Journal of Pediatric Surgery (2013) **48**, 1129–1133

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Journal of Pediatric Surgery

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Diffuse intestinal ganglioneuromatosis in a child

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Received 20 December 2012; revised 14 March 2013; accepted 17 March 2013

Key words:
Intestine;
Ganglioneuromatosis;
MEN 2B;
NF-1;
Cowden syndrome

Abstract A 7 year old male with a history of congenital neutropenia and growth hormone deficiency presented with abdominal pain, fevers, and diarrhea. Imaging and endoscopy revealed significant inflammation of the ascending colon with stenosis at the level of the hepatic flexure. A right hemicolectomy was performed, and pathologic findings were consistent with diffuse intestinal ganglioneuromatosis. Due to recurrent mass effect at the intestinal anastomotic site detected radiologically, a second intestinal resection was performed 7 months later. Genetic testing was negative for mutations in the RET protooncogene, NF1 and PTEN tumor suppressor genes. We report a case of diffuse intestinal ganglioneuromatosis in a child with congenital neutropenia.

Ganglioneuromas are benign neurogenic tumors often diagnosed in children. While they typically develop from sympathetic ganglia and adrenal glands, some arise from the viscera. Intestinal ganglioneuromas are rare and consist of 3 subgroups: 1) solitary polypoid ganglioneuromas, 2) ganglioneuromatous polyposis, and 3) diffuse ganglioneuromatosis [1]. Intestinal ganglioneuromatosis often leads to thickening of the bowel wall leading to stricture formation, abdominal pain and diarrhea [2]. Diffuse ganglioneuromatosis is typically associated with several diseases including neurofibromatosis-1 (NF1), Cowden syndrome (CS), and most frequently multiple endocrine neoplasia type 2B (MEN 2B) [2]. In this report, we describe a case of diffuse intestinal ganglioneuromatosis in a 7 year old patient with congenital neutropenia.

1. Case report

A 7 year old male with a past medical history significant for chronic neutropenia and growth hormone deficiency, had a 2 week history of abdominal pain, nausea, and decreased oral intake leading to a diagnosis of colitis. He presented to the emergency department with a 2 day history of increasing

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0022-3468/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jpedsurg.2013.03.066

abdominal pain, right-sided abdominal fullness, diarrhea, and hematemesis. His physical examination was remarkable for diffuse tenderness to palpation. Acute abdominal series demonstrated several mildly dilated loops of small bowel with air fluid levels, and a relative paucity of bowel gas in the right lower abdomen. CT scan of the abdomen revealed significant ascending colonic wall thickening with fat stranding, and extensive fatty proliferation around the ascending colon (Fig. 1). In addition, there was mild distention of the cecum and ascending colon. Diagnostic laparoscopy revealed significant thickening of mesenteric fat that wrapped around the anterior surface of the ascending colon. Esophagogastro-duodenoscopy (EGD) revealed moderate esophagitis, and colonoscopy showed stenosis in the ascending colon with edematous and pale mucosa. Endoscopic colonic biopsy specimens revealed focal epithelial hyperplasia, edema and expansion of the lamina propria, and patchy mucosal hemorrhage.

Resection of the ascending colon and 4 cm of the distal ileum was performed, with a stapled side-to-side functional end-to-end ileocolonic anastomosis performed in grossly normal appearing bowel. Pathologic examination of the specimen revealed prominent proliferation of thick nerve fibers with ganglion cells in the submucosa that extended focally through the muscular coat into the subserosal bowel wall, consistent with a diagnosis of diffuse intestinal ganglioneuromatosis. The ileum, appendix, and cecal margin had mildly increased numbers of enlarged nerve fibers along with ganglion cells in the muscular coat and subserosa. There was microscopic disease at the resection margins. Subsequently, serum and urine metanephrine and normetanephrine levels were obtained but were not consistent with the presence of pheochromocytoma. Genetic testing for the RET protooncogene mutation, and deletions in the NF1 and PTEN genes were performed and were also negative.

