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Review Article

Peripartum Cardiomyopathy

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Abstract

Peripartum cardiomyopathy (PPCM) is a rare but potentially lethal complication of pregnancy occurring in approximately 1in 3000 live births in the United States although some series report a much higher incidence. African-American women are particularly at risk. Diagnosis requires symptoms of heart failure in the last month of pregnancy or within five months of delivery in the absence of recognized cardiac disease prior to pregnancy as well as objective evidence of left ventricular systolic dysfunction. Obstetricians should suspect the diagnosis, particularly if the patient has risk factors. Evaluation should include an echocardiogram to assess the LV systolic function. Treatment includes ACE inhibitors or angiotensin receptor blockers, beta-blockers, and diuretics. Consideration should be given to anticoagulation. A number of causes are being investigated, including nutritional, infectious, and genetic, which, hopefully, lead to more targeted treatments. This paper provides an updated, comprehensive review of PPCM, including emerging insights into the etiology of this disorder as well as current treatment options.

Epidemiology

Peripartum cardiomyopathy is a rare and potentially fatal form of heart failure. The true incidence of peripartum cardiomyopathy is unknown secondary to diagnostic difficulty and the lack of population-based estimates[1]. It is estimated that the incidence of PPCM in the United States is between 1 in 1300 to 4000 live births[1-3]. PPCM can affect women of all races. It is more prevalent in some countries; estimates suggest that PPCM occurs at rates of one in 1000 live births in South African Bantus, and as high as one in 300 in Haiti[2, 4].

Some studies assert that PPCM may be slightly more prevalent among older women who have had higher numbers of live born children and among women of older and younger extremes of childbearing age[3,4]. However, quarters to a third of PPCM patients are young women who have given birth for the first time[5,6,7,8]. While the use of tocolytic agents or the development of preeclampsia (toxemia of pregnancy) and pregnancy-induced hypertension (PIH) may contribute to the worsening of heart failure but they do not cause PPCM. The majority of women have developed PPCM who neither received tocolytics nor had pre-eclampsia nor PIH[2,7]. In short, PPCM can occur in any woman of any racial background, at any age during reproductive years, and in any pregnancy[9].

Definition

The research definition of peripartum cardiomyopathy has four criteria. The patient must develop cardiac failure, specifically dilated cardiomyopathy, due to decreased systolic dysfunction of the left ventricle in the last month of pregnancy or within five months of delivery. There must be an absence of an identifiable cause for the cardiac failure. There must be an absence of recognizable heart disease prior to the last month of pregnancy. Additionally, left ventricular systolic dysfunction should be demonstrated by classic echocardiography criteria, such as depressed shortening fraction (less than 30 percent) or decreased ejection fraction (less than 45 percent) [10,11,12].

Risk Factors and Etiology

Risk factors for peripartum cardiomyopathy include obesity[1], previous peripartum cardiomyo-pathy, multiparity, advanced maternal age, multifetal pregnancy, gestational hypertension, preeclampsia, use of tocolytics, and African-American race[13,14,15,16,17].

An exact cause of peripartum cardiomyopathy has yet to be identified[13,14]. The hypothetical causes of peripartum cardiomyopathy include myocarditis, a maladaptive response to the hemodynamic stresses of pregnancy, hypertension, an abnormal immune response to pregnancy, stress-activated inflammatory

Designation

cytokines, cardiac myocyte apoptosis[10,13]. Other factors include prolonged tocolysis, viral infection, a relaxin abnormality, selenium deficiency, malnutrition, unmasked familial dilated cardiomyopathy, and familial peripartum cardiomyopathy[3, 4,12,13].

