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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/14378
DOI URL: http://dx.doi.org/10.21474/IJAR01/14378

RESEARCH ARTICLE

MEADOWS SYNDROME: UNUSUAL, MULTI-FACTORIAL AND POTENTIALLY SERIOUS DISEASE: ABOUT 5 CLINICAL CASES

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Manuscript Info

Manuscript History
Received: 10 January 2022
Final Accepted: 15 February 2022
Published: March 2022

Abstract

Meadows syndrome is a rare pathology with a poor prognosis. Its etiopathogenesis remains unknown and its clinical, echocardiographic and histological signs are non-specific. The PPCM prognosis is dark and its evolution is unpredictable, sometimes favorable with complete remission, but often there is persistence or worsening of heart failure that can be deleterious for both mother and fetus. The risk of recurrence in subsequent pregnancies remains high despite apparent remission. Indeed, its fast evolution and its seriousness require a good knowledge of the diagnostic and therapeutic means in order to improve the prognosis of these young women.

Introduction:-

Peripartum cardiomyopathy (PPCM) or Meadows syndrome is a rare form of pregnancy-associated congestive cardiomyopathy defined as an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction toward the end of pregnancy or inthe months following delivery, where no other cause of the heart failure is found. It accounts for less than 1% of cardiovascular pregnancy problems [1,2,3]. The etiology and pathophysiological mechanism remain unclear.

The PPCM prognosis is dark and its evolution is unpredictable, sometimes favorable with complete remission, but often there is persistence or worsening of heart failure that can be deleterious for both mother and fetus. The risk of recurrence in subsequent pregnancies remains high despite apparent remission.

Indeed, its fast evolution and its seriousness require a good knowledge of the diagnostic and therapeutic means in order to improve the prognosis of these young women.

Through these clinical cases, we propose to focus on the particularities of this form of cardiomyopathy, to address risk factors, therapeutic and preventive means with review of the literature.

Observations:-

Case 1:

This29-years-old, without cardiovascular risk factors, no specific medical or surgical history including no known system disease or vasculitis, no notion of tubercular contamination or known heart disease, having on her past obstetric history: G2P1, her first pregnancy went well, her second pregnancy was intrauterine fetal death, shecomes

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at 34 weeks of pregnancywith dyspnea class IV of NYHA andorthopnea associated with lower limbs and abdomenswelling.

Clinical examination found a conscious patient, tachypnea at 28 cpm, tachycardia at 130 bpm, BP = 120/65 mmHg, with signs of right heart failure and crackling at the pulmonary bases. The ECG records sinus tachycardia. Chest X-ray showed cardiomegaly with diffuse interstitial syndrome. Herbiological assessment revealed renal insufficiency with hepatic cytolysis and spontaneously low Prothrombin Time.

Transthoracic echocardiography (TTE) objectified dilated cardiomyopathy and severe left ventricular dysfunction (**figure 1**).

The etiological investigations of this cardiomyopathy went unsuccessful.The patient received bromocriptine, inotropes and conventional treatment for heart failure. Unfortunately, the patient died as a result of cardiogenic shock with multiple organ failure.

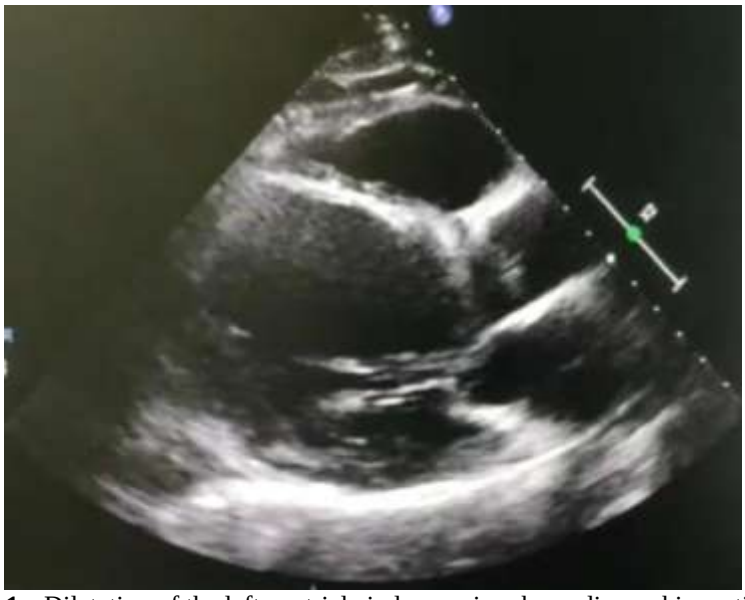

Fig 1:- Dilatation of the left ventricle in long axis echocardiographic section.

