Mauriac syndrome: A rare hepatic glycogenosis with metabolic bone disease in poorly controlled type 1 diabetes

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Received: 23 August, 2023, Manuscript No. fmcp-23-111099, **Editor assigned:** 24 August, 2023, PreQC No. fmcp-23-111099 (PQ), **Reviewed:** 28 August, 2023, QC No. fmcp-23-111099 (Q), **Revised:** 31 August, 2023, Manuscript No. fmcp-23-111099 (R), **Published:** 08 September, 2023, DOI. 10.37532/fmcp.2023.20(4).

Abstract

We report a case of 20 year old female, diagnosed with type 1 diabetes mellitus (T1DM) when she was 5 years of age when she presented with Diabetic ketoacidosis, she had poor glycemic control as she had multiple hospital admissions due to diabetic ketoacidosis. During adolescence she presented with delay puberty, short stature and hepatomegaly. Which end diagnosing this patient by liver biopsy as Mauriac syndrome.

Learning points:

• Mauriac Syndrome (MS) is a rare complication that occurs in patients with type 1 diabetes mellitus.

• Herein, a patient with MS presented with additional features including low bone density and delayed puberty.

• The early recognition and management of this syndrome may improve patient outcomes.

• Continuous glucose monitoring may be an appropriate approach for treating these patients to improve clinical outcomes and avoid complications.

Keywords: rare syndrome, metabolism, diabetes, glycogenosis, mauriac.

Background

Mauriac Syndrome (MS) is a rare syndrome that occurs in patients with poorly controlled Type One Diabetes Mellitus (T1DM) with diabetic complications. The cardinal features of MS include delayed growth, delayed puberty, hepatomegaly, dyslipidemia, and metabolic bone disease [1, 2].

Mauriac syndrome was first described by Pierre Mauriac in a 10-year-old girl with poorly controlled Type One Diabetes Mellitus (T1DM). Since then, several cases of Mauriac Syndrome (MS) have been reported. The exact etiology of the Mauriac Syndrome (MS) remains unknown. It is speculated to probably occur due to a combination of factors including inadequate glucose uptake and utilization in the tissues, decreased insulin-like growth factor-1 and growth hormone levels [3,4], and impaired bioactivity of these hormones. Additionally, hepatomegaly and impaired liver function are thought to be due to glycogen deposition in hepatocytes [5,6].

We performed a literature review published on Mauriac Syndrome (MS) over the past 20 years using the PubMed database. In total, 50 case presentations, studies, and reviews published were identified. Currently, most cases of Mauriac Syndrome (MS) do not have all of the characteristics initially described, and usually, the unique feature at presentation is glycogenic hepatopathy.

Here, we present the case of a young adult with all characteristics of Mauriac Syndrome (MS), with onset in the prepubertal stage and persistence until adulthood with delayed puberty and metabolic bone disease, despite access to insulin therapy and therapeutic education. These were considered additional features that were not identified during the literature review. Therefore, this case is of clinical importance for sharing with other clinicians so that they are aware that patients with Mauriac Syndrome (MS) may also present with these features.

Case Presentation

Here, we report the case of a 20-year-old female diagnosed with type 1 diabetes mellitus when she was 5 years old. She presented with diabetic ketoacidosis and had poor glycemic control as she had multiple hospital admissions due to diabetic ketoacidosis She did not experience other

TABLE 1. Laboratory result of the patient at the time of diagnosis.

Laboratory	Result	Comment
HbA1c	>14%	
Aminotransferase (AST)	1305 U/L	elevated since 2014
Aminotransferase (ALT)	427 U/L	elevated since 2006
Alkaline phosphatase	174 U/L	elevated since 2006
Total bilirubin	6 Umol/L	always been normal
25-Hydroxy D Total	16 nmol/L	Low
Serum cortisol random	230 nmol/L	Normal
somatomedin-C (IGF-1)	34.07 ng/mL	Low
insulin-like growth factor binding protein (IGFBP-3)	2.4 ug/mL	Low
Antinuclear Ab (ANA)	<1:40	
Smooth muscle Ab	Negative	
Anti-transglutaminase IgA	Negative	
Anti-LKM Ab	Negative	
Anti-hepatic cytosol Ab	Negative	
Anti-gliadin Abs	Negative	
Hepatitis serology (Hep C Ab, HepB Surface Ag)	Negative	

diabetic complications; her glycated hemoglobin was around 14% at the time of diagnosis.

The patient was on insulin glargine 28 IU at night and insulin aspart 5 IU before each meal, with a corrective dose of 1 IU for every 50 mg.

