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A 31-year-old man with abdominal pain and a rectal nodule

A 31-YEAR-OLD MAN presents to the emergency department with abdominal pain and diarrhea, which began 4 days ago. The pain is in both of the lower quadrants, is crampy and persistent, and is relieved with bowel movements. He has been having watery stools five to six times per day, without frank blood.

He reports no fevers, chills, nausea, or vomiting, and he has never travelled outside the country. He underwent laparotomy 6 months ago for a gunshot wound. He takes no prescription drugs. He smokes and he drinks alcohol, and he says he has used heroin and oxycodone recreationally.

His blood pressure is 134/74 mm Hg, and he is afebrile. An abdominal examination reveals no mass or tenderness.

Results of a complete blood count, serum chemistry panel, and serum amylase level are normal. His lipase level is slightly elevated at 80 U/L (reference range 12–70). His stool is negative for *Clostridium difficile* toxin on enzyme immunoassay.

Computed tomography of the abdomen reveals diffuse pericolic hyperemia and possible thickening of the rectosigmoid colon, raising the concern that he might have infectious or inflammatory colitis. The patient is admitted for further evaluation.

Colonoscopy to evaluate the abnormalities on computed tomography finds only a 5-mm submucosal nodule in the rectum (FIGURE 1). Biopsy of the nodule shows it to be a well-differentiated neuroendocrine neoplasm (carcinoid tumor). Random colon biopsy samples are normal.

The patient's symptoms resolve over the next 24 hours without any treatment.

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FIGURE 1. A rectal nodule was identified endoscopically at presentation.

WHAT EXPLAINS THE PATIENT'S SYMPTOMS?

1 Which of the following best explains the patient's clinical presentation?

- Narcotic withdrawal
- Carcinoid syndrome
- Viral gastroenteritis
- Acute pancreatitis

Viral gastroenteritis is common and affects people of all ages. The very young and the elderly are at higher risk of adverse outcomes, but few people die of it in the United States.

Our patient's symptoms were consistent with viral gastroenteritis that resolved spontaneously while he received only supportive care.

Narcotic withdrawal can also cause watery stools and abdominal pain. However, this patient lacked other signs and symptoms of withdrawal, and his symptoms improved without any detoxification or maintenance treatment.

Pancreatitis. Although the patient had a mildly elevated lipase level, his lack of nausea and vomiting and the location of the pain were not consistent with acute pancreatitis.

Carcinoid syndrome. Carcinoid tumors are rare, typically indolent neuroendocrine neoplasms. The carcinoid syndrome consists of cutaneous flushing, gut hypermotility with diarrhea, and bronchospasm.¹⁻⁵ Our patient did not have the full range of these symptoms. However, the presentation of carcinoid tumors varies broadly depending on the location, morphology, or biology of the tumor.⁶ Although our patient had diarrhea, his symptoms improved without any specific treatment. Rectal carcinoid tumors rarely cause diarrhea, and therefore the tumor noted on colonoscopy was almost certainly an incidental finding unrelated to his clinical presentation.

The classic symptoms are caused by production of 5-hydroxyindoleacetic acid, typically by a carcinoid tumor of the small bowel. Rectal carcinoids do not produce the 5-hydroxyindoleacetic acid responsible for this “malignant” serotonin-driven syndrome and are typically asymptomatic. When rectal carcinoid tumors are symptomatic, patients may have symptoms of local irritation or obstruction, such as hematochezia, constipation, other changes in bowel habits, rectal pain, pruritis ani, or weight loss.^{2,7}

Nearly 50% of rectal carcinoid tumors are discovered incidentally. The National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) registry database documented a 10-fold increase in the incidence of rectal carcinoids in the last 35 years, attributed in part to an increase in screening colonoscopy.⁸ Furthermore, although studies of large national or multicenter databases have found that 65% to 80% of all rectal carcinoid tumors are smaller than 1.0 cm, 93.3% to 100% of those discovered on screening endoscopy were 1.0 cm or smaller.⁸

Rectal carcinoid tumors have a characteristic feel on digital examination, with a hard, “buckshot” consistency, and are freely mobile.⁵

They have also been described as firm, nodular, rubbery, yellow, submucosal, and polypoid.⁸

■ WHERE DO CARCINOID TUMORS TEND TO ARISE?

2 Which of the following sites is the most commonly recognized site of a primary carcinoid tumor?

- Small bowel
- Lung
- Liver
- Pancreas
- Rectum

The small bowel is the most common site.

Carcinoid tumors derive from neoplastic proliferation of cells of the diffuse neuroendocrine system. Therefore, they can be found anywhere neuroendocrine cells are present, commonly in the gastrointestinal tract, urogenital tract, and the bronchial epithelium.

