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A Case Report with the Very Rare Association of KS with IBD

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ABSTRACT

This is a unique case characterizing the very rare association of KS with IBD. The presence of KS, incidentally identified in submucosal nodules adjacent to a polypoid mass in the terminal ileum of a Crohn's patient, highlights the additional importance of submucosal intestinal biopsies to yield an accurate diagnosis.10,11 In the absence of physical findings such as skin lesions, a careful histologic evaluation is needed to exclude this rare complication in patients with inflammatory bowel disease on prolonged immunosuppressive therapy

KEYWORDS

Kaposi's sarcoma, Crohn's disease, HIV, inflammatory bowel disease, ulcerative colitis, Kaposi sarcoma–associated.

1. Case Presentation

A 21-year-old HIV-negative Ethiopian male with IgA nephropathy, diagnosed by kidney biopsy in 2011 and treated with prednisone, presented in July 2014 with several months of postprandial abdominal pain, anorexia, and weight loss, without associated diarrhea or rectal bleeding. He did not have any other significant personal medical history. His family history was significant for Crohn's disease in his younger brother. An abdominal and pelvic computed tomographic scan from an outside hospital revealed a 10-cm segment of inflammatory changes within the terminal ileum and cecum concerning for an inflammatory or infectious process. A follow-up colonoscopy and esophagogastroduodenoscopy with biopsies performed in August of 2014 showed involvement of the ileocecal valve and cecum and granulomatous inflammation of the stomach. No mass was radiographically appreciated in the bowel at that time. These endoscopic and histologic findings were in keeping with Crohn's disease. In light of the clinical suspicion for Crohn's disease, his immunosuppression with prednisone was continued to treat his IBD symptoms.

In November 2014, the patient was hospitalized for a partial small bowel obstruction. Serologic testing confirmed Clostridium difficile colitis, which resolved with antibiotic therapy. He subsequently returned to the hospital in December 2014 with a persistent partial small bowel obstruction and was given one dose of Infliximab to stave off surgical resection. Unfortunately, he required 2 additional hospitalizations in early and late January 2015 for the same symptoms. Despite 2 additional doses of infliximab, the decision was made to proceed with a laparoscopicassisted partial colectomy with ileocolostomy for a highgrade small bowel

obstruction secondary to Crohn's disease. Laparoscopy revealed markedly distended loops of small bowel in the lower abdomen with inflammation in the terminal ileum, cecum, and a portion of the ascending colon. The terminal ileum appeared dilated and edematous with a focal area of narrowing compatible with an obstruction.

The surgical resection specimen comprised of an 8.5cm segment of terminal ileum and a 29.0-cm portion of cecum and ascending colon with an attached appendix. The mucosal surface of the terminal ileum was notable for a 3.8-cm polypoid mass, proximal to the ileocecal valve, and the ileal wall adjacent to the polyp was markedly thickened.

Histologic examination of the nonpolypoid small bowel mucosa revealed a background of moderately to severely active Crohn's disease with transmural inflammation, fissure formation, aphthous ulceration, and mucosal pseudopyloric metaplasia (Figure 1A and B) involving the terminal ileum and extending up to the ileocecal valve.

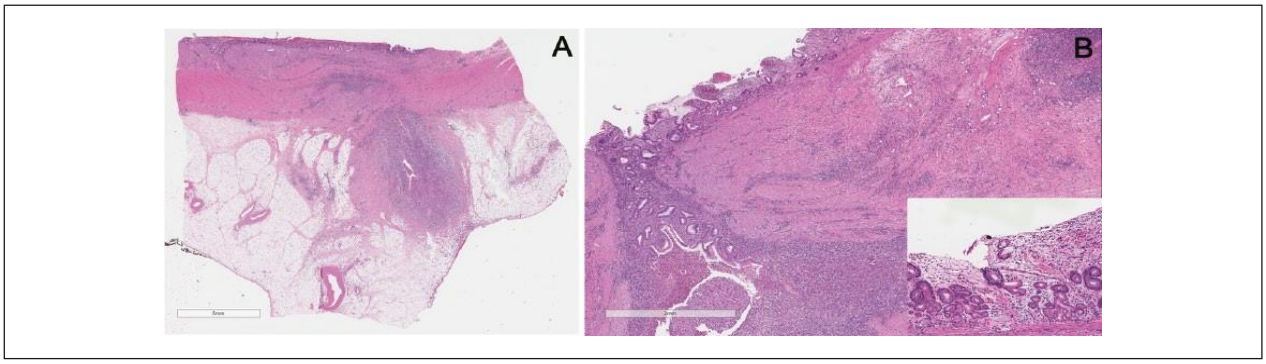

Figure 1. Crohn's disease involving nonpolypoid terminal ileal mucosa.

