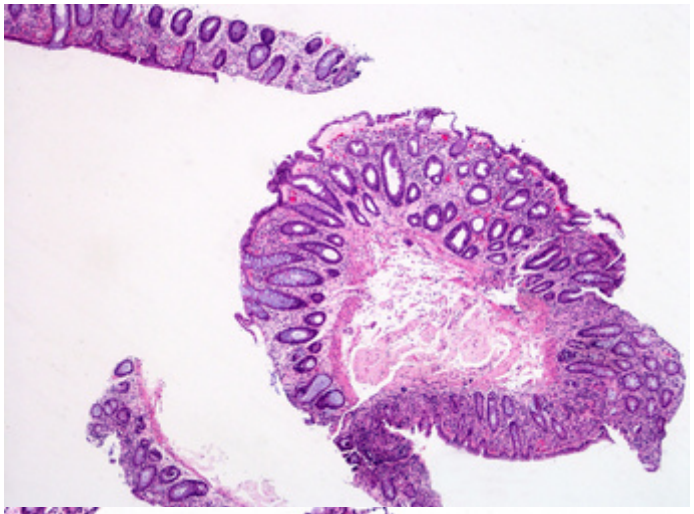
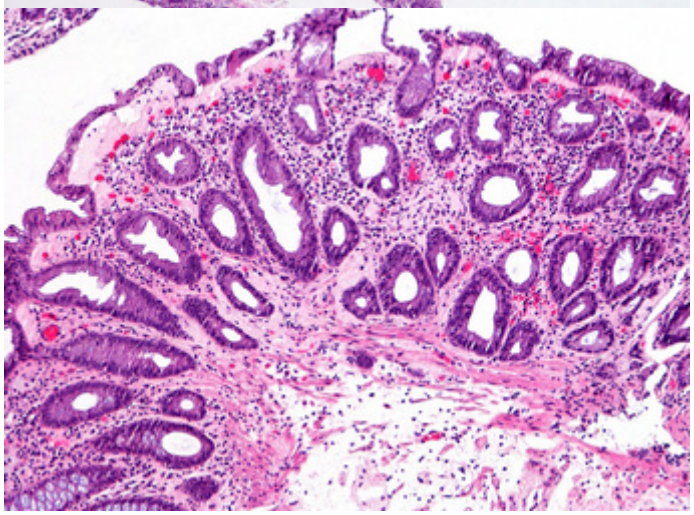
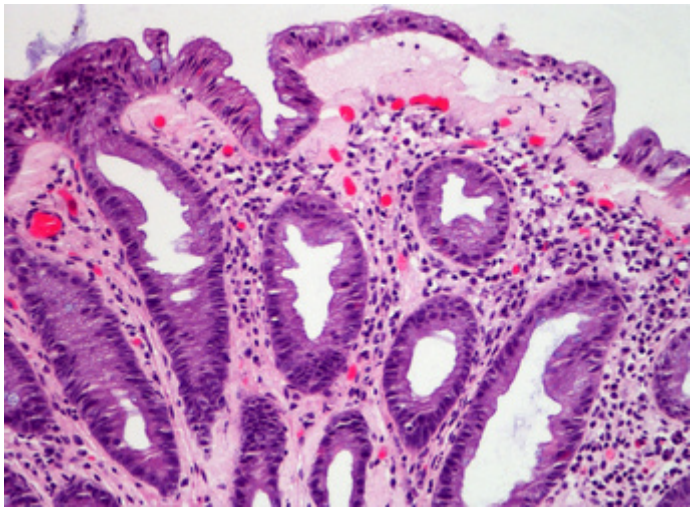
May 2019

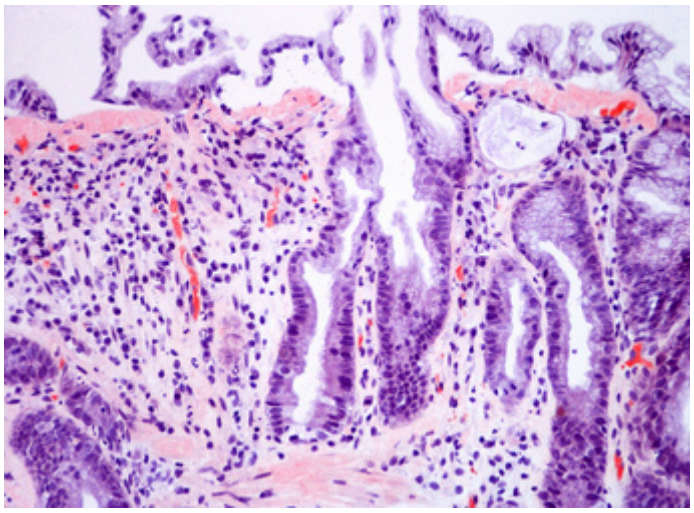
Rectal biopsy from a 60-year-old male with an unexplained weight loss and diarrhea.

