



Primary Effusion Lymphoma: Small Bowel Recurrence After Stem Cell Transplant

Sarah Mushtaq, MD¹, Sabrina Prabakaran, MD¹, Maher Elharake, MD¹, Sayeef Mirza, MD, PhD¹, Adharsh Ravindran, MD², Rawan Faramand, MD³, and Lubomir Sokol, MD, PhD⁴

¹Department of Internal Medicine, University of South Florida, Tampa, FL

²Department of Internal Medicine, University of Buffalo, NY

³Department of Hematology and Oncology, Moffitt Cancer Center, Tampa, FL

⁴Department of Malignant Hematology, Moffitt Cancer Center, Tampa, FL

ABSTRACT

Primary effusion lymphoma (PEL) is a rare AIDS-associated non-Hodgkin lymphoma, growing in the serous body cavities as a lymphomatous effusion. The endoscopic features of PEL can mimic Kaposi sarcoma (KS). We present a case where PEL presented as small intestinal masses which had a similar macroscopic appearance to KS. Endoscopic evaluation was used with biopsies which confirmed the diagnosis of PEL. PEL is a differential of gastrointestinal KS. Accurate diagnosis is crucial for prognostication in these patients. Our case emphasizes that PEL presenting as intestinal tumors can mimic KS macroscopically. Although treatment for PEL and KS includes standard chemotherapy with concurrent antiretroviral therapy, early detection of PEL can improve overall survival in these patients.

INTRODUCTION

Primary effusion lymphoma (PEL) is a form of AIDS-associated non-Hodgkin lymphoma related to human herpesvirus-8 (HHV-8) with predilection for body cavities.^{1,2} PEL can present with masses in the gastrointestinal (GI) tract, lung, central nervous system, or skin.^{3,4} Patients with PEL involving more body cavities have decreased median overall survival of 4 months compared with 18 months in patients with only 1 cavity involved.⁵ In another study, chemotherapy extended survival from 6 to 10 months.⁶ Therefore, early detection and initiating treatment may increase survival in these patients. Kaposi sarcoma (KS) is a vascular tumor associated with HHV-8. The GI tract is the most common area of visceral involvement, and it is possible to present with GI lesions in the absence of cutaneous involvement.⁷ KS-associated herpesvirus-positive solid lymphomas can present with severe systemic symptoms, have GI manifestations, and may be similar to that of PEL.⁸ Cases of KS and PEL involvement of the GI tract are diagnosed by histopathological and immunohistochemistry investigation. Immunohistochemistry for KS and PEL differs. However, they both involve HHV-8. Endoscopic evaluation for PEL is not well characterized. Previous endoscopic evaluation describes KS lesions as red or purple lesions which can be nodular or flat maculopapular lesions.⁷ As these lesions grow, complications such as bleeding, intestinal or biliary obstruction, abdominal pain, perforations, intussusception, protein-losing enteropathy, and diarrhea can arise.⁹ Endoscopic biopsy using hematoxylin and eosin staining, HHV-8 staining, and lymphatic and blood vessel endothelial cell markers has shown high accuracy, which is increased with endoscopic tumor staging.⁹

CASE REPORT

A 39-year-old man with no medical history was diagnosed with AIDS after presenting to his physician's office with purple skin lesions (clinically consistent with KS) and CD4 count of 58. Later, he presented to the emergency department with fever, weight loss, chest pain, and difficulty breathing. Vital signs demonstrated fever and tachycardia. Cardiac work-up was negative. Thoracic computed tomography showed pericardial effusion and pleural effusions. Thoracentesis studies revealed malignant pleural effusion, and immunohistochemistry was consistent with PEL. The patient was placed on highly active antiretroviral therapy and received 6

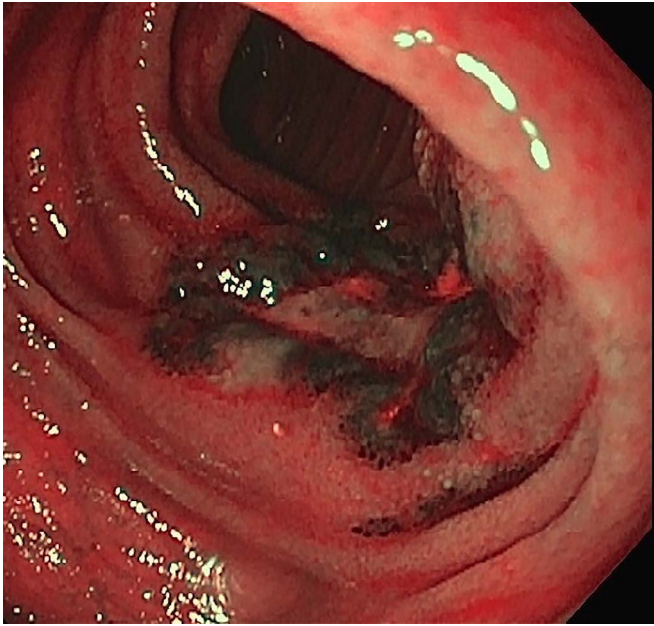


Figure 1. Endoscopic image with small bowel stricture at 300 cm from the incisor. The mass appears hard, friable, and erythematous.

cycles of dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), achieved complete remission, and proceeded to autologous hematopoietic stem cell transplant 6 months later.

