

A Case of Accelerated Development of Proliferative Diabetic Retinopathy in a Woman with Type 2 Diabetes Mellitus after Pregnancy

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Abstract

Whilst it is recognised that diabetic retinopathy is a consequence of prolonged elevation of blood glucose levels, recent studies suggest rapid normalisation of blood sugar as a causal factor in accelerating its development. In this case report, a non-insulin dependent diabetic with poor blood glucose control but no retinopathy in early pregnancy had normalisation of glucose control by the third trimester. However, glucose control deteriorated rapidly postnatally, and she had a sudden blurring of vision three months after delivery of her baby, at which time severe proliferative diabetic retinopathy was diagnosed. The reason for the unusually rapid development of proliferative retinopathy was uncertain, but appeared to have a temporal association with the deterioration of her glycaemic control postnatal after a period of strict diabetes control in the perinatal period.

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Key words: Normalisation of blood glucose levels, Ophthalmic examination, Poor diabetic control, Severe diabetic retinopathy

Introduction

Diabetic retinopathy is the leading cause of blindness in persons between the age of 24 and 64 years both in the US and the UK.^{1,2} Peak fertility and childbearing years correspond to the first half of this period. Thus, careful ophthalmic evaluation and follow-up are essential for pregnant women with diabetes.

In the management of such patients, regulation of hyperglycaemia is important so as to avoid foetal morbidity and mortality. However, recent evidence suggests that accomplishing normoglycaemia too rapidly may actually worsen diabetic retinopathy. Laatikainen et al³ noted rapid ischaemic retinal deterioration in two patients on insulin-pump therapy. Phelps et al⁴ showed a highly significant correlation between worsening retinopathy and the degree of hyperglycaemia at entry into their study, and the magnitude of improvement in glycaemic control in pregnant diabetics. Other reports⁵⁻¹² support the notion of cautious normalisation of serum glucose in patients with retinopathy and poor diabetic control.

Case Report

Mdm RBS, a 34-year-old Malay woman, gravida 4 para 2, attended the combined obstetric-diabetic clinic for antenatal booking in October 1995, at 10 weeks gestation. She had had non-insulin dependent diabetes mellitus for 3 years.

She had 2 previous pregnancies before the diagnosis of diabetes was made. Both of them had been complicated by gestational diabetes, for which she was prescribed insulin treatment. The pregnancies had been otherwise uneventful, culminating in the births of 2 healthy babies, 3.2 kg and 3.6 kg, respectively, by elective Caesarean section. Postpartum oral glucose tolerance tests had been normal on both occasions. Three years after her second delivery, diabetes was diagnosed by her family physician and treatment with an oral hypoglycaemic agent was started. She was first admitted to our hospital 2 years later (a year before this present pregnancy) for a missed abortion at 8 weeks amenorrhoea. During that admission, insulin treatment was initiated as blood glucose monitoring showed unsatisfactory sugar control.

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Haemoglobin A1c (HbA1c) at that time was 11.3%, indicating poor glycaemic control.¹³

Mdm RBS was subsequently followed up by a diabetologist. Besides being given dietary advice and education about diabetes, she was continued on insulin and the regimen was adjusted frequently. This led to improvement in her HbA1c levels, from 11.3% to 8.9%. She was also told of the importance of normalising her blood glucose before conception in her future pregnancies. Until that time, Mdm RBS had not had any known diabetic complications. There was no family history of diabetes and Mdm RBS, a non-smoker, did not have any other significant past medical history.

About a year after commencing follow-up at the diabetic clinic, Mdm RBS became pregnant. This was an unplanned pregnancy; her HbA1c level was 9.7% at her first antenatal booking at 10 weeks gestation. Ophthalmic consultation undertaken at this time (at 12 weeks amenorrhoea in October 1995) revealed no evidence of diabetic retinopathy. She was subsequently closely followed up at the combined obstetric-diabetic clinic.

The initial blood sugar profiles at the clinic were unsatisfactory, with the 2-hour postprandial sugar levels ranging around 10 to 11.2 mmol/l in the first trimester. Vigorous efforts were made, by intensive dietary counselling and adjustment of insulin dosages, to establish normalisation of blood glucose. This led to an improvement in the 2-hour postprandial glucose levels which ranged between 4.5 and 9.2 mmol/l in the second trimester, and between 6.0 to 7.4 mmol/l in the third trimester. The HbA1c levels decreased to 8% by the 14th week of gestation, 7.3% by the 29th week of gestation, and 6.8% just 2 weeks before delivery (Fig. 1).

An appointment was made for Mdm RBS to undergo

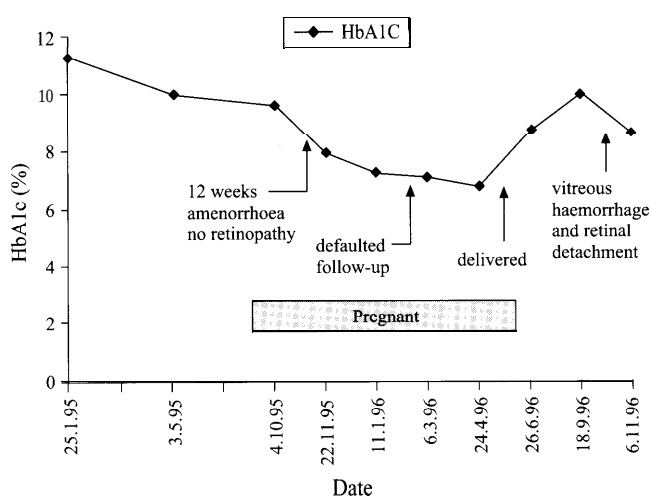


Fig. 1. Trend of HbA1c with relation to ophthalmic examinations during pregnancy and after delivery.

a second ophthalmic examination at 24 weeks of gestation, but she did not turn up for this visit. She however, did not have any visual complaints throughout the pregnancy.

