

## Case History

A 26 year old male presented with a history of chronic diarrhea and hematochezia. Past medical history was significant for severe immunosuppression due to HIV and HAART therapy noncompliance. HIV viral load was extremely high and very low CD4+ T cell counts were detected. Upper EGD detected reddish polypoid lesions on the gastric body and fundus. Multiple cold forceps biopsies were performed and sent for histologic examination. Representative H&E images of the stomach biopsies are depicted below along with selected immunohistochemical stains.



Figure 1. Endoscopic image of the lesion

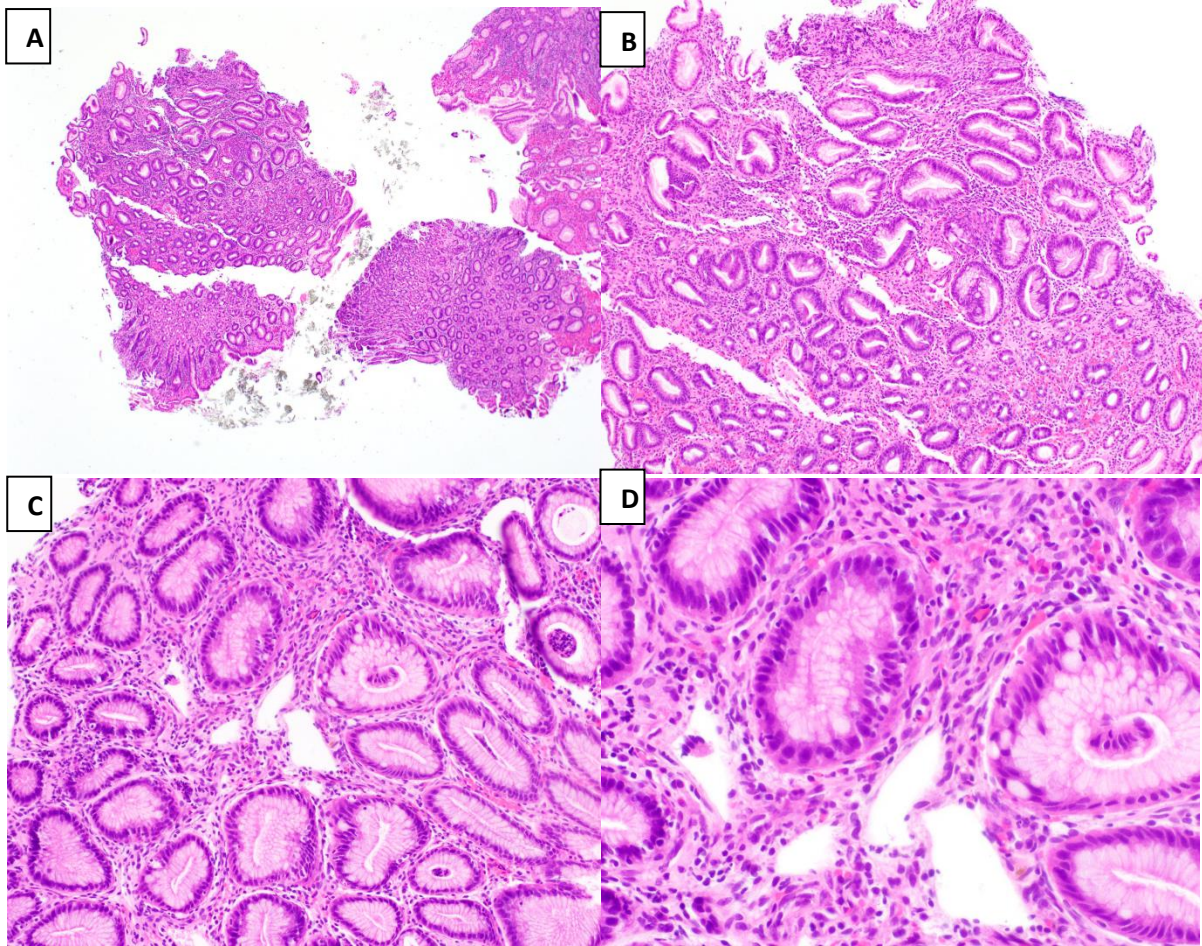


Figure 2: A) H&E 4x, B) H&E 10x, C) H&E 20x, D) H&E 40x

