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Gestational pancreatitis complicating uncontrolled diabetes mellitus

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A 36-year-old G₅ P₂ AB₂ woman was admitted to our hospital due to nausea, vomiting and severe epigastric pain for one day at 24 weeks gestation. She had a history of diabetes for one year, but was not receiving any medical treatment. The patient also denied any other drug history or alcohol drinking. Physical examination revealed a blood pressure of 150/100 mmHg, body temperature 37°C, weight 60 kg, and height 159 cm. Cutaneous eruptions or xanthomas were not seen. The epigastric tenderness was severe, but without rebounding pain or muscle rigidity. Pelvic examination was unremarkable. Fundus height was 22 cm and foetal heart rate 140 beats/min. Laboratory studies showed a serum amylase level of 457 U/l (normal range <180 U/l) and lipase 1056 U/l (<190 U/l). Plasma sugar was 12.9 mmol/l, triglycerides 81.8 mmol/l and total cholesterol 20.7 mmol/l. HbA_{1c} was 10.2% (4–6%), and postprandial serum C-peptide 0.2 nmol/l. Arterial blood gasses were pH_a 7.23, p_aO₂ 113 mmHg at room air, p_aCO₂ 21 mmHg, base deficit 15 mmol/l. Blood ketone reaction was strong with 1:4 dilution. Abdominal sonography disclosed a swelling pancreas, but no evident biliary tract disease. Under a provisional diagnosis of acute pancreatitis, parenteral dextrose (2000 kcal/day by 50% glucose water and 0.9% glucose saline) and intravenous insulin were administered. Ketoacidosis was promptly corrected in one day and serum triglyceride was decreased to 13.5 mol/l by the seventh day. Thereafter a low fat diet was resumed and plasma sugar was well controlled by daily subcutaneous insulin. The serum triglyceride was further lowered to 3.3 mol/l after 2 weeks. The patient had a weight gain of 3 kg within 3 weeks of hospitalisation and finally gave birth to a healthy baby of 2600 g by caesarean section at the 38th week of pregnancy.

Questions

- 1 What is the most likely cause of acute pancreatitis in this pregnant woman?
- 2 What are the possible mechanisms of her extreme gestational hypertriglyceridaemia?
- 3 How should her hypertriglyceridaemia be managed?

Answers

QUESTION 1

Gestational pancreatitis is a rare complication with a high mortality for mother and foetus, the most common cause being biliary tract disease.¹ However, in women with an underlying disorder of lipid metabolism, the possibility of gestational hypertriglyceridaemic pancreatitis should never be overlooked.² Pregnancy is normally associated with a hyperlipoproteinaemia, and may be associated with as much as a 2.5-fold increase of very low density lipoprotein triglycerides (VLDL-TG) over pre-gestational levels in the middle of third trimester.³ In the presence of a pre-existing lipid disorder such as familial hypertriglyceridaemia, a marked gestational hypertriglyceridaemia may occur.² In view of the negative sonographic study of the hepatobiliary tract, denial of alcohol drinking and an extremely high plasma triglyceride level, our patient probably suffered from an acute attack of hypertriglyceridaemic pancreatitis.

QUESTION 2

Diabetes is known as a common cause of secondary lipid metabolism disorder and is often associated with increased plasma VLDL-TG levels and a marked hypertriglyceridaemia, over 2000 mg/dl, may even occur in some patients.⁴⁻⁵ Recently, some authors have stated that oestrogen therapy in diabetic women may lead to an extreme hypertriglyceridaemia, particularly in an uncontrolled glycaemic state, and then possibly induce acute pancreatitis.⁶ However, gestational hypertriglyceridaemic pancreatitis complicating uncontrolled diabetes has rarely been reported.

