

Crohn's Disease and Hereditary Hemochromatosis, a Case Report

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Research Article

Keywords: Hereditary hemochromatosis, Crohn's disease, Iron overload, Anemia

Posted Date: October 11th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-597413/v1>

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Abstract

Hereditary hemochromatosis (HH) is a genetic disorder characterized by increased total iron body storage. It is one of the most commonly identified genetic causes of liver cirrhosis. Here we report a 43-year-old male who was previously diagnosed with crohn's disease, found to have normal hemoglobin and hematocrit. Additional lab tests revealed high ferritin and transferrin saturation. Upon further evaluation, he was diagnosed with hereditary hemochromatosis. The presented case will shed some light on the rare coexistence of crohn's disease and hemochromatosis and some problems in diagnostics related to the presence of the two conditions in the same patient.

Introduction

Crohn's disease is one of the two main types of inflammatory bowel diseases. It usually manifests as abdominal pain, fever, constipation or diarrhea sometimes with passage of blood in stool [1]. Extra-intestinal manifestations may include arthritis, uveitis, ankylosing spondylitis, erythema nodosum among others [2]. The most common extra-intestinal manifestation of crohn's disease is anemia, which affects up to 74% of patients. It is usually a combination of iron deficiency anemia and anemia of chronic disease, but can be caused by other etiologies such as folate or vitamin B12 deficiency, or as a side effect of medications [3]. The gold standard to diagnose of crohn's disease is ileocolonoscopy with biopsies. CT enterography or MR enterography can be helpful in detecting and following some complications like fistulas, abscesses or intestinal obstruction [1]. Patients diagnosed with Crohn's disease have higher risk to suffer from other autoimmune conditions like primary sclerosing cholangitis, celiac disease, type 1 diabetes, sarcoidosis, psoriasis, rheumatoid arthritis and ankylosing spondylitis [4].

Hereditary hemochromatosis (HH) is an inherited disease characterized by iron overload on multiple organs in the body. The most common mutation happens on the *HFE* gene, resulting in a cysteine to tyrosine substitution at amino acid 282 (C282Y). The cardinal clinical findings in this disease are fatigue and arthralgia, but other features can be found like hyperpigmentation, loss of libido and hyperglycemia. Phlebotomy is considered the mainstay of treatment for hemochromatosis [5].

Case Report

We report a 43 year old Indian male patient, who has an established diagnosis previously of Crohn's disease for 5 years on maintenance therapy of oral Azathioprine 100mg daily and oral Mesalazine 1000mg BID. This is the patient's first encounter with us, where he presented with a history of abdominal pain for 1 month duration, the pain was colicky in nature and moderate in severity, associated with constipation. Upon initial assessment and physical examination, the patient had low grade fever of 37.9 C, other vitals were normal and his examination was marked for left lower quadrant abdominal tenderness and abdominal distention.

He was assessed by Gastroenterology team and they elected to do a colonoscopy which revealed

a polypoid mass causing luminal narrowing extending 22 centimeters from the anal verge and the scope was difficult to negotiate beyond the obstructive mass (Figure 1).

He was assessed by the surgical team who decided to go for surgical removal of the mass, so the patient underwent an MRI enteroclysis as a part of the preoperative evaluation, which revealed diffuse low T2 signal intensity of the liver suggestive of iron overload of the liver (Figure 2), then he underwent left partial colectomy and the mass was sent for histopathology (figures 3,4). Afterwards he was referred to Hematology for further evaluation of iron overload.

Initial laboratory investigations including CBC and Iron profile are given in (table 1).