Case 2:
A 26-year-old primigravida woman with a history of pregnancy hypertension, no history of heart disease, admitted to the cardiac ICU, one month after delivery, for acute respiratory distress. Clinical examination found a left heart failure signs with a blood pressure of 100/70mmHg. ECG showed sinus tachycardia at 130 bpm without repolarization disorders. Chest X-ray showed cardiomegaly and diffuse interstitial pulmonary syndrome. Transthoracic echocardiography highlights a hypokinetic dilated left ventricle with 36% impaired LVEF and high filling pressures. The patient soon went into refractory cardiogenic shock and needed assisted ventilation,even though higher doses of inotropes, the evolution was dramatic. The patient died two weeks after her admission.

Case 3:
Mrs. A.S, 24 years-old, was having as obstetrical history: 4 miscarriages and 2 pregnancies carried to completion, the last birth is one month earlier. She was admitted to our service in a NYHA class III dyspnea with heart failure panel and abdominal pain. Transthoracic echocardiography had shown systolic dysfunction DCM of the LV without thrombus (**figure 2**).

The abdominal CT scan showed renal and splenic microinfarction, finally the Cardiac MRI supports the diagnosis (**figure 3**). The patient received conventional treatment for heart failure associated with anticoagulation with clear clinical improvement. She was discharged home 60 days after admission.

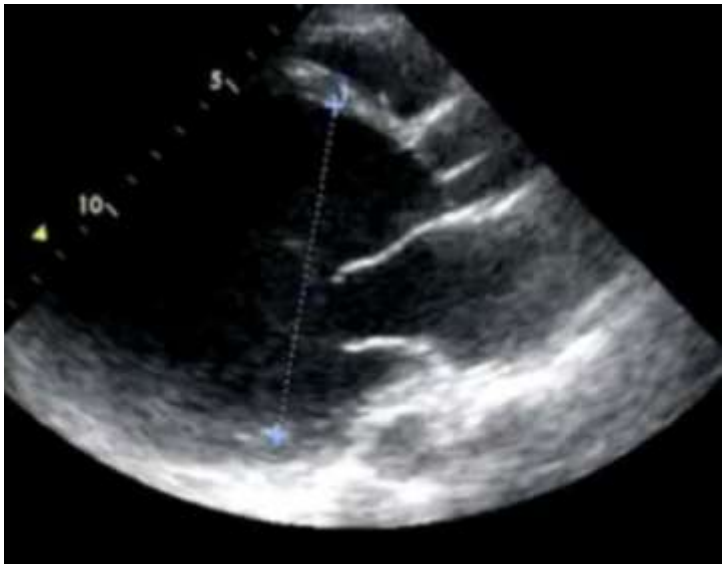

Fig 2:- Echocardiographic long axis section showing dilatation of the left ventricle.

