Warning Signs: Kaposi's Sarcoma in Late HIV Diagnosis

Arianne D. Kalra, OMS IV, Lindsay Tjiattas-Saleski, DO, Michelle Carney, MD.
Spartanburg Regional Medical Center, Department of Infectious Disease, Spartanburg, SC

Edward Via College of Osteopathic Medicine CAROLINAS

Spartanburg Regional Healthcare System

Abstract

- Kaposi sarcoma (KS) is a vascular neoplasm considered an AIDS-defining illness, with a rate of occurrence of 12% in previously diagnosed patients and is associated with HHV-8.
- A 29-year-old Black male with a past medical history of non-Hodgkin's lymphoma, Type 2 Diabetes Mellitus, and no preventative care presented to an infectious disease clinic following a positive HIV test. He had papular, hyperpigmented, nonpruritic lesions present on his lower extremities for the last six months. Multiple ED visits and unsuccessful treatment of perceived cellulitis and eczema.
- Despite HAART therapy, his lesions continue to ascend to the groin with inguinal lymphadenopathy and edema from the knees to hip flexors. He was diagnosed with KS via biopsy. Refractory to chemotherapy, lesions progressed to his colon and small intestines. After admission for recurrent pleural effusions and atelectasis from pulmonary KS, the patient expired.
- This patient has an unusual disease timeline of KS with rapid dissemination of disease to internal organs leading to pulmonary failure, despite chemotherapy and prompt initiation of HAART treatment. There is no literature known for a patient with a similar timeline despite well studied nature of his condition, treatment, and epidemiology.

Introduction and Methods

Introduction

- Kaposi sarcoma (KS) is a well-known vascular neoplasm that is associated with an infection with human herpes virus 8 (HHV-8), also known as Kaposi sarcoma associated virus (KSHV).
- Discovered in 1872 by Moritz Kaposi, KS has since been divided into four types: classic, endemic, iatrogenic, and AIDS-associated.
  - Classic KS is the "idiopathic multiple pigmented sarcoma of the skin," typically found to affect more men than women and is more often in people from the Mediterranean area, as well as in Central and Eastern Europe [1, 8].
- KS is considered an AIDS-defining illness, and AIDS-related KS is one the most common neoplasm in patients with HIV worldwide. More often seen in men who have sex with men (MSM) than in other HIV risk groups, which prompted investigation into other etiologies [5]. HHV-8 was later identified in biopsy studies and found to be the etiologic cause of all subtypes of KS. Detections of HHV-8/KHSV found in peripheral blood mononuclear cells preceded development of KS, which supported the conclusion that HHV-8 was the defining marker behind KS [5].
- Given that HHV-8 is a virus that can avoid cellular defenses and subvert immune system processes through its genetic mechanisms, it is an important consideration for patients in high-risk demographics [3].

Methods

Literature over the past 40 years were reviewed along with case reports, review articles and online resources pertaining to Kaposi's sarcoma. The goal of the literature review was to investigate the presentation of Kaposi's sarcoma and its presentation associated with HIV and Castleman disease, and the timeline of disease progression of Immune Reconstitution Inflammatory Syndrome (KS-IRIS).

