

Background

Glycogenic hepatopathy (GH) was first described by Mauriac in 1930. It is characterized by excessive hepatic glycogen storage as a part of a syndrome comprising growth retardation, delayed puberty, and Cushingoid features in young patients with type 1 diabetes (T1DM).

The proposed pathophysiology of GH is that insulin activates glycogen synthase, allowing conversion of glucose to glycogen in hepatocytes. The occurrence of frequent episodes of hyperglycaemia and supraphysiological doses of insulin leads to glycogen accumulation in the liver.

However, there have been several case reports in the literature describing glycogenic hepatopathy as the sole presentation of Mauriac syndrome in children with poorly controlled diabetes. Recent reports [1] also highlighted hyperlactatemia as a new presentation of Mauriac syndrome in young adults with type 1 diabetes mellitus, but this has not been reported in younger children previously.

We describe a case of GH in our 11 year old patient with poorly controlled T1DM who presented with persistent lactic acidosis and transaminitis despite resolution of diabetic ketoacidosis.

Presenting Problem

Our patient is an 11 year old girl who was diagnosed with T1 DM since she was 7 years old and has a long standing history of poorly controlled diabetes. Her glycosylated haemoglobin level averaged 10-13.5% prior to admission.

She presented with severe DKA (arterial pH 7.02, serum bicarbonate 3.6 mmol/L and serum beta-hydroxybutyrate 8.1 mmol/L). She was managed with intravenous hydration and intravenous insulin therapy.

Within 48 hours of therapy, despite complete resolution of ketosis, there was worsening metabolic acidosis secondary to lactic acidosis. Her serum lactate measured 10.1 mmol/L. In addition, she also developed tender hepatomegaly of 11 cm. Biochemically, there was severe transaminitis with a serum aspartate transaminase (AST) of 6681 U/L (20-40) and a serum alanine aminotransferase (ALT) of 1493 U/L (10-25). Her synthetic liver function was preserved.

References:

1. Torbenson, M; Chen, Y; Brunt, E; Cummings, O.W.; Gottfried, M; Jakate, S; Liu, Y; Yeh, M. M.; Ferrell, L. (2006) Glycogenic Hepatopathy: An Underrecognized Hepatic Complication of Diabetes Mellitus. *The American Journal of Surgical Pathology*: 30(4) 508-513
2. Brouwers, MCGJ; Ham, JC; Wisse, E; Misra, S; Landewe, E; Rosenthal, M; Patel, D; Oliver, N; Bilo, HJG; Murphy, E. (2015) Elevated lactate levels in patients with poorly regulated type 1 diabetes and glycogenic hepatopathy: a new feature of mauriac syndrome. *Diabetes Care* 38(2) e11–e12
3. Rosner, EA; Strezlecki, KD; Clark, JA; Lieh-Lai, M. (2015) Low Thiamine Levels in Children With Type 1 Diabetes and Diabetic Ketoacidosis: A Pilot Study. *Pediatric Critical Care Medicine*: 16(1) 114-118. DOI:10.1097

Evaluation

She was evaluated for viral, autoimmune and metabolic causes, which all returned negative. The patient subsequently underwent a liver biopsy which demonstrated the presence of glycogen-laden hepatocytes, confirming the diagnosis of GH (Figures 1 and 2)

