DOI: https://doi.org/10.22516/25007440.813

Case report

Neuroendocrine Tumor Polypoid Presentation: Case Report and Literature Review

Sergio Andrés Romero-Serrano,[1] Edwin Alirio Báez-Ariza,[2] Sheyla Pardo-González,[3*] Sebastián Martínez-Martínez.[4]

OPEN ACCESS

Citation:
Romero-Serrano SA, Báez-Ariza EA, Pardo-González S, Martínez-Martínez S. Neuroendocrine Tumor Polypoid Presentation: Case Report and Literature Review. Rev Colomb Gastroenterol. 2022;37(3):325-329. https://doi.org/10.22516/25007440.813

[1] General Surgery Resident, Universidad Industrial de Santander. Bucaramanga, Colombia
[2] Coloproctologist, Universidad Industrial de Santander, Universidad Militar Nueva Granada, Clínica Foscal, Hospital Universitario de Santander. Bogotá, Colombia.
[3] General Physician, Universidad Industrial de Santander. Bucaramanga, Colombia
[4] Pathology Resident, Universidad Industrial de Santander. Bucaramanga, Colombia

***Correspondence:** Dra. Sheyla Pardo-González.
sheypardo@gmail.com

Received: 06/08/2021
Accepted: 21/01/2022

Abstract

Diagnosis of rectal neuroendocrine tumor (NET) has increased due to the implementation of colonoscopies as a screening method. Most rectal NETs are less than 1cm at diagnosis time, confined to the submucosa, and well differentiated. They generally have a benign course and are treated mainly using endoscopic methods. Metastases are rare and depend on tumor size and other factors such as submucosal invasion, lymphatic spread, and histologic classification, which will determine the prognosis and treatment. We present a case of a rectal neuroendocrine tumor as a polyp during routine endoscopic screening and a review of the current literature.

Keywords

Neuroendocrine tumor, rectal neoplasia, polyp.

INTRODUCTION

In the last decades, neuroendocrine tumors (NETs) have been diagnosed more frequently through the implementation of colonoscopy and complementary imaging studies in gastrointestinal diseases. They have distinctive histological, biological, and clinical characteristics[1]. These tumors originate in neuroendocrine cells from the endoderm along the mucosa and submucosa of the gastrointestinal tract[1]. They can synthesize and secrete monoamines, peptides, and hormones and transmit and receive nerve signals[2]. Lubarsch discovered these tumors in 1888. Later, Obendorfer named these tumors carcinoid (carcinoma-like). Nowadays, they are known as *neuroendocrine tumors* (NETs) according to their etiology, behavior, and location[3,4].

NETs constitute 0.5% of all malignant cancers and 2% of malignant tumors in the gastrointestinal tract[2]. They have an incidence of approximately 0.86 per 100,000 inhabitants, frequent in Black males and more prevalent in the Asian population[4-7]. Rectal NETs account for 18% of total NETs and 27% of gastrointestinal NETs[5].

Clinical presentation is nonspecific. Rectal bleeding, functional gastrointestinal disorders, abdominal pain, and carcinoid syndrome may be present in 10% of cases[6,7]. However, nearly half of the patients are asymptomatic and are diagnosed in screening colonoscopy or other colorectal

pathology studies[7-9]. They are usually found as single small polypoid tumors, metastatic disease is rare, and tumor size and invasion determine the prognosis of the disease[10-13].

In the latest digestive tumor classification edition (fifth edition, published in 2019) of the World Health Organization (WHO), the classification of well-differentiated NETs or poorly differentiated neuroendocrine tumors with small cell and large cell subtypes remains[14]. Histological classification is based on the mitotic and Ki-67 indexes recorded at tumor hot spots. During cell division, the Ki-67 protein is found in the cell nucleus. The proportion of Ki-67-positive tumor cells (Ki-67 index) correlates with cell proliferation, clinical course, and prognosis[2,14-16]. The 2019 WHO NET classification is described in **Table 1**.

