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Pathology

PRIMARY SIGNET RING CELL CARCINOMA OF COLON – A CASE REPORT

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ABSTRACT Primary signet ring cell carcinoma of the colon is an exceptionally rare subtype of colorectal carcinoma, accounting for less than 1% of cases. The classification of a tumor as signet-ring cell carcinoma is based on the presence of prominent intracytoplasmic mucin in over 50% of the tumor cells, accompanied by displacement and molding of the nucleus. In this case study, we describe a 54-year-old male patient who presented with obstructive symptoms, and a CT scan revealing thickening of the wall of the sigmoid colon. The patient underwent laparoscopic sigmoid resection, leading to the diagnosis of primary signet ring cell carcinoma of the colon. Primary signet ring cell colorectal carcinoma tends to be more prevalent among young adults. Before confirming a diagnosis of primary signet ring cell carcinoma of the colon, it is essential to consider and rule out possible primary gastric carcinoma. Further examination of molecular characteristics can contribute to refining therapeutic approaches and may lead to a favorable prognosis.

KEYWORDS : Primary signet ring cell carcinoma; colorectal carcinoma; rare lesion; linitis plastica colon

INTRODUCTION

Signet-ring cell carcinoma (SRCC), a rare type of colorectal cancer accounts for less than 1% of all colorectal carcinomas (CRC)[1,2]. Primary signet-ring cell carcinoma (SRCC) is predominantly seen in the stomach and therefore metastatic gastric carcinoma should be excluded during endoscopy. Histologically, SRCC shows neoplastic cells with abundant intracytoplasmic mucin, and peripherally displaced nuclei, imparting the cells a signet ring-like appearance. The clinical symptoms tend to occur late in the course of the disease and this leads to late detection at advanced stages and poor survival rate[2]. A tumor is designated as signet-ring cell carcinoma if more than 50% of the tumor cells have prominent intracytoplasmic mucin leading to displacement and molding of the nucleus. When the signet-ring cell component is less than 50% of the tumor, they are considered to have a signet-ring cell component. Signet ring cell carcinomas are more aggressive than other colonic adenocarcinomas[4]. A slight association with inflammatory bowel disease has been suggested. The majority of cases are sporadic and manifest at a younger age compared to typical colorectal adenocarcinoma.

CASE PRESENTATION

A 49-year-old male patient presented with acute onset of abdominal pain, diarrhea, nausea, and vomiting which progressed over a period of 2 days. He is a known case of ulcerative colitis and has been on naturopathic treatment for the past 10 years. On admission, physical examination revealed tenderness in the whole abdomen and a fading gurgling sound. Routine tests were done and all were normal. CT scan revealed thickening of the wall of the sigmoid colon extending over a length of 7 cm and with a thickness of 1.5 cm from the lumen to the outer wall causing significant luminal narrowing. The rest of the bowel showed no lesion.

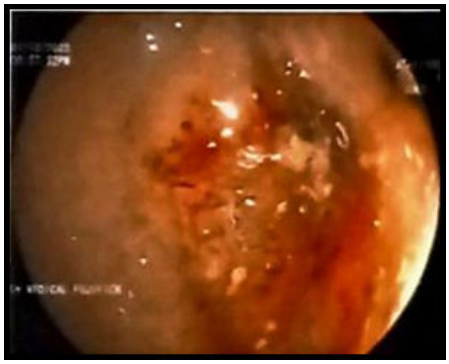

Fig. 1 Laparoscopy Image Showing Stricture At Rectosigmoid Junction

Sigmoidoscopy was done which revealed a stricture at the rectosigmoid junction and the scope could not be negotiated further. Biopsy from the site of obstruction suggested the possible diagnosis of a mucin-secreting adenocarcinoma.

Laparoscopic sigmoid resection was done with colorectal anastomoses and was sent for histopathology evaluation

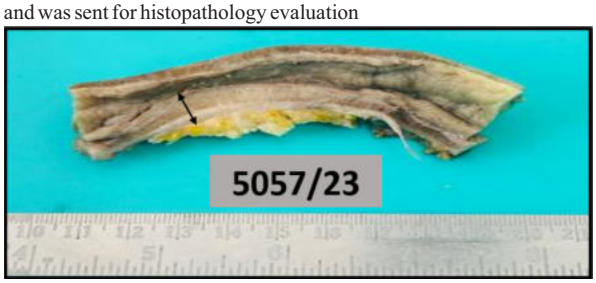

Fig. 2 : Colon With Thickening Of The Wall

MACROSCOPY:

Received segment of colon with attached pericolic fat measuring 12 cm in length. On opening, identified an area of mucosal irregularity with loss of mucosal folds measuring 7 x 5 cm. The wall appeared thickened and the lumen constricted.

