Unrecognized peripartum cardiomyopathy: Case series and comprehensive review of the literature

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Abstract

Peripartum cardiomyopathy (PPCM) is an uncommon type of heart failure of unknown cause occurring late in pregnancy or in the postpartum period. Because of its low incidence and the unspecific symptoms PPCM is often undetected or misdiagnosed. Unfortunately, PPCM is a disease whose underlying etiology and natural history remain incompletely understood. Nevertheless, it is incumbent on the intensivists as well as on the anesthetists to be cognizant of this disease, due to its high maternal morbidity and mortality.
A number of recent reviews have described in detail the clinical picture, pathophysiology and management of PPCM. To avoid duplications we use an illustrative case series of peripartum cardiomyopathy to introduce this topic and proceed to give a short but comprehensive review of published data for daily working clinician.

Introduction

Peripartum cardiomyopathy (PPCM) is a rare type of heart failure of unknown cause occurring late in pregnancy or in the postpartum period. Although PPCM is associated with high morbidity and mortality it is often undetected or misdiagnosed because of its low incidence and nonspecific symptoms. Additionally, pregnancy-related diseases may have similar clinical presentations. Only a few case series have been published to date, but a number of recent reviews have described in detail the clinical picture, pathology and therapy of PPCM. To avoid duplications the goal of this case series is to generally introduce this topic and to give a short but comprehensive review of published data for general anesthetists and intensivists, respectively.

Case reports

Case 1

A 17-yr-old caucasian woman, 7 hours postpartum status post caesarean section, was admitted to our intensive care unit with symptoms of acute respiratory insufficiency. A caesarean section was performed under spinal anesthesia, because of preterm labour and breech position. The patient was obese with a history of asthma, but no other current medical problems. Initial clinical findings were dyspnea (about 35 shallow breaths/min), a peripheral O_2 saturation of 85% on room air, a blood pressure of 150/100 mmHg, tachycardia (150 beats/min) and peripheral edema. Auscultation of the chest revealed severe rhonchi and a gallop rhythm. The suspected diagnosis was status asthmaticus, and therapy was started by the resuscitation team with 250 mg Solu-Decortin (Cortison) i.v. and 1 mg epinephrine (in 5ml H_2O) nebulized with 10 l O_2.

Laboratory studies including electrolytes, complete blood count, basic coagulation panel, renal and liver function parameters, all showed no abnormal findings (Tab.1), whereas arterial blood gases revealed a respiratory acidosis with hypoxia. Chest radiograph showed an enlarged heart and severe signs of pulmonary congestion (Fig.1 I), whereas primary ECG was normal. These findings led to a clinical diagnosis of acute heart failure based on peripartum cardiomyopathy with the tentative diagnosis of an acute pulmonary embolism of unknown etiology. Transthoracic echocardiography (TTE) revealed no evidence of right sided obstruction, but a dilated left ventricle with moderate impaired ejection fraction (48%). Additionally a mitral regurgitation Grade II° was found (Fig.2 I/II). To support the diagnosis, a thoracic CT-scan was done. The scan confirmed the diagnosis PPCM, showing a global heart enlargement with signs of left heart decompensation. An acute pulmonary embolism could be excluded. Additional coagulation, heart failure and infection studies were obtained and completed the diagnosis of PPCM (Tab.1). Significant clinical improvement occurred after 2 days of treatment with diuretics, angiotensin-converting enzyme (ACE) inhibitors and vasodilators. After 5 days of therapy the echocardiography study was normal (Fig.2 III/IV) and the patient was discharged home.

Table 1. Laboratory values at the time of admission, at day 2 after transfer and at the time of ICU discharge or transfer to the medical department (for all three cases).