Case Report

- A 29-year-old African American man with PMHx of non-Hodgkin's lymphoma treated with chemotherapy and therapy-induced Type 2 Diabetes Mellitus presented to an infectious disease clinic with a positive HIV test in January 2018 for initiation of treatment.
- He noted papular, hyperpigmented, nonpruritic lesions present on his lower extremities for the last six months [Figures 1, 2].
  - Lesions were previously treated for eczema and cellulitis with no improvement and subsequent increase in edema in his lower legs.
  - DVT was ruled out during a previous medical visit.
- A daily combination of bictegravir 50 mg/emtricitabine 200 mg/tenofovir 25 mg (Biktarvy) and trimethoprim-sulfamethoxazole was initiated.
- Despite HAART therapy, skin changes continued to worsen. Kaposi's sarcoma was confirmed via skin biopsy.
- Chemotherapy was initiated.
- 1 month later patient developed rectal discomfort, diarrhea and lymphedema with progression to his groin and penis [Figure 3].
- An anal pap smear and biopsy of a nodular lesion at the squamocolumnar junction confirmed visceral Kaposi's sarcoma.
- Patient developed a pleural effusion and intra-abdominal swelling. Endoscopy showed KS lesions in the distal transverse colon and polyps in the rectum. [Figure 4]
  - There was increasing concern for Immune Reconstitution Inflammatory Syndrome (KS-IRIS) due to the rapidly worsening lymphadenopathy and bilateral lower extremity pain after initiation of HAART.
- Patient developed increased fluid retention, abdominal distention and dark colored emesis and increased pleural effusion. Colonoscopy was performed with further extension of lesions [Figure 5] The patient was admitted to the ICU for respiratory distress and expired due to acute hypoxic respiratory failure and anoxic brain injury. No autopsy was requested.

Figure 1. Initial presentation of KS lesions on lower leg and foot

Figure 2. Closer detail of papular KS lesions

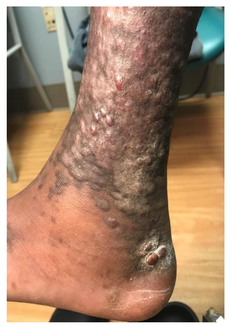


Figure 3. Extension of papular KS lesions to groin

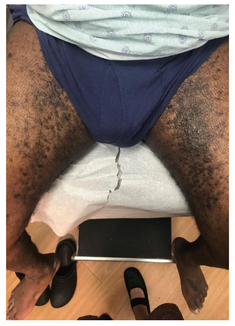


Figure 4. Images of colonoscopy with nodular lesions suspect of KS.

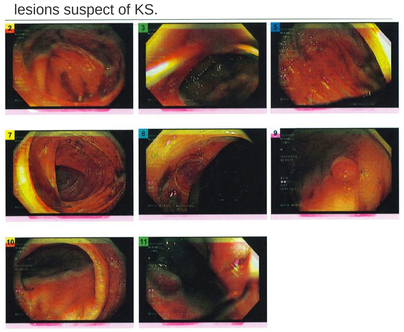
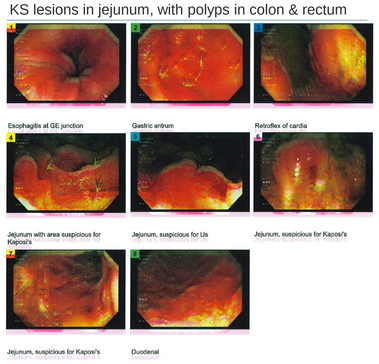


Figure 5. Images of colonoscopy suspect of KS lesions in jejunum, with polyps in colon & rectum



Discussion

- This is a case of Kaposi's sarcoma (KS) in a patient with a positive HIV status, presenting initially with cutaneous lesions and progressing to visceral involvement [12, 13]. Due to early diagnosis, treatment of HIV with HAART therapy, as well as with more targeted viral susceptibility in chemotherapy, cases of AIDS-related KS are extremely rare, with an incidence of 1397.11 per 100,000 person years, approximately 1.3% [2, 7, 11].
- There was concern in this case for exacerbation of KS upon initiation of HAART treatment, known as Immune Reconstitution Inflammatory Syndrome (KS-IRIS) [9, 10].
- Castleman Disease was also a concern for this patient due to his HIV status confirmation 6 months after the KS had developed.
- This case identifies the need for the promotion of early and regular HIV testing as well as provider education in identification of HIV associated skin conditions. The USPSTF recommends annual HIV testing for adults ages 15-65, and especially for those at an increased risk of infection [4]. Pre-exposure prophylaxis (PrEP) is recommended for those at high risk of contracting HIV [6].
  - This patient satisfied two of highest risk demographics as an African American male and MSM.
  - The health care providers who treated the patient for his lesions prior to the diagnosis of KS provided failed therapies.
  - The patient did not receive HIV testing until he presented to the ID clinic.
  - This patient did not receive prophylactic therapy for HIV.

