

CASE REPORT

Mucinous Adenocarcinoma Arising from Perianal Fistulae in Crohn's Disease: A Rare Case Report and Review of the Literature

Zhichun Lu, Veena Shah

Zhichun Lu, Veena Shah, Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, Michigan, the United States

Correspondence to: Zhichun Lu, Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, Michigan, the United States

Email: zlu1@hfhs.org

Telephone: +1-313-916-8330

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the first time diagnosis of Crohn's disease and development of adenocarcinoma in the perianal fistula tracts.

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ABSTRACT

Perianal fistula is a common manifestation of Crohn's disease. Adenocarcinoma arising from perianal fistulae in patients with Crohn's disease is rare. There are only 65 cases in English literature with anorectal adenocarcinoma arising from a perianal fistula in patients with Crohn's disease reported from January 1946 until September 2009. We present a case of 44 year old male diagnosed with Crohn's disease in 2012. Patient presented with worsening perirectal fistulas and posterior anal mass in 2014. Biopsy of posterior anal mass and right lateral anal margin, revealed mucinous adenocarcinoma. Given the findings of a perianal adenocarcinoma and extensive perianal Crohn's disease, the patient underwent neoadjuvant treatment, followed by abdominoperineal resection. Tumor size was 4.0 cm, estimated, as a discreet mass was not seen. This moderately differentiated adenocarcinoma was arising from the lining of the perianal fistulae tracts. The malignant cells and mucinous pools were diffusely involving the anal canal and part of the perianal fibroadipose tissue. The tumor demonstrated irregularly shaped tubules lined by cells with basally located, uniform, and hyperchromatic nuclei with abundant mucinous cytoplasm. The positive staining with CK20 and CDX2 in the tumor cells by immunohistochemistry suggests that tumor originated from colonic epithelium lining the fistula tracts. This case is unusual because of the very short duration between

INTRODUCTION

Perianal fistula is a common manifestation of Crohn's disease. Up to 43% of Crohn's disease patients will develop perianal fistulizing Crohn's disease^[1]. However, adenocarcinoma arising from perianal fistulae in patients with Crohn's disease is rare^[2]. To date, less than 70 cases of Crohn's disease fistula-associated adenocarcinoma have been reported in English literature^[3].

The purpose of this study was to report an unusual case with fistula-associated perianal mucinous adenocarcinoma in the setting of Crohn's disease with very short duration between the first time diagnosis of Crohn's disease and the development of adenocarcinoma, and to perform a systematic review of reported cases of this rare pathologic entity.

CASE REPORT

A 44 year old African-American male (former smoker for 27 years) had a history of Crohn's disease, which was diagnosed in 2012 and treated with Remicade/Imuran. As part of his first presentation, he also had perirectal fistulas associated with Crohn's disease. In April 2014, he presented with posterior anal mass with worsening

perirectal disease. Biopsies of the posterior anal mass revealed mucinous adenocarcinoma. On CT chest/abdominal /pelvis, no distant metastases were identified, but there were mildly enlarged right external iliac and inguinal Lymph nodes; fine needle aspiration was done which was negative for malignancy. After completion of concurrent chemo-RT with Xeloda, patient underwent exploratory laparotomy, abdominoperineal resection (APR) with cutaneous vertical rectal flap reconstruction. Pathologic examination revealed that tumor size was 4.0 cm, estimated, as a discreet mass was not seen. This moderately differentiated adenocarcinoma was arising from the lining of the perianal fistulae tracts, diffusely involving the anal canal and part of the perianal fibroadipose tissue. The tumor demonstrated irregularly shaped tubules lined by cells with basally located, uniform, and hyperchromatic nuclei with abundant intracytoplasmic mucin. The positive staining with CK20 and CDX2 in the tumor cells by immunohistochemistry suggests that tumor originated from colonic epithelium lining the fistula tracts (Figures 5 and 6). Twenty-six lymph nodes (0/26) were dissected from perirectal and perianal areas with no evidence of metastatic adenocarcinoma. However, the cancer was involving the perianal skin; clinical stage T4N0M0. Subsequently, patient had post-surgery chemotherapy with Xeloda. Currently, patient is stable on Remicade/Prednisone treatment, with no evidence of recurrence after 13 months follow-up.