Signs/Symptoms

The diagnosis of peripartum cardiomyopathy may be challenging in the last month of pregnancy since normal pregnant patients experience dyspnea, fatigue, and pedal edema[10,11,12,13,14,18]. Peripartum cardiomyopathy may go unrecognized leading to an under-estimation of incidence[11,14]. Symptoms that may raise suspicion include paroxysmal nocturnal dyspnea, chest pain, tachycardia, arrhythmias, tachypnea. Other features those are suggestive of PPCM are cough, neck vein distention, third heart sound, new murmurs consistent with AV valve regurgitation, pulmonary crackles, hemoptysis, hepatomegaly, ascites, and embolic events[19, 20].

Electrocardiography may demonstrate no abnormalities or may show sinus tachycardia, atrial fibrillation, nonspecific ST segment and T wave changes, evidence of left ventricular hypertrophy, prolongation of the PR or QRS intervals, low voltage, and occasionally left bundle branch block[10, 11,14]. Chest films reveal typical signs of congestive heart failure (CHF), which include interstitial edema, pulmonary venous congestion, cardiomegaly, and occasionally pleural effusion[11, 12, 20].

Echocardiography may demonstrate dilated cardiomyopathy involving all four chambers of the heart, with the left heart being most affected[13]. Normal wall thickness with diffuse symmetric hypokinesis and high intracardiac pressure with low cardiac output are very characteristic[13]. A common finding is left atrial enlargement with mitral regurgitation along with a high incidence of mural thrombi and/or a left ventricular thrombus[13]. A small pericardial effusion may be present[7]. Pulmonary hypertension is common[16].

Diagnosis

The diagnosis requires satisfaction of the research definition for peripartum cardiomyopathy and exclusion of other causes of cardiomyopathy with confirmation by standard echocardiographic assessment of new left ventricular systolic dys-function during a limited period surrounding parturition[10, 14]. Most patients (78 percent) present with symptoms in the first four months post-partum[15, 16]. Fewer patients (9 percent) present in the last month before delivery and others (13 percent) present either more than one month antepartum or more than four months postpartum. [16]. Another report found that over 90 percent of patients pre-sented in the first two months postpartum and only 3.5 percent presented in the antepartum period[16, 17].

Treatment

Currently the treatment of peripartum cardiomyopathy is the standard therapy for heart failure[12,13]. Treatment aims to reduce afterload and preload, and to increase contractility.[10] Primary therapy consists of bed rest, sodium and fluid restriction, vasodilators, digoxin, and diuretics[10,11,12,16]. Cesarean section is reserved for obstetric indications only. [14] Vaginal deliveries are recommended[14].

Care should be taken when deciding which medications to use during the prepartum period and postpartum period, especially with breastfeeding.

In the prepartum period, afterload reduction is accomplished with a combination of medications. Most of these medicines are considered pregnancy class C. The drug of choice during pregnancy is hydralazine, which dilates peripheral vessels and decreases afterload[10,14]. Cardiac after loads may be further reduced by using beta-blockers. Carvedilol and Metoprolol are preferred due to evidence that they improve cardiac function and prolong survival in patients with CHF and decreased contractility[10, 14, 19]. Nitrates may add to the overall effect by decreasing afterload and preload[12]. Diuretics are used to reduce preload and circulating volume[10, 11,12]. Spironolactone may be used since it also improves the prognosis of patients with CHF[19]. Additional preload reduction and positive inotropy are achieved using Digoxin[11, 14].

In the postpartum period, ACE inhibitors are the drugs of choice to reduce afterload[10, 13,14]. ACE inhibitors are absolutely contraindicated in pregnancy[10,11]. Patients intolerant of ACE inhibitors should be placed on angiotensin receptor blockers (ARBs)[10]. Both beta-blockers and ACE inhibitors have been shown to improve overall survival in patients with non-specific cardiomyopathy[10,12]. Long-term use of beta-blockers during pregnancy may associate with low-birth-weight babies[10,12]. Amlodipine is considered the calcium channel blocker of choice because it has been shown to improve survival in patients with non ischemic cardiomyopathy.[12,14,,16] Patient education, dietary

consultation, early ambulation to prevent DVT, and exercise rehabilitation should be an integral part of the treatment regimen[12,19].

