



A MASKED MENACE - Signet Ring Cell Carcinoma of Colon Masquerading as Crohn's Disease: A Review of Literature

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Abstract

According to WHO's International Agency for Research on Cancer, Colorectal carcinomas are the 3rd most commonly occurring cancer worldwide. Incidence of Colorectal cancers have been on a rise for the past 2 decades in India and is currently the 7th most common cancer in India according to Global Cancer Observatory. However, signet ring cell carcinoma of the colon is an extremely rare variant with a reported incidence of around 1%.^[1]

Signet ring cell carcinoma is a subtype of colorectal carcinoma characterised by a diffuse lesion. It usually metastasises to lymph nodes, peritoneum, ovary and rarely to the liver and stomach.

Most common risk factors being age, family history, unhealthy dietary habits, sedentary lifestyle, obesity, smoking and alcohol consumption.

Patients often present with changes in bowel movement, bleeding per rectum, abdominal pain and unexplained loss of weight/ appetite.

These cancers can be diagnosed through imaging (CT scan or MRI), colonoscopic changes, histopathological examination of tissue biopsy. FDG PET CT is often used to diagnose metastasis.

Colorectal malignancies have a variety of specific genetic mutations and biomarkers that guide us to the best possible treatment and better outcome.

However, patients with Crohn's disease may also have a similar presentation causing a delay in diagnosis of SRCC and poor outcomes.^[2]

Here, we present a rare case of recurrent metastatic signet ring cell colonic cancer mimicking Crohn's disease.

Keywords: Colorectal carcinoma, Crohn's disease, Ileocaecal carcinoma, Ileocolic anastomosis, Inflammatory bowel disease, Recurrent metastatic carcinoma, Signet ring cell carcinoma, Skip lesion

Case Report

The case of a 66-year-old gentleman vividly illustrates the dangers of SRCC's resemblance to Crohn's disease.

Three years prior in August 2021, a 63 year old gentleman, a chronic smoker underwent right hemicolectomy with ileocolic anastomosis for caecal malignancy. Biopsy revealed poorly differentiated signet ring cell carcinoma of Colon with metastatic tumour deposits in lymph nodes pT3 N2.^[3] Post operative period was uneventful. FDG PET scan taken post operatively shows features suggestive of post procedural changes with no other abnormal metabolic activity or nodal or distal metastasis. Extensive gene testing and immunohistochemistry including NTRK1 gene rearrangement, micro satellite instability, PIK3CA, KRAS, BRAF, TP53, PTEN, HRAS and NRAS were done and revealed no mutations. Following this, he underwent 5 cycles of adjuvant chemotherapy CAPEOX (CAPECITABINE AND OXALIPLATIN) regimen.

He presented to the hospital several times with complaints of abdominal pain associated with nausea and vomiting and was treated conservatively.

Recently he came with complaints of lower abdominal pain for two days, vomiting and obstipation for one day. Per abdomen examination revealed soft, non-distended abdomen with tenderness over the right iliac fossa and a healthy midline vertical scar. Routine blood investigations done were within normal limits. CECT

Abdomen done was suggestive of few small transmural skip lesions (Figure 3) with minimal thickening (Figure 4) in the ileal loop^[4] He was further evaluated through colonoscopy (Figures 8-10) to rule out inflammatory bowel disease (Crohn's disease) which revealed post right hemicolectomy anastomotic site erythema, erosions, and rectal ulcer. Biopsies from the anastomotic site revealed signet ring cell carcinoma.

However, PET CT showed no evidence of a metabolically active disease. Patient was taken up for diagnostic laparoscopy and proceed which was converted to open exploratory laparotomy due to dense adhesions. Multiple metastatic deposits were noted in the peritoneum, stomach, and small bowel from which tissue biopsy was performed for further evaluation and proceeded with a diversion procedure and an ileocolic anastomosis bypassing the obstruction. The postoperative period was uneventful and the patient was gradually started on oral feeds and tolerated well. Biopsy report received was suggestive of metastatic poorly differentiated signet ring cell carcinomatous deposits in the small bowel, stomach and peritoneum. The patient has been on regular follow up and is on palliative chemotherapy.



