# Glycogen Storage Disease Type III

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Glycogen storage disease (GSD) type III is caused by deficiency of the enzyme amylo-1,6 glucosidase (debranching enzyme) leading to the storage of an abnormal glycogen with short outer chains called limit dextrins(l). Clinical manifestations are usually due to decreased hepatic glycogenolysis and occasionally due to a myopathy associated with an increase in muscle glycogen. We report a case of GSD type III with predominantly liver involvement. This is the second report of this disorder from India(2).

## Case Report

A four-year-old female child was admitted with progressive abdominal distension since the age of two years and inability to walk for four months. The child was born of a non-consanguinous marriage. At the age of six months, she suffered from acute gastroenteritis, when the liver was moderately enlarged but no further investigations were done. On examination, the child was small built with a doll like face and weight and height were less than the 5th centile of NCHS standards, but weight for height was appropriate. There was gross motor developmental retardation, while the fine motor, language and social adaptive development was appropriate for age. She had hypotonia, weakness of lower limbs and a massive hepatomegaly (13 cm below costal margin with a span of 17 cm) with firm consistency, smooth surface and rounded margins. Spleen was not palpable.

Detailed routine and special investigations are shown in *Table I.* Liver biopsy revealed liver cells with central nuclei and vacuolated granular cytoplasm. RAS stains showed accumulation of glycogen within the hepatocytes. Portal areas showed inflammatory infiltrate and fibrosis with spurring into the parenchyma and enclosing liver lobule *(Fig. 1).* The above findings were consistent with glycogen storage disease type 111(3). The patient was put on a high protein and frequent round the clock carbohydrate diet. She was re-examined after 3 months when there was no change in the hepatomegaly. The child did not come for further follow up.

## Discussion

GSD type III is an autosomal recessive disorder, protean in its manifestations. Liver, skeletal muscle and heart are the main organs involved in various levels of severity. In the present case, hepatic involvement was predominant with minimal skeletal muscle involvement and no involvement of the heart. In majority of the reported cases liver pathology has been predominant, characterized by a protruded

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**TABLE I**—*Routine and Specialized Investigations*

| S.No. | Investigations | Result |
|---|---|---|
| 1. | *Hematological profile* | |
| | Hemoglobin | 11.4 g/dl |
| | TLC | 9,800/mm$^3$ |
| | Platelet count | 1.6 lakh/mm$^3$ |
| 2. | *Urine examination* | |
| | Microscopic | Normal |
| | Sugar | Nil |
| | Aminoacidogram | Normal |
| 3. | *Liver function tests* | |
| | Serum bilirubin | 0.6 mg/dl |
| | SGOT | 100 U/L |
| | SGPT | 140 U/L |
| | Alkaline phosphatase | 64.3 KA°U |
| | Prothrombin time | 12 sec |
| | Serum total proteins | 5.5 g/dl |
| | Serum albumin | 2.7 g/dl |
| 4. | HBsAg | Negative |
| 5. | Blood sugar (fasting) | 65 mg/dl |
| 6. | Serum cholesterol | 315 mg/dl |
| 7. | Serum triglycerides | 535 mg/dl |
| 8. | Serum uric acid | 3.8 mg/dl |
| 9. | Serum calcium | 9 mg/dl |
| 10. | Serum phosphorus | 4.5 mg/dl |
| 11. | Serum copper | 84 µg/dl |
| 12. | Serum ceruloplasmin | 0.77 |
| 13. | Serum LDH | 1094 U/L |
| 14. | Serum CPK | 168 U/L |
| 15. | Bone marrow | No storage cells |
| 16. | Abdominal ultrasound | Kidneys normal in size and echotexture |
| 17. | Electrocardiogram | Normal |
| 18. | Echo cardiography | No evidence of cardiomyopathy |
| 19. | Nerve conduction velocity | Normal |
| 20. | Electromyogram | Low amplitude, polyphasic potentials suggestive of a myopathic pattern |
| 21. | Fasting glucagon test, fasting blood sugar<br>Blood sugar 1 hour after glucagon 0.7 mg/m$^2$ | 60 mg/dl<br>70 mg/dl |
| 22. | Post prandial glucagon test, post prandial blood sugar<br>Blood sugar 1 hour after glucagon | 95 mg/dl<br>160 mg/dl |

