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Hepatic Glycogenosis: A Modern Reality in Children with Type 1 Diabetes

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Abstract **Case Report**

Background: Mauriac syndrome (MS) is a rare complication of type 1 diabetes (T1D). It is related to low insulin concentrations and is less common since longer-acting insulins became available. It is characterized by hepatomegaly, growth and puberty delay, and the presence of elevated transaminases and serum lipids. Case reports of patients with Mauriac syndrome are found infrequently in the literature given historic improvements in diabetes management due to readily available insulin therapy. ***Case:*** We report a case of Mauriac syndrome diagnosed in a 15-year-old male. The patient maintained poor glycemic control since childhood, presenting glycated hemoglobin persistently higher than 10% and recurrent episodes of ketoacidosis. He was referred for hepatomegaly evolving for 6 months. The clinical examination objectified a distended abdomen with hepatomegaly at 16 cm. Biological examinations showed hyperglycemia, major cytolysis and cholestasis anicteric. Support based on therapeutic education of the child and his family, as well as adequate insulin therapy have been established. The etiological investigation of hepatic disturbances was negative. The clinical and biological evolution was favorable. The diagnosis of hepatic glycogen storage disease was retained on a bundle of anamnestic and clinical arguments, in the absence of other anomalies responsible for the disturbances liverworts. The diagnostic certainty is histological, and the treatment is based on the equilibration of the diabetes. ***Conclusion:*** Although MS is an ancient entity described in T1D, it still exists, particularly in adolescent patients. Being aware of MS is of extreme importance since most of the clinical features are reversible with better glycemic control.

Keywords: T1D, Mauriac syndrome, hepatomegaly, short stature, hepatic glycogenosis, insulin.

INTRODUCTION

Poorly controlled type 1 diabetes remains a major apprehension in underdeveloped countries, exposing many complications to a lack of insulin. Hepatocyte glycogen overload, previously called Mauriac syndrome, is one of them [1].

Mauriac syndrome (MS) is a rare complication of type 1 diabetes (T1D), characterized by hepatomegaly (hepatic glycogenosis), puberty and growth delay, dyslipidemia, transaminase elevation and reduction of IGF1 (insulin-like growth factor 1). Cushingoid features may also be present [2, 3]. The diagnosis of hepatic glycogenosis (HG) requires the exclusion of other causes of liver damage, including infectious, metabolic, or autoimmune.

The incidence of this syndrome decreased significantly with the introduction of long-acting insulin resulting in better glycemic control.

Although its real incidence is not well-known, due to the reduced number of reported cases in the literature, equal incidence is reported in males and females, with most of the cases occurring in adolescents and young adults [4].

CASE REPORT

We report the case of a 15-year-old patient, known T1D since the age of two, with poor glycemic control since the diagnosis, due to poor therapeutic compliance, with the notion of repeated hospitalizations for episodes of ketoacidosis. Having a background of iron deficiency anemia with notion of geophagia in childhood and newly diagnosed autoimmune thyroiditis under levothyroxine.

The beginning of the symptomatology goes back to 6 months by the installation of a pain of the right hypochondrium with type of gravity. The physical exam founds a patient in good general condition, with a stature-ponderal delay at - 3DS (a height of 132 cm and

a weight of 28 kg), and significant pallor. Abdominal exam revealed a distended abdomen with painless hepatomegaly (hepatic arrow = 16cm) homogeneous, with a regular surface and the absence of splenomegaly.

The laboratory data included poor glycemic control with glycated hemoglobin at 15%, and fasting blood sugar at 2.5 g/dl, aminostransferases were high (AST = 13× normal), ALT = 9× N), anicteric cholestasis with high gamma-glutamyl transpeptidase and alkaline phosphatase (GGT = 2 × N, ALP = 1.6 × N, total bilirubin = 6 µmol/l), without stigma of hepatocellular insufficiency (PT = 72% and albuminemia at 41 g/l). The ionogram and renal function and lipid panel were normal. Severe hypothyroidia was noted (TSH us at 100 mIU/L and a T4l at 2.4 pmol/l).

An etiological investigation of the liver disturbances was started, the abdominal ultrasound found a hepatomegaly of 16cm with regular contours and homogeneous echostructure without detectable focal lesion and without dilation of the intra and extrahepatic bile ducts, the supra-hepatic veins and the portal trunk were permeable with normal caliber. Viral serology (EBV, HAV, HBV, HCV, HEV, CMV and HSV) was negative, antibodies for autoimmune liver disorders, and anti-transglutaminase antibody were also negative. The liver biopsy showed chronic liver disease lesions with moderate fibrosis without septa. Hepatocytes were bloated without noticeable hepatocyte steatosis. Numerous glycogenic nuclei were present. Staining with periodic acid Schiff (PAS) before and after diastasis revealed the glycogen overload of hepatocytes.

