Successful Treatment of Peripartum Cardiomyopathy with Plasmapheresis

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Peripartum cardiomyopathy (PPCM) is a rare, life-threatening disease of late pregnancy and early puerperium among previously healthy women. Management of this challenging disease is similar to other forms of systolic heart failure. Unfortunately, only 30% to 50% of patients recover completely. Among the remaining patients, continued poor ejection fraction indicates irreversible cardiomyopathy and portends a poor outcome. Immune complexes, autoantibodies, or toxic proteins are likely causative agents. Herein, we report first two PPCM cases that were successfully managed with plasmapheresis.

Key Words: Peripartum cardiomyopathy • Plasmapheresis

INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a rare disorder characterized by left ventricular dysfunction and heart failure symptoms experienced by previously healthy women during the peripartum period. PPCM typically occurs in the final month of pregnancy, and can persist for up to five months post-delivery. Although PPCM occurs in less than 0.1% of pregnancies, rates of mortality associated with the condition are high, ranging from 5% to 32%. Treatment of PPCM is similar to that of acute and chronic heart failure due to other causes of left ventricular systolic dysfunction. Unfortunately, only 30% to 50% of women with PPCM experience a complete recovery. Persistence of ventricular dysfunction beyond six months indicates irreversible cardiomyopathy and foreshadows worse survival. While the etiology of PPCM is unclear, immune complexes, autoantibodies, and toxic protein are thought to play major roles. Accordingly, we propose that plasmapheresis may benefit PPCM patients through the removal of inflammatory mediators. The use of plasmapheresis for severe heart failure in PPCM has not been previously reported. Herein, we present the first two reported cases of PPCM that were successfully treated with plasmapheresis.

CASE REPORTS

Case 1

A 41-year-old female was transferred to our hospital having complained of dyspnea on exertion, orthopnea, and bilateral lower leg edema. This patient had an uneventful delivery of a full-term twin pregnancy (gravida 1, para 1) eight months earlier, but began experiencing symptoms approximately two months after delivery that progressively worsened. The pregnancy was complication-free, and the patient reported no personal or family history of cardiovascular disease. On admission the patient had a systolic/diastolic blood pressure of 130/64 mm Hg, a heart rate of 105 beats/min, and a respiratory rate of 24 breaths/min. Echocardiography revealed a left ventricular ejection fraction (LVEF) of...
19% (Figure 2A) and coronary angiography revealed patent arteries (Figures 1A, B and C). Candesartan, carvedilol, and spironolactone were administered, and plasmapheresis was performed every other day beginning on the third day post-admission for a total of five sessions. By the six month follow-up, her symptoms had resolved, and her LVEF increased to 43% and 60% at 12 and 22 months after delivery, respectively (Figure 1D). Medications were also gradually tapered and completely discontinued within two years.

Case 2
A 30-year-old female (gravid 2, para 0, abortus 2) experienced preeclampsia at 38 weeks’ gestation due to cardiogenic shock (LVEF = 10%, Figure 2C) followed by multiple organ failure, and emergency delivery was performed. The only significant findings in the patient’s medical history included a cesarean section two years prior due to placental abruption and fetal distress at 36 weeks’ gestation. Despite optimal medical therapy, her hemodynamic status was dependent on the use of inotropes and an intra-aortic balloon pump. Hemodialysis was performed for severe metabolic acidosis, subsequently followed by plasmapheresis. Hemodialysis and plasmapheresis were performed on alternating days for a total of five sessions of plasmapheresis and six sessions of hemodialysis. The patient’s condition gradually improved, resulting in successful weaning from mechanical ventricular support. At the nine month follow-up, myocardial function had improved to 35%, and by 23 months post-delivery myocardial function had returned to normal (LVEF: 62%) (Figure 2D).

Plasmapheresis protocol
Plasmapheresis was initiated as soon as possible after admission. Blood from the patient was pumped through an extracorporeal blood circuit via a standard dual lumen, venovenous dialysis catheter. The volume of plasma to be exchanged per treatment was calculated as follows:

Total apheresis volume = \(rac{\text{body weight in kilograms}}{c_{180}}\times\frac{1}{13}\times(1-\text{haematocrit})\)

The treatment course was QOD (alternate day). Heparin was loaded at 2000 IU and followed by 1000 IU/hr every hour for the duration of the plasmapheresis. Bleeding risk was judged by surveillance of clotting factors and monitoring of hemodynamic status.

DISCUSSION
Multiparity, twin births, advanced maternal age,
and preeclampsia are known risk factors for PPCM.\(^1\)\(^-\)\(^4\) Although the etiology of PPCM remains unclear, infection, inflammation, and autoimmune processes are considered to be likely pathogenic factors. Currently, the practical value of previous viral and bacterial studies is unclear, as the results of these tests were nonspecific and have limited prognostic value in patients with PPCM. Most evidence supports an autoimmune process as the cause of PPCM.\(^1\) Inflammatory cytokines and high titers of autoantibodies against specific cardiac tissue proteins and increased levels of tumor necrosis factor-alpha, interleukin-6 and soluble Fas receptors have been described.\(^4\) While pregnancy is characterized by a state of immunomodulation, an abnormal fetal-maternal antigen interaction produces an inflammatory cascade that causes PPCM.

Since most reported PPCM cases have nonspecific biopsy findings, and drugs are associated with significant adverse effects with no clear benefit, immunosuppressive agents were not routinely administered.\(^5\) Intravenous immune globulin produced a good response among PPCM patients in a small retrospective study.\(^6\) Additionally, the authors suggested plasmapheresis could be used as an alternative to immune globulin therapy for the same purpose.

Plasmapheresis involves the removal of injurious macromolecules from the plasma of patients with various medical conditions. The American Society for Apheresis states that plasmapheresis is indicated for many autoimmune diseases, and its benefit occurs through the removal of all inflammatory mediators and toxic proteins, including autoantibodies, complement components, and cytokines.\(^7\) The available literature suggests that plasmapheresis can better improve the survival of patients with idiopathic dilated cardiomyopathy than standard medical therapy.\(^8\) Houck et al. proposed that peripartum myocardial infarction, a disease similar to PPCM, was successfully treated with plasmapheresis without coronary intervention.\(^9\) To the best of our knowledge, the application of plasmapheresis for patients with PPCM is novel, and the two PPCM cases presented herein are the first to be successfully treated with plasmapheresis.

The persistence of poor ventricular function after six months indicates irreversible cardiomyopathy and portends worse survival. Unfortunately, only 30% to 50% patients with PPCM recover completely. Due to the importance of early recovery of LVEF in determining prognosis with this disorder, we suggest that plasmapheresis should be initiated as soon as possible. The intent of this approach is to rapidly eliminate all toxic protein and attenuate the overall inflammatory cascade which can result in irreversible PPCM. The first patient in this case study experienced PPCM for eight months despite the administration of optimal medical therapy. Fortunately, LVEF was dramatic improved within 2 months of plasma exchange and finally recovered completely at 14 months. Plasmapheresis was also suitable for the second patient in whom hemodynamic status was maintained.

In conclusion, PPCM is a rare but fatal disease. Under conventional treatment PPCM has a high mortality rate, and a low probability of complete recovery. We propose a feasible management for PPCM through the implementation of plasmapheresis. The results presented herein on two successfully treated cases merit further investigation, particularly large randomized controlled trials. In this regard, the detection of cardiac autoantibodies can be used to identify patients requiring treatment and to guide therapy.

REFERENCES

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