

Thromboembolic disease: a frequent complication of dilated cardiomyopathy of the peripartum experience in Ivory Coast

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Abstract

Aim: To highlight the thromboembolic complications of peripartum cardiomyopathy (PPCM) and to specify the factors of occurrence in our series.

Material and methods: This was a retrospective and analytical study from January 2016 to March 2019 in the Cardiovascular and Thoracic Diseases Department of Bouaké Teaching Hospital.

Results: Forty patients were admitted (29.1 ± 6.3 years) with PPCM. The main contributing factors were the unfavorable socio-economic background (97.5%) and multiparity (77%). The most common signs found were dyspnea (62.5%), edema of the lower limbs (100%) and cough (87.5%). Nonspecific repolarization disturbances (77.5%) dominated the EKG data. The left ventricle in diastole was dilated (64.6 ± 6 mm) with low ejection fraction in all patients (0.35 ± 0.08). The mode of cardiac decompensation was right and left side heart failure in all cases, favoured by non-compliance of diet regimen (74.5%), anaemia (56.5%) and bronchopneumonia (38.5%). The major complications were persistence of heart failure (17.5%), venous or cardiac thromboembolism (15%) and one case of atrial fibrillation. The occurrence of thromboembolic complications was closely related to high pregnancy, multiparity ($p = 0.029$) and stage IV of dyspnoea ($p = 0.046$). Increased haemoglobin and collapse of left ventricular ejection fraction were more correlated with the presence of intracavitary thrombus ($p = 0.027$). Its management was that of heart failure, associated with anticoagulant therapy and sometimes bromocriptine. The average length of hospital stay was 5 days. No one died.

Conclusion: Thromboembolic complications seem to be common in PPCM and must be systematically sought out.

Keywords: peripartum cardiomyopathy, heart failure, Thromboembolic disease

Introduction

Peripartum dilated cardiomyopathy (PPCM) is defined as heart failure of unknown etiology, with the onset of symptoms during a period including the last month of pregnancy and the first five months postpartum. This definition excludes patients with an history of heart disease

or a family history of cardiomyopathy or sudden cardiac death.¹ It is a condition frequently encountered in sub-Saharan Africa.^{2,3} This condition, the mechanism of which remains to be discussed, has been the subject of numerous studies focusing on its epidemiology, clinical aspects, and prognosis.⁴⁻⁶ Thromboembolic complications, which can be pregnant because they lead to sudden death, are described and most often as anecdotal.^{7,8} However, regional differences could exist with this condition. The general objective of our work was to highlight the thromboembolic complications of our series and investigate the factors of their occurrence.

Patients and methods

We carried out a retrospective study of patients with PPCM received from January 2016 to March 2019 in the cardiology department of the University Hospital of Bouaké. The selection criteria included patients of childbearing age, hospitalized, or outpatient with heart failure between the eighth month of pregnancy and the first five months postpartum with no identified etiology. Dilated cardiomyopathy (DCM) was diagnosed with echocardiography Doppler. We excluded patients who had anemia less than 7 g / dl, concomitant arterial hypertension > 160 mmHg, a history of heart disease, or a family history of cardiomyopathy or sudden cardiac death.

These criteria made it possible to retain 40 files. The parameters studied concerned epidemiological (age, gravidity, parity, twinning, and socio-economic background), clinical, paraclinical, and outcomes data. We compared these parameters to patients with thrombus to those without.

Statistical analysis:

Variables were presented as means for continuous variables and as a percentage for discontinuous variables. The continuous variables were compared with the Student test and the discontinuous variables with the Fisher exact test when the calculated numbers were upper 5. Otherwise, the Yates corrected Chi 2 test was applied. A p-value <0.05 was considered statistically significant.

Ethical considerations

The Bouake teaching Hospital ethics committee approved the study. The data collected were analyzed under the data protection laws for individuals, following ethical principles according to the Declaration of Helsinki.

Results

➤ **Clinical and para-clinical epidemiological characteristics of our patients**

The mean age of the patients was 29.1 ± 6.3 years (range 17 and 45 years) (table 1). The main factors favoring PPCM were unfavorable socio-economic background (97.5%), multiparity (77%), and twinning (10%). We have seen all patients after delivery with lower limb edema (100%) and dyspnea (100%). Dyspnea was in stage III (37.5%) or IV (62.5%) of the New York Heart Association. The other most common functional signs were cough (87.5%) and chest pain (60%) (Table 2). On the electrocardiogram, sinus tachycardia was noted in 82.5% of cases, left ventricular hypertrophy in 37.5% of cases, diffuse non-specific repolarization disorders in 77.5% of cases (table 3). One

case of atrial fibrillation was found. Cardiomegaly was noted in all patients with a cardiothoracic ratio at 0.64 ± 0.0 and extremes at 0.57 and 0.78.

The left ventricle on echocardiography was dilated in all of our patients with an indexed end-diastolic mean diameter of $35.7 \pm 3.4\text{mm} / \text{m}^2$ and a mean systolic ejection fraction of $35\% \pm 0.08$.