References

1. Angeloni A, Heston L, Uccini S, Sirianni MC, Cottoni F, Masala MV, Cerimele D, Lin SF, Sun R, Rigsby M, Faggioni A. High prevalence of antibodies to human herpesvirus 8 in relatives of patients with classic Kaposi's sarcoma from Sardinia. *Journal of Infectious Diseases*. 1998;177(6):1715-8.
2. Cheng CH, Hsu YH. Immune reconstitution inflammatory syndrome-associated disseminated Kaposi's sarcoma in a patient infected with human immunodeficiency virus: Report of an autopsy case. *Ci Ji Yi Xue Za Zhi*. 2017;29(1):41-45. doi:10.4103/tcmj.tcmj_9_17
3. Dittmer DP, Damania B. Kaposi sarcoma-associated herpesvirus: immunobiology, oncogenesis, and therapy. *J Clin Invest*. 2016;126(9):3165-3175. doi:10.1172/JCI84418
4. Final Recommendation Statement: Prevention of Human Immunodeficiency Virus (HIV) Infection: Preexposure Prophylaxis. U.S. Preventative Services Task Force. Published June 11, 2019. Accessed May 15, 2020.
5. Gonçalves PH, Uldrick TS, Yarchoan R. HIV-associated Kaposi sarcoma and related diseases. *AIDS*. 2017;31(14):1903-1916. doi:10.1097/QAD.0000000000001567
6. Human Immunodeficiency Virus (HIV) Infection: Screening. U.S. Preventive Services Task Force. Published June 11, 2019. Accessed May 15, 2020.
7. Hymes KB, Cheung T, Greene JB, Prose NS, Marcus A, Ballard H, et al. Kaposi's sarcoma in homosexual men-a report of eight cases. *Lancet*. 1981;2(8247):598–600.
8. Kaposi M. Idiopathic multiple pigmented sarcoma of the skin. *CA: A Cancer Journal for Clinicians*. 1982;32(6):342-7.
9. Letang E, Lewis JJ, Bower M, Mosam A, Borok M, Campbell TB, Naniche D, Newsom-Davis T, Shaik F, Fiorillo S, Miro JM, Schellenberg D, Easterbrook PJ. *AIDS*. 2013 Jun 19; 27(10):1603-13.
10. Levy JA, Ziegler JL. Acquired immunodeficiency syndrome is an opportunistic infection and Kaposi's sarcoma results from secondary immune stimulation. *Lancet*. 1983;2(8341):78–81.
11. Liu Z, Fang Q, Zuo J, Minhas V, Wood C, Zhang T. The world-wide incidence of Kaposis sarcoma in the HIV / AIDS era. *HIV Medicine*. 2018;19(5):355-364. doi:10.1111/hiv.12584.
12. Mehta S, Garg A, Gupta LK, Mittal A, Khare AK, Kuldeep CM. Kaposi's sarcoma as a presenting manifestation of HIV. *Indian J Sex Transm Dis AIDS*. 2011;32(2):108-110. doi:10.4103/0253-7184.8541.
13. Moore PS, Chang Y. Detection of herpesvirus-like DNA sequences in Kaposi's sarcoma in patients with and those without HIV infection. *New England Journal of Medicine*. 1995 May 4;332(18):1181-5.

Acknowledgements

The author of this case study would like to thank Dr. Michelle Carney and Dr. Blair Clementson of Spartanburg Regional Medical Center for their support throughout the project. Thank you to Melissa at Spartanburg Regional for her communication in providing images for the use of this project. Thank you to Dr. Lindsay Tjiattas-Saleski and Ashwin Sharma, MA, MSIII for advising and support in the preparation of this project to be presented today. In addition, we are grateful to the patient LA and his family for their consent and kindness to use the case for research and to take photos for educational purposes.