MICROSCOPY:

Sections from the colon showed ulceration of mucosa with an infiltrating neoplasm composed of cells arranged as sheets, islands and trabeculae. Individual neoplastic cells were round to polygonal with abundant cytoplasm and hyperchromatic nucleus pushed to the periphery by intracellular mucin. Pools of extracellular mucin were noted. Tumor was seen perforating the visceral peritoneum. Resected margins were free of neoplastic involvement. 12/14 lymph nodes showed metastatic deposits from the above-mentioned neoplasm.

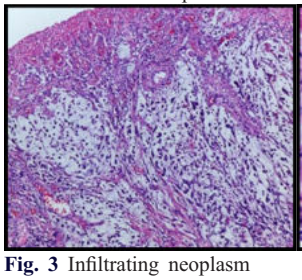

Fig. 3 Infiltrating neoplasm with cells arranged as sheets

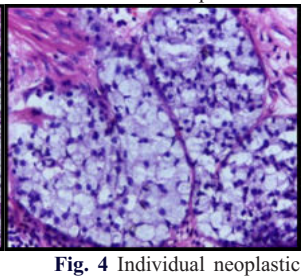

Fig. 4 Individual neoplastic cells with signet ring morphology morphology

DISCUSSION

Signet ring cell colon carcinoma, like its more prevalent gastric counterpart, presents as diffuse infiltration of the bowel wall. It was originally described as a linitus-type carcinoma of the colon by Laufman and Saphir [5]. This uncommon histologic variant of CRC accounts for less than 1% of all histological subtypes. Unlike the intraluminal mass observed in colorectal adenocarcinoma, colorectal SRCC exhibits thickening of the bowel wall which may be accompanied by a significantly constricted lumen. SRCC is more prevalent among young patients (ages 20-40 years) than among older adults (>40 years) with a median age of presentation of less than 40 years of age. A slight male preponderance is noted with M: F - 2:1. Metastases may develop rapidly and can occur in multiple locations that are not typical for CRC.

In this particular case, the patient received a diagnosis at an earlier age (54 years old) than the average age (65 years old) associated with colorectal carcinoma. This highlights the crucial need for attentiveness when dealing with colorectal SRCC cases that manifest atypical features, including an earlier onset, clinical signs indicating incomplete intestinal obstruction, and the potential for a negative endoscopy result.

Signet ring cell carcinoma differs from mucinous adenocarcinoma of the colon by its distinct molecular features. Microsatellite instability is associated with both these tumors but signet ring cell carcinoma exhibits a lower frequency of KRAS mutations[6]. Genomic alterations such as loss of expression of CDH1 (cadherin-1) and upregulation of genes regulating epithelial-mesenchymal transition facilitate an invasive phenotype and set signet ring cell carcinoma apart from mucinous adenocarcinoma colon. [7,8].

SRCC is associated with a high incidence of microsatellite instabilities and has a strong association with Lynch syndrome. They have a relatively poor survival rate. Higher prevalence of *BRAF* and CIMP (CpG island methylator phenotype) mutations in patients with SRCC have also been identified.

In our patient, other features suggestive of syndromic associations or a family history of similar complaints could not be found after an extensive search. No other lesions were detected in other possible primary sites for signet ring cell carcinomas.

In cases of colonic carcinomas displaying signet ring morphology, the differential diagnostic categories to be considered comprise metastatic signet ring cell carcinoma, benign lesions with signet ring cell changes, and primary mucinous adenocarcinoma.[9]

Mucin-poor variant of signet ring cell carcinoma is a differential for metastatic signet ring cell carcinoma. Both tumors may have diffuse infiltration by poorly cohesive cells. Primary colonic adenocarcinoma will show co-expression of CDX2, SATB2 and CK20. The metastatic tumor can be differentiated by correlating with clinico-radiological findings as well by its immunohistochemical profile[10,11].

The distinction of mucinous adenocarcinoma from signet ring cell carcinoma of the colon is based on the percentage (> 50%) of signet ring cells present. This differentiation holds significance since signet ring cell carcinoma is regarded as a separate entity with a poorer prognosis.

In a population-based study comprising 1,972 cases of colorectal SRCC, there was a significant association between SRCC and poorer 5-year survival when compared to conventional colorectal cancer (CRC)[12]. Several studies have reported that SRCC histology stands as an independent adverse prognostic factor even after accounting for variables such as tumor stage and location.

Following the surgical procedure, the patient, in this case, is undergoing standard postoperative chemotherapy. Our patient survived for 5 months until the time when this article finished.

CONCLUSION

Primary SRCC of the colon is a rare disease with an overall 5-year survival of 0 -12%. It has a poor prognosis due to the late clinical presentation of the symptoms. Before making a diagnosis of primary SRCC it is imperative to rule out primary gastric malignancy. Additional assessment of the molecular characteristics can help improve the therapeutic modalities leading to a good prognosis. This case report adds to the existing literature on this uncommon and poorly understood subtype of colonic carcinoma.

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