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Case Report

Metastatic Mayhem

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ABSTRACT
Signet-ring cell carcinoma (SRCC) is a rare type of adenocarcinoma characterised by cancer cells that contain and secrete mucin. We present a unique case of SRCC with the primary lesion in ascending colon and numerous (>100) tumour deposits over the entire length of the gastrointestinal tract along with multiple metastasis in the peritoneum, liver, both lobes of lungs and cervical, mediastinal and abdominal metastatic lymphadenopathy. Primary presentation with such extensive metastatic disease has rarely been described in literature.

Key words: Signet-ring cell carcinoma, Synchronous gastrointestinal lesions, Metastatic disease.

CASE REPORT

A 65 year old retired businessman presented to the gastroenterology department with one month history of pain in abdomen and loss of appetite. Abdominal pain was located in the right iliac fossa and hypogastric region, intermittent and dull in character, aggravated with food intake and affected his quality of life. His appetite had halved over one month and he had lost 7 kg during the same period. He complained of easy fatigability, generalized weakness, breathlessness and malaise. He also gave history of recent onset constipation, nausea and vague abdominal bloat.

He consumed a mixed diet and had no addictions or drug allergies. He had no major medical and surgical co-morbidities in the past. His family history was non-contributory.

On examination, he had pallor and mild right iliac fossa tenderness. However, there was no guarding or rigidity. Virchow's node was palpable, raising a strong suspicion of underlying malignancy. There was no organomegaly on palpation. The cardiovascular, respiratory and central nervous systems were normal on examination.

Laboratory investigations revealed hemoglobin of 8.9 g/dl with normal total leucocyte and platelet count. He had microcytic and hypochromic anemia, Erythrocyte Sedimentation Rate (ESR) was 110 mm at the end of 1h. He had low serum iron and transferrin saturation level and a normal total iron binding capacity (TIBC). Liver function tests revealed hypoalbuminemia (2.9 g/dl); elevated transaminases (SGOT – 63; SGPT – 1,260 IU/ml) and mildly elevated serum bilirubin (1.7 g/dl). Renal function tests and serum lactate dehydrogenase (LDH) levels were normal. Stool for occult blood was strongly positive.

For further evaluation of anemia with possible underlying gastrointestinal malignancy, upper and lower gastrointestinal endoscopies were performed. Gastroscopy revealed numerous nodules (<5mm) with superficial ulcerations in the fundus and body of the stomach and first part of duodenum. Colonoscopy revealed an ulcero-proliferative polypoid fungating growth in the cecum along with multiple tiny sessile polyps throughout the colon including the rectum Figures 1,2. Biopsy from the stomach, duodenal nodules and colonic lesions was diagnostic of moderately differentiated signet ring cell carcinoma in all specimens. Rectal biopsy revealed a tubulovillous adenoma with high grade dysplasia.

Contrast enhanced computerized tomogram (CECT) of neck, chest, abdomen and pelvis showed a soft tissue mass involving the ascending colon with pericolic fat stranding and nodularity. Multiple hepatic metastatic lesions were observed. CT also revealed left supraclavicular, mediastinal and abdominal lymphadenopathy with diffuse nodular peritoneal deposits. There was mild ascites and right sided pleural effusion. F-18 Fluorodeoxyglucose (FDG) labeled whole body Positron Emission Tomogram (PET) showed a heterogeneously enhancing soft tissue mass in the ascending colon (Standardized Uptake Value (SUV) max 18.3) representing primary neoplastic etiology with mild ascites and diffuse hypermetabolic omental thickening. Hypermetabolic bilobar hepatic and bilateral lung lesions were observed along with hypermetabolic left supraclavicular (1.7 x 1.0, SUV max 10.3), mediastinal (SUV max 20.3) and abdominal lymph nodes (metastatic) Figures 3,4. His CT scan of the brain was normal.

In view of extensive disease with metastasis he was referred for palliative chemotherapy. However, he succumbed to his illness within a month.