➤ Treatment

The management was that of a classical heart failure, associated with anticoagulant therapy and sometimes Bromocriptine (table 4). The mean length of hospital stay of the patients was 5.59 ± 2.64 days. There were no deaths in all of the cases.

➤ Thrombi

Intra cardiac thrombi are described in table 5. Most of them are localized on the septo-apical wall in left ventricle.

➤ The prevalence and characteristics of thromboembolic complications

All patients were admitted in acute cardiac decompensation, favored by the deviation diet (74.5%), anemia (56.5%), and bronchopneumopathy (38.5%). The major complications were represented by the transition to the chronicity of heart failure (17.5%) and venous or cardiac thromboembolism (15%). Our cohort of six patients with thromboembolic complications was a mural thrombus of varying size and apical site (Table 5). The occurrence of these thromboembolic complications was closely related to high pregnancy ($p = 0.029$), multiparity ($p = 0.029$) and stage IV dyspnea ($p = 0.046$). (Table 1 and 2) with a long hospital stay ($p = 0.001$) (Table 4).

➤ Predictors of cardiac thrombosis

High number of pregnancy ($p = 0.029$) and multiparity ($p = 0.029$) favor the occurrence of intracardiac thrombus. Stage IV dyspnea ($p = 0.046$) is linked to the presence of intracardiac thrombus.

The increase in hemoglobin level and the collapse of the ejection fraction ($p = 0.027$) were more correlated with the presence of intracavitary thrombus (Table 3).

Discussion

Most of the series report that PPCM is a condition that occurs in very young, multiparous subjects. But it can appear as in our work in all childbearing age groups.⁹⁻¹² Our study's main factors favoring PPCM were the unfavorable socio-economic background (97.5% of cases), multiparity (77%), and twinning. Twinning was found in four patients (10%). These prevalences observed in our work are similar to those found in Senegal in 2010, which were respectively 9.09% and 90.90% for twinning and low socio-economic status.¹³ Ferriere et al. report a frequency of three percent of twinning in France.¹⁴ Dyspnea, almost constant in our work, is frequently described during PPCM varying between 81 and 89%.^{15,16}

In our work, sinus tachycardia (82.5%) and repolarization disorders (77.5%) were prominent electrocardiographic abnormalities. On the other hand, in the paper of Kane et al.¹³, the most observed anomalies were sinus tachycardia (90.1%) and left ventricular hypertrophy (66.6%). He also noticed a high frequency of secondary repolarization disorders (42.4%) and peripheral low voltage (18.1%). We observed left ventricular hypertrophy in only 37.5% of cases.

In echocardiography, we found an enlargement of the left ventricle with an average ejection fraction of 35%.

This significant enlargement of the left ventricle with a severe drop in the ejection fraction had been found in several series.^{13,17,18} The systolic dysfunction of the left ventricle is constant and constitutes a mandatory diagnostic criterion of CMPP.

Two-dimensional trans-thoracic ultrasound is a key examination for the detection of intracardiac thrombosis. The frequency of thrombosis in our series was 15%, while it was 30.3% in the series by Kane et al.¹³ The higher frequency of thrombosis in Kane's series than ours could be explained by lower ejection fractions, which is more correlated with the occurrence of thrombi.¹⁹ The literature reports a frequency of three to 10.5% of intracavitary thrombosis.^{20,21}

In our study, high pregnancy and parity significantly influenced the occurrence of intracavitary thrombosis ($p = 0.029$). Likewise, there was a close correlation between stage IV dyspnea and the occurrence of intracavitary thrombus ($p = 0.046$). In our series, the presence of intraventricular thrombus was significantly related to the collapse of the left ventricular ejection fraction ($p = 0.027$). There was a good correlation between increased hemoglobin level and thromboembolic complications ($p = 0.029$). Kane et al. had made the same observation for a high hemoglobin level of between 10 and 14 g / dl.¹³ Anemia leads to an increase in cardiac output and an acceleration of the circulatory speed, protecting against stasis and the occurrence of thrombosis.

These thromboembolic complications may be provoked by hypokinesia of the ventricular walls, systolic dysfunction of the left ventricle, enlargement of the heart chambers, and heart failure. Reduced maternal mobility during the last months of pregnancy and estrogen-related hypercoagulability of the blood during pregnancy increase the activity of fibrinogen and factors VII, VIII and X and decreases that of antithrombin III as well as the intensity of physiological fibrinolysis^{19,22}.

The implication of this physiopathological disposition in the management is the administration of bromocriptine (an anti-prolactin) in addition to other conventional treatments. Bromocriptine has been shown to be effective in a randomized controlled trial²³. This would justify a short average hospital stay of 5 days, without death in all cases.

