Revisit of a rare complication of type 1 diabetes mellitus: Mauriac syndrome

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Abstract
Mauriac syndrome is an uncommon complication of poorly-controlled type 1 diabetes mellitus (T1DM) reported in children 13–17 years of age. It manifests as delayed growth, hepatomegaly, elevated liver enzymes and serum lipids, and glycogen accumulation in hepatocytes. Common presenting features include short stature, growth retardation, moon facies, protuberant abdomen and proximal muscle wasting. Since the advent of long- and intermediate-acting insulin, this syndrome is now rarely encountered.

We report the case of a 16-year-old male who had a 13-year history of T1DM and was diagnosed with Mauriac syndrome. He was treated with biphasic isophane insulin and recovered – good glycaemic control was maintained, his height increased from 128cm to 141.5cm, hepatomegaly disappeared with normal liver enzymes, and the onset of pubertal spurt at eight months’ follow up was shown.

In conclusion, ensuring compliance with insulin therapy, and providing supportive treatment, nutritional support and good follow-up care can help to mitigate most of the complications relating to Mauriac syndrome. Copyright © 2017 John Wiley & Sons. Practical Diabetes 2017; 34(4): 132–134

Key words
type 1 diabetes mellitus; Mauriac syndrome; hypoglycaemia; hepatomegaly; insulin

Introduction
Mauriac syndrome is a rare complication of very poorly-controlled type 1 diabetes mellitus (T1DM) in adolescence. Mauriac syndrome manifests as short stature, glyco-gen-laden enlarged liver, limited joint mobility, tight waxy skin, growth maturation delay, moon facies, protuberant abdomen, and proximal muscle wasting. It is also frequently associated with retinopathy and nephropathy.1,2

Case history
A 16-year-old male patient with T1DM of 13 years’ duration had polyuria, polydipsia, polyphagia, weight loss and diabetic ketoacidosis (DKA) at the time of his diagnosis of T1DM. He had poor control of T1DM since the diagnosis was made. In the past he had required frequent hospitalisations for attacks of DKA and hypoglycaemic convulsions. His parents were very anxious regarding his uncontrolled hyperglycaemia in spite of using different insulin preparations as advised by many consultants.

The patient was admitted to our hospital, the main complaint being recurrent attacks of symptomatic hypoglycaemia in the form of unconsciousness and episodic convulsions. At the time of admission, he was receiving short-acting (Human Actrapid) insulin 12 IU before breakfast, lunch and evening meal, and ultra-long acting (Lantus) insulin 14 IU at ≈10pm, subcutaneously (SC). His diet was both vegetarian and non-vegetarian. He was immunised in accordance with his age. He had no family history of diabetes.

On examination, the patient was conscious and oriented. He was short in stature (128cm in height), 31kg in body weight, and his BMI was 18.92kg/m². Vital examinations were normal. He had a moon-like face and a protruded abdomen. He had delayed secondary sexual characteristics for his age. His pubic hair had not grown and his puberty Tanner stage was between 1 and 2. He had restricted finger movements due to stiffness of the metacarpal joint and could not make a fist.

The patient’s blood group was B+ve. His haemoglobin was 11.6gm/dl; total WBC 13.23×10⁹/µL; platelet count 4.22×10⁹/µL; PCV 34.6%; MCV 71.6fL; MCH 24.0pg; MCHC 33.5gm/dl; serum cholesterol (CHO) 177mg/dl; triglycerides 66mg/dl; high-density lipoprotein (HDL) 74mg/dl; low-density lipoprotein (LDL) 89.8mg/dl; very low-density lipoprotein (VLDL) 13.2mg/dl; CHO/HDL 2.39; LDL/HDL 1.21;
and INR 0.85. He had normal renal function tests.