Traditionally, neuroendocrine tumors were classified by their embryologic origin: foregut (including the respiratory tract, thymus, stomach, and pancreas), midgut (including the small intestine, appendix, and right colon), and hindgut (including the transverse, descending, and sigmoid colon and rectum). Functionally, this was sensible, as each class of tumors presented similarly due to the similar hormonal secretory products.^{2,3,9}

A 2004 population-based review of the SEER database¹⁰ classified incidence rates of carcinoid tumors and their distribution throughout the body. Most (54.5%) were discovered in the gastrointestinal tract, and of these, 44.7% were in the small intestine, 19.6% were in the rectum, 16.7% were in the appendix, 10.6% were in the colon, 7.2% were in the stomach, and the remaining 1.2% were at other gastrointestinal sites. Nongastrointestinal sites included the lungs and bronchi (30.1%), pancreas (2.3%), female reproductive tract and ovaries (1.2%), biliary system (1.1%), and head and neck (0.4%).¹⁰

The incidence rates have increased and the distribution of sites in the body has changed over time. For example, the appendix was once considered the site of highest incidence, with tumors often discovered incidentally

He has had pain and diarrhea for 4 days; what is the likely cause?

during surgical resection. However, these data were based on anecdotal or single-institution reports and so may have been subject to reporting bias. According to the SEER data, the small intestine is now the leading site, perhaps because of increased awareness or improved diagnostic technology and imaging.^{10,11}

The liver is a common site of metastasis, but it is an exceptionally rare location for a primary tumor.

■ HOW SHOULD THIS PATIENT BE MANAGED?

3 What is the appropriate management of rectal carcinoid in this patient?

- Since the nodule is 1.0 cm or smaller, watchful waiting is acceptable
- Since the nodule is 1.0 cm or smaller, local excision is appropriate, and no follow-up is required
- Because all carcinoid tumors are potentially malignant, radical resection (eg, abdominal perineal resection) is appropriate
- Because all carcinoid tumors are potentially malignant, radical resection with chemotherapy with 5-fluorouracil (Adrucil) and doxorubicin (Adriamycin) is required

Since the nodule is 1.0 cm or smaller, local excision is appropriate, and no follow-up will be required. Rectal carcinoid tumors generally have a favorable prognosis, with a 5-year survival rate of 87.5%.¹⁰

■ PROGNOSIS DEPENDS ON TUMOR SIZE, OTHER FACTORS

Many studies have examined risk factors contributing to poor prognosis, and this is an area of active study. Early research categorized rectal carcinoid risk in terms of tumor diameter, and this is still widely used to guide management. As early as 1959, Hanley et al⁵ recognized that tumors that were likely to metastasize were often larger than 1 cm, had infiltrated the muscularis, or were ulcerated. Today, it is understood that only 3% to 10% of rectal carcinoids smaller than 1 cm metastasize, whereas 17% to 42% of those 1 to 2

cm and 60% to 80% of those larger than 2 cm do.^{2,8,12,13}

However, size is not the only consideration. Wang et al¹² showed that muscular invasion is an independent risk factor for survival, and that tumor diameter is a significant predictor of invasion and metastasis. Similarly, a meta-analysis by Mani et al¹³ recognized tumor size and muscularis invasion as the most important predictors of malignancy in these neoplasms.

To aid in predicting prognosis, staging systems have been developed from institutional or national registries. Landry et al¹⁴ developed a TNM (tumor, node, metastasis) staging system for rectal carcinoids, in which the T value was based on tumor size and degree of invasion. A group at Memorial-Sloan Kettering Cancer Center¹⁵ developed a system for risk stratification of carcinoid of the rectum that is based on tumor size, muscularis invasion, lymphovascular invasion, and the mitotic rate.

■ TREATMENT IS BY EXCISION

Despite these new prognostic systems, there is no new guidance on therapeutic management. Surgical therapy is still largely guided by tumor size.

Lesions smaller than 1 cm are resected endoscopically or by another local transanal technique.^{2,3,15,16} Standard endoscopic mucosal resection is performed, and recent studies have suggested that endoscopic submucosal dissection is as effective¹⁷ or even preferred, because it resects to the deeper submucosa (as the name suggests).¹⁸ This *en bloc* technique may be appropriate for lesions with evidence of local invasion.¹⁸ Other situations may call for deeper resection, such as transanal resection for higher lesions and full-thickness mucosal-muscularis resection.

Tumors 1 to 2 cm are currently evaluated for other factors such as ulceration and umbilication, which influence the choice of local vs radical resection. Otherwise, there is little guidance for tumors of 1 to 2 cm.

Tumors larger than 2 cm have a high risk of muscularis invasion and metastasis, and hence they are resected with wide margins and imaging is then used to evaluate for metastasis.^{8,19} In cases of metastasis, local resection is often palliative, providing local symptom relief.¹⁹

Nearly 50% of rectal carcinoids are discovered incidentally

■ **AN INCIDENTALLY DISCOVERED CASE; PATIENT LOST TO FOLLOW-UP**

Our patient's case is typical of rectal carcinoid in that it was discovered incidentally during colonoscopy. His clinical presentation was likely unrelated to his carcinoid tumor, and he improved without specific treatment. His symptoms resolved within 24 hours with supportive treatment and he was discharged.

Pathologic confirmation of carcinoid tumor occurred after his discharge. Despite persistent attempts to contact the patient, he never returned for a follow-up appointment.

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■ **TAKE-HOME POINTS**

- Carcinoid tumors are rare neoplasms of neuroendocrine origin.
- Rectal carcinoids are the third most common carcinoid of the gastrointestinal tract.
- Most rectal carcinoids are asymptomatic.
- Diagnosis is most often incidental and histologic.
- Treatment is by excision.
- Prognosis is favorable for smaller carcinoids and depends on size (and therefore, invasion).

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Carcinoids > 2 cm have a high risk of muscularis invasion and metastasis