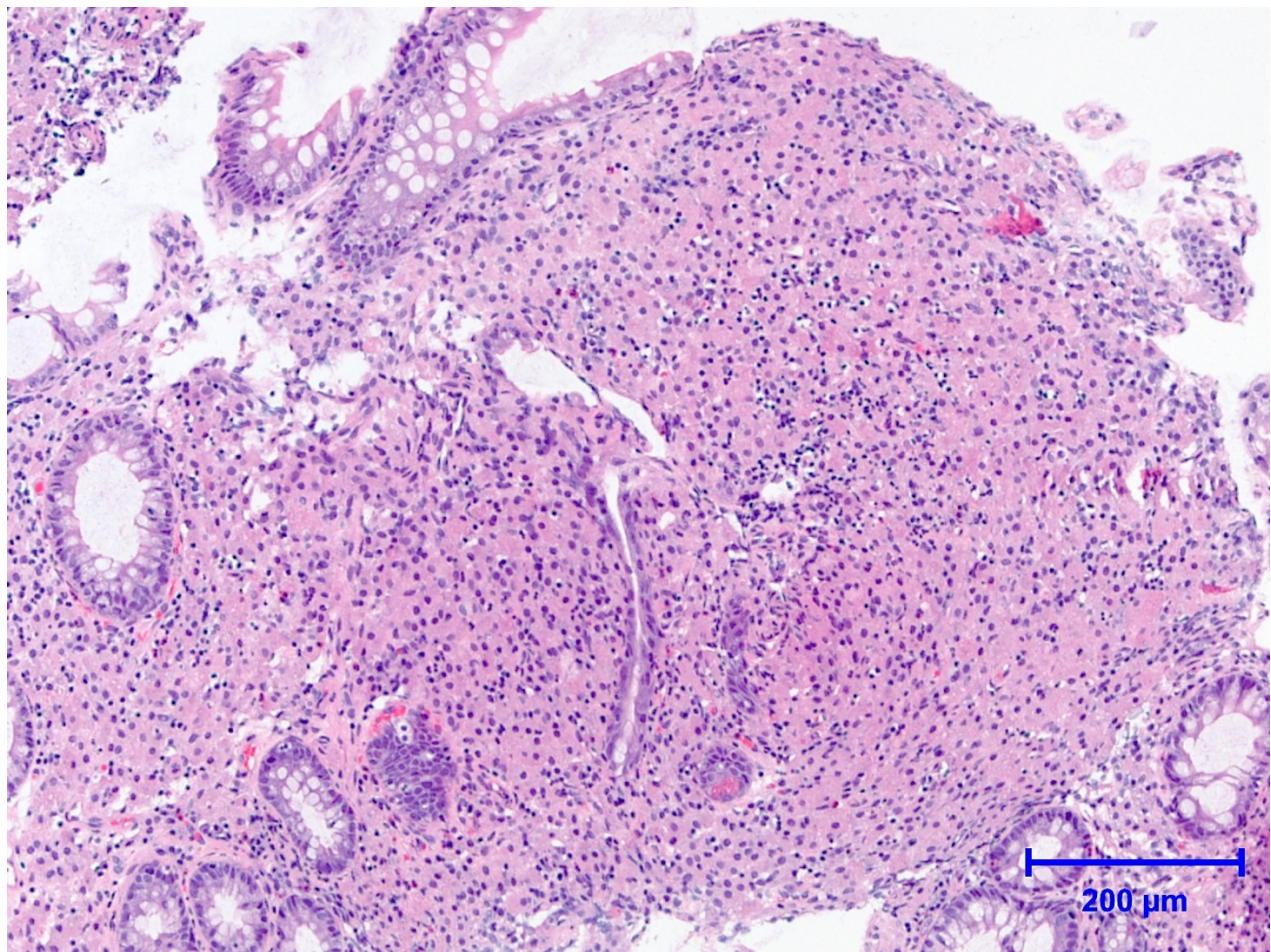
