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Diffuse Intestinal Ganglioneuromatosis in an Infant - A Case Report

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Abstract: ***Intestinal diffuse ganglioneuromatosis is a rare, benign, neoplastic condition arising from the enteric nervous system. This is a case of 2-month-old female baby, who presented with abdominal distention and decreased stool passage and suspected to have hirschsprung disease. Patient underwent ileostomy with multiple seromuscular biopsies, on histopathological examination and immunohistochemistry found to have Intestinal diffuse ganglioneuromatosis.***

Keywords: Ganglioneuromatosis, MEN 2B, NF1, ganglion cells

1. Introduction

Ganglioneuromas typically arise from sympathetic ganglia and adrenal glands, rarely some arise from the viscera [1]. It is composed of nerve fibres, ganglion cells and supporting cells like schwann cells [2]. They can arise in the gastrointestinal tract rarely, originating from the enteric nervous system [3]. Though uncommon, intestinal ganglioneuromas are more frequently observed in children than in adults [1]. It is typically associated with systemic conditions such as Cowden syndrome, neurofibromatosis type 1 (NF1), and multiple endocrine neoplasia type 2B (MEN 2B) [4].

Herein we discuss a case of 2-month-old child with diffuse intestinal ganglioneuromatosis without any known syndromic association

2. Case Report

The case involves a 2-month-old female baby, presented with abdominal distention since 1-month, poor weight gain, decreased feeding and passes small quantity of stool with straining. The child was not improving with lactulose. There was no history of meconium delay or bilious vomiting in neonatal period.

On examination, the following were observed:
Weight - 2.4 kg, pulse rate - 140 bpm, temperature - afebrile, oxygen saturation - 99%, per abdomen - soft, grossly distended with visible and palpable loops, per rectum - passed small quantity of pellet like yellow stool with no flatus.

USG abdomen showed dilated content filled bowel loops, X-ray showed gaseous distended bowel loops following which barium enema was done. Barium enema as in Figure 1 showed narrowed featureless colon, grossly dilated small bowel, no transition zone visualised. The possibility of hirschsprung disease was considered. Blood investigation showed low sodium levels which was then corrected.

Child was taken up for exploratory laparotomy, multiple biopsies and divided ileostomy under general anaesthesia. Multiple seromuscular biopsies were taken from rectosigmoid, descending colon, transverse colon, ascending colon, appendix, ileum at about 20 cm from ileo-colic junction (ICJ) and doughnut biopsy of ileostomy.

Microscopy showed diffuse hyperplasia of ganglion cells and neural tissue in submucosa and in myenteric plexus extending into serosa as shown in Figure 2. Immunohistochemistry was done. Calretinin, synaptophysin and S100 highlighted ganglion cells and neural cells as in Figure 3. With the above finding, a possibility of diffuse intestinal ganglioneuromatosis was considered.

Post op, ileostomy started functioning on post operative day 2 and oral feed restarted on post operative day 3.

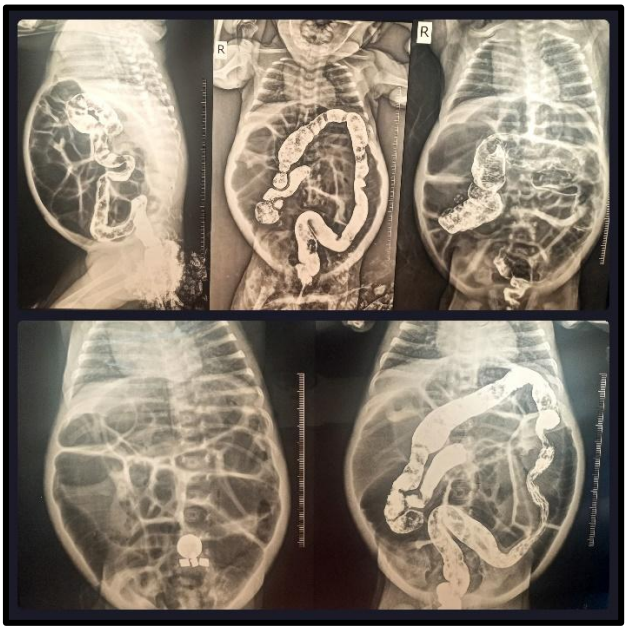

Figure 1: X-ray and Barium enema

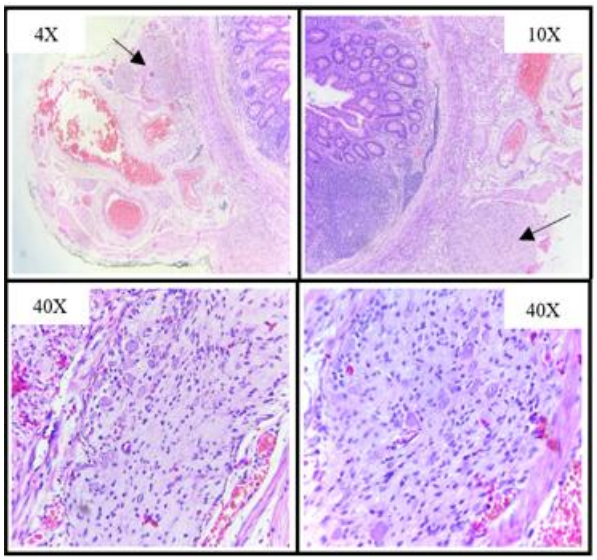

Figure 2: H&E showing diffuse hyperplasia of nerve bundles and ganglion cells in the submucosa, muscularis propria and serosa

