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**Michael Herman, Jean Abed, Wenjing Shi, Arzu Buyuk,
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ABSTRACT

Introduction: Colonic ganglioneuromas are classified as hamartomatous polyps that are composed of ganglion cells, nerve fibers, and enteric nervous system cells. The GNs of the gastrointestinal tract can be classified into three groups based on the size and the number of polyps: polypoid GN, ganglioneuromatous polyposis, and diffuse ganglioneuromatosis. Polypoid GNs, seen in patients with Cowden's syndrome, are small, sessile or pedunculated polyps that have a similar appearance to hyperplastic and adenomatous polyps. Ganglioneuromatous polyposis, seen most commonly in patients with MEN IIB, NF1, Cowden's syndrome, usually manifests as more than 20 sessile or pedunculated polyps. Lastly, diffuse ganglioneuromatosis, seen in MEN IIB7 and NF1, involves proliferation of neuronal cells in the entire colon, but does not extend into the ileum.

Case Report: A 57-year-old African-American male with a history of untreated chronic hepatitis C cirrhosis with viral load of over 4 million copies, seizure disorder, mild mental retardation, hypothyroidism, hypertension, diabetes mellitus type 2, presented to the gastroenterology clinic for scheduling of a screening colonoscopy. At that time, he was completely asymptomatic. On colonoscopy, one 4 mm sessile polyp was resected in the sigmoid colon and was histologically diagnosed as a ganglioneuroma (GN).

Conclusion: The finding of an asymptomatic, solitary GN in our patient does not warrant more frequent colon cancer screening given its benign nature.

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CASE REPORT

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Keywords: Cancer, Colonoscopy, Cowden's syndrome, Ganglioneuroma, Neurocutaneous syndromes

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INTRODUCTION

Ganglioneuromas (GNs) are a subset of neuroblastomas. They are rare, slow growing, well-differentiated large tumors that arise from sympathetic ganglion cells. They are often benign and have excellent prognoses even when the tumor is not completely resected, regardless of where they are located in the body. Epidemiologically, GNs are seen more frequently

in females, with 60% occurring before the age of 20 years [1]. The most common locations for GNs to appear are the mediastinum, retroperitoneum, and adrenal glands, and less commonly the colon. Patients with intestinal GNs usually have (1) neurocutaneous syndromes, such as neurofibromatosis type 1 (NF1) and tuberous sclerosis, (2) genetic polyposis syndromes, such as juvenile polyposis, polyposis coli, or Cowden's disease, or (3) multiple endocrine neoplasia type IIB (MEN IIB). However, solitary lesions do not embody the same association. Colonic GNs are relatively asymptomatic and patients with the above syndromes have the same risk of having gastrointestinal manifestations of GNs as the general population [1].

CASE REPORT

A 57-year-old African-American male with a history of untreated chronic hepatitis C cirrhosis with viral load of over 4 million copies, seizure disorder, mild mental retardation, hypothyroidism, hypertension, diabetes mellitus type 2, presented to the gastroenterology clinic for scheduling of a screening colonoscopy. At that time, the patient was asymptomatic and did not report any fever, chills, nausea, vomiting, abdominal pain, diarrhea or constipation. He never had any alarming symptoms such as weight loss, melena and hematochezia. In addition to denying toxic habits (i.e., tobacco, alcohol, drugs), he also denied any personal or family history of colon or small bowel cancer. His physical examination was unremarkable, as he did not have scleral icterus, murmurs, wheezing, abdominal distention, organomegaly, café au lait spots or fibromas on his skin. At home, the patient was taking metformin, levothyroxine, ferrous sulfate, tamsulosin, lactulose, omeprazole, divalproex sodium, propranolol, aripiprazole, vitamin C, multivitamin, and saline nasal spray. Initially, patient underwent a screening colonoscopy, one 8 mm pedunculated polyp in the ascending colon was removed with a cold biopsy forceps and was histologically identified as a tubular adenoma. Additionally, a pink, tan sessile polyp-like lesion was identified, measuring 4 mm in diameter, and resected with a hot snare from the sigmoid colon (Figure 1). After the procedure, the patient had no complications and was discharged home. The histology of the biopsied 4 mm lesion revealed a solitary small sessile colonic polyp at low magnification (Figure 2). At high magnification, there are irregular distributions of dysmorphic ganglion cells in the lamina propria (Figures 3 and 4).