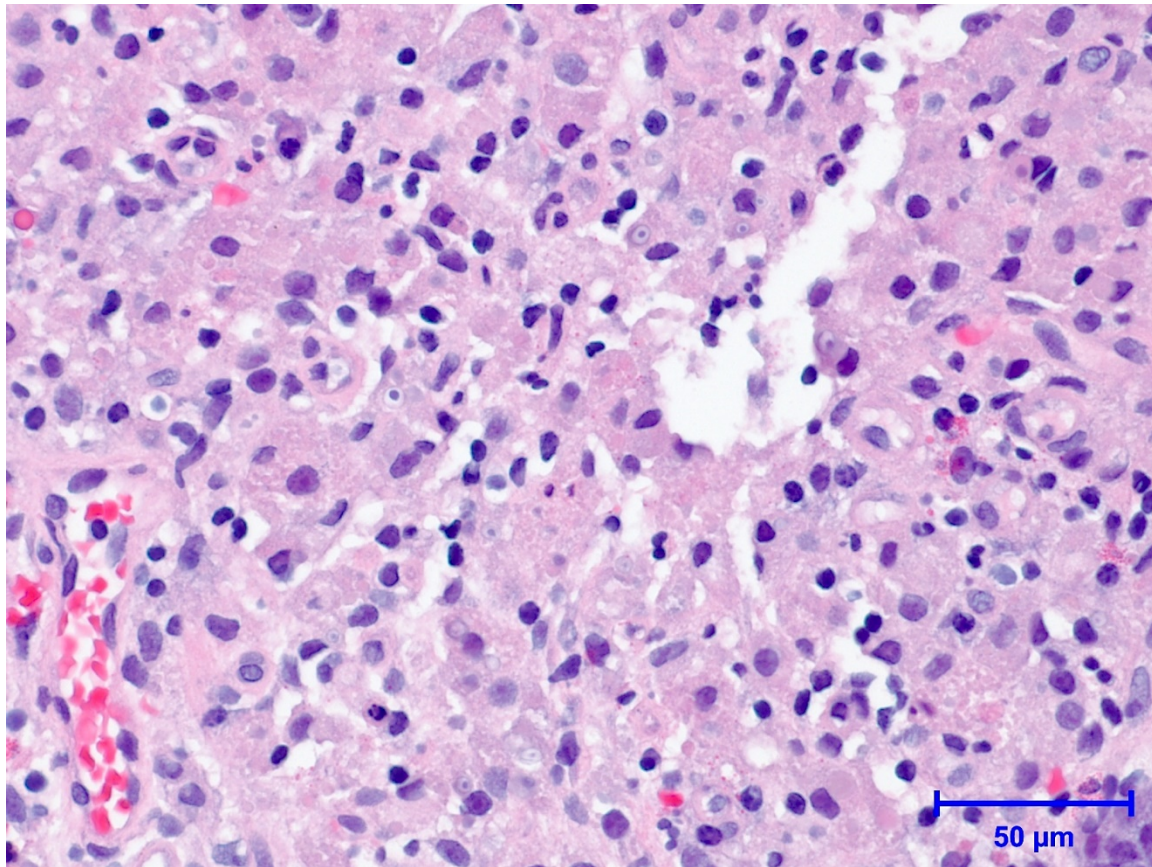