Critical patients may be treated with IV inotropic therapy, right-sided heart catheterization and IV pressor or after-load reducing therapy, intra-aortic balloon pump counter pulsation, and left ventricular or biventricular assist device[1,2,7]. An endomyocardial biopsy to diagnose myocarditis should be performed on patients who fail to improve within two weeks[12]. A trial of immunosuppressive agents such as prednisone, azathioprine, or cyclosporine may be administered to patients with biopsy-proven myocarditis who fail to improve with standard heart failure therapy[16]. Studies with these agents have shown mixed results[4]. Recent studies have shown that pentoxifylline inhibits inflammatory cytokines and markers of apoptosis while improving ejection fractions in patients with left ventricular dysfunction[12,13,19]. Improved ejection fraction in women with peripartum cardiomyopathy has also been shown with the use of intravenous immune globulin[10,12,19]. Heart transplantation is an option for those who do not respond to medical treatment or have persistent cardiomegaly[12,19].

Patients with significant ventricular dysfunction also require anticoagulation to prevent thrombosis and emboli. These patients typically have an ejection fraction of less than 25-35 percent or a previous history of emboli[11,13,16]. Enoxaparin (low molecular weight heparin) should be used during pregnancy to avoid unnecessary volume loading[12]. Warfarin should only be used in the post-partum period or possibly during the second trimester[10,16]. The most important complication of peripartum cardiomyopathy is thromboembolism[7]. The incidence of pulmonary and systemic embolism has been reported to be as high as 50 percent and may be the presenting problem. [16] The tendency for thromboembolism is likely caused by the hypercoagulant state of late pregnancy in combination with stasis and turbulent flow in the dilated heart[16]. This high rate may also reflect prolonged bed rest[16].

Treatment should continue up to one year in patients who respond to standard therapy[13, 19]. A dobutamine stress echo should be performed to determine whether or not the patient has impaired myocardial reserve and if there is complete resolution of left ventricular dysfunction at three and six months[11,13,19]. Therapy can be tapered gradually in patients with normal heart size and function at rest and normal cardiac enhancement with dobutamine or exercise[19].

Prognosis

Prognosis depends on normalization of left ventricular size and function within six months after delivery[10,11,14,16]. About 30-50 percent of patients with peripartum cardiomyopathy are reported to recover baseline ventricular function within 6 months of delivery[10,11,19]. A fractional shortening value less than 20 percent and a left ventricular end diastolic dimension 6 cm or greater at the time of diagnosis are associated with a more than 3-fold higher risk for persistent left ventricular dysfunction[1,2]. Persistent left ventricular dysfunction may result in mortality as high as 85 percent over five years[11,14,16,19].

Mortality has slowly increased since 1971, but new medications have helped survivors significantly improve left ventricular function[14,15]. The five-year survival rate increases to 94 percent when using the strict definition of peripartum cardiomyopathy[11,18]. Patients with persistent or abnormal ventricular dysfunction should not become pregnant and should be treated using the guidelines for heart failure[11,14]. Subsequent pregnancy after peripartum cardiomyopathy in women with recovery of left ventricular function may result in recurrence of peripartum cardiomyopathy and possible permanent decrease in left ventricular function or even death[13,17].

Conclusion

The outcome of patients with peripartum cardiomyopathy is highly variable. In some patients, the clinical and echocardiographic status improves rapidly and returns to normal[14, 20]. In contrast, some patients with this disorder deteriorate rapidly, do not have a response to medical therapy, and require cardiac transplantation or die[20]. Still others have persistent evidence of cardiac dysfunction, and a few have a slow return to normal cardiac function over several years[11,15]. The key points are to develop better incidence and prevalence estimates, determine risk factors and prognostic variables, ascertain cardiovascular risks for subsequent pregnancies, establish a central serum and tissue bank, and evaluate therapeutic interventions[14]. These excellent goals are yet to be achieved[10].

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