Composite carcinoma of the colon: A case report with literature review

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Citation

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Abstract

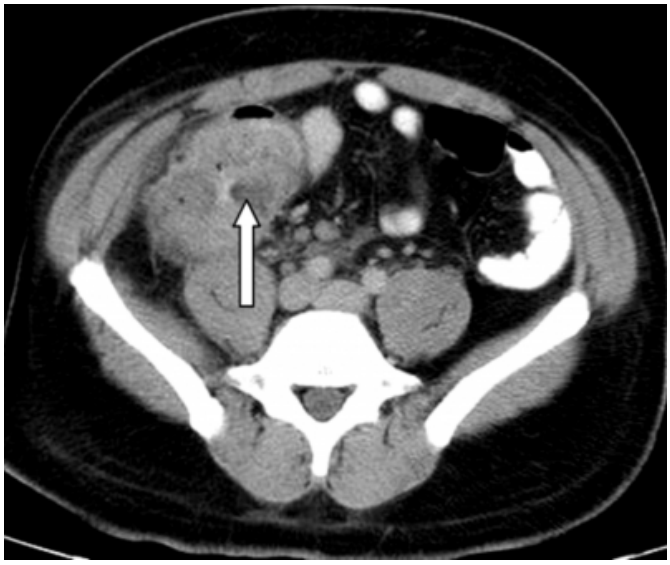
Mixed composition carcinomas of the large intestine are rare. The aggressiveness of these malignant tumors depends on the components of the tumor. We present the case of a middle-aged man who developed an acute surgical abdomen due to perforation of a mixed composition carcinoma with a dominant small cell component. To the best of our knowledge this is the first case report of a composite cecal carcinoma with lymph node metastases from both the small cell and adenocarcinoma components.

CASE HISTORY

A 47-year-old gentleman was admitted with severe crampy right lower quadrant pain, nausea & fever of one-day duration. He had an episode of severe watery diarrhea approximately 12 hours after the onset of abdominal pain. On examination all the vital signs were normal except for pyrexia (38^{O} c) and tachycardia. Local examination revealed the classical clinical findings of acute appendicitis with severe local peritonitis. His hematological and biochemical parameters on admission were as follows: hemoglobin 11.8g/dl, white cell count 18.5×10^{9} /l, and c-reactive protein 256mg/l. All other investigations were normal. He was scheduled for an emergency appendectomy. When examined under anesthesia, there was a firm irregular 10x10 cm intra abdominal palpable lump in the right iliac fossa. The surgery was cancelled and a conservative approach was adopted. Subsequent CT of the abdomen revealed (Figure 1) a mass in the cecal area extending to the pelvis, with streaking of the surrounding fat.

Figure 1

Figure 1: CT-scan of the cecal mass.



As he improved on conservative management, he was discharged on the seventh day of admission with a week course of antibiotics. After 4 weeks, he had a barium enema and a repeat CT scan of the abdomen. The barium enema demonstrated a large irregular filling defect occupying the cecal pole giving the impression of a soft tissue mass.

Figure 2

Figure 2: Barium enema, showing a large irregular cecal defect filling the cecal pole.

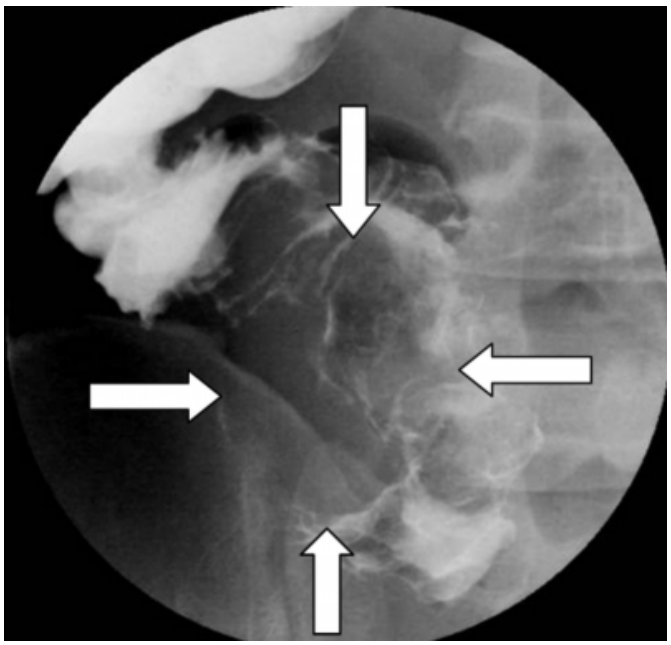
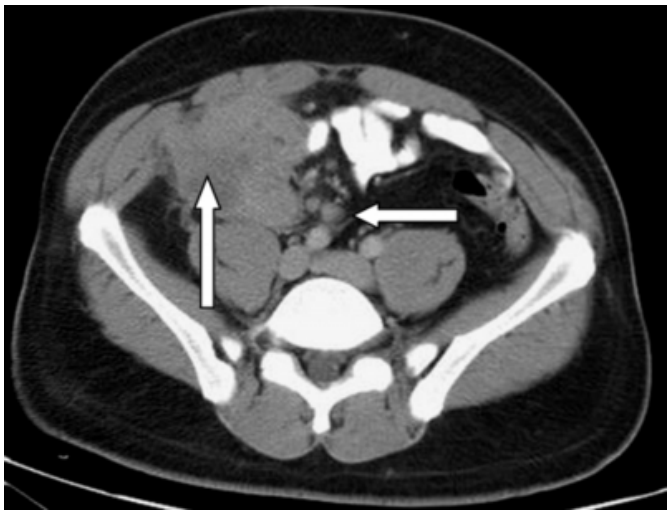


