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Synchronous Gastrointestinal Metastatic Large Cell Neuroendocrine Tumor and Metastatic Colon Adenocarcinoma: Case Report

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Abstract
This article reports a case involving a synchronous silent metastatic rectal adenocarcinoma and metastatic large cell neuroendocrine tumor of the cecum and ascending colon. The patient presented with left sided abdominal pain and hematochezia with a noncontributory family, social, and medical history. This case presents a rare pathology not only due to the low incidence of synchronous gastrointestinal malignancies, but due to the unusual silent patient presentation.

Introduction
Colorectal carcinoma is the third most common carcinoma diagnosis and second deadliest carcinoma in either sex greater than 50 years of age **[2,3]**. Colorectal carcinoma can present with hematochezia, abdominal pain, unintentional weight loss, fatigue, bowel obstruction, and anemia. Large cell neuroendocrine tumor is a rare and aggressive subtype of neuroendocrine tumors at risk for early metastasis **[1]**. Presentation of a large cell neuroendocrine tumor can vary depending on multiple factors; however, it typically presents with abdominal pain, hematochezia, melena, and altered bowel movements.
The coexistence of a large cell neuroendocrine tumor and primary colorectal adenocarcinoma presenting as synchronous tumors are rarely known to occur. Synchronous tumors are two primary tumors occurring simultaneously or within a 6-month span after diagnosis of the primary tumor. Patients presenting with large cell neuroendocrine tumors in the gastrointestinal tract have an incidence of adenocarcinoma located in the colorectal region ranging from 17 to 53% in some case series **[4,5]**. Prognosis of patients is primarily based on the adenocarcinoma portion rather than the large cell neuroendocrine tumor. A case literature analysis revealed synchronous colorectal cancers incidence rates range from 2.3 to 12.4% **[4,5].** The analysis indicated that these lesions are mainly located on both sides of the colon. In contrast, lesions localized to the right side rather than the left side of the colon are typically seen in older patients. Average ages for the lesion locations right vs left sided are 72 and 64, respectively **[6].** We describe a synchronous carcinoma consisting of adenocarcinoma of the rectum and metastatic large cell neuroendocrine carcinoma of the rectum and ascending colon. This case reports a rare opportunity wherein an adult patient presents with synchronous gastrointestinal carcinoma.

Case Presentation
A 67-year-old Hispanic male with no medical history of coronary artery disease, cerebrovascular accidents, hypertension, or diabetes mellitus. The patient had no past

surgical history or colonoscopies, family history of any malignancies, and denied history of smoking. The patient presented to the surgical clinic with left sided abdominal pain and hematochezia. He did not report any nausea, vomiting, hematemesis, constipation, diarrhea, weight loss, change in appetite, or fever.

CBC and BMP were collected prior to procedures. CBC revealed decreased hemoglobin and hematocrit of 12.8 and 38.2, respectively. Glucose was slightly elevated at 109. The other lab value was unremarkable.

An esophagogastroduodenoscopy and a colonoscopy were performed which revealed invasive cancer in the cecum and sigmoid colon. CT of the chest, abdomen and pelvis wo/w contrast revealed no signs of metastatic disease. An exploratory laparotomy was performed, and visualization of adenocarcinoma located in the cecum, rectosigmoid lesions, and metastatic disease throughout the liver were seen. Biopsies were taken and a total abdominal colectomy with proximal and mid proctectomy and ileorectal anastomosis with diverting loop ileostomy was performed.

The pathology report of the liver biopsy revealed a high-grade (large cell) neuroendocrine carcinoma. Second specimen of cecum and proximal ascending colon revealed a 3.5 x 3.0 x 1.3 cm high-grade (large cell) neuroendocrine carcinoma with the tumor invading through the muscularis propria into the sub serosal adipose tissue. Three regional lymph nodes revealed metastatic high grade neuroendocrine carcinoma and three other regional lymph nodes revealed metastatic adenocarcinoma with lymph-vascular and perineural invasion. Terminal ileum and proximal/distal anastomosis donuts specimens revealed no malignancies.

Immunohistochemical stains of the deepest area of invasion revealed CDX2, CD56, and synaptophysin. Immunohistochemical staining of the rectal mass towards the proximal margin revealed marked reduction in MSH6 expression which could be a result of DNA mismatch repair deficiency and lynch syndrome should be considered in patients with this expression.

Overall, the total colectomy specimen shows two distinct primary tumors which are high-grade (large cell) neuroendocrine carcinoma of the cecum/proximal ascending colon and invasive adenocarcinoma (moderately differentiated involving the rectum).

Postoperatively, the patient was stable and plans for a Port-A-Cath and adjuvant chemotherapy were made. Laboratory values postoperatively revealed WBC: 6.8, Hgb 12.8, Platelet count: 237, Na: 139, K: 3.7, BUN: 14, Creatinine 1.1, and Calcium 9.4 which are within normal limits.

Discussion

Colorectal cancer is one of the most common cancers in the United States. However, synchronous adenocarcinoma of the rectum and large cell neuroendocrine carcinoma of cecum/ascending colon is a rare occurrence. This case is an atypical presentation of synchronous carcinoma of the gastrointestinal tract has limited representation within the

literature. Synchronous multiple primary malignant tumors typically occur in male patients older than 50 years of age. Synchronous cancers have an incidence rate of around 0.7% to 11.7% **[7].** Synchronous carcinomas typically occur in proximal portions of the gastrointestinal tract. Out of multiple primary malignant tumors, the current prevalence of synchronous versus metachronous cancers ranges from 30-55%**[7].**

Double malignancies of the gastrointestinal tract are rare, and typically occur in patients with genetically related cancer syndromes. Case series revealed 17 case reports of synchronous large cell neuroendocrine tumor and colon carcinomas with most of the patients being female **[5].** The median age of these case reports were around 64 years. This series states that large cell neuroendocrine tumors in the rectum are more common than large cell neuroendocrine tumors located in the ileum. Out of the 17 cases, the most common location of adenocarcinoma was the sigmoid colon. Treatment options for these cases ranged from no treatment to subtotal colectomy and snare resection with chemotherapy.

Notable features seen in our patient that coincide with other limited case reports are the vague symptoms of abdominal pain and hematochezia without any other signs in the history and physical exam. The lack of significant family history, social history, and medical history did not pinpoint as to why this patient could have developed a gastrointestinal malignancy or the diagnosis of synchronous malignancies. In all, synchronous metastatic malignancies of the gastrointestinal tract are extremely rare in an individual with noncontributory history.

Conclusion

This adult patient presenting with synchronous gastrointestinal carcinoma with vague symptoms may have led to a delayed diagnosis identification and sequential treatment. The incidence of synchronous carcinoma with this presentation is extremely rare. Our case provides a unique presentation of synchronous tumors affecting various locations in the gastrointestinal tract, severity of malignancy, and vagueness of patient presentation which helps contribute to the limited literature of synchronous gastrointestinal carcinomas and promotes screening for gastrointestinal malignancies.

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