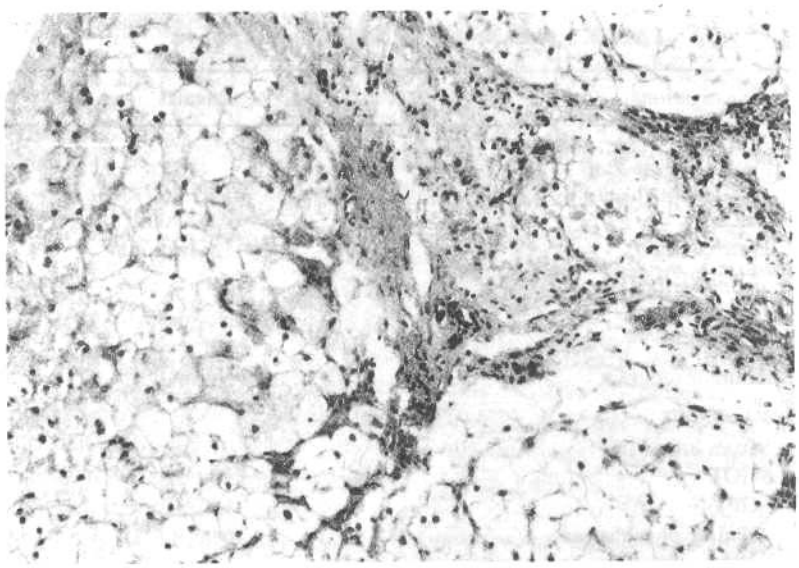

*Fig. 1. Liver biopsy specimen of the patient. High power view showing liver cells which appear empty with nucleus pushed to one side. Portal tracts show mononuclear cell infiltrate.*

abdomen because of-a markedly enlarged liver, and high concentration of serum transaminases and lipids (mainly cholesterol). Liver has a normal consistency but jaundice and the slow development of cirrhosis may occur in individual instances(4). Liver size decreases for unknown reasons at or before puberty and 'the elevated serum transaminases also .decrease. There may be mild muscle hypotonia at a young age. The infant usually has growth retardation, but it gradually catches up(5). Cerebral development is usually normal, and there is truncal obesity and a doll like face. There was no history suggestive of hypoglycemic episodes in the present case. Hypoglycemia is less frequent in GSD III as compared to type I. The serum concentration of uric acid, lactate and ketones are normal.

In the myopathic form, slight to severe impairment of muscle function and slowly progressive distal muscular wasting develops during later childhood or adulthood(6). Accumulation of glycogen in heart may lead to moderate cardiomegaly with nonspecific ECG changes, although rarely accompanied by clinical symptoms(7). Rarely one can observe clinical, electrophysiological and electronmicroscopic evidence of neuropathic lesions in peripheral nerves(6).

In the present case the glucagon test did not show a significant rise in fasting blood sugar; however, the rise in post prandial blood sugar was significant. Differentiation between type I and type III GSD is made by the intravenous glucagon test in the immediate post-prandial period when there usually is a rise in blood sugar levels in type III but not in type I patients(8). The liver histopathology in type III GSD is very similar in appearance to that seen in type I GSD; universal distension of hepatocytes producing a mosaic architecture and periportal nuclear hyperglycogenation are prominent. The notable distinctions from type I glycogenosis are the presence of fibrous

septa formation and the paucity of fat(3). Our case showed similar findings with fibrous septa in the portal area. Serial biopsy specimens, do not demonstrate a progression of septa formation and cirrhosis has not been reported. Deficiency of amylo-1,6 glucosidase can be demonstrated in one of the following tissues; leucocytes, erythrocytes, liver, muscle, fibroblasts, or chorionic villi. Immunoblot analysis of the enzyme has been recently reported(9).

Treatment is mainly dietary. Carbohydrates should be given frequently round the clock when the patient is. young. Gastric drip feeding at night may be introduced in the infant if hypoglycemia is a problem(10). Corn starch therapy can be started in the older child and is useful(11). Diet should be rich in high class proteins(12) because some aminoacids serve as substrate for gluconeogenesis. Fat intake should be reduced.

The prognosis for a relatively normal life is good, although the development of myopathy and cardiomyopathy is a matter of concern. Prenatal diagnosis has been performed by enzyme analysis of amniotic fluid fibroblasts or chorionic villi(13).

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