A Case of Mauriac Syndrome Caused by Social Inequities in Healthcare: A Call to Action

Authors:	Steven Iglesias,[1] Noelle Dayal,[1] Varinder Bansro,[2] Sahra Akbari,[1] Temur Hannan,[1] *Zachary I. Merhavy,[1] Imran Siddiqi[2] 1. Ross University School of Medicine, Bridgetown, Barbados 2. University of Maryland, Capital Region Medical Center, Largo, Maryland, USA *Correspondence to zackmerhavy@gmail.com

Disclosure:	The authors have declared no conflicts of interest.
Received:	11.03.24
Accepted:	17.06.24
Keywords:	Diabetes, hepatomegaly, lactic acidosis, Mauriac syndrome, socioeconomic, Type 1 diabetes mellitus (T1DM).
Citation:	EMJ Diabet. 2024;12[1]. https://doi.org/10.33590/emjdiabet/NOGQ9587.

Abstract

Presented here is a case of Mauriac syndrome with persistent lactatemia in a 21-year-old female with a history of poor glycaemic control. Mauriac syndrome is a severe complication of Type 1 diabetes mellitus (T1DM) characterised by glycogen accumulation in the liver leading to hepatomegaly. Mauriac syndrome is considered to be a very rare and preventable complication due to better treatment options for T1DM. Most cases of Mauriac syndrome today involve children and adolescents who face socioeconomic inequities that prevent them from accessing adequate healthcare and affording insulin, as is the case with this patient. The combination of low health literacy, insulin unaffordability, and difficulty accessing healthcare for her chronic condition all contributed to her poorly controlled T1DM. It has been well established that insulin has become difficult to afford for insulin-dependent patients. An alarming one out of four insulin-dependent patients have rationed their doses due to the high cost of insulin. Progress has been made to cap the price of insulin at 35 USD to prevent price-gouging for certain populations in the USA but not all. Young patients with poorly controlled T1DM and low socioeconomic status require higher levels of social support and public health intervention to prevent serious complications of T1DM such as Mauriac syndrome.

Key Points

1. The people most affected by Mauriac syndrome (MS) are young adults who have social barriers that prevent them from managing their chronic disease. Healthcare providers are responsible for identifying these patients so that better education and early public health interventions can be implemented to support these patients and prevent MS.

2. A case report describing the identification and treatment of a severe complication of uncontrolled Type 1 diabetes and investigating the socioeconomic factors that impact a young patient with Type 1 diabetes's ability to manage their chronic condition.

3. MS was once considered rare, but healthcare providers should remain suspicious of it in patients with Type 1 diabetes mellitus and low socioeconomic status. Additionally, healthcare providers should advocate for better public health interventions to make diabetes management more accessible and affordable.

CASE PRESENTATION

A 21-year-old female with a history of Type 1 diabetes mellitus (T1DM) with baseline HbA1c ranging from 8.8–12.5%, delayed menarche, recurrent hospitalisations for diabetic ketoacidosis (DKA), and hepatomegaly presented to the emergency department with complaints of multiple episodes of intractable emesis, fatigue, feelings of dehydration, and dizziness for the past 2 days. On physical exam, the patient had hepatomegaly, abdominal tenderness, and moon facies. Vitals on presentation were as follows: blood pressure 119–148/77–103 mmHg, pulse 129–136 bpm, maximum temperature 36.7 °C, respiratory rate 20, and saturation 100% RA. Her physical exam was significant for dry mucous membranes. Other significant lab findings include a complete blood count suggesting haemoconcentration, an elevated anion gap of 23, abnormal liver enzymes (aspartate aminotransferase 73, alanine transaminase 60, alkaline phosphatase 210), blood urea nitrogen 31, creatinine 1.8, blood glucose of 443, beta-hydroxybutyrate 3.94, and lactate 8.5. Her BMI was 17.6. Ultrasound of the abdomen was ordered and showed a liver span of 18.18 cm with increased echogenicity. The patient grew up in the foster care system and lived with her grandparents at the time of presentation. The patient was diagnosed with acute DKA and managed with continuous insulin and aggressive fluid resuscitation, and her electrolytes were replaced. The patient was transferred to the intensive care unit (ICU) for further management.

