Case History

A 24 year old male presented with abdominal pain, nausea, vomiting and decreased oral intake for seven days. His past medical history included diagnoses of paroxysmal nocturnal hemoglobinuria (PNH) and idiopathic thrombocytopenic purpura (ITP) for which he was receiving the pro-hematopoietic drug, eltrombopag. At the time of admission, the patient had an elevated CRP (140.1 mg/L, reference range < 10), white blood cell count (14.08 thousand/ul, reference range 4.3-10), lactate dehydrogenase (527 U/L, reference range 80-190), and total bilirubin (2.7 mg/dL, reference range 0.2-1.3); and a decreased haptoglobin (12 mg/dL, reference range 26-279). Initial platelet count was 48 thousand/ul (reference range 150-400); this decreased to 4 thousand/ul over the course of 48 hours. D-dimer level at the time of the platelet drop was elevated to 3.5 mcg/ml (reference range < 0.59). On CT scan, inflammation of the retroperitoneum in the region of the 3rd and 4th portions of the duodenum was noted. Esophagogastroduodenoscopy (EGD) revealed mildly mottled mucosa in the 2nd portion of the duodenum and areas of abnormal mucosa with erythema, edema, and distorted architecture in the 3rd portion of the duodenum (see image below).

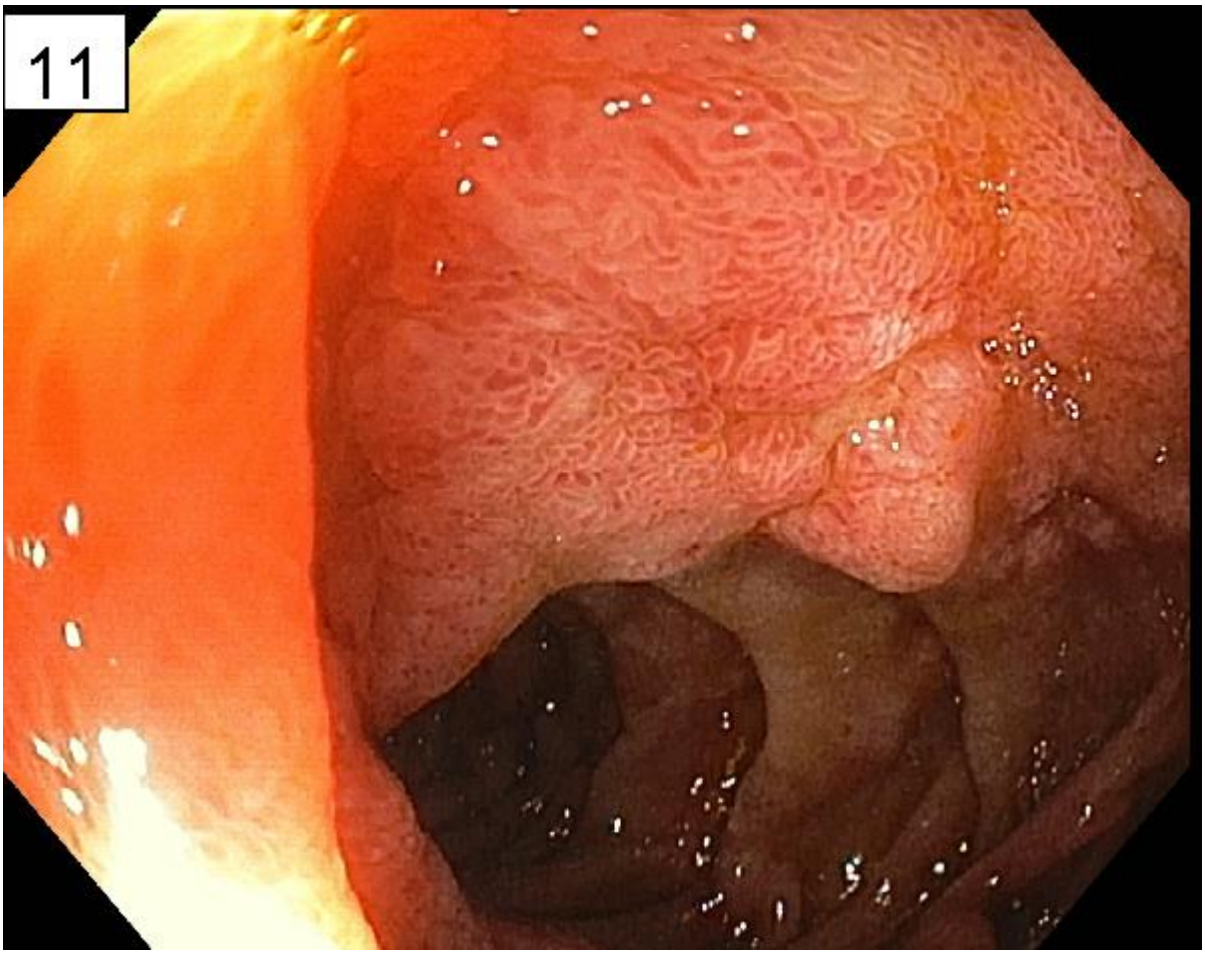

Image 1: Representative endoscopic image of the 3rd portion of the duodenum, showing architectural distortion, erythema and edema.

