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Case Report

A Rare Incidental Finding of Appendiceal Ganglioneuroma During Screening Colonoscopy

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Abstract:

Ganglioneuromas are rare, benign tumors of the autonomic nervous system that arise from neural crest cells. They most commonly occur in the adrenal glands, posterior mediastinum, and retroperitoneum, with gastrointestinal (GI) involvement being particularly uncommon. Colonic ganglioneuromas are typically asymptomatic, and thus are often discovered incidentally during routine screening colonoscopies. However, depending on their size, location, and extent, they may present with nonspecific GI symptoms.

Herein, we present a case of a 52-year-old male with a history appendectomy who was incidentally found to have a benign submucosal ganglioneuroma at the appendiceal orifice during his first colorectal cancer screening. The lesion was successfully removed using a hot snare polypectomy without complications. Our patient was recommended for a follow-up colonoscopy in 5 years given the absence of adenomatous tissue and the lack of established management guidelines. This case highlights the importance of considering ganglioneuroma in the differential diagnosis of submucosal lesions, even when endoscopic appearance suggests a benign polyp.

Key words: appendiceal orifice; colonoscopy; ganglioneuroma; genetic syndromes; inverted colonic diverticulum; lipoma

Introduction

Ganglioneuromas are benign, slow-growing tumors that are comprised of ganglion cells, glial cells, Schwann cells, nerve fibers, and fibrous tissues. They may arise as single or multiple lesions and can occur in isolation or in association with genetic syndromes, such as Cowden syndrome, familial adenomatosis polyposis, multiple endocrine neoplasia (MEN) or neurofibromatosis (NF).[1,2] While ganglioneuromas are largely asymptomatic, symptomatic cases may present with abdominal pain, hematemesis, melena, hematochezia, diarrhea, constipation, bowel obstruction or perforation.[3] Most cases are detected incidentally during colonoscopy as polypoid lesions.[2]

Histologically, ganglioneuromas are categorized into three types: polypoid ganglioneuroma, ganglioneuromatous polyposis (GP), and diffuse ganglioneuromatosis (DG). These lesions can occur anywhere along the sympathetic chain but are commonly located in the thoracic region (60-80%, posterior mediastinum), the abdominal cavity (10-15%, adrenal gland, retroperitoneum, and pelvic/sacral sympathetic ganglia), and the cervical region (5%).[4] While ganglioneuromas can occur throughout the GI tract, isolated intestinal cases are much rarer, most commonly involving the colon and rectum, and less frequently the ileum and appendix.[2] In a large study of 71,000 appendix specimens, Collins identified ganglioneuromas only in 0.27% of specimens.[5] Ganglioneuromas in the appendix are extremely rare, and due to their rarity, the exact incidence of colonic ganglioneuroma remains unknown.

Therefore, we report a case of appendiceal ganglioneuroma that developed in a 52-year-old patient with a history of appendectomy and was incidentally discovered during his initial screening colonoscopy.

Case Presentation

A 52-year-old Polish male with a medical history of hypertension, type 2 diabetes mellitus, and hyperlipidemia and a surgical history of appendectomy in his 20s presented for his first colonoscopy for colorectal cancer screening. He had no active complaints or symptoms and was not taking any anticoagulant or antiplatelet agents. Vital signs, physical

examination, and review of systems were all unremarkable. No additional imaging was performed at this time.

During colonoscopy, one 15-mm non-bleeding sessile polyp was identified at the appendiceal orifice and removed with a hot snare. Subsequently, a hemostatic clip was placed to prevent post-polypectomy bleeding. Pathological examination revealed a benign submucosal ganglioneuroma. The examination was otherwise normal on both direct and retroflexion views. The patient tolerated the procedure well without any complications and was discharged on the same day after the procedure.

