A 63 year-old male with a history of HIV controlled on HAART, HCV cirrhosis, ESRD s/p renal transplant and squamous cell carcinoma of lung, presents with clinically significant watery diarrhea of unexplained origin. On colonoscopy, the examined colonic mucosa is normal. Images of the colonoscopic biopsies are demonstrated below.

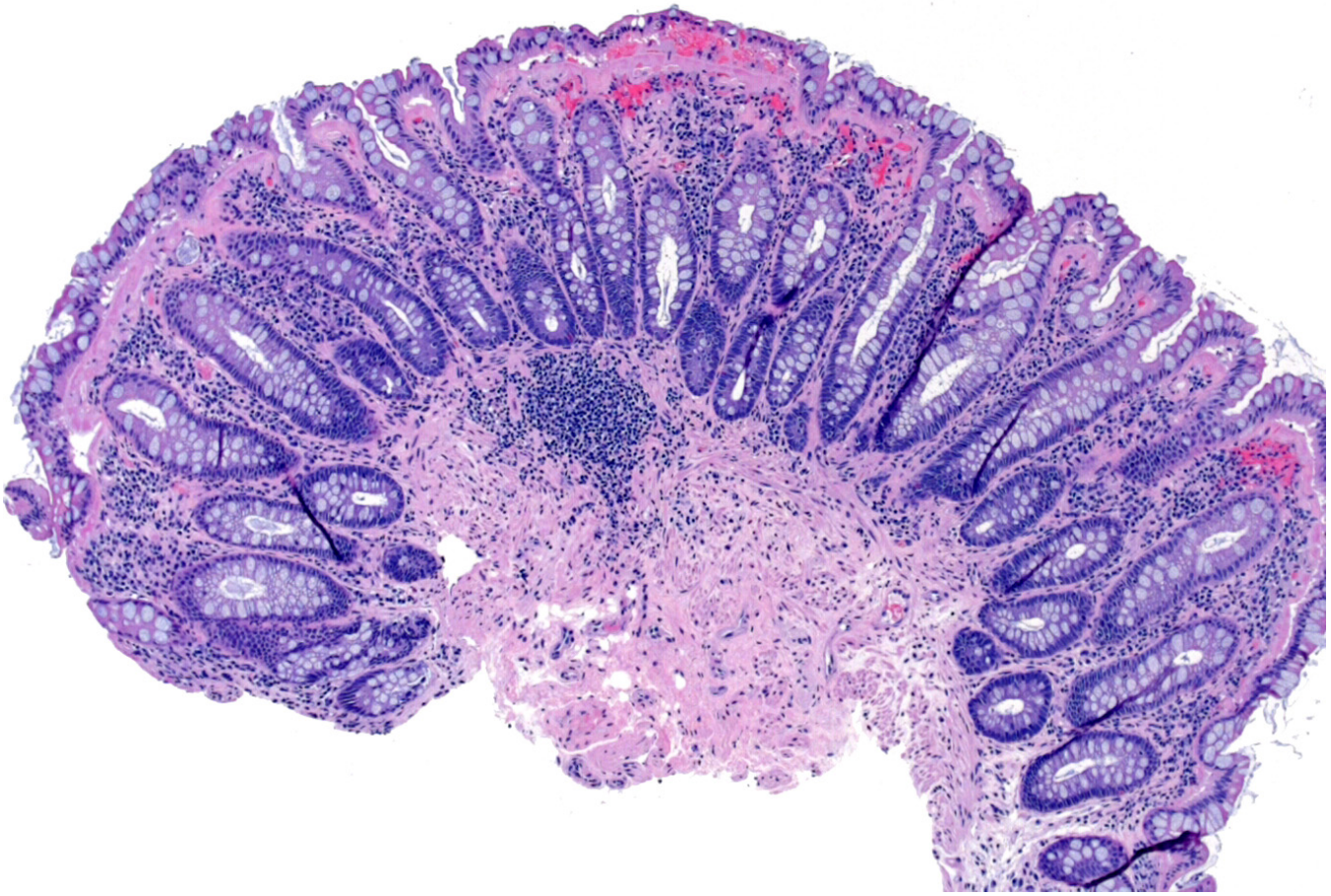