It had been shown that diabetic pregnancies are associated with higher plasma triglycerides than normal ones.³⁻⁷ Moreover, the increased levels of plasma triglycerides has been shown to be related to diabetic control.⁷ The accentuated hypertriglyceridaemia may be produced by a synergistic effect of diabetes and pregnancy on VLDL synthesis.⁷ In our patient, who had an uncontrolled diabetes before pregnancy, this is the most probable explanation for her extreme hypertriglyceridaemia. Nevertheless, we did not perform any other investigation of genetic lipid abnormalities on our patient or her family and could not exclude the possibility of an endogenous lipid disorder, in spite of the good recovery of hypertriglyceridaemia after insulin infusion.⁵ Diabetic ketoacidosis, another acute metabolic complication noted in our patient, could also be associated with hypertriglyceridaemia.⁸ How-

Learning points

- pre-existing hypertriglyceridaemia may be exacerbated by pregnancy and thus induce a risk of acute hypertriglyceridaemic pancreatitis
- uncontrolled diabetes may exacerbate gestational hypertriglyceridaemia
- strict glycaemic control is effective in managing gestational diabetic hypertriglyceridaemia

ever, in the reported cases, hypertriglyceridaemia over 7000 mg/dl has rarely been found and our patient's hypertriglyceridaemia could not be attributed to diabetic ketoacidosis alone.⁸

QUESTION 3

Management of gestational hypertriglyceridaemic pancreatitis lies in correction of lipoprotein metabolism disturbances, and maintenance of nutritional support.⁹ Dietary fat restriction, lipid-free parenteral nutrition or plasma exchange have all been used to achieve this.⁹⁻¹⁰ However, antihypertriglyceridaemic drugs, such as fibric acid derivatives should not be considered, due to the possibility of teratogenic effects. Strict glycaemic control would provide another rational therapy.⁷⁻¹¹ In our patient, diabetic VLDL-TG metabolism was normalised by intensive insulin therapy, possibly mediated by decreased hepatic VLDL synthesis and enhanced lipoprotein lipase due to the effects of insulin.¹²⁻¹³

Conclusion

A moderate hypertriglyceridaemia due to uncontrolled diabetes may have existed in our patient before pregnancy and was markedly exacerbated by the gestation. In consequence, acute hypertriglyceridaemic pancreatitis occurred, complicated by diabetic ketoacidosis.

Pancreatitis is a rare but serious event during pregnancy. Pregnant women with inadequately controlled diabetes may be at risk of hypertriglyceridaemia. Strict diabetic control during pregnancy is warranted to prevent hypertriglyceridaemic pancreatitis and achieve an optimal outcome for mother and foetus.

Final diagnosis

Gestational hypertriglyceridaemic pancreatitis and diabetic ketoacidosis, due to uncontrolled diabetes mellitus.

Keywords: diabetes; hypertriglyceridaemia; pregnancy; pancreatitis

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A young woman with fluctuating hypo- and hyperthyroidism

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A 30-year-old woman presented for the first time in August 1990 with signs and symptoms of hypothyroidism: weight gain, fatigue, and muscle aches. She had a small goitre, but no ophthalmopathy or dermopathy. She was a non-smoker and mother of two (last childbirth 2 years previously). There was no history of thyroid disease or drug consumption. Thyroid function tests confirmed the diagnosis of primary hypothyroidism: thyroid-stimulating hormone (TSH) 74 mU/l (reference range 0.4–5 mU/l), free thyroxine (FT₄) 2.4 nmol/l (9–24). Thyroid microsomal antibody (TMA) and antithyroglobulin antibody were positive (one in 256 000 and 1600, respectively). Replacement therapy with thyroxine was started (100 µg daily). Over the next 6 months her dose requirement for thyroxine was reduced to 50 µg daily and the drug was stopped altogether one year after the initial diagnosis while she remained clinically and biochemically euthyroid. In July 1997, she developed symptoms and signs of thyrotoxicosis: weight loss, palpitations, and increased sweating. The diagnosis of thyrotoxicosis was confirmed (TSH undetectable, tri-iodothyronine (T₃) 2.5 nmol/l (0.7–2.1), and FT₄ 29 nmol/l). No treatment was given. While on follow-up over the next 2 months her symptoms subsided and she gained weight; thyroid function confirmed hypothyroidism (TSH 84 mU/l, FT₄ 8.8 nmol/l). In November 1997, although symptomatically she remained well, thyroid function tests showed thyrotoxicosis (TSH undetectable, FT₄ 30 nmol/l) but she has remained euthyroid on follow-up. Her TMA titre remains the same.

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Figure Fluctuation of thyroid function during the follow-up period.

Questions

- 1 What is the diagnosis?
- 2 Why is the thyroid function fluctuating?
- 3 How would you treat this patient?