	Case 1 (B.H., 17 yrs)			**Case 2 (R.Z., 33 yrs)**			**Case 3 (C.H., 38 yrs)**			
	Adm.	**day 2**	**day 5**	**Adm.**	**day 2**	**day 5**	**Adm.**	**day 2**	**day 3**	
WBC	13,2	10,4	8,4	17,9	11,1	10,1	11,9	9,8	8	C/µl
Hb (Hk)	9,6 (29)	8,6 (26)	10 (30)	10,4 (30)	10,6 (30)	12 (34)	8,7 (28)	9,3 (31)	9,3 (30)	G/dl (%)
Thromb.	209	248	392	254	236	449	216	238	233	C/µl
Sodium	140		140			139		137		mmo/l
Potassium	4,1		3,9			4,2		3,8	4,2	mmo/l
Urea	2,3		2,9		9,4	5,4	5,2	6,2		mmo/l
Creatinine	63		42		72	85	106	100	77	µmol/l
AST	19		20			35	27	26		U/l
ALT	7		12			40	8			U/l
GGT	5		9			23		<5		U/l
LDH	242		249			249		224		U/l
CRP	21,9	61	39,8	21,2	59	15.5	32,9	62,9		mg/
Quick	112	104	102	119	121	121	91	109		%
PTT	25	32	31	24	24	24	35	25		sec
Fibrinogen	5,1		5,5			4,9				g/l
AT-3	88		110			94				%
Trop I	0,02			0,11	0,12		0,12	0,14	0,12	µg/l
D-Dimer	750						203			µg/l
NT-proBNP	4449	4179		2622	626,9		4128	3333		µg/l

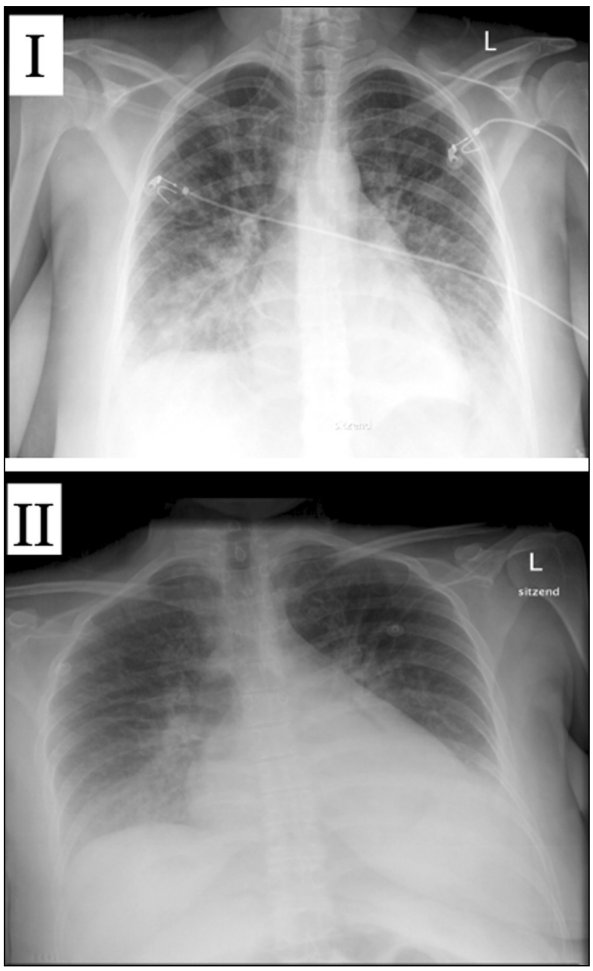

Figure 1. A PA chest radiogram of case 1 (Fig.1 I) and case 3 (Fig.1 II) at time of admission: Allusively cardiomyopathy and severe signs of pulmonary congestion are visible, suggesting the diagnosis of acute left heart decompensation.

Case 2

A 33-yr-old caucasian woman, pregnant with twins following in vitro fertilization, was admitted in gestational week 27+1 with a developing infection of the amnionic fluid and preterm labor. Caesarean section was performed under general anesthesia after an ineffective spinal anesthesia. Approximately two hours before the c-section, the patient complained about mild dyspnea for the first time. During anesthesia the oxygen saturation, as measured by a fingertip pulse oxymeter, fell from 99% to 89% when the inspiratory oygen concentration was lowered from 1.0 to 0.5. After the delivery of two healthy babies, the operation concluded and the patient became severely dyspneic. As a result she was admitted to the intensive care unit.