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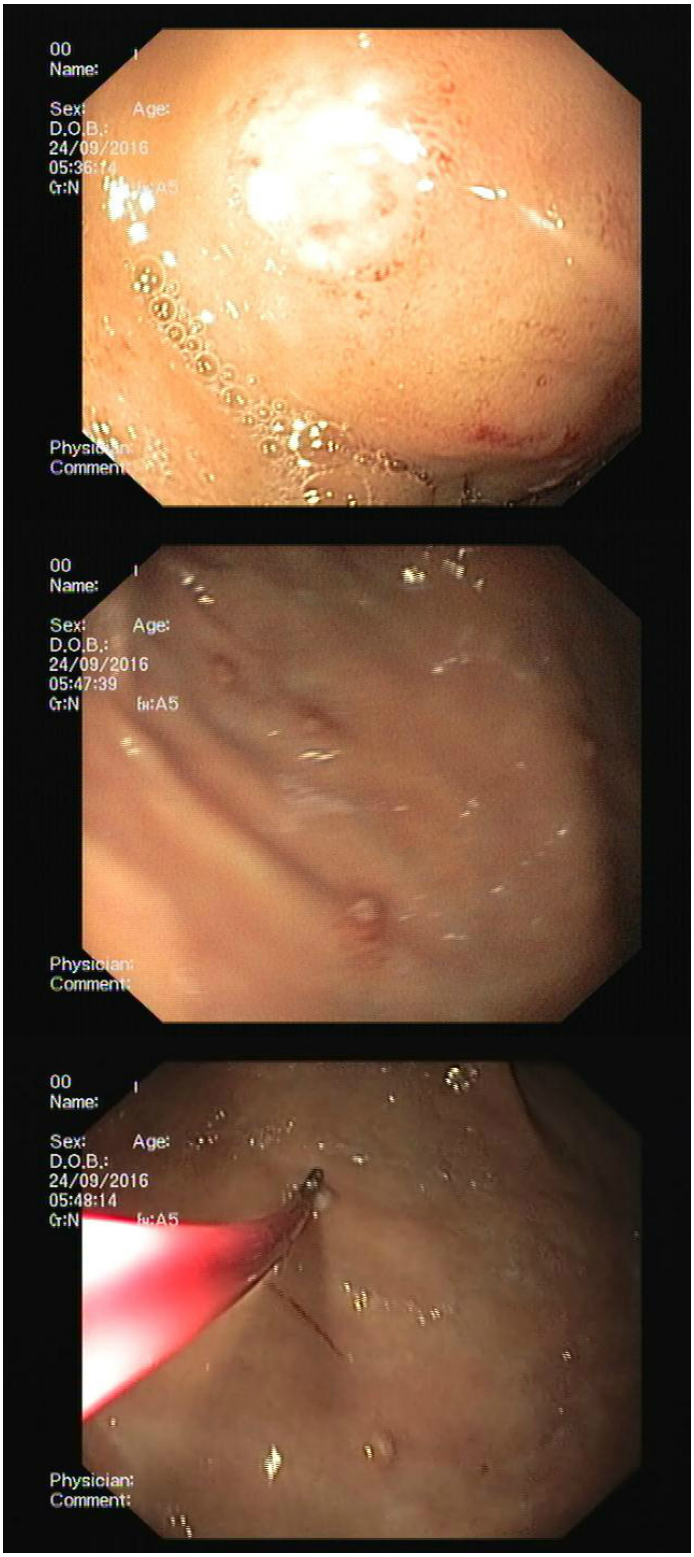

Figure 1: Upper Gastrointestinal Endoscopy: Multiple nodules in the duodenum (top) and stomach (middle and bottom).

