Successful Management of Myocardial Infarction during Pregnancy in a Renal Transplant Recipient

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Summary: Myocardial infarction (MI) complicating pregnancy in a renal transplant recipient is described. Management challenges of MI in pregnancy and the possible predisposing roles of renal transplantation and erythropoietin (EPO) use are discussed.

Key words: myocardial infarction, pregnancy, renal transplantation, erythropoietin

Introduction

Myocardial infarction (MI) during pregnancy is rare and is reported to occur in one of every 10,000 gestations.¹ Many renal transplant recipients are in the child-bearing age group, and pregnancy after renal transplantation has been associated with several risks.² Since accelerated coronary atherosclerosis can occur in the renal allograft recipient,³ this group is also prone to myocardial ischemia and infarction. We report a patient who had undergone renal transplant in the past and developed MI during pregnancy. Our patient had received erythropoietin for the first time just prior to the MI and her coronary angiography revealed no significant coronary stenosis. The possible role of erythropoietin in this patient's MI is also discussed.

Case Report

A 30-year-old Caucasian woman G3P2 at 27 weeks gestation presented with a history of chest pain. She had received a living-related renal allograft 8 years earlier. The indication for transplantation was chronic renal failure due to chronic glomerulonephritis. Accelerated rejection occurring in the early postoperative period led to transplant nephrectomy, and retransplantation from a cadaveric donor 16 months later. She had been found to be hypercholesterolemic 5 years earlier (total cholesterol 277 mg%) and had been treated with lovastatin until the diagnosis of pregnancy was made. There was also a history of hypertension treated with long-acting nifedipine. On the night prior to admission she experienced "heart burn" and restlessness. On the day of admission, she complained of severe chest heaviness radiating to both arms, associated with nausea, diaphoresis, and shortness of breath. The patient gave no history of tobacco use. Her admission medications were cyclosporine 175 mg twice daily, nifedipine extended release 30 mg daily, azathioprine 50 mg daily, and prednisone 10 mg daily. She had received recombinant human erythropoietin 10,000 IU subcutaneously for her anemia for the first time 8 h prior to the onset of chest discomfort.

Physical examination revealed an obese female with an intrauterine pregnancy in no distress. Blood pressure was 130/80 mmHg, pulse rate 90 beats/min, and respiration 14/min. There was no jugular venous distension, and the venous pressure was normal. There was no significant murmur or gallop. Electrocardiogram (ECG) revealed normal sinus rhythm with new Q wave in lead III and T-wave inversions in leads III and aVF (Fig. 1B) compared with an earlier ECG taken 6 years previously (Fig. 1A). Laboratory values were significant for hematocrit of 22.5%, total cholesterol 430 mg/dl, triglycerides 541 mg/dl, and cyclosporine A level of 192 ng/ml. Creatinine kinase was 284 IU on admission and peaked at 549 IU with an MB of 85 IU (15%) at 24 h. Transthoracic echocardiography performed during chest pain revealed normal left ventricular function with severe inferior and inferoseptal hypokinesis. Transesophageal echocardiography excluded aortic dissection and confirmed severe inferior hypokinesis.

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Received: September 10, 1997

Accepted with revision: November 6, 1997

FIG. 1 (A) Baseline normal electrocardiogram. (B) Admission electrocardiogram revealing new Q wave in lead III and T-wave inversion in leads III and aVF.

Based on the clinical and investigative information, an acute MI was diagnosed and therapy with aspirin, metoprolol, nitrates, and intravenous heparin was instituted. Emergent efforts at revascularization were not pursued because of pain resolution more than 12 h after onset of chest pain and the absence of ST-segment elevation. The patient had an uneventful postinfarction course and was discharged on Day 5 of her hospital stay. She was pain free on medical therapy and successfully delivered a male infant vaginally with vacuum cup assistance at term. Labor and immediate postpartum course were uneventful.