Table 1. Classification of Neuroendocrine Tumors, WHO, 2019[16]

	Ki-67 Index (%)	Mitotic index/10 HPF
Well-differentiated neuroendocrine neoplasms		
- Grade 1 (Low)	< 3	< 2
- Grade 2 (Intermediate)	3-20	2-20
- Grade 3 (High)	> 20	> 20
Poorly differentiated neuroendocrine neoplasms		
- N/A (no numerical assignment: high grade)	> 20	> 20

HPF: high-power fields; N/A: not applicable. Taken and adapted from: Lloyd RV, Osamura RY, Kloppel G, Rosai J. WHO Classification of Tumors of Endocrine Organs. 5th edition. WHO; 2019.

In general, well-differentiated tumors are low or intermediate-grade tumors. Well-differentiated high-grade NETs are less frequent but have a better prognosis than poorly differentiated NETs, a fundamental classification to know the course of the disease and define the most appropriate treatment for the patient[1,12-14]. Below is a case of a neuroendocrine tumor as a polyp in the rectum.

CASE PRESENTATION

This is an 88-year-old female patient with a medical history of hypertension, hyperlipidemia, type II diabetes *mellitus*, breast cancer in remission, and grade I internal hemorrhoids. She sought medical assistance for a long-standing clinical picture characterized by constipation with no other gastrointestinal symptoms. The patient underwent a colonoscopy where a polyp was evidenced in the upper third of the rectum, 12 cm from the anal edge of 2 cm in diameter (**Figure 1**). A polypectomy was performed, and a sample was sent for pathologic study, which reported morphologic findings compatible with a well-differentiated neuroendocrine tumor. Tumor size was 1 cm in greatest dimension, submucosal location, and lateral and deep negative resection margins for tumor involvement (**Figures 2** and **3**). Immunohistochemistry staining showed a well-differentiated neuroendocrine tumor with a low mitotic rate with Ki-67 < 1%. Outpatient follow-up with colonoscopy check-up in 1 year was indicated.

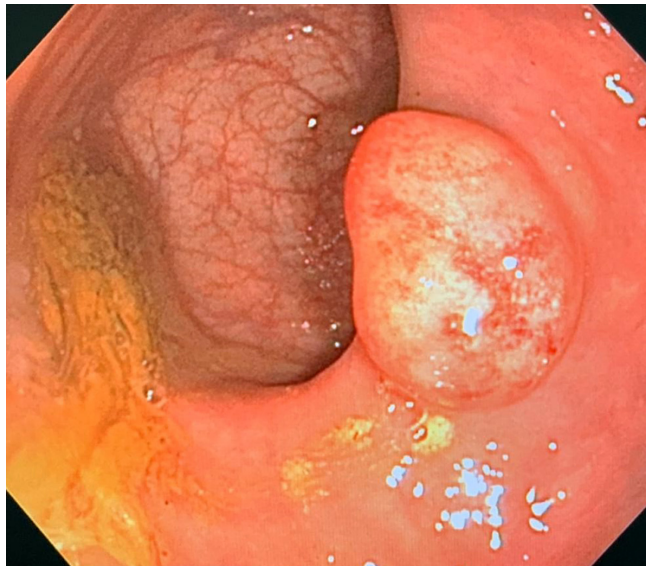

Figure 1. Colonoscopy image showing a neuroendocrine polyp in the upper third of the rectum, 2 cm in diameter.

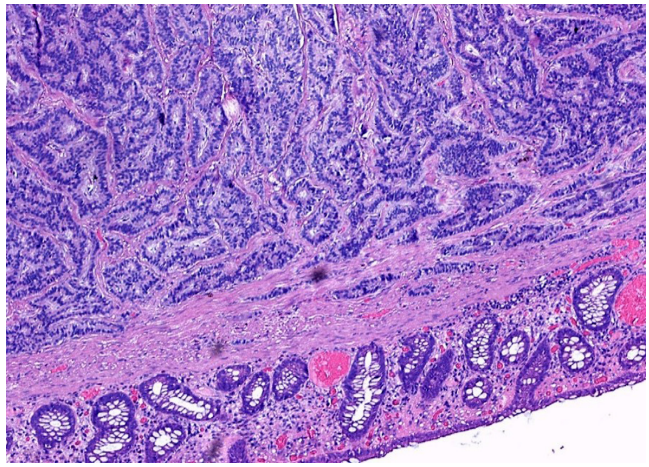

Figure 2. The colonic cut shows a submucosal lesion with an organoid pattern (4x). Hematoxylin and eosin (H&E) stain.