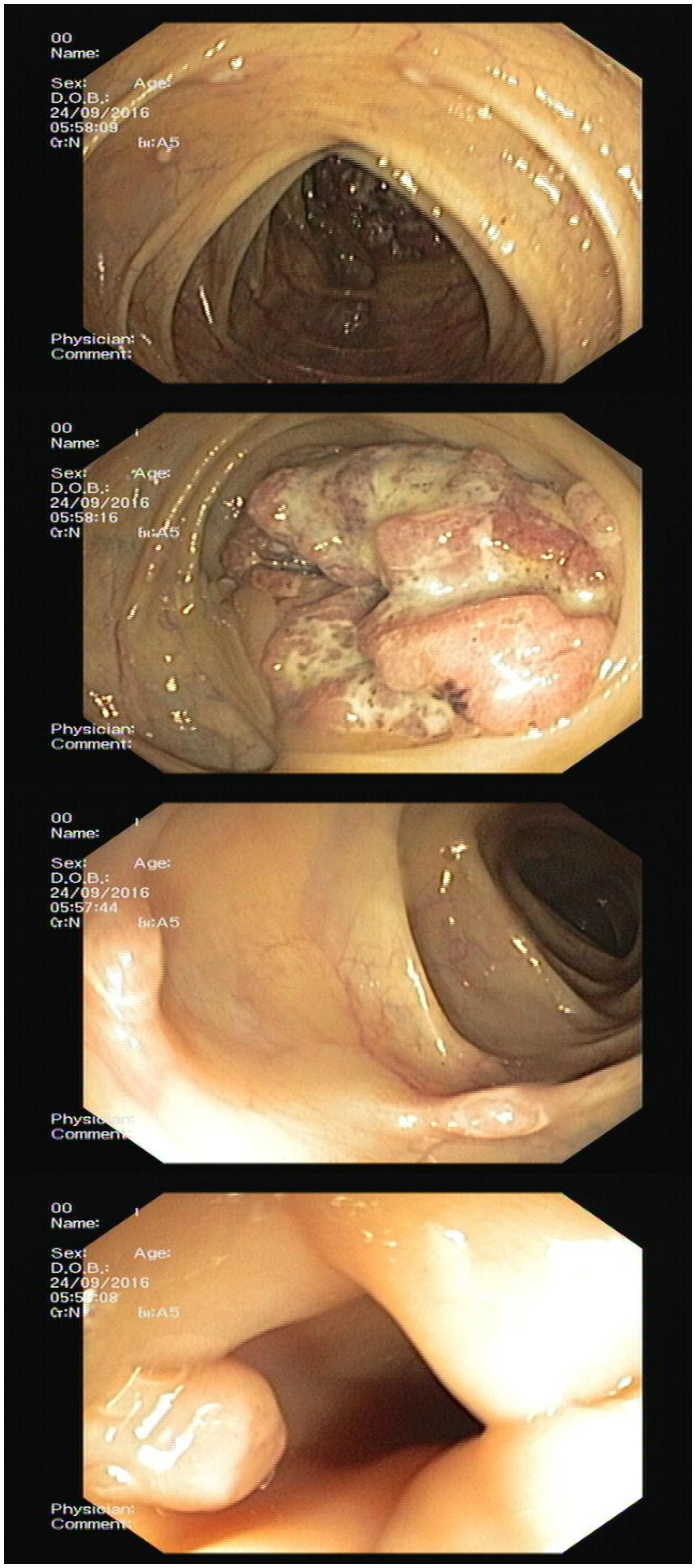

Figure 2: Lower Gastrointestinal Endoscopy: A large fungating ulcero-proliferative growth in the ascending colon just above cecum along with multiple nodules throughout the colon. Large rectal polyp (bottom).

DISCUSSION

Signet ring cell carcinoma (SRCC) of the colon and rectum is a rare variant of colorectal adenocarcinoma. The incidence is reported to range between 0.1% and 2.6%.[1,2] SRCC is more common in younger age group and female patients. SRCC commonly presents with advanced lesions. The diagnosis of colorectal SRCC is based on the histological examination with exclusion of a gastric primary. These tumors have an aggressive clinical course and a poor prognosis.[3] There is high incidence of peritoneal metastases and relatively low incidence of hepatic metastases, a characteristic feature