Pubertal timing was not within normal limits, and her parents reported shorter stature than her siblings. The patient had no family history of endocrine disease; however, she was diagnosed with low bone density with recurrent presentations of non-traumatic fractures.

The patient was referred to the internal medicine department because of altered liver enzyme levels. The patient reported having no gastrointestinal symptoms. The patient denied the use of alcohol, tobacco, or illicit drugs.

Investigation

Clinical examination revealed that the patient was 150 cm tall, weighed 40 kg, and had a body mass index of 17.7. Her height was plotted below the third percentile line, Tanner stage 2, and her liver span was 11 cm under the right costal margin with cushioned features (moon face) as reffered in (**TABLE 1**).

Bone radiography showed delayed bone age (13) according to the Greulich and Pyle Technique, with diffuse osteopenia and narrowed growth plates (**FIGURE 1**).

Abdominal ultrasound showed an enlarged liver measuring 21 cm, showing increased homogenous echogenicity, and no gross focal lesion or intrahepatic biliary ductal dilatation. Both portal and hepatic veins appeared patent; the color and waveform of the hepatic artery appeared normal, and hepatomegaly was related

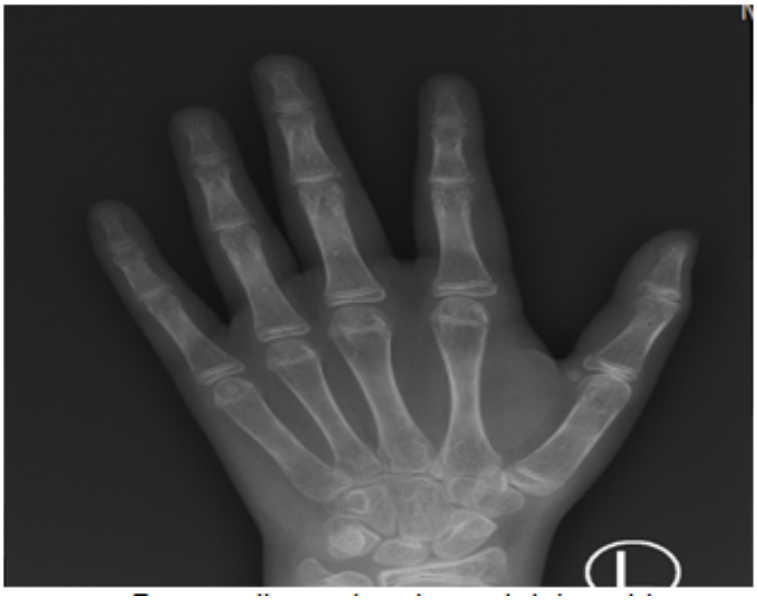

FIGURE 1. Bone radiography showed delayed bone age with diffuse osteopenia and narrowed growth plates.

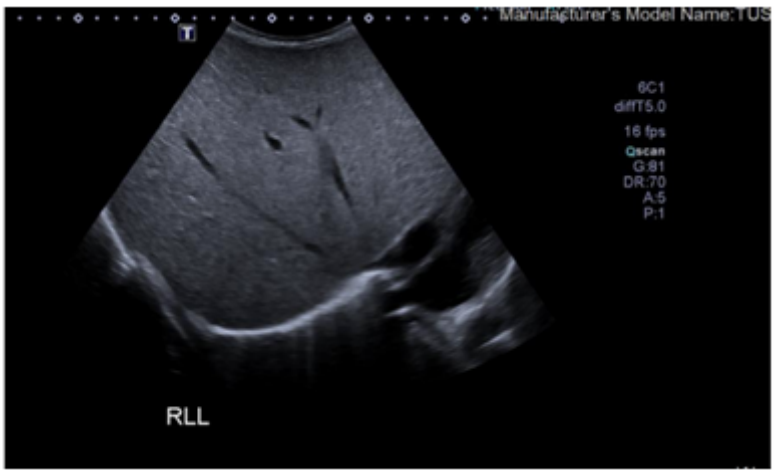

FIGURE 2. Ultrasound liver of the patient shows enlarged liver measuring (21 cm) demonstrates increased hepatic echogenicity.

to diffuse fatty liver infiltration. (**FIGURE 2**).

Magnetic Resonance Imaging scan showed that the pituitary gland had a microadenoma of 3 mm. Further investigation was performed to rule out a case of functioning adenoma; the morning serum cortisol level post dexamethasone suppression test was below 50 nmol/L and the prolactin level was 5 ng/dL.

