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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Ulcerative Colitis or Not? A Case of Dysplasia, Gastrointestinal Bleeding, and Juvenile Polyposis in a 27-Year-Old Man

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ABSTRACT

Juvenile polyposis syndrome lies within the family of hamartomatous polyposis syndromes characterized by polyps that appear benign but harbor an increased risk of colorectal and gastric cancer. This 27-year-old man with severe ulcerative colitis was discovered to have concomitant juvenile polyposis syndrome during diagnostic workup for gastrointestinal bleeding. The implications of this rare association complicate both diagnostic and treatment modalities since both diseases confer an increased risk of cancer.

KEYWORDS: juvenile polyposis syndrome; dysplasia; ulcerative colitis; inflammatory bowel disease; hamartomatous polyps; juvenile polyps

INTRODUCTION

Juvenile polyposis syndrome (JPS) is an autosomal dominant condition with incomplete penetrance and an estimated worldwide incidence of 1 in 100,000. Up to 45% of individuals diagnosed with JPS have mutations in the *SMAD4* or *BMPR1A* genes.[1] The syndrome is diagnosed when 1 of 3 clinical criteria are met, ie, more than 5 juvenile polyps in the colon and rectum, juvenile polyps in other parts of the gastrointestinal tract, or any number of juvenile polyps and a positive family history.[2]

Given the high number of polyps, most patients are symptomatic by the age of 20 years. Rectal bleeding is the most common presenting symptom. Other symptoms include prolapse, abdominal pain, diarrhea, and anemia.[3] Our patient had a previous diagnosis of ulcerative colitis (UC) and was subsequently found with JPS.

A patient with UC and a rare undiagnosed underlying condition such as JPS presents with diagnostic difficulty as there is significant overlap in associated symptoms. Moreover, both conditions are independently associated with increased risk of cancer. In UC, the duration and extent of inflammation have been associated with increased risk of colorectal cancer (CRC).[4,5] Specifically, mucosal inflammation evidenced on histologic and endoscopic examination were associated with an increased risk of colorectal neoplasia.[5]

For individuals with JPS, the mean age of diagnosis of CRC is 44 years and the cumulative lifetime risk is 38.7%. In addition, JPS confers a lifetime risk of gastric and duodenal cancer of 11%–20%.[6,7] Those with UC have a 2.4 fold increased risk of developing CRC.[8] The cumulative incidence of CRC was 2.5% after 20 years and 7.6% after 30 years of disease.[9] However, to date, there have been no studies to quantify the risk of CRC in patients with both JPS and UC.

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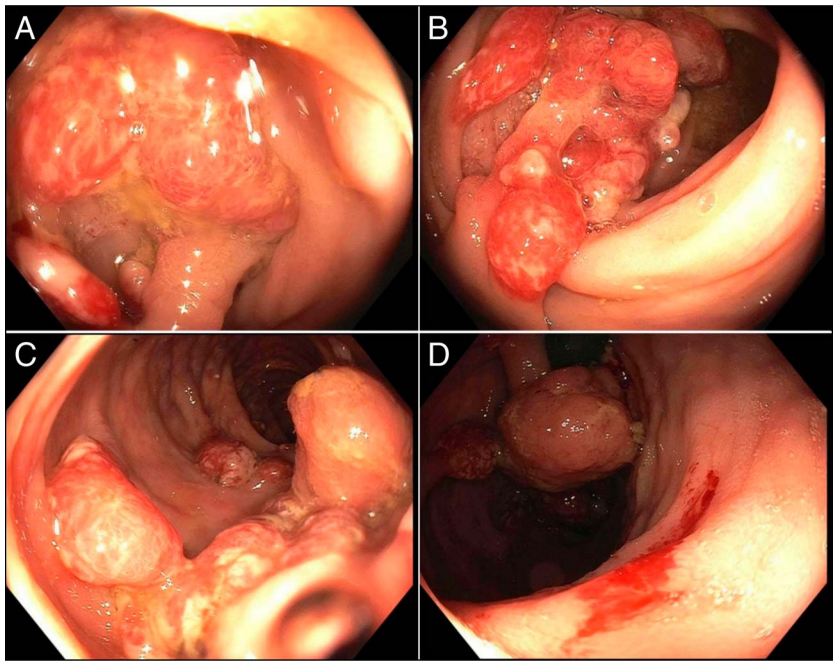

Figure 1. Colonoscopy showing multiple polyps in the (A) ascending, (B) descending, and (C) sigmoid colon. (D) Another view of single polyp in the sigmoid colon.

CASE REPORT

A 27-year-old man with a medical history of UC diagnosed in 2011. He discontinued medications due to insurance costs and then was admitted to the hospital for severe anemia, shortness of breath, fatigue, and maroon-colored stools up to 9 times a day. He was found to be tachycardic to 105 bpm and normotensive with a blood pressure of 120/67.

