Reversible Heart Failure with Left Ventricular Dysfunction in a Postpartum Woman with Familial Hypertrophic Cardiomyopathy

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KEY WORDS: pregnancy, hypertrophic cardiomyopathy, left ventricular dysfunction

IMAJ 2013; 15: 324–325

Peripartum cardiomyopathy is a cardiomyopathy of unknown etiology that affects women during the latter part of pregnancy or the postpartum period in the absence of any demonstrable heart disease before pregnancy [1]. Clinical deterioration in women with hypertrophic cardiomyopathy during pregnancy or postpartum with the development of symptoms of congestive heart failure is uncommon and is related to left ventricular diastolic dysfunction [2]. To the best of our knowledge there are no previous reports of reversible LV systolic dysfunction in women with hypertrophic cardiomyopathy related to pregnancy.

PATIENT DESCRIPTION

A 38 year old pregnant woman presented to the high risk pregnancy unit with a past medical history of familial hypertrophic non-obstructive cardiomyopathy as well as a family history of sudden death of two siblings. At age 36 she underwent placement of an automated implantable cardioverter-defibrillator. At 13 weeks of her first pregnancy she had good functional capacity with no limitation on physical activity. Echocardiography demonstrated LV hypertrophy (wall thickness 13 mm), LV ejection fraction 50% (lower limit of normal), mild mitral and tricuspid regurgitation and no pulmonary hypertension. LV function remained preserved during the second and third trimester of pregnancy. Her obstetric follow-up was unremarkable until 35 weeks gestation when she presented with premature contractions. Physical examination in the upright or supine position was normal, with no signs or symptoms of congestive heart failure. However, the lithotomy position or Valsalva maneuver caused dyspnea and deterioration in the oxygen saturation. Echocardiography revealed no significant cardiac deterioration compared with her previous imaging tests. Low dose beta-blockers (metaprolol 25 mg twice a day) were administered with a good clinical response, and an elective cesarean section was scheduled for 38 weeks gestation. At 37 weeks gestation spontaneous active labor ensued and an emergent cesarean section was performed. A healthy baby girl was born. At the end of surgery the patient developed pulmonary congestion with improvement after intravenous furosemide and was transferred to the cardiac intensive care unit. Echocardiography again showed no changes in LV function. She was treated with beta-blockers for short runs of non-sustained ventricular tachycardia and the puerperium was uneventful.

Four months later she presented with symptoms and signs of overt heart failure: shortness of breath upon minimal exertion and rest, peripheral edema and ascites. At admission, physical examination revealed sinus tachycardia of 100/minute, blood pressure 94/64 mmHg, elevated jugular venous pressure, bilateral basal rales, an S3 and S4 gallop, 2/6 mid-systolic murmur at the apex, hepatomegaly, 3+ extremity edema and ascites. Electrocardiography showed sinus tachycardia. Chest X-ray revealed an enlarged cardiac silhouette and pulmonary congestion. Echocardiography demonstrated depressed LV dysfunction (LVEF 30%) with a large mobile apical thrombus, moderate mitral and tricuspid regurgitation, and moderate pulmonary hypertension of 58 mmHg. Anticoagulation with low molecular heparin was initiated, while congestive heart failure was managed with furosemide, angiotensin-converting enzyme inhibitor, beta-blockers and aldosterone. Coronary angiography revealed normal coronaries. Her blood serology workup for myocarditis was negative. Her condition improved and she was discharged on warfarin and optimal doses of heart failure therapy (enalapril 10 mg twice a day, furosemide 40 mg/day, metaprolol 50 mg twice a day, aldactone 25 mg/day).

At follow-up a month later, she felt better and was classified as New York Heart Association class II. Echocardiography no longer revealed the thrombus, and near complete LV function recovery was apparent (mild systolic LV dysfunction, LVEF 48%). A diagnosis of superimposed peripartum cardiomyopathy with overt severe heart failure and apical thrombus was suggested. Two years later, the patient

LV = left ventricle

LVEF = left ventricular ejection fraction

has good functional capacity; the LV systolic function remains stable.