Figure 1; H&E, 40x

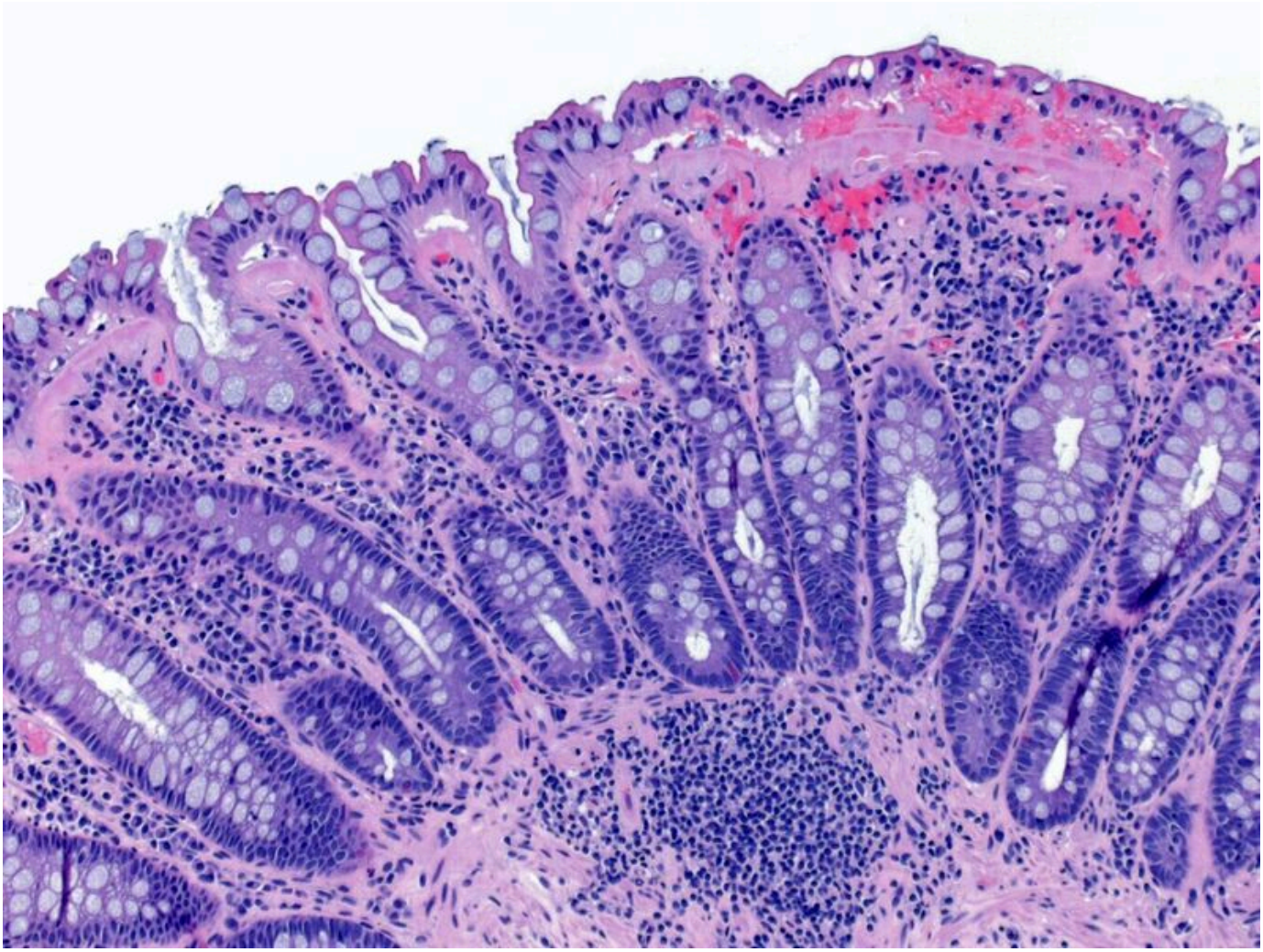


Figure 2; H&E, 200x

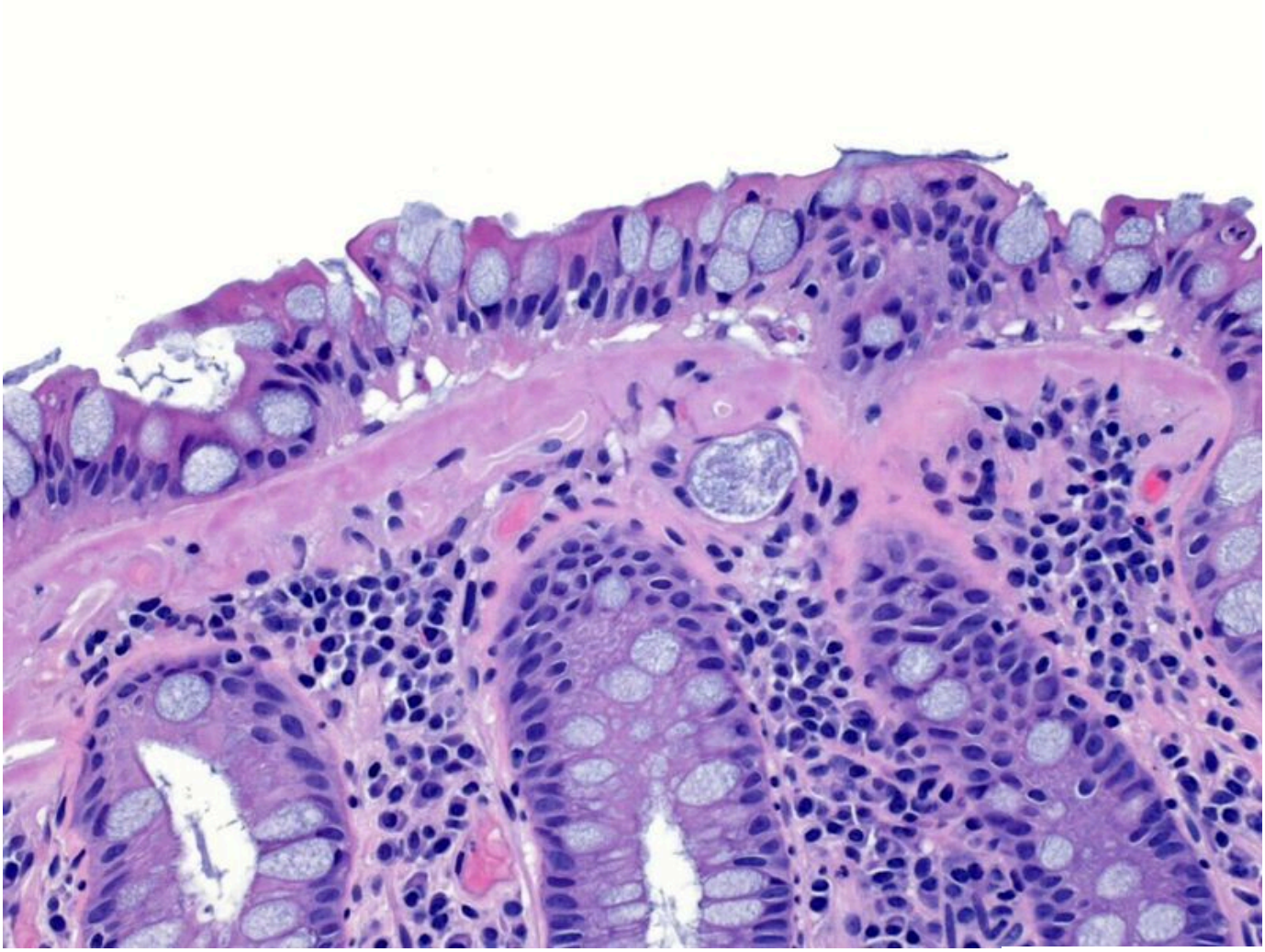


Figure 3; H&E, 600x

SCROLL FOR SPECIAL STAIN IMAGES