His hemoglobin was 5 g/dL, ferritin was 1 ng/mL, and iron was 14 μg/dL. Computed tomography (CT) angiography revealed mild bowel wall thickening of the rectosigmoid colon and concern for active extravasation. He received a total of 3 units packed red blood cells and intravenous iron supplementation. His fecal calprotectin was 367 μg/g. A carcinoembryonic antigen was within normal limits. Subsequent upper endoscopy revealed 3 gastric polyps which were resected. Colonoscopy revealed numerous hamartomatous polyps throughout the entire colon, the largest measuring 80 mm (Figure 1). Segmental mucosal biopsies were performed, and polypectomy was performed on several large representative polyps. Histologically, the stomach polyp was both hamartomatous and hyperplastic. The colon polyps were juvenile and inflammatory polyps with dysplasia ranging from indeterminate in the ascending colon, low grade in the descending colon, and high grade in the rectal biopsy with p53 null expression and loss of *SMAD4* expression throughout. Mucosal biopsies from the left colon and rectum revealed hyperplastic change but no inflammation or colitis.

Following colonoscopy, the patient was deemed stable for discharge with a short interval CT scan recommended while awaiting biopsy results to assess for new inflammation as the patient continued to experience hematochezia.

In the initial 2011 colonoscopy, when he was first evaluated for UC, multiple polyps were seen throughout the gastrointestinal tract, including the cecum and sigmoid areas. Multiple biopsies resulted as inflamed hamartomatous polyps; however, no dysplasia was seen at that time. Repeat colonoscopy in 2013 and 2014 showed no evidence of inflammation or dysplasia near the terminal ileum; however, there were persistent inflamed hamartomatous polyps at the cecum and splenic flexure. In colonic mucosa, mucosal biopsies revealed crypt architectural distortion, advanced chronic active inflammation, and granulation without dysplasia. Prior esophagogastroduodenoscopy performed in 2011 did not reveal any polyps, only nonspecific gastritis and duodenitis. Patient was started on mesalamine afterward in 2016 which was stopped in 2019 due to lack of insurance coverage. Since 2016, in the interim, he has had multiple bowel movements daily but without hematochezia.

Magnetic resonance imaging of the rectum demonstrated vascular engorgement and heterogeneous enhancement, consistent with active inflammation/colitis in addition to a primary 4.9 × 5.9 × 4.1 cm polypoid T3a tumor with a superior rectal lymph node, although none of the biopsies confirmed carcinoma (Figure 2).

The patient underwent a proctocolectomy with ileal pouch-anal anastomosis and diverting loop ileostomy. Owing to the presence of dysplasia in the rectum, a mucosectomy and handsewn anastomosis was performed. The colectomy revealed numerous hamartomatous polyps, the largest polyp measuring 6.5 × 4.3 × 4.0 cm with pathology revealing varying low-grade and focal

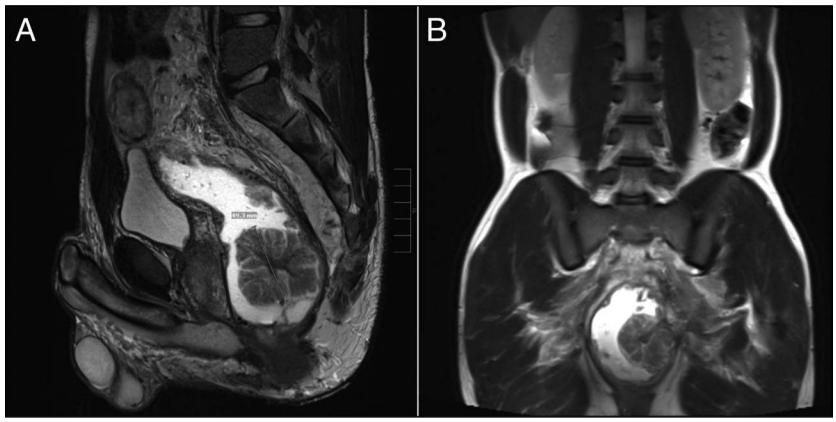

Figure 2. Magnetic resonance imaging of mass in (A) sagittal and (B) coronal views. Size of mass: 4.9 × 5.9 × 4.1 cm (Craniocaudal × Anteroposteior × Transverse).

high-grade dysplasia (Figure 3). Immunohistochemical stain was positive for desmin and P53 null expression. Given the absence of carcinoma in the rectum, a loop ileostomy reversal was planned.