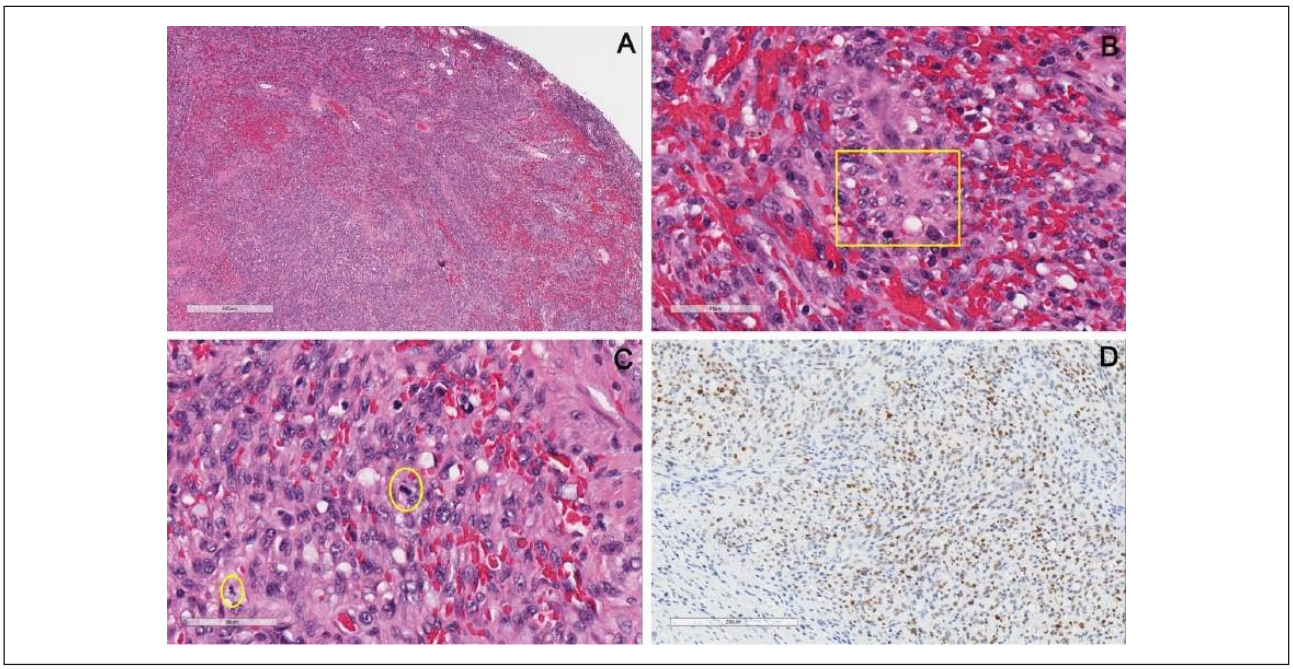

Figure 2. Submucosal nodules adjacent to polypoid mass.

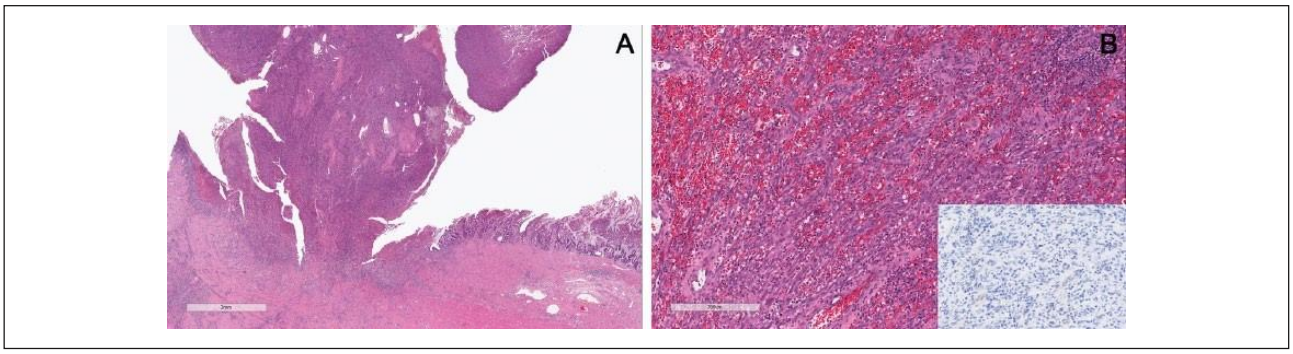

Figure 3. A 3.8-cm polypoid mass in terminal ileum.

