Bangabandhu Sheikh Mujib Medical University Journal 2024;17(4):e75378 bsmmuj.org
ISSN 2074-2908 | eISSN 2224-7750 | © CC-BY-NC-4.0 | Open access doi: 10.3329/bsmmuj.v17i4.75378

CASE REPORT

Ganglioneuromatous polyposis and ileal adenocarcinoma: A case report

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Keywords: *neurofibromatosis, ganglioneuroma, polyposis*

INTRODUCTION

Von Recklinghausen's disease, or neurofibromatosis type 1 (NF1), is an autosomal dominantly inherited neurocutaneous syndrome with the potential to involve the gastrointestinal tract. The gastrointestinal manifestations include gastrointestinal tumours and vasculopathy. Ganglioneuromas are rare autonomic nervous system tumours that have been linked with NF1 and are considered benign.[1,2,3] The published literature reports an unclear but increased incidence of adenocarcinomas, especially colonic, in patients with NF1. Ileal adenocarcinomas are relatively rare neoplasms. It remains unclear whether NF1 and intestinal ganglioneuromatosis are causally linked.

LEARNING POINTS

1. Neurofibromatosis is associated with gastrointestinal lesions in 10-25% of cases, including tumours or vasculopathy.
2. Ganglioneuromas are tumours arising from the autonomic nervous system and are associated with neurofibromatosis and multiple endocrine neoplasias.
3. Neurofibromatosis is increasingly linked with gastrointestinal carcinomas, though the association remains unclear.

CASE DESCRIPTION AND MANAGEMENT

A 57-year-old man presented with a one-month history of abdominal pain accompanied by three days of bilious vomiting and constipation. He had been experiencing abdominal distension, decreased appetite, and significant weight loss for several months. Physical examination revealed a frail, malnourished man with multiple neurofibromas, café au lait spots, and freckling. The abdomen was distended with tenderness, particularly in the left iliac fossa, where a vague mass was palpable. A rectal examination did not show evidence of bleeding or palpable masses. Laboratory examinations revealed mild anaemia, haemoglobin 10.4 g/dL, hypokalemia (3.2 mEq/L), and acute kidney injury (blood urea nitrogen 54 mg/dL and creatinine 2.1 mg/dL). Abdominal ultrasound demonstrated prominent small bowel loops, multiple mesenteric lymph nodes, focal liver lesions, possibly metastases, and mild ascites (**FIGURE 1.A-B**). Non-contrast computed tomography confirmed the ultrasound findings and suggested likely malignant distal ileal obstruction.

The patient underwent surgery after conservative attempts to relieve the bowel obstruction were unsuccessful. During the procedure, a firm, ball-shaped tumour mass measuring approximately 15 cm was identified, with the distal end about 25 cm from the ileocecal junction (**FIGURE 1.C-D**). Gross examination revealed multiple peritoneal, mesenteric, bowel, and hepatic nodules. A segmental resection was performed, followed by end-to-end anastomosis of the ileum. Samples were collected from peritoneal nodules and mesenteric lymph nodes, and all were sent for histopathological examination. Upon opening the resected specimen, numerous polypoidal lesions were observed within the lumen with a mass with luminal

Received: 9 Aug 2024 | **Revised version received:** 2 Oct 2024 | **Accepted:** 2 Oct 2024 | **Published online:** 14 Oct 2024
Responsible Editor: M Mostafa Zaman | **Reviewer B:** Sukriti Das; **D:** Sanjida Ahmed

constriction in its lower part. The histopathological examination revealed a moderately differentiated adenocarcinoma in the ileum, extending to the serosa, forming an annular growth that produced an 8.3 cm stricture. The remainder of the intestine exhibited ganglioneuromatous polyposis, polyps ranging from pinhead size to 2.5 cm on either side of the tumour mass, staining positive with S100 and synaptophysin (**FIGURE 1.E-F**). Following an uneventful post-operative period, the patient was referred to medical oncology and started chemotherapy.

DISCUSSION

Ganglioneuromas are tumours arising from the autonomic nervous system. Gastrointestinal ganglioneuromas are uncommon, sporadic, or associated with neurocutaneous syndromes, where the large intestine is typically affected.[1,2,3] Gastrointestinal ganglioneuroma may follow three discrete morphological patterns: (a) Polypoid ganglioneuroma (single or a small number of mucosal or submucosal polyps, most often reported in the large intestine and less frequently in the stomach, duodenum, ileum, and appendix); (b) Ganglioneuromatous polyposis (multiple, typically more than 20 in the mucosa or submucosa); (c) Diffuse ganglioneuromatosis (diffuse hypertrophy of the autonomic plexus within the gastrointestinal tract, which may involve both the submucosal and myenteric plexus, larger and poorly demarcated, potentially distorting the surrounding tissue architecture).[1,2]

Isolated ganglioneuromas may be sporadic or associated with neurocutaneous syndromes. Ganglioneuromatous polyposis and intestinal ganglioneuromatosis are often associated with MEN2b, NF1, Cowden's disease, Juvenile polyposis, and Ruvalcaba-Myhre-Smith syndrome.[1,2,3] Mucosal neuromas and intestinal ganglioneuromatosis are early markers of MEN IIB, invariably within the first three decades of life, and are detected before the onset of medullary carcinoma of the thyroid and pheochromocytoma.

