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Case Report

Signet-ring cell carcinoma of the caecum: A case report ☆

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ABSTRACT

Colorectal cancer (CRC) ranks as the third most prevalent cancer globally, with adenocarcinomas being the most frequent type. Signet ring cell carcinoma (SRCC) is a very rare subtype of adenocarcinoma, it commonly occurs in the stomach. However, other digestive localizations are possible including the colon, rectum, and gallbladder. Herein, we report a rare case of a metastatic caecal SRCC in a young male patient, presented to our department for abdominal diffuse pain and distention evolving for 3 months, associated with remarkable weight loss and asthenia. The clinical examination revealed abundant ascites and abdominal tenderness. Laboratory tests showed an elevated C-reactive protein at 35 mg/l (normal value: <6 mg/l), a microcytic hypochromic anemia at 11.2 g/dl (normal value for a man > 13 g/dl), increased carcinoembryonic antigen (CEA) levels, as well as CA 19-9 and CA-125.The abdominal scan showed irregular and asymmetrical thickening with peripheral speculation of the caecum measuring 2.1 cm *5.8 cm. Additionally, adjacent adenopathies, abundant ascites, and peritoneal carcinomatosis were observed to be associated with suspicious bilateral pulmonary nodules and micronodules. The colonoscopy identified a bulging ulcerative tumor of the ileocecal valve extended to the ileum. Further histologic examination confirmed the presence of signet-ring cell carcinoma. The patient was referred to the medical oncology department to initiate palliative chemotherapy following a multidisciplinary consultation meeting. We can underline that SRCC of the caecum is a rare entity with a bad prognosis. Usually, the diagnosis is made at late stages due to the lack of obvious symptoms earlier.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Introduction

Colorectal cancer (CRC) is the third most commonly prevalent cancer globally in males and the second in females, according to the World Health Organization [1]. With adenocarcinomas being the most frequent type. Signet ring cell carcinoma (SRCC) is one of the rare histologic variants of colorectal carcinomas, occurring in less than 1% of all CRCs [2]. It has a distinct molecular and tumor biology. Additionally, it is associated with advanced tumor grade, an occurrence at a young age, and an extremely poor prognosis. Here, we report and discuss a rare clinical case of a young male patient with metastatic cecal SRCC, to expand our knowledge base regarding such a rare situation.

Case presentation

Our patient is a 38-year-old man who presented to our department for abdominal diffuse pain and distention that evolved over 3 months, associated with a remarkable weight loss of 10% of his initial weight, asthenia, and anorexia. The patient was an active consumer of chewing tobacco, without any specific personal or familial medical history, particularly concerning cancers or colic polyps. Physical examination revealed abdominal distension with dullness related to abundant ascites and a mild diffuse abdominal tenderness. No abdominal mass or peripheral adenopathies were detected. The digital rectal examination was normal. The test lab results indicated an elevated C-reactive protein at 35 mg/L (normal value: <6 mg/L) and microcytichypochromic anemia at 11.2 g/dL (normal value for a man > 13 g/dL). Tumor-related cell markers were elevated: CA 19-9 at 265 U/mL (reference range: < 33 U/mL), CA 125 at 506 U/mL (reference range: <28 U/mL), and ACE at 66 (reference range: < 10 U/mL). A contrast-enhanced chest-abdomen-pelvic scan results showed irregular and asymmetrical thickening with peripheral speculation of the caecum, measuring 2.1 cm *5.8 cm (Fig. 1), associated with adjacent adenopathies, abundant ascites, and an appearance of an omental cake suggestive of carcinomatosis (Fig. 2). No other digestive thickening was observed, notably in the stomach. Hepatic metastasis was not detected, but there were suspicious bilateral pulmonary nodules and micronodules (Fig. 3).

A colonoscopy revealed a bulging ulcerative tumor of the ileocecal valve extended to the ileum (Fig. 4), the rest of the colon and rectum were macroscopically normal.

Histologically, the tumor biopsies revealed an abundant mucin in the cytoplasm which displaces the nucleus towards the cell periphery, giving the cells the characteristic signet ring aspect (Fig. 5).