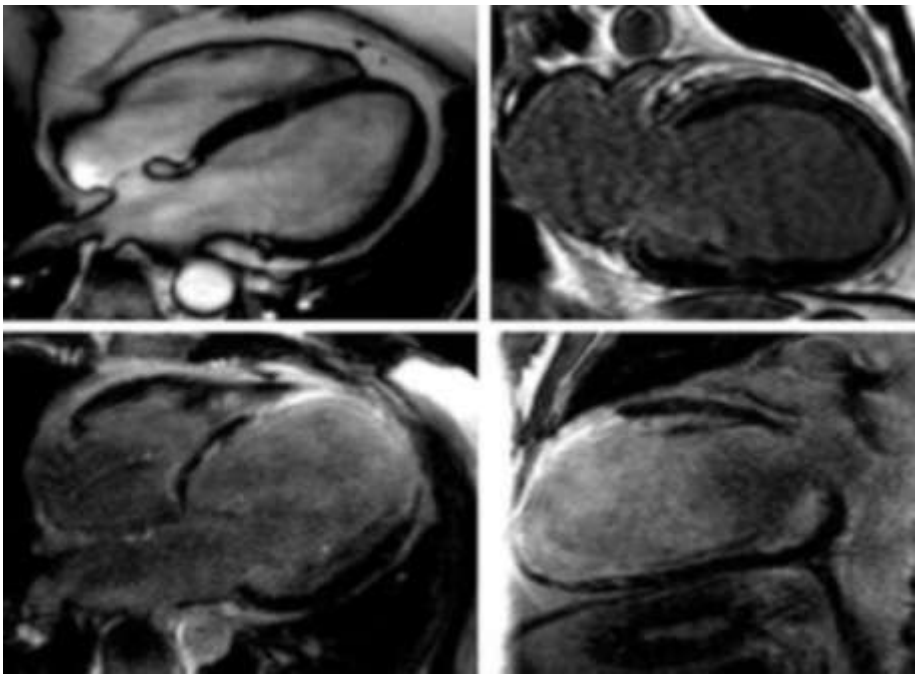

Fig 3:- Cardiac MRI showing dilatation and dysfunction of left ventricle.

Case 4:

Mrs.A.R, 21-years-old, second parity, hospitalized in cardiology unit following an acute global heart failure one week after normal delivery at 39 weeks of amenorrhea, the two pregnancies went well. She has no specific medical history, especially no cardiac history. At admission, the patient was orthopneic, heart rate up to 120, normotensive(110/70 mmHg), bilateral crackling rattles at two-third of both pulmonary fields with signs of right heart failure. The examination also found swelling of the right lower limb with a decrease of calf bloating and a positive Homans sign. The TTE showed dilated left heart chambers with a 30% altered left ventricle ejection fraction (LVFE) with a left intra ventricular thrombus (**figure 4a, 4b**). The venous ultrasound of the lower limbs founded a deep phlebitis of the right lower limb.

The patient received Cabergoline associated to conventional heart failure therapy and effective anticoagulation with compression stockings. The evolution was clinically favorable.

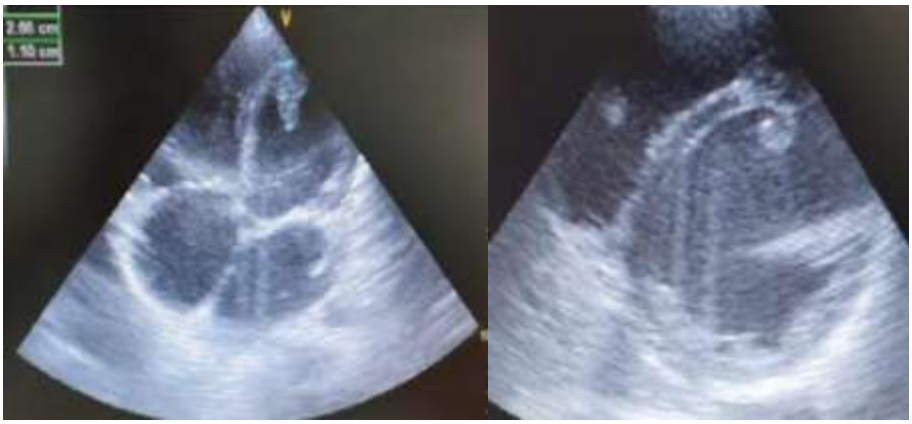

Fig 4a, 4b:- Echocardiographic image showing ventricular thrombi.

Case 5:
This 28-year-old patient with no specific risk factors or history, G2P1, admitted to the emergency obstetric department for progressive dyspnea, 30 days after giving birth to her second child, which began 1 week before delivery. At the examination the patient is in acute decompensated heart failure. ECG showed frequent ventricular extrasystoles right type delay. The angio-CT for pulmonary embolism was negative but showed cardiomegaly. TTE showed a dilated LV with global hypokinesia and left ventricular dysfunction with ejection fraction of about 40% and high filling pressures. The patient has achieved clinical and ultrasound improvement under diuretic treatment, conversion enzyme inhibitor and beta-blockers.