Intestinal ganglioneuromas, especially the isolated polypod lesions, are often asymptomatic and are incidentally detected. However, depending on the location and size, it may present with intestinal obstruction or bleeding.[1,2,3,4] Lesions are phenotypically indistinguishable from other gastrointestinal polyps. Histology reveals the presence of neurons, Schwann cells, and ganglion cells on conventional staining. Immunochemical staining might demonstrate a positive reaction to S-100, synaptophysin, neuron-specific enolase, and other neurofilament proteins. Genetic testing (NF1, PTEN, RET, SMAD4) helps diagnose the associated inherited syndromes. To date, there is no consensus on managing these rare tumours. Isolated lesions are amenable to endoscopic removal and can be resected by endoscopic measures. Symptomatic and extensive lesions might require surgical resection.[2,3,4]

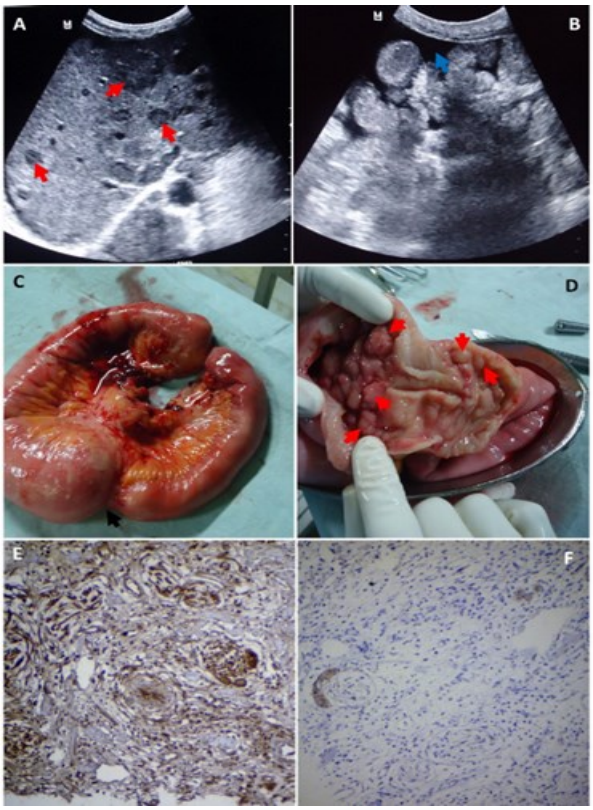

FIGURE 1 **Ultrasound images, panels A & B, revealed hypoechoic liver lesions (red arrow) and ascites (blue arrow). Panels C & D are surgical resection specimens that depict the area of luminal narrowing (black arrow) and upstream dilatation. When cut open longitudinally, the specimen reveals multiple discrete polypoidal lesions (red arrows). Panels E & F are immunohistochemical staining demonstrating S100 (left) and synaptophysin (right) reactivities.**

Intestinal ganglioneuromas are considered benign lesions. Few case reports have documented the occurrence of adenocarcinomas, mostly colonic, in individuals with ganglioneuromatous polyposis and intestinal ganglioneuromatosis.[1,4,5,6] We here report an exceedingly rare case of ileal adenocarcinoma in a patient with NF1 and gangliomatous polyposis. Hwangbo *et al*. had previously reported two similar cases in 2007.[7] We hope our case adds to the increasing reports of carcinomas in extensive intestinal ganglioneuroma patients. However, whether this is a premalignant lesion or if the association is merely a coincidental finding remains uncertain. Also, it remains unclear if the underlying NF1, rather than the ganglioneuromatosis, is linked to ileal carcinoma. There are no cancer screening recommendations for these patients; hitherto, an increasing number of case reports might lead to recommendations in the future. Patients with relevant symptoms or signs of obstruction should be suspected of having intestinal adenocarcinoma. Careful history-taking and examinations are key to detection and early treatment.

Acknowledgments

We thank the patient for his cooperation.

Author contributions

Manuscript drafting and critical revision: AJ, GZK, SK. *Approval of the final version of the manuscript:* GSZ, SK, AJ. *Guarantor of accuracy and integrity of the work:* GSZ.

Funding

We did not receive any funding for this case report.

Conflict of interest

We do not have any conflict of interest .

Ethical approval

Ethical approval was not sought because this is a case report. However, informed written consent was obtained from the patient for preparation of this manuscript.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author.

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