His fasting blood glucose (FBG) was 453mg/dl, and post-prandial blood glucose (PPBG) 400mg/dl; serum C-peptide was <0.01ng/ml; he had very low (44.4ng/ml) IGF-1 (somatomedin C); serum cortisol was 7.5µg/dl (normal); glutamic acid decarboxylase (GAD) antibody was 184 IU/ml; and HbA1c was 13.7%. Islet-cell antibody and anti-insulin antibody results were not significant. He had proteinuria of 0.48g/day with urine albumin 25mg/dl. His serum TSH, T3 and T4 were respectively: 2.21MU/ml (normal 0.27–4.20), 1.7nmol/L (1.30–3.10), and 139nmol/L (66–181). Follicle stimulating hormone level was 3.2mIU/ml (normal 1.27–11.95); luteinizing hormone was 0.46mIU/ml (normal 1.14–8.75); serum testosterone of 5.9ng/dl was low (puberty Tanner stage 1: 2–23); and prolactin was 15.58ng/ml (normal 3.46–19.40). He had negative report of serum antinuclear antibody, anti-double stranded deoxyribonucleic acid and tissue transglutaminase IgA. Serum vitamin D was 17.8ng/ml (normal 30–47), and serum vitamin B12 was 450pg/ml (normal 191–663).

The patient had diabetic retinopathy grade 1 on fundus examination, with myopic astigmatism reported by the ophthalmologist.

His two-dimensional echocardiography report suggested mild left ventricular diastolic dysfunction with ejection fraction of 60%.

He had altered liver function tests with SGPT 234U/L and SGOT 256U/L.

He had normal chest X-ray and sinus rhythm on electrocardiogram.

He had right kidney 8.7×3.9cm and left kidney 8.7×4.7cm, with normal echo-pattern and preserved corticomedullary differentiation, small size of both testes and hepatomegaly on ultrasound examination. His liver biopsy suggested diffuse microvesicular steatosis in the liver when compared with normal histopathology (Figure 1).

He had sensory-motor neuropathy on electromyography and nerve conduction velocity study. He had a bone age of around 10.5 years. His MRI brain was normal.

The patient was admitted to our hospital for 28 days. He and his parents were well counselled and educated regarding the disease, its complications and treatment. Psychological support was also provided to the patient and his parents during his hospitalisation.

He was initially kept on short-acting insulin 4-hourly and as per need, according to the sliding scale for blood glucose. He received dextrose 25%, 2ml/kg of body weight for hypoglycaemia. Gradually, he was shifted to SC biphasic isophane insulin (30/70) 36 IU administered at 8am each morning and 20 IU at 8pm. He received short-acting (regular) SC insulin 7 IU before lunch and 4 IU before the evening meal. He was also advised to take short-acting insulin as per need in between, according to hyperglycaemia by sliding scale. Oral atenolol 25mg once a day was continued to maintain normal blood pressure. For the low level of vitamin D, vitamin D₃ granules 6000 IU, one sachet, once a week for 10 weeks was started. Oral Folvite 5mg, vitamin B complex capsule, and calcium supplement were started. Injection of testosterone 100mg/ml, deep intramuscularly, was started once a month for the patient’s low testosterone level.

The patient was discharged after the 27th day of hospitalisation. Subsequently, he regularly attended for follow up every 15 days.

At eight months’ follow up, he is on SC biphasic isophane insulin injection (30/70): 36 IU at 8am and 20 IU at 8pm. He is also taking SC short-acting insulin: 7 IU before lunch and 4 IU before the evening meal.

To date, our patient has had no episode of fluctuations in high or low blood glucose, nor of DKA or of hypoglycaemic attacks producing convulsions. His height has increased to 141.5cm from the previous 128cm, and his weight is 36kg body weight (previously 31kg). The patient’s puberty Tanner stage is now between 3 and 4. His serum testosterone levels and FSH are 169.1ng/ml and 0.199MIU/ml. Ultrasound examination revealed right testis 2.7×1.1cm and left testis 2.5×1.2cm in size. His FBG, PPBG, HbA1c and serum C-peptide were 198mg/dl, 204mg/dl, 7.6%, and <0.01ng/ml, respectively. His hepatomegaly disappeared. His liver enzymes were within normal limits.