Discussion:-

The PPCM was first time described in 1971 by Demakis et al., defined as an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction toward the end of pregnancy or in the months following delivery. Then in 1997, it was redefined by the National Heart, Lung and Blood Institute (NHLBI) based on the association of 4 criteria:
- Development of cardiac failure in the last month of pregnancy or within five months of delivery.
- Absence of an identifiable cause for the cardiac failure.
-Absence of recognizable heart disease prior to onset of symptoms (last month of pregnancy).
-And the presence of ultrasound signs of systolic left ventricular (LV) dysfunction with a LV ejection fraction (EF) of less than 45% and/or a shortening fraction of less than 30%, and/or a LV end-diastolic diameter (LVEDD) of more than 2.7 cm/m2.[4]

More recently, this definition has been adopted by a working group on heart failure of the European society of cardiology and is more pragmatic:

"PPCM is an idiopathic cardiomyopathy with signs of heart failure secondary to left ventricular systolic dysfunction at the end of pregnancy or within five months of delivery, where no other cause of heart failure is found. Ventriculardilatation is not mandatory, but LVEF is always less than 45%" [5]. The incidenceof PPCM varies from a country to another [1]. It concerns one birth over 3000 to 15 000 with a large geographical variety and a higher frequency in Africa and Haiti(1/100 births in Nigeria, 1/299 births in Haiti and 1/1000 births in South Africa versus 1/4000 births in the United States)[6], this variation cannot be confirmed, because of the limited epidemiological data and the small series in most registries listed in literature[7]. Several risk factors have been identified: age over 30 years, obesity, the black race, multiparity and twin pregnancy[1]Poverty and malnutrition are likely to be predisposing factors especially in Africa but cannot alone explain the occurrence of a PPCM[8].A recent study reports that pre-eclampsia and tocolysis by beta-mimetics promote the occurrence of PPCM. Indeed, the frequency of the association between pre-eclampsia and PPCM is found in 22 to 43% of cases[1]. Pre-eclampsia and PPCM can be clinically confounding, both associating signs of left heart failure and pulmonary edema[9]. To date, none of these risk factors have a sufficient predictive value -positive or negative- to allow its use as a screening tool, one third of patients developing a PPCM having none of them[7].

Its etiopathogenesis remains poorly understood and several hypotheses are established but none of them could be affirmative. Myocarditis is often suspected as the origin of thePPCM that can be linked to a viral infection (enteroviruses, parvovirus B19, adenoviruses and herpes viruses). In addition, physiological and hemodynamic changes associated with pregnancy are believed to increase the susceptibility to viral myocarditis [7].An autoimmune origin is also evoked, indeed, a passage of fetal cells in maternal blood could trigger a maternal immune response with production of auto-antibodies directed against the heart muscle. Another hypothesis has been suggested, that upon delivery, the uterine tropocollagen is degraded by enzymes that will release actin, myosin and other metabolites leading to the formation of auto-antibodies that cross react with the myocardium and thus contribute to the development of thePPCM through the destruction of cardiac cells. The latest data from the literature confirm the involvement of genetic factors in the development of this disease, including genes involved in cardiomyocyte apoptosis[10], it seems that the pro-apoptotic gene Nix or Bnip3 would play an important role in the development of PPCM[11]. More recently, the Hilfiker-Kleiner team pointed out the role of a peptide resulting from the cleavage of the lactation hormone prolactin[12]. The protease: Cathepsin D,divides prolactin into small molecular weight with anti-angiogenesis and apoptotic properties, 16Kda-prolactin, this protein is responsible, in animals, of endothelial dysfunction, myocardial vascular abnormalities, and cardiomyocyte dysfunction.The high level of circulating estrogens during pregnancy would play a cardioprotective role by its hypertrophic effects (increase of the heavy chains of ß-myosin and decrease of the heavy chains of amyosine), decrease of calcium-ATPase sarcoplasmic, increased synthesis of atrial natriuretic peptides and transcription of protective cellular signals. The sudden drop in post-partum estrogen levels is thought to be the cause of an imbalance between protective estrogen-dependent factors and the cardiotoxic effects of the cascade oxidative stress–cathepsin D–16KDa prolactin[7,12].

The other etiologies proposed are nutritional disorders including selenium and other micronutrients. A study by Cénac et al. involved the direct relationship between selenium deficiency and PPCM as they had found plasma selenium levels significantly low in women with PPCM compared to the control group[1]. However, none of these assumptions are confirmed. It could also be excessive left ventricular dilation in response to physiological increases in blood volume and cardiac output during pregnancy, this exaggerated response could become symptomatic when the reduction in the ejection fraction described at the end of pregnancy is increased.