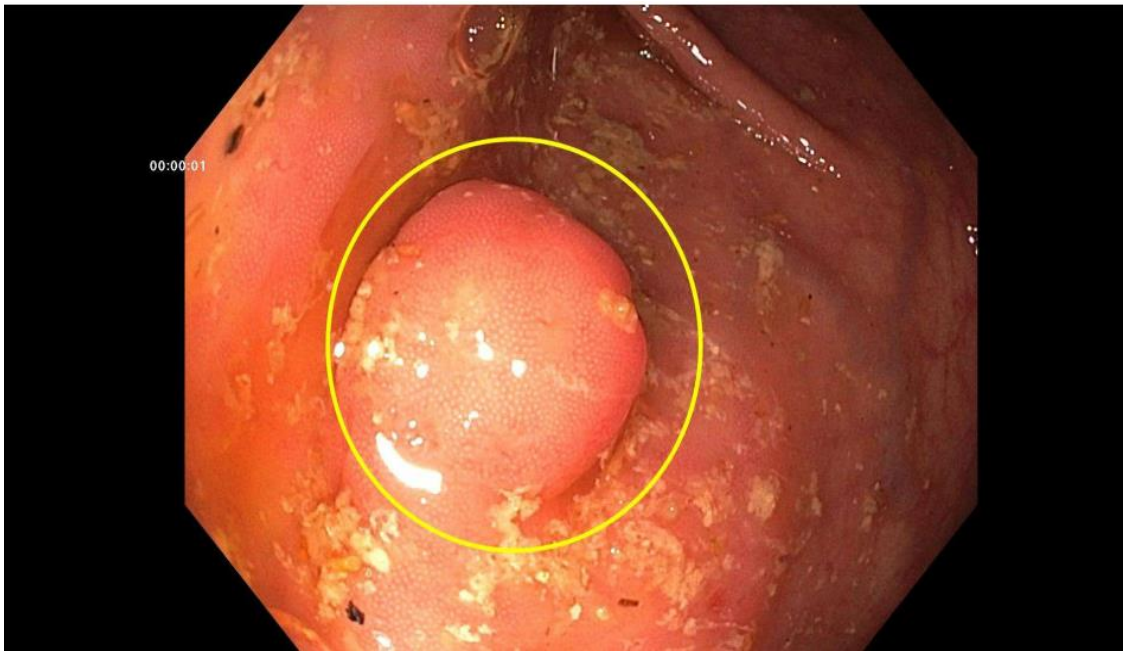

Figure 1: Appendiceal orifice polyp: a well-defined nodule with smooth morphology.