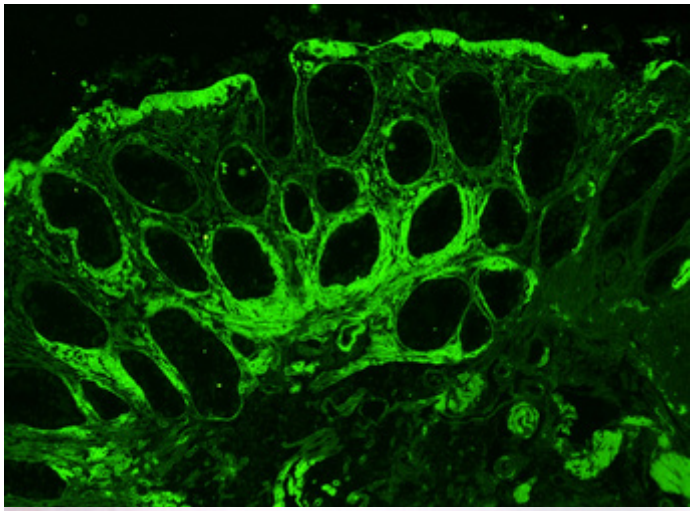
What is your diagnosis?

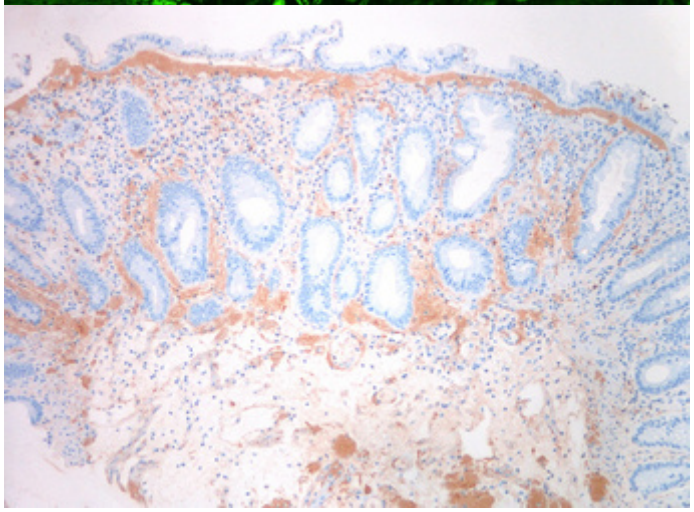












Diagnosis:

Primary lambda light chain amyloidosis (AL amyloidosis).

Comment:

Endoscopically, rectal mucosa appeared normal. Microscopically, it shows mild crypt distortion, focal detachment of the surface epithelium and deposits of amorphous, eosinophilic material beneath the basement membrane and in the submucosal blood vessels (Panel A-C). Deposits stain with Thioflavin T and Congo red and show green birefringence on polarized microscopy (Panel D). Immunohistochemistry and immunofluorescence reveal strong positivity for lambda light chain (Panel E and F), whereas immunohistochemistry for kappa light chain, amyloid A, transthyretin, and beta2-microglobulin was negative.

Amyloidosis constitutes a heterogenous group of disorders that share the feature of deposition of amorphous, extracellular deposits of abnormal fibrillary protein at various sites. It may be hereditary or acquired, localized or systemic in distribution. The diagnosis of amyloidosis is based on histologic demonstration of amyloid deposits in the tissue, using Congo red staining, with green birefringence on polarized microscopy. The next step is to identify the amyloidogenic protein in order to establish the type of amyloidosis. This is usually done by immunohistochemistry, in combination with clinical, laboratory and genetic results. Immunohistochemistry is a highly sensitive and specific method, enabling definite classification of amyloidosis in more than 90 % of cases.

Amyloidosis in the GI tract is usually part of a systemic disease, the most common being amyloidosis AL, followed by the senile, hereditary and AA amyloidoses. Amyloid AA tends to deposit in the blood vessels and lamina propria, whereas amyloid AL is usually found in the muscular layers and blood vessels. The deposits may be abundant and easy to recognize, but may also be very subtle. When deposition is abundant below the basement membrane, it can be misdiagnosed as collagenous colitis. Whatever the pattern, if eosinophilic, amorphous material is found in a GI biopsy, special stains for amyloid must be used.

GI amyloidosis may be asymptomatic or may present with malabsorbtion, diarrhea, weight loss, abdominal pain, ischemia, haemorrhage, perforation, or motility disorder.

Systemic amyloidoses have been regarded as intractable conditions, but improvements in the understanding of pathogenesis over the past decade have led to the development of different therapeutic approaches ranging from chemotherapy and autologous stem cell transplantation for AL amyloidosis to liver transplantation for some hereditary forms.

For further reading:

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