White blood cells	4.1*10 ³ (4.0-10.0 *10 ³)
Red blood cells	4.3*10 ⁶ (4.5-5.5*10 ⁶)
Hemoglobin	14.1 gm/dL (13.0-17.0 gm/dL)
Hematocrit	39.9% (40.0-50.0 %)
Mean corpuscular volume	92.6 fL (83.0-101.0 fL)
Mean corpuscular hemoglobin	32.7 pg (27.0-32.0 pg)
Mean corpuscular hemoglobin concentration	35.3 gm/dL (31.5-34.5 gm/dL)
Platelets	287*10 ³ (150.0-400.0 *10 ³)
Iron	37 umol/L (6-35 umol/L)
Total iron binding capacity	48 umol/L (45-80 umol/L)
Iron saturation %	77% (15-45 %)
Transferrin	1.9 gm/L (2.0-3.6 gm/L)
Ferritin	1710 ug/L (30-490 ug/L)

Table 1: Initial laboratory investigations

Based on the findings of blood tests, there was a strong suspicion of hemochromatosis, so genetic testing was sent and showed homozygous for C282Y variant in the HFE gene, H63D variant was not detected. MRI cardiac and hepatic iron load was done and showed moderate hepatic iron overload and no evidence of myocardial iron overload. Currently the patient is on maintenance therapy for crohn's disease and regular follow up for hemochromatosis and he is not requiring any treatment or intervention until now.

Discussion

We described a patient with a history of complicated crohn's disease found to have hereditary hemochromatosis, the coexistence of inflammatory bowel disease and hereditary hemochromatosis is very rare, few case reports discussed this combination [6, 7], However upon reviewing the literature extensively, we could not find any paper that reported a patient with both hereditary hemochromatosis and crohn's disease. Crohn's disease is an inflammatory disease characterized by a relapsing nature that primarily affects the whole gastrointestinal tract with skipping involvement [8]. It is well known that crohn's disease is a multifactorial disease including hereditary, genetic and environmental factors, but the precise mechanism and cause are not well understood [9].

The evidence of the importance of the genetic factor to play a significant role in causing crohn's disease was supported by studies from families and twins with crohn's, a susceptibility locus for crohn's has been mapped to chromosome 16, that mainly affects the nucleotide-binding oligomerization domain (NOD) proteins NOD1 and NOD2 and the final gene product will lead to susceptibility of crohn's over activating of NF-kB in the intestinal epithelial cells [8]. Another confirmation of the importance of the genetic predisposition is the association of Human leukocyte Antigen "HLA" and crohn's disease, even HLA typing varies according to the race, and one of the common association is HLA-DR4 and DQ 4 which is carried on chromosome 6 , the same chromosome that carries the HFE gene for Hereditary hemochromatosis [8,10].

Hereditary hemochromatosis is an autosomal recessive disease characterized by disturbed iron regulation in the body that leads to iron deposition in multiple organs. This dysregulation caused by gene mutation to HFE gene on chromosome 6, and the most common mutation is the homozygous mutation C282Y, which compromises 85-90% of the phenotypically affected patients. The disease may be asymptomatic early then may manifest as arthralgia, impotence, cirrhosis, cardiomyopathy, diabetes mellitus and hypogonadism [11].

The diagnosis of Hereditary hemochromatosis mandates confirmed raised serum ferritin (>300µg/L in male and postmenopausal female and >200µg/L in premenopausal female) and elevated fasting transferrin saturation (45%), with or without symptoms. The genetic study for HFE gene is used for subtyping, and liver biopsy to determine the stage and the degree of liver fibrosis [10], and Cardiac MRI is usually done once cardiac involvement is suspected to quantify the iron overload [12].

Anemia is a common finding in crohn's disease with a prevalence of 9-74% [13],

which may be due to chronic blood loss or the chronic inflammatory state among other causes, but it was not found in our patient who had normal Hemoglobin readings, which can be attributed to iron overload.

Conclusion

Hereditary hemochromatosis and crohn's disease are both autoimmune diseases which were never reported to occur in the same patient. The coexistence of these disorders might result in less chance of having anemia, and less incidence of iron overload complications which may warrant treatment. Nonetheless, patients with these disorders need close follow up to avoid the disease's devastating complications.

Declarations

Statement:

Acknowledgment:

Authors would like to acknowledge the internal medicine and hematology departments at Hamad Medical Corporation for supporting this publication.

Funding sources

Qatar National Library.

Conflict of interest:

The authors report no conflicts of interest in this work.