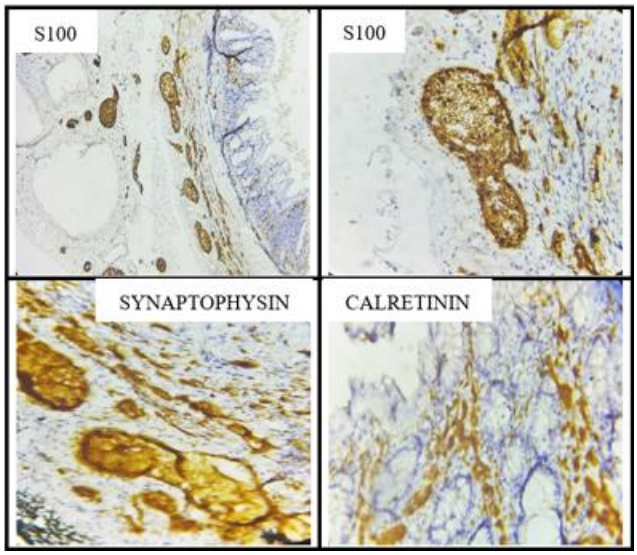

Figure 3: S100, synaptophysin and calretinin highlighting the proliferated nerve bundles and ganglion cells

3. Discussion

Intestinal ganglioneuromatosis is an uncommon benign neurogenic tumor characterized by abnormal growth of intestinal wall schwann cells, nerve fibers, and ganglion cells in the intestinal wall [5]. Any part of the gastrointestinal tract might be affected, though the ileum, colon, and appendix are more frequently affected. They are more common in children [6].

The three main categories of intestinal ganglioneuromatosis, as classified by the WHO in 2019, which are, solitary ganglioneuroma; ganglioneuromatous polyposis and diffuse ganglioneuromatosis [6]. The first one can be mucosal or submucosal, seen mostly in colon as a solitary or small polyps [7]. Ganglioneuromatous polyposis, which is usually observed in the colon and terminal ileum, is characterized by numerous tiny mucosal polyps usually > 20 in number and ≤ 2.2 cm in diameter, and is composed of loose aggregates of mature ganglia. It may resemble familial adenomatous polyposis and can be associated with MEN2b, NF1, Cowden disease or juvenile polyposis [4], [7], [8]. In diffuse intestinal ganglioneuromatosis, there is hyperplasia of myenteric plexus with infiltrative intramural or transmural ganglioneuromatous proliferation in ileum, colon, and appendix and can show association with tuberous sclerosis, Cowden disease, MEN 2B, NF1 or juvenile polyposis [6], [7]. It can occur in two forms: mucosal and transmural. In children, both the forms can be seen, while in adults, the mucosal variant is more common [3].

Clinical manifestations of intestinal ganglioneuromatosis typically include bleeding, constipation or diarrhea, altered bowel habits, abdominal pain, and intestinal obstruction from stricture formation. But depending upon the location and extent of the lesion the signs and symptoms can vary. When a syndromic association is present, intestinal ganglioneuromatosis may be the first manifestation of these syndromes[5]. There is no pathognomic signs of any associated syndromes in our case. The clinical diagnosis of diffuse intestine ganglioneuromatosis becomes challenging due to its nonspecific clinical presentations and imaging findings [5].

Hirschsprung's disease, intestinal tuberculosis, inflammatory bowel disease, cytomegalovirus infection, amyloidosis and tumours such as adenocarcinomas, gastrointestinal stromal tumors (GIST), lymphomas, leiomyomas come under the differential diagnosis. Definitive diagnosis is mainly based on histopathological examination [6]. Other investigations include colonoscopy, abdominal X-rays and CT scans [1].

Histologically it is a well differentiated tumour with muscularis propria and other layers showing abundant, ill defined, nodular, or diffuse proliferation of nerve fibers, ganglion cells, and supporting cells of the enteric nervous system [9]. When ganglion cells are few, immunohistochemical staining may be useful because the ganglion cells are positive for NSE, synaptophysin, and neurofilament protein, but S-100 is positive in spindle cells [3]. In case of our patient, the major differential diagnosis was Hirschprung's disease as was suggested by preoperative radiologic and clinical findings. However, the definitive diagnosis established by pathologic examination revealed diffuse intestinal ganglioneuromatosis.

Since conservative measures have shown to be ineffective for treating diffuse intestinal ganglioneuromatosis, surgical resection of the affected bowl is the preferred course of treatment [9].

4. Conclusion

Diffuse intestinal ganglioneuromatosis is a benign tumour of enteric nervous system, usually seen in children. Due to its rarity and nonspecific symptoms and radiological findings, clinically and radiologically it is often misdiagnosed as motility disorders in children. Therefore, histopathological examination is necessary to come to a definitive diagnosis. Since it often has syndromic association, accurate diagnosis is critical for prevention and management of neoplasms arising in individuals with germline mutation in protooncogene.

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