

# Protein-Losing Enteropathy as the Initial Presentation of Gastrointestinal Kaposi's Sarcoma in Previously Undiagnosed HIV Disease

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## ABSTRACT

Occult Kaposi's sarcoma (KS) presenting as a protein-losing gastroenteropathy is a rare occurrence. We report the case of a 23-year-old male presenting with leg bilateral swelling and epigastric discomfort. A workup revealed human immunodeficiency virus seropositivity, hypoalbuminemia, and small bowel wall thickening on computed tomography scan. Initially there were no mucosal or cutaneous lesions visible. An upper endoscopy demonstrated subepithelial lesions with a reddish appearance involving the palate, cardia, duodenum, and jejunum, consistent with KS. Gastrointestinal involvement is the most common extracutaneous site of KS and is found in about half of the acquired immune deficiency syndrome (AIDS)-related cases. However, only one out of 5 patients are symptomatic in the absence of skin lesions. Antiretroviral therapy along with anthracycline chemotherapy must be promptly initiated to improve chances of survival.

## INTRODUCTION

Kaposi's sarcoma (KS) is an angioproliferative malignancy in which human herpesvirus-8 (HHV-8) is isolated in more than 90% of the lesions. HHV-8 transmission occurs through saliva as well as sexual contact, similar to other herpesviruses.<sup>1</sup> The most aggressive form is seen in acquired immune deficiency syndrome (AIDS). Visceral involvement of KS compromises the gastrointestinal tract leading to mucosal dysfunction and lymphatic congestion. In turn, hypoalbuminemia and systemic edema develop, an entity known as protein-losing enteropathy (PLE).<sup>2</sup> We present the case of PLE as the initial presentation of human immunodeficiency virus (HIV) caused by intestinal KS, which was diagnosed by gastrointestinal endoscopy.

## CASE REPORT

A 23-year-old African-American male presented with 2 weeks of progressive leg swelling, rapid weight gain, vague epigastric discomfort associated with meals, and one episode of blood in stool. He denied the presence of any associated chest pain, dysphagia, odynophagia, cough, or fevers. There was no past medical or surgical history. He smoked marijuana daily but denied other illicit drug use, alcohol, or tobacco. He had sex with men, and the family history was unknown when he was adopted. On presentation, his blood pressure was 137/94 mm Hg; heart rate 93 beats/min; respiratory rate 18/min; oxygen saturation of 97% on room air; and temperature of 98.1°F. He was in mild distress. Ear, nose, and throat examination revealed a purple lesion on the left lateral posterior pharyngeal wall. Heart and lung examination were unremarkable. Abdominal examination was pertinent for a diffuse tenderness without peritoneal signs, greater in the periumbilical area. Extremities revealed non-pitting edema extending up to his thighs. No cutaneous or mucosal lesions were seen.

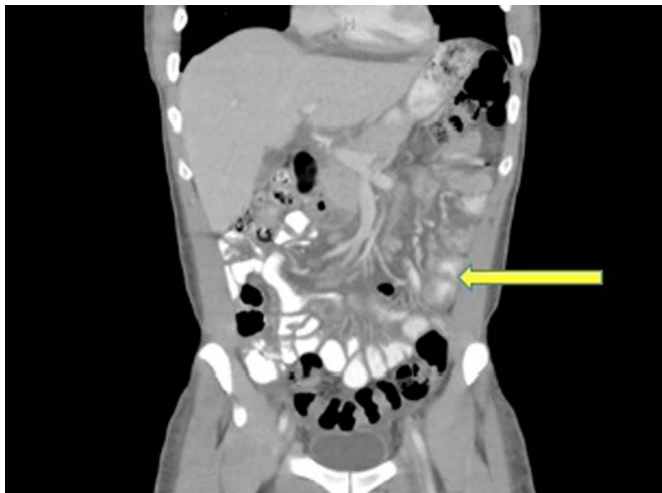
Laboratory data revealed an albumin of 1.3 g/dL, a white blood cell count of 3.8 K/ $\mu$ L, antibodies to HIV-I, viral load of 123,863 copies, CD4 count of 6 cells/ $\mu$ L, iron-deficiency anemia, and low B12. A 24-hour urine test was negative for proteinuria. Stool test

was negative for Cytomegalovirus, *Clostridium difficile*, ova, parasite, and acid-fast bacilli. Fecal  $\alpha$ -1 antitrypsin concentration of 271 mg/dL was used as a surrogate marker of  $\alpha$ -1 antitrypsin clearance. Thyroid, kidney functions, and liver enzymes were normal. Neither celiac or *Helicobacter pylori* testing was performed.

