

Long Standing Crohn's Disease and Signet Ring Cell Carcinoma of the Ileum

by David M. Schwartzberg, H. Tarik Kirat, Feza H. Remzi

INTRODUCTION

Chronic intestinal inflammation caused by Crohn's disease (CD) has been associated with malignant transformation into aggressive forms of small bowel adenocarcinoma. The overall incidence of small bowel adenocarcinoma is less than 2%.^{1,2} Signet ring cell carcinoma (SRCC) is an aggressive subtype and is associated with poor differentiation and a poor survival, often presenting as T4 lesions in Crohn's patients.³ Mid-small bowel CD is difficult to survey and subtle symptomatology maybe the only clue in deciding between biologic therapy or surgical intervention. Before deciding on medical therapy, including a

number of possible biologic therapies, malignancy must be ruled out, or surgical resection must be offered.⁴

We report a case of SRCC in a patient with long-standing Crohn's disease who was suspected to have increasing symptoms secondary to Crohn's ileitis. Escalation of medical therapy failed to control his symptoms and operative intervention was ultimately required. Pathology revealed a poorly differentiated, pT4aN2M1 SRCC adenocarcinoma in the setting of active Crohn's disease. This case highlights the importance of considering malignant transformation of the small intestine in the setting of long-standing inflammatory bowel disease.

Case Report

A 63-year-old male with a 32-year history of Crohn's disease presented with increasing abdominal pain, fatigue, weight loss and intolerance to solid food.

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A CASE REPORT

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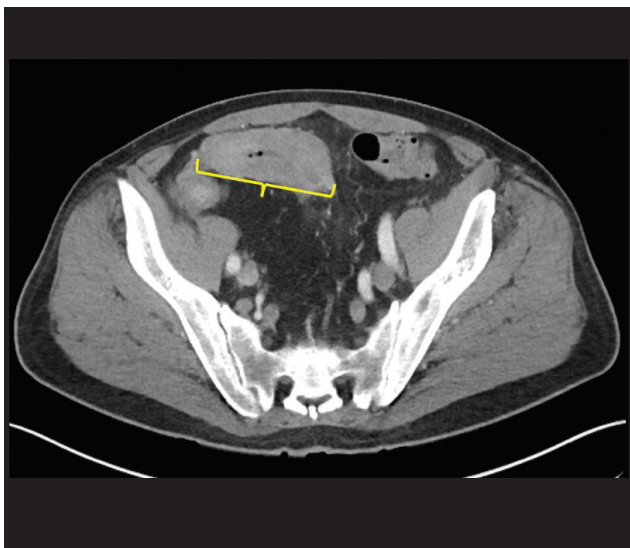


Image 1. CT showing axial imaging of ileal inflammation showing an increase of ileal bowel wall inflammation to 16.9mm while on biologic therapy for Crohn's disease (brackets).

Historically he had been treated with budesonide and mesalamine only requiring sporadic corticosteroid tapers. Recent colonoscopy revealed a scarred ileocecal valve, which prompted initiation of infliximab. Ileal thickening (to 16.9mm) was noted on computed tomography (CT) ordered for persistent symptoms despite two months of infliximab treatment (Image 1). Aggressive inpatient therapy failed to control his symptoms and surgical intervention was recommended. Peritoneal implants were noted on the anterior abdominal wall; frozen section was positive for mucinous adenocarcinoma. En bloc resection was performed (Image 2). His final pathology showed a poorly differentiated, pT4N2M1 signet ring cell carcinoma measuring 23 cm in length. Mismatch repair was stable. There was metastatic lymph node spread (12 of 15 lymph nodes), lymphovascular and perineural invasion, omental and peritoneal metastasis. CDX2, CK20 and CK7 stains were positive. The surrounding bowel was consistent with active Crohn's disease.

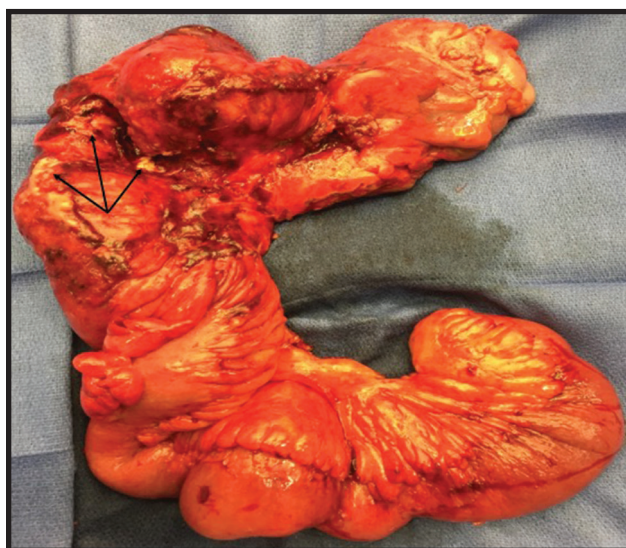


Image 2. Small bowel consistent with Crohn's disease and a 23cm length signet ring cell adenocarcinoma; note the tumor depots on the bowel wall (arrows).

Discussion

This case describes malignant transformation of the ileum to an aggressive form of small bowel adenocarcinoma, signet ring cell carcinoma, in a patient with long-standing Crohn's disease. The subtype of SRCC is rare with only one other case arising in the presence of Crohn's disease.⁸ SRCC originate from undifferentiated stem cells and are mucin secreting tumors with an abundance of intracellular mucin that peripherally displaces the nucleus.² SRCC is most commonly found in the stomach and colon, with small bowel SRCC only occurring in 1.1% of reported cases. It is generally associated with poor-differentiation and T4 lesions with a reported 5-year overall survival of 16.1%.^{2,3}

Overall, small bowel adenocarcinoma is uncommon, and its symptoms non-specific. Its association with Crohn's disease, however, increases the risk 40 to 60-fold relative to the general population.^{1,6} Though adenocarcinoma is rare, and the exact mechanism of malignant degeneration unknown, malignancy must be ruled out prior to escalating medical therapy, especially in patients with long-standing CD.⁶

Surveillance of CD is possible in upper and lower gastrointestinal disease. Small bowel disease is often difficult to access endoscopically, thus

location of disease must factor into the treatment algorithm. The aggressive nature of small bowel adenocarcinoma, specifically SRCC, should be considered when small bowel CD fails to improve with escalating medical therapy, or long-standing disease becomes increasingly worrisome. Surgical resection may be the only opportunity for cure, and it must be considered to be diagnosed.¹¹ ■

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