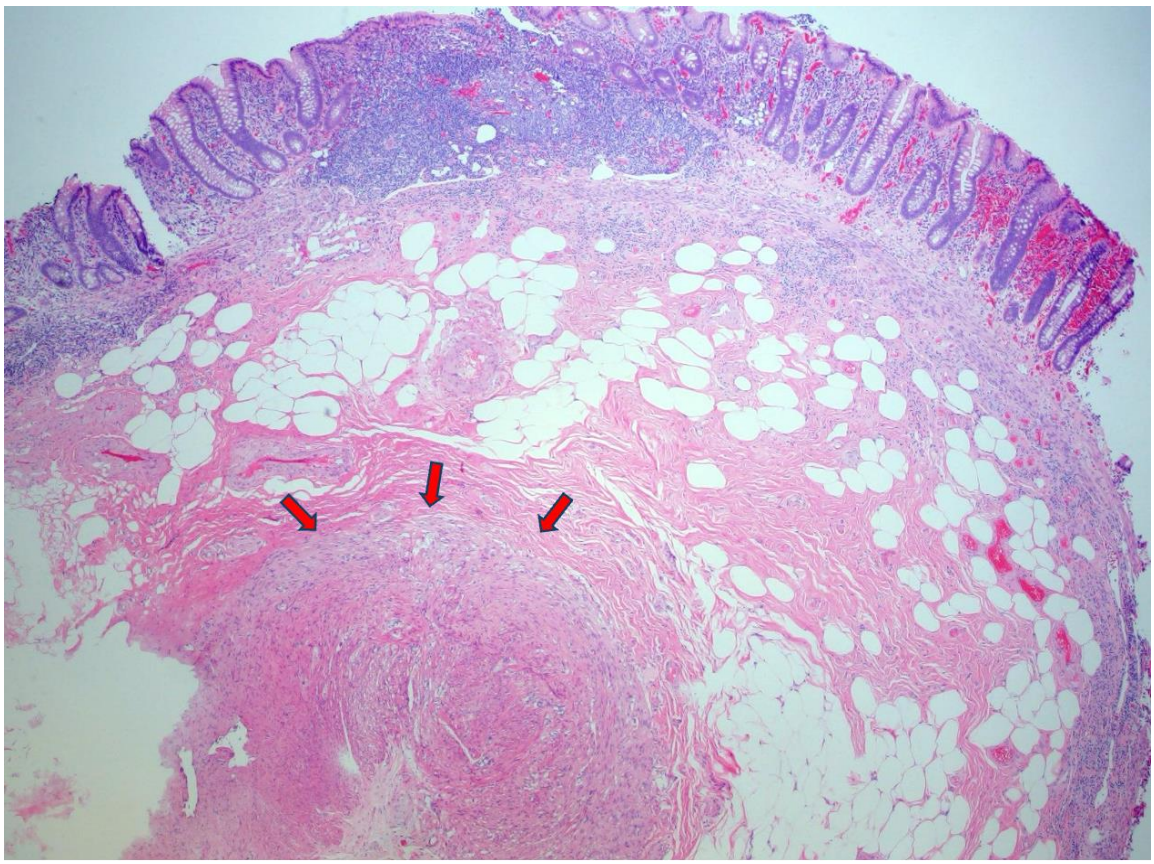

Figure 2: Colonic type mucosa showing a well-defined nodule within the submucosal layer (red arrows) (Hematoxylin and Eosin, 20x).