In addition, a bone density scan indicated severe osteoporosis (lumbar Z score -7, femoral neck Z score -4). (**FIGURE 3**).

Upper endoscopy revealed a clean-based ulcer at the gastro-esophageal junction grade C esophagitis, and no esophageal or fundal varices. Ileocolonoscopic examination and histology of biopsies taken from the anal verge, right and left colon, and terminal ileum were performed. The patient was negative for dysplasia and malignancy. The anal verge biopsy showed a clean-based linear ulcer (2 cm × 3 cm) and mucosal prolapse. Furthermore, histological findings did not suggest celiac disease.

There was a need for further investigation. A liver biopsy was performed, which showed features of glycogen storage disease, enlarged hepatocytes showing a mosaic pattern, hyperglycemic nucleus, chronic inflammation, and fibrosis of the portal traces; the hepatic lobules showed a low level of neutrophils and were negative for malignancy (**FIGURE 4**).

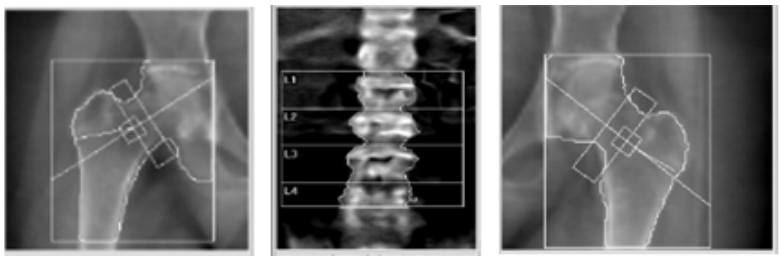

FIGURE 3. Bone densitometry (Hologic Explorer) shows following result. Lumbar spine (L1-L4): BMD (g/cm(2)): 0.459 (T-score: -5.3 Z-score: -7.0) Femoral neck: BMD (g/cm(2)) : 0.404 (T-score: -4.0 Z-score: -4.0)

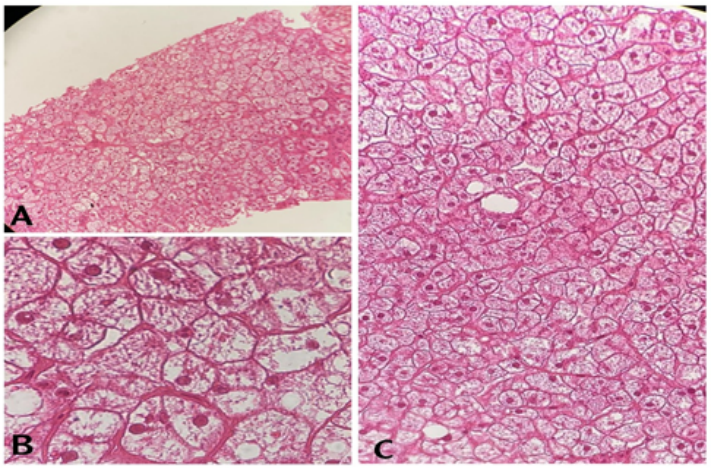

FIGURE 4 . (A) Hematoxylin and Eosin stain, hematoxylin-eosin, original magnifications 10x. Microscopic discerption: Mosaic pattern due to enlarged hepatocytes compressing sinusoids. (B) Hematoxylin and Eosin stain, hematoxylin-eosin, original magnifications 40x: Microscopic discerption: Large hepatocytes with prominent cell membrane and increased hepatocellular glycogen. (C) Hematoxylin and Eosin stain, hematoxylin-eosin, original magnifications 20x: Microscopic discerption: the hepatocytes are swollen with pale staining cytoplasm.

Treatment

The insulin dosage was gradually increased to glargine 36 IU SC once daily and aspart 8 IU TID pre meals, with a corrective dose of 1 IU for each 30 mg over 6 months. ethinylestradiol 35 mcg PO once daily started on 5th day of the period was initiated with full replacement with calcium carbonate 600 mg PO BID and vitamin D 50,000 IU PO once weekly.

■ Outcome and follow-up

After implementing strict glycemic control, hepatomegaly improved and elevated transaminase levels returned to normal ranges. The HbA1c level decreased to 10.5% after 3 months. The patient experienced menarche and a regular menstrual cycle thereafter. BMD was evaluated after 1 year with a significant improvement in the Z-score (lumbar Z score -5.9, femoral neck Z score -3.9), without a history of further fractures (**FIGURE 5**).

