Chronic constipation leading to total colectomy: A rare case to illustrate the controversial entity of intestinal neuronal dysplasia

Mona Deerwester, Katherine Weng, Steven Drexler

ABSTRACT

Introduction: Intestinal neuronal dysplasia (IND) encompasses a group of histological anomalies of bowel innervation characterized by clinical symptoms of constipation, abdominal pain, and delayed intestinal transit time. However, despite numerous scientific research conducted with over 250 articles published, IND remains a controversial entity due to lack of consensus on diagnostic criteria.

Case Report: We present a unique case of a patient with chronic constipation and with clinical symptoms consistent with IND but the histopathological findings revealed hypoganglionosis of Meissner’s plexus and hyperganglionosis of Auerbach’s plexus, neither of which met the diagnostic criteria of IND.

Conclusion: This unique case illustrates the controversy of the diagnostic criteria of IND and exemplifies the need for definite treatment regardless of the diagnosis.

Keywords: Chronic constipation, Colectomy, Intestinal neuronal dysplasia

INTRODUCTION

Intestinal dysganglionosis is a group of disorders that constitute malformations of the enteric nervous system, which includes intestinal neuronal dysplasia (IND), Hirschsprung disease, hypoganglionosis, and ganglioneuromatosis. Although they have distinct histological features, they have overlapping clinical symptoms most often characterized by constipation, abdominal pain, and delayed intestinal transit time [1]. Intestinal neuronal dysplasia is defined as a disorder of the submucous plexus of the intestine where there is an increase of ganglionic cells in the submucous plexus, often accompanied by hyperplastic changes in the myenteric plexus [2]. The etiology of IND also remains unclear. Since IND is associated with chronic intestinal obstruction, it has been proposed that it is caused by either an inflammatory process or a reaction of the enteral nervous system to intestinal obstruction [3]. Clinically, IND presents as acute and chronic intestinal obstruction with vomiting, abdominal pain and distention, diarrhea, and malabsorption. No unified method of treatment is accepted; both successful surgical treatment and conservative treatment have been described.

The diagnosis is controversial due to lack of consensus on diagnostic criteria. The criteria purposed by Meier-Ruge in 2006 is based on the proportion of giant ganglia in the submucosal, defined as more than 8 ganglion in...
a 15 micron thick frozen section that has been stained histochemically for lactate dehydrogenase (LDH) to highlight the ganglion cells. Additional criteria are a minimum of 25 submucosal ganglia, more than 20% of submucosal ganglia must be giant ganglia and the biopsy should be at least 8 cm proximal to the pectinate line. In addition, the patient must be older than 1 year [4]. These criteria’s technical requirements are available at only a few diagnostic centers, which led to the rise of nonuniform diagnostic criteria and led to diagnosis of IND without specifically using Meier-Ruge criteria. This further contributed to the ambiguity of a diagnosis of IND. Hence, IND remains a controversial entity with disparity in diagnosis. At present, documented cases have a geographic distribution with the highest rates in Europe, which correlates to published cases in this region [5]. Intestinal neuronal dysplasia will remain a controversial diagnosis until further studies are conducted to establish diagnostic criteria that can be universally implemented. We present a unique case of chronic constipation that led to total colectomy, which highlights that despite the inconsistencies of the diagnostic criteria of IND, definitive treatment and follow up is essential.

CASE REPORT

Clinical

A 23-year-old female presented to the emergency department of our hospital complaining of abdominal pain, nausea, and constipation. She reported long standing constipation and abdominal pain for many years starting in her teenage years. There was no family history of dysmotility in the patient’s family. The patient has tried non-surgical treatment including over the counter laxatives, diet, and exercises, all without symptomatic relief. The patient had no previous surgical history and denied any other significant medical history. Previous anal manometry results were within normal values. Laboratory tests conducted on admission were within normal range. Physical exam revealed abdominal tenderness. Abdominal X-ray showed distented bowel without obstruction. Magnetic resonance imaging (MRI) enterography showed dense stool throughout the large bowel (Figure 1). Colectomy was offered to the patient due to longstanding constipation and radiological findings. During laparotomy, no obvious mechanical cause was found, and a total abdominal colectomy with ileo-rectal anastomosis was performed. The patient had an uneventful postoperative course and was discharged. On follow-up, the patient reported feeling well with resolution of her symptoms.