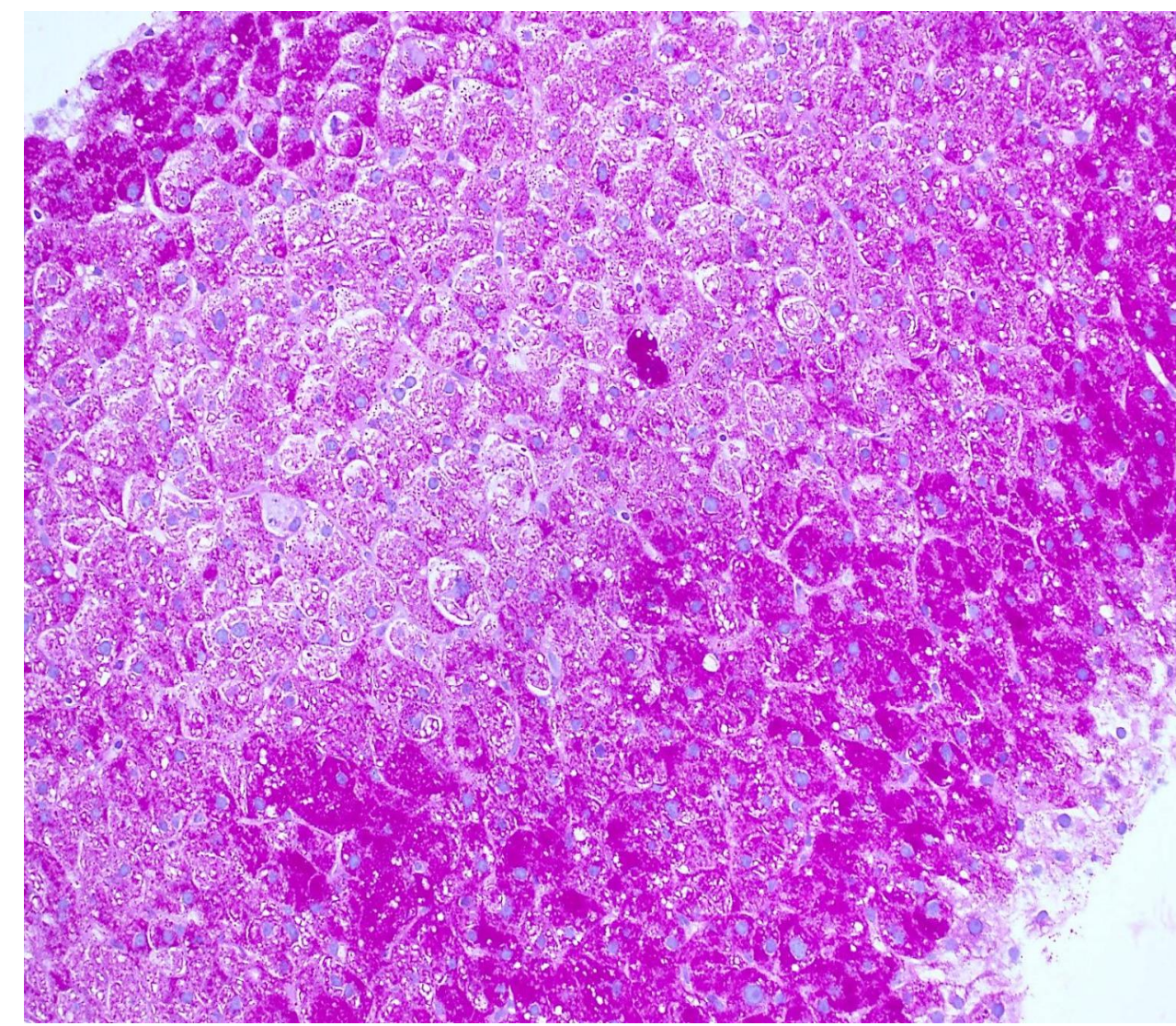


Figure 1: Abundant intracytoplasmic glycogen highlighted on PAS stain.

