A case report of a neuroendocrine tumor in the small intestine with manifest dark digestive bleeding

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Abstract

We present the case of a young patient with no history of illness who developed obvious bleeding in the form of melena, hematochezia, and severe anemia. Initial endoscopic studies were normal, but video capsule endoscopy (VCE) revealed an ulcerated subepithelial lesion in the jejunum leading to suspicion of GIST or a neuroendocrine tumor. It was marked in enteroscopy, extension studies showed that it was normal. Therefore, local resection was scheduled by laparoscopy, making diagnosis and management of a neuroendocrine tumor.

Keywords

Hemorrhage, small intestine, neoplasms of the jejunum, neuroendocrine tumor.

INTRODUCTION

In 10% to 20% of patients with gastrointestinal bleeding, the cause cannot be documented in initial endoscopic studies. For the doctor and patient, this may be a manifestation of obscure digestive bleeding if there is evidence of hemorrhaging (melena, hematochezia), or it could be a case of occult digestive bleeding if blood is found in fecal matter or if there is unexplained iron deficiency anemia without clinical evidence of bleeding. (1) Recent development of new diagnostic methods for exploring the small intestine including video capsule endoscopy (VCE), enteroscopy and angiography have made it possible to diagnose most sources of digestive bleeding in this segment. A recently published clinical guideline recommends change the term obscure digestive bleeding to bleeding from the small intestine. (2) It reserves the term obscure digestive bleeding for bleeding that cannot be identified after the entire gastrointestinal tract has been evaluated. (1-3) Of all the causes of gastrointestinal bleeding, only a small percentage (5%) is attributed to sources in the small intestine. In young people, the causes vary from tumors such as gastrointestinal stromal tumors (GIST), neuroendocrine tumors, lymphomas and adenocarcinomas, to inflammatory lesions especially due to the use of non-steroidal anti-inflammatory drugs (NSAIDs) and Crohn's disease. Rarer causes have also been described. They include ulcerated or eroded Meckel's diverticulum and the Dieulafoy's lesion. In our environment, we cannot stop thinking about ancylostomiasis as a cause of anemia and obscure bleeding (3).

The initial approach to digestive bleeding from the small intestine should be to use VCE to establish the etiology and clarify the location in order to define the subsequent best approach.

CLINICAL CASE

The patient was a 26 year old man with no history of illness. He said that he did not take NSAIDs or smoke, but that he occasionally drank alcoholic beverages. He was admitted with digestive bleeding manifested by melena and hematochezia and had severe anemia. His initial hemoglobin level was 5.8 g/dL which required a transfusion of two units of red blood cells. Initial suspicion of upper gastrointestinal

bleeding led to performance of esophagogastroduodenoscopy which was normal and without evidence of bleeding. A total ileocolonoscopy was also normal but showed blood coming from the small intestine. A VCE revealed a subepithelial ulcerated lesion with a visible vessel located in the jejunum at 52% of the transit of the VCE through the small intestine (Figure 1). Because of these findings, antegrade double-balloon enteroscopy was performed, the most distal site was marked, and local resection was requested. Staging studies with computed tomography (CT) of the thorax and contracted abdomen found no additional lesions are identified.

Laparoscopy identified the lesion and local oncological resection removed a 10 cm segment. The patient's clinical evolution was satisfactory without new episodes of bleeding, and he was discharged two days later. Currently, he is asymptomatic.

DISCUSSION

Obscure digestive bleeding is a great challenge for the clinician. In the case described, we adhere to the current recommendations of the guidelines of the American Society of Gastrointestinal Endoscopy (ASGE) for study of bleeding from the small intestine. (1) For patients with manifest and stable obscure bleeding, the initial approach should be made with VCE in order to determine the location and type of lesion and to determine the most appropriate method and approach. In this case, we documented an ulcerated subepithelial lesion in the jejunum. Bearing in mind that the most common causes of these lesions in this age group are GIST and neuroendocrine tumor, additional studies were carried out to define resectability. Given the absence of additional findings from these negative studies, we decided to perform local laparoscopic resection (Figure 2) after marking with ink using double balloon enteroscopy.

Currently, we have multiple techniques for evaluating the small intestine. These include: VCE, double balloon enteroscopy, enterography by multiphasic CT scan, magnetic resonance enterography (MRE) and, intraoperative enteroscopy which is rare. These modalities can recognize small bowel injuries and can impact therapeutic strategies. Unnecessary surgical intervention can often be avoided, but when necessary, surgical time can be decreased by better identification of the location of the lesion. Despite these advances, the most cost-effective approach for management of patients with suspected small bowel bleeding has not been fully determined. Still, the strongest recommendation at present is to address small bowel bleeding with VCE (1, 3-5).