Ethics approval:

Case approved by HMC Medical Research Center.

Consent to participate:

Written informed consent was obtained from the patient to allow the publication of information including images.

Consent for publication:

Written informed consent was obtained from the patient to allow the publication of information including images.

Availability of data and material:

Data and material are available whenever required

Code availability:

Not applicable

Authors' contribution:

Ibrahim Khamees: manuscript writing and literature review.

Nabeel Mohammad Qasem: case presentation writing.

Mousa Alhiyari: literature review.

Lujain Salahaldeen Malkawi: literature review.

Orwa Elaiwy: pathology slides.

Mohamed A Yassin: mentorship, manuscript writing, and literature review.

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Figures

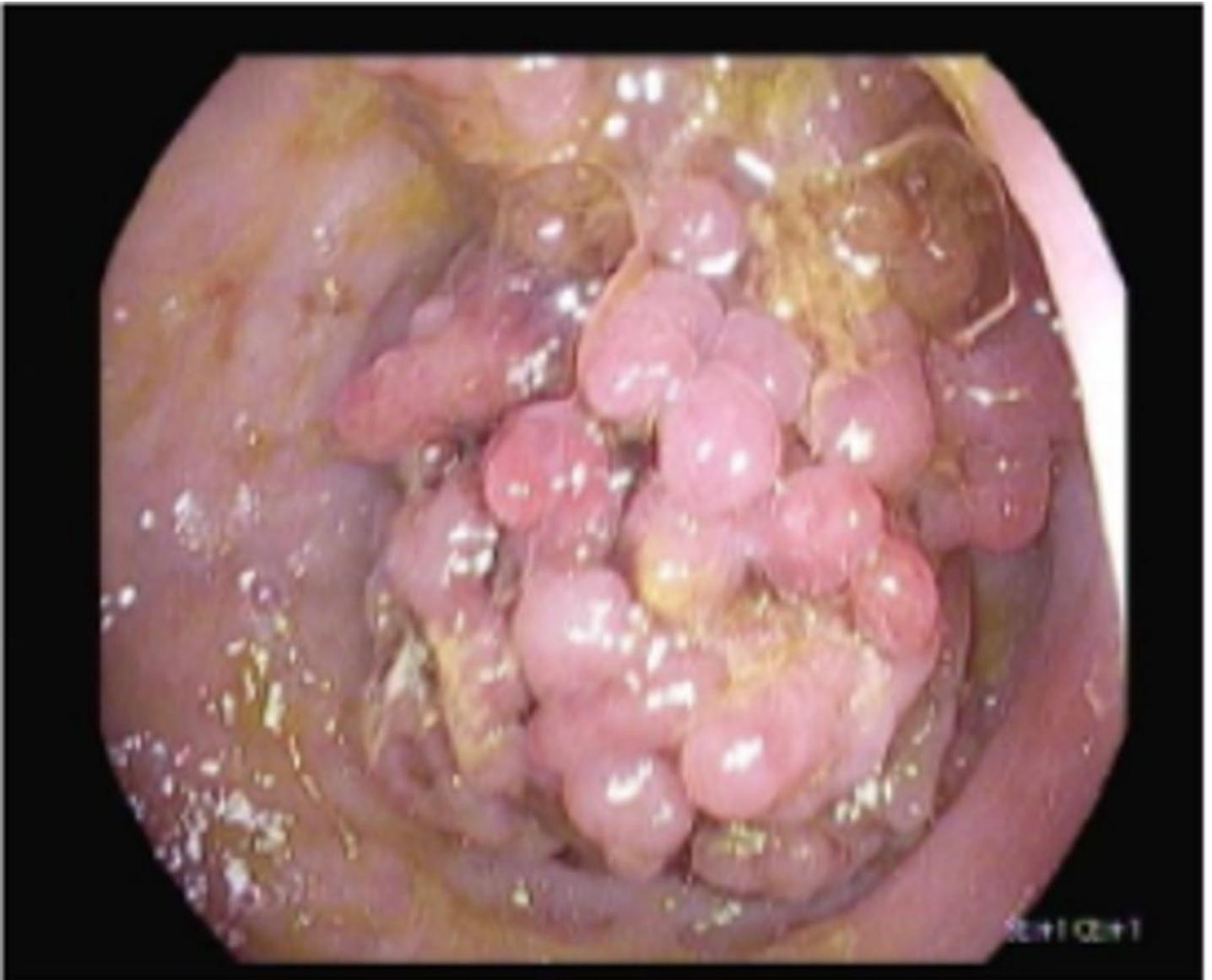


Figure 1

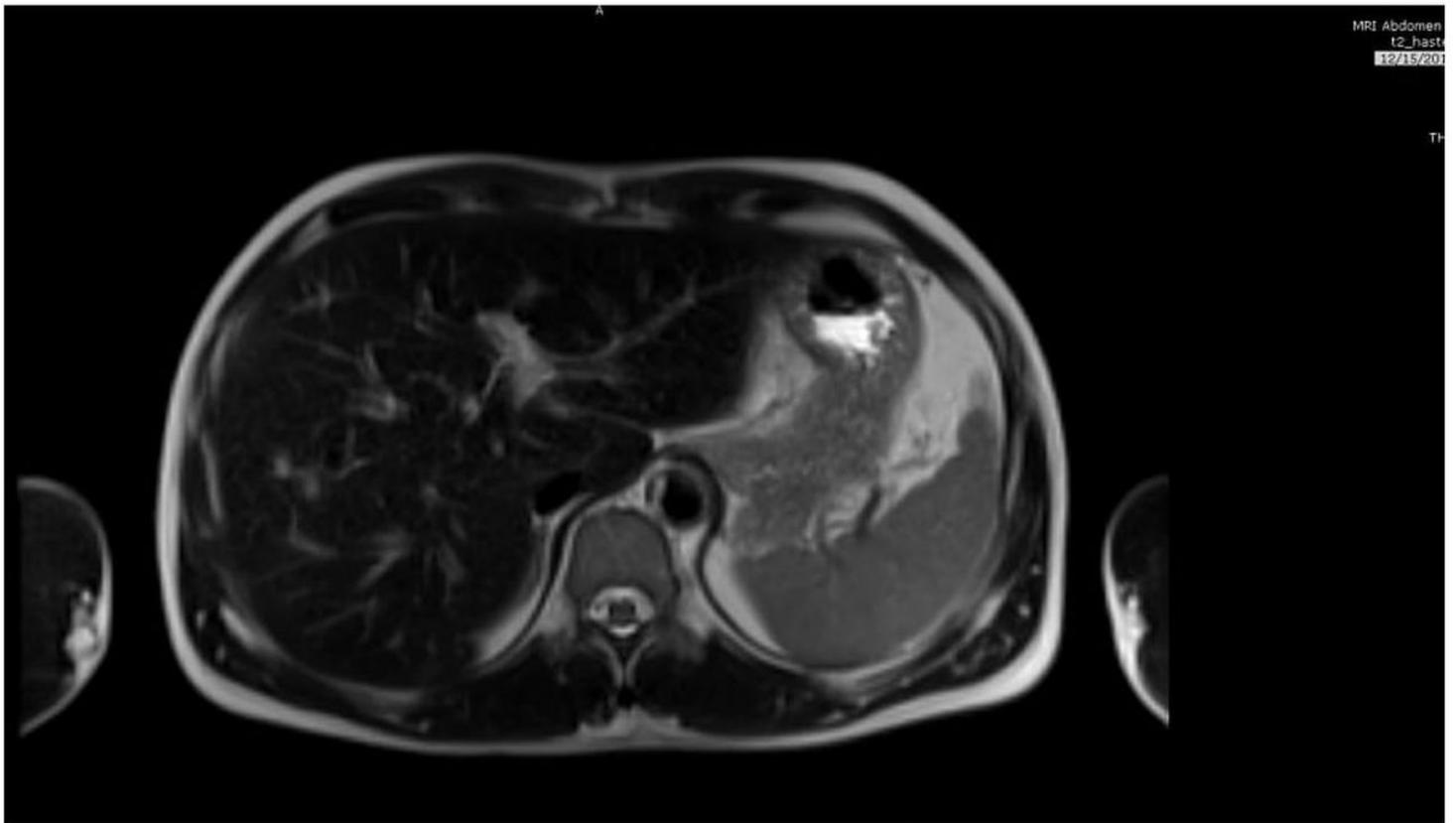


Figure 2

MRI enteroclysis showing hepatic iron overload.