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Table 1: Epidemiological characteristics of PPCM patients with or without intraventricular thrombus in our population study

	All patients (n=40)	PPCM patients without thrombus (n=34)	PPCM patients with thrombus (n=06)	p-value
Mean age	29,17 ± 6,36	29,17 ± 6,34	29,16 ± 6,44	0,9
Pregnancy mean	3,30 ± 1,93	3,39 ± 1,95	2,83 ± 1,94	0,029
Average parity	3,17±1,84	3,27 ± 1,84	2,67 ± 1,96	0,029
Multiparity	3,17±1,56	3,67±1,56	3,5±1,56	0,806
Low economic level	39(97,5%)	34(100%)	05 (83,3%)	0,150
Caesarean section	04(10%)	04(11,8%)	00(00%)	0,507

Table 2: Clinical characteristics of PPCM patients with or without intraventricular thrombus in our population study

	TOTAL (n=40)	PPCM patients without thrombus (n=34)	PPCM patients with thrombus (n=06)	p-value
Dyspnéa stage IV	25 (62,5%)	19 (55,9%)	06 (100%)	0,046
Cough	35 (87,5%)	29 (85,3%)	06 (100%)	0,423
Chest pain	24(60%)	19 (55,9%)	05 (83,3%)	0,212
Palpitations	14(35,0%)	10(29,4%)	04 (66,4%)	0,099
Dyscomfort	03(7,5%)	01(2,9%)	02(33,3%)	0,053
Dizziness	01(2,5%)	01(2,9%)	0(0%)	0,85
Clinical anémia	17(42,5%)	16(47,1%)	1(16,7%)	0,175
Global HF	40(100%)	34(100%)	06(100%)	-
Systolic BP	113,01±15,42	119,64±15,05	106,33±12,09	0,052
Diastolic BP	75,82±18,15	77,94±17,57	73,67±3,88	0,572
Heart rate	113,41±16,10	108,62±15,27	118,17±11,44	0,128
Tachycardia	33(82,5%)	27(79,4%)	6(100%)	0,289

Galop	10(25,0%)	7(20,6%)	3(50,0%)	0,153
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Captions: HF (heart failure) BP (blood pressure)

Table 3: Paraclinical characteristics of PPCM with or without intraventricular thrombus in our study population

	TOTAL (n=40)	PPCM without thrombus (n=34)	PPCM with thrombus (n=06)	p-value
LVH	15(0,37%)	13(38,23%)	2(33,33%)	0,426
Repolarization disorders	31(77,5%)	25(73,52%)	06(100%)	0,095
AF	1(2,5%)	1(2,9%)	0(0,0%)	0,850
Size LV (mm)	64,55±5,89	64,57±5,85	64,48±6,69	0,9
LVEF (%)	34,8±7,7	35,88±7,44	28,67±6,69	0,027
LVEF <30%	11(24,63±4,59)	6(24,51±5,44)	4(24,75±3,30)	0,42
Tx Hb (g/dl)	10,68±1,77	10,49±1,78	11,80±1,37	0,029
Hematocrit	33,11±4,42	32,51±4,19	36,47±4,51	0,029
Creatinine (mg/l)	13,42±8,59	14,18±9,07	9,10±2,56	0,187

Legend: LVH (left ventricular hypertrophy) AF (Atrial fibrillation), ICT (Cardio Thoracic Index), FE (ejection fraction), Hb (hemoglobin)

Table 4: Therapeutic characteristics of PPCM with or without intraventricular thrombus in our study population

	TOTAL (n=40)	PPCM without thrombus (n=34)	PPCM with thrombus (n=06)	p-value
Diuretics	40(100%)	34(100%)	6(100%)	-
Spironolactone	36(83%)	30(83%)	06(100%)	0,25
ACEI	40(100%)	34(100%)	06(100%)	-
Digital	38(95%)	32(94,1%)	06(100%)	0,71
Bisoprolol	39(97,5%)	33(97,05%)	06(100%)	0,43
Thromboprophylaxis	17(42,5%)	17(50%)	0(0,0%)	0,026
Anticoagulation curative	09(22,5%)	03(08,8%)	06(100%)	<0,001
Vitamin K antagonist	08(20%)	02(05,9%)	06(100%)	<0,001
Antiplatelet agent	2(5%)	2(5,9%)	0(0,0%)	0,71
Antianemic	16(40%)	15(44,1%)	1(16,7%)	0,21
Bromocriptine	29(72,5%)	29(85,3%)	0(0,0%)	-

Length of hospital stay	5,59±2,64	4,62±1,45	8,17±2,23	0,001
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Legend: ACEI (ACE inhibitor), AAP (antiplatelet agent) DOA (direct oral anticoagulant)

Table 5: Characteristics of thrombi

	Length (mm)	Width (mm)	Localisation	Characteristic
Thrombus 1	23	10,2	Septoapical	Mural
Thrombus 2	18	13	Apical	Mural
Thrombus 3	10	10	Septoapical	Sessile
Thrombus 4	26	18	Septoapical	mural
Thrombus 5	16,2	14,1	Apical	pedicled
Thrombus 6	17	11,3	Septoapical	mural
Average	18,3	12,76		



Figure 1: Four-chamber ultrasound image showing a mural thrombus at the apex of the left ventricle



Figure 2: Four-chamber view cardiac ultrasound image showing a pedicled thrombus at the apex of the left ventricle and a thrombus at the lateral wall of the right ventricle