DISCUSSION

Juvenile polyps may be pedunculated or sessile, containing dilated crypts filled with mucus, neutrophils, and a lamina propria with edema and inflammatory cells with surface erosions. These structural abnormalities lead to gastrointestinal bleeding and resultant anemia.[10]

Both inflammatory bowel disease (IBD) and JPS can present with anemia, fever, abdominal pain, diarrhea, and hematochezia. Histologically, inflammatory polyps and pseudopolyps, seen more frequently in IBD, can have granulation tissue-like stroma, which makes it difficult to distinguish from juvenile polyps.[11]

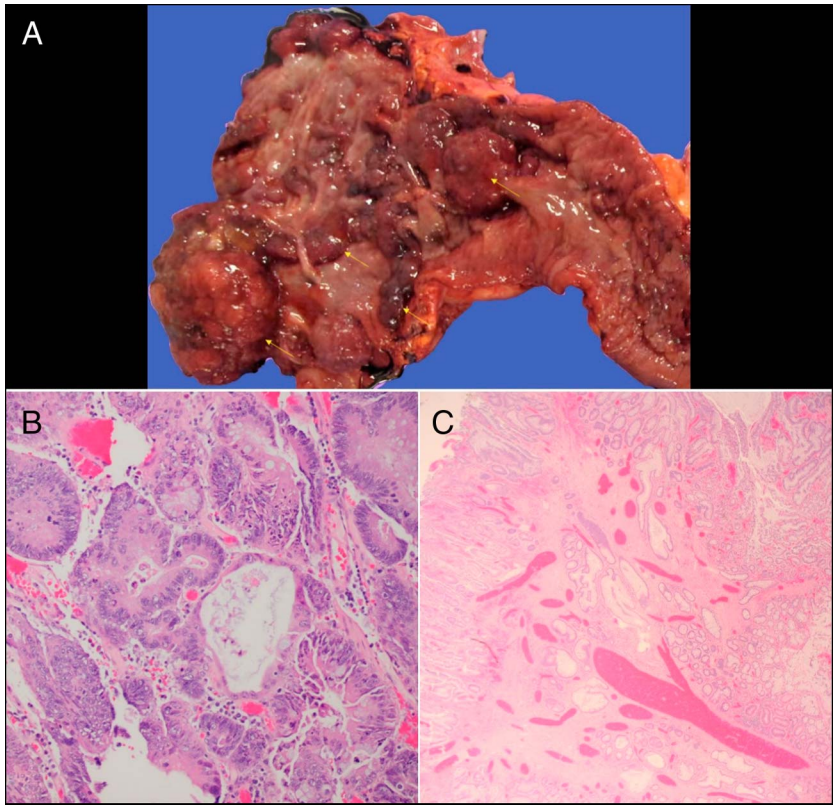

Figure 3. (A) Gross specimen with yellow arrows pointing at numerous tan-brown, pedunculated, and sessile polyps located diffusely throughout the colonic mucosa, with largest a 6.5 × 4.3 × 4.0 cm polypoid mass within the rectum, 1.5 cm from the distal margin. (B) High power (40×) of focal high-grade dysplasia. (C) Low power (4×) of the largest polyp with vascular core.

Although solitary juvenile polyps have low malignant potential, patients with JPS carry an increased lifetime risk of 50% of multiple types of gastrointestinal cancer.[4]

To our knowledge, there have only been 3 case reports discussing simultaneous IBD and JPS.[12,13] Although several cases describe UC with solitary juvenile polyps, there are no direct associations between juvenile polyps and IBD.[11,14]

UC cells release reactive oxygen and nitrogen species, resulting in DNA damage and inaccuracies in intrinsic repairs of coding and regulatory genetic sequences.[15] One proposed mechanism of cancer pathogenesis in JPS is the landscaper mechanism, which postulates that genetic alterations at the chromosomal level results in cancer as a result of an abnormal stroma environment.[16]

The average median age of CRC in JPS is reported at the age of 41 years,[17] yet our patient aged 27 years exhibited evidence of focal high-grade dysplasia. We initially hypothesized that the inflammation from uncontrolled UC was contributory to the high-grade dysplasia; however, not only was there limited inflammation observed on direct visualization, but mucosal biopsies from the left colon and rectum also revealed only hyperplastic change in the absence of inflammation. Biopsies of the polyps themselves were juvenile and inflammatory histologically. This is likely also true for the CT findings after discharge describing left-sided colitis; the inflammatory burden that was observed on imaging was secondary to wall thickening from significant polyposis burden rather than inflammatory colitis.

Nevertheless, further investigation is needed to determine if IBD can alter the regulatory genes of these hamartomatous polyps, leading to an accelerated progression to malignancy. The increased cancer risk in JPS may require shorter time intervals of surveillance and anti-inflammatory therapy.

DISCLOSURES

Author contributions: T. She, S. Ren, and S. Katz made substantial contributions to the conception or design of the work and interpretation of data for the work. T. She drafted the work, revising it critically for important intellectual content along with the help of S. Ren, H. He and M. Symer. Images created by T. She. All Authors reviewed all content and made several revisions and edits for intellectual and grammar content. S. Katz is the article guarantor. Final approval of the version to be published was reviewed by all authors.

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