Finally, a diagnosis of primary SRCC of caecum with peritoneal carcinomatosis and pulmonary metastasis was made based on the radiographic, endoscopic, and pathological findings. Considering the advanced stage of the disease, palliative chemotherapy was decided according to a multidisciplinary consultation meeting. The patient has undergone 1 cycle of chemotherapy based on Folfox and Bevacizumab, with good clinical tolerance. A radiological assessment is scheduled after 3 cycles to evaluate the treatment's effectiveness.

Discussion

CRC is the third most common cancer worldwide and the second leading cause of cancer-related death globally [1]. The most frequent type is adenocarcinomas which represent more than 90 % of cases [2]. Among all subtypes of CRC, SRCC accounts for less than 1% of all cases [3].

SRCC of the colon is a rare and aggressive adenocarcinoma subtype, characterized by a distinct molecular and tumor biology, with a poor prognosis [2]. It is defined according to the WHO's classification as a poorly cohesive carcinoma composed predominantly of tumor cells with prominent cytoplasmic mucin and an eccentrically placed crescent-shaped nucleus [4]. It is frequently observed in the stomach in about 96% of cases. However, other digestive localizations are possible including the colon, rectum, pancreas, and gallbladder [5]. SRCC of the colon occurs in the younger population usually less than 40 years old, with male predominance [4]. It is also characterized by a high incidence in the right colon and large tumor size (> 5 cm) [4]. It can present with symptoms such as abdominal pain, unintentional weight loss, changes in bowel habits, and blood in the stools, which are typically similar to those of other colorectal cancers.

Since the clinical manifestations are nonspecific and appear lately. It is usually diagnosed at an advanced stage with node-positive disease and metastatic spread, making surgery impossible and the prognosis grim [5]. Diagnosis delay can also be explained by the radiographic aspect of those tumors resembling inflammatory processes [6], and by the high false-negative rates of endoscopic biopsy [4].

The endoscopic features of this type of carcinoma include an impassable stenosis in the colon, as observed in our patient. Other nonspecific endoscopic aspects may be observed, such as scattered patches of edematous colonic mucosa, which can make the endoscopic diagnosis challenging.

Pathologically, SRCC demonstrates unique features that distinguish it from other ADK of the colon, and confer aggressiveness to these cells. The histological appearance of the tumor is characterized by cells with abundant intracytoplasmic mucin (more than 50%) pushing the nuclei to the periphery, which makes the cells look like signet rings. These cells have a slightly lower occurrence of KRAS mutation but a higher BRAF mutation rate as compared to classical AC. Also, the MSI tends to be more prevalent in SRCC [7].

SRCC is characterized by a high incidence of peritoneal seeding and a low incidence of liver metastases. The treatment of metastatic disease not amenable to curative therapy is chemotherapy, the choice between the different chemotherapy schemes, Fluoropyrimidinesalone, or associated with Irinotecan and/or Oxaliplatin ± Bevacizumab, Cetuximab or Panitumumab, is to be discussed according to the patient's wishes, toxicities, contraindications, biological characteristics of the disease [8].

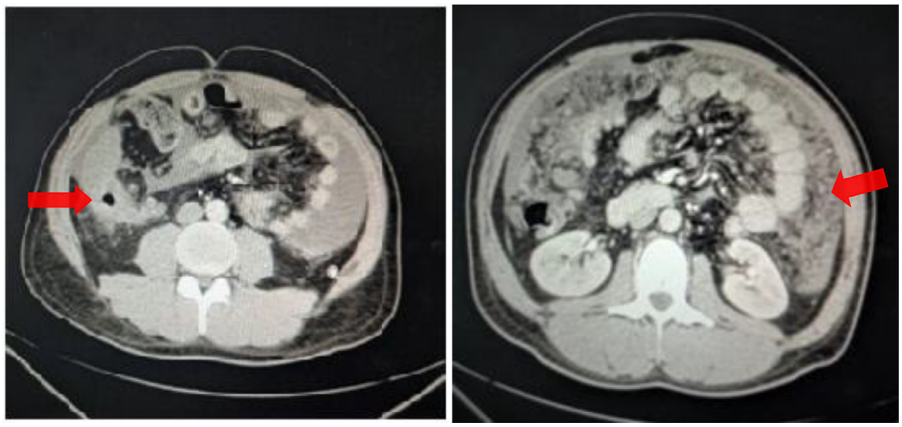


Fig. 1 – Contrast-enhanced computed tomography of the abdomen showing cecal thickening.