Figure 3

Figure 3: CT scan of the abdomen at showed further enlargement of the cecal pole mass with more streaking of the surrounding fat. Multiple regional lymph nodes were also noted.

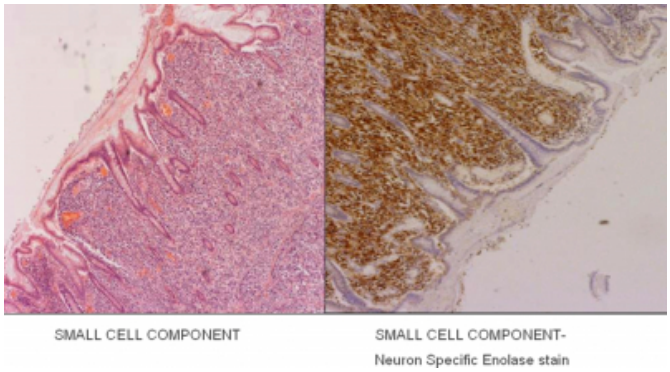


A colonoscopy was arranged, but prior to this, the patient presented with another episode of acute abdomen. He underwent an urgent right hemicolectomy. His baseline CEA level before surgery was 16 mcg/L. Intraoperatively there was a perforated cecal mass, which was seen adherent to the posterior abdominal wall. The appendix was normal and was not involved in the mass. The presence of prominent mesenteric adenopathy was also noted. There was no evidence of any hepatic involvement.

Histopathological examination of the specimen showed a variegated cream colored tumor in the right colon measuring 35mm x75mm x70mm. It had perforated through the serosa over an area of 35x25 mm. Sections of the tumor showed a large component composed of islands of epithelial cells with granular nuclear chromatin and scant to moderate amounts of cytoplasm with extensive necrosis. The morphology was that of a small cell (neuroendocrine) carcinoma (Figure 4). Adjacent to this, there was an area of moderately differentiated adenocarcinoma (Figure 5).

Figure 4

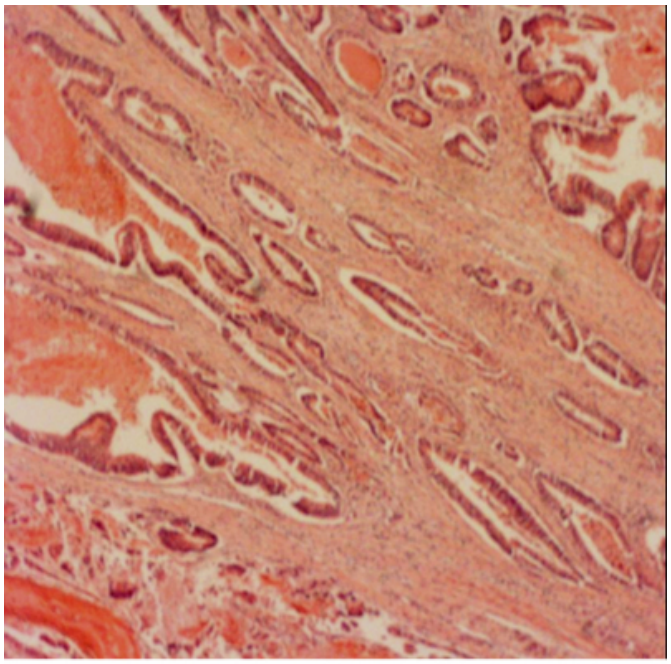
Figure 4: Histologic picture



The small cell component extended to the serosal surface (pT4) and infiltrated between the crypts in the overlying mucosa. There was lymphovascular invasion without extramural vascular invasion. Immunostaining showed that the small cell component was strongly positive for Neuron Specific Enolase stain.

Figure 5

Figure 5: Histologic picture with adenocarcinoma



The adenocarcinomatous component was positive for CEA and CK20. Lymphocyte common antigen, chromogranin, and TTF-1 were negative. Eight of twenty-six lymph nodes contained metastatic deposits (8/26). One of the metastases has an adenocarcinomatous appearance and the others were from the small cell component of the tumor.