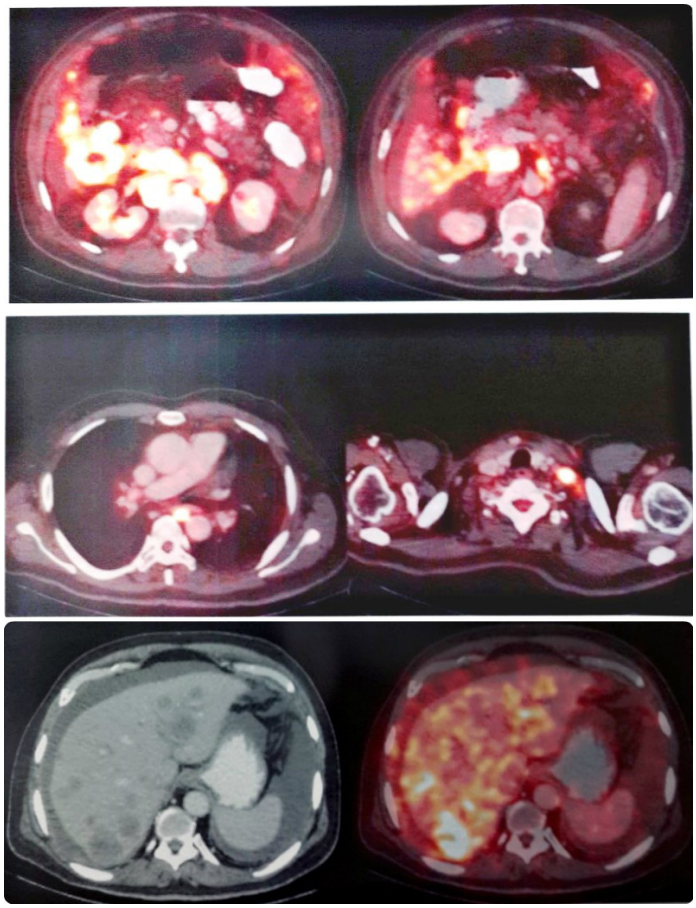

Figure 3: PET scan images showing extensive hypermetabolic lesions in chest, abdomen and liver.

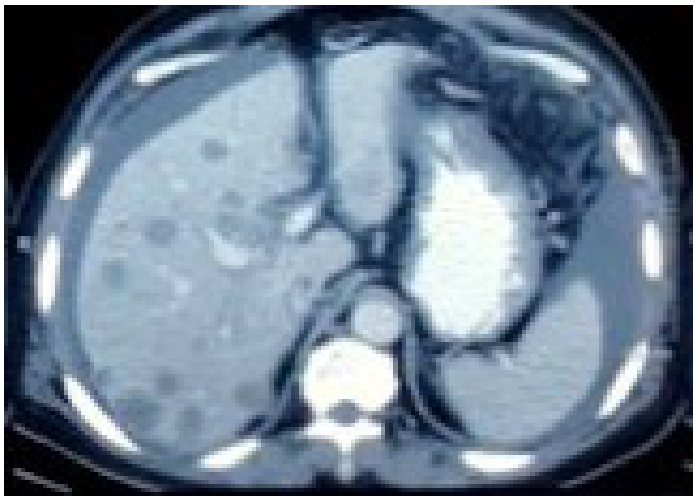

Figure 4: Contrast enhanced CT scan of abdomen showing gastric wall thickening and hepatic metastasis.

distinguishing colorectal SRCC from non-signet colorectal carcinoma. SRCC have higher rates of metastasis than conventional colorectal adenocarcinomas. They metastasize through lymphatic and haematogenous routes.[4] Common sites of metastasis include liver, uterus, prostate, lung and skin. Brain, kidney, adrenal gland, ovary, heart, omentum, bone, pleura, pancreas and spleen are involved uncommonly. SRCC patients frequently have metastasis at multiple sites (>70%).[5] However, synchronous tumour dissemination across the gastrointestinal tract is rare.

According to Secco *et al*, the 5-year survival rate of primary colorectal SRCC was 0% (median 15 months) and disease recurrence was 100%.[6] It is important to identify disseminated peritoneal disease at the time of the initial diagnosis as these patients are unlikely to benefit from surgery. The histological appearance of the tumor is characterized by cells with abundant intracytoplasmic mucin which pushes the nucleus to the periphery. The tumor cells may be arranged individually or in loose clusters, and may spread diffusely through the bowel wall. Mucin lakes containing small, primitive and abortive gland structures may be present.[7] The question of a primary colonic malignancy or metastatic gastric adenocarcinoma frequently arises when signet ring cell carcinoma is seen on colonoscopic biopsy.

Immunostaining profiles for CK7 and CK20 have been used to characterize and differentiate signet ring cell carcinomas of breast, stomach and colon.[8] CK20 is a low molecular weight cytokeratin that is normally expressed in the gastrointestinal epithelium, urothelium and in Merkel's cells. CK7 is expressed by tumors of the lung, ovary, endometrium and breast, but not of the lower gastrointestinal tract. It has been suggested that when a signet ring cell adenocarcinoma is encountered on colonic biopsy, the diagnosis of a colon primary is supported by the presence of CK7 (-)/CK20 (+) staining pattern in the neoplastic cells, while gastric primary is diagnosed if the cells have a CK7 (+)/CK20 (-) staining pattern.

The present case illustrates the aggressive nature of signet ring cell carcinoma, with extensive dissemination of tumor in gastrointestinal tract and at extraintestinal sites. Such widespread dissemination carries grave prognosis.

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