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CASE REPORT | LIVER

Systemic Mastocytosis Complicated by Non-Cirrhotic Portal Hypertension and Variceal Bleeding

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ABSTRACT

Systemic mastocytosis is a myeloproliferative disorder characterized by extracutaneous involvement of at least one organ. Although rare, infiltration of inflammatory mast cells within the portal vein may lead to obstruction of the sinusoids resulting in non-cirrhotic portal hypertension. We present a patient with known history of systemic mastocytosis with bone marrow involvement presenting with new-onset esophageal variceal bleeding. Although systemic mastocytosis is uncommon, the subsequent development of hepatic involvement and non-cirrhotic portal hypertension are discussed. Further highlighted is a lack of organization guidelines and the potential for gastrointestinal and hepatic screening of mastocytosis patients with known extracutaneous involvement.

INTRODUCTION

Systemic mastocytosis is a myeloproliferative disorder characterized by mast cell hyperplasia with infiltration and accumulation in at least one extracutaneous organ.[1] While the most common site of extracutaneous involvement in systemic mastocytosis is the bone marrow, hepatic involvement may result in hepatic fibrosis and sinusoidal, non-cirrhotic portal hypertension.[1,2]

CASE REPORT

An 82-year-old woman presented to the emergency department with maroon-colored stool. She had a prior history of systemic mastocytosis, confirmed by bone marrow biopsy 3 years prior to admission. Mastocytosis was well-controlled on prednisone (20 mg orally), which she had been taking continuously. She reported no previous episodes of gastrointestinal (GI) bleeding nor family history of liver disease. She denied tobacco or recreational drug use and self-reported no prior history of alcohol use with negative ethanol levels on previous hospitalizations.

On arrival, the patient was hemodynamically stable. Exam disclosed a thin, elderly woman with anicteric sclera, scattered purpura on all extremities, and benign abdominal exam with no clinically evident liver or spleen enlargement. She had external hemorrhoids and maroon-colored stool on digital rectal exam. Initial laboratory data was notable for hemoglobin 6.8 mg/dL, albumin 2.9 g/dL, platelets 76 x 10^3/μL, creatinine 0.4 mg/dL, international normalized ratio 1.22, and an unremarkable liver panel aside from a chronically elevated alkaline phosphatase 249 U/L. The patient was started on intravenous pantoprazole and famotidine twice daily. She was transfused with 1 unit of packed red blood cells with appropriate response, and oral montelukast was added prior to endoscopy.

Endoscopy demonstrated 3 columns of large esophageal varices at 28 cm with extension to the gastroesophageal junction with red wale sign, moderate portal hypertensive gastropathy in the gastric cardia, and no ulcerations

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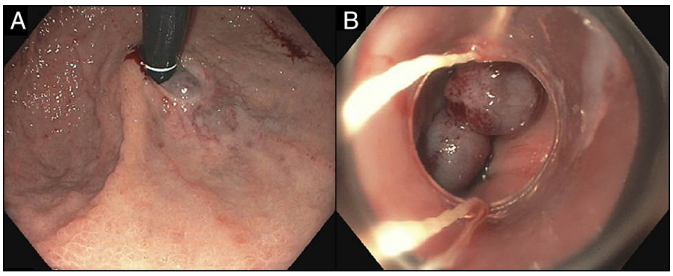

Figure 1. (A) Portal hypertensive gastropathy with active oozing of blood in the stomach cardia. (B) Band ligation of large esophageal varices in the distal esophagus.

(Figure 1). Five bands were placed with obliteration of the varices, and nadolol was started for secondary prophylaxis. The patient had no further episodes of bleeding. Abdominal ultrasound with doppler demonstrated splenomegaly, normal appearing liver with no evidence of steatosis, and patent hepatic and portal veins without thrombus. Review of abdominal computed tomography obtained approximately 1 year prior also demonstrated no evidence of liver nodularity.

Laboratory testing to evaluate the etiology of portal hypertension (viral hepatitis panel, iron studies, alpha-1-antitrypsin, ceruloplasmin, and autoimmune markers including anti-nuclear antibody, immunoglobulin classes, smooth muscle antibodies, and antimitochondrial antibodies) was unremarkable. No liver biopsy was performed as the patient was already on prednisone for treatment of mastocytosis and was high risk for bleeding given worsening thrombocytopenia.

