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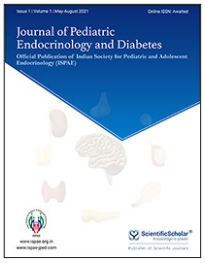

Case Report

Unique presentation of Mauriac syndrome with associated celiac disease in an adolescent with type 1 diabetes mellitus: A case report

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ABSTRACT

We report an adolescent girl with Mauriac syndrome diagnosed in merely 3 years of diagnosis of type 1 diabetes mellitus with poor glycemic control and associated celiac disease. A 11-year-old girl with poor metabolic control characterized by recurrent hypoglycemia and hyperglycemia presented with Mauriac syndrome comprising stunting, hepatosplenomegaly, and elevated serum transaminases without cushingoid features, within 3 years of diagnosis of type 1 diabetes mellitus. Serum tissue transglutaminase antibodies were elevated. The girl also had coexisting celiac disease. She improved with adequate glycemic control along with a gluten-free diet, iron, and other supplements with regression in the size of the liver and reduction of liver enzymes. Mauriac syndrome should be considered in type 1 diabetic patients with poor metabolic control and hepatomegaly irrespective of the duration of diabetes mellitus. Recurrent hypoglycemia and the presence of Mauriac syndrome are signs of associated autoimmune disorders.

Keywords: Type 1 diabetes mellitus, Mauriac syndrome, Poor glycemic control, Celiac disease, Hepatomegaly

INTRODUCTION

Recurrent hypoglycemia in a patient with type 1 diabetes mellitus may be associated with other autoimmune endocrinopathies such as Addison disease, celiac disease, and autoimmune thyroiditis with hypothyroidism. These autoimmune conditions are also more common when a child with type 1 diabetes mellitus presents with the features of Mauriac syndrome.[1] Mauriac syndrome is a rare complication of type 1 diabetes presenting with growth failure, hepatomegaly, delayed puberty, cushingoid features, and elevated serum transaminases.[2,3] Inadequate insulin therapy and poor metabolic control along with inadequate diet are important factors for the development of Mauriac syndrome.[4] Several case reports in the literature have described that this syndrome may present without the full spectrum of features described for Mauriac syndrome.[4,5] In this review, we summarize the unique presentation of this syndrome without obesity and cushingoid features in a young girl. In addition, we highlight the development of Mauriac syndrome in an adolescent girl merely 3 years after a diagnosis of type 1 diabetes with persistently poor glycemic control, along with the associated celiac disease.

CASE REPORT

An 11-year-old girl, from a low socioeconomic strata with a history of poorly controlled type 1 diabetes mellitus, presented with a history of abdominal distension, nausea, vomiting on and off, and pain in both lower limbs of 1-month duration. She also had a history of failure to gain weight and height, anorexia, and paleness of the body for the previous 2 years, along with episodes of unexplained recurrent hypoglycemia requiring intervention by hospitalization that led to the reduction in insulin requirements. She was diagnosed as a case of type 1 diabetes mellitus 3 years back at the age of 8 years. Since then, she was on treatment with multiple daily subcutaneous insulin injections, with an initial insulin dosage of 1 IU/kg. However, compliance with insulin administration was poor with inadequate blood glucose monitoring due to financial constraints. Her blood glucose measurements were variable with recurrent episodes of documented hypoglycemia and many episodes of hyperglycemia as well.

She was hospitalized thrice in the past 2 years and was treated symptomatically with intravenous antibiotics, antacids, and antiemetics as indicated and required a red blood cell transfusion. However, the symptoms were not relieved and the girl became anorexic, stunted, pale, and kept losing weight. There was no family history of hypertension, diabetes mellitus, and autoimmune disorders.

On presentation, the anthropometric data revealed severe growth retardation, with height 112 cm (<3rd percentile), weight 15.6 kg (<3rd percentile), body mass index 12.4 kg/m^2, mid-upper arm circumference 11 cm, and upper segment to lower segment ratio of 1:1. The patient was prepubertal with Tanner stage 1 for breast and pubic hair development. Physical examination revealed severe pallor, cold skin, protuberant abdomen, hepatomegaly, and muscle wasting of extremities [Figure 1]. The liver was enlarged 8.5 cm below the right costal margin and the left lobe was also palpable, with a span of 12.5 cm. The spleen was also enlarged 5 cm below the left costal margin with no evidence of free fluid in the abdomen. There was no stigmata of chronic liver disease such as palmar erythema, spider angiomas, or pedal edema.

Laboratory analysis revealed hemoglobin of 4 g/dL and blood picture revealed microcytic hypochromic anemia. Liver function tests showed serum aspartate aminotransferase 133 IU/L, alanine aminotransferase 55 IU/L, and alkaline phosphatase 813.7 IU/L. Blood urea was 84 mg/dL and serum creatinine was 1.56 mg/dL. Serum electrolytes were within normal limits. Hemoglobin A1c was 11%. Vitamin D levels were 8.32 ng/mL suggestive of vitamin D deficiency. An ultrasonogram of the whole abdomen revealed fatty liver with hepatosplenomegaly and raised renal echotexture.

In view of severe pallor with moderate splenomegaly and renal involvement, associated autoimmune diseases such as systemic lupus erythematosus (SLE) were thought of as a possibility. However, there was no skin involvement or arthritis. There was no pancytopenia and no evidence of pleural or pericardial effusion was seen on the radiograph of the chest and ultrasonography of the thorax. Thus, the possibility of SLE was clinically excluded. A normal smear for malarial parasite ruled out chronic malaria**.** Autoimmune liver disease antibody testing could not be done due to financial constraints.