The consensus of the multidisciplinary team was that it represented a mixed composition carcinoma of the colon with a dominant small cell (neuroendocrine) element and focal adenocarcinoma, of stage III C, Dukes' C1. His staging CT scan of the chest was normal. It was decided to start him on adjuvant chemotherapy based on Oxaliplatin, 5-Flourouracil and Levamisole for 12 cycles, each cycle lasting for 2 weeks. He tolerated adjuvant chemotherapy well with no evidence of disease recurrence within 6 months. His CEA level was less than 1 during this period. He presented with rapid and extensive tumor recurrence in abdomen, including the bladder, within a year and did not respond to further chemotherapy.

DISCUSSION

Small cell carcinomas of the large intestine comprise less than 1% of colorectal cancers. Extrapulmonary small cell carcinoma is a distinct entity that can occur in many sites and it is similar to small-cell lung cancer in pathology and clinical behaviour [1]. It is an aggressive malignant tumor characterized by rapid local progression and early metastases [2]. Typically the duration of symptoms is short (running only a few weeks) and they include crampy abdominal pain, malaise, weight loss, and alteration of bowel habits [3]. On CT, a colonic small cell tumor appears as a poorly enhancing heterogenous mass often with extensive regional lymph node metastases. Barium enema may show a segmental annular narrowing with thickened irregular interhaustral folds [4].It may appear as a bulky mass projecting into the bowel lumen or perforating the bowel wall (as in this case). It may be picked up incidentally as a tiny focus in an adenomatous polyp.

Topographically, it has a predilection for the right side of the colon and most commonly the cecum. The frequency of hepatic metastases at the time of surgery is much higher (71%) compared to that of poorly differentiated carcinoma (7%) or non–small cell undifferentiated carcinomas of large bowel (50%) [5,6,7,8,9]. The gross features of small cell carcinoma of colon do not distinguish it from adenocarcinoma. By light microscopic examination, small cell carcinoma of colon resembles small cell carcinoma of lung. Numerous mitoses, apoptotic cells, foci of necrosis, and vascular invasion are usually obvious. The characteristic pattern of encrustation of the nuclear material around blood vessels (Azzopardi effect) has been reported at the site of metastases in 2 cases [10]. These tumors usually show evidence of neuroendocrine differentiation either by electron microscopy or by immunohistochemistry. Positivity for neuron-specific enolase, chromogranin, synaptophysin and cytokeratin are the most common finding. The highest rates of positivity are reported with neuron-specific enolase (87%) and synaptophysin (56%) [7]. The features of the metastatic lesions in the liver or the lymph nodes are similar to those of the primary lesion, and the morphologic and immunohistochemical characteristics can be readily identified. Differentiation from carcinoid may pose diagnostic difficulty. Typically, carcinoids show a characteristic growth pattern with less than 1 mitosis per high-power field, and lack of necrosis. Imaging appearance may be very similar.

Small cell carcinomas are believed to arise from uncommitted stem cells or the reserve cells of colonic crypts, probably in pre existing adenomas. These are believed to be capable of differentiating into a number of types of neoplastic cells, including neuroendocrine tumors triggered by genetic alteration from an unidentified stimulus. A few cases of primary small cell undifferentiated carcinoma of the

rectum associated with ulcerative colitis have been reported in literature [11]. Awareness by the pathologist that the cecum may be a potential site of small cell carcinoma may help to prevent misdiagnosis as poorly differentiated adenocarcinoma. This is crucial because extrapulmonary small cell carcinomas usually have a significantly worse prognosis [14]

Due to the extremely aggressive behaviour of colonic small cell carcinoma with early metastatic spread, CT scans of the chest-abdomen and radionuclide bone scan should be performed. The importance of this tumor is due to its great aggressivity and its great tendency to produce early hematogenous and lymph node metastases. Because of these facts, treatment must include, beside surgical resection, an aggressive systemic protocol [15]. In the presence of metastatic disease, multiagent chemotherapy with cisplatin should be instituted [16]. Despite a variety of regimens, they respond poorly to treatment.

CONCLUSION

Appendicular mass that fails to resolve on conservative management should be thoroughly investigated. It is wiser to do serial follow up scans on suspicious appendicular mass. Even though rare, malignant tumors of the cecum can mimic acute appendicitis. Perforated malignant tumors carry a poor prognosis. It is ideal to rescan earlier, particularly if there is high index of suspicion in a young patient. Cecum is a common site for extra pulmonary small cell carcinoma, which carry a poor prognosis. Awareness by the pathologist that the caecum may be a potential site of small cell carcinoma may help to prevent misdiagnosis as poorly differentiated adenocarcinoma.

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