Figure 1: CECT Abdomen demonstrating post-operative anastomotic site



Figure 2: CECT ABDOMEN showing prominent bowel loops

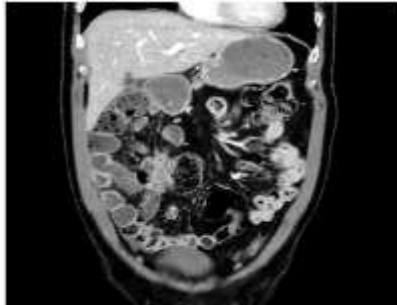


Figure 3: CECT Abdomen revealing transmural skip lesions

Discussion

Colonic signet ring cell carcinoma is an exceedingly rare and aggressive subtype of colorectal cancers characterised by the presence of mucin producing cancer cells that exhibit a signet ring appearance on microscopic examination.

This variant poses diagnostic challenges due to its clinical presentation that mimics Crohn's disease and other disorders of the gastrointestinal tract. SRCC generally has an infiltrative growth pattern which also causes a delayed presentation. Carvalho JR et al ^[2] also suggests a similarity between the presentation of Crohn's disease and signet ring cell carcinoma of colon which pose as a diagnostic challenge

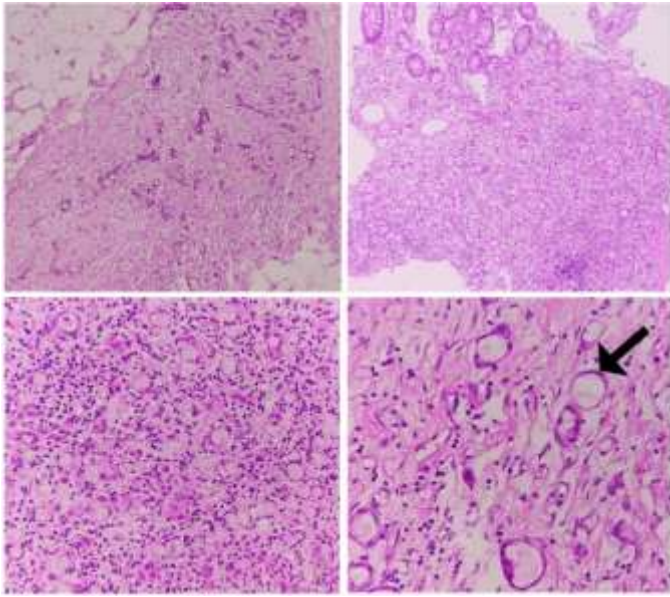


Figure 4: CECT Abdomen showing thickened bowel loops and abdominal aortic aneurysm

In India, the incidence of colorectal carcinomas is on a rise but however less than in western population. Patients with either colorectal carcinomas or Crohn's can both present with abdominal pain, bloating, altered bowel habit (constipation or diarrhoea), bleeding per rectum, anaemia and unexplained loss of weight or appetite.

In addition, the two diseases also share similar endoscopic findings like ulceration, strictures, mucosal skip lesions and cobblestone appearance of the mucosa. These overlapping symptoms and signs often tend to cause a delay in the diagnosis of carcinoma which is particularly detrimental in case signet cell variant due to its aggressive nature of progression leading to poorer prognosis.

A case report by Ali Z Ansari et al^[2] emphasises the diagnostic challenge and similarities between Crohn's disease and colorectal carcinoma, which aligns with our discussion of how the signet ring cell carcinoma's mimics Crohn's disease.



Figures 5-8: Biopsy depicting recurrent signet ring cell carcinoma

The presence of signet ring cells within the mucin content is a key distinguishing feature in SRCC but these can be sparse and overlooked, especially in initial stages or in poorly differentiated tumours. While tumour markers like Carcinoembryonic antigen (CEA) may be elevated in colorectal carcinomas, they are not specific and can be elevated in other inflammatory diseases as well.

