Hepatocellular Failure in Glycogen Storage Disorder Type 3

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Abstract

A case of a 21 years male patient with type 3 glycogen storage disorder diagnosed at necropsy, who died suddenly with hypovolemic shock following a massive upper gastrointestinal bleeding due to hepatocellular failure is reported. Salient features of GSD type 3 are briefly discussed. ©

INTRODUCTION

The glycogen storage disorders [GSD] include various genetic defects that impair glycogen breakdown, primarily in liver, muscle or both. Even the types most frequently encountered [GSD-1a and GSD-3] are uncommon, each with an incidence of approximately 1 in 100,000 births. The hepatic symptoms in GSD-3 improve with age and usually disappear after puberty. Overt liver cirrhosis appears to be a rare complication, except in Japanese patients. We present a case of 21 years male with GSD-3, who developed this rare complication of hepatic cirrhosis and hepatocellular failure.

CASE REPORT

A 21 years nonalcoholic male presented to us with progressive distension of abdomen noticed over last 3-4 years. He had several episodes of hematemesis and malena in past for which surprisingly he never sought any medical advice. He also had history of dyspnoea on exertion and chest pain which had progressed from NYHA grade 2 to grade 4 in the last three months. He also developed edema feet since a week. He did not have any episode of jaundice, altered sensorium, oliguria, bleeding from any site, palpitations and syncope. He did not receive any blood transfusion in past and he denied any high risk behavior. Family history was not contributory.

General examination revealed a pale and malnourished cachexic male with underdeveloped secondary sexual characters, tachycardia, bounding peripheral pulses, raised jugular venous pressure with a blood pressure of 100/40 mmHg. Dilated veins were visible on his distended abdomen with demonstrable fluid thrill due to massive ascitis. Liver was enlarged (10 cms below the right costal margin) which was nontender with a firm consistency and irregular surface.

Spleen was moderately enlarged. His hyperkinetic apex beat was displaced outside the left midclavicular line. Cardiac auscultation revealed grade 3 ejection systolic murmur in the aortic area with a loud second heart sound. Rest of the clinical findings were unremarkable.

At this point, a clinical diagnosis of hepatocellular failure with portal hypertension due to cirrhosis of liver with cardiac failure to rule out left ventricular outflow obstruction due to aortic stenosis was made. In view of massive hepatomegaly and cardiac involvement possibility of storage disorder was suspected.

Further laboratory investigations revealed a haemoglobin

Fig. 1: Gross necropsy specimen of heart showing marked ventricular hypertrophy
Fig. 1: Photograph of the heart showing marked hypertrophy and congestion.

Fig. 2: Gross necropsy specimen of liver showing mild hepatomegaly with mixed nodular cirrhosis.

Fig. 3: Section of heart on microscopy showing vacuolated myocytes. (H/E staining)

Fig. 4: Section of liver showing hyperglycogenated nuclei, enlarged hepatocytes and occasional fatty change. (H/E staining)

Fig. 5: Section of spleen showing congested red pulp and gamma gandy body

of 6.5 gm/dl with hypoalbuminemia, reversal of A/G ratio and prolonged prothrombin time. Total white cell count, liver enzymes, bilirubin and random blood sugar were normal. Viral markers for hepatitis and HIV were negative. Ascitic fluid was transudate. Slit lamp examination ruled out KF ring. Ultrasonography of abdomen confirmed gross hepatomegaly with coarse echotexture, massive ascitis and congestive splenomegaly with increased portal vein diameter. X-ray chest revealed cardiomegaly. ECG documented biventricular hypertrophy and 2D echo revealed hypertrophic obstructive cardiomyopathy (HOCM). Upper GI endoscopy showed grade 3 oesophageal varices, for which prophylactic sclerotherapy was given.

Patient was also treated with propranolol for portal hypertension and HOCM. Vitamin K, packed cell and fresh frozen plasma transfusion was given for correction of anaemia and coagulation profile. Unfortunately patient had a massive bout of hematemesis, hypovolemic shock and cardiac arrest during his hospital stay from which he could not be revived.

A postmortem examination was performed which revealed on gross examination - massively enlarged, globular, congested heart which on cut-section showed marked right and left ventricular hypertrophy with normal valves and aorta (Fig. 1). Liver was enlarged with a nodular surface suggestive of mixed nodular cirrhosis (Fig. 2). There was moderate congestive splenomegaly with thickened serosa.

On histopathological examination of heart, there was marked vacuolisation of myocytes with few bizarre nuclei seen (Fig. 3). Hepatic lobules divided into irregularly sized nodules of various sizes by fibrous septa. Hepatocytes were enlarged showing presence of glycogenated nuclei and occasional fatty change (Fig. 4). Spleen showed red pulp congestion, dilated and congested sinusoids with presence of gamma gandy bodies suggestive of fibrocongestive splenomegaly (Fig. 5). All the above findings on gross and histopathological examination suggested a diagnosis of type 3 glycogen storage disease involving heart and liver (GSD type 3a).

**DISCUSSION**

Glycogen storage disorder 3 (Limit dextrinosis, debrancher enzyme deficiency, Cori or Forbes disease) was originally reported by Snappes and Van Crevald in 1928. It is an autosomal recessive disorder in which deficiency of glycogen debranching enzyme activity leads to the accumulation of an abnormal glycogen with short outer branch chains resembling limit dextrin in the tissues. The gene locus for debrancher enzyme is on chromosome 1p21. More commonly this disorder involves both liver and muscle and is termed as GSD 3a. However in about 15% of patients, only liver is involved.
and is classified as GSD 3b.\textsuperscript{2} Our patient had both liver and muscle (cardiac) involvement and was classified into type 3a. GSD 3a may present in infancy and childhood with hepatomegaly, hypoglycemia, hyperlipidemia and growth retardation. Hepatic symptoms however improve with age and usually disappear after puberty while the slowly progressive weakness and wasting of muscles become severe after the 3rd and 4th decade. Most patients with GSD 3 run a relatively benign course. Ventricular hypertrophy is frequent and was noticed in our patient also, but overt cardiac dysfunction is rare. Thus, adults with GSD 3a present predominantly with muscular symptoms\textsuperscript{3,4} contrary to the observation in our case where hepatic cirrhosis and hepatocellular failure predominated the clinical features.

Histopathology of liver is characterised by a universal distension of hepatocytes by glycogen and the presence of fibrous septa; with paucity of fat. Definitive diagnosis requires enzyme assay in liver, muscle or both.\textsuperscript{5} Dietary management which includes frequent meals high in carbohydrates with cornstarch supplements and a high protein.\textsuperscript{6}

**REFERENCES**


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