In cases of neuroendocrine tumors in the small intestine, a large number of authors propose a multi-image presurgical approach using transverse or functional images to define
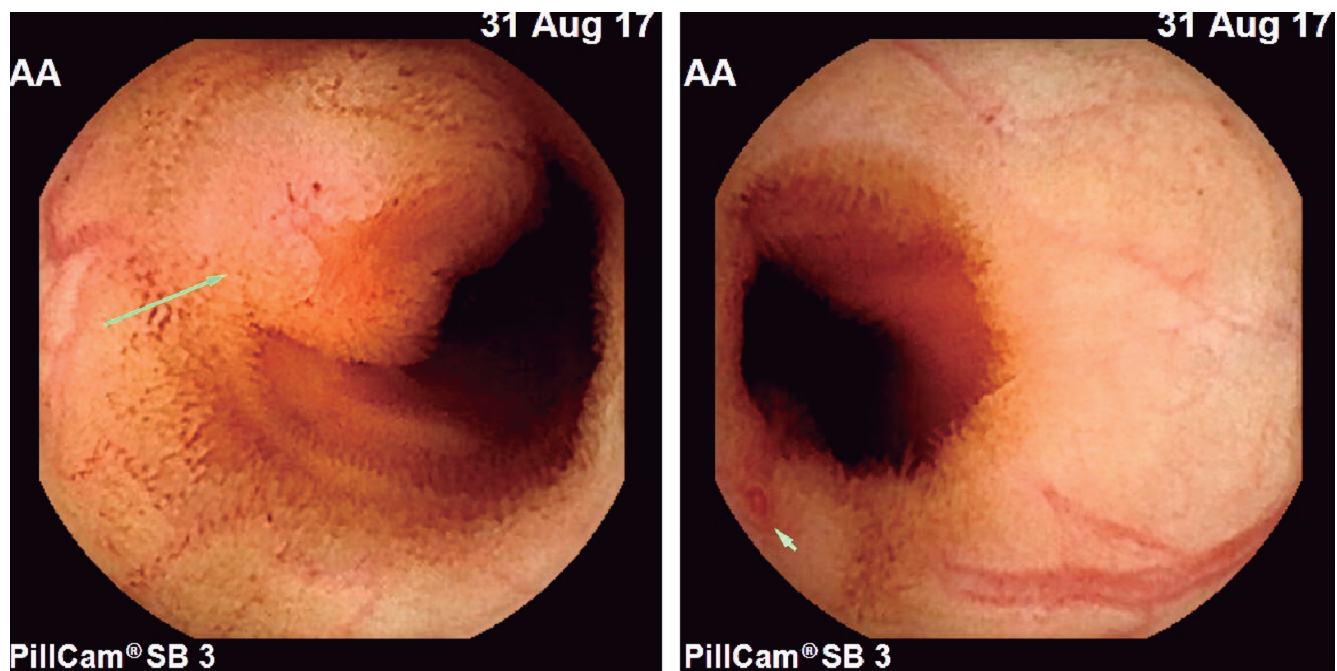

Figure 1. Endoscopic videocapsule shows ulcerated subepithelial lesion with a vessel visible in the jejunum.
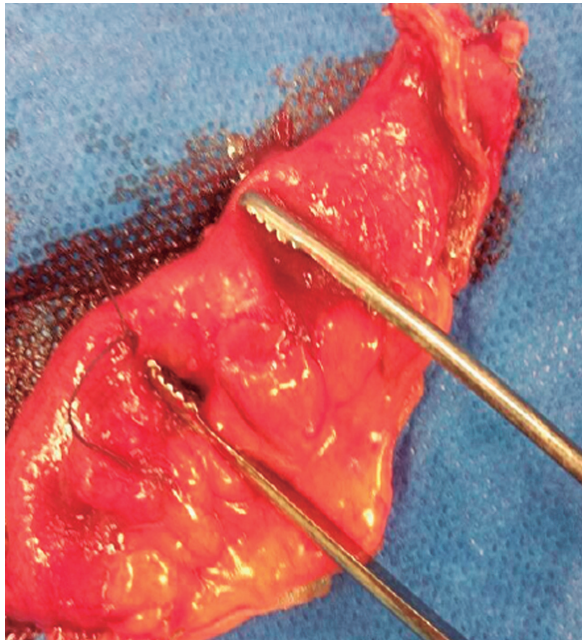
Figure 2. Resected intestinal segment