The main clinical manifestation of PPCM is congestive heart failure, most often global as foundin the majority of our patients, sometimes purely left and rarely right heart failure alone. In severe forms, the onset is fast, even brutal as in the first 2 cases. Functional signs are dominated by respiratory symptoms. Chest pain is observed in 50% of cases, which may be as atypical precordialgia, sometimes angina pain. The ECG shows no specific signs. Apart from the tachycardia found in our series and which is almost constant in case of cardiac decompensation, we can find a left branch block in 30% of cases, and sometimes a reversion of T-waves from V4 to V6[13].

Transthoracic echocardiography (TTE) is primordial, it direct towards the diagnosis, eliminate an unknown pre-existing heart disease and monitor the progress of PPCM. It searches a global systolic dysfunction with a LVEF less than 45% and/or a SF less than 30%, this systolic dysfunction is generally bi-ventricular with a dilatation of the left ventricle and a LVEDD greater than 2,7cm/m^2 and globalheart hypokinesis without segmental kinetics abnormalities. Indeed, chamber dilation is not constant, as shownin some trials where they found at least one case without dilation of the heart chambers[14].

The TTE is used also to screen for complications such as heart cavities thrombosis (like the case of our 4th patient), effusions and associated valve disease including mitral insufficiency.

In the case 3, our patient benefited from cardiac MRI exam which is valuable and interesting for the PPCM diagnosis, by objectifying a late enhancement after gadolinium injection, unsystematized, under epicardic predominancy, and whose intensity appears to be correlated with the prognosis and probability of LV functional recovery[15,16].

The severity and context of the disease require emergency hospitalization and specialized follow-up by a multidisciplinary team including cardiologist, obstetrician and neonatologist. Management of PPCM is essentially symptomatic. The conventional treatment is the same as for heart failure, which was prescribed for all our patients, combining: conversion enzyme inhibitor, beta-blocker and diuretic, anticoagulation is necessary when thromboembolic complications are associated, it was prescribed for 2 of our patients[7,17].

Thromboembolic accidents, which occur in nearly 50% of cases, are promoted by secondary hypercoagulability during pregnancy and blood stasis in dilated chambers. Effective anticoagulation is then justified and must be continued as long as the ejection fraction is less than 35%[18]. In severe forms of acute postpartum onset, as described by Merson et al, patients generally respond to conventional cardiogenic shock treatment, sometimes the tracheal intubation is required[10], but, in somecases, when poor response to treatment and/or major left ventricular dysfunction persists, the use of circulatory assistance is useful. However, some molecules have recently shown their effectiveness in the management of PPCM such as: Pentaxifylline that inhibits the production of TNF alpha, which seems to play a major role in the development of the disease.Bromocriptine, by inhibiting the secretion of prolactin, improves the functional prognosis of patients and prevents the alteration of ventricular function. Nett team describes the benefit of Cabergoline on left ventricular functional recovery in patients with PPCM[19]. Also, Sliwa et al. in their randomized trial, which compared two groups of 10 women receiving conventional versus conventional and bromocriptine treatment, they were able to show that at 6 months follow up, the second group had a better cardiac function measured by MRI, a lower mortality rate and a lower rate of occurrence of the judgment criteria (death and/or heart failure class III/IV NYHA and/or FEVG < 35%) [20] Currently, a randomized multicenter trial is being included in Germany (NCT 00998556) with a higher dosage (5mg twice daily for two weeks, then once daily for four weeks) and a larger population (60 patients) this would reinforce these results[6]. Brogly et al. demonstrated the beneficial effect of Levosimendan in a woman with PPCM, this new calcium sensitizing inotropic agent, improves cardiaccontraction withoutinducing tachycardia, its vasodilatory action sometimes responsible for severe hypotension; it also has an action on the diastolic function of the LV[10]. Two other clinical cases described its use inPPCM[21] which had introduced it,five days after childbirth, to a patient with acute pulmonary edema associated to severe left heart failure (LVEF 20%) but without circulatory failure. Also, Benloloet al.[22] introduced it after hemodynamic stabilization in a 22-year-old primiparous that had undergone cardiogenic shock during labor. In the three cases above, the authors observed an improvement in systolic function of the LV.

Based on the assumption that PPCM is secondary to myocarditis, some authors report the beneficial effect of immunosuppressive drugs prescribed to patients who remain symptomatic despite optimal conventional treatment and in whom myocarditis has been confirmed by endomyocardial biopsy. Melvin et al.[23] described three cases of PPCM in which the ejection fraction improved under Immunosuppressive treatment. Similarly, Mideiet al.[24]reports that nine of ten patients went well under immunosuppressive drug.

