CASE REPORT

Ganglioneuromatous Polyposis of the Colon: a Case Report and a Review of the Literature

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ABSTRACT

This report discusses a case of ganglioneuromatous polyposis of the colon in a woman without any other systemic manifestations. To our knowledge, this is the first report of the few cases of intestinal ganglioneuromatosis described in the literature presenting with abdominal pain and bloody diarrhea as unique clinical signs, with multiple polyps confined in the right side of the transverse colon and in the ascending colon. Of note, the endoscopic feature of such a rare entity - which involves the enteric nervous system - may mimic that of sessile adenomatous polyps which are diagnosed at routine colonoscopy. We emphasized that this condition may be misdiagnosed, and we reviewed the reported cases in the literature. (*J Dig Endosc* 2011;2(1):18-21)

Key words: Colonic polyps - Ganglioneuromatous polyposis - Enteric nervous system

Introduction

Intestinal ganglioneuromatosis is a benign proliferation of nerve ganglion cells, nerve fibers, and supporting cells of the enteric nervous system that can result in abnormally large enteric neuronal cells in the myenteric plexus, which can be associated with the von Recklinghausen's disease and other multiple tumor syndromes.[1,2] We report a case of a woman diagnosed with colonic ganglioneuromatous polyposis of the colon following surgery. We reviewed the literature and discussed the endoscopic pitfall of this rare condition.

Case report

A 64-year-old woman was referred to our Unit because a 2-year history of recurrent episodes of abdominal pain with mild bloody diarrhoea and mucus in the stool. Barium-contrast study demonstrated the presence of multiple filling defects in the ascending colon (Figure 1). The patient had no family history for intestinal diseases or neoplasia. Examination revealed tenderness in the lower abdomen, with normal bowel sounds, and no detectable masses. Rectal examination showed the presence of haemorrhoids. Colonoscopy revealed diverticulae in the sigmoid and descending colon and presence of flat, multiple, agglomerated, sessile polyps, 2-4 mm in size, located in the right side of the transverse colon and in the ascending colon (Figure 2). The histology of a resected polyp was adenomatous polyp with low grade dysplasia. Because of the extensive nature of polyposis, the patient underwent right hemicolectomy to rule out an attenuated form of familial adenomatous polyposis. Unexpectedly, the post-surgical

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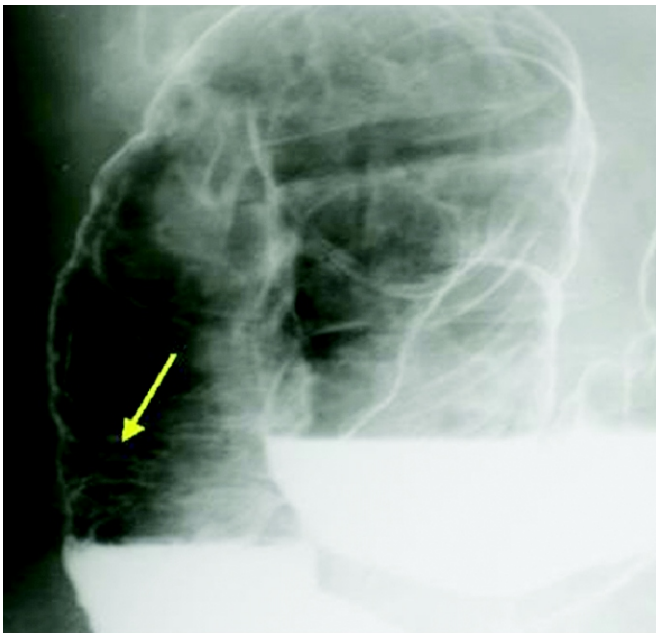

Figure 1: Figure 1: Barium-contrast study showing small filling defects in the ascending colon (arrow).