## CASE HISTORY:

73-year-old man with multiple myeloma presented with several months history of progressive, watery diarrhea. He had a previous autologous stem cell transplantation and was undergoing treatment with lenalidomide, bortezomib, and dexamethasone. A lower endoscopy showed an unremarkable terminal ileum and two sub-centimeter sessile colonic polyps. The terminal ileum biopsy showed no specific histologic abnormalities. The two colonic polyps were tubular adenomas. Representative H&E stains of the colonic mucosa adjacent to the tubular adenomas are depicted below. Grocott-Gomori's methenamine silver (GMS), Ziehl-Neelsen/acid-fast stain (AFB), and Wade-Fite/modified acid-fast stain (Fite) stains were negative for microorganisms (not shown).



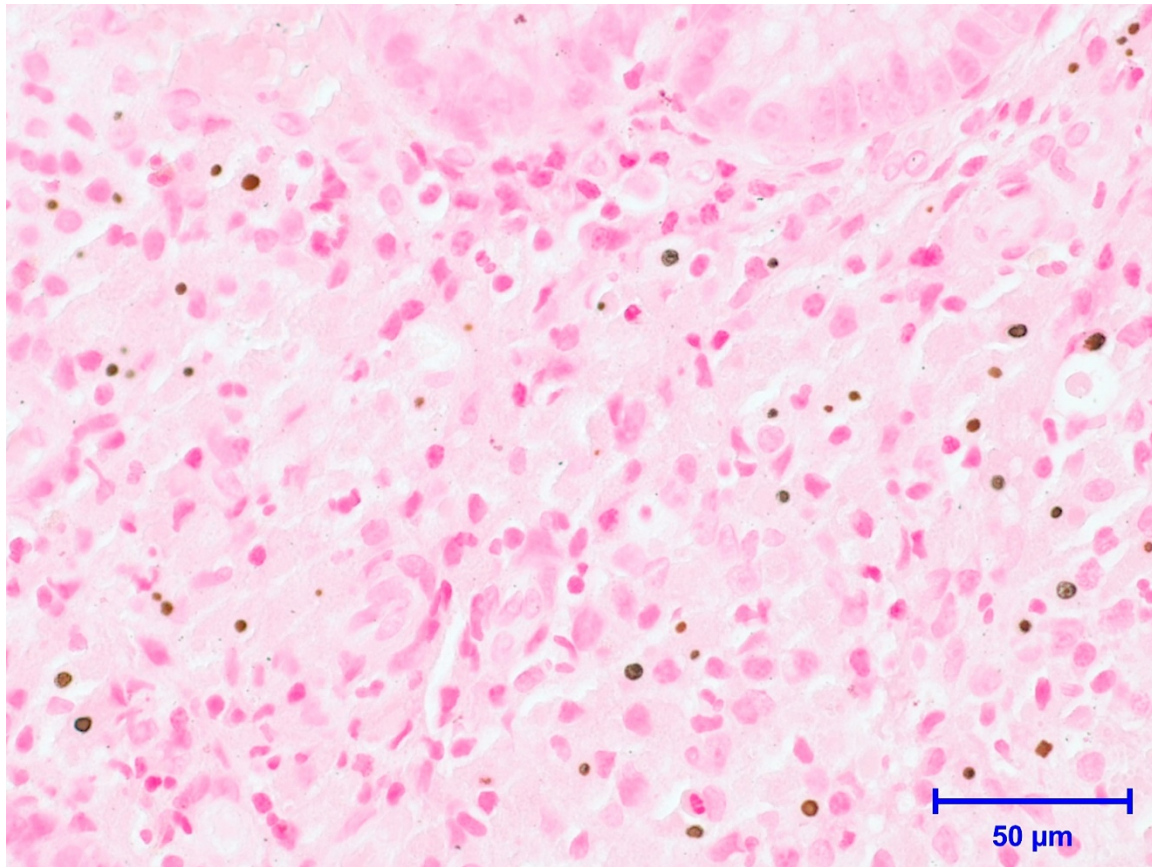


What is your preliminary diagnosis?

- A. Histoplasmosis
- B. Leishmaniasis
- C. *Mycobacterium avium-intracellulare* infection
- D. Whipple's disease
- E. Malakoplakia

An additional histochemical stain was performed.





1. What histochemical stain was performed?
2. What is your final diagnosis?

Answers:

1. von Kossa stain
2. Malakoplakia

## Discussion

### E: Malakoplakia

Malakoplakia is a histiocytic inflammatory condition that is thought to be caused by defects in macrophage phagocytic response to certain bacterial infections and can occur concurrently with inflammatory disorders and immunosuppression. Although it is predominantly seen in the urinary tract, other organ systems can be affected, with the second most common site being the gastrointestinal tract. Endoscopically, malakoplakia may present as a mass, plaque, polyp, or nodule. It can be associated with colonic adenomas, as in our case, as well as adenocarcinoma. Histologic sections show aggregates of von Hansemann cells, which are histiocytes with PAS-positive, granular eosinophilic cytoplasm that contain the characteristic Michaelis-Gutmann bodies. Michaelis-Gutmann bodies are basophilic inclusions that have a “targetoid” appearance and range from 5-15 micrometers in size and are believed to represent phagolysosomes that accumulate due to the inability of histiocytes to completely digest bacteria. Michaelis-Gutmann bodies stain positive for PAS, Prussian blue, and von Kossa stains due to their contents of sugar, calcium, and iron salts. The above images of PAS and von Kossa stained sections highlight forms consistent with Michaelis-Gutmann bodies.

### A: Histoplasmosis

Gastrointestinal histoplasmosis is likely an underdiagnosed entity due to most patients being asymptomatic or having non-specific symptoms, but it is important to recognize this entity since patients can progress to disseminated histoplasmosis (as discussed in the September 2018 edition of the GIPS Case of the Month). Routine H&E stains generally show macrophages containing small ovoid to spherical organisms that have a clear halo between the organism and its cell wall. Although the organisms are PAS-positive, they can be distinguished from malakoplakia by positive staining on GMS stain. *Histoplasma* are also smaller and more uniform compared to Michaelis-Gutmann bodies, measuring 2-4 microns in size. Von Kossa stain should be negative for *Histoplasma* sp.