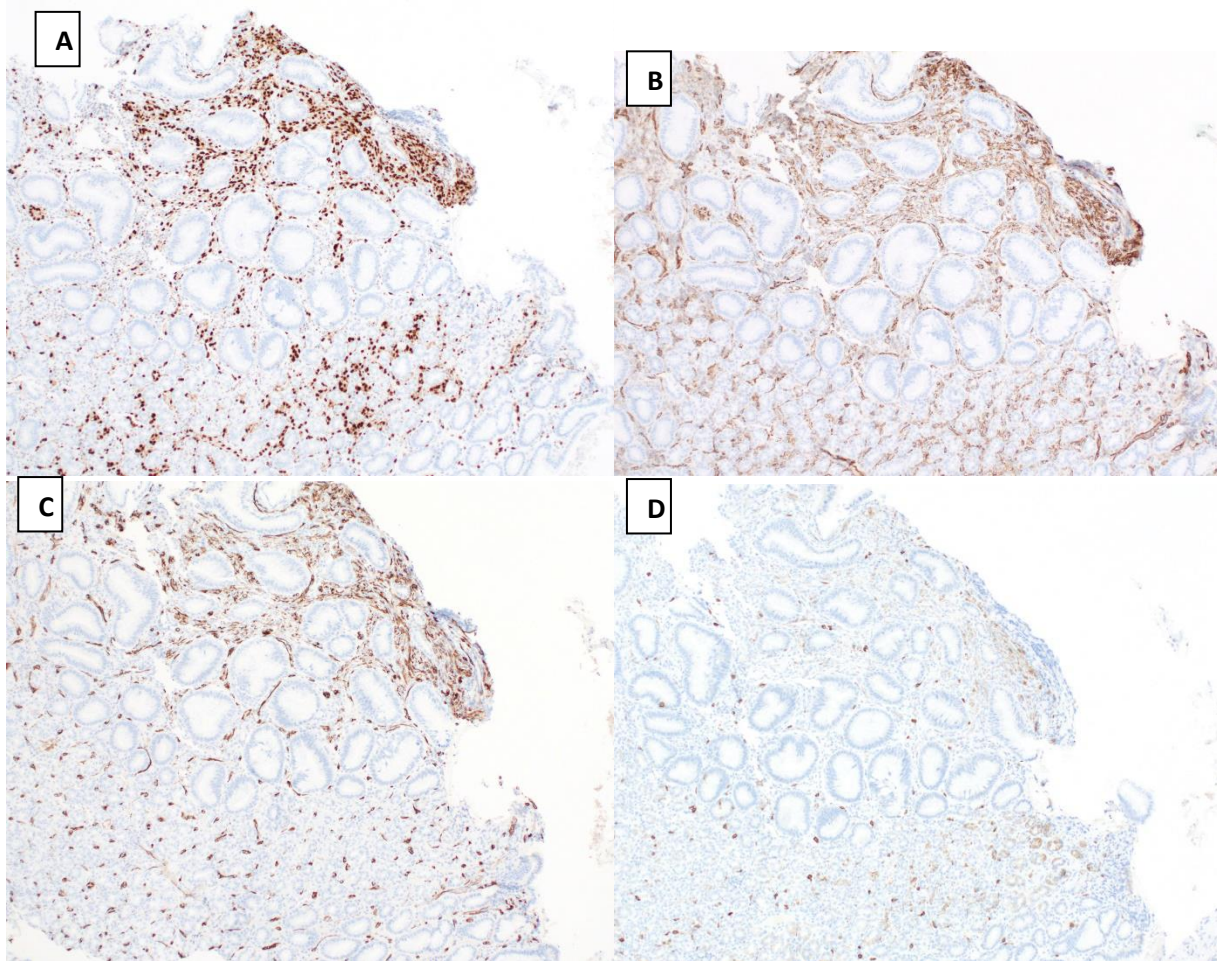


Figure 3: A) CD31 10x, B) CD34 10x, C) ERG 10x, D)c-kit 10X

**What is the most likely diagnosis?**

- a. Gastric angiosarcoma
- b. Gastrointestinal stromal tumor
- c. Inflammatory fibroid polyp
- d. Kaposi sarcoma
- e. Metastatic melanoma

ANSWER AND DISCUSSION ON THE NEXT PAGE.

**Correct answer: D, Kaposi sarcoma.**

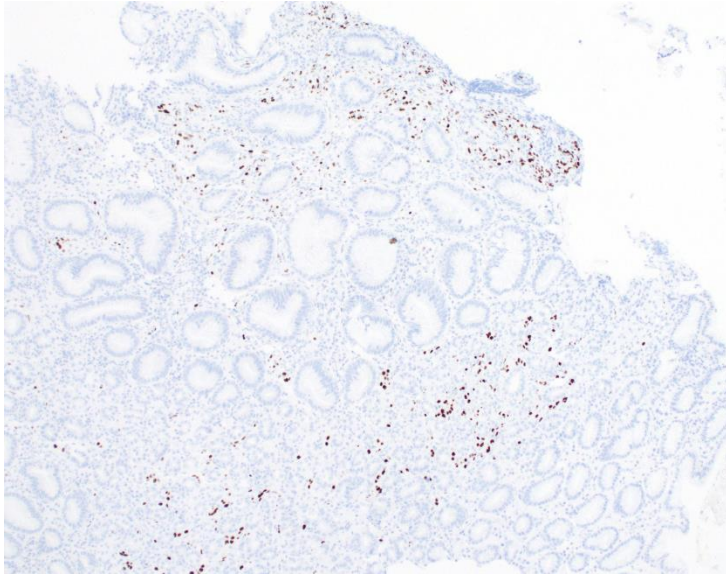


Figure 4. HHV-8, 10x

Histology sections show a spindle cell proliferation in the lamina propria. Multiple “slit-like” vascular spaces and red blood cells are seen. These spindle cells stain for CD 34, CD 31 and ERG. The diagnosis is further confirmed by positive staining with human herpes virus 8 (HHV-8) immunohistochemical stain (Figure 4).

