Peripartum cardiomyopathy

Peripartum cardiomyopathy is classified as an idiopathic cardiomyopathy.[1] The pathophysiological mechanisms are not yet fully understood. Diagnosis usually takes place by **exclusion**.[2] In order to make this diagnosis, three basic diagnostic criteria must be met - the presence of **acute heart failure** with reduced ejection fraction, manifestations of difficulties in the **peripartum period** or in several months after delivery (possibly abortion), and the exclusion of other possible causes of heart failure.[2][3][4] The clinical picture of peripartum cardiomyopathy is diverse. Pharmacological intervention is limited with regard to fetal health. **This is a potentially life-threatening disease that requires early diagnosis.**[1][2][4]

Etiopatogenesis

The pathophysiological mechanisms leading to the development of pregnancy cardiomyopathy are not yet completely clear. **Genetic, nutritional, hormonal, metabolic, other factors and, above all, their combination** contribute to the manifestation of the disease. [1][2][3] In particular, low selenium levels, cardiotropic virus infections (myocarditis), autoimmune or other inflammatory reactions, oxidative stress and hormonal imbalances may play a role in the pathophysiology of the disease.[2][3] According to recent research, oxidative stress leads to the breakdown of **prolactin** molecules. Its fragments then act proapoptically in the myocardium, lead to vasoconstriction and inhibit angiogenesis and neovascularization.[2][3] The role of other hormones, such as VEGF and sFlt-1, is also being studied (it also occurs in patients with preeclampsia).[2][3]

Genetic predisposition also plays a significant role. **Genetic mutations, eg for titin and beta myosin heavy chain,** have been detected in 15-20% of patients. [2][3] However, not all patients with identified mutations will develop the disease, so there will be a significant **proportion of other factors**. [3]

Epidemiology

In addition to risk factors, the incidence of peripartum cardiomyopathy also **depends on the patient's ethnicity.**[2][3] It occurs more frequently in **African and African-American women.** In Nigeria, the incidence of pregnancy cardiomyopathy is **1: 100**, while in Germany, for example, only **1: 1500**.[2] In the United States, the incidence is 1: 1000 to 1: 4000.[3] In African-American women, cardiomyopathy manifests at a younger age and often with poorer ejection fraction values.[2]

In addition to the ethnic group, the risk factors for the development of peripartum cardiomyopathy are **preeclampsia, hypertension**, diabetes, a positive family history of cardiomyopathies, multiparity and **old age**.[2][3]

Clinical picture

The clinical picture is similar to other cases heart failure. Most patients report **slow occurring dyspnea, peripheral edema, chest pain and dizziness**..[3] In a large number of cases, these symptoms are attributed to the normal physiological state at the end of pregnancy or after childbirth.[2][3] **Early diagnosis** at the same time is very important for this disease and its prognosis is significantly based on it.[2][3]

In the differential diagnosis of patient's difficulties, it is necessary to **exclude other possible causing (even pre-existing and as yet unmanifested) diseases**. This includes, in particular, other types of cardiomyopathies, acute myocarditis, embolization, pre-existing valve or congenital heart defects and others.[2][3]

Diagnosis

Diagnosis is per exclusion. Patients with suspected pregnancy cardiomyopathy must have an **echocardiographic and laboratory examinations**.[1] The role of endomyocardial biopsy in this diagnosis is controversial and is only used in very specific situations.[3]

ECG findings are non-specific and may be normal. Repolarization changes and QTc prolongation are common pathologies.[2]

Echocardiography, or magnetic resonance imaging of the heart, are useful in terms of differential diagnosis and estimation of the patient's prognosis. The **ejection fraction is reduced**, mostly below 45%, changes in the dimensions of the heart compartments are also seen, the presence of functional valve regurgitation and signs of pulmonary hypertension are also seen. .[2][3] The methods also serve to exclude the formation of intracardiac thrombi. **If the patient has not given birth yet, magnetic resonance imaging of the heart should not include gadolinium contrast agent.**[2][3]