the extent of the disease. Once the diagnosis of tumor in the small intestine has been made, a CT scan or magnetic resonance imaging (MRI) are most commonly used during the preoperative approach. (6-8) The value of each diagnostic tool varies. CT scans are usually better at identifying the primary lesion, and MRI seems to be better at evaluating liver metastases. However, up to 15% of lesions may not be evident in these studies, so the extent of abdominal metastases may be underestimated. (7, 8) CT enterography is a promising new modality for evaluating small bowel bleeding. It uses high-volume neutral oral contrast to distend the small intestine and thus improve evaluation of the wall. In addition, contrast material is administered intravenously, and images are typically acquired 30 seconds after the intravenous bolus in the arterial phase, 50 seconds after the bolus in the enteric phase, and 90 seconds after the bolus in the delayed phase. (9) This technique can detect inflammatory lesions, neoplasms and vascular lesions including angiectasis, varicose veins, Dieulafoy's lesions, aortoenteric fistulas and pseudoaneurysms. (1, 9) Like VCE, CT enterography scans can help clinicians determine whether an antegrade or
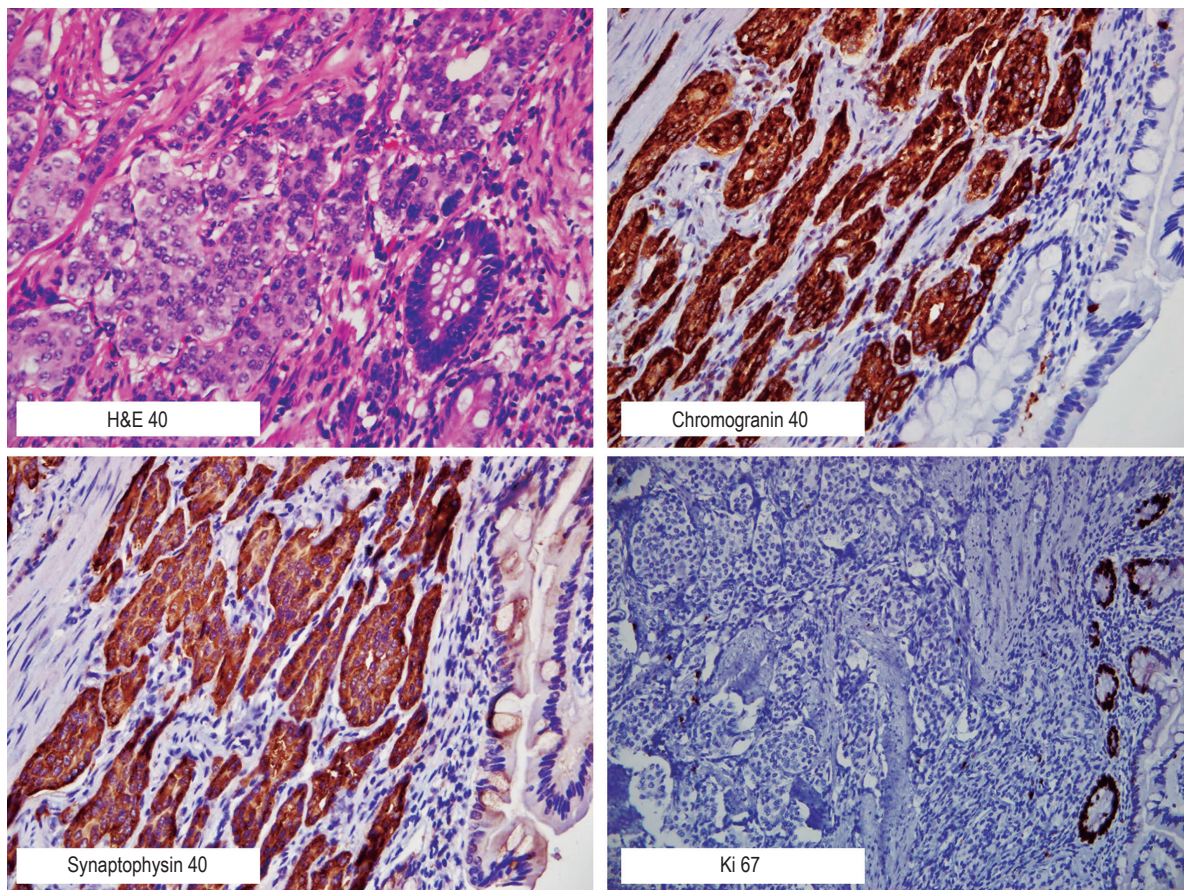

Figure 3. Neuroendocrine tumor pathology with several positive markers.

retrograde approach is more appropriate for enteroscopy. A study published by Hakim et al. has even found higher rates of detection of small bowel tumors with CT enterography than with VCE. (10) CT enterography could an option in cases of digestive bleeding from the small intestine in young patients for whom a neoplastic etiology is considered in the differential diagnosis.

