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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Rare Finding of Rectal Squamous Metaplasia in Inflammatory Bowel Disease

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ABSTRACT

Rectal squamous metaplasia in inflammatory bowel disease is rare. We present 2 cases of rectal squamous metaplasia, one in a patient with Crohn's disease and another with ulcerative colitis. Given the risk of malignant transformation, dysplasia surveillance is important particularly in areas of chronic inflammation. Furthermore, human papilloma virus (HPV) is involved in the pathogenesis of anal squamous cell carcinoma (SCC), but no guidelines exist in the United States for HPV prophylaxis against anal SCC in inflammatory bowel disease. HPV vaccination should be considered in high-risk patients younger than 45 years for prevention of anal SCC, including those with rectal squamous metaplasia.

KEYWORDS: squamous metaplasia; Crohn's disease; ulcerative colitis; dysplasia surveillance; human papilloma virus

INTRODUCTION

Squamous metaplasia of the colon in inflammatory bowel disease (IBD) is a rare finding that presents as a thin whitish area with a distinct margin at conventional colonoscopy.[1] It may arise with chronic inflammation and/or high-risk strains of human papilloma virus (HPV), and the immunosuppression secondary to chronic inflammation compounded with immunosuppressive treatments for severe inflammation further increases the risk of metaplastic changes. Rectal squamous metaplasia without carcinoma has been occasionally reported in patients with ulcerative colitis (UC), and less so with Crohn's disease (CD).[1–8] We present 2 cases of rectal squamous metaplasia, one in a patient with long-standing CD and another in a patient with UC. As metaplasia might serve as a precursor to dysplasia and neoplasia, we also discuss dysplasia surveillance and the role of HPV and its vaccine in IBD.

CASE REPORT

Case 1: A 34-year-old man presented with nausea, vomiting, abdominal pain, and weight loss and was diagnosed with colonic CD in 2009. He did not respond to infliximab, adalimumab, certolizumab, and azathioprine. A colonoscopy in 2016 showed scattered inflammation throughout the colon and a rectal stricture with pathology from the rectum showing active colitis without metaplasia or dysplasia. He was started on vedolizumab (VDZ) and budesonide and went into clinical remission. In September 2019, a colonoscopy showed a rectal stricture at 10 cm with at least 2 to three 1–3 mm ulcers found proximal to and within the stricture. Biopsies from the stricture revealed chronic inflammation and squamous mucosa. The patient continued to be in clinical remission. An October 2021 colonoscopy showed mild stenosis in the rectosigmoid colon with an area of hypopigmented mucosa extending from rectosigmoid to the anus (Figure 1). Pathology from the hypopigmented tissue was consistent with rectal squamous metaplasia. Pathology from 3 different hypopigmented areas during a December 2021 sigmoidoscopy reaffirmed colonic mucosa with squamous metaplasia. The patient was recommended to undergo the HPV vaccine but declined. Repeat colonoscopy in December 2022 showed no rectal stricture and hypopigmented mucosa extending from the anus to 12 cm with multiple biopsies revealing squamous metaplasia. The patient self-discontinued VDZ in 2023 after being lost to follow-up for 1.5 years and remained in clinical remission. Continued surveillance colonoscopy was recommended, but the patient was again lost to follow-up.

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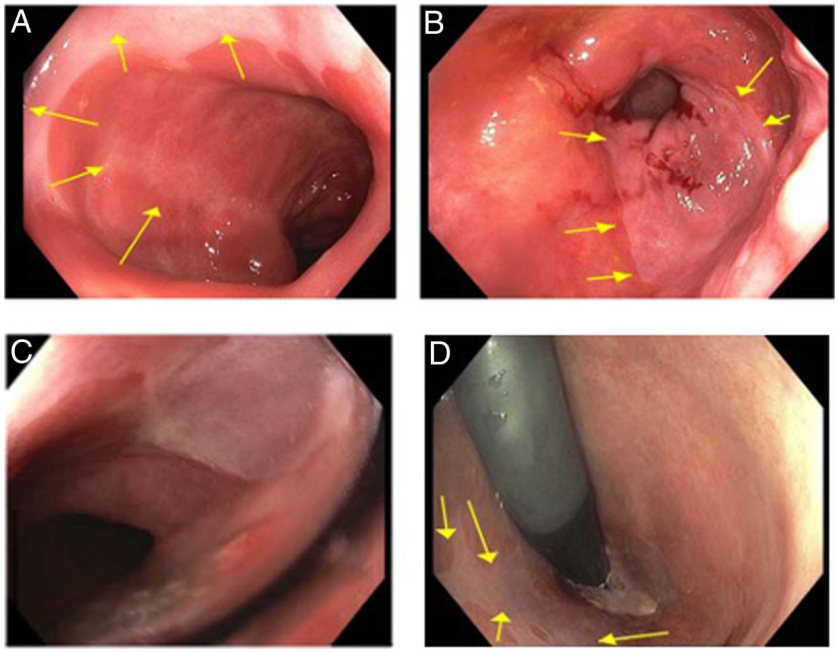

Figure 1. Endoscopic surveillance of squamous metaplasia in inflammatory bowel disease. (A) Salmon colored rectal mucosa and (B) hypopigmented region extending to the anus in 10/2021 colonoscopy (case 1, Crohn's disease). (C) Hypopigmented mucosa extending from the anus in 7/2022 sigmoidoscopy (case 2, ulcerative colitis). (D) Hypopigmented mucosa in the distal rectum with biopsies negative for metaplasia or dysplasia following human papilloma virus vaccination in 5/2024 sigmoidoscopy (case 2, ulcerative colitis).