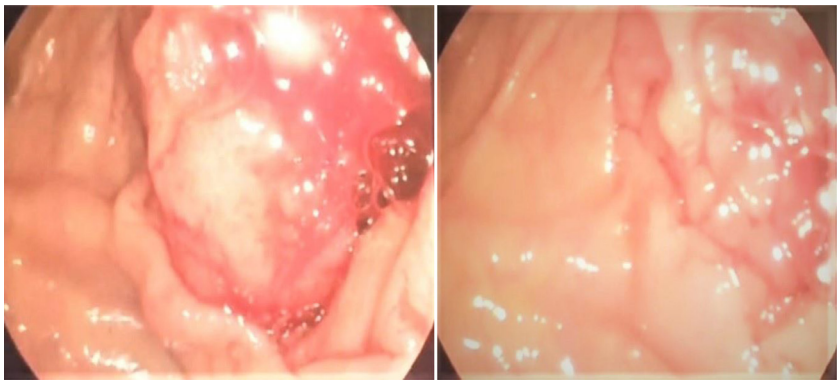
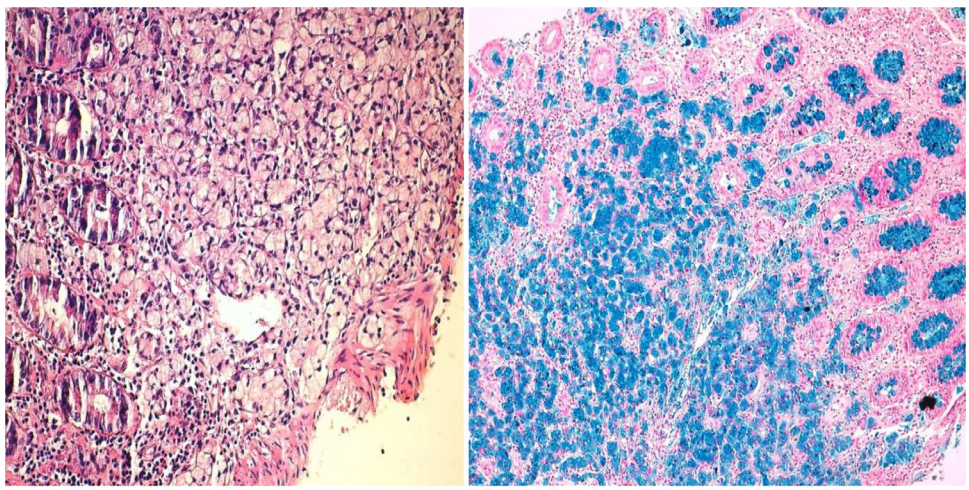


Fig. 2 – Contrast-enhanced computed tomography of the abdomen showing peritoneal carcinomatosis.



(a) (b)

Fig. 3 – Contrast-enhanced computed tomography of the chest showing suspicious bilateral pulmonary nodules and micronodules.