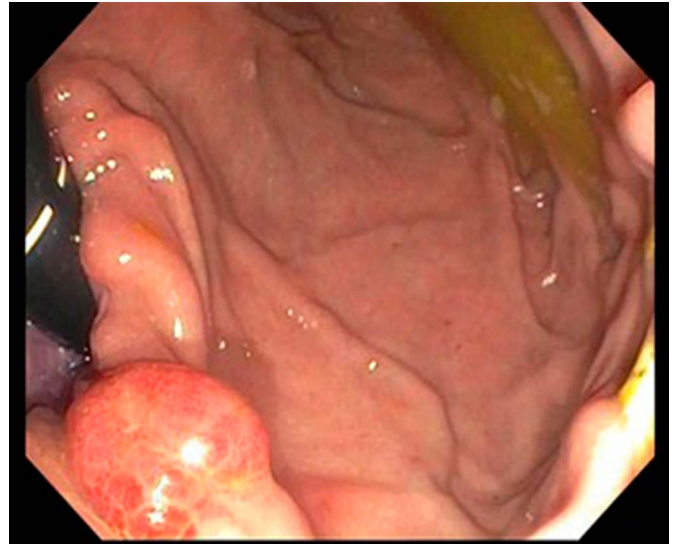
Abdomen CT scan revealed diffuse small bowel wall thickening, bilateral pleural effusions, and ascites (Figure 1). The ascites fluid was clear and the serum-ascites albumin gradient was 0.3 g/dL. Transthoracic echography revealed a normal ejection fraction. On upper endoscopy multiple 2–3 cm patches of subepithelial lesions with a reddish appearance were visualized throughout the soft palate, stomach, duodenum, and jejunum (Figures 2 and 3). The pathology was consistent with KS, and positive HHV-8 nuclear staining was detected in the nuclei of the spindle cells and endothelial cells (Figures 4 and 5). Over the following week, he developed oral and cutaneous lesions. Our patient was subsequently started on bictegrovir, emtricitabine, tenofovir, and doxorubicin liposomal infusion every 21 days. At 4-month follow-up, his viral load had decreased, the diarrhea had resolved, and the cutaneous and oral lesions had flattened. However, he had developed a chylothorax and was referred for thoracic duct embolization.

## DISCUSSION

The presentation of KS is variable and ranges from indolent, solely dermatologic manifestations, to fulminant, with extensive visceral involvement of lungs, gastrointestinal tract, and less commonly liver, spleen, heart, and kidney.<sup>1</sup> Four variants have been described in medical literature: The first variant is the classical KS, which mainly affects elderly men of Mediterranean or eastern European descent. Endemic KS is a more aggressive form that occurs in men in Eastern and Central Africa with a lympho-adenopathic subvariant found in children. The



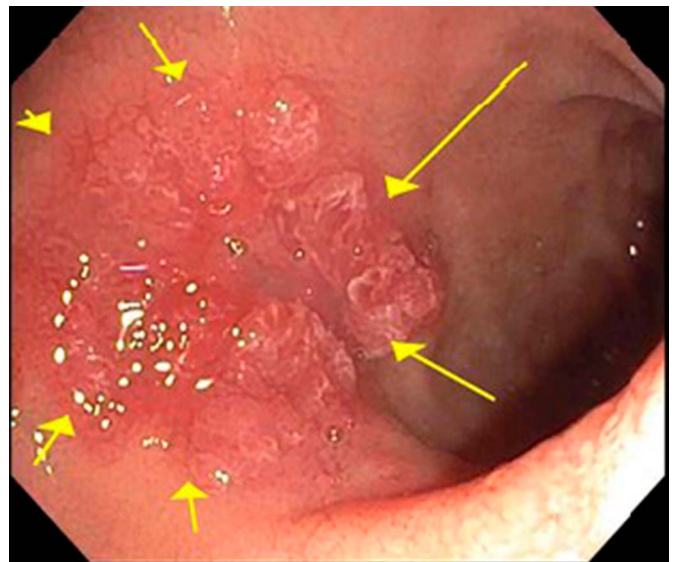
**Figure 1.** Computed tomography scan of abdomen and pelvis with contrast showing moderate to severe circumferential mucosal thickening of the jejunum (arrow), ascites, and mesenteric adenopathy.



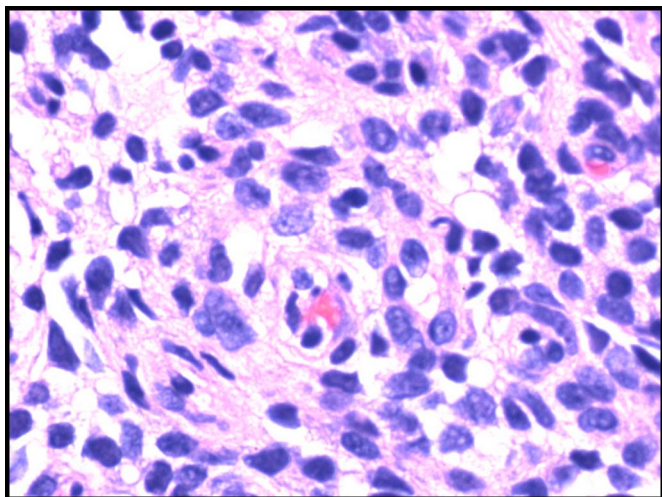
**Figure 2.** Gastric cardia lesion.