They range from nearly normal ganglion cells with large round nuclei, prominent nucleoli and abundant cytoplasm to abnormal ganglion cells with hyperchromatic nuclei with irregular nuclear membrane, invisible nucleoli, and scanty cytoplasm.

Scattered spindle cells are also seen. Both of them are highlighted by immunostain S100 (Figure 5), but negative for AE1/AE3 and EMA (markers for 69 epithelium) or

CD117 (the marker for GIST). No mitosis or cell necrosis is seen. Diagnosis of ganglioneuroma was subsequently made by the pathologist.

Figure 1: Endoscopy view of ganglioneuroma.

Figure 2: Colonic sessile polyp (H&E stain, x40)

DISCUSSION

Colonic GNs are classified as hamartomatous polyps that are composed of ganglion cells, nerve fibers, and enteric nervous system cells. The GNs of the gastrointestinal tract can be classified into three groups based on the size and the number of polyps: polypoid GN, ganglioneuromatous polyposis, and diffuse ganglioneuromatosis [1].

All three types of GNs are usually incidental findings found on colonoscopy and typically do not present with symptoms. Polypoid GNs, which can be sessile or

Figure 3: Ganglion cells and scattered spindle cells in the lamina propria (H&E stain, x200). Ganglion cells (red arrow) and spindle cells (black arrow).

Figure 4: Ganglion cells and scattered spindle cells in the lamina propria (H&E stain, x400). Ganglion cells (red arrow) and spindle cells (black arrow).

pedunculated, are small and appear to be very similar to hyperplastic and adenomatous polyps endoscopically [1]. This subset is most commonly seen in patient with Cowden's syndrome, characterized by ganglioneuromas found in the breast, thyroid, genitourinary tract, and mucocutaneous areas [2].

Ganglioneuromatous polyposis is seen most commonly in patients with MEN IIB, NF1, Cowden's syndrome, often accompanied by more than 20 sessile or pedunculated polyps [3]. Lastly, diffuse ganglioneuromatosis involves proliferation of neuronal cells in the entire colon, but does not extend into the ileum. Polyps can be as large as 17 cm in diameter with a variable (intramural or transmural) penetration into the colonic wall. They are seen as a

Figure 5: Ganglion cells and Schwann cells demonstrated immunoreactivity to S100, but not to AE1/AE3, EMA, or CD117 (x100).

component of MEN IIB7 and NF1 [4]. Histologically, the polyp is confirmed to be a GN by immunohistochemical staining with S100 protein confirming the presence of ganglion cells. The histological features of isolated polypoid GNs show disturbed crypt architecture and expanded lamina propria at low magnification. Higher magnification demonstrates the spindle cells in the fibrillary matrix and irregular groups of ganglion cells within the expanded lamina propria. The isolated GNs may also present submucosal extension and a plexiform-like arrangement involving submucosal nerve plexus. This pattern is suggestive of neurofibromas, but the presence of ganglion cells distinguishes them from neurofibromas. The GNs in ganglioneuromatous polyposis have overlapping features with isolated GNs. However, they are more variable and consist of more numerous ganglion cells. Diffuse ganglioneuromatosis may exhibit fusiform expansion of the myenteric plexus or confluent transmural ganglioneuromatous proliferations involving nerve fibers, ganglion cells, and supporting cells of enteric nervous system. The management of GNs depends on the patient's clinical history and presentation. For the polypoid subgroup, polypectomy is the cure, however, colectomy may be required for ganglioneuromatous polyposis and diffuse ganglioneuromatosis, particularly if the patient is symptomatic [5]. Rarely, large GNs may cause symptoms of abdominal pain, constipation, obstruction, or bleeding secondary to the size and location within the colon. In general, solitary polypoid GNs are asymptomatic [6, 7].

CONCLUSION

To our knowledge, no guideline is available for repeat colonoscopy, although there are reports of association

with tubular adenomas. The finding of an asymptomatic, solitary ganglioneuroma in our patient, does not warrant more frequent colon cancer screening given its benign nature.

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Author Contributions

Michael Herman – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Jean Abed – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Wenjing Shi – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Arzu Buyuk – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Pavan Kumar Mankal – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Donald Kotler – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Gabriel Ionescu – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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