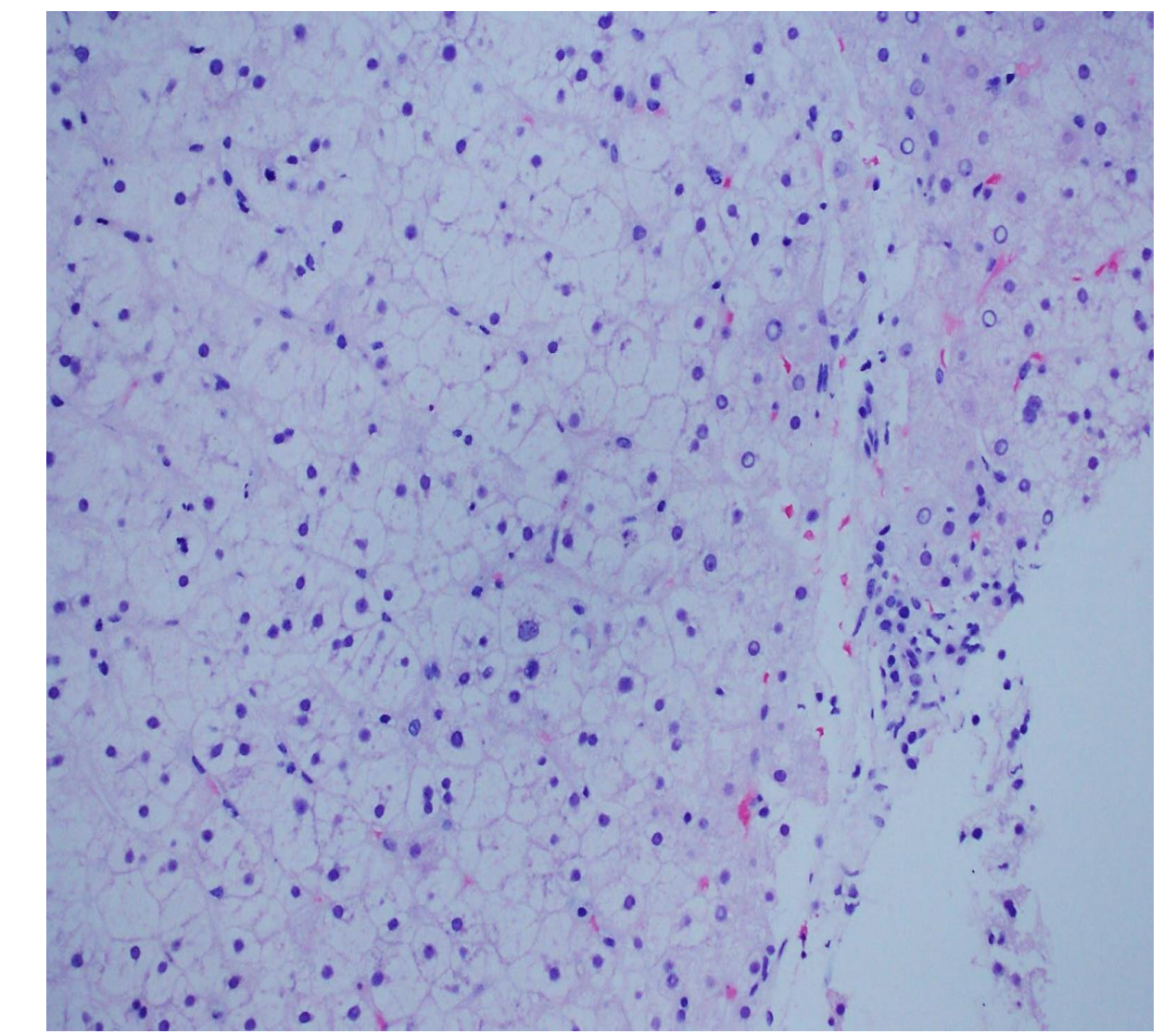


Figure 2: Diffuse hepatocytic swelling with abundant clear cytoplasm on H&E stain.

Discussion

In our patient, she had been non-compliant to insulin therapy for a prolonged duration. Treatment with intravenous insulin as part of DKA management likely resulted in acute glycogen accumulation in the hepatocytes, leading to hepatomegaly and hepatocellular damage reflected through the severe transaminitis occurring 48 hours into therapy which was not noted at presentation.

Lactic acidosis in GH could be related to the reduction of hepatic gluconeogenesis during insulin administration for DKA management and glycogen accumulation, resulting in the conversion of pyruvate to lactate. The presence of abnormal giant mitochondria in electron microscopy of liver biopsy specimens from patients with GH has also been described. [2] We postulate that GH could also result in a secondary inhibition of the respiratory chain resulting in lactic acidosis.

T1DM patients have also been shown to have thiamine deficiency [3] which may be worsened by treatment. Thiamine is used as a cofactor in the pyruvate dehydrogenase complex in the generation of acetyl-CoA from pyruvate for the Krebs cycle. In thiamine deficiency, pyruvate is converted to lactate by lactate dehydrogenase. As treatment with thiamine is safe and inexpensive, we initiated this for our patient. She was treated with 1 week of thiamine. Her transaminitis and hyperlactemia gradually resolved after 2 months.

Conclusion

Clinicians should be vigilant for this rare complication of insulin therapy in children with poorly controlled DM. Thiamine is a safe and inexpensive adjunct and can be considered to aid recovery in such cases.