iatrogenic variant is a consequence of immunosuppressive therapy following organ transplant. Lastly, the most aggressive clinical variant is found in AIDS patients and frequently resolves after initiating highly active antiretroviral therapy (HAART).<sup>2,3</sup>

KS, along with cervical cancer and certain high-grade non-Hodgkin lymphoma, are considered AIDS-defining cancers, as they mark the onset of clinically relevant immunosuppression and arise through the loss of immunologic control of oncogenic viral infections.<sup>4</sup> Similar to other DNA oncogenic viruses, HHV-8 expresses viral genes that directly or indirectly down-regulate p53 protein functions, including DNA repair, cycle cell arrest, and apoptosis in response to a variety of stimuli such as stress signals, genotoxic agents, and hypoxia and oncogene activation.<sup>1,5</sup> Studies have demonstrated that homosexual men,



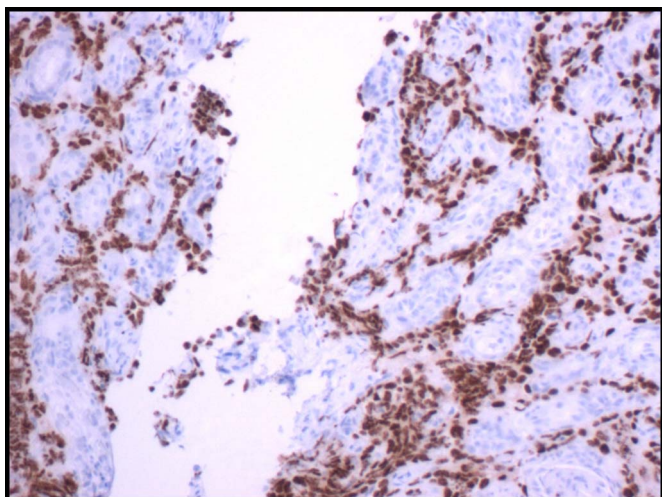
**Figure 3.** Duodenal bulb lesion.



**Figure 4.** Biopsy of duodenum and jejunum with hematoxylin and eosin stain showing atypical vascular lesion with increased vascular structure, spindle cell proliferation and extravasated red blood cells, involving small bowel mucosa consistent with Kaposi sarcoma.

regardless of their HIV serostatus, have a higher rate of KS than the general male population.<sup>6</sup>

Although KS is known to have a viral etiology, the pathogenesis is multifactorial and ultimately, it is immune dysfunction and genetic predisposition that will lead to oncogenesis. Gastrointestinal involvement is the most common extracutaneous site and is found in about half of AIDS-related cases. Still, only 1 out of 5 patients are symptomatic without the presence of skin lesions. Endoscopic evaluation is not recommended in asymptomatic patients; however, it is reasonable in homosexual men with a low CD4 count (<100 cells/ $\mu$ L) even without cutaneous KS.<sup>7-9</sup> The most common presentations are abdominal pain, nausea, diarrhea, and iron-deficiency anemia. Obstruction and perforation are less common. Very rarely does a patient present with PLE.<sup>1,10,11</sup>



**Figure 5.** Human herpesvirus-8 nuclear staining positive in the nuclei of the spindle cells and endothelial cells from jejunum.

The first mention of PLE due to intestinal KS in medical literature was in 1987.<sup>12</sup> In 1989, Bouhnik et al<sup>2</sup> discussed the importance of investigating hypoalbuminemia in AIDS patients, as there is a possibility that this is the only sign of otherwise symptomless intestinal KS. Nevertheless, none of the previous reported cases, to our knowledge, developed PLE as the initial presentation of AIDS caused by KS. As seen in inflammatory bowel disease and intestinal lymphoma, PLE in KS results from mucosal ulcerative changes and inflammation, leading to exudation and loss of absorption. Mesenteric lymphatic obstruction and congestion might also play a role in the pathogenesis of PLE in KS.<sup>13,14</sup> Treatment is directed at the underlying cause, HIV, with HAART as the initial step. In cases with visceral involvement and rapid progression of KS, anthracycline chemotherapy is indicated with pegylated liposomal doxorubicin or liposomal daunorubicin being recommended as first-line agents.<sup>15,16</sup>

Gastrointestinal symptoms in HIV-positive patients with low CD4 count warrant prompt imaging and luminal evaluation. Hypoalbuminemia is seen frequently in HIV patients; however, severe cases associated with anasarca would suggest underlying small intestine pathology. Intestinal KS in the absence of skin involvement is uncommon but should be considered in HIV patients presented with prominent intestinal symptoms. This entity and the risk of potential gastrointestinal bleed post biopsy of this highly vascular lesions should be recognized by the endoscopist. HAART therapy along with chemotherapy should be initiated to improve the clinical outcome.

## DISCLOSURES

Author contributions: All authors discussed the medical literature. D. Curras-Martin presented the idea. A. Copca-Alvarez, N. Campbell and D. Curras-Martin wrote the manuscript with input from all authors. MA Hossain is the article guarantor.

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