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## Case Report

# Large cell neuroendocrine carcinoma in the unusual location of the descending colon ☆

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## ABSTRACT

Neuroendocrine neoplasms are most often found in the small intestine, rectum, appendix, and stomach. The colon, excluding the appendix and the cecum, is a rare location for these neoplasms and often gives rise to highly proliferative, poorly differentiated tumors with aggressive features and dismal prognosis. A 32-year-old male presents with a large cell neuroendocrine carcinoma arising from an unusual location, the descending colon. The patient's clinical and imaging characteristics resembles those seen in the much more common neoplasm, colonic adenocarcinoma. Computed tomography and In-111 octreotide scan are limited in diagnosing large cell neuroendocrine carcinoma. Pathologic correlation of a surgical specimen is required to make the correct diagnosis.

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## Introduction

Neuroendocrine neoplasms (NENs) are uncommon, slow growing neoplasms of the neuroendocrine system that most frequently occur in the ileum (30%), the rectum (21%–27%), the appendix (17%–20%), and the stomach (6%–9%) [1,2]. The colon, excluding the appendix and the cecum, is a rare origin for NENs with a reported incidence of 0.2 per 100,000 persons [3]. The overall median age at diagnosis is 63 years [3]. Colonic NENs are not normally associated with hereditary tumor syndromes such as multiple endocrine neoplasia, type 1 [4]. Colonic NENs are typically poorly differentiated on histology, and often appear as a large mass with aggressive growth, rapid dissemination, and distant metastases at the time of

diagnosis [4–6]. Once metastasized, the prognosis is dismal with a median survival of 5 months [3].

Patients with NENs typically present with nonspecific complaints such as bleeding, diarrhea, abdominal pain, gastrointestinal blood loss or weight loss [1,4]. Carcinoid syndrome is more often seen in patients with gastric or small intestinal NENs with liver metastasis. In contrast, carcinoid syndrome is rare in patients with colonic NENs because these tumors rarely contain serotonin or secrete serotonin precursors [1,7,8]. Urine levels of the serotonin metabolite, 5-HIAA, are not significantly elevated in patients with colonic NENs [8]. Serum chromogranin A may be elevated in 80% of all gastrointestinal NENs and correlate with tumor burden [8]. However, its diagnostic accuracy can be lower for poorly differentiated NENs [2,9]. Also, it may be falsely elevated in proton

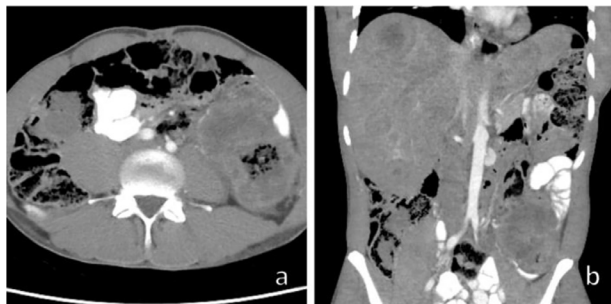
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**Fig. 1 – Axial (a) and coronal (b) images of CT with IV contrast with multiphasic acquisition. Irregular, circumferential wall thickening of the descending colon with a contiguous 4.2 × 5.6 × 6.4 cm heterogeneously enhancing mass.**

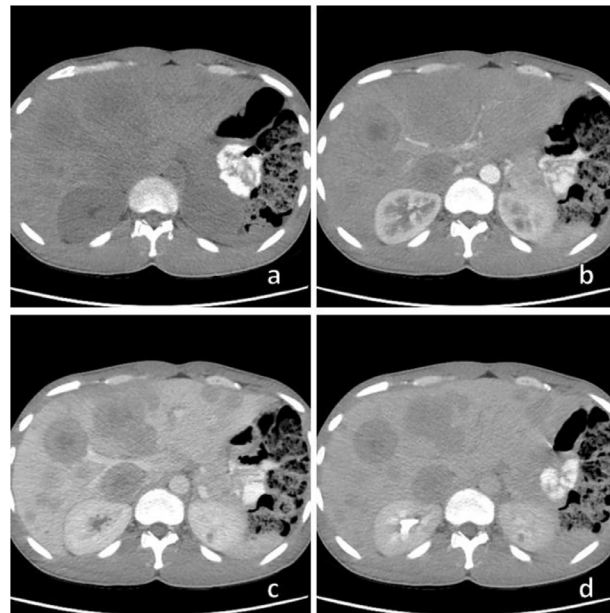
pump inhibitor use, atrophic gastritis, impaired renal function, rheumatoid arthritis, inflammatory bowel disease, and non-neuroendocrine neoplasms such as prostate cancer, ovarian cancer, breast cancer, and colorectal cancer [10].

