CASE REPORTS

Successful pregnancy in a woman with systemic sclerosis while taking nifedipine

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Abstract

The case is reported of successful conception and pregnancy in a woman with systemic sclerosis while receiving continuous treatment with nifedipine 30 mg/day, after a previously poor obstetric record and involuntary secondary infertility.

There is limited experience of pregnancy in women with systemic sclerosis because systemic sclerosis is itself an uncommon condition (4.5-12 new cases per million population per year).¹ The peak onset is in the third to fifth decades and there is possible secondary infertility.

There is also little experience of the use of nifedipine during the first trimester of pregnancy. Only six cases in which the outcome is known have been reported to the manufacturer, Bayer (UK). In later pregnancy it has been shown to be effective in both acute and chronic pregnancy associated hypertension,^{2,3} and also as a tocolytic agent in the treatment of premature labour.⁴ Recently, it has been shown to have beneficial effects on abnormal blood coagulation, in particular the prolonged thrombolysis found in patients with systemic sclerosis.⁵

Case report

The patient, a 36 year old white woman, was diagnosed as having systemic sclerosis when aged 15 on clinical grounds (Raynaud's phenomenon, sclerodactyly, impaired finger flexion, loss of finger pulp substance, dysphagia, and telangiectasia). (Serology: antinuclear antibodies positive 1/160 (100 IU/ml), anti-dsDNA negative, RNP positive, latex positive 1/40, RAHA positive 1/40, Scl 70 negative, Ro negative, La negative, Sm negative, cryoglobulins negative.) She had been a cigarette smoker and had taken the contraceptive pill (ethinyl-oestradiol 30 µg) for five years.

Despite bilateral cervical sympathectomy her Raynaud's phenomenon resulted in digital ulceration, requiring amputation of the left index and middle fingers. Her other main problem was painful, intractable foot ulceration associated with smooth, atrophic, ivory-white scars surrounded by pigmentation and ectatic blood vessels (atrophie blanche, livedoid vasculitis) since the age of 19. The foot ulcers were refractory to both outpatient and inpatient treatment and required pinch skin grafting on four occasions. Doppler ultrasound arterial pressures in the legs were normal both at rest

and after exercise. There was no evidence of venous incompetence. Previous treatment included aspirin, oil of evening primrose, and three eight hour infusions of the prostacyclin analogue, Iloprost. Measurement of her blood coagulation was carried out with a newly designed instrument, the haemostatometer.⁶ Briefly, samples of heparinised and non-heparinised blood were perfused through two polyethylene tubes within a closed pressure system. A standard sized hole was punched into each tube allowing 'bleeding' and a consequent fall in pressure. Non-heparinised blood formed a platelet plug and ultimately clotted. In the heparinised channel clotting was prevented. Haemostatic platelet plug formation and thrombolysis, resulting in weakening and expulsion of the haemostatic plug, were detected as changes in pressure, and the timing of these events was recorded. The time taken to achieve 30% of haemostatic plug information (HPF-30) was a good index of platelet function alone. Results for our patient showed that before she was pregnant she had markedly hyperactive platelets and no measurable spontaneous thrombolysis. The HPF-30 was 57.9% of the normal mean. No thrombolysis was measured after 3600 seconds (normal mean 1804.9 (SD 884.5 seconds), after which spontaneous thrombolysis does not take place. Repeat measurements made while receiving nifedipine 60 mg/day showed a spontaneous thrombolysis time of 1566 seconds—that is, within normal limits.

We decided to use nifedipine for treatment of her foot ulceration on the basis of its normalising effect on thrombolysis. We assumed the patient to be secondarily infertile. The nifedipine was increased gradually to 60 mg/day to minimise side effects associated with hypotension in previously normotensive subjects. The foot ulceration became less painful and healed completely within three months. She was taking nifedipine 60 mg/day when she conceived and for a further six weeks until pregnancy was confirmed. The dose of nifedipine was then halved empirically on the basis of the limited information about its effect in pregnancy and maintained at that dose, 30 mg/day, throughout the remainder of the pregnancy. This dose was less effective at maintaining the healing of her foot, however.

PREVIOUS OBSTETRIC HISTORY

(Gravida 6 para 2+3)

1. April 1977: caesarean section 28 weeks for fetal distress. Male 1.16 kg neonatal death.
2. February 1978: miscarriage, 12 weeks.

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Accepted for publication
18 April 1989

3. December 1979: premature labour, 35 weeks. Male 2.10 kg survived.
4. January 1982: missed abortion, 16 weeks.
5. January 1983: ?miscarriage, 6 weeks.

There followed a period of secondary infertility, 1983–1987, during which she attended an infertility clinic, received clomiphene, and underwent five unsuccessful attempts at artificial insemination by husband, AIH.

LATEST PREGNANCY

Her blood pressure was monitored throughout pregnancy and remained satisfactory. Urine analysis was consistently negative for protein and glucose. Renal function remained within normal limits. Fetal and placental growth were confirmed by serial ultrasound scans. She went into premature labour at 33 weeks' gestation. Initial attempts to halt the progression of the labour were unsuccessful and the labour was allowed to continue: first stage >24 hours. She delivered a normal healthy male infant 1.94 kg, who is alive and developing normally.

Discussion

Giordano *et al* did not find significant infertility among a series of 86 women with systemic sclerosis when compared with matched controls.⁷ The abortion rate was significantly higher, however, in the patients with systemic sclerosis but not restricted to a few habitual aborters. The case controlled postal questionnaire study of Silman and Black did suggest some reduction in fertility and increased recurrent abortion in women with systemic sclerosis.⁸ The mechanisms of infertility and recurrent spontaneous abortion are not known.

Our patient showed a notable reversal in her obstetric fortunes while taking nifedipine. This might have been fortuitous, but we believe nifedipine might have had a beneficial effect on her conceiving and maintaining the pregnancy, primarily through correction of unfavourable haemostatic abnormalities. Rademaker *et al* found hyperactive platelet function and prolonged thrombolysis in systemic sclerosis, which was improved by nifedipine.⁵ Our patient showed both these abnormalities, and repeat measurements while taking nifedipine confirmed restoration of normal thrombolysis. Other possible beneficial effects include: (a) Primary prevention of hypertension. In both previous pregnancies on completing the second trimester

our patient developed pre-eclamptic toxæmia, which did not occur in her latest pregnancy. (b) Prevention of premature labour. Our patient went into labour at 33 weeks despite taking nifedipine. She did experience a prolonged first stage of labour.

Nifedipine used as a tocolytic agent in normotensive women causes a reduction in both systolic and diastolic blood pressures, but these are not significant.⁴ Despite its uterine relaxant properties no patients treated with nifedipine have had excessive uterine bleeding.² The infants had various neonatal problems as would be expected in pregnancies complicated by hypertension, but no adverse effects on the fetus have been reported.

Favourable responses have been reported to treatment of atrophie blanche with antithrombotic drugs,^{9–10} those which stimulate fibrinolytic activity,^{9–11} and haemorrhological agents.¹² There is a previous case report of the use of nifedipine in atrophie blanche.¹³ We support its use in secondary atrophie blanche associated with systemic sclerosis and suggest that its main effect is to normalise deranged thrombolysis.

We thank Mr M D Simanowitz, consultant obstetrician and gynaecologist, Edgware General Hospital, for permission to report his patient; and Dr I B Kovacs for the coagulation data.

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