

Dear Editor,

We are pleased to resubmit for publication the revised version of Manuscript ID 35974 entitled “entitled " HHV-8 Positive Iatrogenic Kaposi's Sarcoma in the Setting of Refractory Ulcerative Colitis.” Thank you for your email dated September 6<sup>th</sup>, 2017. We appreciated the constructive criticisms of the reviewers and assistant editor. We have addressed each of their concerns as outlined below.

**Reviewer 1 comments:**

Authors, you are presenting an interesting case, which has high novelty and clinical relevance, but to achieve its full overall impact, it needs minor language editing throughout by an academic with experience in handling medical literature. It may reflect lack of editing by Dr. Fine. For example, Introduction, line 8: “Interestingly, no association has been noted between the development of KS and either duration of UC disease activity. This sentence is incomplete.

**The sentence has been rewritten to completion.**

Also, please take out the s from backgrounds (line 3).

**This has been changed.**

There is no shortage of many more throughout the report.

**We have gone through and made grammatical edits as noted under track changes of our edited document.**

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Please note the other changes we have made on this current revision:

1. We changed our title to provide a more specific description of our case report. Please feel free to forward any paperwork that must be redone to include our new title: “**HHV-8 Positive Iatrogenic Kaposi’s Sarcoma in the Setting of Refractory Ulcerative Colitis.**”
2. In regards to our IRB Statement, Conflict of Interest, and Informed consent we provided our original statements included at the beginning of our manuscript in PDF format. We would appreciate any further direction from editors in this regard if more action is needed to be taken on our part.
3. We have included the following writing requirements for the comments as indicated at the end of our edited manuscript:
  - a. Case characteristics
    - i. Patient’s symptoms included fever, nausea, diarrhea, and hematochezia.
  - b. Clinical diagnosis
    - i. Patient was found to have a rectal tumor consistent with Kaposi Sarcoma after having had surveillance colonoscopies completed.
  - c. Differential diagnosis
    - i. Ulcerative colitis flare, vascular transformation of lymph nodes, CMV colitis, infectious colitis
  - d. Laboratory diagnosis
    - i. Labs were notable for a hemoglobin of 12.3 g/dL (13.5-16), WBC of  $10.1 \times 10^9/L$  (3.5-11) and a negative HIV antibody.
  - e. Imaging diagnosis
    - i. Esophagogastroduodenoscopy and capsule endoscopy demonstrated that tumor involvement was limited to the rectum.
  - f. Pathological diagnosis
    - i. Histologic sections of the rectal tumor demonstrated a cytologically

bland spindle cell proliferation interspersed by irregular vascular spaces containing extravasated erythrocytes, which on immunohistochemistry were positive for Human Herpesvirus-8 and consistent with Kaposi's sarcoma.

- g. Treatment
  - i. The patient underwent multiple failed attempts to withdraw his regimen of oral corticosteroids, and ultimately received a laparoscopic assisted subtotal colectomy with end ileostomy and since has done well.
- h. Related reports
  - i. While our references include several articles that can be perused for further information, more info can be found within the following articles:
    1. Kumar V, Soni P, Garg M, Abduraimova M, Harris J. Kaposi Sarcoma Mimicking Acute Flare of Ulcerative Colitis. Journal of Investigative Medicine High Impact Case Reports.
    2. Anderson, L., Lauria, C., Romano, N., Brown, E., Whitby, D., Graubard, B., Goedert, J. (2008). Risk factors for classical Kaposi sarcoma in a population-based case-control study in Sicily. Cancer Epidemiology, Biomarkers & Prevention : A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology
- i. Term explanation
  - i. Refractory: resistant to a process or stimulus, in the context of medicine this term often refers to being resistant to treatment.
  - ii. Immunosuppression: reduction of the activation or efficacy of the immune system
- j. Experiences and lessons
  - i. This particular patient's case highlights the importance in considering the diagnosis of Kaposi Sarcoma in the setting of ulcerative colitis patients, as failure to do so delays treatment.
- k. Peer-review
  - i. This patient case illustrates the manifestation of primary gastrointestinal KS in a patient with refractory colitis to medical management.

We hope the reviewed version is now suitable for publication and look forward to hearing from you. We appreciate your time and consideration.

Sincerely,



Erica Duh