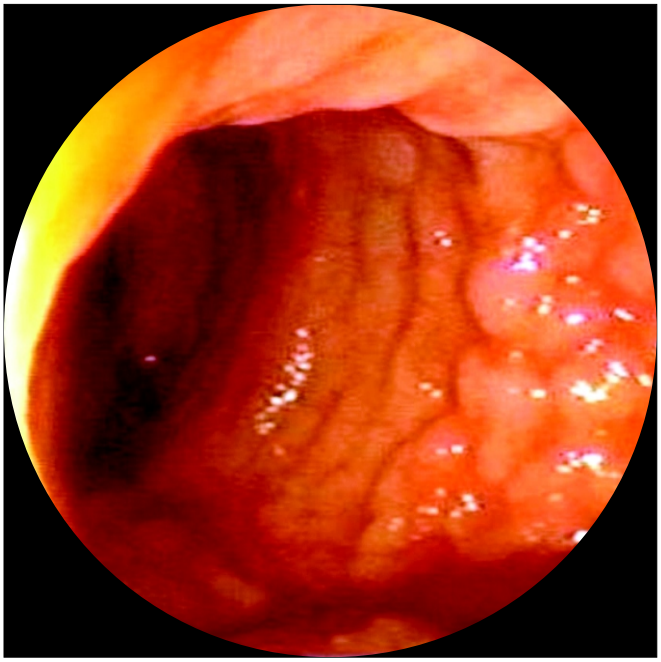

Figure 2: Endoscopic feature of several polyps in the ascending colon.

histological examination showed polyps with normal mucosa, whereas aggregates of neurologic fibers, Schwann cells and rare ganglial cells were present in the submucosa. Immunohistochemical studies using antibodies to S-100 protein, neuronspecific enolase (NSE) and neurofilament protein (NFP) were positive. Therefore, the final diagnosis was ganglioneuromatous polyposis of the colon (Figure 3). A total body CT-scanning did not demonstrate any other

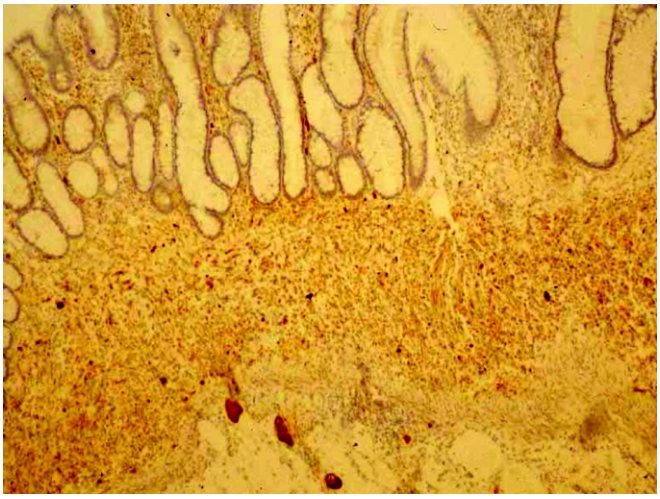

Figure 3: Neuron-specific enolase stain showed the neural nature of the polyps.

abnormality. Following colonic resection, diarrhea resolved. No other polyps in the residual colon were found at 3-year endoscopic follow-up.

Discussion

Intestinal gganglioneuromatosis has been essentially described in children and rarely in adults, generally associated with juvenile polyps or multiple adenomatous polyps. It is characterized by the presence of benign, hamartomatous polyps with an overgrowth of nerve ganglion cells, nerve fibers, and supporting cells in the gastrointestinal tract.[2,4] At endoscopy, the finger-like polyps more likely suggest ganglioneuromatosis, while the raspberry-like polyps correspond to adenomas.[3] Depending on the great variability in neural, supportive, and ganglion cell content and demarcation, three forms have been recognized: 1) polypoid ganglioneuroma, never associated with von Recklinghausen's disease or endocrine multiple neoplasia, with a typical juvenile polyp-like pattern or neuro-fibromatous pattern; 2) diffuse ganglioneuromatosis, associated with systemic disorders, such as MEN IIb, Cowden syndrome, and Ruvalcaba-Myhre-Smith syndrome; and 3) ganglio-neuromatous polyposis. Despite the latter form of intestinal ganglioneuromatosis is quite rare, it may be associated with adenomatous polyps or juvenile polyposis, but not coexists with neoplasia type IIb, neurofibromatous type I, and Cowden syndrome.[5-15] A familial form of such a disease has been once reported.[16] Two morphologic patterns have been described: 1) transmural type, characterized by neural hyperplasia in all layers of the bowel wall with predominant involvement of the myenteric plexus, often associated with multiple endocrine neoplasia IIb, and 2) mucosal type with predominant involvement of the mucosa without concomitant hyperplasia of the myenteric plexus, associated

Table 1: Main data of case reports of intestinal ganglioneuromatosis in the literature