Dobutamine echocardiography performed 4 weeks post delivery showed improvement in overall left ventricular function at peak stress and persistence of inferior hypokinesia

without provokable ischemia. However, maximal heart rate could not be achieved as nonsustained ventricular tachycardia necessitated early termination of the procedure. The patient was readmitted 10 weeks post delivery for evaluation of atypical chest pain and shortness of breath. Coronary angiography revealed normal coronary arteries except for a 30% lesion in the intermediate ramus artery (Fig. 2A and B). The patient has done well without chest pain or congestive failure 1 year after the infarction.

Discussion

Renal transplant recipients may be at increased risk for coronary artery disease (CAD).² An atherogenic lipoprotein

FIG. 2 (A) Right coronary arteriogram showing no major occlusive disease. (B) Left coronary arteriogram showing no major occlusive disease in left anterior descending and left circumflex arteries; curved arrow indicates 30% stenosis of the origin of the intermediate ramus branch. RCA = right coronary artery, LAD = left anterior descending, Cx = left circumflex, IR = intermediate ramus.

profile often associated with renal transplant recipients, along with underlying hypertension, diabetes, or autoimmune disease results in increased risk.⁴ Hyperhomocysteinemia, an independent cardiovascular risk factor, occurs in renal transplant patients, especially in association with cyclosporine therapy.⁵ Pregnancy in renal transplant patients is considered high risk, secondary to a high incidence of preeclampsia, prematurity, and low neonatal birth weight. Pregnancy may also have adverse effects on the renal graft.⁶

Myocardial Infarction in pregnancy is rare and presents unique management problems which have recently been reviewed.⁷ Thrombolysis is contraindicated during pregnancy while angioplasty and coronary artery bypass surgery have been performed on rare occasions.^{8,9} Coronary angiography in our patient revealed no significant coronary atherosclerosis. Up to 29% of patients with MI in pregnancy have normal coronaries when angiography is performed.⁷ Explanations for this finding have included coronary vasospasm and healed dissection, but these hypotheses have not been substantiated. The potential role of erythropoietin administered the day prior to admission is also relevant as a possible cause of the MI in our patient. Whole blood viscosity increases during erythropoietin administration and is thought to be primarily mediated by an increase in hematocrit. Since whole blood viscosity is greater with erythropoietin than with red cell transfusion, achieving the same hematocrit, other unknown factors may play a role.¹⁰ Erythropoietin increases vascular resistance, both by a loss of hypoxic vasodilatation and by a probable direct vascular effect.¹¹ High-dose erythropoietin (20–200 IU/ml) can cause direct vasoconstriction in the isolated renal and mesenteric vessels. It should be noted that these effects

have never been demonstrated on the coronary vascular bed. All the above effects of erythropoietin occur with prolonged therapy, and the impact of a single dose of erythropoietin on coagulation and viscosity is unclear. Thromboembolic complications in erythropoietin-treated patients with advanced renal disease is about 7.1%.¹² Abnormalities in the coagulation system with erythropoietin use that portend a thromboembolic risk include decreased protein C, free protein S, and antithrombin III, as well as increased collagen-induced platelet aggregation. Of note, free protein S is decreased in pregnancy and renal disease as well.¹³ Since our patient did not have a measured free protein S at the time of her infarction, the mechanism of MI remains conjectural. Similarly, the role of nifedipine in the genesis of MI cannot be overlooked,¹⁴ although our patient had received relatively smaller doses of the longer acting nifedipine.

Conclusion

Pregnancy in renal transplant recipients is considered high risk, and MI in pregnant patients is associated with a relatively poor prognosis. Our patient, a renal transplant recipient, sustained an MI during pregnancy and was conservatively managed until her normal delivery. Aggressive attempts at revascularization have been reported in MI complicating pregnancy but were not employed in our patient. While this, to the best of our knowledge, is the first reported case of MI during pregnancy in a renal transplant recipient, factors such as improved quality of life in renal transplant recipients, increased prevalence of smoking in young women, and increas-

ing age of pregnant women might lead to frequent occurrence of this condition. Although speculative, erythropoietin may contribute to coronary risk in similar patients.

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