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# Sudden Abdominal Pain: A Unique Case of Metastatic Mixed Neuroendocrine and Adenocarcinoma of the Colon

**Swetha Paduri[1], MD; Nehal Patel[1], MD; Nitish S Nandu[1], MD; Capt. Paul Roach[1], MD; Mukta Pant-Purohit[1], MD; Peter Morawiecki[1], MD and Aravind Kuchkuntla[1*], MD**

Department of Internal Medicine, Rosalind Franklin University of Medicine

***Corresponding author**
Aravind Reddy, Kuchkuntla, PGY 2, Rosalind Franklin University of Medicine 3333 Green Bay Road, North Chicago, USA. E-mail: Aravindreddy.rkuchkuntla@rosalindfranklin.edu

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## Case Description

A healthy 48-year-old male with no significant or pertinent medical history presented with complaints of sudden, progressively worsening severe right lower quadrant (RLQ) pain over the course of two days. He denied any other constitutional symptoms. A palpable mass was noted in the RLQ. Laboratory findings were consistent for anemia and CEA and CA 19-9 markers were normal. CT of the abdomen revealed a heterogeneous exophytic mass in the RLQ measuring 9.8 cm x 7.9 cm x 12.1 cm, colonic intussusception, and liver metastases.

An explorative laparotomy with an eventual right hemicolectomy demonstrated an extremely large and friable mesenteric mass with neovascularization within the mesentery and a large intraluminal mass within the ascending colon. The mass was situated immediately adjacent to the terminal ileum and the cecum. Additionally, there were multiple palpable metastases within the liver. CT scan of the neck and thorax showed lytic lesion within the T4 vertebral body and scattered pulmonary nodules which were indeterminate. Examination of the gross anatomical specimens revealed a right colectomy specimen with two discrete masses: a large, exophytic mucosal mass and a second large mesenteric mass. The two masses exhibited distinctly different histologic characteristics.

The mucosal mass was a gland forming adenocarcinoma associated with an adenoma. The mesenteric mass displayed a sheet of mitotically active malignant cells with high nuclear to cytoplasmic ratios that express neuroendocrine markers, consistent with a high-grade neuroendocrine carcinoma. The findings were consistent with well differentiated adenocarcinoma and poorly differentiated small cell neuroendocrine carcinoma with stains positive for CD56 and synaptophysin. His eventual diagnosis was stage IV adenocarcinoma (T1N1Mx) and neuroendocrine (T2N2aMx). (Figures 1,2,3,4 and 5)

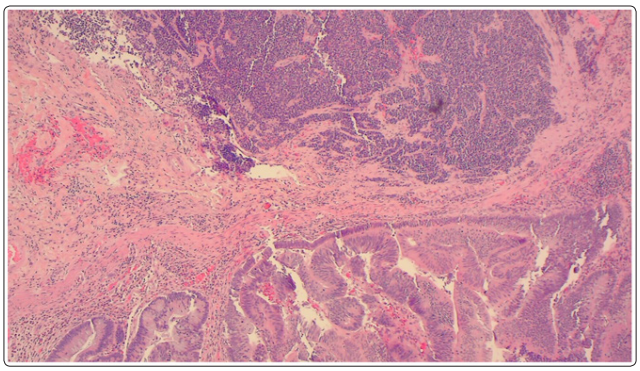

**Figure 1:** Small cell neuroendocrine carcinoma (top) adjacent to adenoma (bottom) (H&E, X1000)

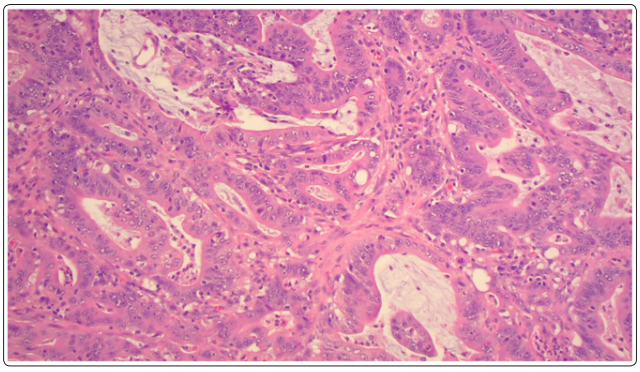

**Figure 2:** Adenocarcinoma component forming irregular glands lined by pleomorphic cells with large nuclei with prominent nucleoli. (H&E, X400)

