Triple Synchronous Neoplasm in the Cecum of an Older Adult: A Case Report Highlighting Diagnostic Challenges and Individualized Screening

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Introduction

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related death in the United States with an incidence of approximately 37 per 100,000 annually. Colonic neuroendocrine tumors (NETs) and low-grade appendiceal mucinous neoplasms (LAMNs) are far less common, with incidence of approximately 1 per 100,000 AND 1-3 per million, respectively. The simultaneous discovery of a colonic adenocarcinoma, a metastatic-well0differentiated NET of unknown primary origin, and a synchronous LAMN within a single surgical specimen is exceedingly unusual, raising questions about diagnostic strategies, screening guidelines, and colonoscopy quality in older adults.

Many colorectal cancers—estimated 60%-85%-- are diagnosed after the onset of symptoms, rather than through screening. Symptomatic presentation typically reflects advanced disease, as tumor growth into the lumen or adjacent structures produces clinical manifestations. Common presenting signs and symptoms include hematochezia or melena, abdominal pain, unexplained iron-deficiency anemia, and changes in bowel habits. Less common symptoms such as abdominal distention, nausea, and vomiting may indicate obstruction. Iron-deficiency anemia from occult blood loss is particularly common in right-sided colorectal cancers, which also more likely to be missed by colonoscopy with a repeated miss ratees of 27-40% in the proximal colon.

Case Description

An 82-year-old male Vietnam War veteran with a history of congestive heart failure (EF 30%), COPD, atrial fibrillation, hyperlipidemia, hypertension, prostate cancer, abdominal aortic aneurysm (AAA) status post repair and Agent Orange exposure presented with a two-year history of unexplained anemia, intermittent abdominal pain with vomiting, and a 30-pound unintentional weight loss. Despite multiple emergency department visits and hospitalizations for symptomatic anemia requiring transfusions, the source of bleeding remained unidentified, as workups were directed toward concurrent obstructive uropathy, bilateral hydronephrosis and recurrent urinary tract infections. A colonoscopy performed six years earlier had revealed only hemorrhoids.

On presentation, the patient was hemodynamically significant with a blood pressure of 90/35 mmHg. Laboratory evaluation revealed a hemoglobin of 6.3 g/dL with microcytic indices (MCV 79fl, MCH 23.2 pg), hypoalbuminemia (2.3 g/dL), elevated BUN (56 mg/dL) and creatinine (2.5 mg/dL), elevated NT-proBNP (4,297 pg/mL,) and a positive fecal immunohistochemical test (FIT). CT abdomen and pelvis without contrast demonstrated bilateral hydronephrosis, non-obstructing renal calculi and colonic diverticulosis, but no colonic wall thickening, peri colonic inflammatory changes or lymphadenopathy. The appendix was described as unremarkable. A subsequent CT abdomen and pelvis with contrast similarly failed to identify any colonic mass, enlarged lymph nodes or appendiceal abnormality.

EGD and colonoscopy revealed a large exophytic mass in the cecum encompassing approximately 50% of the lumen, two rectal hyperplastic polyps, internal hemorrhoids, diverticulosis and possible Barrett's esophagus. Biopsy confirmed invasive moderately differentiated adenocarcinoma. Immunohistochemistry for mismatch repair proteins (MLH1, PMMS2, MSH2, MSH6) demonstrated retained nuclear staining, consistent with microsatellite stable (MSS) phenotype.

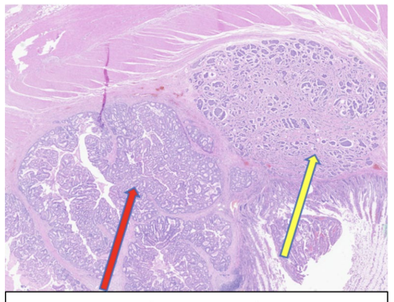
Robot assisted right hemicolectomy was performed. Gross examination revealed a 5.5 cm exophytic mass filling the cecum and extending to the ileocecal valve, with a 4.5 cm appendix containing a dilated lumen filled with mucoid material. Final pathology demonstrated three synchronous neoplasms: (1) a 5.5 cm moderately differentiated colonic adenocarcinoma invading the visceral peritoneum (pT4aN0), with negative lymphovascular and perineural invasion, all margins negative and 0 of 13 lymph nodes positive for carcinoma; (2) a well differentiated neuroendocrine tumor (NET G1), positive for synaptophysin and CD56 with a Ki-67 index 3% (Figures 1a, 1b), identified adjacent to the primary adenocarcinoma and within a single lymph node metastasis—reported as metastatic NET of unknown primary origin; and (3) a 4.5 cm low-grade appendiceal mucinous neoplasm (LAMN; pTisN0) (Figure 2) with negative margins and no lymphovascular invasion. A mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) was considered but deemed unlikely given the low-grade nature of the NET component. The patient recovered well post operatively.