Table 1. Published cases of colorectal Kaposi's sarcoma in known and suspected hiv-negative patients with crohn's disease.

First Author and Year	HHV-8 Status	Skin Lesions	Immunosuppression Therapy for Crohn's Disease	HIV Status	Surgery/Biopsy	Medical Management of Kaposi's Sarcoma
Koop, 1987	NR	Yes	Prednisone	Negative	Small bowel resection	None
Puy-Montbrun, 1991	NR	No	Steroids, azathioprine	Negative	Colonic biopsies	Discontinuation of immunosuppressive therapy
Cohen, 2001	NR	No	Prednisone	Negative	Ileocolic resections, proctosigmoidectomy	Discontinuation of immunosuppressive therapy
Present case	IHC of colonic sample: Negative Serology: Negative	No	Prednisone, infliximab	Negative	Partial colectomy with ileocolostomy	Discontinuation of immunosuppressive therapy

2. Discussion and Conclusion

Here we report the fourth case of intestinal KS associated with Crohn's disease in the setting of prolonged immunosuppression in an HIV-negative patient. Table 1 summarizes features from the 3 previously documented cases of KS-associated Crohn's disease reported in the English literature along with the features of the current case. There have been 12 documented cases of colorectal KS arising in a background of ulcerative colitis in HIV-negative patients.

Histologic examination of this case highlighted some interesting features of KS. While, the submucosal nodules in the ileum were unequivocally confirmed to be lesions of KS, HHV-8 staining was notably absent in sections from the adjoining 3.8-cm polypoid mass. Repeat staining on multiple blocks of paraffin-embedded tissue yielded the same result, excluding the possibility of technical failure. We postulate that the lack of HHV-8 staining in the polypoid mass highlights the unique mechanisms of KSHV-induced oncogenesis. KSHV uses both latent transcripts and lytic proteins, and the interplay between these two entities induces oncogenesis. Latent viral transcripts such as latency-associated nuclear antigen (LANA), viral cyclin, viral FLICE inhibitory protein (v-FLIP), and viral-encoded microRNAs influence growth and proliferative signals, evade apoptosis, and promote proangiogenic and inflammatory signals.24 However, latent transcripts alone cannot transform endothelial cells, and a small proportion of infected cells undergo lytic replication leading to the development of a mature virus and cell lysis. Lytic proteins include K1, viral interferon response factors (vIRFs), vIL-6, viral-encoded chemokines (vCCLs), and viral G protein-coupled receptor (vGPCR). While lytic viral gene expression is more involved Nonetheless, in this patient, we favor transplant-associated/iatrogenic KS in the context of long-standing immunosuppressive therapy. He only presented with the lesions of KS, after years of

immunosuppressive therapy for IgA nephropathy and Crohn's disease, and was never found to have any other features of endemic KS such as lymphadenopathy, skin lesions, or other visceral symptoms prior to his diagnosis of Crohn's disease. Additionally, he did not manifest with other lesions of KS in the short available postoperative time frame. His postoperative serologic testing for HHV-8 DNA was also negative. This may be explained if he had a low postoperative viral load, which can correlate with low/subclinical KSHV-specific antibody titers. The low viral load could therefore have been missed by serologic testing, giving the false impression of the absence of a systemic HHV-8 infection.24

IgA nephropathy is the most common form of glomerulonephritis in children, adolescents, and adults worldwide. The association between IgA nephropathy and IBD is known, with several reported cases of IgA nephropathy in patients with Crohn's disease.29-34 While the exact mechanism of this association has not been proven, one hypothesis suggests a link between increased intestinal mucosal permeability and the influx of food and bacterial antigens in Crohn's disease resulting in the formation of immune complexes that get trapped in the glomerular mesangium.30,35 In most patients, therapy for the intestinal disease also results in improvement of the renal manifestations.

In summary, this is a unique case characterizing the very rare association of KS with IBD. The presence of KS, incidentally identified in submucosal nodules adjacent to a polypoid mass in the terminal ileum of a Crohn's patient, highlights the additional importance of submucosal intestinal biopsies to yield an accurate diagnosis.10,11 In the absence of physical findings such as skin lesions, a careful histologic evaluation is needed to exclude this rare complication in patients with inflammatory bowel disease on prolonged immunosuppressive therapy.

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