CLINICAL AND IMMUNOMORPHOLOGICAL FEATURES OF LIVER DAMAGE IN SEVERE PREECLAMPSIA

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Abstract: Pregnancy-associated liver diseases occur in 0.7–3% of pregnant women, are often accompanied by the development of liver dysfunction/failure, and cause increased morbidity and mortality for both mother and child. Pathomorphological examination helps to understand the pathophysiology of severe liver damage in preeclampsia and to optimize the management tactics of such patients. The purpose of the thesis is to study the morphological and immunohistochemical features of liver damage in the most severe forms of preeclampsia and eclampsia, which are fatal.
Keywords: Preeclampsia, eclampsia, HELLP syndrome, liver failure.

INTRODUCTION

Liver diseases associated with pregnancy are reported in 0.7–3% of pregnant women and are often accompanied by the development of liver dysfunction/failure. Severe forms of liver damage cause increased morbidity and mortality for both mother and child [1, 2]. HELLP syndrome develops in 10–20% of pregnant women with severe preeclampsia, acute fatty hepatosis - from 1 in 7 thousand to 1 in 20 thousand pregnancies [1].

Liver diseases during pregnancy are divided into two groups:

1) associated with pregnancy (severe vomiting of pregnant women, intrahepatic cholestasis, liver damage due to hypertensive disorders - preeclampsia, eclampsia, HELLP syndrome, acute fatty hepatosis, liver infarction / liver rupture);

2) not related to pregnancy (pre-existing liver diseases - viral hepatitis, cirrhosis and portal hypertension, autoimmune liver lesions, complications of liver transplantation, various forms of thrombotic microangiopathy; diseases manifesting during pregnancy - autoimmune, viral, vascular, such as Budda-Chiari, drug hepatotoxicity).

MAIN PART

Currently, acute fatty hepatosis is considered to be a mitochondrial hepatopathy, similar to Reye's syndrome and drug-induced hepatotoxicity (caused, for example, by valproic acid), the pathogenesis of which is based on a defect in mitochondrial β-oxidation of fatty acids [5]. In this case, the placenta plays an important role in the pathogenesis of fatty hepatosis. A defect in the oxidation of fatty acids in placental mitochondria leads to mitochondrial dysfunction and increased oxidative stress in the placenta and blood serum. At the same time, defective oxidation of fatty acids leads to the accumulation of toxic intermediate compounds (free fatty acids, such as arachidonic acid) in the placenta and blood serum of pregnant women. These results were demonstrated in a series of experiments back in 2020 [3].

It has been shown that about 20% of newborns born to mothers with fatty liver disease have a defect in β-oxidation of fatty acids and a deficiency of the key enzyme LCHAD (long-chain 3-hydroxyacyl coenzyme A dehydrogenase) due to heterozygous or even homozygous - new mutation of the corresponding allele [7]. Due to a genetic defect, fetal fatty acids accumulate and are returned transplacentally to the mother, deposited in her liver cells, which leads to the development of fatty hepatosis. It has been shown that mothers of newborns with LCHAD deficiency are 20 times more likely to develop fatty liver disease or HELLP, reaching up to 80% [2].

Since there are significant similarities in the clinical manifestations of HELLP syndrome and acute fatty liver disease, the role of fatty acid oxidation defects in HELLP syndrome has also been studied. A certain correlation was obtained, but rather weak [5].

In recent years, severe preeclampsia and HELLP syndrome are considered to be secondary forms of thrombotic microangiopathy (TMA), which also include such rare and severe diseases as atypical hemolytic uremic syndrome (aHUS), thrombotic thrombocytopenic purpura (TTP), nocturnal paroxysmal hemoglobinuria, etc. These pathological conditions are characterized by microangiopathic hemolytic anemia, thrombocytopenia and multiple organ dysfunction/failure, including liver.

However, despite the similarity of clinical and laboratory features of the listed forms of TMA, they have different trigger mechanisms of development and, accordingly, require a differentiated therapeutic approach [3]. The main treatment method for preeclampsia and HELLP syndrome is still delivery, after which the symptoms of these complications usually disappear. But to stop aHUS, it is necessary to use specific therapy (eculizumab, a monoclonal antibody that blocks the C5 component of complement) [4], with TTP plasma exchange is required and the introduction of platelets is not recommended, despite severe thrombocytopenia [10], the issue is also resolved individually about the prescription of glucocorticoids and the need for hemodialysis.

Due to the similarity of clinical symptoms of severe preeclampsia, HELLP syndrome, aHUS and TTP, differential diagnosis of different forms of TMA during pregnancy and the postpartum period is often either absent or extremely delayed. For example, a delay in accurate diagnosis of aHUS and the resulting lack of specific therapy often lead to progression of the disease, up to end-stage renal failure, the need for dialysis or kidney transplantation. At the same time, the International Registry reports only 4 cases of eculizumab use during pregnancy [4], so the use of this drug in this category of patients is not yet regulated by relevant documents.

CONCLUSION

Thus, the study showed the need to optimize the management tactics of patients with severe preeclampsia, taking into account the following recommendations.

1. Preeclamptic liver dysfunction, HELLP syndrome, acute fatty hepatosis are life-threatening emergency conditions, and early diagnosis and adequate treatment are important in preserving the life and health of both mother and fetus. Urgent delivery is the cornerstone in the treatment of severe preeclamptic liver dysfunction to prevent complications such as acute renal failure, seizures, infarction and rupture of the liver capsule.

2. With the development of preeclampsia and especially eclampsia, careful monitoring of the dynamics of blood pressure and controlled administration of antihypertensive drugs is necessary—an unacceptably sharp and/or significant decrease in blood pressure, which can lead to a drop in organ perfusion, up to necrotic changes. At the same time, prolonged and high hypertension is also dangerous due to the occurrence of cerebral hemorrhage, placental abruption, retinal detachment and other complications.

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