The cross-sectional imaging features of colonic NENs include irregular circumferential wall thickening or large polypoidal mass with lymphadenopathy, closely resembling those of colonic adenocarcinoma [6,7,11,12]. Metastasis to the liver is common and appear as hypervascular lesions that demonstrate moderate-to-intense homogenous or peripheral rim enhancement during hepatic arterial phase on multiphasic computed tomography or magnetic resonance imaging [12,13]. In-111 octreotide scintigraphy utilizes a synthetic somatostatin analog to characterize NENs [14]. Neuroendocrine tumors containing somatostatin receptors demonstrate increased radiotracer uptake. We present a rare case of large cell neuroendocrine carcinoma in the descending colon with metastasis in the liver, which demonstrates clinical and imaging features closely resembling those of metastatic colonic adenocarcinoma.

## Case presentation

A 32-year-old male with a past medical history of depression and schizophrenia presented with constant, left abdominal pain radiating down to the hip and groin. No pertinent surgical or family history was noted. The patient admitted to daily use of alcohol and tobacco and denied recreational drug use. The review of systems was positive for fatigue, intermittent blood-streak stools, and unintentional weight loss of 20 lbs. The patient denied fever, night sweats, decreased appetite, nausea, vomiting, diarrhea, cutaneous flushing, sweating, or bronchospasm. The physical exam was unremarkable except for tenderness over the left flank and mid abdomen.

Computed tomography of the abdomen and pelvis with IV contrast revealed irregular circumferential wall thickening of the descending colon with a contiguous 4.2 × 5.6 × 6.4 cm heterogeneously enhancing mass (Fig. 1). Innumerable hypoattenuating lesions with hypovascular peripheral enhancement



**Fig. 2 – Axial images of CT of the abdomen and pelvis at the level of the right portal vein. Noncontrast axial CT image (a) demonstrates innumerable ill-defined, hypoattenuating masses throughout the liver, suspicious for metastatic lesions. Contrast axial CT image on arterial phase (b) demonstrates the same masses with peripheral rim enhancement and a hypoattenuating center. The masses remain hypodense to the background hepatic parenchyma. Each mass contains a faint, hypoattenuating, and nonenhancing halo. Contrast axial CT image on portal venous phase (c) and delayed phase (d) demonstrate persistent peripheral enhancement with no rapid washout.**

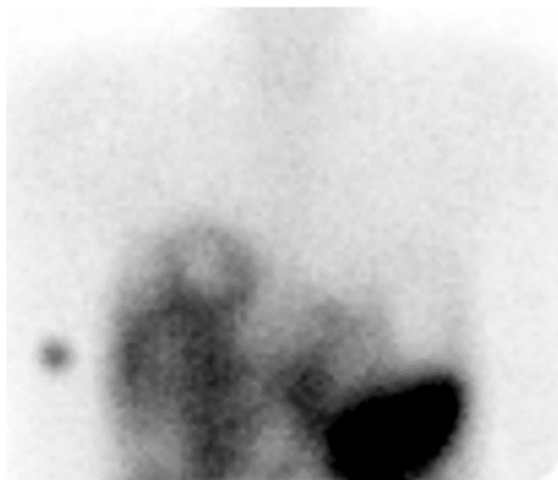
were observed throughout the hepatic parenchyma (Fig. 2). No skeletal metastasis was appreciated. In-111 octreotide scan demonstrated multiple photopenic lesions within the liver (Fig. 3).

After an unsuccessful attempt with colonoscopy, left hemicolectomy and surgical pathology were pursued. Surgical pathology of the colonic mass revealed poorly differentiated, large cell neuroendocrine carcinoma with tumoral invasion into the visceral peritoneum and positive 3 of 7 lymph nodes (Fig. 4). Additionally, interventional radiology was consulted for CT-guided biopsy of the liver lesions. Tissue biopsy of the hepatic lesions confirmed metastasis from the colonic mass.

Evaluation of 5-hydroxyindoleacetic acid (5-HIAA) in a 24-hour urine specimen was within normal limits at 4mg/24h. The patient was treated with intravenous 80 mg/m<sup>2</sup> cisplatin for 3 weeks in combination with 80 mg/m<sup>2</sup> etoposide for first 3 days.

