) patients in this group presented between 1 and 7 days of life. In hypoganglionic group, 2 patients had definite surgeries and 7 presented for the first time. In this group, the mean age at diagnosis was 28.03 months (2.3 years) among those presented for the first time (table 1). In this group, maximum (28.5%) patients presented between 1 and 2 years of age. In IND type B group, one case was for definitive surgery and the other presented for the first time at 9 months of age.

The main presenting complaints were difficulty in passing meconium, abdominal distension, constipation and vomiting during the course of diseases. In most of the cases, more than one symptom was present. Figure 1 shows the details of presenting complaints in all the groups separately. Among HD group, 4 (7.4%) patients suffered intestinal perforation (3 caecal and 1 ileal), 2 (3.9%) came with imperforate anus and 2 (3.9%) with anal stenosis, 2 (3.9%) were diagnosed as Down’s syndrome and one (2%) had mental motor delay. Among IGC group, 2 (22.2%) showed caecal perforation. In hypoganglionic group, one (11.1%) was diagnosed as Down’s syndrome.

DISCUSSION
As regard the sex in HD the present study showed a predilection for the males i.e., 4.1 : 1. This is also supported by other studies on HD reported M : F ratio of 4 : 1. This is consistent with the present study showing a predilection for boys. The mean age at diagnosis in the present study was 1.9 years; this was likely to be due to late presentation. A Pakistani study reported from...
Islamabad, showed late presentation i.e., 2.4 years in their study population. Another study reported from this region revealed that the mean age at diagnosis was 2.11 years (35-28 months). Similarly a high mean age at diagnosis (4.4 years) was also reported from India. Late presentation of HD was also reported from various other countries and has been attributed to cultural differences, neglect of initial symptoms, poverty and prolonged treatment with herbal enemas. In a study conducted in Kuwait on HD reported that 57% patients were diagnosed during neonatal period, whereas 21% were of more than 4 months of age. On the contrary, in the present study 67.7% among the HD group were diagnosed during first year of life and of these 47.6% (32.3% among all age groups) were diagnosed in the neonatal period and 66.7% (51.6% among all age groups) within the first 6 months. The time when newborn passes the first meconium is an important prognostic factor. A few authors quoted that 58 – 90% of patients presented with delayed passage of meconium on the other hand in the present study, 47.9% of patients gave the history of delayed passage of meconium. Abdominal distension was observed in 76 – 88% patients on the other hand, the present study showed a higher incidence (91.7%). Askarpour and Samimi reported constipation in 33% patients in their study group whereas Ziad et al. reported that 82% presented with constipation, however, they also included the patients who had delayed passage of meconium or intermittent passage of stool of increasing consistency in older children. When comparing this with the present study, 78% of our patients were constipated whereas 58.3% had vomiting which is similar to those reported by Lewis et al. (61 – 67%). Intestinal perforation was the presenting complaint in 2.9% subjects. As regard perforation, we received 7.8% (n = 4) patients, three were with caecal; and one with ileal perforation. Imperforated anus was seen in 1.5% of patients in a study reported from USA whereas this association is also on the higher side in the present study i.e., 3.9%. The incidence of intestinal perforation is variable (2 – 10%) in different studies. Down’s syndrome was seen in 3.9% (n = 2) of our patients and mental motor delay in 2% cases.

As regard the IGC, Markiewicz – Kijewska and associates, showed that initial symptoms in most of their patients occurred during the first week of life (1 – 6 days) whereas others (5 out of 15 children) were diagnosed between 1 and 12 months of life.

This is similar to the present study in which patients with IGC presented between the ages of 2 – 40 days and majority (87%) of them were diagnosed within 0 – 7 days of life. Schärli reported that the mean age at diagnosis was 6 months in IGC group, on the other hand in the present study, the age at diagnosis was 0.39 months (12 days) of life. In the present series, all (100%) the patients with IGC had abdominal distension, 66.7% had constipation, and 28.6% presented with vomiting.

In a report on isolated hypoganglionosis, there were 10 males and 7 females making the M : F ratio of 1.4 : 1. On the other hand in the present study, hypoganglionic group comprised of 7 (77.8%) males and 2 (22.2%) females, with M : F ratio of 3.5 : 1. This is similar to the present study, Meier – Ruge concluded that hypoganglionosis is usually diagnosed during the later childhood. A common complaint with hypoganglionosis was intractable constipation, that was also the most common feature in the present study i.e., 88.9% of patients. Among the 9 cases of isolated hypoganglionic group, 3 (33.3%) complained of delayed passage of meconium. Abdominal distension was observed in 7 (77.8%) and absent in 2 (22.2%) cases. Vomiting was present in 3 (33.3%) patients and one (11.1%) was diagnosed as Down’s syndrome.

The mean age at diagnosis of IND type B was reported as 1.5 years and 50% of the children investigated were between 1 year and 12 years of ages. Two years of mean age was reported in another study of IND type B with an equal male to female ratio whereas in the present study there were two patients and both were males.
The clinical course of IND type B is insidious with progressive development of severe constipation similar to HD. Another study reported progressive constipation in IND type B. However, in the present study, two children were found to have isolated IND type B, both complained of constipation and abdominal distension whereas one gave the history of delayed passage of meconium (4th day of life) and another complained of vomiting. This is the first such study in this region which report clinicopathological features of patients with clinical presentation of Hirschprung’s disease.

We, therefore, conclude from the present study that HD is the commonest among the enteric neural abnormalities and in which common presenting complaints are abdominal distension, constipation, vomiting and delayed passage of meconium in all the groups.

Conflict of interest: None to declare.

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