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Case Report

Peripartum Cardiomyopathy Complicated with Massive Cardioembolic Stroke, a Treatment Challenge

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Abstract

Peripartum Cardiomyopathy (PPCM) is a life-threatening condition affecting women during their late pregnancy or early postpartum period. This clinical entity, till date, has remained as a diagnosis of exclusion. We share our experience in treating a 27 years old lady with PPCM during puerperium. Despite being treated with standard anti-failure therapy, bromocriptine and prophylactic anticoagulation, she developed massive cerebral infarct secondary to left ventricular thrombosis. She underwent a long journey of rehabilitation and suffered severe debilitation.

Since the recognition of this entity, various guidelines have been published to focus on the treatment plan. However, diagnosis of this condition is often delayed due to its overlapping features with other types of heart failure, especially hypertension related heart disease. This case emphasizes on the importance of recognition of this entity and early intervention by the treating physician.

Keywords: Peripartum cardiomyopathy; Echocardiography; Heart failure

Introduction

Peripartum cardiomyopathy is a distinct form of cardiomyopathy which is fatal. The incidence data are not widely available in many countries causing it to be frequently under diagnosed. The Heart Failure Association of the European Society of Cardiology Study Group on PPCM has included the definition in its position statement, and the same has been published in 2018 ESC guidelines for the management of cardiovascular diseases in pregnancy. Pregnancy predisposes to a hypercoagulable state, and coupled with Left Ventricular (LV) dysfunction due to PPCM, it imposes a very high risk of developing stroke.

Case Presentation

A 27 years old primigravida at 37 weeks presented with sudden onset of dyspnoea without any cough/orthopnoea/lower limb swelling prior to that. She was not diagnosed as hypertension antenatally. BP on presentation was 180/110 with pulse rate of 100 beats per min, respiratory rate 30/min; saturation was 89% under room air. Physical examination showed raised jugular venous pulsation with bilateral crepitations up to midzone. ECG revealed sinus rhythm with left ventricular hypertrophy, while chest X-ray showed pulmonary congestion and cardiomegaly. Other laboratory tests were unremarkable. She underwent emergency lower segment caesarean section due to fetal distress. Post operatively echocardiography showed global hypokinesia with severely depressed left ventricular function (EF 27%). The patient was treated as hypertensive cardiomyopathy and was given diuresis, fluid restriction of 800 ml/day and standard anti-failure medications. She responded well to diuretics and was discharged after optimising her anti-failure therapy.

The patient readmitted 3 days after discharge with gradual worsening of shortness of breath and orthopnoea. The diagnosis on admission was acute decompensated heart failure secondary to non compliance to fluid restriction. She was decongested with diuretics and showed remarkable clinical improvement. Unfortunately on Day 4 of admission, she developed sudden onset of slurring of speech and right upper limb weakness. A plain head CT showed left internal capsule infarct. Within 24 hours, she sustained another catastrophic drop in GCS with right sided complete hemiplegia. An urgent MRI demonstrated right middle cerebral artery infarct with M3 and M4 segment complete occlusion. A repeated echocardiography was done showing left ventricular ejection fraction of 32% with a large thrombus 2 cm × 2 cm in the left ventricle. The impression was revised to peripartum cardiomyopathy with massive cardioembolic stroke. She was started on bromocriptine 2.5 mg BD for 7 days then OD for 42 days, full dose anticoagulant and standard anti failure therapy.

This patient underwent tracheostomy and was admitted for a month for rehabilitation. Her MRS (Modified Rankin Scale) on discharge was 5.

Discussion

Peripartum Cardiomyopathy (PPCM) is an idiopathic entity due to unexplained left ventricular systolic dysfunction. It was recognized as early as the 1870s as possible relationship between pregnancy [1] and subsequently as a disease entity in the 1930's. It presented with symptoms of heart failure toward the end of pregnancy or in the months after pregnancy. The disease is more common in women with pre-eclampsia, hypertension, smoker, multiparity, advance age of more than 30 years or malnourished.

Diagnosis requires 3 clinical criteria; development of heart failure

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symptoms towards the end of pregnancy and post-partum, absence of another identifiable cause of HF and evidence of LV systolic dysfunction with LV ejection fraction of less than 45%. It remains a challenge as disease may overlap with co-morbidities, especially those with pre-eclampsia and hypertension. 2013 meta-analysis found 22% prevalence of pre-eclampsia amongst women with PPCM, more than 4-fold of global prevalence [2,3]. Early symptoms suggestive of heart failure may be mistaken for symptoms of late pregnancy, such as dyspnea and limb edema. Even when heart failure symptoms were recognized early, final diagnosis of PPCM usually get delayed as other causes need to be excluded. Known heart disease, such as valvular heart diseases are amongst diseases excluded in diagnosing PPCM. It is possible however, that they may have developed the disease but was not recognized due to similar presentations, hence treated for decompensation of underlying pre-existing heart disease. All these are challenges that lead to delay in identification and initiation of appropriate treatment.