**Discussion**

In 1930, Mauriac first described a syndrome in children with T1DM presenting with clinical features of growth failure, maturation delay, hepatomegaly and protruded abdomen. Since the advent of the long- and intermediate-acting insulins, T1DM with hepatomegaly and the various manifestations of Mauriac syndrome are rarely encountered. Most of the cases occur in adolescence with an equal sex ratio.

Mauriac syndrome is classified into two subgroups depending upon the presence or absence of obesity. In the obese variety of the syndrome, poor glycaemic control involves wide fluctuations between hyper- and hypoglycaemia, suggestive of a pattern of over- and under-insulination of glucose, respectively. In the non-obese variety of the syndrome, patients were inadequately insulinised without a...
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A history of alternating hypoglycaemia and ketoacidosis. The pathogenesis of this syndrome is unclear but is thought to be multifactorial. Inadequate glucose to the tissues, decreased IGF-1 and growth hormone levels, hypercortisolism, and resistant/defective hormone receptor action may lead to stunted growth and delayed puberty.

MacDonald et al. discovered a mutation in the catalytic subunit of liver glycogen phosphorylase kinase in a patient with Mauriac syndrome who developed growth failure and massive hepatomegaly. In their patient, PHKG2 G→A mutation in exon 9 was identified for excess glycogen accumulation in liver cells. Glycogen phosphorylase kinase activates glycogen phosphorylase, the enzyme that catalyses the first step in glycogen breakdown. This case proves that the effect of a mutant enzyme of glycogen metabolism can combine with hyperglycaemia to directly hyper-inhibit glycogen phosphorylase, in turn blocking glycogenolysis causing the massive liver in Mauriac disease. Thus, neither hyperglycaemia alone nor a mutated enzyme alone are sufficient to cause this syndrome: a mutant enzyme of glycogen metabolism combined with chronic hyperglycaemia can cause the syndrome. Hepatomegaly developed because of glycogen deposited in the liver due to periods of supraphysiological levels of insulin. Blood glucose passively enters the hepatocytes in which glycogen synthesis is promoted by high cytoplasmic glucose concentration reliant on the presence of insulin. Then glycogen is deposited within the hepatocytes as a result of a vicious cycle of hyperglycaemia and insulin treatment. Poor glycaemic control due to hypoinsulinaemia leads to lipolysis and ketone generation. Ketosis activates cortisol synthesis promoting the release of fatty acids and hyperglycaemia.

In this case, poor compliance because of illiteracy was the main cause of poorly-controlled diabetes – even when using short- and long-acting insulin preparations. After achieving the better glycaemic control with modified insulin therapy, the patient recovered from the complications, and improvement in growth and development was observed.

To conclude, Mauriac syndrome is a rare complication of poorly-controlled T1DM in adolescence. It requires a high index of suspicion so that proper growth and pubertal maturation can be accomplished; this can be done by timely intervention ensuring compliance with insulin therapy, and providing supportive treatment, nutritional support and good follow-up care.

Key points

- Mauriac syndrome is a rare complication of very poorly-controlled type 1 diabetes in adolescence which may be presented as either the obese or the non-obese variety
- This syndrome can be manifested as short stature, hepatomegaly, limited joint mobility, tight waxy skin, growth maturation delay, moon facies, proptuberant abdomen and proximal muscle wasting, and can be associated with retinopathy and nephropathy
- Timely intervention ensuring compliance with insulin therapy, supportive treatment, nutritional and psychological support, regular exercise and good follow-up care can help in recovery from Mauriac syndrome

References


Declaration of interests

There are no conflicts of interest declared. Funding: none. Ethics committee approval: confirmed. Consent of patient’s relative: obtained.

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