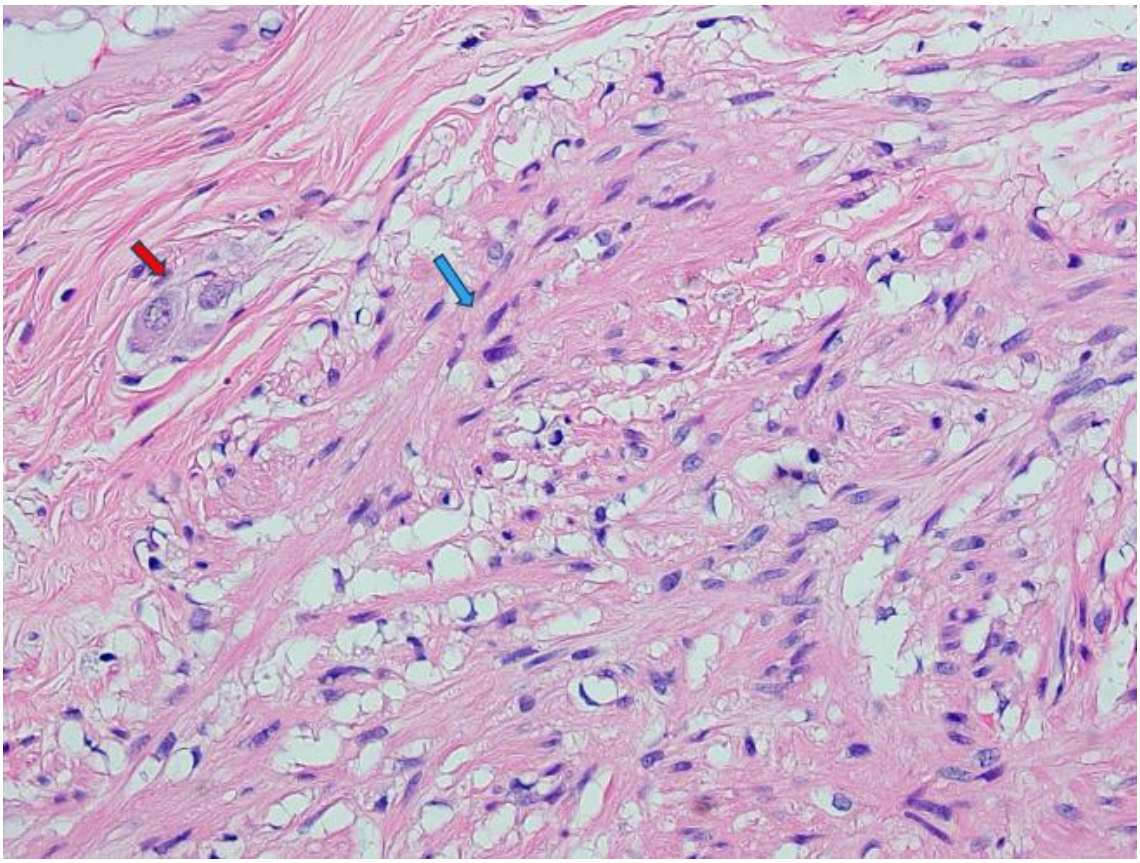

Figure 3: Higher power view showing admixture of small cluster of ganglion cells (red arrow), and abnormally proliferating spindle-shaped Schwann cells (blue arrow). The Schwann cells that composed the lesion are bland, with elongated hyperchromatic nuclei with tapering ends and inconspicuous nucleoli (Hematoxylin and Eosin, 400x).

Discussion

Ganglioneuromas are benign neuroectodermal neoplasms that occur anywhere along the autonomic nervous system, most commonly in the mediastinum, retroperitoneum, adrenal glands. They are less frequently found in the GI tract, rarely in the colon, and even more rarely in the appendix, small intestine, and terminal ileum.[2] In a review by Collins (1963) of 71,000 appendectomies, only 0.28% contained ganglioneuromas.[5] The most recently reported incidence of ganglioneuromas in the general population is approximately 1 per million.[4,6,7] The peak incidence occurs between the first and fifth decades of life, with 60% of cases occurring before age 20.[8,9] Although there is no consensus on gender predilection, some studies indicate a higher prevalence in females.[8,9,10]

Shekitka et al. classified ganglioneuroma into three types: polypoid ganglioneuroma, ganglioneuromatous polyposis (GP), and diffuse ganglioneuromatosis (DG).[11] Polypoid ganglioneuromas are solitary, small (< 2 cm), and sessile or pedunculated.[12] GP consists of multiple (> 20), small (1 mm to > 2 cm), sessile or pedunculated polyps, often with filiform morphology and greater variability than sporadic lesions.[12,13] Lastly, DG presents as diffuse, large (< 17 cm), nodular polyps that may be mucosal or transmural and involve the myenteric plexus.[13] Ganglioneuromas can also be divided into either solitary isolated lesion or multiple lesions. Because polypoid ganglioneuromas usually occur as a solitary lesion, they are not associated with genetic syndromes. On the other hand, GP and DG are often linked to familial syndromes, such as MEN IIB and NF1.[12,13] Notably, DG is found in nearly all patients with MEN IIB.[12]

Ganglioneuromas are mainly asymptomatic but can present with a wide range of clinical symptoms depending on the location, size, and extent of the lesion. Symptoms can range from abdominal pain, diarrhea, constipation, hematochezia, irritable bowel syndrome, appendicitis, and megacolon with intestinal obstruction.[3,8,10,13,14] Diagnosis is confirmed through histopathologic evaluation. Additionally, hematoxylin and eosin staining can be performed to demonstrate spindle and ganglion cells. Immunohistochemistry can further ascertain a neural origin of the lesion with S100 and neuron-specific enolase positivity.[2,4]