### B. Leishmaniasis:

Leishmaniasis is caused by infection by an obligate intracellular protozoa from the *Leishmania* species and is spread by sandflies. Visceral leishmaniasis is often associated with AIDS and is endemic in Algeria and East Africa, but rarely occurs in the gastrointestinal tract. Histologically, the lamina propria usually shows histiocytes containing amastigotes of *Leishmania* that are visible on H&E stain. The amastigotes measure 2-4 microns in size and can be highlighted by Wright-Giemsa stain. Given the microorganism size, identification of the rod-like kinetoplast within amastigotes is important in order to distinguish *Leishmania* from the morphologically similar *Histoplasma* yeast forms. Diagnosis can also be confirmed by culture or PCR.

### C. *Mycobacterium avium-intracellulare* infection:

*Mycobacterium avium-intracellulare* infection (MAI) of the gastrointestinal tract occurs in immunocompromised individuals and predominantly involves the duodenum and rectum rather than the colon. In rare cases of MAI in the colon, H&E stain should show histiocytes within the lamina propria, but without readily identifiable organisms or inclusions. Mycobacteria will stain positive for PAS, but Ziehl-Neelsen and Fite stains also highlight the bacilli, and von Kossa stain should be negative.

#### D. Whipple's disease:

Whipple's disease is a rare infection caused by *Tropheryma whipplei* that is often seen in middle-aged men. Clinical symptoms include weight loss, diarrhea, abdominal pain, arthralgia, and abdominal lymphadenopathy. Similar to MAI, Whipple's disease is more often seen in the small intestine, with rare cases reported in the colon. Histologically, aggregates of foamy macrophages can be seen within the lamina propria containing globular or coarse cytoplasmic inclusions. Histiocytes of Whipple's disease will stain positive for PAS similar to malakoplakia, but von Kossa stain will be negative. Immunohistochemistry or PCR for *T. whipplei* can be used for confirmatory testing.

#### Contributing authors:

Enoch Kuo, MD

PGY-3 in Anatomic & Clinical Pathology

Kari D. Caradine, MD

Assistant Professor of Pathology

Eric U. Yee, MD

Assistant Professor of Pathology

Department of Pathology

University of Arkansas for Medical Sciences

4301 W. Markham St.

Little Rock, AR 72205

#### References:

1. Arnold CA, Moreira RK, Lam-himlin D, De petris G, Montgomery E. Whipple disease a century after the initial description: increased recognition of unusual presentations, autoimmune comorbidities, and therapy effects. *Am J Surg Pathol.* 2012;36(7):1066-73.
2. Cipolletta L, Bianco MA, Fumo F, Orabona P, Piccinino F. Malacoplakia of the colon. *Gastrointest Endosc.* 1995;41(3):255-8.
3. Gray JR, Rabeneck L. Atypical mycobacterial infection of the gastrointestinal tract in AIDS patients. *Am J Gastroenterol.* 1989;84(12):1521-4.
4. Karasavvidou F, Potamianos SP, Barbanis S, et al. Malakoplakia of the colon associated with colonic adenocarcinoma diagnosed in colonic biopsies. *World J Gastroenterol.* 2007;13(45):6109-11.

5. Laura W. Lamps. Surgical Pathology of the Gastrointestinal System: Bacterial, Fungal, Viral, and Parasitic Infections. New York, NY: Springer, 2009. pp 84-6.
6. Rizzo E, Sandmeier D, Hack I, Matter M, Bouzourene H. Malakoplakia and colonic adenoma: a rare association. Ann Diagn Pathol. 2004;8(6):364-6.
7. Sagaert X, Tousseyn T, De hertogh G, Geboes K. Macrophage-related diseases of the gut: a pathologist's perspective. Virchows Arch. 2012;460(6):555-67.
8. Sun HY, Chen MY, Wu MS, et al. Endoscopic appearance of GI mycobacteriosis caused by the Mycobacterium avium complex in a patient with AIDS: case report and review. Gastrointest Endosc. 2005;61(6):775-9.
9. Wolke A, Meyers S, Adelsberg BR, et al. Mycobacterium avium-intracellulare-associated colitis in a patient with the acquired immunodeficiency syndrome. J Clin Gastroenterol. 1984;6(3):225-9.