Osteopetrosis: A New Cause of Upper Gastrointestinal Bleeding

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Abstract

Osteopetrosis is a genetic disorder of bone remodeling caused by osteoclast dysfunction. Clinical features include short stature, frequent fractures, and recurrent infections. Abnormal bone obliterates the marrow cavity, resulting in pancytopenia and extramedullary hematopoiesis in the liver and spleen. The splenomegaly can lead to left-sided portal hypertension. We report the second case of osteopetrosis-induced portal hypertension and the first case of upper gastrointestinal bleeding in a 52-year-old woman with osteopetrosis.

Introduction

Osteopetrosis is an extremely rare congenital syndrome characterized by osteoclast dysfunction resulting in overly dense but fragile bones. Clinical features include recurrent fractures, stunted growth, failure to thrive, blindness and deafness from cranial nerve entrapment, and recurrent infections from impaired immune function. Another major feature is pancytopenia and bone marrow failure from infiltration with abnormal bone tissue. As a compensatory mechanism, extramedullary hematopoiesis occurs in the spleen and/or liver. Over time, excessive flow through the portal circulation can lead to portal hypertension, resulting in ascites and gastroesophageal variceal formation.

Case Report

A 52-year-old woman with childhood-onset osteopetrosis complicated by multiple long bone fractures, recurrent osteomyelitis, and transfusion-dependent pancytopenia was admitted for coffee ground emesis and a hemoglobin of 5.0 g/dL. She had 2 episodes of maroon stool on the day of admission without abdominal pain or hematochezia. She had no history of non-steroidal anti-inflammatory drug or alcohol use, peptic ulcer disease, or prior history of gastrointestinal (GI) bleeding. She had never had an upper endoscopy or colonoscopy. With the exception of osteopetrosis, her past medical history was unremarkable. Her medications included amoxicillin-clavulanate for chronic osteomyelitis and hydromorphone for musculoskeletal pain. Her brother died from osteopetrosis-related complications at age 46 years.

She was tachycardic and hypotensive with scleral icterus on admission. She was a thin, short-statured female with forehead bossing, enlarged mandibles with open sinus tracts draining purulent material, and a small oropharynx. Her abdomen was soft but mildly distended with normal bowel sounds with a palpable splenic tip in the left lower quadrant and normal liver span. Her leukocyte count was 2,100/uL, hemoglobin 5.0 g/dL with MCV of 94.4, platelet count 39,000/uL, albumin of 3.1 g/dL, and alkaline phosphatase of 119 IU/L. Chest x-ray was limited due to markedly dense overlying bones showing diffuse bony sclerosis and multiple healed rib fractures (Figure 1). Nasogastric lavage returned clear non-bilious fluid.

ACG Case Rep J 2014;2(1):45–47. doi:10.14309/crj.2014.80. Published online: October 10, 2014.
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She was admitted to the intensive care unit for gastrointestinal bleeding and started on intravenous pantoprazole and octreotide drips with fluid resuscitation using colloids and blood products. Upper endoscopy revealed grade III esophageal varices and severe portal gastropathy (Figure 2). Hepatic viral serologies were negative, and she refused a liver biopsy. Her serum iron level was normal and ferritin was mildly elevated. An abdominal ultrasound with Doppler showed a homogenous liver, enlarged spleen measuring 18 cm, and normal portal blood flow. CT of the abdomen and pelvis revealed marked splenomegaly measuring 23 cm longitudinally with extension into left iliac fossa, moderate abdominal ascites, and a normal-appearing liver (Figure 3).

The patient’s hemoglobin improved and remained stable after transfusion and upper endoscopy. The octreotide drip was discontinued after 5 days and pantoprazole drip after 72 hours. She was started on oral pantoprazole and a diuretic regimen of spironolactone and furosemide for her ascites. Nadolol was initiated for her varices and titrated to a goal heart rate in the 60s. She was discharged home, and upon follow-up at our clinic, was tolerating her medication regimen well.

**Discussion**

Portal hypertension is the result of long-standing resistance to blood flow through the portal circulatory system. Etiologies are divided into pre-, intra-, and post-hepatic causes. Pre-hepatic causes include excessive blood flow through the splenic vasculature or veno-occlusion of the splenic or portal venous system due to thrombosis or compression. Those that are the result of excessive blood flow or obstruction of the splenic vein are known as left-sided portal hypertension. In the former scenario, splenic venous outflow increases to a level greater than the hepatic capacity, resulting in impaired drainage into the liver and enlargement of splenic vein tributaries. The elevated pressures in the splenic vasculature result in dilatation of collateral vessels (e.g., esophageal, short gastric, and fundal veins) resulting in varices and left-sided portal hypertension. Patients may remain asymptomatic or may present with jaundice, weight loss, nonspecific abdominal pain, or have manifestations of elevated portal pressures including varices, splenomegaly, and ascites. Variceal bleeding is the most life-threatening complication, and may require balloon tamponade or sclerotherapy. Splenectomy is reserved for cases of recurrent or intractable variceal bleeding.

Our case highlights the rare occurrence of left-sided portal hypertension in a patient with osteopetrosis presenting...
with varices and ascites. Other common causes of portal hypertension, such as liver disease and thrombosis or fibrosis in the portal circulation, were ruled out. We hypothesize that our patient had left-sided portal hypertension from extramedullary hematopoiesis in the spleen. Given her bone marrow failure, her spleen served as the major reservoir for production of blood cells. The increased drainage of blood through the spleen overwhelmed the liver’s capacity, resulting in portal hypertension.

We found only 1 prior reported case of left-sided portal hypertension in osteopetrosis. That patient had biopsy-proven extramedullary hematopoiesis in her liver and spleen. As a result of elevated portal pressures, the patient presented with a dilated and tortuous epigastric collateral vein found on imaging. However, that patient did not present with gastrointestinal bleeding. Our case is the second case of portal hypertension from osteopetrosis and the first manifesting with gastrointestinal bleeding.

Disclosures

Author contributions: KN Katz and MA Shafqet wrote, edited, and reviewed the manuscript. SD Rampertab and N. Pooran edited and reviewed the final manuscript. KN Katz is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received: June 9, 2014; Accepted: September 9, 2014

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