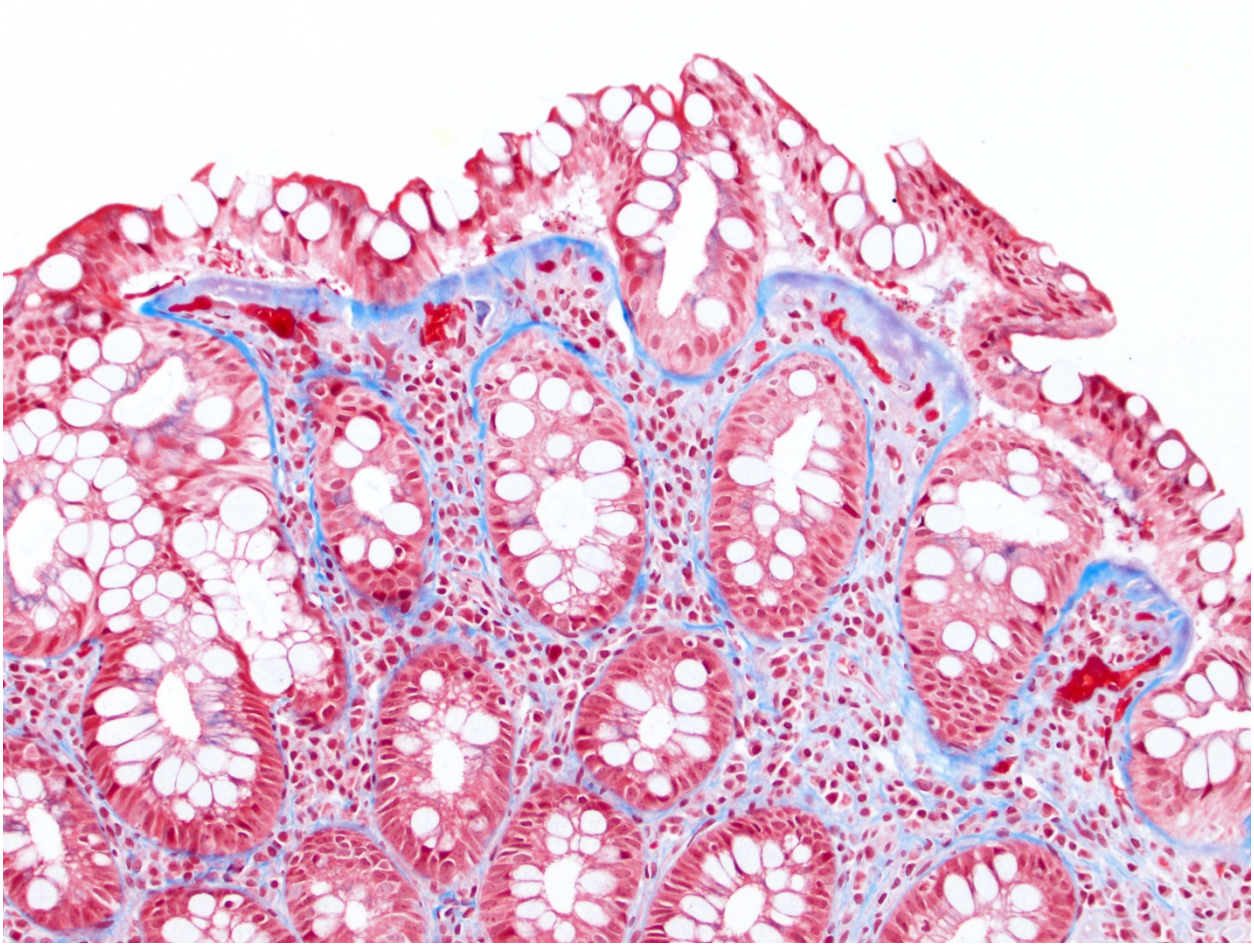


Figure 4; Trichrome stain, 400x

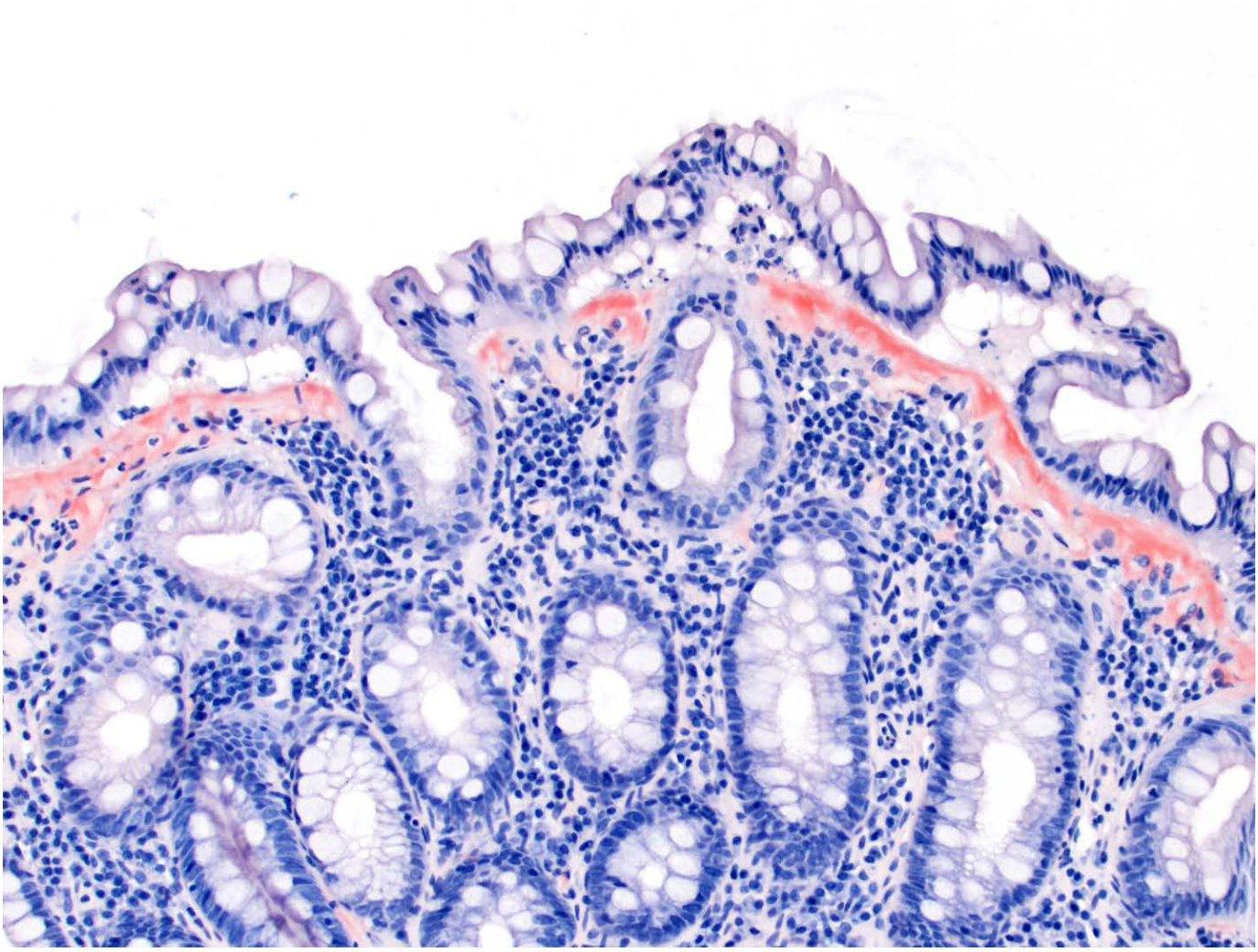


Figure 5; Congo-red stain, 400x

Question: Based on the morphology and special stain results, what is the diagnosis?
A) Collagenous colitis
B) Amyloid colitis
C) Mucosal prolapse
D) Ischemic colitis
E) Quiescent inflammatory bowel disease