COMMENT

Peripartum cardiomyopathy is an idiopathic cardiomyopathy that affects women during pregnancy or postpartum and is characterized by LV systolic dysfunction (LVEF < 45%) and symptoms of heart failure. The original description of this condition defined it as an idiopathic disease that occurs during pregnancy or postpartum in the absence of recognizable pregestational heart disease [1]. Peripartum cardiomyopathy shares many features with other forms of dilated cardiomyopathies. Severely depressed LV systolic function with thrombus formation is not unusual. Patients often have dramatic presentations with severe symptoms and signs of heart failure. Spontaneous and complete recovery of the depressed ventricular function occurs frequently (50–70%), usually within the first 6 months of presentation. These patients have a favorable prognosis, but they are still at risk for deterioration of LV function during a subsequent pregnancy. The outcome of peripartum cardiomyopathy has changed favorably over the years due to improvements in medical therapy for heart failure and aggressive use of implantable defibrillators. Nevertheless, maternal morbidity and mortality remain relatively high in this young population [3]. Early treatment with bromocriptine (a prolactin blocker) was recently reported to have a beneficial effect on LV recovery in women with this condition [4].

Women with hypertrophic cardiomyopathy usually tolerate well the hemodynamic burden imposed by volume overload associated with pregnancy, despite marked LV hypertrophy, small cavity and reduced compliance. Clinical deterioration with the development of critical symptoms of heart failure is relatively uncommon, occurring in < 5% of the patients without symptoms before pregnancy and related to their functional class before pregnancy. No impairment of systolic LV function and LV dilatation has been reported in those women. Their symptoms were related mostly to severe LV diastolic dysfunction [2].

As mentioned, peripartum cardiomyopathy is a diagnosis of exclusion and other causes of cardiac dysfunction should be ruled out [5]. The recently published review on peripartum cardiomyopathy, however, emphasizes that the diagnosis should not be excluded in patients with heart disease, which is otherwise not likely to cause LV dysfunction during or after pregnancy [5].

In our patient with hypertrophic cardiomyopathy and preserved LV systolic function who was completely asymptomatic before pregnancy, the development of severe LV dysfunction with thrombus formation together with the dramatic presentation of overt congestive heart failure were uncharacteristic of the usual postpartum course of hypertrophic cardiomyopathy. Therefore, this case clearly suggests that patients with preexisting conditions can develop superimposed peripartum cardiomyopathy and that this entity must be suspected in a patient with pregnancy-associated deterioration of LV systolic function even if she has a preexisting condition like hypertrophic cardiomyopathy, which is not expected to lead to LV dysfunction during pregnancy or the postpartum period. This observation may be important when considering the use of novel disease-specific treatment for peripartum cardiomyopathy such as bromocriptine.

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Capsule

CCR5 is a receptor for *Staphylococcus aureus* leukotoxin ED

Pore-forming toxins are critical virulence factors for many bacterial pathogens and are central to *Staphylococcus aureus*-mediated killing of host cells. *S. aureus* encodes pore-forming bi-component leukotoxins that are toxic towards neutrophils, but also specifically target other immune cells. Despite decades since the first description of staphylococcal leukocidal activity, the host factors responsible for the selectivity of leukotoxins towards different immune cells remain unknown. Alonzo et al. identify the human immunodeficiency virus (HIV) co-receptor CCR5 as a cellular determinant required for cytotoxic targeting of subsets of myeloid cells and T lymphocytes by the *S. aureus* leukotoxin ED (LukED). The authors further demonstrate that LukED-dependent cell killing is blocked by CCR5 receptor antagonists, including the HIV drug maraviroc. Remarkably, CCR5-deficient mice are largely resistant to lethal *S. aureus* infection, highlighting the importance of CCR5 targeting in *S. aureus* pathogenesis. Thus, depletion of CCR5+ leukocytes by LukED suggests a new immune evasion mechanism of *S. aureus* that can be therapeutically targeted.

Nature 2013; 493: 51

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