Uneventful pregnancy in a patient with ketosis-prone type 2 diabetes mellitus

Déroulement normal d’une grossesse chez une patiente ayant un diabète de type 2 cétosique

Keywords: Ketosis-prone type 2 diabetes; Pregnancy; Insulin resistance

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Ketosis-prone type 2 diabetes is typically revealed by acute metabolic decompensation, followed by remission and subsequent relapse [1]. The mechanisms of this phasic course are not fully understood, but may involve both a progressive defect of insulin secretion and insulin resistance [2]. Since pregnancy is associated with insulin resistance, it may be a situation at high risk for decompensation in such patients. However, there have been no reports on the prognosis of pregnancy in patients with this particular form of diabetes.

1. History and examination

A 30-year-old woman from Mali was admitted with metabolic decompensation revealing diabetes. She had no significant past medical history and no known family history of diabetes. Her body weight was previously normal (70 kg, BMI 24.2 kg/m²). She reported the onset of polyuria and mouth dryness, followed by vomiting and abdominal discomfort, eight days before admission. On admission, her physical examination was unremarkable apart from signs of dehydration. The patient had lost 8 kg of body weight. Plasma glucose concentration was 40 mmol/L and urine ketone bodies were 4+. Arterial pH was 7.32 and bicarbonates were 7 mmol/L. Plasma sodium was 151 mmol/L, potassium was 4.8 mmol/L, protides were 103 g/L and creatinine was 148 µmol/L. Liver and pancreas enzymes were normal. No precipitating factor was identified. HbA1c was 13.2% (normal 4.3–5.7%).

The diagnosis of diabetic ketoacidosis with moderate hyperosmolarity (calculated plasma osmolarity was 361 mmol/L) was made, and the patient was treated by fluid and potassium replacement, and intravenous regular insulin. Insulin requirements were 240 IU during the first 24 h, and 120 IU the next day. Thereafter, insulin was administered subcutaneously. Good glycaemic control was achieved with 66 IU/day of insulin on day 4 after admission. Metformin (2550 mg/day) and glyburide (15 mg/day) were then instituted while the insulin dosage was tapered. The patient was discharged on day 10 while taking insulin therapy and oral hypoglycaemic agents, with normal glycaemic control. Islet-cell antibodies, anti-GAD and anti-IA-2 antibodies were all negative.

During the following six weeks, insulin therapy and glyburide were progressively tapered, and the patient remained on metformin alone with good glycaemic control. She was followed-up for 15 months and remained in remission (HbA1c 5.2–5.6%). At this time, the patient had regained her initial weight loss. Because the patient planned a pregnancy, metformin was discontinued with no deterioration of glycaemic control (preconceptional HbA1c 5.3%). Throughout the entire pregnancy, the patient was treated with diet alone and glycaemic control remained good, as indicated by capillary blood glucose self-monitoring (mean value of four to six daily determinations: 5.6–6.1 mmol/L) and HbA1c values (5.1–5.7%). Total weight gain during the pregnancy was 10 kg. Pregnancy was uneventful and the patient spontaneously delivered, at 40 weeks of gestation, a healthy 3710-g girl, who had no neonatal hypoglycaemia. Thirty months after the initial decompensation, the patient remains in remission.

2. Conclusion

In this patient, the diagnosis of ketosis-prone type 2 diabetes was established on the basis of her ethnicity, the uncovering of diabetes by severe decompensation in the absence of a precipitating event, the subsequent progression to complete remission within a few weeks, and the absence of type 1 diabetes-associated autoantibodies.

The definite pathophysiology of ketosis-prone type 2 diabetes remains unknown. It has been shown that insulin secretion and insulin sensitivity, which are deeply suppressed at presentation, both recover at least partially after treatment with insulin. However, after the first remission and cessation of insulin therapy, up to 60% of patients with ketosis-prone type 2 diabetes have a recurrence of hyperglycaemia within two years when treated by
In patients in remission, progressive hyperglycaemia precedes, and is a strong risk factor for subsequent relapse [2]. More recently, short-term studies have shown that glucotoxicity, but not lipotoxicity, is involved in the occurrence of β-cell dysfunction and abnormal muscle insulin signalling [3]. Thus, both insulin secretion defect and insulin resistance may be involved in relapse.

The case we have described shows that the insulin resistance normally associated with pregnancy was not sufficient to trigger metabolic decompensation in our patient. This suggests that, despite the severe initial presentation, recovery of β-cell function was near-normal, or at least able to counteract insulin resistance. Since glucotoxicity is a major determinant of the insulin secretion defect observed in ketosis-prone type 2 diabetes, maintenance of normal glucose control is crucial to avoid relapse of metabolic decompensation. In this respect, monotherapy with metformin, which is not associated with the risk of hypoglycaemia, should be used during the remission phase in patients who have ketosis-prone type 2 diabetes.

References


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Inclusion of C-reactive protein in the identification of metabolically healthy but obese (MHO) individuals

To the Editor:

There has been considerable interest recently in the establishment of clinical criteria to identify individuals who are potentially at risk for metabolic and cardiovascular complications. For example, much attention has been paid to the establishment of criteria to identify individuals who have the metabolic syndrome [1]. This clustering of the risky phenotypes (such as central body fat, hyperglycaemia and dyslipidaemia) in which insulin resistance may play a central role could predispose individuals to an increased risk of cardiovascular disease and type 2 diabetes [1].

Interestingly, a unique subset of obese individuals has been described in the literature that appears to be ‘protected’ from the development of metabolic disturbances associated with obesity [2]. These individuals—termed ‘metabolically healthy, but obese’ (MHO)—despite having large quantities of fat mass exhibit a healthy metabolic profile, including remarkably high levels of insulin sensitivity, a favourable lipid and inflammatory profile, and no signs of hypertension. Evidence suggests that MHO individuals may account for as much as 20–30% of the obese population [2]. This is a striking finding that underscores the need to identify these individuals using simple clinical markers.

Recognition of MHO patients is important because the absence of metabolic complications could influence their prognosis and treatment. We recently proposed simple clinical markers that could identify MHO individuals [3]. It should be noted that these criteria have recently been duplicated by an independent research team, thereby confirming that they are appropriate for identifying a specific subgroup of the obese population [4]. In that study, the authors showed that these individuals displayed a more favourable metabolic and inflammatory state than ‘at-risk’ individuals.

In addition, C-reactive protein (CRP) has been suggested for the identification of the metabolic syndrome [5]. The findings of Cook et al. [6] further showed that CRP may be an important marker for clinical use. Moreover, we reported that MHO individuals (identified using the hyperinsulinaemic–euglycaemic clamp) have 92% lower CRP levels than those ‘at risk’ [2]. Therefore, we considered it timely to attempt to redefine the simple clinical metabolic criteria that identify MHO individuals.

The proposed selection of MHO clinical markers is based on those previously described [3], except that CRP is included as a clinical marker for the identification of MHO individuals, and total cholesterol is excluded as it is highly correlated with LDL cholesterol. Based on the review by Bassuk et al. [7], which showed that CRP levels above 3 mg/L significantly increased the risk of cardiovascular disease, we suggest that the cut-off point for this new marker be less than or equal to 3 mg/L. Furthermore, based on the recent study by Karelis et al. [2], we now suggest the new defining level for homoeostasis model assessment (HOMA)