Heart transplantation is the last alternative in patients who remain symptomatic despite optimal medical treatment.

For patients with PPCM before the end of pregnancy, there are no systematic recommendations for obstetric management. The decision to give birth prematurely will be discussed on a case-by-case basis depending on the severity of the left ventricular dysfunction, the response to treatment, and eventual fetal distress[13].Based on the hormonal theory, breastfeeding would not be recommended. [8]

The risk of recurrence in subsequent pregnancies is not negligible, sometimes making a future pregnancy unauthorized and life-threatening, hence the need of effective contraception in these young women is mandatory after a first episode of PPCM. Elkayan et al. reported in a study of 44 patients with PPCM, that patients with an ejection fraction less than 50% in prepartum had an unfavorable evolution with a very high mortality rate[11].

In a review published in 2004,the recurrence of left ventricular systolic dysfunction has been shown to occur in 27% of women who had normalized their heart function prior to this new pregnancy and in 48% of women who maintained ventricular dysfunction; with 16% mortality rate was reported in the latter group.[9]

The evolution of PPCM is highly variable and completely unpredictable, punctuated by the occurrence of early complications and the possibility of late death secondary to the sequellary dilated cardiomyopathy of primary heart disease[25].

The mortality rate is 25 to 50%, it was 40% in our series; in fact, half of the deaths occur early in the first month of the symptomatology as well as in the first three months of the post-partum[26].

For surviving patients, the evolution is often favorable with recovery of left ventricular function for about 50 to 75% of patients.

The pejorative criteria seem to be the black race, women over 30 years old, and multiparous or in case of twin birth. Similarly, women who remain symptomatic after two weeks post-partum and those whose symptoms begin early in post-partum appear to have a more unfavorable evolution. The functional prognosis remains reserved with high risk of persistent heart failure, indeed, the lower the ejection fraction and the higher the end diastolic diameter of the left ventricle, the poorer is the prognosis[18]. The European Society of Cardiology recommends performing screening echocardiography in the third trimester for women with a history of fully recovered PPCM or in the case of a first-degree relative family history of PPCM.

Conclusion:-

Peripartum cardiomyopathy is a rare cause of heart failure, the etiology of which is still poorly understood. Although rare, it affects young women and can cause severe heart failure or death. There is currently no specific treatment for total recovery of myocardial function. EF and LV end diastolic diameter are statistically significant prognostic factors. The recurrence risk in subsequent pregnancies remains high and requires rigorous monitoring.

Acknowledgments:-

None

Consent:

The authors confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient.

Conflict Of Interest

The authors declare that they have no conflict of interest to report.

Author Contributions

All authors have contributed to the elaboration of the manuscript.

Ethical Approval

We confirm that the manuscript has been read and approved by all named authors. The protection of intellectual property associated with this manuscript had been in our consideration.

References:-

1. Bahloul M, Ben AhmedMN,Laaroussi L, Chtara K, Kallel H,Dammak H, Ksibi H, Samet M, Chelly H, Ben Hamida C, Chaari A, Amouri H, Rekik N, Bouaziz M. Peripartum cardiomyopathy: Incidence, pathogenesis, diagnosis, treatment and prognosis. Ann Fr Anesth Reanim.2009;28:44–60.
2. Beus E, Mook WN, Ramsay G, Stappers JL, Putten H. Peripartum cardiomyopathie: acondition intensivists should be aware of. Intensive Care Med 2003;29:167–74.
3. Grison P, Le Douarin, Senotier JM, Levy M, Soussana J. œdème pulmonaire deux jours après une césarienne réglée. Ann Fr AnesthReanim1994;13:414–6.
4. Aachak M. La cardiomyopathie du péripartum: à propos d'un cas. Thèse, Université Mohamed 5, faculté de médecine et pharmacie-Rabat. 115(2016).
5. Sliwa K ,Hilfiker-Kleiner D,Petrie MC,Mebazaa A,Pieske B,Buchmann Eet al. Current state of knowledge on aetiology, diagnosis,management, and therapy of peripartum cardiomyopathy: a positionstatement from the Heart Failure Association of the European Society ofCardiology Working Group on peripartum cardiomyopathy. Eur J HeartFail, 2010. 12(8): 767-78.
6. Massou E, Lebon A, Vardon D, Dreyfus M, Benoist G. Peripartum cardiomyopathy: A rare, unknown and potentially fatal disease. GynécologieObstétrique&Fertilité 41 (2013) 667–71.
7. Vanzetto G, Martin A, Bouvaist H, Marlière S, Durand M,Chavanon O. Cardiomyopathie du péripartum : une entité multiple.Presse Médicale. 2012;41(6): 613-20.
8. Fennira S, Demiraj A, Khouaja A,Boujnah M-R. Peripartum cardiomyopathy. Ann Card Angéiol. 2006;55(5): 271–5
9. Le Gloan L, Piriou N, Cueff C, Trochu J-N. La cardiomyopathie du peripartum. e-cordiam.fr. 2018:20-24.
10. Brogly N, Guasch E, Puertas L, Alsina E, Lopez T, Gilsanz F. Défaillance cardiaque aigue associée à une cardiomyopathie dilatée en post-partum précoce : traitement par ballon de contrepulsion aortique et lévosimendan. Ann Fr AnesthReanim. 2010;29(11):807–810