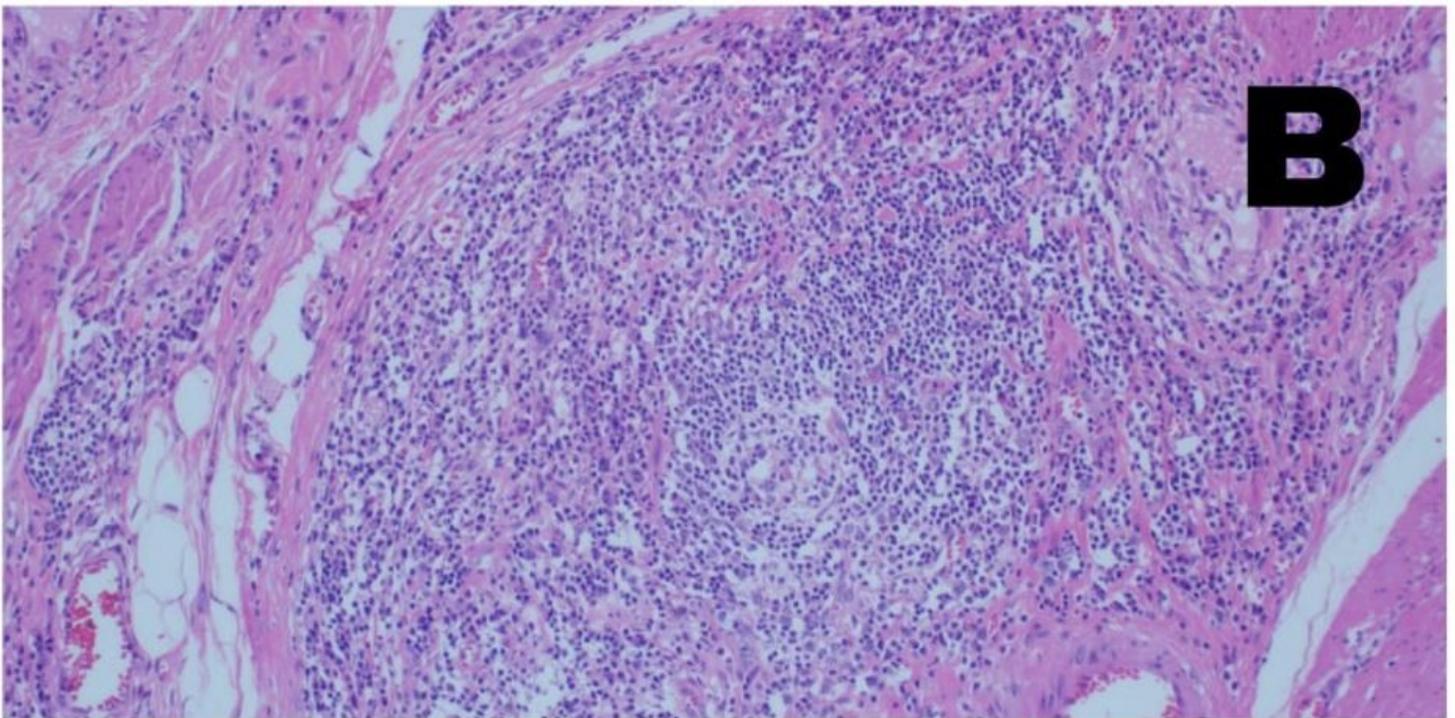