Kaposi sarcoma is the most common HIV associated malignancy despite the effectiveness of HAART treatment. Gastrointestinal involvement as initial presentation has been described in up to 40% of patients and is as high as 80% on autopsies. The stomach is the most commonly involved site and polyps and nodules are the most frequent presentations. In the HIV positive population this entity is mostly asymptomatic, but can manifest with abdominal pain, nausea and vomiting, digestive bleeding, obstructive symptoms or rarely perforation. Risk factors include low CD4 T cell counts (<200 cells/  $\mu$ L) and high viral load. The endoscopic appearance of violaceous, erythematous or hemorrhagic plaque-like, polypoid or nodular lesion(s) in an immunocompromised patient is a useful clue to the diagnosis. Kaposi sarcoma can be extremely subtle on biopsies. It may sometimes appear more spindled and sclerotic and can be easily mistaken for fibrosis. Stains for CD31, CD34, ERG are useful for diagnostic purposes. Angiosarcoma (metastatic or primary to the GI tract) can pose a diagnostic challenge due to similar immunophenotypical and morphological profile. However, HHV-8 immunohistochemical stain shows an excellent sensitivity and specificity for detection of Kaposi sarcoma. False negative diagnosis may occur when the tumor originates in deeper regions of the stomach wall in which case extensive sampling of the ulcer wall is required.

### **Incorrect Answer A, Gastric angiosarcoma**

Angiosarcomas are rare sarcomas that usually present in the skin and subepidermal tissue. Involvement of liver, heart, spleen and GI tract has been reported. Gastric angiosarcoma is exceedingly rare and usually displays two distinctive histological growth patterns: vascular and solid. The vascular pattern is composed of spindle, plumped anaplastic endothelial cells. The solid pattern exhibits epithelioid cells that are spindled or polygonal with abundant eosinophilic cytoplasm. The immunophenotype is concordant with a vascular origin: CD31, CD34 and factor VIII positive. HHV-8 facilitates the distinction from Kaposi sarcoma. In very rare instances gastric angiosarcoma can present concomitantly with Kaposi sarcoma.

### **Incorrect Answer B, Gastrointestinal stromal tumors (GIST)**

These tumors arise from interstitial cells of Cajal and their precursors. The stomach is the most common location. Spindle cell GISTs are composed of uniform, monomorphic bland spindle shaped cells similar to those of Kaposi sarcoma. Blood vessels can be inconspicuous or elongated and prominent. Activating mutations in KIT and platelet-derived growth receptor alpha (PDGFRA) have been identified in 80% and 10% of GISTs, respectively. Most GISTs will be diffusely positive for CD117 (c-kit) immunohistochemical stain. This can pose a diagnostic challenge since approximately 40% of Kaposi sarcomas can show positivity for CD117. DOG1, a more recently described immunostain appears to be immunoreactive even among CD117-negative GISTs and is negative in Kaposi sarcoma. Additionally, HHV-8 can also help to distinguish between these entities.

### **Incorrect Answer C, Inflammatory fibroid Polyp**

Inflammatory fibroid polyps frequently present as sessile lesions with mucosal ulcerations. They commonly arise in the gastric antrum in close relation or overlying the pyloric sphincter. These tumors arise in the mucosa and very infrequently involve the muscularis propria. The classic morphologic findings are bland spindle cells admixed with inflammatory cells, small capillaries, and an edematous or myxoid background. Immunostains for CD34, smooth muscle actin and CD68 are positive, while CD117, S100 and cytokeratins are negative. HHV-8 immunostain is useful as it would be negative in the inflammatory fibroid polyp.

### **Incorrect Answer E, Metastatic melanoma**

Melanoma metastases to the gastrointestinal tract are rare and are commonly associated with metastases to other organs. They usually present as multiple ulcerated polypoid lesions that can occur at initial presentation or years after the diagnosis. Histologically, melanoma cells can be spindled or epithelioid, with a plasmacytoid appearance. Other distinguishing features are intranuclear pseudoinclusions, increased eosinophilic cytoplasm, and enlarged nucleoli. In many instances, the presence of melanin pigment yields the diagnosis, however melanomas metastatic to the GI tract are frequently amelanotic. Patients may have a remote history of malignant melanoma or lack a prior diagnosis. Immunohistochemical stains such as S100, Sox10 and HMB-45 are particularly useful in establishing the diagnosis. Additionally, HHV-8 will be negative in cases of metastatic melanoma.

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