Ref.	No. of Patients	Age	Sex	Symptoms	Clinical features	Endoscopic finding	Histological diagnosis
1	28	48	14/14	Rectal bleeding Weight loss Abdominal pain	Intestinal tumour (2)	NA	Polypoid ganglioneroma
	7	39	5/2	Abdominal pain Rectal bleeding	Multiple cutaneous(3) Elephantiasis (1)		Polyposis GNM
	8	35	7/1	Rectal bleeding Megacolon Abdominal pain			Diffuse GNM
2	2	45	2/0	Unknown	None	Polyps	Diffuse GNM
3	10	55	6/4	Abdominal pain Diarrhea Obstruction	MEN IIb(1) vRN (2) Adenomatous polyp (1) Cowden disease (1)	Megarectum(1) finger-like polyp (2) Rasberry like polyp (2)	Diffuse GNM (4) Appendicular GNM Rectal GNM (1) Sigmoid GNM (2) Polyposis GNM (1)
4	1	41	1/0	Rectal bleeding	Cutaneous lypomas	100 sessile polyps 1-2 mm colon, 3 sessile polyps in stomach	Polyp GNM
9	1	68	1/0	Unknown	unknown	Polyp	Polyp GNM
10	1	77	0/1		Adenocarcinoma Hyperparathyroidism	Polyposis	Polyposis GNM
11	1	40	1/0	Unknown	Adenocarcinoma	Polyposis	Polyposis GNM
12	3	67	2/1	Diarrhea	None	Polyposis cecum and right colon	Diffuse GNM
13	1	32	1/0	Unknown	NF type I	Unknown	Diffuse GNM
14	1	0/1	None	None	Sessile polyp	Polyp GNM	
15	1	5	0/1	Intussusception	Unknown	Polyp	Polyp GNM
16	1	38	1/0	Unknown	Unknown	Juvenile polyposis	Polyposis GNM
17	5			Unknown	3 MEN 2b, 1 WRN 1 adenocarcinoma 1 adenomatosis polyposis		
18	1			Diarrhoea	Intrathoracic noduclear stroma	Normal	Diffuse GNM

vRN = von Recklinghausen neurofibromatosis; GNM = ganglioneuromatosis; NF = Neurofibromatosis

with von Recklinghausen's disease, adenocarcinoma of the colon, and multiple adenomas.[17] Differently from our report, in most cases polyps were found in the entire colon. Rectal bleeding, abdominal pain, watery diarrhoea of several months duration have been observed in these patients.[18]

The pathogenesis remains unclear, representing an unusual hyperplasia of the nerve plexus related to circulating nerve growth factors and /or selective expression of the mutated neurofibromatosis gene within subpopulation of autonomic neurons. The pathophysiology is related to a complex hyperplasia of several peptidergic, cholinergic, and probably adrenergic nerve fibres.[4,17]

Diagnosis of intestinal ganglioneuromatosis has to be exclusively established on the basis of the microscopic examination by diffuse Schwann cell hyperplasia expressing S100 protein in close contact to nerve fibers expressing neurofilament, tau protein, synaptophysin, and to ganglion cells (Table 1). Symptoms including rectal bleeding, watery diarrhoea, abdominal pain and, seldom, acute occlusion have been reported. The endoscopic feature comprises presence of multiple finger-like polyps localized in colon. The von Recklinghausen's disease, multiple endocrine neoplasia type IIb or Cowden's disease, a nonfamilial adenomatous polyposis or colonic adenocarcinoma can be associated disorders.[1,6,8,10,17,18]

To our knowledge, this is the first report of a transmural type ganglioneuromatous polyposis presenting with abdominal pain and bloody diarrhea, associated with multiple adenomatous polyps which are confined in the ascending and transverse colon, without any evidence of other neuroendocrine or inherited associated diseases. The coexistence of ganglioneuromatous polyposis and adenomatous polyps into the colon remains unclear. However, after colonic surgery no other polyps were found in the residual colon. At 3-year follow-up neither polyp recurred nor the patient developed features suggestive of multiple endocrine neoplasia or other diseases.

Conclusion

Ganglioneuromatous polyposis of the colon is a rare condition characterized by the presence of 20-40 sessile or pedunculated polyps, which may be detected in the colon. This rare condition may be associated with adenomatous polyps or juvenile polyposis or multiple endocrine neoplasia. Its pathogenesis remains unclear, although an unusual hyperplasia of the nerve plexus due to circulating nerve growth factors and/or selective expression of the mutated neurofibromatosis gene within subpopulation of autonomic neurons have been showed. Gastroenterologists have to be aware of the higher risk of occlusion and intestinal neoplasia associated with this rare condition which should be also kept in mind when multiple, adjacent polyps are detected at colonoscopy.

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