Pathology

Gross examination of the colectomy specimen showed cobblestoning (Figure 2). Paraffin-embedded tissue was cut to 5-μm-thick sections. The morphology of the muscle cells in the muscularis propria showed no significant histopathological changes. No significant interstitial fibrosis in the muscularis propria was evident on hematoxylin and eosin stain. Immunohistochemical expression of calretinin was used to highlight nerve fibers in the muscularis mucosa and submucosa (Figures 3 and 5). Microscopic examination demonstrated hypoganglionosis of the Meissner’s plexus, hyperganglionosis of Auerbach’s plexus (Figure 3) and “giant ganglia” (Figure 4). Immunohistochemistry for calretinin was performed which highlighted giant ganglia in the Auerbach’s plexus of the submucosa (Figure 5). While additional immunohistochemistry studies, such as Bcl2 to highlight the ganglia and CK117/c-kit to study other elements of the neuromuscular apparatus would certainly be enlightening, these studies were not performed as they were deemed of insignificant prognostic value. Although a putative diagnosis of IND was established, this histopathological features of this case did not meet the 2006 Meier-Ruge criteria (Table 1).
DISCUSSION

This case report highlights the controversial entity of IND due to lack of consensus on diagnostic criteria. This case caused confusion with IND, because clinically, IND is an entity of exclusion and definitive treatment is colectomy in setting of unrelenting constipation and failure of conservative management. Although the pathology did not entirely conform to the controversial diagnostic criteria of IND, the patient’s clinical course was consistent with IND and all other possible disease entities were excluded. Hence, a colectomy was offered for treatment, which was successful in alleviating the patient’s symptoms.

Since IND is a controversial histopathologic phenotype, its clinical significance remains unclear. Intestinal neuronal dysplasia has two subtypes, IND-type A which is characterized as congenital aplasia or hypoplasia of the sympathetic nerves seen in infancy, whereas IND-type B is caused by malformation of the parasympathetic submucosal and myenteric plexi often seen in adults and children. The pathogenesis is not clear but speculations of smooth muscle contraction by 5-hydroxytryptamine produced by neuroendocrine cells has been made [6]. Intestinal neuronal dysplasia is characterized by morphological changes, such as giant cells, and increased neuroendocrine cells [6]. Unlike some of the other intestinal dysganglionosis, such as Hirschsprung disease, the surgical treatment of IND-type B lacks consensus. Conservative management of IND is effective in 33–64% of patient [7], which is why surgery is often delayed.

A recent case study illustrated that a 71-year-old patient with longstanding idiopathic constipation remained without proper treatment for more than 60 years despite long-term attempts for conservative treatment [8]. A subtotal colectomy was the only successful therapeutic approach. Colectomies have been successful in many other documented cases [9, 10].

We present a unique case in which total colectomy was performed in the setting of chronic constipation with the putative diagnosis of IND. This case study highlights the importance of initiating definitive treatment despite the enigma surrounding the diagnosis of IND. The aim of this case report is to highlight the controversy surrounding IND and to illustrate that colectomy is curative although the final diagnosis remains unclear. This case does not fit hypoganglionosis or other conditions and does not fulfill

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<td><strong>2006 Meier-Ruge Criteria</strong></td>
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<td>• A minimum of 25 submucosal ganglia</td>
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<td>• More than 20% of submucosal ganglia must be giant ganglia</td>
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<td>• A giant ganglion contains &gt;8 nerve cell cross sections</td>
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<td>• Patient must be older than 1 year</td>
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the diagnostic criteria of IND, which further exemplifies the controversy surrounding the diagnostic criteria of IND and demonstrates that although the diagnostic criteria of IND was not completely met, definite treatment of colectomy without delay to alleviate symptoms is needed regardless of the diagnosis.

Clinicians should be mindful of IND in patients with long standing history of chronic constipation and nonspecific imaging, as timely diagnosis with discussion of treatment options can significantly improve quality of life.

CONCLUSION

Though intestinal dysganglionosis is rare, clinicians should have a high index of suspicion of IND (even when not all diagnostic criteria are met) when patients present with severe chronic constipation. Timely diagnosis is essential in initiating appropriate treatment to prevent further complications from intestinal obstruction. The entity of IND remains controversial due to lack of consensus on diagnostic criteria. Despite this controversy, diagnosis and treatment should not be delayed.

REFERENCES


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Author Contributions

Mona Deerwester – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Katherine Weng – Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Steven Drexler – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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