Case 2: A 31-year-old woman presented with abdominal pain, tenesmus, and rectal bleeding and was diagnosed with UC in 2015. She did not respond to mesalamine, infliximab, and VDZ. She was started on tofacitinib in 2021 and went into clinical remission. A flexible sigmoidoscopy in July 2022 showed lack of haustral folds and decreased vascular markings from 0 to 20 cm as well as hypopigmented tongues of mucosa extending from 10 cm to 3 cm proximal to the anus with biopsies showing rectal squamous metaplasia (Figure 1). She was referred to gynecology and had a papanicolaou test with no findings of HPV. Follow-up colonoscopy in October 2023 revealed 4 inflammatory polyps at the rectosigmoid colon and sigmoid colon and decreased vascular pattern from 30 to 40 cm proximal to the anus but no evidence of hypopigmented mucosa in the rectum. She received the HPV vaccine in December 2023. Her most recent flexible sigmoidoscopy in May 2024 showed decreased mucosa vascular pattern in the descending colon and transverse colon and redemonstrated hypopigmented mucosa in the distal rectum with one of 3 distal rectal biopsies revealing colonic mucosa with mild chronic active colitis and marked reactive epithelium but no evidence of metaplasia or dysplasia (Figure 1).

DISCUSSION

Rectal squamous metaplasia in the setting of IBD is rare, even less common than rectal primary squamous cell carcinoma (SCC). Only few isolated case reports are found in the literature.[1–8] The exact pathogenesis of squamous metaplasia is not well defined and poorly understood. One proposed mechanism may be due to a reparative response from chronic mucosal injury and inflammatory damage.[1,7] For instance, several reported cases, including our 2 cases, demonstrate areas of squamous epithelium in the vicinity of colonic strictures and pseudopolyps, which support this.[2,4,6,7] Although squamous metaplasia is generally benign, there is concern in patients with IBD about the potential of malignant transformation, especially in the context of chronic inflammation and long-term immunosuppression. Cheng et al. described a case of SCC arising from an area of squamous metaplasia in the rectum in a patient with long-standing UC.[9] While our first patient self-discontinued VDZ and remained in clinical remission, it is unclear whether IBD therapies and/or remission status have any role in the progression or regression of rectal squamous metaplasia. This is an area that warrants further individualized study. However, owing to the potential risks of progression of metaplasia to dysplasia and carcinoma, patients with long-standing disease or those on advanced therapies should be closly monitored endoscopically. Although the frequency and approach to dysplasia surveillance in IBD patients with squamous metaplasia is unclear, it is nonetheless important to consider, particularly in areas of chronic inflammation.

Anal SCC is rare in IBD as the annual incidence rate of anal SCC is slightly elevated in UC and higher in CD compared with the general population.[10] Furthermore, anal SCC presents at an earlier age and is associated with worse outcomes in those with CD. HPV has been established as a risk factor for multiple cancers including anal SCC, as HPV infection of damaged keratinocytes by high-risk variants (e.g., HPV 16 and 18) leads to integration of oncogenes E6 and E7 in the host genome-

inducing carcinogenesis. Advanced therapies in IBD may be risk factors, as HPV 16 has been associated in 2 cases of rectal SCC in UC.[11,12] Owing to the rarity of anal SCC in IBD, no current guidelines in the United States exist for HPV prophylaxis in IBD. The European Crohn's and Colitis Organization recommends routine prophylactic HPV vaccination for both male and female patients with IBD through 26 years of age, and for older patients between 27 and 45 years of age to engage in shared clinical decision-making on vaccination.[13] After the HPV vaccination, our patient with UC had spontaneous resolution of squamous metaplasia, albeit there is a possibility of sampling error given that the hypopigmented mucosa persisted in sigmoidoscopy despite the absence of evidence for metaplasia or dysplasia on repeat rectal biopsies. Nevertheless, it is worthwhile to consider HPV prophylaxis in patients younger than 45 years for prevention of anal SCC in high-risk patients, including those with rectal squamous metaplasia. Ultimately, further studies are warranted to determine the frequency and approach to dysplasia surveillance in rectal squamous metaplasia, and whether HPV prophylaxis and close endoscopic monitoring in this subset of patients impact long-term outcomes.

DISCLOSURES

Author contributions: Conceptualization and Supervision: S. Taleban. Data collection: All authors. Drafting of the manuscript: All authors. Critical review of the manuscript: All authors. Approval of the final version of the manuscript: All authors. S. Taleban is the article guarantor.

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