DISCUSSION

Fistula-associated perianal adenocarcinoma (FAPA) is uncommon. To date, there is no population-based study, literatures consist mainly of case reports and small series study. The largest systematic review reported by Lesalnieks *et al*^[4] in 2010, which consisted of 65 cases of Crohn's disease diagnosed with adenocarcinoma arising from perianal fistulae. The mean duration between the first time diagnosis of Crohn's disease and development of adenocarcinoma in the perianal fistula tracts was 11 (range, 0-24) months^[4]. 95 % patients had T3 or T4 stage carcinoma at the time of cancer diagnosis. 44% had perirectal or inguinal lymph nodes involvement and 13% had distant metastases^[4]. A mean tumor recurrence was 16.6 (range, 2-55) months of following APR, with median follow-up of 20.5 (range, 3-60) months^[4]. The overall survival rate following APR was 88% at 1 year, 54% at 3 years, and 26% at 5 years^[4]. In contrast to the literature, this male patient is quite unusual, with younger age, very short duration between the first time diagnosis of Crohn's disease and development of adenocarcinoma in the perianal fistula tracts. Clinical stage is T4 with no lymph node involvement and distant metastases, 13 months follow-up with negative signs for recurrence.

The pathogenesis of carcinoma arising in fistula of Crohn's disease is not well understood. Traube *et al* have suggested that the environment of constant mucosal regeneration occurring within a fistula may cause dysplastic changes and ultimately lead to adenocarcinoma^[5]. Church *et al*^[6] supported that a fistula formation may be a result of the cancer itself, and it was more likely that carcinoma caused the fistulas in patients with shorter duration of fistulas. For the pathologic evidence, Smith *et al.* have documented that mucinous adenocarcinoma can arise in a fistula tract in association with adenomatous mucosa. The colonic epithelialization of the fistula tract may have a dysplastic potential that gives rise to subsequent mucinous adenocarcinoma^[7]. Smoking as an independent prognostic factor has been found to worsen the natural history of Crohn's disease, leading to an increased incidence of fistula formation and recurrence following intestinal resection, as well as an increased risk for cancer-related death in Crohn's disease patients with fistula-associated perianal adenocarcinoma^[4,8-9].

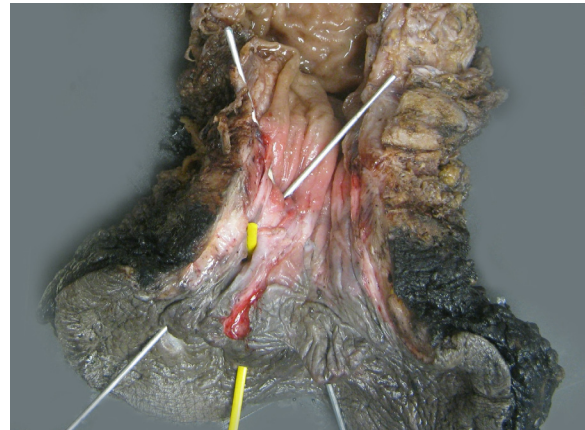


Figure 1 Gross photograph, anal canal with multiple perianal fistulas perforating skin.

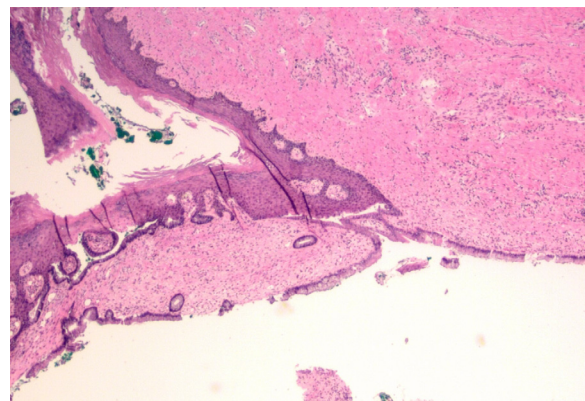


Figure 2 H&E, perianal fistula with overlying skin, malignant adenomatous epithelial lining of the fistula.

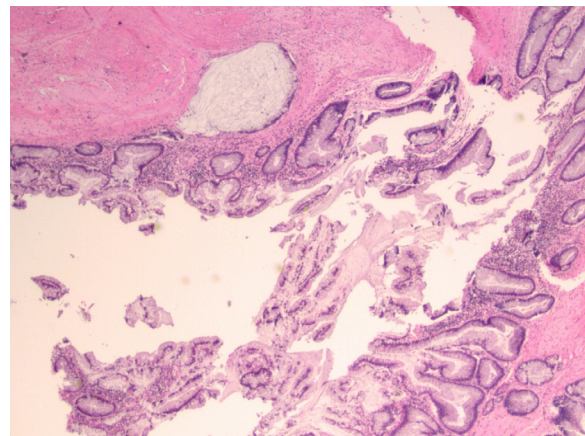


Figure 3 H&E, moderately differentiated adenocarcinoma arising from the lining of the perianal fistula tract, infiltrating perianal fibrotic stroma along with extracellular mucinous pool.

