Unsuspected Small Bowel Neuroendocrine Tumor

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Introduction

Neuroendocrine tumors (NETs) are epithelial tumors that arise from neuroendocrine cells of the digestive system. The incidence of well-differentiated NETs in the U.S. is around 4.7 per 100,000.[1] Within the digestive system, the majority occur in small intestine (45%), followed by rectum (20%), appendix (16%), colon (11%) and stomach (7%).[2] Histologic grade and differentiation correlate closely with clinical presentation. Symptoms include abdominal pain, nausea, vomiting, diarrhea, bowel obstruction, bleeding, anemia, and weight loss.[3] The majority of NETs are not associated with clinical symptoms.[3] Therefore, diagnosis is usually made accidentally during a routine workup or from the patient experiencing symptoms from the tumor. We report a difficult-to-diagnose unsuspected NET of the ileum in a young, otherwise healthy individual.

Case Report

A 57-year-old female with a history of hypertension and hyperlipidemia presented to the emergency department (ED) with multiple episodes of dark, burgundy-colored stools that started one day prior to admission. She was in her usual state of health until the day before, when she had four episodes of dark, foul-smelling stools.

On the morning of admission, she had another episode and felt fatigued. She denied abdominal pain, nausea, vomiting, or any other associated symptoms. She was not taking NSAIDs or blood thinners. In the ED, her initial hemoglobin was 9.8 g/dL, her baseline being 13.4 g/dL from one year ago. Within a few hours, her hemoglobin was 7.7 g/dL. She was transfused blood and started on intravenous fluids and acid suppression therapy. The patient had a screening colonoscopy a year ago showing moderate internal hemorrhoids. In the ED, the gastroenterologist performed a diagnostic upper endoscopy, but it did not show any signs of bleeding. The patient then had a CT angiogram that showed high density fluid in the small bowel with no active bleeding and a 2 mm hypervascular focus in the right lobe of the liver.

Overnight, she bled again and had a near syncopal episode. She had a second CT angiogram. This time, it showed active bleeding within an intraluminal segment of the small intestine in the pelvis (Image 1). The patient was taken to the cath lab for an urgent angiogram for embolization, but no active bleeding was noted in any of the mesenteric blood vessels.

The following day, she had an MR enterography which showed focal thickening of the same segment of the small intestine that had shown active bleeding on the repeat CT angiogram the day before. General surgery was consulted, who along with the gastroenterologist, agreed to take the patient to the operating room for a laparoscopy and possible intra-operation small bowel enteroscopy.

During the procedure, the surgeon identified what felt to be a tumor with adherent fat in the distal ileum, about 60 cm from the ileocecal valve. Five cm of small intestine was resected and sent to pathology (Image 2). The patient had end-to-end primary anastomosis of the distal small bowel. Pathology revealed a well-differentiated neuroendocrine tumor, 2.2 cm (WHO grade 1 of 3) with focally-penetrating serosa with negative margins (Image 3). The patient recovered from the surgery and was sent home without further complications. She will be followed by oncology for further observation.

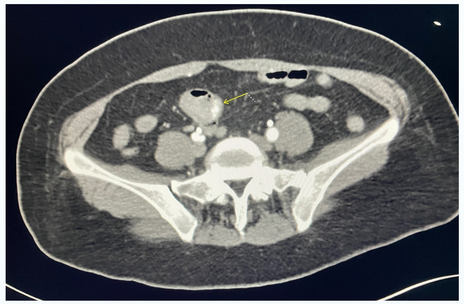

Image 1: Extravasation of contrast in the distal small bowel suggestive of active small bowel bleeding.

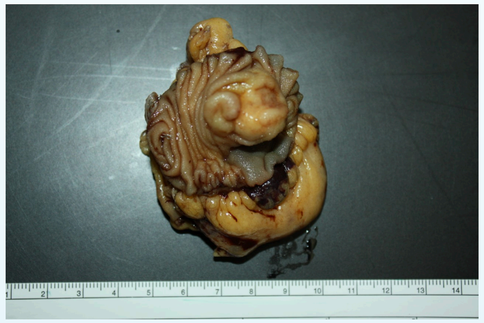

Image 2: Ulcerated submucosal mass in distal small bowel measuring 2.8x1.8 cm.