Representative images from the duodenal biopsies are shown in images 2-4 below.

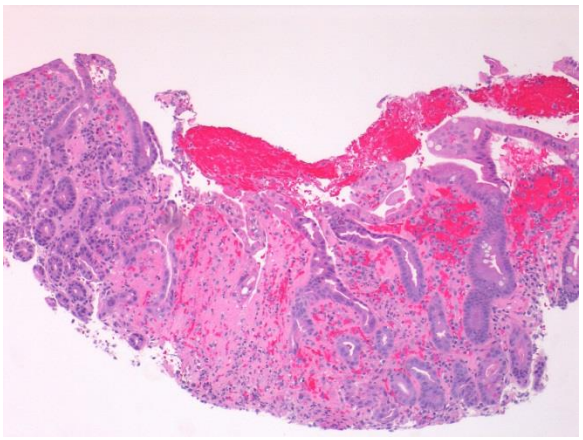

Image 2: Crypt withering and intramucosal fibrin deposition

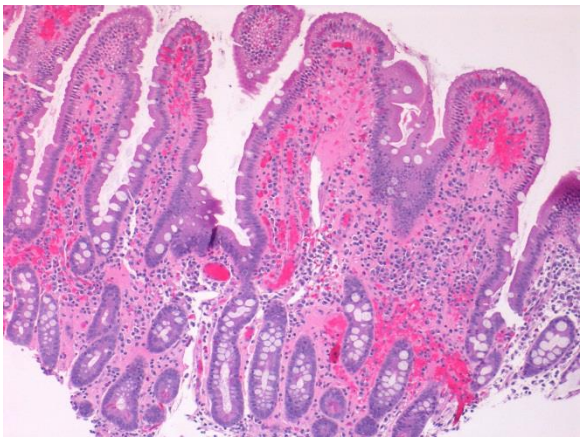

Image 3: Intramucosal hemorrhage

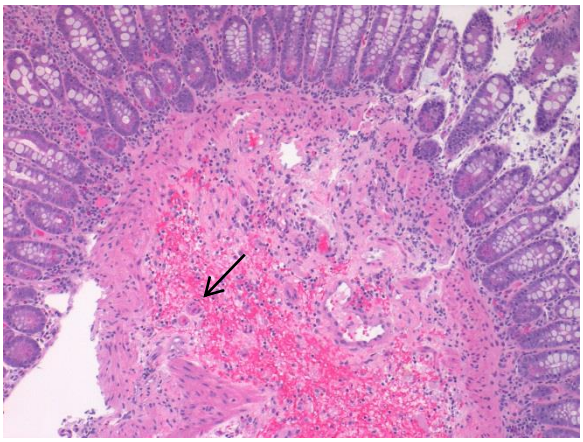

Image 4: Submucosal hemorrhage and microvascular occlusion (arrow)

Questions:

What is your diagnosis?

A. Amyloidosis
B. PNH-associated small bowel ischemia
C. Waldenstrom's macroglobulinemia
D. Peptic duodenitis

(scroll down for answer)

Answer:

This is a case of PNH-associated small bowel ischemia. Although highly eosinophilic at low power, histologic feature of amyloidosis (dense acelluar deposits of eosinophilic material, particularly around vessels) or Waldenstrom's macroglobulinemia (acellular, eosinophilic material within lymphatic channels) are ABSENT from this biopsy. PNH is an acquired clonal hematopoietic stem cell disorder in which mutations arise in the phosphatidylinositol glycan class A gene (*PIG-A*, located on the X chromosome). The *PIG-A* gene product is necessary for the formation of the glycosylphosphatidylinositol anchor that attaches certain proteins to the cell membranes of hematopoietic cells, including the complement regulators, CD55 and CD59. Lack of these proteins results in complement-mediated intravascular hemolysis, peripheral blood cytopenias, and an increased risk of venous thrombosis (Brodsky 2014). Approximately 1/3 of patients with PNH will present with abdominal pain (Peffault de Latour 2008), and more than 1/2 of patients will have abdominal pain at some time in their disease course (Schubert 2015). Small bowel ischemia has been infrequently reported (Blum 1966, Doukas 1984, Williamson 1987, Zapata 1998, Adams 2002). Where histology has been described, the findings have included patchy areas of necrosis, hemorrhage and edema with lamina propria fibrosis and microvascular thrombi (Adams 2002, Zapata 1998). In our patient, the presence of rare venous thrombi, crypt withering and lamina propria fibrosis were consistent with an ischemic pattern injury. Many coagulation disorders (e.g. PNH, HUS, TTP, Protein C or S deficiency, DIC and Homocystinuria) can lead to GI ischemia. Correlation with clinical history is essential. Unfortunately, many of the patients with PNH-associated small bowel ischemia have recurrent episodes (Adams 2002, Hino 2014), though eculizumab, the C5-C9 membrane attack complex inhibitor recently approved for the treatment of PNH-related hemolysis, has been associated with durable relief of abdominal symptoms in at least one patient (Hino 2014).

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Authors:
Cheryl Mather, MD
Fellow, GI & Hepatic Pathology
University of Washington

Maria Westerhoff, MD
Assistant Professor
Department of Anatomic Pathology
University of Washington