11. BhattacharjeeR, Raithata N, Patel M, Vaishnav S. Peri-partum cardiomayopathy - not a rare entity, clinical profile in a rural tertiary care center in Gujarat, India t. Int J Reprod Contracept ObstetGynecol 2017;6:1544-9.
12. Hilfiker-Kleiner D, Sliwa K, Drexler H. Peripartum cardiomyopathy: recent insights in its pathophysiology. Trends in cardiovascular medicine. 2008;18(5):173-9.
13. Mouquet F, Bouabdallaoui N. Cardiomyopathie du péripartum. Presse Med. (2015), http://dx.doi.org/ 10.1016/j.lpm.2015.05.010
14. Ferrière M, Sacrez A, Bouhour JB, Cassagnes J, Geslin P, Dubourg O, et al. La myocardiopathie du péripartum : aspects actuels. Etudes multicentriques : 11 observations. Arch Mal Coeur 1990;83:1563–9.
15. Bouzeda A. Cardiomyopathie du péripartum: à propos d'une observation et revue de la littérature. Pamj. 2016; 25:21
16. Barone-RochetteG ,Rodière M, Lantuejoul S.Value of cardiac MRI in peripartum cardiomyopathy. Archives of Cardiovascular Disease (2011) 104, 263—264.
17. Ben Letdifa D, Slama A, Khemakhem K, Ben Jazia K, M'hamdi S, Jegham H, Essaydi H, Khaii H, Khaii H, Ammar H. Cardiomyopathie du péripartum: série de cascliniques. Ann Fr AnesthRéanimation. 1999;18(6):677–8
18. Merson L, Stecken L, Morel N, Lélias A, Dabadie P. Défaillance cardiaque en postpartum : cas clinique d'une cardiomyopathie du péripartum.Ann Fr AnesthRéanim 27 (2008) 731–734.
19. de Jong JS, Rietveld K, van Lochem LT et al; Rapid left ventricular recovery after cabergoline treatment in a patient with peripartum cardiomyopathy. Eur J Heart Fail 2009;11:220-2.
20. Sliwa K, Blauwet L, Tibazarwa K et al. Evaluation of bromocriptine in the treatment of of acute severe peripartum cardiomyopathy: a proof-of-concept pilot study. Circulation. 2010;121(13):1465-73.
21. Benezet-Mazuecos J, De la Hera J. Peripartum cardiomyopathy: a new successful setting for levosimendan. Int J Cardiol2008;123:346–7.
22. Benlolo S, Lefoll C, Katchatouryan V, Payen D, Mebazaa A. Successful use of levosimendan in a patient with peripartum cardiomyopathy. AnesthAnalg2004;98:822–4.
23. Melvin KR, Richardson PJ, Olson EGJ, Daly K, Jackson G. Peripartum cardiomyopathy due to myocarditis. N Engl J Med 1982;307:731–4.
24. Midei MG, Dement SH, Feldman AM, Hutchins GM, Baughman KL. Peripartum myocarditis and cardiomyopathy. Circulation 1990;81:922–8.
25. Ardehali H, Kasper EK, Baughman KL. Peripartum cardiomyopathy. DivCardiol2003;51:41–8.
26. Bhakta P, Biswas BK, Banerjee B. Peripartum cardiomyopathy: review of the literature. Yonsei Med J 2007;48:731–47.