

# PD1 Inhibitor Induced Hemorrhagic Gastritis

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## Introduction

Immune checkpoint inhibitors are a mainstay of treatment for a range of cancers, including melanoma, squamous cell carcinoma, non-small cell lung cancer and Hodgkin's lymphoma. These drugs work by disinhibiting host immunity to help target tumors, but consequently, this can lead to immune related adverse effects. Check point inhibitor colitis is a well described complication involving the gastrointestinal tract, but gastric involvement is a rare occurrence. In this unusual case, we report endoscopic and histologic findings consistent with hemorrhagic gastritis in a patient treated with pembrolizumab, an anti-PD-1 immunomodulator.

## Case Presentation

- 76 year old M with PMH of small lymphocytic lymphoma with recurrence s/p chemotherapy, basal cell carcinoma and squamous cell carcinoma of R ear s/p tx with pembrolizumab, from 1/2021- 3/2022, 42 courses, and microcytic anemia who presented to the hospital with dyspnea on exertion, weakness, and melena, found to have a profound microcytic anemia with a hemoglobin of 4 with heme positive stool. Symptoms of SOB, edema of the lower extremities, muscle cramps, marked fatigue, weight changes, and tremulousness reportedly started since 3/2022.
- During admission he was transfused with 4U PRBC and given 2 doses of inpatient parenteral iron. An EGD at that time showed bleeding angioectasias, which were cauterized, and pt was discharged on oral iron but continued having dark stools and weakness.
- Outpatient colonoscopy showed blood throughout the colon.
- Had cardiac and pulmonary evaluation of his pulmonary complaints with no obvious explanations.
  - CT PET fusion (4/2022) - normal appearing lung parenchyma but revealed a hypermetabolic external iliac chain hypermetabolic uptake measuring 1 cm in diameter and there was associated mild SUV uptake in subcentimeter left inguinal lymph nodes.
  - Normal TTE and EKG.
  - US of the leg, negative for DVT, possible Baker's cyst in the popliteal area.
- He was referred to hematology for the anemia to rule out hemolysis, versus nutritional deficits, versus other hemoglobinopathy. Anemia workup included EPO levels (normal), iron/TIBC were normal, ratio = 20% (low end of normal), normal ferritin, normal reticulocyte count. Hence, there were no clear signs of either hemolysis or iron deficiency.
- He re-presented to the hospital 2 months later with the same presentation and admitted with acute on chronic anemia, melena, and concern for small bowel bleeding. Video endoscopy which showed "red blood in the stomach and another site of active bleeding in the proximal to mid jejunum" with the remainder of the exam masked by old blood.
- The following day he underwent a double balloon endoscopy (upper device assisted enteroscopy w/o fluoroscopy) which showed red blood throughout the stomach, patchy severe inflammation with hemorrhage depicted as adherent blood, friability, and granularity in all of the stomach.

## Case Presentation (continued)

- Argon plasma was used as the source of coagulation for hemostasis and was successful in treating around forty sites of punctate hemorrhage with active bleeding. Normal examination of the duodenum, jejunum and proximal ileum although the small bowel mucosa was somewhat friable on exam.
- A biopsy with cold forceps for histology of the stomach was obtained that revealed chronic inactive gastritis.
- The active bleeding from the multifocal punctate hemorrhage in the gastric body and antrum were consistent with checkpoint inhibitor-induced hemorrhagic gastritis due to pembrolizumab therapy. He has been started on prednisone at 60 mg daily and states that he has had marked improvement, with dose reductions in 2 week intervals.
- His recommended treatment was twice daily proton-pump inhibitors, potential future therapy with octreotide depot injections then tranexamic acid if bleeding persists. He was given one infusion of venofer 200mg IV prior to discharge. Discussion with the oncologist was noted for future medication changes.

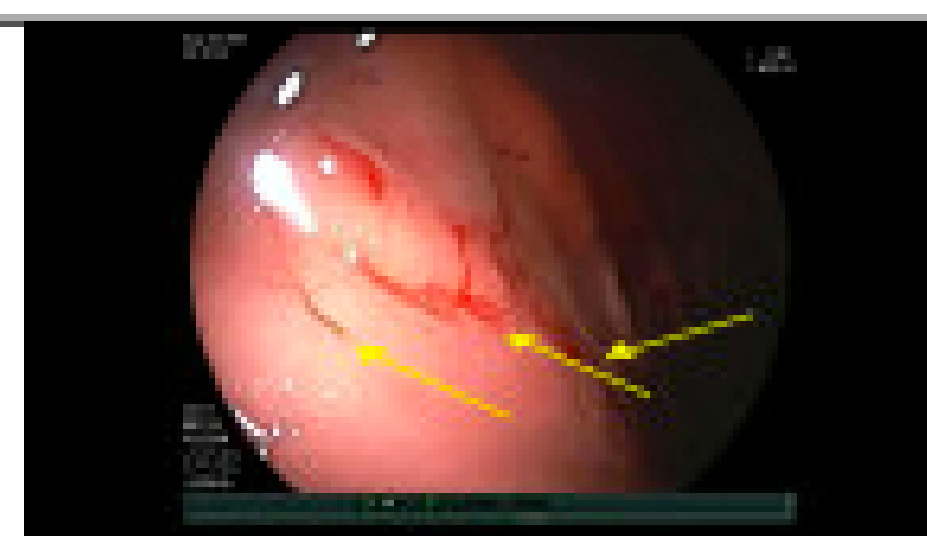
## Diagnosis



**2** Multifocal punctate hemorrhage



**3** Gastric Antrum ; Focal hemorrhage in the gastric antrum



**1** Gastric Body ; Multifocal punctate hemorrhage in the gastric body



**4** Pre-pyloric Stomach : \*Inflammation



**5** Proximal Ileum : Normal

## Discussion

- The patient presented with symptoms of SOB, edema of the lower extremities, muscle cramps, marked fatigue, weight changes, and tremulousness since 3/2022, after completing ~1 year treatment course of pembrolizumab for SCC. Outpatient workups were unrevealing for the cause of his microcytic anemia.
- He showed symptoms of subacute and overt evidence of gastrointestinal bleeding and was hospitalized twice for symptomatic anemia requiring multiple blood transfusions.
- Upper endoscopy showed slow hemorrhaging from multiple focal punctate lesions located diffusely throughout the gastric body and antrum, at least 40 sites of punctate hemorrhage.
- Biopsies of these areas showed histology consistent with chronic inactive gastritis.
- Endoscopic appearance was consistent with immunotherapy induced colitis, most consistent with checkpoint inhibitor-induced hemorrhagic gastritis (due to pembrolizumab therapy).
- After the diagnosis, patient was started on steroids with marked improvement.
- Treatment consists of immunosuppression with use of corticosteroids or immunomodulators such as infliximab in refractory cases as well as PPIs and Octreotide for persistent bleeding.
- Patients should be told to report any abdominal discomfort/melena to their oncologist to keep in mind immune check point inhibitor adverse effects.
- PPIs or histamine H2 receptor antagonists may be used for preventing gastritis and upper GI hemorrhage in high risk patients.
- This case highlights the need to assess for possibility of hemorrhagic gastritis in patients using pembrolizumab presenting with melena as well as the need for further investigation in standardizing prophylaxis in high risk patients.

## References

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