Elevation of natriuretic peptides occurs in laboratory parameters.[3]

Treatment

The treatment of pregnancy cardiomyopathy is not easy and it is essential that it be started as soon as possible.[3] It is limited, among other things, by the fact that some drug groups commonly used in the treatment of heart failure have toxic and teratogenic effects on the fetus.[2][3][5] **ACE inhibitors, sartans, aldosterone receptor blockers and ivabradine are contraindicated in pregnant patients**.[2][3][5] Digoxin should be used with caution. [2] **Beta-blockers, nitrates and diuretics** are mainly used to treat heart failure in pregnant patients.[2][3][5] In patients with peripartum cardiomyopathy there is an **increased risk and incidence of thromboembolic complications**.[2][3] Therefore, prophylactic anticoagulant therapy with low molecular weight Heparin is also recommended in indicated cases..[2] **Warfarin is contraindicated** due to its teratogenic effects.[2][3]

The situation with pharmacological treatment changes as soon as the patients give birth.[2][3] At this stage, it is possible for patients to use some drug groups that are contraindicated during pregnancy. In any case, caution is needed, mainly because not enough data from large studies are available yet.[2]

In addition to anticoagulant therapy, treatment of more severe conditions may require ionotropic support, mechanical support, including ECMO, or even heart transplantation.[2][3][5] In the United States, heart failure due to pregnancy cardiomyopathy is the primary cause of heart transplantation in women in 5% of cases.[5]

A promising drug is the dopamine D2 receptor agonist **bromocriptine**.[2][3] Several studies have shown its beneficial effect in reducing mortality. However, some studies have not confirmed such results.[3] Currently, bromocriptine is more widely used in Europe than in the United States, where it is still considered an experimental treatment.[2][3] Prophylactic anticoagulant therapy is also given due to the higher risk of thromboembolic events with bromocriptine.[2]

It is not yet clear how long pharmacological treatment should last after normalization of cardiac function. **However, it is at least 12-24 months**, and in some patients the therapy is longer.[2] The need for longer-term pharmacological treatment for this disease is supported by cases in which cardiac dysfunction has recurred after discontinuation of treatment. [3]

Childbirth and breastfeeding

If the patient is hemodynamically stable, doctors prefer to give birth the classical way.[2] In hemodynamically unstable patients, premature birth is sometimes necessary by caesarean section.[2]

The issue of breastfeeding is still under discussion. There are no uniform recommendations yet. In patients with a severe course, experts are more inclined to suspend breastfeeding.[2] In other cases, according to studies, breastfeeding is well tolerated by patients.[2][3]

Prognosis

Many factors affect the prognosis of patients. Among the major ones are **early diagnosis and early treatment, ethnicity, severity of heart failure and pre-existing conditions such as preeclampsia**.[2][3] Roughly 50-75% of patient will improve and their heart function will normalize within 6-12 months.[2][3] Almost 20% of patients have arrythmias(of which 5% malignant arrhythmias)[3], intracardiac thrombi are found in 10-17%[3] and according to some studies, almost half of the patients diagnosed with peripartum cardiomyopathy had preceding conditions such as pulmonary edema, signs of hemodynamic instability, thromboembolic events, etc.[3] Mortality is therefore highly variable. **In the United States, the annual mortality rate is in the range of 4–11% (higher data, especially for African American women), in African countries, it is even more than 20%.**[3]

The question of **other pregnancies** is difficult. All patients have a **higher risk of developing complications**, chronic heart failure and possibly death.[2][3][5] Although patients with normal cardiac function do not have such an increased mortality rates, a relapse rate of about 20% is observed.[3][5] If the patient does not have normalized heart function at conception, the mortality rate is 16-25% according to some studies.[3] The risk of developing chronic heart failure is also higher.[3] Decisions about further pregnancies are therefore highly individual and may require changes in medication and close monitoring of the patient's condition.

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- Cardiomyopathy

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