Elevated Lactate Levels in Patients With Poorly Regulated Type 1 Diabetes and Glycogenic Hepatopathy: A New Feature of Mauriac Syndrome

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Glycogenic hepatopathy is a rare but probably underdiagnosed feature of poorly controlled diabetes, in particular type 1 diabetes. It is characterized by excessive hepatic glycogen storage as first described in 1930 by Mauriac as a part of a syndrome comprising growth retardation, delayed puberty, and Cushingoid features in young patients with type 1 diabetes (1). Recent case reports have demonstrated that glycogenic hepatopathy can be the sole presenting feature of Mauriac syndrome (reviewed in ref. 2).

Here, we describe four strikingly similar cases of young adults with poorly controlled type 1 diabetes who presented with excess hepatic glycogen storage *and* increased plasma lactate levels. The combination of these metabolic abnormalities led to the initial presumption of an inherited disorder of metabolism.

All patients presented to the emergency department with either nausea and vomiting or abdominal pain (Table 1). Laboratory investigations showed elevated liver enzymes, absence of ketoacidosis, negative viral hepatitis serology, and elevated lactate levels (3.1–10.8 mmol/L). All patients had palpable hepatomegaly and excess glycogen accumulation on liver biopsy.

Given the increased hepatic glycogen storage in combination with poorly controlled type 1 diabetes, a diagnosis of glycogenic hepatopathy was suspected. Though once previously reported (3), elevated plasma lactate levels are not a well-recognized feature of this syndrome and a differential diagnosis of an inherited glycogen storage disorder was therefore queried.

Additional investigations in patient 1 identified that plasma lactate levels were at their nadir in the fasting state (1.4–3.9 mmol/L) and that the lactate-to-pyruvate ratio was elevated (25.1). These observations are in contrast with glycogen storage disease type 1, in which hepatic glycogen accumulation is accompanied by elevated *fasting* plasma lactate levels as a consequence of impaired gluconeogenesis (4). Instead, high postprandial lactate levels and an elevated lactate-to-pyruvate ratio (>25) point toward a defect in the mitochondrial respiratory chain (4). Electron microscopy of liver biopsy material in patient 1 showed abnormal, giant mitochondria, in line with previous reports on glycogenic hepatopathy (1).

It could be argued that the patients reported here have been misdiagnosed with type 1 diabetes and actually have a primary mitochondrial disorder with concomitant diabetes and lactatemia. However, the age of onset of diabetes in all patients was much younger than commonly observed in patients with mitochondrial diabetes (5). No patient had signs of a systemic mitochondrial defect, such as stroke-like episodes, epilepsy, deafness, or (cardio)myopathy. Nor was there maternal inheritance of disease. Patient 1 did not carry the A3243G mitochondrial DNA mutation. Finally, improved glucose regulation (HbA_{1c} 7.0% [53 mmol/mol]) in patient 4 resulted in normalization of liver enzymes *and* plasma lactate levels (0.6 mmol/L), supporting the assumption that these metabolic abnormalities are all the consequence of poor glucose control.

Based on these findings, we believe that elevated plasma lactate levels are part of the clinical spectrum of glycogenic hepatopathy in patients with poorly controlled type 1 diabetes. In such patients, these metabolic abnormalities are reversible, and glycemic control should be prioritized

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Table 1—Patient characteristics

Patient	Sex	Age	Age of T1D diagnosis	Clinical presentation	BMI (kg/m^2)	Hepatomegaly	ALT (units/L)	HbA_{1c} (% [mmol/mol])	Lactate levels at presentation (mmol/L)	Maximum lactate levels ever measured (mmol/L)
1	F	19	3	Nausea, vomiting	23.0	Yes	88	9.5 [80]	8.3	10.8
2	F	19	6	Nausea, vomiting	18.1	Yes	39	13.3 [122]	2.4	3.1
3	M	17	7	Abdominal pain RUQ	24.9	Yes	908	12.7 [115]	7.9	7.9
4	F	20	3	Nausea, vomiting	17.2	Yes	1,471	14.7 [137]	10.2	10.2

ALT, alanine aminotransferase; F, female; M, male; RUQ, right upper quadrant; T1D, type 1 diabetes.

over the search for rare inborn errors of metabolism.

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