CASE REPORT

A 33-year-old albino woman of Puerto-Rican origin presented with complaints of rectal bleeding. The rectal bleeding had been painless and intermittent for the last few months but had worsened over the last few weeks. At the time of presentation she was having at least six bowel movements a day with symptoms of frequency and urgency. Bright blood was found mixed with stool in almost every bowel movement. She denied any fevers or chills but admitted to some discomfort in her abdomen. She had lost about 5 lbs over the last 4 weeks. Physical exam revealed a small albino woman with blond hair in some discomfort. She had nystagmus. Conjunctival pallor was present. No oral lesions were noted. She was hypovolemic without evidence of orthostatic hypotension. Examination of the abdomen revealed mild tenderness in the left lower quadrant without peritoneal signs and normal bowel sounds. Blood work revealed a microcytic anemia, mild hypokalemia and an ESR of 40 mm/hr. She did not have a significant past medical history except a history of poor visual acuity requiring

Figure 1.

Figures 1–3. Erythematous and inflamed colonic mucosa with pseudopolyp formation and areas of hemorrhage.

Visvanathan Muralidharan, M.D., MRCP, Fellow in Gastroenterology, Bridgeport Hospital, Yale New Haven Health, Bridgeport, CT. Priya Jamidar, M.D., FACG, Associate Professor, Section of Digestive Diseases, Yale New Haven Hospital, New Haven, CT.
optical lenses. She had no known drug allergies but had been told not to take aspirin. There was no family history of inflammatory bowel disease.

She underwent a colonoscopy, which revealed granular and friable mucosa with contact bleeding with superficial ulcerations involving the left colon from the splenic flexure down to the rectum. Some pseudopolyps were also seen. (Figures 1–3) Biopsies were taken (Figure 4).

Questions
1. What is the diagnosis?
2. What are the clinical features of this condition?
3. How would you treat this condition?

(continued on page 110)
DISCUSSION

Hermansky Pudlak Syndrome (HPS)

This syndrome was first described by two Czechoslovakian pathologists (1) and consists of a collection of genetically distinct autosomal recessive defects, which share clinical manifestations of hypopigmentation and a platelet storage deficiency. These findings reflect abnormalities in the melanosome of the melanocyte and the platelet’s dense body—two intracellular organelles related to lysosomes (2). The two main genetic defects have been described in human HPS—a frame shift mutation in HSP1 gene (3) which codes for an mRNA vital for vesicle formation—and a mutation in the ADTB3 gene which codes for an adaptor complex important in vesicle formation (4). The clinical manifestations of HPS arise from disorders of vesicle formation intra-cellular trafficking. A significant portion of the population of north-western Puerto Rico is homozygous for HPS1 mutation (more than 400 patients). Accumulation of ceroid lipofuscin has been considered a hallmark of this disease (5) however this is not necessary to establish the diagnosis of HPS.

It accumulates in the visceral organs including the kidney, lung, bone marrow, spleen, liver and the large intestine. Clinical features of this disease include: oculo-cutaneous albinism, bleeding diathesis, pulmonary fibrosis, and granulomatous colitis.

There is a wide range of severity in the oculo-cutaneous albinism associated with HPS. The hematological manifestations are due to platelets deficient in dense granules (5). It usually involves spontaneous soft tissue bruising and bleeding from mucosal membranes (5). Coagulation factors, prothrombin and partial prothrombin times are normal. Bleeding time can be prolonged. Fatalities due to bleeding are rare but a significant number of patients have received transfusions of red blood cells and platelets. For minor bleeding in HPS topical thrombin can be used and DDA VP can be administered prophylactically (6). The pulmonary involvement in HPS is extremely variable and usually manifests as a restrictive defect (7). Granulomatous colitis in HPS was first described by Schinella, et al (8). About 15% of these patients suffer from a granulomatous colitis (7). The distal colon is most often affected by this complication. However, it can affect both the small and large intestine. Granulomatous gingivitis has also been described (5). The colitis of HPS can resemble Crohn’s disease (8). It is possible that the deposition of the ceroid lipofuscin in the intestinal mucosa causes a granulomatous colitis. The colitis can manifest as diarrhea or bright red blood per rectum. Some of these patients may have symptoms of lactase deficiency and may actually have a positive hydrogen breath test (7). The lymphocyte and neutrophil function appear to be normal in HPS in contrast to other related conditions like Chediak-Higashi Syndrome (9).

Management

There is very little information available on the management of colitis in HPS. The general approach is to use 5-ASA preparations and topical corticosteroids. There is a theoretical risk of some systemic absorption of the 5-ASA compound with regular 5-ASA, which may then worsen platelet function. Hence a case can be made for the use of balsalazide, which may have very little systemic absorption when compared with other 5-ASA preparations. It is important to avoid any medication that can interfere with platelet function. If bleeding is profuse platelet and blood transfusions may be necessary. Desmopressin can be used to help platelet function. In severe cases intravenous steroids can be used after excluding infectious colitis. Apart from anecdotal data there is very little literature on the use of immuno-modulatory agents like anti-TNF antibodies. Refractory cases have required colectomy although the post-operative course can often be complicated by bleeding (10).

References