DISCUSSION

In recent years, the diagnosis of rectal NETs has increased thanks to colonoscopy as a screening method for colon can-

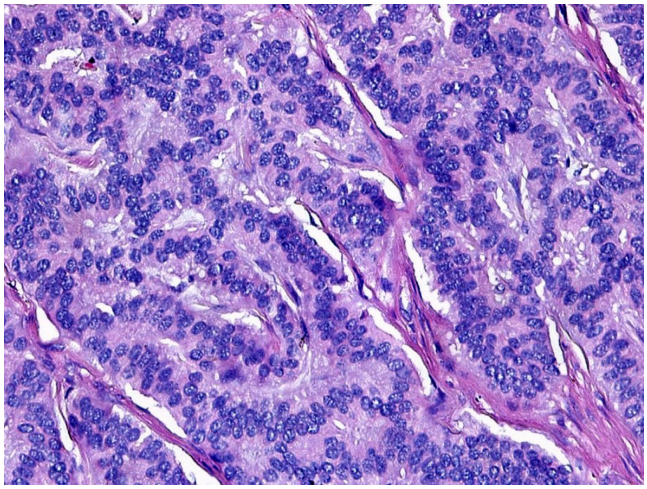

Figure 3. The cut reveals a submucosal lesion composed of monotonous cells with a salt and pepper chromatin appearance (40x). Hematoxylin and eosin (H&E) stain.

cer and the implementation of other imaging studies of the gastrointestinal tract[5]. In a British cohort of 13,061,716 patients who were screened with fecal occult blood, 259,765 of the participants obtained abnormal results, and 216,707 screening colonoscopies were performed; 146 patients were diagnosed with NETs, and it was evidenced that the diagnostic rates per 100,000 colonoscopies were 29 rectal, 18 colonic and 11 ileal NETs[17].

There is a tendency to delay the diagnosis of all types of NETs, which can take up to 5 years, related to their asymptomatic clinical presentation[17,18]. The vast majority (93%-100%) of rectal NETs are < 1 cm in size at diagnosis, limited to the submucosa, well-differentiated, and generally have a benign clinical course[14,19].

The risk of metastatic disease of NETs increases with tumor size, which is up to 60%–80% when the tumor is ≥ 2 cm[20]. Tumor size > 10 mm and muscle and lymphovascular invasion are independently associated with an increased risk of metastasis[20,21]. However, there is a higher detection of the disease in the early stages related to a lower risk of metastasis. A retrospective study that evaluated 48 patients showed that stage I tumors (TNM) accounted for 78.8% and were the most frequent. At the same time, distant metastases had a lower incidence[22], which is related to the findings of a recent systematic review in which it was evidenced that only 5% measured more than 20 mm at the time of diagnosis[20.21]. Endoscopic ultrasound and magnetic resonance imaging (MRI) are used to evaluate the tumor's exact size, extension into the rectal wall, and the condition of the perirectal lymph nodes, facilitating better treatment selection and improving the complete resection rate[10].

Various endoscopic procedures can be used in rectal NET resection, including conventional polypectomy, endoscopic mucosal resection, and endoscopic submucosal dissection[10,19]. According to the European Neuroendocrine Tumor Society consensus, well-differentiated rectal NETs below 1.5 cm without invasion of muscularis propria or lymph node involvement can initially be treated endoscopically[10,20]. Transanal excision should be considered when the margins of endoscopic resection are positive[19]. The distance between the tumor and the anal canal and the potential of the tumor to cause an obstruction should be considered when choosing the most appropriate treatment[19-21]. When there are positive locoregional lymph nodes or invasions of the muscularis propria, more radical methods such as excision with low anterior resection or abdominoperineal resection should be chosen[20,21].

According to the European Neuroendocrine Tumor Society (ENETS), patients should be monitored after the complete resection of rectal NETs, as described in **Table 2**.