Seven months after the transplant, our patient presented to the emergency department for fever and bloody mucus-filled loose bowel movements. Vital signs demonstrated fever, tachycardia, and hypotension. He was found to have KS skin lesions with an otherwise normal physical examination. Laboratory evaluation was significant for hemoglobin of 10.9 g/dL, white blood cells

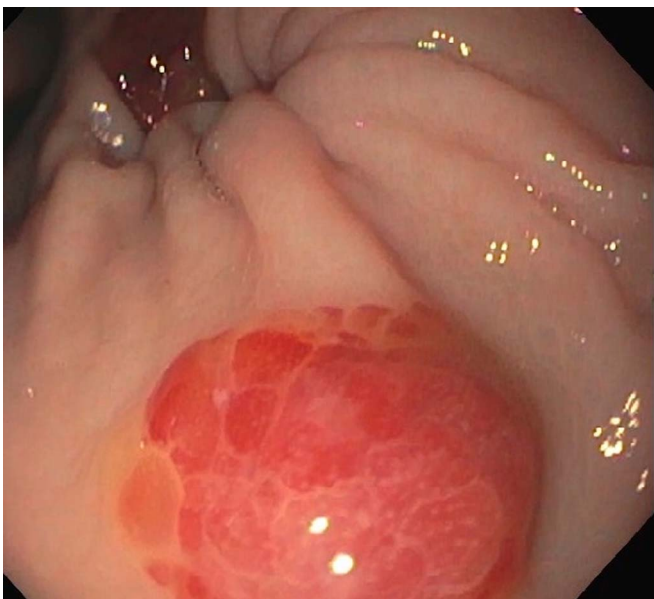


Figure 2. Endoscopic image of gastric antral lesion that appears erythematous and consistent with Kaposi sarcoma.



Figure 3. A 2-cm mass that extended submucosally was found in the lower third of the esophagus, 35 cm from the incisors. The mass involved one-half of the lumen circumference and was partially obstructive.

$4.26 \times 10^3/\mu\text{L}$, and CD4 count $131/\mu\text{L}$. Abdominal and pelvic computed tomography demonstrated a circumferential small bowel mass measuring $7.9 \times 4.4 \times 4.2$ cm causing a high-grade partial small bowel obstruction. Single balloon enteroscopy revealed hard, friable, erythematous masses at 200, 250, and 300 cm, as well as in the antrum, body, and fundus of the stomach (Figures 1 and 2). All lesions had appearances consistent with KS. Biopsies revealed recurrence of PEL with lymphoma cells strongly immunoreactive for HHV-8, MUM-1, and EBER and negative for pankeratin, CD117, S-100, and desmin. Given multiple GI lesions and a lack of a complete bowel obstruction, he was managed medically. Repeat esophagogastroduodenoscopy

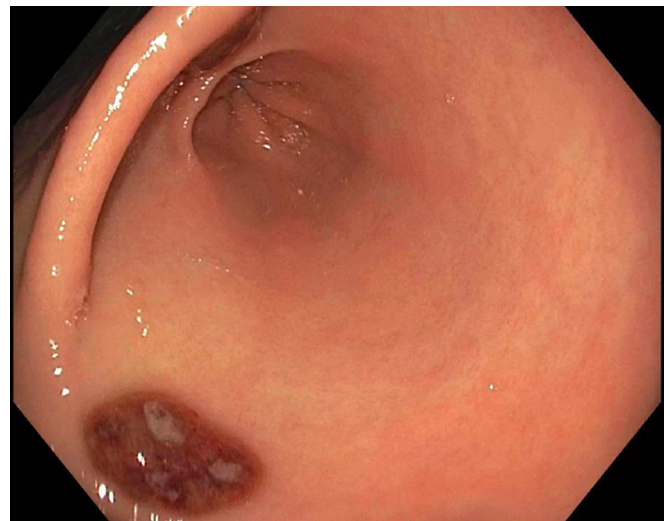


Figure 4. Multiple medium-sized, infiltrative smooth masses with no bleeding or stigmata of recent bleeding were found in the gastric body and the gastric antrum. The masses were 10–15 mm. These were seen on our previous endoscopy.

noted a partially obstructing mucosal mass in the lower third of the esophagus, gastric tumors in the body and antrum, and a malignant duodenal mass (previously biopsied and consistent with lymphoma) (Figures 3 and 4). He started a salvage chemotherapeutic regimen with ifosfamide, carboplatin, and etoposide, and gemcitabine and oxaliplatin that he tolerated poorly. Unfortunately, the patient died 15 months after the initial diagnosis.

