Gaucher's Disease Presenting with Portal Hypertension

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Gaucher's disease is a rare lysosomal storage disorder characterized by abnormal accumulation of lipid-laden macrophages in different organs. Though hepatosplenomegaly is commonly found, symptomatic presentation with portal hypertension is rare. We report a child with liver cirrhosis and bleeding esophageal varices who was diagnosed with Gaucher's disease disease.

Key words: *Gaucher's disease, Portal hypertension.*

Gaucher's disease (GD) is an autosomal recessive lysosomal storage disorder usually presenting with hematological or skeletal manifestations [1]. Symptomatic portal hypertension in GD is rare [2,3]. We report two siblings with GD who presented in early childhood with esophageal variceal bleeding due to accompanying cirrhosis.

CASE REPORT

A three-year-old male child, born to non-consanguinous parents, presented with insidious onset progressive swelling of abdomen, early satiety, poor weight gain and generalized weakness for one year. There was no history of fever, jaundice, bleeding, abdominal pain, respiratory or urinary symptoms. His birth history and postnatal period were normal. He had a history of hospital admission for anemia on two occasions, eight and six months back, and was discharged after blood transfusion. Patient had two episodes of hematemesis two days back and was referred to us.

Previous investigations had revealed microcytic hypochromic anemia, normal liver and renal function tests, and hepatosplenomegaly on abdominal ultrasound. Bone marrow aspiration was suggestive of iron-deficiency. His elder brother, four years older to him, also had similar history and clinical features and died at five years of age during an episode of variceal bleeding. Complete hematological workup in that child also did not reveal anything apart from iron deficiency.

On presentation, moderate mental retardation, moderate pallor, right axillary lymphadenopathy, sternal tenderness, mild hepatomegaly and huge splenomegaly were present, but no edema, jaundice or ascites. Neurological examination was normal. Routine investigations were essentially normal apart from microcytic hypochromic anemia. Grade II esophagal varices were noted on upper gastrointestinal endoscopy. Apart from a low albumin (2.6 g/d), liver function test were normal. Doppler study revealed dilated portal vein with collaterals at the splenic hilum. Portal venous flow was hepatopetal, and vena cava and hepatic veins were normal. Liver biopsy showed pericellular and perisinusoidal increased and thickened reticulin fibers along with portal, periportal and irregular lobular fibrosis. Features were consistent with cirrhosis. Tests for hepatitis B, hepatitis C, human immunodeficiency virus, Wilson's disease, α-1 antitrypsin deficiency, autoimmune liver disease and cholestatic liver disease were negative.

Patient was treated with sclerotherapy for variceal bleeding. Biopsy of the axillary lymph node showed numerous large cells with abundant pale streaky cytoplasm infiltrating the sinusoids and suggested the possibility of storage disorder. Bone marrow biopsy revealed increased reticulin fibers and replacement of hematopoietic elements by periodic acid Schiff (PAS)-positive large cells having small oval nuclei with abundant eosinophilic wrinkled cytoplasm suggesting the possibility of GD. Finally, acid-α glucosidase activity in peripheral blood lymphocytes was found to be low (12%; normal greater than 30%). A diag-

nosis of GD (type I) with portal hypertension was made. As his parents could neither afford the genetic analysis nor enzyme replacement, he is being treated with transfusion and iron supplement for his anemia, and repeated sessions of sclerotherapy till the obliteration of varix. Presently, he is under regular follow up.

DISCUSSION

Many patients with GD have varying degrees of hepatomegaly, and infiltration of liver with Gaucher's cells may occur preferentially after splenectomy. In majority, the liver infiltration is clinically silent and the serum tests of liver function are generally normal or only marginally disturbed [4,5]. Hepatic failure and complications of portal hypertension are rare and their presence suggests poor prognosis [2,3,5]. Bleeding from esophageal varices has been rarely noted [6]. Patient affected are usually in first two decades of life and usually have other florid manifestations of the disease [5-7].

Liver histology in patients with GD with portal hypertension is characterized by fibrosis [5-7]. The accumulation of glucocerebroside in the macrophages is undoubtedly the mechanism of progressive onset of hepatic fibrosis and cirrhosis. Neither viable Gaucher's cells nor hepatocytes are seen in the central parts of these fibrotic zones, which are acellular suggesting that the fibrosis in part have followed ischemia and infarction [7].

Of the two siblings reported, the first was lost to follow up before the work up for portal hypertension could be initiated. The younger one was found to have GD by relevant investigations. However, his liver biopsy showed features consistent with cirrhosis, but no Gaucher's cells. As the etiological workup in this patient could not identify any other cause of cirrhosis, we conclude that hepatic fibrosis occurred in response to metabolic insult to the liver.

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