Table 2. Follow-up and surveillance indications per tumor size and grade according to ENETS[6,10,14,21]

Size	Grade	Follow-up
< 1 cm	1-2	No surveillance needed
< 1 cm	3	Annual colonoscopy for 5 years
1-2 cm	N/A	Colonoscopy, ultrasound, and MRI at 12 months, then colonoscopy every 5 years
> 2 cm	1-2	Colonoscopy and annual MRI for 5 years
> 2 cm	3	Colonoscopy and MRI every 4 to 6 months for the first year, then annually for 5 years

N/A: not applicable; MRI: magnetic resonance imaging; ENETS: European Neuroendocrine Tumor Society.

Rectal NETs have the best overall survival of all gastroenteropancreatic NETs, largely due to the high incidence of small rectal NETs with no evidence of invasion and an excellent long-term prognosis[21,23].

Localized rectal NETS (T1, N0, M0) have a 5-year survival of 98%-100%, while those with regional (N1) and distant (M1) metastases have a 54%–74% and 15%–37% survival, respectively[5,23,24].

We stress the importance of performing regular endoscopic screening in selected patients, detecting and diagnosing the presence of NETs early to avoid complications related to advanced stages of the disease and, thus, reducing morbimortality rates. When evaluating polyps of the gastrointestinal tract, the diagnosis of NETs should be considered a possibility, and its characteristics should be considered to define prognoses and follow-up.

CONCLUSION

Thanks to the incursion of colonoscopy as a screening method for colorectal cancer, the diagnosis of rectal NETs has increased. The risk factors that may lead to their appearance are still unknown due to the lack of large epidemiological studies. In general, at the time of diagnosis, tumors are mostly less than 1 cm, well-differentiated, and can be found in polypoid form, as in our case, which gives patients a better long-term prognosis. Given their smaller size, they can be treated endoscopically without any risk. However, histological classification, size, and location must be considered to define the need for more radical treatments. Rectal NETs have better overall survival than all NETs. It is important to continue population screening through endoscopic studies for early detection and treatment of these tumors.

