Abstract
Ganglioneuroma (GN) of colon is a rare tumor of gastrointestinal (GI) tract. GNs of GI tract are usually confined to colon particularly rectum. GNs are usually found incidentally but can be associated with MEN IIb, von Recklinghausen’s neurofibromatosis or Cowden syndrome. A 21-year-old female with past medical history of bulimia, bipolar disorder and hypothyroidism, who presented with complaints of hematemesis and hematochezia. Her physical exam was unremarkable. She subsequently underwent an EGD and colonoscopy for further evaluation. EGD revealed mild gastritis. Colonoscopy revealed two 5 mm sessile polyps in the sigmoid colon and the rectum. Biopsy of the rectal polyp showed ganglioneuroma. This represents a case of polypoid ganglioneuromatosis. These polyps are endoscopically small sessile or pedunculated polyp indistinguishable from hyperplastic and adenomatous polyps. They are not associated with increased risk of colon cancer and don’t require additional screening. On the other hand, gangliomatous polyposis and diffuse ganglioneuromatosis can be associated with increased risk of colon and other cancers, and may require further work up.

Keywords: Ganglioneuroma; Gangliomatous polyposis; Diffuse ganglioneuromatosis; Gastrointestinal

Abbreviations: GN: Ganglioneuroma; GI: Gastrointestinal; GP: Gangliomatous Polyposis; DG: Diffuse Ganglioneuromatosis; CS: Cowden Syndrome; NCCN: National Comprehensive Cancer Network

Discussion
GNs as mentioned in detail below are mainly divided into three categories.
1. Polypoid ganglioneuromatosis
2. Gangliomatous polyposis (GP)
3. Diffuse ganglioneuromatosis (DG) [1].

Endoscopically they are indistinguishable from adenomas or hyperplastic polyps [1]. Diagnosis is made by immunohistochemical staining which is positive for S-100, glial fibrillary acidic protein and vimentin (which stains spindle cell elements). Neuron specific enolase and neurofilament protein, confirm the presence of ganglion cells. Differentials are neurofibroma and Schwannoma but they don’t contain ganglion cells [5].

Polypoid ganglioneuromatosis
Polypoid ganglioneuromatosis lesions are solitary or few in number, found incidentally on colonoscopy, endoscopically small sessile or pedunculated polyp indistinguishable from hyperplastic and adenomatous polyps. Patients are usually asymptomatic but may get symptomatic depending upon the lesion size.
They are not associated with increased risk of colon cancer and don’t require additional screening [1].

Ganglioneuromatous polyposis (GP)

GP is characterized by multiple and often innumerable sessile or pedunculated mucosal or sub mucosal polyoid lesions [5-7]. Histologically there is greater variability in ganglionic, neural and supportive cell content and more demarcation when compared to polyoid ganglioneuroma but microscopically indistinguishable from polyoid GNs. GP can be associated with intestinal or extra intestinal manifestations like cutaneous lipomas, skin tags (achrochordon formation) [8], or with a syndrome such as Cowden syndrome (CS), juvenile polyposis, coexistent colonic adenoma or carcinoma and rarely von-Recklinghausen disease [1]. Patient can be symptomatic or asymptomatic and diagnosed incidentally.

Most common symptoms reported are constipation or diarrhea producing stricture like thickening of segments of bowel [4,6]. Transmural infiltration of ganglioneuromatosis tissue with risk of colon cancer, which requires cancer screening starting at age 40 and then every 2 years. Juvenile Polyposis (SMAD4 mutation) has also been associated with increased risk of colon cancer, which requires cancer screening starting from mid teens. NCCN recommends consideration of baseline esophagogastroduodenoscopy and colonoscopy at age 15 years then every year in patients with Juvenile polyposis. Several cases of non-Cowden Syndrome-related Ganglioneuromatous polyposis developing into adenocarcinoma have been reported, leading Kanter et al. [6] to suggest the condition to be considered premalignant. Discussion with patient about possible proctocolectomy can be considered on case-to-case basis, as it is difficult to monitor for the development of an adenocarcinoma amongst innumerable polyoid lesions [4].

Diffuse ganglioneuromatosis (DG)

DG is characterized by poorly demarcated, mucosal or transmural infiltration of ganglioneuromatous tissue with massive atypical proliferation of the myenteric plexus, often producing stricture like thickening of segments of bowel [4,6]. Most common symptoms associated with MEN 2B, these symptoms often begin in the first months of life, before the diagnosis of MEN 2B. Recognition of these symptoms can lead to early diagnosis if MEN 2B and potentially lifesaving thyroidectomy [4] von Recklinghausen syndrome is associated with neurofibrosarcoma.

We conclude that our patient had polyoid ganglioneuromatosis, which is not associated with increased risk of cancer. She didn’t need any further follow up. Her symptoms may or may not be related to her polyps. It is important to differentiate this entity from others as we can avoid unnecessary surveillance colonoscopies in this subgroup of patients. On the other hand, ganglioneuromatous polyposis and diffuse ganglioneuromatosis can be associated with increased risk of colon and other cancers, and requires further work up.

References

1. Bagdasaryan R (2012) Ascending colon ganglioneuroma. Med Health R195(1): 18.
2. Artaza T, Garcia JF, González C, Amengual M, Mazarro A, et al. (1999) Simultaneous involvement of the jejunum and the colon by type 1 neurofibromatosis. Scand J Gastroenterol 34(3): 331-334.
3. Trufant JW, Greene L, Cook DL, McKinnon W, Greenblatt M, et al. (2012) Colonic ganglioneuromatous polyposis and metastatic adenocarcinoma in the setting of Cowden syndrome: a case report and literature review. Hum Pathol. 43(4): 601-604.
4. Grobmyer SR, Guillem JG, O'Riordain DS, Woodruff JM, Shriver C, et al. (1999) Colonic manifestations of multiple endocrine neoplasia type 2B: report of four cases. Dis Colon Rectum 42(9): 1216-1219.
5. Srinivasan R, Mayle JE (1998) Polypoid ganglioneuroma of colon. Dig Dis Sci 43(4): 908-909.
6. Kanter AS, Hyman NH, Li SC (2001) Ganglioneuromatous polyposis: a premalignant condition. Report of a case and review of the literature. Dis Colon Rectum 44(4): 591-593.
7. ShaziaRafiq, Hussein Hameer, Michael D Strin (2005) Ganglioneuromatous Polyps Associated with Juvenile Polypos and a Tubular Adenoma. Dig Dis Sci 50(3): 506-508.
8. Chao, Owen T M, Haghghi, Parviz (2006) Hamartomatous polyps of the colon - Ganglioneuromatous, stromal, and lipomatous. Arch Pathol Lab Med 130(10): 1561 - 1566.
9. Heald B, Mester J, Rybicki L, Orloff MS, Burke CA, et al. (2010) Frequent gastrointestinal polyps and colorectal adenocarcinomas in a prospective series of PTEN mutation carriers. Gastroenterology. 139(6): 1927-1933.
10. Nguyen AT, Zacharin MR, Smith M, Hardikar W (2006) Isolated intestinal ganglioneuromatosis with a new mutation of RET proto-oncogene. Eur J Gastroenterol Hepatol 18(7): 803-805.
11. Dellenberg G, Lynch C, Mihas A (1996) Colonic Ganglioneuroma Presenting as Filiform Polyposis. J Clin Gastroenter 22(1): 66-70.