The pregnancy was otherwise uneventful. There was no documented hypertension. Serial ultrasound scans were normal.

Mdm RBS delivered her baby in May 1996 at 37 weeks and 5 days of amenorrhoea by elective Caesarean section. A live baby boy, weighing 3340 g, was delivered. Apgar scores were 5 at 1 minute and 9 at 5 minutes. The baby was sent to the neonatal intensive care unit for monitoring but was subsequently well and discharged.

After the delivery and an uneventful puerperium, Mdm RBS resumed follow-up at the diabetic clinic. At this time, her blood glucose control deteriorated, her HbA1c levels increased from 6.8% prenatal to 8.9% and 10.0% at 2 and 3 months postnatal, respectively. At this last visit, Mdm RBS complained of a progressive blurring of vision over one week's duration. An urgent ophthalmic referral was made and she was found to have bilateral neovascularisation of the discs, new vessels elsewhere in the fundus and fibrovascular proliferations around the disc. It had only been a year since the last ophthalmic consultation and three years since the diagnosis of diabetes was made. Urgent treatment with pan-retinal photocoagulation was instituted. This was repeated at a later stage, with improvement in vision. Mdm RBS is still being followed up by the diabetologist. Her last HbA1c, 4 months after documented retinal complications, was 8.4%.

Discussion

Diabetic retinopathy consists of a spectrum of lesions, extending from background diabetic retinopathy, through preproliferative diabetic retinopathy, including cotton-wool infarcts, venous loops, beading and intraretinal microvascular abnormalities; to proliferative diabetic retinopathy, marked by retinal neovascularisation. Background retinopathy is common in diabetes and practically universal if investigated in patients with diabetes of more than 20 years' duration. Ten per cent of patients with diabetic retinopathy go on to develop neovascularisation and proliferative retinopathy.

The factors influencing the development and progression of diabetic retinopathy in pregnancy have been extensively studied.^{14,15} These include: the duration of diabetes (which was shown to be most closely associated with the presence of retinopathy),¹⁶ hyperglycaemia as documented by a raised HbA1c level,^{17,18} the severity of retinopathy at the beginning of pregnancy,¹⁷ current age or age at the time of examination,¹⁶ hormone levels,¹⁹ hypertension,^{20,21} rapid normalisation of blood glucose

(which may accelerate retinopathy in the already compromised eye)^{3-12,22,23} and smoking.¹⁶

Preliminary reports¹⁴ suggest that retinopathy may continue to progress after tight control of glucose levels has been achieved. It is not possible to determine in this patient the cause for the development of retinopathy. The following are possibilities: the natural progression of the disease was unaffected, normalisation of blood glucose levels actually adversely affected diabetic retinopathy, or the pregnancy itself influenced the disease. The unusual feature of our patient is that no retinopathy was detected at initial examination in the first trimester when diabetes control was poor. Retinopathy must have occurred after the first ophthalmic examination although she remained asymptomatic. Normalisation of blood glucose was achieved by the third trimester. However, there was an acute onset of symptoms of blurred vision 3 months postnatally (within only a year of her previous normal ophthalmic examination) which was found to be due to traction on the retina secondary to proliferative diabetic retinopathy. This appears to be associated with her deterioration of glycaemic control at this time.

The effects of normalisation of blood glucose levels in various stages of pre-existing diabetic retinopathy are unknown. The current methods of achieving tight control of glucose levels invariably result in episodes of hypoglycaemia. This has been implicated as a causal factor in the development of vitreous haemorrhage in proliferative diabetic retinopathy.²² Another issue concerns retinal blood flow changes in pregnant diabetics. The risk of returning an abnormal retinal circulation that has adapted to a raised blood glucose level (by an osmotically induced increase in blood volume) to an environment of normal blood glucose is undetermined.¹⁴ Murata and Yoshimoto²⁴ studied the microscopic appearance of retinopathy following rapid normalisation of blood glucose and found the characteristic appearance of nerve-fibre-layer infarctions and intraretinal vascular lesions, possibly secondary to a relatively acute decrease in blood flow.

Pregnancy itself may have effects on diabetic retinopathy. Chen et al²⁵ have suggested that an increased retinal blood flow occurs in pregnant diabetics and this may be associated with worsening retinopathy. However, whether pregnancy influences the development of retinopathy or the progression of established retinopathy remains controversial.²⁶⁻³³

In the light of the aforementioned reports and our observations, it would be prudent to advocate that a pregnancy be planned so as to normalise the blood glucose gradually before conception. Unfortunately, clinicians often are faced with a *fait accompli*—a diabetic woman with poor blood glucose control presenting to them already pregnant. While emphasising that rapid

control to attain euglycaemia may actually increase the risk for progression of retinopathy, it does not mean that less rigid control would be appropriate, inasmuch as euglycaemia is necessary to optimise foetal outcome. Rather, total diabetic management during pregnancy should include, after normalisation of blood glucose, a protocol for rigorous ophthalmic follow-up for all diabetic parturients before, during, and after pregnancy.

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