TTE performed two hours after ICU admission showed only mild dilation of the left ventricle and atrium but a severely reduced left ventricular ejection fraction of 30%. The blood samples taken revealed also heart failure as indicated by an initial n-terminal pro-brain natriuretic peptide (NT-proBNP) value of 2622.0 pg/ml (Tab.1).

She responded to treatment with continuous positive airway pressure, diuretics and nitrates; the symptoms improved quickly and the NT-proBNP fell to 626.9 pg/ml on the following day. The patient was discharged from the intensive care unit after three days.

Case 3

The third case to be discussed was more severe. A 38-yr-old patient who was pregnant with twins (her ninth and tenth child) was scheduled for elective caesarean section. On the day before section was planned, labor began and she was admitted to the labor and delivery suite. She complained of dyspnea, which had begun a few days before. She also reported similar problems by the end of her previous pregnancy. She was hypertensive (BP 180/100 mmHg), tachycardic (HR 160/min) and the oxygen saturation was 99% breathing room air. Since delivery was urgent, caesarean section was performed under spinal anesthesia without further work-up. The spinal procedure had been uneventful with negative blood aspirate and clear spinal fluid. After injection of 15mg of Bupivacain intrathecally, the patient became hypotensive (systolic blood pressure about 90 mmHg) and she was treated with colloidal infusions and sympathomimetics. Later the patient was discharged from the operating room in stable cardiopulmonary condition (RR 110/60, HR 110/min and oxygen saturation 96% breathing room air).

12 hours later the patient complained of dyspnea again and was admitted to the intensive care unit in a state of cardiac decompensation. She was tachycardic (HR 150-180/min) and the oxygen saturation on room air was 76% while the systolic blood pressure was normal (100-120 mmHg). The echocardiography showed severe impaired left ventricular function (EF 15%) and suggested cardiomyopathy. The x-ray showed global cardiac decompensation (Fig.1 II). The NT-proBNP at admission was 4128 pg/ml (Tab.1).