Our case is similar to cases reported by Smith *et al.* and Nishigami *et al*^[7,10]. The adenocarcinoma was arising from the colonic epithelial lining of the perianal fistulae tracts with positive immunohistochemical stains (CK20 and CDX2 were both positive) demonstrating colonic type epithelium. However, the very short duration between the first time diagnosis of Crohn's disease and development of adenocarcinoma in the perianal fistula tracts, might suggest that fistulas formation is a result of cancer itself. Adenomatous transformation of the epithelial lining of the fistula tract and long term smoking are the potential etiologies of mucinous adenocarcinoma arising in fistulating Crohn's disease.

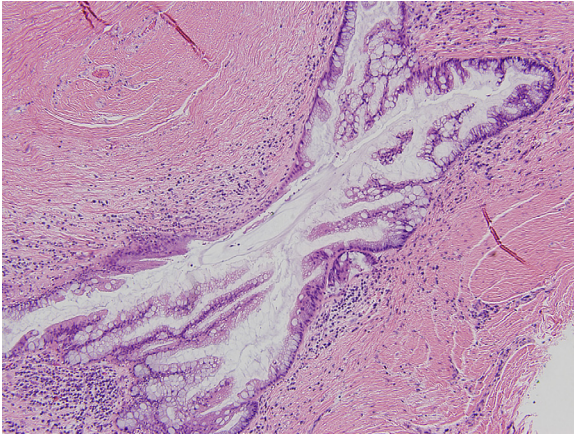


Figure 4 H&E, mucinous adenocarcinoma, invading perianal fibromuscular tissue.

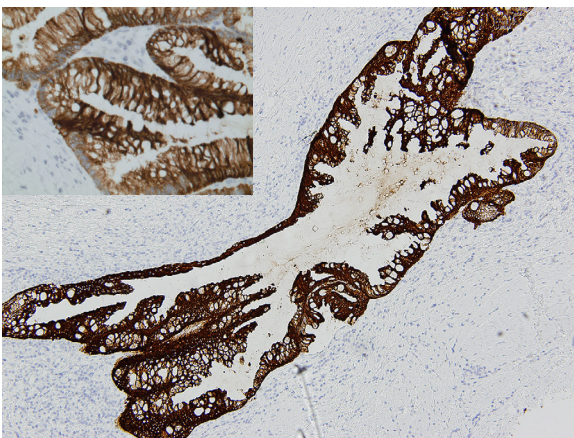


Figure 5 CK20, Strong cytoplasmic and membranous positivity in malignant mucinous glandular cells is supporting tumor originated from colonic epithelial lining of the fistula tracts. Inset demonstrates high-power view.

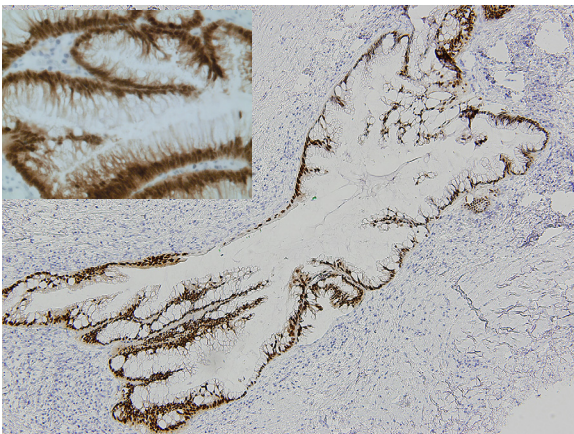


Figure 6 CDX2, Strong nuclear positivity in malignant mucinous glandular cells is supporting tumor originated from colonic epithelial lining the fistula tracts. Inset demonstrates high-power view.

CONCLUSION

Mucinous adenocarcinoma can arise in a patient with a long term history of smoking with perianal fistulas in the setting of Crohn's disease during a very short period. Close attention should be paid to this variable in patients with Crohn's disease.

CONFLICT OF INTERESTS

The authors declare that they do not have conflict of interests.

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Peer reviewer: Luis Rodrigo, Professor, Gastroenterology Department, University Hospital Central of Asturias, c/ Celestino Villamil s. n°, 33.006. Oviedo. Spain.