Case reports

Successful pregnancy with scleroderma renal disease and pulmonary hypertension in a patient using angiotensin converting enzyme inhibitors

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SUMMARY A patient with scleroderma renal disease and pulmonary hypertension who had a successful pregnancy with the use of angiotensin converting enzyme inhibitors is presented. The routine use of these inhibitors during pregnancy is not recommended, however, owing to the reported potential risks to the fetus.

The occurrence of pregnancy in patients with scleroderma is uncommon and has been associated with significant morbidity for the mother, including accelerated hypertension, renal failure, and death.^{1 2} We present a patient with scleroderma renal disease and pulmonary hypertension who had a successful pregnancy with the use of angiotensin converting enzyme inhibitors.

Case report

A 27 year old black woman with classic scleroderma presented to the rheumatology clinic at Louisiana State University Medical Center in Shreveport on 13 April 1988 with complaints of abdominal discomfort, described as a feeling of fullness with mild nausea, and episodes of spontaneous nosebleeds two and three days before the clinic visit. She was unexpectedly found to be pregnant. She claimed to have had a normal menstrual period two weeks previously but was using no birth control methods. She was taking nifedipine 20 mg three times a day and enalapril 10 mg a day for hypertension.

The past medical history was remarkable for the onset of Raynaud's phenomenon at age 11. She subsequently developed diffuse skin changes of scleroderma. At age 23 she was admitted to hospital for treatment of malignant hypertension after presenting with headaches, a blood pressure of 160/120 mmHg, anaemia, and nephrotic range

proteinuria. A calculated 24 hour urine creatinine clearance was 25 ml/min with her weight of 35 kg. A diagnosis of scleroderma renal disease was made. Her blood pressure was controlled with difficulty before the regimen of nifedipine and enalapril was started. The renal disease improved with the antihypertensive treatment and by 1987 proteinuria averaged one gram per gram of creatinine as determined by spot urine protein/creatinine ratios. Echocardiography on 3 February 1988 showed evidence of pulmonary hypertension with 'notching' of the pulmonic valve and minor dilatation of the right sided chambers. There was no evidence of left ventricular dysfunction.

On physical examination the patient was afebrile with blood pressure of 140/100 mmHg, heart rate 88 beats/minute, and respiratory rate 12/minute. There were classic sclerodermal skin changes with taut, hidebound skin over the face, neck, extremities, anterior chest, and abdomen. The skin of the face was so retracted that the patient could not close her mouth over protruding upper incisors. Multiple telangiectasias were present on the face, but there were no signs of bleeding or ulcerations in the nostrils. Old, healed fingertip ulcerations were present without evidence of recent ischaemia. Chest examination showed clear lung fields with a normal cardiac examination. The abdomen was protuberant with a firm, non-tender palpable uterus up to the level of the umbilicus. Fetal movements were palpated, and auscultation showed fetal heart tones at greater than 120 beats/minute.

The patient was admitted to the high risk pregnancy service for further evaluation. A pelvic

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examination performed by an obstetrician was unremarkable except for the gravid uterus. An ultrasound evaluation of the pelvis showed a healthy fetus estimated to be at 29 weeks' gestation. Admission laboratory tests showed a microcytic anaemia with haemoglobin 98 g/l, serum creatinine 88.6 μ mol/l, and blood urea nitrogen 8.8 mmol/l. Urine protein was 0.295 g/24 hours, and calculated creatinine clearance was 58 ml/min. Pulmonary function testing indicated a mild restrictive ventilatory impairment with a reduced forced vital capacity (FVC), a reduced forced expiratory volume at 1 second (FEV₁), and a normal FEV₁/FVC ratio.

Concern about the possible harmful effects on the fetus of nifedipine and enalapril prompted a change of antihypertensive treatment to alpha-methyldopa 500 mg twice a day. On 18 April 1988 the patient was discharged only to return within 24 hours with vaginal bleeding. Readmission examination showed a blood pressure of 138/104 mmHg and 50% effacement of the cervix with no evidence of rupture of the fetal membranes. There was no evidence of fetal distress and no significant change in the patient's laboratory values. Intravenous magnesium sulphate was given for premature labour. The history of significant renal disease with hypertension and the failure of alpha-methyldopa to control the blood pressure adequately forced the decision to begin treatment with captopril 50 mg three times a day. By 28 April 1988 the patient had no evidence of progression of labour and was discharged from the hospital with good blood pressure control.