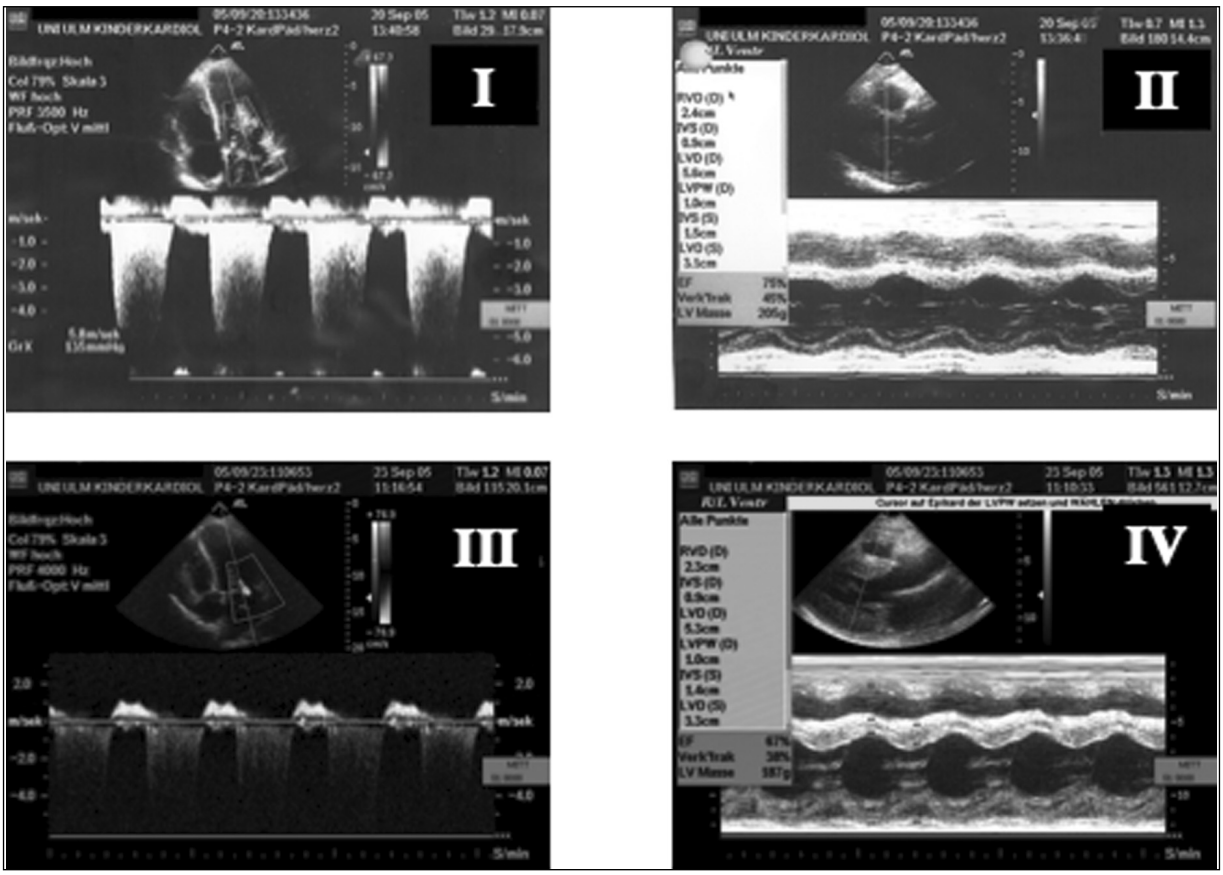

Figure 2. Doppler echocardiographic assessment of mitral valve regurgitation in an apical view (Case 1) showing moderate mitral valve regurgitation as a sign of acute heart failure (I).
Measurements of left ventricular function and dimension at the end of systole and diastole by M-mode echocardiography in a parasternal long-axis view, showing enlargement of the left ventricle and impairment of the left posterior wall motion as signs of acute heart failure (II).
Almost normal findings in the control assessments after 5 days (III/IV).

Again, conservative treatment with continuous positive airway pressure (CPAP), diuretics and ß-adrenergic blockers was initiated and the patient was transferred to the medical service on the following day. The dyspnea improved only slightly and the repeat echocardiography performed five days after delivery still showed severely impaired left ventricular function. The therapy was converted to oral medications with angiotensin converting enzyme blockers, ß-blockers and diuretics. The patient was discharged seven days post partum.

Short-Review

Heart failure associated with pregnancy was first observed and recorded as early as the 19th century by Ritchie and Virchow. Adapted from work by Demakis et al. (1), PPCM is defined as the development of heart failure in the last month of pregnancy or in the first 5 months postpartum in patients with no demonstrable heart disease before the last month of pregnancy and no discernible etiology for heart failure.

Epidemiology

The exact incidence of PPCM is unknown but is estimated to be 1 in 3000-4000 deliveries in the United

States (2). Specific data is rare because mild forms are often unrecognized and the manner in which authors define PPCM shows great variability. PPCM constitutes less than 1% of all cardiovascular events related to pregnancy (3). Risk factors classically identified in the literature include black race, increased age (>30 years), multiparity, twin pregnancy, preeclampsia and gestational hypertension (1;4).

Etiology

Despite many hypotheses, the cause und mechanism of pathogenesis of PPCM remain unknown. Early investigations proposed myocarditis as the cause for PPCM where anti-inflammatory treatment resulted in clinical improvement (5). Further studies failed to establish this causal link between mycarditis and development of PPCM (6;7). Additionally, Felker et al. confirmed that the absence or presence of inflammation on endomyocardial biopsy tissue did not predict outcome in patients with PPCM (8).

