Neuroendocrine Tumor Polypoid Presentation: Case Report and Literature Review

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Abstract
Diagnosis of rectal neuroendocrine tumor (NET) has increased due to the implementation of colonoscopies as a screening tool in rectal treated neo/endoscopic examps. Metastases are rare and prognosis and treatment. We present a case of rectal neuroendocrine tumor as a polyp during 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 (5). 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. They are usually found as single small polypoid tumors, metastatic disease is rare, and tumor size and invasion determine the prognosis of the disease.

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. 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. The 2019 WHO NET classification is described in Table 1.

<table>
<thead>
<tr>
<th>Ki-67 Index (%)</th>
<th>Mitotic index/10 HPF</th>
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<tbody>
<tr>
<td>Well-differentiated neuroendocrine neoplasms</td>
<td></td>
</tr>
<tr>
<td>- Grade 1 (Low)</td>
<td>&lt; 3</td>
</tr>
<tr>
<td>- Grade 2 (Intermediate)</td>
<td>3-20</td>
</tr>
<tr>
<td>- Grade 3 (High)</td>
<td>&gt; 20</td>
</tr>
<tr>
<td>Poorly differentiated neuroendocrine neoplasms</td>
<td></td>
</tr>
<tr>
<td>- N/A (no numerical assignment: high grade)</td>
<td>&gt; 20</td>
</tr>
</tbody>
</table>

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. 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.

**DISCUSSION**

In recent years, the diagnosis of rectal NETs has increased thanks to colonoscopy as a screening method for colon can-
Various endoscopic procedures can be used in rectal NET resection, including conventional polypectomy, endoscopic mucosal resection, and endoscopic submucosal dissection\(^\text{[10,19]}\). 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\(^\text{[10,20]}\). Transanal excision should be considered when the margins of endoscopic resection are positive\(^\text{[19]}\). The distance between the tumor and the anal canal and the potential of the tumor to cause obstruction should be considered when choosing the most appropriate treatment\(^\text{[19-21]}\). 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\(^\text{[20,21]}\). 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\(^\text{[6,10,14,21]}\)

<table>
<thead>
<tr>
<th>Size</th>
<th>Grade</th>
<th>Follow-up</th>
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<tr>
<td>&lt; 1 cm</td>
<td>1-2</td>
<td>No surveillance needed</td>
</tr>
<tr>
<td>&lt; 1 cm</td>
<td>3</td>
<td>Annual colonoscopy for 5 years</td>
</tr>
<tr>
<td>1-2 cm</td>
<td>N/A</td>
<td>Colonoscopy, ultrasound, and MRI at 12 months, then colonoscopy every 5 years</td>
</tr>
<tr>
<td>&gt; 2 cm</td>
<td>1-2</td>
<td>Colonoscopy and annual MRI for 5 years</td>
</tr>
<tr>
<td>&gt; 2 cm</td>
<td>3</td>
<td>Colonoscopy and MRI every 4 to 6 months for W_K_H_U_V_W_H_D_U_W_K_H_Q_D_Q_Q_X_D_O_O_U_R_U_H_D_U_V</td>
</tr>
</tbody>
</table>

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\(^\text{[21,23]}\).

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\(^\text{[21,23,26]}\).

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 morbillimortality 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.

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**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.
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