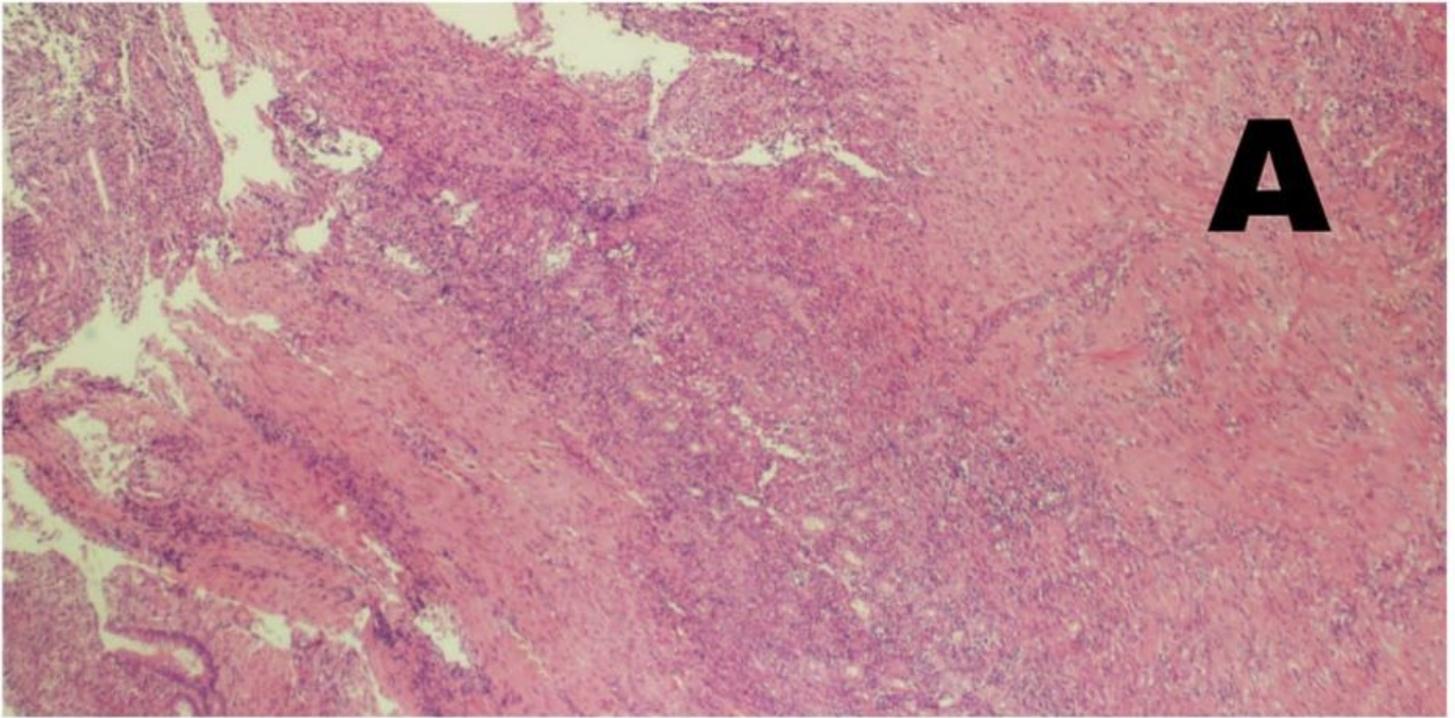