In this case, a 66 year old gentleman with recurrence of signet ring cell carcinoma at the anastomotic site 3 years post right hemicolectomy presented with abdominal pain, vomiting and obstipation mimicking Crohn's disease. Serum CEA levels were elevated and CECT Abdomen revealed transmural skip lesions (Figure 2) with minimal thickening (Figure 3) in the ileal loop raising the suspicion of IBD. The patient was taken up for Diagnostic laparoscopy and proceed which was converted to open exploratory laparotomy due to dense adhesions and multiple metastatic deposits were noted in the peritoneum, stomach and small bowel from which tissue biopsy was taken for further evaluation and

proceeded with diversion procedure and ileocolic anastomosis bypassing the obstruction. The biopsy reports confirmed metastatic poorly differentiated signet ring cell carcinoma at the anastomotic site (Figures 4-7) with carcinomatous deposits in the stomach, small bowel and peritoneum. Owing to this aggressively progressed stage of the tumour, the patient has a very poor prognosis and is on palliative care.

According to Muhammad Baraa Hammami et al ^[1], not only colonic SRCC but also signet ring cell carcinoma of ileum may also be masked by Crohn's disease.

Similar case report by Gaurav Mohan et al^[13] also suggest that Signet cell carcinoma can mimic Crohn's disease on radiological and endoscopic findings, including the presence of a fistula tract.

However, there are studies that suggest other types of colorectal carcinoma being masked by features of Crohn's disease.^[7,12]

Lammer J et al ^[11] suggested similarity between Crohn's disease and anaplastic colonic carcinoma.

This case highlights the critical need for a high index of suspicion for SRCC in patients presenting with symptoms suggestive of Crohn's disease, especially those with a history of SRCC. While Crohn's disease is significantly more common, the possibility of SRCC should not be overlooked, particularly in cases that show atypical features or not responding to standard Crohn's treatment. Hence reliance on conventional imaging may fail to diagnose the disease at an early stage and often present at progressed stage.

A comprehensive multidisciplinary approach involving surgeons, gastroenterologists, radiologists, and pathologists is essential for accurate diagnosis and timely intervention.^[4] Advanced imaging modalities like PET CT, along with serum tumor markers like CEA, can

be play a vital role in differentiating SRCC from Crohn's disease.

Jianfei Fu et al^[4] also suggested that SRCC had significantly higher rates of unsuccessful surgical outcomes compared to other carcinomas of colon.

Takahiro Zenda et al^[7] reported that anaplastic cancer with exuberant desmoplastic reaction and infiltration along the mesenteric border accounted for the morphological similarities noted between Crohn's disease and metastatic colon cancer.

However, so far all the cases reported were related to tumours in the small bowel or adenocarcinoma colon being masked by features of Crohn's disease and our case is probably the first case to be reported eliciting the relation between presentation of signet ring cell carcinoma in colon and Crohn's disease.



Figure 9: Colonoscopic view of previous anastomotic site



Figure 10-11: Multiple skip ulcerations in the large bowel

Conclusion

The rising incidence of signet ring cell carcinoma of the colon coupled with its diagnostic challenges justifies the

need for heightened awareness and a multidisciplinary approach to management.^[14] Skip lesions, characterized by areas of normal-appearing bowel interspersed between inflamed segments, are a hallmark of Crohn's disease. However, they can also be seen in SRCC, particularly when it spreads transmurally, mimicking the inflammatory pattern of Crohn's.^[9] These findings points towards inflammatory bowel disease, making Crohn's disease a strong suspect.

The mimicry of Crohn's disease by SRCC underscores the importance of a comprehensive evaluation, including a thorough clinical assessment, advanced endoscopic and imaging modalities as well as accurate histopathological examination for precise diagnosis and early curative intervention. For patients with this aggressive variant on colorectal carcinomas, addressing these stumbling blocks is crucial for enhancing survival rates and improving outcomes in patients with this aggressive variant of colorectal carcinoma.^[10,13,14]

Ethics Approval

This study was conducted after obtaining approval from the Institutional Human Ethics Committee.

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