Discussion

Mauriac Syndrome (MS) is a rare condition; however, it was more prevalent prior to the development of long-acting insulin for the management of type 1 diabetes mellitus and the introduction of HbA1c as a measure of long-term glycemic control. This syndrome has been documented in isolated patients [2]. It was initially described in 1930 in children with type 1 diabetes mellitus, and exhibits clinical symptoms of failure to thrive, maturation delay, hepatomegaly, and abdominal distension. The etiology of delayed growth in Mauriac Syndrome (MS) is multifactorial, these factors include inadequate tissue glucose levels, decreased growth hormone levels and IGF-1, impaired or resistant hormone receptor activity, and hypercortisolism. Hepatomegaly and impaired liver function are thought to be caused by glycogen deposition in the hepatocytes [5,6]. Due to the lack of a stimulatory impact of insulin, sex steroid usage, or malnutrition, circulating IGF-1 levels may be lowered due to decreased IGF-1 synthesis and secretion, as was also reported in this case [3,4].

Several cellular mechanisms have been postulated to mediate bone metabolic disease in poorly controlled type 1 diabetes mellitus

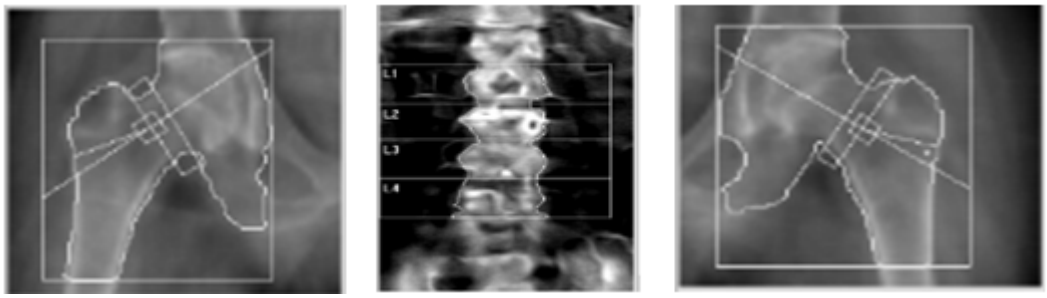

FIGURE 5 : Bone densitometry (Hologic Explorer) shows the following result Lumbar spine (L1-L4): BMD (g/cm (2)): 0.490 (T-score: -5.1 Z-score: -5.9)Total Hip: BMD (g/cm (2)): 0.482 (T-score: -3.8 Z-score: -3.8).

with type 1 diabetes mellitus Defects in osteoblast differentiation and activity are the main mechanisms underlying metabolic bone disease. Despite the increased risk of fractures, bone fragility remains an underrepresented complication of type 1 diabetes mellitus [7].

Conclusion

Early recognition and management of this syndrome may improve the outcome of these patients. Applying continuous glucose monitoring might be an appropriate approach to treat these patients to improve the clinical outcome and avoid complications. However, further investigation of these methods in-patient with Mauriac Syndrome (MS) is warranted.

Funding statement

Non.

Declaration of interest

No interest

References

1. Patita M, Nunes G, Alves de Matos et al. "Mauriac syndrome: a rare hepatic glycogenosis in poorly controlled type 1 diabetes." *GE-Port. J. Gastroenterol.* 26(5),370-374(2019).
2. Kocova, Mirjana, and Liljana Milenkova. "Old syndrome–new approach: Mauriac syndrome treated with continuous insulin delivery." *SAGE Open Med. Case Rep*. 6 (2018): 2050313X18785510.
3. Kim, Mimi S., and J. B. Quintos. "Mauriac syndrome: growth failure and type 1 diabetes mellitus." *Pediatr. endocrinol. rev*. 14(5), 989-993(2008).
4. Mauras, Nelly, Thomas Merimee, and Alan D. Rogol. "Function of the growth hormone-insulin-like growth factor I axis in the profoundly growth-retarded diabetic child: evidence for defective target organ responsiveness in the Mauriac syndrome." *Metabolism* 40(10),1106-1111(1991).
5. Giordano S, Martocchia A, Toussan L, et al. "Diagnosis of hepatic glycogenosis in poorly controlled type 1 diabetes mellitus." *World j. diabetes* 5(6), 882(2014).
6. Chatila, Rajaa, and Brian A. West. "Hepatomegaly and abnormal liver tests due to glycogenosis in adults with diabetes." *Medicine* 75(6), 327-333(1996):.
7. Mitchell, Deborah M. "Growth in patients with type 1 diabetes." *Curr. opin. endocrinol. diabetes obes*. 24(1), 67(2017).