The exact pathophysiology of the disease remains unknown. A relation between increases in approximately 45% plasma volume in third trimester suggest possible cardiovascular stress in pregnancy [4]. Research by Felker et al. [5] found that 26 of 51 women with PPCM had histologic evidence of myocarditis on endomyocardial biopsy. Other researchers propose PPCM as an inflammatory response in pregnancy, evidenced by an elevated tumor necrosis factor-alpha and interleukin-6 level [6,7]. Current hypotheses favors "two-hit" models, with interaction between genetic predisposition followed by vascular insult caused by antivascular and/or hormonal effects during late pregnancy and the early post-partum period. The vascular-humoral changes, in particular, prolactin, was studied for its relation between similar rise in serum level towards the end of pregnancy and continues post-partum, in comparison to PPCM timing.

Prolactin

Cathepsin D, secreted through mechanism that is not well understood cleaves prolactin from 23kDa to 16kDa prolactin. A study done in 2007 demonstrate that 16kDa prolactin is associated with endothelial injury and capillary dropout in pregnant mice. Administration of bromocriptine in these mice blocks prolactin production and subsequently reverse the PPCM in the affected pregnant mice. Subsequent research done by same group showed that 16kDa prolactin exerts cardiotoxic effects through upregulation of mRNA-146a (miR-146a). Similar effect seen with administration of bromocriptine, in which miR-146a level normalized resulting in decrease in the amount of observed systolic dysfunction, capillary dropout and cardiac fibrosis.

Placental angiogenic factors

Another research focused on vasculo-humoral hypothesis with soluble Fms-Like Tyrosine kinase 1 (sFLT1) involved in the disease pathophysiology. This anti-angiogenic protein secreted by the placenta in exponential amounts towards end of pregnancy. sFLT1 was found in higher concentration in pre-eclampsia and twin pregnancy. Study in murine model suggested the loss of vascular Endothelial Growth Factor (vEGF) in pathogenesis of PPCM. sFLT1 neutralize vEGF, thereby reducing circulating vEGF leading to development of the disease. The study again demonstrates administration of bromocriptine mitigated the cardiomyopathy partially when administered and fully when administered together with vEGF.

Treatment and prognosis

While treatment of heart failure for PPCM is similar to standard care for heart failure, care should be observed in particular to those who still in ante partum stage. Treatment strategy should take into consideration both maternal and fetal health. Close monitoring care, such as in intensive care unit should be considered. Patient should follow strict low salt diet and venous thromboembolic prophylaxis must be instituted, especially those with severe LV systolic dysfunction. Patient is preferably need continuous cardiac monitoring for arrythmias. Medical therapy for heart failure is similar to those with heart failure with systolic dysfunction. While digoxin, beta-adrenergic blocker, loop diuretics are generally safe, angiotensin-converting enzymes inhibitor and angiotensin-receptors blockers must be avoided in pregnancy due to fetal renal agenesis and death. After load reduction agents such as hydralazine and nitrates are also generally safe in pregnancy.

Recent data showed 50% to 80% of women with PPCM recover to normal LV systolic function (LVEF ≥ 50%) with most recoveries occurs within the first 6 months. These statistics showed great improvement as compared to 1970s, which reported mortality, was 30%-50%. Perhaps this improvement reflects both better disease entity recognition and advancement in heart failure treatment.

In the Investigations of Pregnancy Associated Cardiomyopathy (IPAC) study of 100 women in US, majority (71%) improved their LV systolic functions of above 50% by 6 months post-partum. Approximately 13% had major events with persistent cardiomyopathy and LVEF below 35%. Poor predictors include initial LVEF <30% and LV End-Diastolic Diameter (LVEDD) of more than 60 mm. The disease has recurrence risk with subsequent pregnancy of about 56%.

Despite improvement, it is of note while evidences are evolving diagnosing women with PPCM early remains a challenge. Given recent understanding on role of prolactin in endothelial injury and myocyte death, we propose early recognition of the disease may help to halt the disease or at least, severity of the disease. Based on IPAC study mentioned earlier, the disease fare worst in severe disease. With early recognition and prolactin inhibition, perhaps development of heart failure can be prevented, and if at all, resulted in milder disease. Journal by Mattia Arrigo et al. incorporate bromocriptine into treatment regime with dosage and durations tailored to severity of PPCM. The study incorporates bromocriptine as central part of the therapy coined as BOARD therapies (Bromocriptine, Oral HF drugs, Anticoagulation, Relaxant (vasodilators) and Diuretics). Perhaps with better understanding of the disease, combined with early recognition and treatment institution, we can improve further on morbidity and mortality.

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