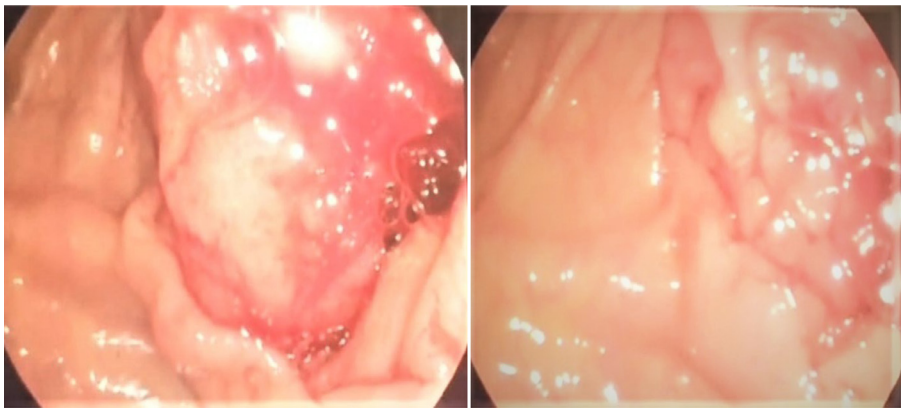
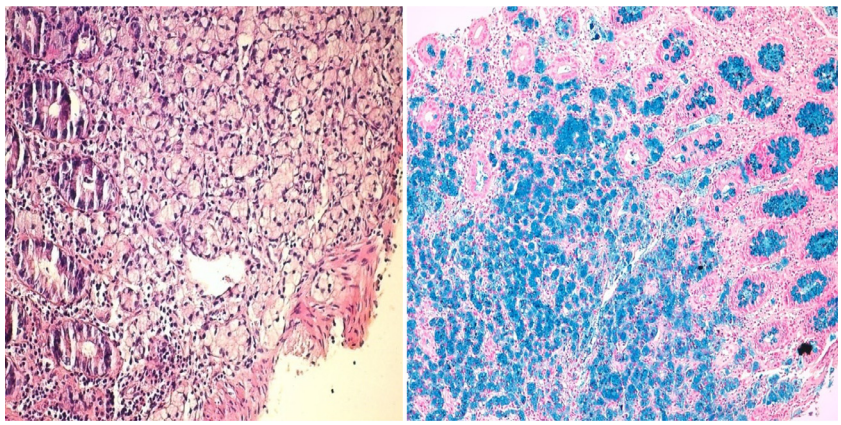


Fig. 4 – Endoscopic images showing ulcerating and stenosing tumor of the ileocecal valve.



(a) **(b)**

Fig. 5 – Anatomopathological images showing tumor cells with abundant and vacuolated cytoplasm, pushing the nucleus to the cell periphery, realizing a "signet ring" aspect. (A) Hematoxylin Eosin stain, x 20; (B) Signet ring cells within crypts highlighted by Alcian blue, x 10.

Table 1 – Comparative table of our case with different studies on the clinicopathological features of colorectal SRCC.

	Our case	Psathakis [9]	Chew [10]	Liang [11]
Age	38	67.5 ± 16.9	63.5	50
Gender M/F	M	1/1	0.4/1	1.5/1
Predominant Location	Proximal colon	Proximal colon 50.0%	Distal colon 46%	Proximal colon 48.6%
TNM stage III–IV	IV	92.9%	94%	89.1%
Site of metastasis (%)	Peritoneum Lung	Peritoneum 64.3% Liver 14.3% Lung 0 %	Peritoneum 50% Liver 7% Lung 22%	Peritoneum 66.7% Liver 19.1% Lung 4.8%

The prognosis of this entity is very poor. Median and mean survival times are reported respectively as 20 and 45 months [9]. The 5-year survival rate ranges from 0% to 12%, and disease recurrence is more frequent compared to other Adenocarcinomas [10]. Early diagnosis and a multidisciplinary approach are essential for better management and prognosis.

By comparing our case to the literature series, we observe that our patient is younger compared to the other cases. Additionally, there are variations in gender ratios and tumor locations across different series. However, our case aligns with the literature's findings regarding advanced TNM stages upon the diagnosis, as well as the prevalence of peritoneal metasta-

sis. Here is a table (Table 1) comparing our patient with several case series in the literature.

Conclusion

Colon SRCC tends to affect young people and is usually diagnosed at an advanced stage, with low rates of curative resection and a poor prognosis. It is characterized by a high incidence of peritoneal seeding and a low incidence of liver metastases. Early diagnosis and a multidisciplinary strategy are crucial for optimal management and prognosis.

Patient consent

Informed consent was obtained from the patient.

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