DISCUSSION

KS is an angioproliferative neoplasm which commonly presents as red or purple skin lesions but can include visceral involvement.⁷ KS lesions are a rare endoscopic finding and not documented frequently in the literature. As previously stated, endoscopic evaluation for GI KS is valuable for early diagnosis, staging, and treatment. Bower et al¹⁰ evaluated newly diagnosed KS patients and found that 15% of late-stage disease had visceral involvement. Most patients were treated with combination antiretroviral therapy and liposomal anthracycline chemotherapy and had a 5-year overall survival of 85%. Early diagnosis and management of KS achieved high survival in patients with advanced KS.

Coinfection with HHV-8 plays a critical role in the pathogenesis and diagnosis of PEL and KS. PEL can include cases of solid lymphomas without malignant effusions.³ There are approximately 50 cases of extracavitary PEL, with a handful of them involving the GI tract. There have been no previous reports of endoscopic evaluation of PEL within the GI tract. A surgical approach in these patients with multiple GI lesions carries a significant risk of morbidity. Small bowel involvement of high-grade lymphoma is associated with perforation and increased mortality.¹¹ It is also important to remember that patients may present with GI bleeding because of GI lymphoma. Therefore, the role of endoscopic evaluation for PEL will be critical for the early diagnosis and management of this disease process.

The case we present highlights that PEL can present as a solid tumor and may have macroscopic features in common with KS. GI physicians should consider PEL when evaluating lesions consistent with KS and should ensure histopathologic and immunohistochemistry investigation to confirm HHV-8. Given the poor prognosis with PEL, differentiating between PEL and KS is essential because treatment options differ between these 2 malignancies. Endoscopic evaluation can be an invaluable tool in the diagnosis of PEL and thus leading to

earlier recognition and treatment of these patients and improved overall survival.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. M. Elharake is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report

Previous presentation: This case was presented at the American College of Gastroenterology Annual Scientific Meeting, October 5-10, 2018; Philadelphia, Pennsylvania.

Received November 22, 2020; Accepted June 21, 2021

REFERENCES

1. Das DK. Serous effusions in malignant lymphomas: A review. *Diagn Cytopathol.* 2006;34(5):335–47.
2. Jiang Y, Xie W, Hu K, Sun J, Zhu X, Huang H. An aggressive form of non-Hodgkin's lymphoma with pleural and abdominal chylous effusions: A case report and review of the literature. *Oncol Lett.* 2013;6(4):1120–2.
3. Chen YB, Rahemtullah A, Hochberg E. Primary effusion lymphoma. *Oncologist.* 2007;12(5):569–76.
4. Okada S, Goto H, Yotsumoto M. Current status of treatment for primary effusion lymphoma. *Intractable Rare Dis Res.* 2014;3(3):65–74.
5. Castillo JJ, Shum H, Lahijani M, Winer ES, Butera JN. Prognosis in primary effusion lymphoma is associated with the number of body cavities involved. *Leuk Lymphoma.* 2012;53:2378–82.
6. Khoury J, Willner CA, Gbadamosi B, Gaikazian S, Jaiyesimi I. Demographics and survival in primary effusion lymphoma: SEER database analysis. *Blood.* 2018;132(Suppl 1):5397.
7. Carmo J, Marques SC, Bispo M, Pinto D, Chagas C. Clinical and endoscopic features of gastrointestinal Kaposi sarcoma: A single-center Portuguese experience over the last decade. *GE Port J Gastroenterol.* 2017;24(5):219–26.
8. Carbone A, Gloghini A, Vaccher E, et al. Kaposi's sarcoma-associated herpesvirus/human herpesvirus type 8-positive solid lymphomas: A tissue-based variant of primary effusion lymphoma. *J Mol Diagn.* 2005;7(1):17–27.
9. Nagata N, Igari T, Shimbo T, et al. Diagnostic value of endothelial markers and HHV-8 staining in gastrointestinal Kaposi sarcoma and its difference in endoscopic tumor staging. *World J Gastroenterol.* 2013;19(23):3608–14.
10. Bower M, Dalla Pria A, Coyle C, et al. Prospective stage-stratified approach to AIDS-related Kaposi's sarcoma. *J Clin Oncol.* 2014;32(5):409–14.
11. Wong Y, Lum H, Fook-Chong S, Lim S, Salazar E. Do total parenteral nutrition and bowel rest reduce the risk for perforation in patients with gastrointestinal tract lymphoma receiving chemotherapy? *Nutrition.* 2019;67-68:110515.

Copyright: © 2021 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The American College of Gastroenterology. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.