A study of 52 patients with digestive bleeding from the small bowel which could not be diagnosed by VCA, found that CT enterography could diagnose half of the cases. (11). Another study which included 30 patients with negative CT enterography results found that subsequent VCE had a diagnostic yield of 57%. (12) These data support the complementary role of the VCE and the CT enterography when one has negative results, thus adding a second examination to the diagnostic performance.

MRE could be an alternative when there is suspicion of obstruction in the small intestine and for young patients who require periodic monitoring as in the cases of polyposis and Crohn's disease. Radiation exposure is much less than that in CT enterography although data related to MRE are still limited. (1, 13, 14) In all cases of obscure digestive bleeding, the individual characteristics of the patients, the resources available, and the experience in the institution with different diagnostic methods should all be taken into account in order to have a more rational and effective approach.

In our case, we defined the surgical treatment due to the suspicion of malignant lesion before we found the subepithelial lesion with a visible vessel in the jejunum. The pathology report showed a 15 x 10 x 5 mm unifocal lesion compatible with a well-differentiated neuroendocrine tumor. The tumor had deeply compromised the subserosa but had not reached the serosa. It had negative margins (markers of synaptophysin, chromogranin, CD56 with strong and diffuse positivity in the neoplastic cell, with Ki-67 proliferation index less than 1%) (Figure 3).

According to the literature, neuroendocrine tumors located in the duodenum or proximal jejunum are the rarest of

Table 1. WHO Classification of Gastroenteropancreatic Neuroendocrine Tumors (9)

2000 WHO Classification (pancreas)	Local invasion	Characteristics
Well-differentiated benign endocrine tumor	Confined	<2 cm, no LVI or PNI, <2 mitosis/10 HPF, proliferation index Ki 67 <2%
Well-differentiated endocrine tumor of uncertain behavior	Confined	One or more ≥2 cm, LVI, PNI, 2-10 mitosis/10 HPF, proliferation index Ki 67 ≥2%
Well-differentiated endocrine carcinoma	Local invasion or metastasis	One or more ≥2 cm, LVI, PNI, 2-10 mitosis/10 HPF, proliferation index Ki 67 ≥2%
Poorly-differentiated endocrine carcinoma	Widespread invasion or metastatic	High grade carcinoma with> 10 mitosis/HPF

2017 WHO Classification	Mitotic count	Index of proliferation Ki 67 (%)
NET grade 1	<2	<3
NET grade 2	2-20	3-20
NEC	>20	>20

2017 WHO Classification (changes NEC the classification of WD-NET G3 and PD-NEC) (9, 11, 12)			
High-grade neuroendocrine neoplasm characteristics: tumor necrosis, increased mitotic activity> 20/10 HPF, Ki 67 index> 20%			
Classification	Thorough examination of pathological material	Immuno-histochemical studies	Clinical information
WD-NET grade 3	Low-grade component (OMS G1-G2) WD-NET; Early samples are lower grade than later samples	Loss of DAXX or ATRX expression	Incidental finding without associated symptoms of high grade malignancy Elevated neuroendocrine markers in plasma (chromogranin A) Diffuse avidity in gamma grafting with octreotide
PD-NEC	Component of conventional adenocarcinoma or squamous cell carcinoma	Loss of Rb or abnormal expression of p53	Symptoms associated with high-grade malignancy Elevated markers of carcinoma in plasma (CEA, CA19.9, CA 125ect) Negative or weak focal activity on octreotide scintigraphy

GEP-NET: gastroenteropancreatic neuroendocrine tumors; HPF: high power field(s); LVI: lymphovascular invasion; PNI: perineural invasion; NEC: neuroendocrine carcinoma; WHO: World Health Organization; PD-NEC: poorly differentiated neuroendocrine carcinoma; WD-NET: well differentiated neuroendocrine tumor.

those in the small intestine. It is estimated that their prevalence is between 5.7% and 7.9%. (15, 16) All except gangliocytic paragangliomas are considered to be malignant. Most patients with this type of tumor in the small intestine have metastatic disease or multiple lesions when the diagnosis is made. The case we have presented corresponds to grade 1 in the classification of neuroendocrine tumors which has excellent oncological prognosis and low risk of relapse. (1, 17) We recommend Table 1 where we summarize classifications of neuroendocrine tumors and the recent proposal to classify neuroendocrine carcinoma. (9, 18, 19)

Financing

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Case report