The patient's hospital course was further complicated by acute hypoxemic respiratory failure secondary to hypertensive urgency with improved response to anti-hypertensive medications and aggressive diuresis. Transthoracic echocardiogram revealed preserved ejection fraction and unremarkable right-sided heart pressure. Follow-up endoscopy 2 weeks post-esophageal banding was not performed as the patient did not return to clinic. The patient was subsequently lost to follow-up so an outpatient liver biopsy was not obtained.

DISCUSSION

Based on this patient's evaluation, we believe that her portal hypertension and esophageal variceal bleeding was secondary to aggressive systemic mastocytosis, likely involving the liver. Gastrointestinal involvement may be seen in up to 80% of patients with systemic mastocytosis and commonly manifests as abdominal pain, diarrhea, and nausea or vomiting.[3] Bleeding from the gastrointestinal tract is typically due to peptic ulcer disease in approximately 11% of patients with systemic mastocytosis, while liver infiltration with portal hypertension is presumed to be rare. First described by Capron et al in 1978, non-cirrhotic portal hypertension as a result of systemic mastocytosis is thought to be either pre-sinusoidal or sinusoidal.[4] While the exact mechanism is unknown, it is postulated that non-cirrhotic portal hypertension may develop as a result of infiltration of inflammatory mast cells within the portal vein and obstruction of the sinusoids.[4] This infiltration is thought to result in increased portal pressures and sinusoidal obstruction.

The initial step to any evaluation of a patient with systemic mastocytosis is to determine the category of disease. Our patient's portal hypertension, thought to be due to hepatic mast cell infiltration, is associated with aggressive disease and suggests an overall poor prognosis.[5] While internal jugular liver biopsy with hepatic venous pressure gradient measurement was deferred due to our patient's age, high risk for rebleeding, and previous bone marrow confirmation of mastocytosis, the high clinical suspicion and unremarkable work-up for alternative liver-related etiologies suggest non-cirrhotic portal hypertension due to aggressive myeloproliferative disease. The patient's lack of steatosis on abdominal ultrasound, unremarkable alcohol history, and benign cardiac work-up eliminate several other causes to explain the patient's portal hypertension. Given the endoscopic findings of esophageal varices, portal gastropathy, and lack of peptic ulcerations, it is reasonable to suspect aggressive systemic mastocytosis complicated by non-cirrhotic portal hypertension and variceal bleeding.

Overall, no study has identified what percent of patients with systemic mastocytosis develop portal hypertension. However, a recent study of 24 cases of systemic mastocytosis involving the GI tract found only 3 patients with liver involvement.[2] Interestingly, these 3 patients with hepatic involvement represented half the patients with aggressive disease as defined by the World Health Organization criteria.[6] Furthermore, liver disease as characterized by hepatomegaly and ascites was present in 2 cases, with 1 patient reported to have an acute upper GI bleed secondary to esophageal varices. While patients in this study underwent tissue biopsy to confirm the diagnosis, our patient was lost to follow-up so we could not definitively confirm the diagnosis.

Given the involvement of mast cells and underlying disease process, the addition of histamine and leukotriene receptor antagonists is an important supplement to the traditional acute management of variceal bleeding. It is also important to note that prior to medical or surgical procedures, including endoscopy, pre-medications designed to prevent mast cell degranulation should include first- and second-generation antihistamines with the option to administer leukotriene receptor antagonists or corticosteroids. The patient in this case was initially managed with pantoprazole given concerns for peptic ulcer disease, along with famotidine and montelukast prior to endoscopy.

The question is then whether this episode of variceal bleeding can be prevented. While there is no cure for mastocytosis at present, targeted treatment with tyrosine kinase inhibitors for eligible patients (ie, those with KIT proto-oncogene mutations) may improve symptoms. Even with other potential available treatments, our patient's symptoms were well-controlled on chronic prednisone. Despite a lack of symptoms, the patient developed mast cell infiltration of the portal vein and subsequent portal hypertension.

At present, no major gastroenterology, hepatology, or hematology organization has proposed specific screening guidelines for patients with systemic mastocytosis. Perhaps liver biopsy or endoscopic screening may help prevent future complications in this select patient population. Furthermore, considering the overall low prevalence of systemic mastocytosis, it is not known whether these measures would be cost effective. Ultimately, this case reinforces the importance of and need for appropriate portal hypertension screening in patients with systemic mastocytosis.

DISCLOSURES

Author contributions: All authors contributed equally to the literature search and composition of the manuscript. JI Allen is the article guarantor.

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Informed consent was obtained for this case report.

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