During the patient's ICU course, she was a very brittle diabetic. Her blood glucose was difficult to control and changed dramatically. The patient was started on insulin drip, but her glucose still fluctuated between 100's–400's. She could not tolerate oral intake despite constant encouragement, proton pump inhibitor, and metoclopramide therapy. On the third day, the patient's anion gap had closed and beta-hydroxybutyrate normalised. Her point of care glucose stabilised, and she appeared clinically improved; however, she had persistently fluctuating levels of lactic acidosis, which vacillated between 4.1–5.9 and never normalised. Her elevated levels of lactic acid did not match her clinical presentation, vitals, or other laboratory findings. Later, the patient was downgraded from ICU to medical–surgical for further monitoring and insulin regimen modifications. Further workup to evaluate her lactic acidosis continued until the patient left against medical advice. Significant lab findings before she left included an abnormal lipid profile (cholesterol: 183; triglycerides: 183; high-density lipoproteins: 42; low-density lipoproteins: 104; Cholesterol/high-density lipoproteins ratio: 4.4), normal hepatitis panel, normal thyroid-stimulating hormone, normal antinuclear antibodies panel, normal LKM-1 IgG, normal antineutrophil cytoplasmic antibodies screen, normal serum IgG, and normal antinuclear antibodies ELISA.

The patient was seen by a social worker and diabetes educator and was referred to 'population health' for assistance with diabetes management. This programme was intended to help the patient access healthcare, afford insulin, and improve health literacy all in an effort to prevent complications of her T1DM. Ultimately, the patient left against medical advice and was lost to follow-up as an outpatient.

DISCUSSION

Mauriac Syndrome (MS) is a rare but ever-present complication of T1DM, characterised by high glycogen accumulation in the liver causing severe hepatomegaly. Patients can also present

with short stature, delayed puberty, and moon facies. MS is highly treatable with insulin and adequate glycaemic control, and most of the reported cases involve children and young adults from lower socioeconomic status who struggle to pay for insulin and properly manage their disease.[1]

The differentials for this patient included hepatic glycogenosis (HG), DKA, and non-alcoholic fatty liver disease (NAFLD). HG is a disease that occurs at any age and can be present without the full spectrum of features described for MS. In few reports, HG is considered as the primary cause of hepatomegaly in young patients with T1DM. HG is an under-recognised condition characterised by pathological storage of glycogen in hepatocytes and represents a rare complication of T1DM.[2] MS not only presents with HG but also short stature, poor weight gain, and delayed puberty, as well as a Cushingoid presentation.

NAFLD is a common misdiagnosis of HG since they both can present with hepatomegaly and hepatic steatosis on CT. One study found that NAFLD can be associated with T1DM but is more commonly confounded by the increased association of NAFLD in T1DM with increased BMI. A liver biopsy is the gold standard to differentiate between NAFLD and HG associated with MS.[3] This patient has a low BMI of 17.6 due to poor weight gain and her other clinical signs are more suggestive of MS.

DKA caused by inadequate insulin levels can lead to hyperglycaemia and lipid breakdown with the production and accumulation of ketoacids. The hyperglycaemic crisis is considered to be resolved with normalisation of the serum anion gap (less than 12 mEq/L) blood beta-hydroxybutyrate levels.[4] While this patient was also treated for DKA during her hospital stay, the DKA alone does not explain her hepatomegaly.

In patients with MS, hyperglycaemia leads to increased glucose absorption into hepatic cells, which induces glycogen synthesis.[5] A defect in the feedback inhibition pathway prevents glycogen synthesis from stopping, and continued hyperglycaemia leads to glycogen accumulation in the liver.[5,6] This can cause hepatomegaly and elevated liver enzymes.[5,6] It has been suggested that there may be a genetic component that causes the defect in feedback inhibition of glycogen synthesis. A genetic mutation in the hepatic glycogen phosphorylase kinase, which inhibits glycogen synthesis, has been found in patients with MS. This mutant glycogen phosphorylase is unable to inhibit glycogen synthesis which allows it to accumulate when the patient is in a hyperglycaemic state. It is important to highlight that this study found that both the mutation and poor glycaemic control were required for MS to develop.[5]

On arrival, the patient's lactate was 8.1, which could have been caused by lactic acidosis that occurred concomitantly with the DKA.[7] However, once the patient was stabilised with insulin, her lactate was persistently elevated from 4.1–5.9, and she remained asymptomatic. A few other case reports have described a patient with MS who also had persistently elevated lactatemia after treatment, and it may be considered to be a new feature of MS.[8-10] While the exact mechanism is unmown, it is thought that insulin could play a role in increasing lactate by inducing glycolysis, which can drive lactic acid production when administered in excess to treat DKA.[11]