The patient was referred to endocrinology for adequate management of his diabetes and therapeutic adjustment for his hypothyroidism.

After six months of insulin therapy, the patient had a well glycemic control with glycated hemoglobin reduced from 15 to 8%, the hepatomegaly diminished and his liver function tests were good as well . A liver biopsy to check this fact was not necessary. Based on the history, the biological and histological data and the favorable evolution after adequate management of the unbalanced diabetes, the diagnosis of hepatic glycogenosis was retained.

DISCUSSION

Adolescence is a critical period , when the child undergoes very important physical, intellectual and emotional changes. Helping the adolescent through this period is a real challenge for parents as well as for doctors. This period is more complex for adolescents diagnosed with type 1 diabetes: in addition to experiencing the same challenges as their peers, these adolescents must deal with intensive medical regimens, regular clinic appointments, carbohydrate calculations and frequent daily monitoring of blood glucose levels. Although new insulins and carbohydrate counting approach are currently available to facilitate more optimal glycemic control, many adolescents with type 1 diabetes achieve suboptimal glycemic control and in some cases we can still find MS [3, 4].

Mauriac syndrome, initially described by Mauriac in 1930, is typically diagnosed in children with T1D, presenting with growth failure, delayed puberty, hepatomegaly with abnormal liver enzymes and hypercholesterolemia [1]. This name has been replaced by the term hepatic glycogenosis or glycogenic hepatopathy.

The pathogenesis of glycogenic hepatopathy is imperfectly known. It seems to be linked to the combined excess of insulin and episodes of hyperglycemia. The mechanisms that contribute to hepatic glycogenosis in the event of overconsumption of insulin associated with phases of hyperglycemia consist of excessive storage of circulating glucose in the form of intrahepatic glycogen by hyperstimulation of glycogenesis and inhibition of glycogenolysis; insulin activates glucokinase and glycogen synthetase and inhibits glucose-6-phosphatase [2].

The pathogenesis of growth and pubertal delay is not clear but rather seems to be multifactorial: insufficient tissue glucose, lack of insulin as a growth factor and hypercorticism may contribute. The Cushingoid signs present during glycogen storage disease are classically described in children [1, 3]. Indeed, during the developmental period, documented large-scale fluctuations between hyperglycemia and hypoglycemia (suggesting a pattern of over- and under-insulinization) are accompanied by activation of counter-regulatory hormones with reactive hypercorticism to excess insulin [1, 2, 4]. Secondary hypercorticism therefore seems to be responsible for the development of Cushingoid obesity. This occurs mainly with children/teenagers, but is almost absent in those who have passed the puberty period [5-7].

Hepatomegaly is secondary to glycogen deposition in the liver. In the event of major hyperglycaemia, glucose passively enters the hepatocytes via GLUT 2 (insulin-independent glucose transporter) and is rapidly transformed into glucose-6P by glucokinase; significant insulin administration leads to the transformation of glucose-6P into glycogen by glycogen synthetase [8, 10].

Abdominal ultrasound found hepatomegaly and the aspect of liver overload reflecting the chronic storage of glycogen. The diagnosis of hepatic glycogenosis, includes the exclusion of other causes of liver injury, namely infectious, metabolic, obstructive, or autoimmune diseases [11].

The diagnosis of non-alcoholic fatty liver disease (NAFLD) should not be overlooked in a context of metabolic overload of the liver and in the presence of risk factors such as overweight (BMI > 25 kg/m2) with central adiposity, hypertriglyceridemia and low HDL-cholesterol levels often seen in diabetics [12]. Imaging does not make it possible to differentiate hepatic glycogenosis from NAFLD [13, 14]. The only examination to formally confirm the diagnosis is liver biopsy which highlights an aspect of glycogen overload visible after with PAS (periodic-acid-Schiff, used in histology to highlight the polysaccharides of the mucopolysaccharide types present in certain connective tissues as well as in the mucus) [15].

Nevertheless, some authors do not recommend performing the biopsy if the liver test normalizes with good glycemic control [8]. The evolution is most often favorable thanks to the glycemic balance, and the liver damage generally disappears in two to four weeks [16].

CONCLUSION

Mauriac syndrome is a modern reality, and although rare, may be going undiagnosed . Hepatic glycogenosis should be considered in the event of hepatomegaly with disturbance of liver function tests in an unbalanced T1D child. The diagnosis is based on a bundle of anamnestic and clinical arguments, after the exclusion of other causes of liver injury. The diagnostic is certainly histological, although rarely obtained, and the treatment is based on the equilibration of the diabetes.