REFERENCES

1. Bolsolino A. Tumores neuroendocrinos de colon y recto. Acta Gastroenterol Latinoam. 2018;48(4):328-338.
2. Ahmed M. Gastrointestinal neuroendocrine tumors in 2020. World J Gastrointest Oncol. 2020;12(8):791-807. https://doi.org/10.4251/wjgo.v12.i8.791
3. Lubarsch O. Uber den primaren Krebs des Ileum nebst Bemerkungen uber das gleichzeitige Vorkommen von Krebs und Tuberkulose. Virchows Arch. 1888;3:280-317. https://doi.org/10.1007/BF01966242
4. Oberndorfer S. Karzinoid Tumore des Dunndarms. Frankf Z Pathol. 1907;1:426-30.
5. Hrabe J. Neuroendocrine Tumors of the Appendix, Colon, and Rectum. Surg Oncol Clin N Am. 2020;29(2):267-279. https://doi.org/10.1016/j.soc.2019.11.010
6. André TR, Brito M, Freire JG, Moreira A. Rectal and anal canal neuroendocrine tumours. J Gastrointest Oncol. 2018;9(2):354-357. https://doi.org/10.21037/jgo.2017.10.01
7. Partelli S, Maurizi A, Tamburrino D, Baldoni A, Polenta V, Crippa S, et al. GEP-NETS update: a review on surgery of gastro-entero-pancreatic neuroendocrine tumors. Eur J Endocrinol. 2014;171(4):R153-62. https://doi.org/10.1530/EJE-14-0173
8. Jann H, Roll S, Couvelard A, Hentic O, Pavel M, Müller-Nordhorn J, et al. Neuroendocrine tumors of midgut and hindgut origin: tumor-node-metastasis classification determines clinical outcome. Cancer. 2011;117(15):3332-41. https://doi.org/10.1002/cncr.25855
9. Tichansky DS, Cagir B, Borrazzo E. Risk of second cancer in patients with colorectal carcinoids. Dis Colon Rectum 2002;45(1):91-97. https://doi.org/10.1007/s10350-004-6119-y
10. Caplin M, Sundin A, Nillson O, Baum RP, Klose KJ, Kelestimur F, et al. Barcelona Consensus Conference participants. ENETS Consensus Guidelines for the management with digestive neuroendocrine neoplasms: colorectal neuroendocrine neoplasms. Neuroendocrinology 2012;95(2):88-97. https://doi.org/10.1159/000335594
11. Starzyńska T, Deptała A, Królicki L, Kunikowska J, Londzin-Olesik M, Nasierowska-Guttmejer A, et al. Colorectal neuroendocrine neoplasms - management guidelines (recommended by the Polish Network of Neuroendocrine Tumours). Endokrynol Pol. 2013;64(6):494-504. https://doi.org/10.5603/EP.2013.0032
12. Ramage JK, De Herder WW, Delle Fave G, Ferolla P, Ferone D, Ito T, et al. ENETS Consensus Guidelines Update for Colorectal Neuroendocrine Neoplasms. Neuroendocrinology. 2016;103(2):139-43. https://doi.org/10.1159/000443166
13. Ramage JK, Ahmed A, Ardill J, Bax N, Breen DJ, Caplin ME, et al. Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours (NETs). Gut. 2012;61(1):6-32. https://doi.org/10.1136/gutjnl-2011-300831
14. Gonzalez RS. Diagnosis and Management of Gastrointestinal Neuroendocrine Neoplasms. Surg Pathol Clin. 2020;13(3):377-397. doi: 10.1016/j.path.2020.04.002
15. Kim JY, Hong SM, Ro JY. Recent updates on grading and classification of neuroendocrine tumors. Ann Diagn Pathol. 2017;29:11-16. https://doi.org/10.1016/j.anndiagpath.2017.04.005
16. Lloyd RV, Osamura RY, Kloppel G, Rosai J. WHO Classification of Tumors of Endocrine Organs. 5.ª edición. WHO; 2019.
17. Basuroy R, O›Donnell CM, Srirajaskanthan R, Ramage JK. Ileocolonic neuroendocrine tumours identified in the English bowel cancer screening programme. Colorectal Dis. 2018;20(4):O85-O91. https://doi.org/10.1111/codi.14033
18. Shim KN, Yang SK, Myung SJ, Chang HS, Jung SA, Choe JW, et al. Atypical endoscopic features of rectal carcinoids. Endoscopy. 2004;36(4):313-316. https://doi.org/10.1055/s-2004-814202
19. Rakici H, Akdogan RA, Yurdakul C, Canturk N. A case of rectal neuroendocrine tumor presenting as polyp. Int J Surg Case Rep. 2015;8C:59-61. https://doi.org/10.1016/j.ijscr.2015.01.031
20. Bertani E, Ravizza D, Milione M, Massironi S, Grana CM, Zerini D, et al. Neuroendocrine neoplasms of rectum: A management update. Cancer Treat Rev. 2018;66:45-55. https://doi.org/10.1016/j.ctrv.2018.04.003

21. Basuroy R, Haji A, Ramage JK, Quaglia A, Srirajaskanthan R. Review article: the investigation and management of rectal neuroendocrine tumours. Aliment Pharmacol Ther. 2016;44(4):332-45. https://doi.org/10.1111/apt.13697
22. Chi Y, Du F, Zhao H, Wang JW, Cai JQ. Characteristics and long-term prognosis of patients with rectal neuroendocrine tumors. World J Gastroenterol. 2014;20(43):16252-16257. https://doi.org/10.3748/wjg.v20.i43.16252
23. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, et al. One hundred years after «carcinoid»: epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol. 2008;26(18):3063-72. https://doi.org/10.1200/JCO.2007.15.4377
24. Dasari A, Shen C, Halperin D, Zhao B, Zhou S, Xu Y, et al. Trends in the Incidence, Prevalence, and Survival Outcomes in Patients With Neuroendocrine Tumors in the United States. JAMA Oncol. 2017;3(10):1335-1342. https://doi.org/10.1001/jamaoncol.2017.0589