Her thyroid profile revealed a free thyroxine (FT4) value of 0.53 ng/dL, free triiodothyronine <1.5 pg/mL, and thyroid-stimulating hormone (TSH) 2.66 μU/mL. Low levels of FT4 and normal TSH were attributed to euthyroid sick syndrome as a consequence of non-thyroidal illness. Early morning (8:00 am) serum cortisol level was 19 μg/dL and an adrenocorticotropic hormone stimulation test was not done.

Serum tissue transglutaminase antibody testing was done to rule out celiac disease, which reported levels of 1070.0 AU/mL, which was strongly suggestive of celiac disease. Anti-endomysial antibody testing and intestinal biopsy were needed to confirm the diagnosis but were not done due to refusal by the attendants due to financial constraints. Although celiac disease is known to cause fluctuations in blood glucose levels in a patient with type 1 diabetes, hyperglycemia due to celiac disease may cause mild or moderate glycogen deposition in the liver but it cannot cause chronic massive deposition of glycogen in the liver. This mild glycogen deposition in the liver improves with short-term improvement in metabolic control.[6] Our patient had very high blood glucose levels as reflected by the high glycosylated hemoglobin levels, and this could inhibit glycogen degradation more than normal.

She was gradually put on a gluten-free diet and supplements. She was also given intravenous iron therapy. Insulin administration was optimized as per blood glucose levels with diet monitoring. On 2 months follow-up of the child, improvement of metabolic control resulted in the reduction of hepatomegaly and normalization of liver enzyme levels. Liver disease regressed but her height remained below the third centile.

DISCUSSION

Mauriac syndrome was first described by Pierre Mauriac in 1930, as a rare disease in patients with type 1 diabetes who presented with short stature, hepatomegaly, delayed puberty, cushingoid features, and elevated transaminases.[2] With the advent of long-acting insulins and insulin analogs, the various classical manifestations of Mauriac syndrome are rarely seen and represent a poor therapeutic compliance.[7]

Our patient presented with stunting, hepatosplenomegaly, elevated liver enzymes but without obesity, and cushingoid features in the setting of poor metabolic control from a low socioeconomic background. Recently, there has been increasing number of case reports stating that Mauriac syndrome in diabetic patients may present without the full spectrum of features of this syndrome.[5,6]

The absence of features such as obesity and cushingoid features as reported in previous cases of Mauriac syndrome was noteworthy. A review of the literature suggested that there are two types of Mauriac syndrome according to the presence or absence of obesity. The first subgroup of Mauriac syndrome which is treated with regular insulin alone is associated with cushingoid features and secondary hyperadrenalism whereas, in the non-obese variety of Mauriac syndrome, inadequate insulinization of patients was seen.[8,9] The index case in our case report resembles the second form of Mauriac syndrome without cushingoid features. Moreover, our child belonged to lower socioeconomic strata which may be a factor for inadequate insulinization and poor compliance by the patient.

Many recent reports have also described that the coexistence of adolescent age, low socioeconomic status, and inadequate diet are important risk factors for the manifestation of Mauriac syndrome.[4] Although obesity was not prominent in our patient, this child exhibited very similar clinical manifestations of Mauriac syndrome. Hepatomegaly is a typical sign and is seen in most patients with Mauriac syndrome.[10] Literature also suggested that good metabolic control with daily insulin therapy can reverse these changes completely.[4,9]

The role of genetic factors in the development of Mauriac syndrome has been identified recently. Heterozygous mutation in the catalytic subunit of liver glycogen phosphorylase kinase has been reported. The glycogen phosphorylase kinase enzyme complex activates glycogen phosphorylase, an enzyme catalyzing the first step in glycogen breakdown in the liver. The mutant subunit inhibits the enzyme glycogen phosphorylase kinase causing inhibition of glycogenolysis and glycogen accumulation in the liver. Mutations in phosphorylase kinase catalytic subunit gamma 2, in the setting of hyperglycemia and glycogenolysis, result in massive hepatomegaly in patients with Mauriac syndrome. We could not undertake genetic studies due to financial constraints.

Mauriac syndrome is a chronic complication of poorly controlled type 1 diabetes and is rarely reported within 3 years of diagnosis of type 1 diabetes. Here, we have reviewed a case of an 11-year-old girl presenting with features of Mauriac syndrome within merely 3 years of diagnosis of type 1 diabetes suggesting that the child had poor glycemic control since the inception of the disease. She was also diagnosed to have associated celiac disease. Thus, in such patients of type I diabetes, presenting with features of Mauriac syndrome, the importance of early recognition of latent celiac disease is stressed.

Figure 1: 11-year-old girl with Mauriac syndrome who presented with severe stunting and hepatomegaly with poorly controlled type 1 diabetes mellitus.

Learning points

Mauriac syndrome may present without the full spectrum of clinical features described earlier. It should be suspected in a diabetic patient with poor metabolic control and hepatomegaly.

Adolescent age, low socioeconomic strata, and poor glycemic control are important clues to the development of Mauriac syndrome.

Although Mauriac syndrome is a chronic complication of poorly controlled diabetes, it can also complicate the disease early in its course.

Other autoimmune disorders, especially celiac disease, should be ruled out when Mauriac syndrome develops in type 1 diabetes patients to avoid more serious complications.

Limitations of the study

Liver biopsy to detect hepatic glycogenosis, duodenal biopsy to confirm celiac disease and genetic markers for Mauriac syndrome could not be performed.

CONCLUSION

Unexplained recurrent hypoglycemia requiring a reduction in insulin requirements and the development of Mauriac syndrome are signs of an associated autoimmune disorder and an early appropriate diagnosis will help improve the clinical outcome and avoid complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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