On 14 May 1988 the patient was admitted to the high risk labour unit with spontaneous rupture of the fetal membranes. To assist in fluid management and monitoring a Swan-Ganz catheter was inserted that gave the following initial readings: blood pressure 151/94 mmHg, pulmonary artery pressure 30/5 mmHg, pulmonary capillary wedge pressure 5 mmHg, and calculated cardiac index 4.14 l/min. The patient had a surprisingly uneventful labour with diastolic blood pressures between 90 and 100 mmHg and successfully delivered a normal boy weighing 1740 g. The patient's postpartum course was unremarkable with no evidence of exacerbation of hypertension or renal disease. The baby was admitted to the neonatal intensive care unit for observation owing to low birth weight and prematurity. The Apgar scores at one and five minutes were 8 and 9. The infant did well with only mild neonatal jaundice and had no evidence of renal insufficiency. He remained in hospital for 18 days.

Six months after delivery the patient continues to have well controlled hypertension and stable renal disease. The infant remains healthy without evidence of renal disease or birth defect.

Discussion

Women with scleroderma have been found to have more spontaneous abortions and fertility problems before onset of the disease than controls.³ Once scleroderma is established the occurrence of pregnancy is also uncommon, which has been attributed to the late age of the usual onset of the disease,¹ and to decreased fertility and increased complications of pregnancy in patients with scleroderma.² A recent review of published work on pregnancies in patients with scleroderma by Scarpinato and MacKenzie recorded only 82 cases with a 15% maternal mortality, though many uncomplicated pregnancies may go unreported.¹ The major complication has been the development of accelerated hypertension, distinct from eclampsia, characteristically appearing in the third trimester¹ with the sequela of postpartum renal failure and often maternal death.⁴⁻⁸ Treatment of severe hypertension during pregnancy in patients with scleroderma has been difficult despite the use of multiple antihypertensive agents and even bilateral nephrectomy.¹ This is the first report of the use of an angiotensin converting enzyme inhibitor during pregnancy in patients with scleroderma. Watson *et al* described the successful use of captopril to control severe postpartum hypertension in a patient with scleroderma.⁷ Unfortunately that patient developed agranulocytosis thought to be secondary to the drug. It has been suggested that captopril should be considered for use with significant hypertension during pregnancy in patients with scleroderma.¹

The use of angiotensin converting enzyme inhibitors during pregnancy is controversial with reports of increased risk of fetal wastage, teratogenic effects, fetal distress, and severe postpartum neonatal renal failure.⁹⁻¹³ There is one report of reversible acute renal failure in a neonate whose mother received enalapril for just 17 days before delivery.¹⁴ Lindheimer and colleagues have suggested that angiotensin converting enzyme inhibitors should be contraindicated during pregnancy.^{15 16} Responding to such reports, the United States Food and Drug Administration is developing new labelling that identifies angiotensin converting enzyme inhibitors as potentially harmful to the fetus for inclusion in drug package circulars.¹⁷

In contrast, Coen *et al* have reported the successful birth of healthy twins to a mother who used captopril throughout gestation.¹⁸ This patient, without scleroderma, who had longstanding hypertension and renal disease had suffered two previous spontaneous miscarriages due to uncontrolled hypertension. Captopril was found to be the only medicine that adequately controlled her blood pressure.

Our patient had taken enalapril and nifedipine until the 29th week of gestation when the pregnancy was discovered. Concern about potentially harmful effects on the fetus prompted a change of treatment to alpha-methyldopa, which did not adequately control the hypertension. In view of the past history of severe hypertension and scleroderma renal disease that was not easily treated the decision was made to use captopril. The patient was thus taking an angiotensin converting enzyme inhibitor for all but three days of her pregnancy. Because of the reported potential risks to the fetus with angiotensin converting enzyme inhibitors we cannot recommend their routine use during pregnancy. The treatment of our patient does show, however, that when the decision is made to use these drugs for the well-being of the mother a successful pregnancy is still possible.

This patient also shows that successful pregnancy can occur in scleroderma even after development of significant renal and pulmonary involvement. The combined evaluations by the high risk obstetric, rheumatology, and nephrology services, with frequent prepartum monitoring visits and non-invasive cardiopulmonary function testing, assisted in pregnancy management decisions. For example, the echocardiographic evidence of pulmonary hypertension led to the prophylactic measurement of pulmonary artery pressures during labour. Aggressive prenatal monitoring and the multi-disciplinary team care approach seem to be prudent in the management of these patients with complications.

Finally, this unexpected pregnancy serves as a reminder that all sexually active young women with scleroderma should be counselled about birth control measures even in the presence of long-standing disease. Prevention of pregnancy in patients with scleroderma with significant cardiopulmonary or renal disease should be emphasised because of the great risk of increased maternal death.

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