Persistent viral antigen has been also postulated as a trigger for the development of PPCM. Presence of viral genomic material, including enterovirus (coxsackie virus), parvovirus B19, adenovirus and hepatitis virus was isolated in biopsy material of patients with idiopathic dilated cardiomyopathy. Further, the authors demonstrated an association between clinical improvement of left ventricular systolic function and viral clearing (9). Despite this promising findings, further studies are needed to clearly identify virus infection as the cause for development of PPCM.

Many animal and clinical investigations support to the hypothesis that immune activation, dysregulation of cellular apoptosis pathways and upregulated humoral immunity contribute to the pathogenesis of PPCM. Whereas the importance of raised high sensitivity c-reactive protein in plasma of patients with new and evolving PPCM merits additional evaluation, concentrations of the inflammatory cytokine TNF-alpha, elevated immunoglobulins against cardiac myosin as well as markers of apoptosis (Fas/Apo-1) are well correlated with left ventricular function and mortality. Additionally, animal data suggest that the cardiac myocyte-specific STAT3 pathway is necessary for protection of the heart from postpartum stress (10).

Taken all available data together, so far no cause has been clearly identified for the development of PPCM.

Clinical features and diagnosis

The clinical presentation of patients of PPCM is similar to that of other forms of left ventricular and systolic failure. Clinical symptoms are dyspnea, cough, chest pain, abdominal pain, and orthopnea. Additionally physical examination may reveal signs such as tachycardia, hypertension, ventricular gallop rhythm, mitral regurgitation murmur, hepatosplenomegaly, ascites, hemoptysis, or jugular venous distension. Ancillary studies include electrocardiogram (ECG), chest radiograph, Doppler-echocardiography and possibly thoracic CT-scan. To recapitulate, proper medical history and an accurate physical examination combined with routine ancillary studies may ensure the diagnosis of PPCM. Clinicians should think of PPCM in any peripartum patient with unexplained disease.

Therapy

Medical therapy of PPCM is similar to that for others forms of congestive heart failure. Thus digoxin, angiotensin-converting enzyme (ACE) inhibitors, diuretics, sodium restriction and after-load reducing agents are the mainstays of medical therapy (11-13). If necessary, catecholamines like dopamine and dobutamine can be given. Arrhythmia treatment should be performed using standard guidelines and protocols. Low molecular weight heparin prophylaxis is routinely advised. Immunosuppressive therapy may be indicated when peripartum myocarditis and cardiomyopathy is present (5). Intra-aortic balloon pumping or insertion of a left ventricular (LVAD) or biventricular assist device (BVAD) should be considered if the patient is not responding to medical management. As a last resort heart transplantation can be considered for nonresponders.

Prognosis

Prognosis in the United States is variable with a maternal mortality of 25 to 50 percent (14). However outcome differs widely between reports. Death is generally attributed to arrhythmia or thrombo-embolism. If congestive cardiomyopathy persists after 6 months it is likely irreversible and portends decreased survival.

Conclusion

Peripartum cardiomyopathy is an uncommon complication of pregnancy with unknown cause and potentially life-threatening complications. Once the diagnosis is confirmed treatment of PPCM does not differ from that of other dilated cardiomyopathies. Echocardiography appears to be extremely valuable in diagnosing PPCM, formulating prognosis of recovery and following the course of the disease. Especially ejection fraction and left ventricular end diastolic dimensions at the time of diagnosis may be predictive of long-term cardiac dysfunction. Currently, there is no consensus regarding recommendations for future pregnancy after PPCM. Nevertheless the risk of developing PPCM, with future pregnancies, remains high. Particularly in the presence of persistent left ventricular dysfunction, a subsequent pregnancy should be discouraged and avoided (14).

PPCM is a disease whose underlying etiology and natural history remains incompletely understood. It is incumbent on the intensivists to be cognizant of this disease, due to its high maternal morbidity and mortality.

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