Correct Answer:

B) Amyloid colitis

The biopsies show dense subepithelial eosinophilic thickening measuring up to 86 micrometers. There is no evidence of surface epithelial damage or intraepithelial lymphocytosis. The eosinophilic thickening is limited to the subepithelium without vascular or interstitial involvement and shows salmon-pink appearance on Congo-red stain with apple-green birefringence under polarized light. The findings are diagnostic of amyloid colitis. The amyloid deposits were typed as amyloid protein A, consistent with AA (serum amyloid A)-type amyloid deposition by liquid chromatography tandem mass spectrometry.

Amyloidosis of gastrointestinal tract is not infrequent and biopsies from gastric and rectal mucosa are part of routine diagnostic workup for systemic amyloidosis. Amyloid protein is commonly deposited around the vessels and in the lamina propria; very rarely, it may be deposited in the subepithelial location mimicking collagenous colitis as seen in our case. To date, only four such cases have been reported in the literature.

In the reported cases, the affected patients were male with a wide age range (29-69 years). In all but one case, there was an underlying systemic inflammatory condition specifically Crohn's disease, urinary tuberculosis and rheumatoid arthritis, and similar to our case, the amyloid was typed as AA in all other cases. The endoscopic findings ranged from mild erythema to subtle orange discoloration/friability of the mucosa.

The patients with subepithelial amyloid deposition are more likely to present with watery diarrhea secondary to perturbations of diffusion caused by the subepithelial deposits, similar to the proposed mechanism for collagenous colitis. In contrast, the clinical presentation with vascular or interstitial amyloid deposition is variable, ranging from asymptomatic, to pseudoobstruction and ischemic colitis-like presentation secondary to amyloid angiopathy or altered gut motility and autonomic dysfunction.