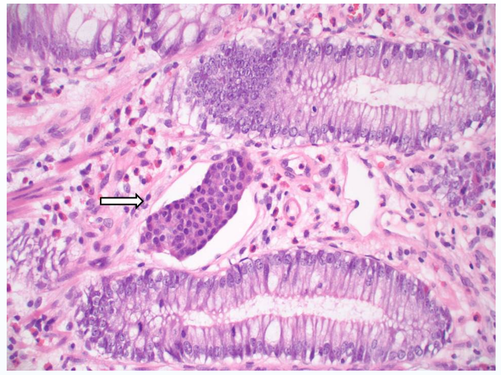

Image 3. Sections of the mass consist of a proliferation of nests of tumor cells with rosette formation. Tumor cells have dispersed chromatin and eosinophilic to granular cytoplasm. Tumor necrosis is absent. Mitotic figures are not identified. Tumor cells involve the surface mucosa and and focally penetrate the serosa. Lymphovascular invasion is identified. Perineural invasion is absent. The submucosa and mesenteric fat surrounding the lesion shows hemorrhage. No lymph nodes are identified.

Discussion

Neuroendocrine tumors (NETs) are epithelial tumors. They are slow-growing and can develop in most organs in the body but have significant neuroendocrine differentiation. Symptoms include abdominal pain, nausea, vomiting, diarrhea, bowel obstruction, bleeding, anemia, and weight loss.[3] The genetic basis of NETs involves chromosomal deletions and additions and cancer-related signaling pathways.[3]
NETs are the most common type of small bowel neoplasms. The majority of NETs are not associated with clinical symptoms.[3] Therefore, diagnosis is usually made accidentally during a routine workup or from the patient experiencing symptoms from the tumor. Small bowel NETs are usually diagnosed at 60-70 years of age.[3] They are divided into duodenal NETs and distal NETs of the jejunum and ileum. Lymph node metastasis occurs in about 60% of cases of duodenal NET.[3] Liver metastasis occurs in less than 10% of duodenal NET cases and about 20% of cases of distal NET of the jejunum and ileum.[3]

The stage of the disease has a large impact on prognosis. Patients with well-differentiated duodenal NETs have a five-year survival rate of almost 85%.[4] The 10-year survival rate is 95% for patients with localized NETs and 10% for those with distant metastasis.[4] Distal NETs of the jejunum and ileum have a poorer prognosis because of their tendency to metastasize.[5] The 5-year survival rate is 65% for patients with localized NETs and 36% for those with distant metastasis.[6]

The annual incidence of NETs has increased over the past five years to forty to fifty cases per million, largely due to better diagnostic tools. For duodenal NETs, upper gastrointestinal endoscopy with biopsy is the most sensitive diagnostic test.[7] Endoscopy can be used to stage the disease locally. Capsule enteroscopy (CE) and balloon-assisted enteroscopy are newer tools that have high diagnostic yield and non-invasiveness.[7] Recently, studies have established that PET/CT, specifically with 68-Gallium-labeled somatostatin analogues, has the greatest sensitivity for diagnosis and staging for all NETs, except insulinomas.[8] Several genetic markers are being evaluated as diagnostic tools. Clinical societies, such as NANETS, ENETS and UKINETS, are emerging to further improve diagnosis and management of NETs.

Treatment depends on the size of the NET. Small (≤ 1 cm) duodenal NETs can be resected endoscopically.[9] Larger duodenal NETs (≥ 2 cm) or lymph node metastasis should be treated surgically.[9] Patients with hepatic metastasis should be offered palliative surgery. Inspection and palpation for additional tumors should be done, especially for distant NETs of the jejunum and ileum which are more likely to metastasize. Systemic chemotherapy is not recommended for well-differentiated NETs.[9]

Conclusion

In conclusion, NETs are neoplasms with many unanswered questions about their pathophysiology. This case describes difficulties in diagnosing NETs of the ileum and highlights the need for improvements in diagnosis and management of NETs and further research into their pathophysiology.

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