Figure 3

(A) A section of large bowel wall showing severe acute inflammation with fissuring ulcer extending to the muscularis, a feature of Crohn's disease. (Hematoxylin & Eosin stain, 40x). (B) A section of large bowel wall showing chronic inflammation with lymphoid follicles in the muscularis, a feature suggestive of Crohn's disease. (Hematoxylin & Eosin stain, 200x)

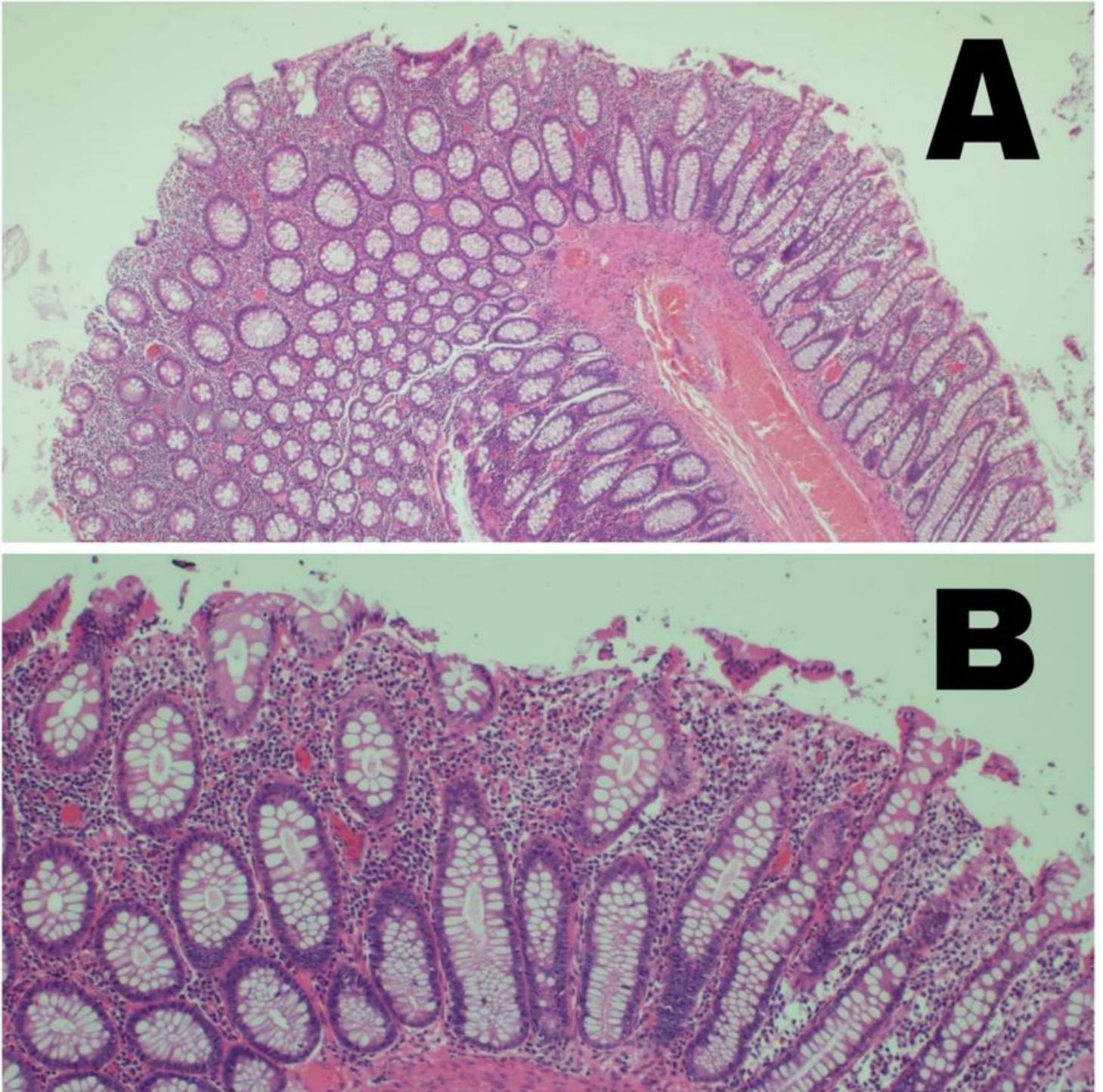


Figure 4

(A) A section of large bowel showing hyperplastic polyposis area. One glandular crypt (Bottom) shows crypt abscess, a feature of inflammatory bowel disease. (Hematoxylin & Eosin stain, 40x) (B) A section of large bowel showing hyperplastic polyposis area with higher magnification. The nuclei show no dysplasia. (Hematoxylin & Eosin stain, 200x)