## Discussion

Colonic NENs demonstrate similar cross-sectional imaging features as colorectal adenocarcinomas [6,7,11,12]. Both



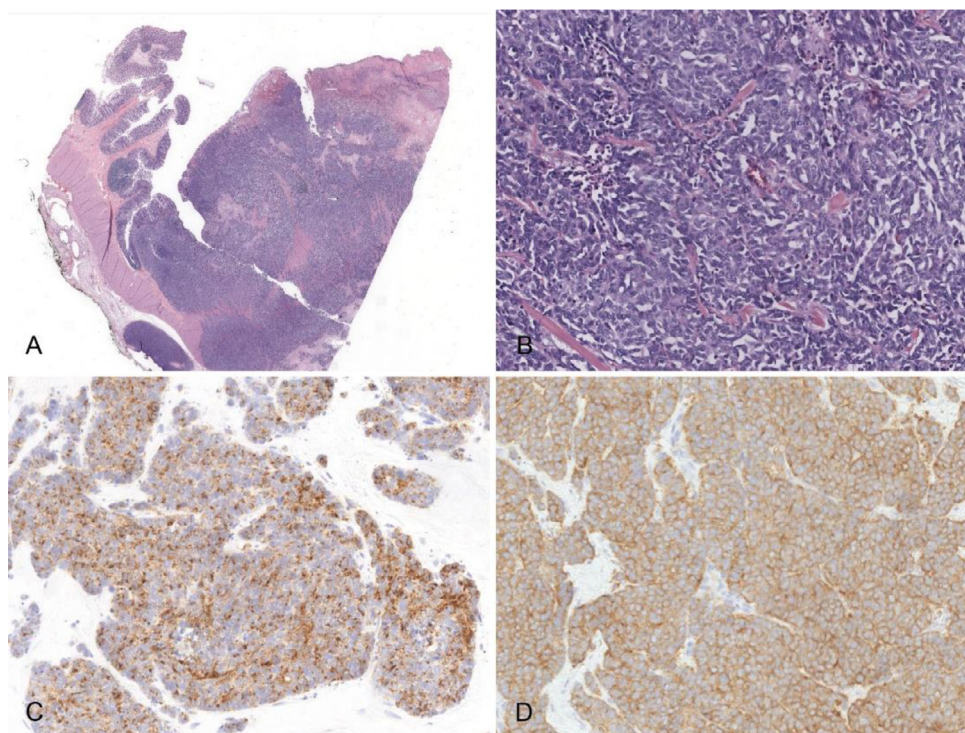
**Fig. 3 – 24 hours delayed anterior projection of the chest In-111 octreotide scintigraphy demonstrates multiple photopenic lesions within the liver.**

feature irregular circumferential wall thickening or polypoid intramural mass with areas of central necrosis and degeneration [6,7,11,12]. Also, both malignancies often metastasize to the liver [12]. Colonic adenocarcinomas often produce hypovascular hepatic metastatic lesions. In contrast, 94% of gastrointestinal NENs metastases feature hypervascular lesions

demonstrating moderate-to-intense homogenous or peripheral rim enhancement during arterial phase [12,13]. Hypervascular hepatic metastasis are nonspecific and can be commonly seen in melanoma, renal cell carcinoma, choriocarcinoma, and thyroid carcinoma [15]. However, in the setting of a patient with a colonic mass, hypervascular hepatic metastatic lesions may be the differentiating imaging feature to suggest colonic NENs rather than adenocarcinoma. In our case, the hepatic metastatic lesions demonstrated hypovascular, peripheral enhancement that resemble those typically seen with colonic adenocarcinoma as opposed to those seen with colonic NENs. We postulate that the appearance of these lesions may be attributed to the fibrogenic nature of NENs [3,16], and central necrosis due to the poor cell differentiation of the mass.

In-111 octreotide scintigraphy is commonly used in diagnosis of NENs with a sensitivity of 80%-90% for all NENs [14]. It utilizes a synthetic somatostatin analog that binds to somatostatin transmembrane receptors, which are expressed in 80%-100% of all NENs [14]. However, poorly differentiated NENs may sometimes express fewer somatostatin receptors or may even completely lack them all together, producing less reliable results [5,14]. In our case, In-111 octreotide scintigraphy demonstrates multiple photopenic lesions in the liver. This may be secondary to the absence or fewer numbers of somatostatin receptors in poorly differentiated NENs.

Our patient presents with abdominal pain, fatigue, weight loss, and hematochezia without the characteristic symptoms of carcinoid syndrome despite having substantial hepatic



**Fig. 4 – H&E stain, scan power view shows sheet-like growth pattern of tumor cells involving whole layer of colon (A). On higher magnification (B), tumor cells show solid growth pattern. Note the vesicular nuclei with salt-and-pepper chromatin. Immunohistochemical staining for chromogranin A (C) and synaptophysin (D) reveals diffuse positive in tumor cells.**

metastasis. Also, laboratory analysis of urine 5-HIAA is unremarkable. CT and In-111 octreotide scan are limited in diagnosing large cell neuroendocrine carcinoma. Ultimately, the correct diagnosis is made through immunohistochemical evaluation of the surgical pathologic specimen.

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