The patient's post-operative course was notable for several admissions for colitis and gastroenteritis. Several months later, a CT scan of the abdomen showed thickening of the distal ileum at the anastomotic site with fatty proliferation and fat stranding, raising the possibility of recurrent tumor. EGD and colonoscopy revealed gastritis and stenosis at the ileocolonic anastomosis, respectively. He was returned to the operating room 7 months after the initial resection where he underwent resection of the ileocolonic anastomosis with a side-to-side functional end-to-end ileocolonic anastomosis performed in healthy appearing bowel. Pathologic examination confirmed the frozen section diagnosis of diffuse ganglioneuromatosis in both the small bowel and colon at the resected anastomotic site, this time with microscopically negative resection margins (Fig. 2). Further genetic testing was performed and was negative for mutations in the NF1 and PTEN tumor suppressor genes. The patient is now 16 months after his second resection and continues to have admissions for fevers, abdominal pain, and diarrhea, with repeat imaging intermittently showing inflammatory changes and bowel wall thickening at the site of the anastomosis. A colonoscopy was recently performed and biopsies obtained showed inflammation at the anastomosis but no evidence of recurrence. Further surgery has not been required to date.

2. Discussion

Intestinal ganglioneuromas are rare, benign neurogenic tumors that are more often identified in adults and are

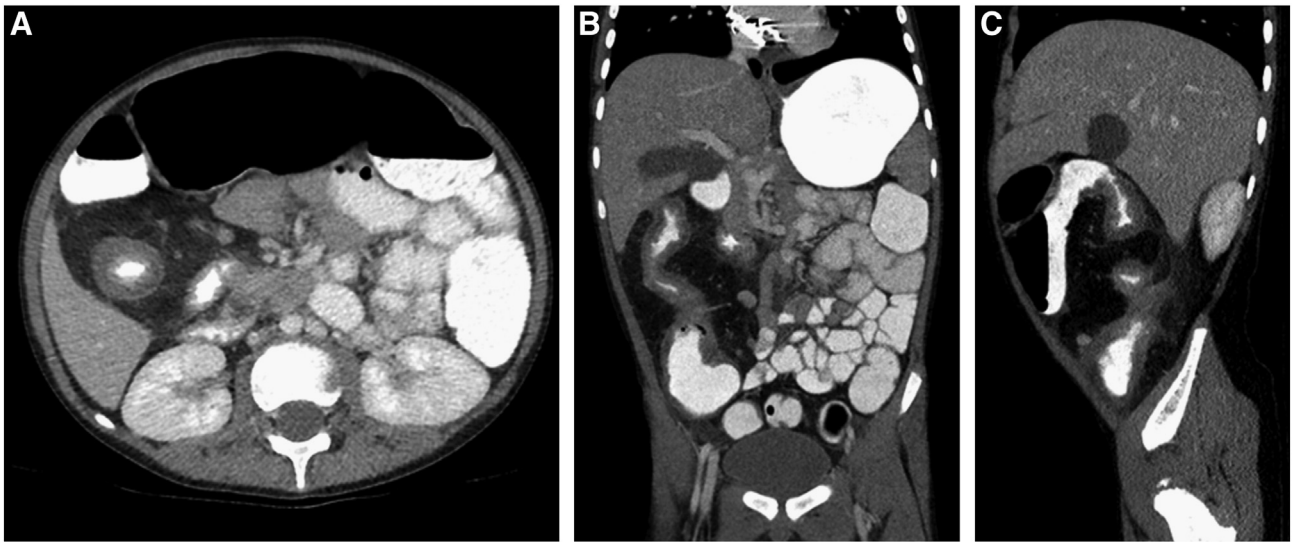

Fig. 1 CT scan of the abdomen. Shown are: (A) axial, (B) coronal and (C) sagittal reconstructed images from the abdominal CT scan. Each image demonstrates marked wall thickening of the ascending colon. The surrounding fat is abnormal and more extensive than is seen with Crohn's Disease. In addition, there is stranding within the fat extending from the ascending colonic serosa, the mucosal surface is nodular and irregular, and the lumen of the colon is narrowed with proximal bowel dilation.