In our case, endoscopic findings revealed a well-defined submucosal nodule at the appendiceal orifice, whose location and characteristics were inconsistent with typical mucosal lesions such as adenomas or hyperplastic polyps. Adenomas are benign, premalignant neoplastic epithelial proliferations characterized by dysplastic glandular architecture that remains confined to the mucosa. The absence of epithelial dysplasia and the lesion's submucosal location made an adenoma an unlikely diagnosis. Similarly, the lesion did not resemble hyperplastic polyps, which exhibit serrated glandular organization within the mucosal layers without dysplasia. Both adenomas and hyperplastic polyps originate from the epithelial lining and are confined to the mucosa, whereas our patient's lesion was clearly located within the submucosa and lacked glandular structures altogether.[6]

The appearance of the lesion raised consideration for a colonic lipoma—a benign, non-epithelial hyperplasia of adipocytes in the GI tract. Lipomas are the second most common colon lesion after adenomatous polyps and present as well-circumscribed masses in the submucosa. Studies have identified the ascending colon near the ileocecal valve (45%) as the most

common site, and the submucosa as the most frequent layer of origin (90%) with occasional extension into the muscularis propria or subserosa.[15] A classic endoscopic finding is the "pillow sign," in which pressure with biopsy forceps results in indentation of the lesion. Histologically, lipomas consist of mature adipose tissue, similar to what was observed in this case (Figure 2). Another possibility to consider is an inverted colonic diverticulum (ICD). Although rare, with an incidence of 0.7-1.7%, ICDs may appear as sessile lesions without a stalk, often leading to misdiagnosis of colonic polyps.[16,17] Additional features include a shiny pink mucosa indistinguishable from surrounding mucosa and pale concentric rings at its base.[18] However, these findings were absent in our patient's endoscopic image.

Given the lesion's submucosal location, neural composition, and the patient's remote history of appendectomy, we believe the most likely etiology is a traumatic neuroma. Traumatic neuroma is a reactive proliferation of nerve fibers and connective tissue arising from Schwann cells triggered by surgical or traumatic nerve injury.[19] Our patient's lesion exhibited an admixture of spindle-shaped Schwann cells with clusters of ganglion cells (Figure 3), which likely resulted from the surgical disruption of nerve fibers resulting in disorganized nerve regeneration, with fibrosis and neural cell hyperplasia contributing to neuroma formation. Although the pathophysiology is not fully understood, an inflammatory state is believed to stimulate the growth of neuroendocrine cells and Schwann cells.[20] This case underscores the importance of considering alternative, non-epithelial lesions and performing careful morphologic assessment when evaluating atypical colonic polyps.

The mainstay of treatment for ganglioneuromas is excisional polypectomy via cold or hot biopsy forceps. Some experts recommend follow-up colonoscopy to confirm complete excision of the lesion and screen for recurrence, while some believe that screening is redundant given the benign and non-recurrent nature of these lesions.[8,12,13] In our patient, polypectomy was successfully performed with a hot snare. Given that there are currently no established guidelines for treatment or post-treatment management, we elected to perform a follow-up colonoscopy in 5 years, as the lesion contained no adenomatous tissue.

Conclusion

In conclusion, colonic ganglioneuromas are extremely rare, with appendiceal involvement being even more uncommon. Clinical presentations vary depending on the location, size, and extent of the lesion. Given that lesions are largely asymptomatic, they are often discovered incidentally on imaging or routine screening. Definitive diagnosis requires pathologic examination. While endoscopic resection is the preferred treatment–partly due to the potential coexistence of malignancy–there are currently no established guidelines for the management or surveillance of ganglioneuroma. When evaluating lesions with normal mucosal architecture, clinicians should consider alternative diagnoses beyond typical polyps. Recognizing these atypical endoscopic features is essential for accurate diagnosis and appropriate management.

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Conflicts of interest: None to report.

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