Discussion

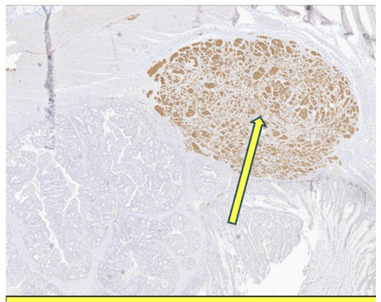
This case is remarkable for the coexistence of three histologically distinct neoplasms discovered in a single surgical specimen. The pathologic finding of a well-differentiated NET adjacent to the colonic adenocarcinoma and within a lymph node raises the question of whether this represents a collision tumor—two independent primary neoplasms arising in the same location—or a metastatic NET from an occult primary deposited within the colonic mass. The pathologist favored the latter interpretation, reporting the NET as "metastatic neuroendocrine tumor of unknown origin" with no definitive primary identified. Clinical and radiologic correlation was recommended to determine the likely primary source. This distinction has important implications for staging, surveillance, and further workup, including considerations of somatostatin receptor scintigraphy to identify a potential occult NET primary.

The MSS phenotype on immunohistochemistry argues against Lynch syndrome as a unifying genetic explanation for the multiple synchronous neoplasms. While Agent Orange exposure is a recognized risk factor for certain malignancies, current evidence does not support a direct association with colorectal, appendiceal or neuroendocrine tumors.

This case powerfully illustrates the diagnostic limitation of cross-sectional imaging in patients with surgically altered anatomy. Two CT scans-one without contrast and one with contrast—performed within weeks of surgery both failed to identify a 5/5 cm cecal mass and a 4/5 cm appendiceal neoplasm. The CT with contrast explicitly described the appendix as "unremarkable" and noted "no abnormally dilated loops of larger or small bowel." dense adhesions and distorted retroperitoneal anatomy from prior AAA repair likely obscured these findings. Intraoperatively, the tumor was found deeply embedded in the retroperitoneum surrounded by adhesions. The colonoscopy performed six years earlier also failed to detect what ultimately became a large cecal mass, raising concerns about examination quality yin the setting of adhesions and distorted anatomy. Despite these limitations, colonoscopy ultimately played the pivotal diagnostic role.



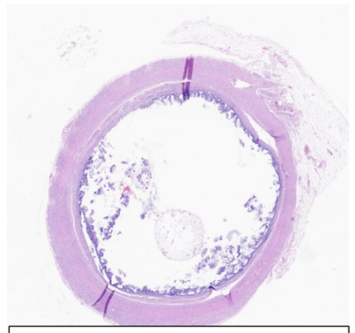
1a. H & E of Invasive adenocarcinoma & adjacent well differentiated neuroendocrine tumor



1b. Synaptophysin staining of Neuroendocrine tumor adjacent to adenocarcinoma

Conclusion

Triple synchronous tumors of the gastrointestinal tract are exceedingly rare, and a literature review failed to identify a reported case of synchronous colonic adenocarcinoma, colonic NET and LAMN within a single specimen. This case underscores the critical role of colonoscopy in patients with altered surgical anatomy where cross-sectional imaging may be unreliable. It reinforces the importance of individualized patient-centered screening decisions in older adults and highlights that age-based screening cessation must not preclude diagnostic evaluation in symptomatic patients. The discovery of a metastatic NET of unknown primary within the surgical specimen necessitates further workup to identify a potential occult primary site. Reporting of such cases further expands the knowledge and understanding of synchronous gastrointestinal neoplasms.



2. Low-Grade Appendiceal Mucinous

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