In the future, the development of non-invasive imaging methods may be useful to differentiate from the NAFLD, but nowadays liver biopsy remains necessary.

REFERENCES

1. Mauriac. (1930). Gros ventre, hépatomégalie, trouble de la croissance chez les enfants diabétiques traités depuis plusieurs années par l'insuline. *Gas Hebd Med Bordeaux*, 26, 402–410.
2. Mahévas, T., Gobert, D., Gatfossé, M., Mekinian, A., & Fain, O. (2017). Œdème insulinique au cours d'une glycogénose hépatique. *La Revue de Médecine Interne*, *38*(3), 201-203.
3. Gutch, M., Philip, R., Saran, S., Tyagi, R., & Gupta, K. K. (2013). Re-emergence of a rare syndrome: A case of mauriac syndrome. *Indian Journal of Endocrinology and Metabolism*, *17*(Suppl1), S283-285.
4. Dias, J., Martins, S., Carvalho, S., Marques, O., & Antunes, A. (2013). Mauriac syndrome still exists. *Endocrinología y Nutrición (English Edition)*, *60*(5), 245-248. doi: 10.1016/j.endonu.2012.12.005. Epub 2013 Mar 26. PMID: 23540612.
5. Patita, M., Nunes, G., de Matos, A. A., Coelho, H., Fonseca, C., & Fonseca, J. (2019). Mauriac syndrome: a rare hepatic glycogenosis in poorly controlled type 1 diabetes. *GE-Portuguese Journal of Gastroenterology*, *26*(5), 370-374. doi: 10.1159/000496094. Epub 2019 Jan 29. PMID: 31559328; PMCID: PMC6751446.
6. Omoy, M. N., Ngoy, D. M., Ilunga, E. K., Ntumba, D. B., a Wakamb, G. K., Okitosho, S. W., & Numbi, O. L. (2017). Le diabète sucré de type I chez l'enfant de moins de 5 ans: à propos d'une observation aux cliniques universitaires de Lubumbashi et revue de la littérature. *The Pan African Medical Journal*, *26*. doi: 10.11604/pamj.2017.26.170.11876. PMID: 28674563
7. Khan, F., Parikh, M. P., & McCullough, A. J. (2018). Hepatobiliary and Pancreatic: Mauriac syndrome: A rare cause of elevated liver enzymes. *Journal of Gastroenterology and Hepatology*, *34*(2), 313-313. doi:10.1111/jgh.14381
8. Mayanda Ohouana, R. L., & Belmejdoub, G. (2022). Syndrome de Mauriac: À Propos d'un Cas. *Health Sciences and Disease*, *23*(3).
9. Parmar, N., Atiq, M., Austin, L., Miller, R. A., Smyrk, T., & Ahmed, K. (2015). Glycogenic hepatopathy: thinking outside the box. *Case Reports in Gastroenterology*, *9*(2), 221-226.
10. Brouwers, M. C., Ham, J. C., Wisse, E., Misra, S., Landewe, S., Rosenthal, M., ... & 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.
11. Fitzpatrick, E., Cotoi, C., Quaglia, A., Sakellariou, S., Ford-Adams, M. E., & Hadzic, N. (2014). Hepatopathy of Mauriac syndrome: a retrospective review from a tertiary liver centre. *Archives of Disease in Childhood*, *99*(4), 354-357.
12. Giordano, S., Martocchia, A., Toussan, L., Stefanelli, M., Pastore, F., Devito, A., ... & Falaschi, P. (2014). Diagnosis of hepatic glycogenosis in poorly controlled type 1 diabetes mellitus. *World journal of diabetes*, *5*(6), 882-888.
13. Ngongo, O. M., Kanteng, A. W., Mabaga, M., Essabe, A., Ebambi, K. T., Bafwafwa, N. D., ... & Luboya, O. (2015). Difficulté de diagnostic et de prise en charge du diabète sucre de l'enfant en milieu sous équipé: à propos de 3 observations. *Rev Méd Gd Lacs*.
14. Bril, F., & Cusi, K. (2017). Management of nonalcoholic fatty liver disease in patients with type 2 diabetes: a call to action. *Diabetes care*, *40*(3), 419-430.
15. Panda, P. K., & Sharawat, I. K. (2020). Mauriac syndrome in a young child with diabetes. *Indian Pediatrics*, *57*(4), 379-379.
16. Alhajjaj, A. H., & Aljishi, F. K. (2021). Mauriac Syndrome Still Exists in Poorly Controlled Type 1 Diabetes: a report of two cases and literature review. *Cureus*, *13*(4), e14704. doi: 10.7759/cureus.14704. PMID: 33927961; PMCID: PMC8076427.