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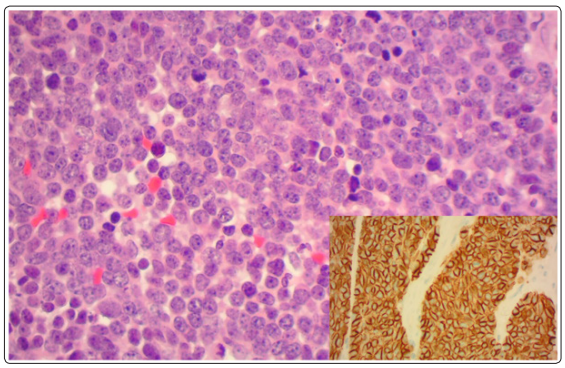

**Figure 3:** Small cell neuroendocrine carcinoma (H&E, X400). Insert; CD56 immunoreactivity in small cell carcinoma

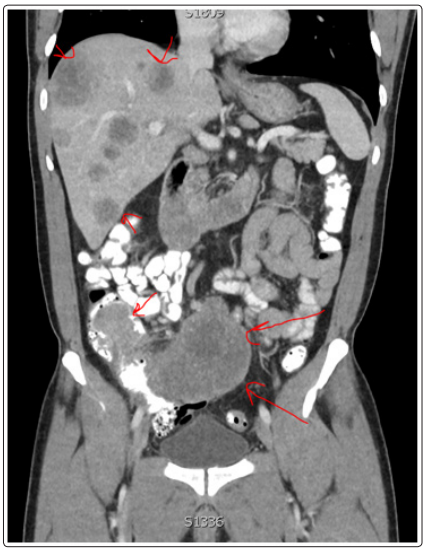

**Figure 4:** CT showing large exophytic mass in ascending colon and multiple liver metastasis

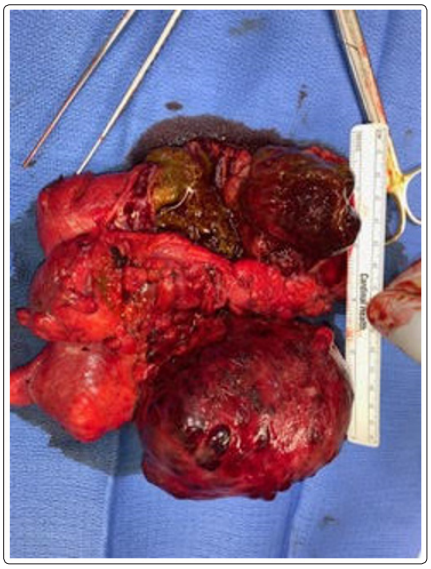

**Figure 5:** Right colectomy specimen with two discrete masses

He was started on palliative chemotherapy with cisplatin and etoposide. A follow up CT scan was done after 6 cycles of chemoimmunotherapy, which showed a mixed response. The patient was then transitioned to a single agent chemotherapy, atezolizumab. Two weeks into this course, he was admitted for intractable abdominal pain with workup showing advancement of metastatic disease.

His course was further complicated when was diagnosed with Coronavirus Disease-2019 (COVID19) and was found to have a thrombus in his port-a-cath. Treatment was initiated with therapeutic anticoagulation and managed for COVID19. After the resolution of the COVID19 infection, he developed fulminant liver failure and additional treatment with mFOLFOX was forgone. Unfortunately, despite aggressive interventions the patient succumbed to the rapid progression of the disease and was deceased within six months of his initial diagnosis.

## Discussion

Colorectal cancer (CRC) is the second leading cancer. Adenocarcinoma accounts for upto 95% of CRCs while MiNENs only accounts for only 1-2% of all colorectal malignancies [1]. Impaired gene expression in the stem cells is believed to be responsible for the simultaneous development of gastrointestinal NET with adenocarcinoma. However, there is no consensus regarding the pathophysiology leading to the development of MiNENs [2]. MiNENs are classified into high, intermediate and low-grade neoplasms [2]. The prognosis of these tumors remains unclear due to the rarity of lesions, heterogeneity of its components and the lack of established well-defined treatment regimens [2]. Localized lesions without distant metastasis are eliminated by surgical resection in combination with perioperative chemotherapy [2]. Systemic chemotherapy with etoposide in combination with cisplatin or carboplatin is the first line of therapy used to manage cases with distant metastasis [2]. Regrettably, most presentations of MiNENs encountered in clinical practice are high grade tumors with poorly differentiated neuroendocrine components and carry a poor prognosis [3].

In the past decade, there has been a great deal of information collected about MiNENs but the core understanding of these tumors continues to be a mystery. Advancement in research is necessary to understand these neoplasms at both a molecular and genetic level, so that targeted therapies can be created. The keystone to appropriate management is accurate histological identification and methodical clinical vigilance [4].

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