The drug manufacturers of insulin have a longstanding history of price-gouging this life-saving drug, and there have been some great advances in policy reform to cap its cost at 35 USD for certain populations in the USA.[12] MS is a severe complication of poorly controlled T1DM and is likely preventable if insulin continues to become more affordable and easily accessible. This case report highlights that although MS is rare, it is important to maintain high clinical suspicion for it as its prevalence seems to be on the rise. The continued advocacy effort to cap the price of insulin will make it more easily accessible for lower-income patients to prevent MS in the future.[12]

Patients with T1DM with lower socioeconomic status face more difficulty affording and accessing insulin, requiring more than 25% of insulin-dependent patients to ration their doses, putting them at a higher risk of poor glycaemic control.[6] The patient presented

in this case was noted to have a lower socioeconomic status and faced financial difficulty, which affected her ability to access healthcare and afford medication. She was referred to 'population health', which is a programme at the hospital designed to help underserved patients manage their chronic diseases, afford medications, and reduce hospital re-admission. She was ultimately lost to follow-up and continues to be at risk for many complications of T1DM. The authors believe that earlier intervention with public health programmes and better social support could have improved the patient's compliance and prevented some of her complications.

One study noted an emerging prevalence of MS in patients with insulin-dependent Type 2 diabetes.[7] Although the prevalence is currently small, with only 2% of cases with MS, it demonstrates a need to emphasise medication compliance and early public health intervention to improve affordability and accessibility to insulin as more patients with Type 2 diabetes become insulin dependent.

CONCLUSION

This patient's presentation of hepatomegaly, delayed puberty, poor weight gain, persistent lactatemia, and moon facies all provide evidence of MS. Her presentation also included persistently elevated lactate levels, for which the exact mechanism is currently unknown. MS was once considered rare, but this patient is one in an emerging population of insulin-dependent patients who struggle with socioeconomic inequities that lead to this preventable complication. Earlier intervention with population health services and better social support could have improved this patient's access to healthcare and prevented complications of her T1DM. Physicians and all healthcare providers should continue to advocate for better public health interventions so as to prevent these severe complications of chronic disease.

References

1. Alhajjaj A H, Aljishi FK. Mauriac Syndrome still exists in poorly controlled type 1 diabetes: a report of two cases and literature review. Cureus. 2021;13(4):e14704.
2. Garcês Soares S et al. Hepatic glycogenosis: an underdiagnosed entity? Cureus. 2022;14(4):e23853.
3. Mertens J et al. NAFLD in type 1 diabetes: overrated or underappreciated? Ther Adv Endocrinol Metab. 2021;12:20420188211055557.
4. Lizzo JM et al, Adult diabetic ketoacidosis [Internet] (2024) Treasure Island: StatPearls. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560723/. Last accessed: 10 March 2024.
5. MacDonald MJ et al. Discovery of a genetic metabolic cause for Mauriac syndrome in type 1 diabetes. Diabetes. 2016;65(7):2051-9.
6. Herkert D et al. Cost-related insulin underuse among patients with diabetes. JAMA Intern. Med. 2019;179(1):112-4.
7. Sherigar JM et al. Glycogenic hepatopathy: a narrative review. World J Hepatol. 2018;10(2):172-85.
8. Feenstra RA et al.(2014). Lactic acidosis in diabetic ketoacidosis. BMJ Case Reports. 2014;2014:bcr2014203594.
9. Deemer KS, Alvarez GF. A rare case of persistent lactic acidosis in the ICU: glycogenic hepatopathy and Mauriac syndrome. Case Rep Crit Care. 2016;2016(1):1-4.
10. Brouwers MC et al. Elevated lactate levels in patients with poorly regulated type 1 diabetes and glycogenic hepatopathy: a new feature of Mauriac syndrome. Diabetes Care. 2015;38(2):e11-2.
11. Baldini N, Avnet S. The effects of systemic and local acidosis on insulin resistance and signaling. Int J Mol Sci. 2019;20(1):126.
12. Shao H et al. (2022). Economic evaluation of the $35 insulin copay cap policy in Medicare and its implication for future interventions. Diabetes Care. 2022;45(11):161-2.