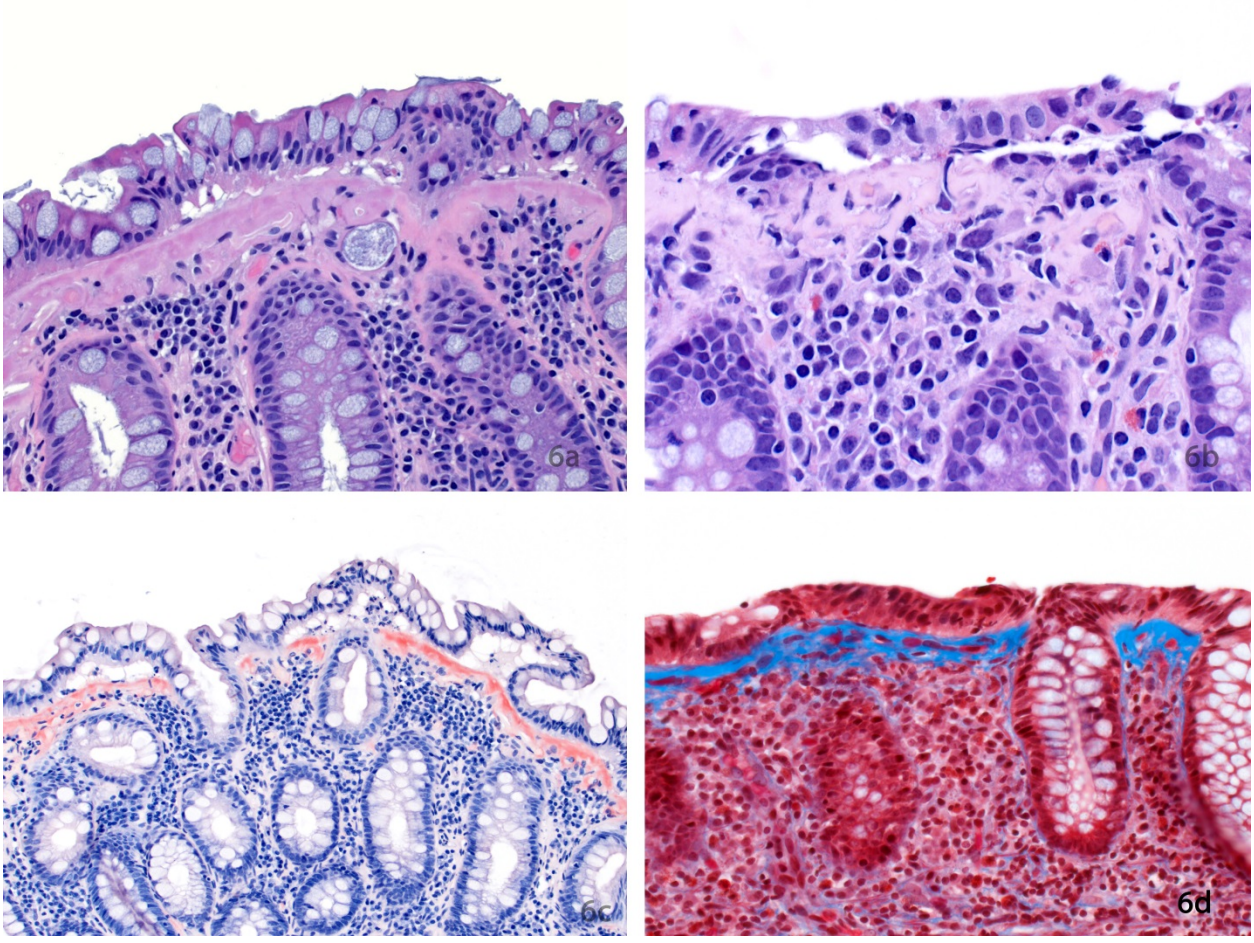
The differential diagnosis of this peculiar histologic presentation of amyloid colitis is rather limited and includes other diseases with subepithelial hyaline deposition. The most important differential is collagenous colitis. Unlike collagenous colitis, surface damage, increase in intraepithelial lymphocytes, entrapment of capillaries and inflammatory cells are not present in amyloid colitis (Figure 6a – d). Other differentials include mucosal prolapse, quiescent inflammatory bowel disease, and ischemic colitis where the collagen may be deposited in the subepithelial location secondary to mucosal injury and repair. The distinction and a definitive diagnosis of amyloid colitis can be readily achieved using Congo red stain, as the subepithelial band in all other entities would lack Congo red staining.

Since amyloidosis is caused by several different disease states, treatment is aimed at limiting the amount of amyloid deposition by treating the underlying systemic disorder. In cases associated with inflammatory diseases, immune suppression may be employed to reduce inflammation associated with the disease. Chemotherapy may be used in cases of amyloidosis arising from diseases such as plasma cell dyscrasias.

KEY POINTS

- Rarely, amyloidosis of the gastrointestinal tract may mimic collagenous colitis where amyloid is deposited in the subepithelial location.
- This pattern of amyloid deposition is associated with chronic watery diarrhea and AA amyloidosis.
- A Congo red stain can reliably and quickly establish the diagnosis.

- Treatment is primarily directed against the underlying condition to reduce the amount of amyloid deposition.



6a and 6c: Amyloid colitis (H&E and Congo-red stain); 6b and 6d: Collagenous colitis (H&E and Trichrome stain). Note the absence of surface damage and the homogenous quality of amyloid deposits in amyloid colitis (left panel) in contrast to the injured surface epithelium with irregular collagen deposition in collagenous colitis (right panel).

SUGGESTED READING

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