YEVROSIYO PEDIATRIYA AXBOROTNOMASI/ЕВРАЗИЙСКИЙ ВЕСТНИК ПЕДИАТРИИ

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ACUTE FATTY LIVER OF PREGNANCY (LITERATURE REVIEW)

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Resume

The review article presents an analysis of the literature data on acute fatty liver in pregnant women. The issues of diagnosis, differential diagnosis, clinical manifestations, peculiarities of labor management and the postpartum period are considered.

Key words: preeclampsia, acute fatty liver of pregnancy, morphology, HELLP syndrome, mortality.

ОСТРЫЙ ЖИРОВОЙ ГЕПАТОЗ БЕРЕМЕННЫХ (ОБЗОР ЛИТЕРАТУРЫ)

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Резюме,

В обзорной статье представлены анализ литературных данных, посвященные острому жировому гепатозу беременных. Рассмотрены вопросы диагностики, дифференциальной диагностики, клинических проявлений, особенностей ведения родов и послеродового периода.

Ключевые слова: преэклампсия, острый жировой гепатоз беременных, морфлогия, HELLP-синдром, летальность.

ҲОМИЛАДОРЛАР ЎТКИР ЁҒЛИ ҒЕПАТОЗИ (АДАБИЁТЛАР ШАРҲИ)

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Резюме

Мақоланинг шарҳида ҳомиладор аёлларда ўткир ёғли гепатоз ҳақида адабиёт маълумотларининг таҳлили тақдим этилган. Диагностика, дифференциал диагностика, клиник-морфологик кўринишлари, тугруқнинг кечиши ва тугруқдан кейинги давр хусуситялари кўриб чиқилди.

Калит сўзлар: преэклампсия, ҳомиладорлар ўткир ёғли гепатози, морфология, HELLP-синдром, ўлим.

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Relevance

Acute fatty liver of pregnancy (AFLP) is one of the most severe complications of pregnancy, leading to high maternal and perinatal mortality. The first mention of acute fatty degeneration of the liver in a woman who died in the postpartum period dates back to 1857. AFLP as a nosological form was first described in 1940 by HL Sheehan [13], who called this disease acute yellow obstetric atrophy of the liver and gave its detailed description. According to the first reports, the mortality rate in acute gallstones was 90-100%. This pathology is rare, which explains the problems of its diagnosis and treatment.

Perinatal mortality of infants born to affected mothers also varies widely 8.9, with recent estimates of perinatal mortality ranging from about 10 to 20% 1, 7, 8, 10-13, with the majority of reported cases due to stillbirth. Perinatal morbidity associated with fetal acidosis and prematurity has also been reported 14, 15. Although the cause is not clear, the severity of maternal disease does not correlate with the incidence or severity of fetal complications [10].

Such pathological conditions as irrepressible vomiting of pregnant women, cholestatic hepatosis of pregnant women, late toxicosis of pregnant women with renal-hepatic syndrome and acute fatty liver of pregnancy can lead to complications of pregnancy with the development of jaundice [2, 9]. Early diagnosis of this disease and the correctly chosen treatment tactics (immediate delivery) can significantly reduce maternal mortality rates, although even under these circumstances it remains very high and amounts, according to various researchers, from 8 to 33% (on average 25%) [1, 2]. AFLP refers to a rare pathology of pregnancy: one case of AFLP occurs in 13,328 deliveries [3]. Consequently, in most maternity hospitals with the number of deliveries 3000-5000 per year, doctors theoretically have the opportunity to observe such pathology of pregnant women once every three to four years. However, it should be emphasized that, the appearance of jaundice and dyspeptic syndrome often becomes the basis for hospitalization of these patients in an infectious diseases hospital with suspicion of viral hepatitis. Thus, a part of pregnant women with AFLP first of all end up in infectious diseases hospitals, and therefore the knowledge of the vast majority of obstetricians-gynecologists working both in polyclinics and in general maternity hospitals is extremely inadequate about this disease [3].

The etiology and pathogenesis of AFLP have not yet been sufficiently studied. According to modern concepts, AFLP is referred to as mitochondrial cytopathies [4, 5], in which fatty degeneration of the liver is a sign of systemic mitochondrial pathology, which also affects the kidneys, muscles, nervous system, pancreas, and heart.

In mitochondria, all reactions of transformation and accumulation of energy take place, except for the breakdown of carbohydrates. Oxidative phosphorylation reactions are accompanied by the breakdown of fatty acids and the synthesis of ATP. This process requires the participation of specific enzymes (3-hydroxyacyl-CoA fatty acid dehydrogenase). It is likely that the deficiency of these enzymes, due to genetics, underlies the development of AFLP and other diseases that also belong to the group of mitochondrial cytopathies (Reye's syndrome, reactions to certain drugs, etc.). This is evidenced by genetic studies [5, 6], conducted among women with AFLP, their husbands and newborns and showed that the development of this complication during pregnancy may be associated with heterozygosity in this category of women for a gene defect caused by the appearance of a mutant gene.

AFLP is referred to as jaundice caused by its own pathology of pregnancy [10]. In the domestic literature, several terms are used to denote this disease: acute fatty liver infiltration of pregnant women (AFLIPW), acute fatty degeneration of the liver of pregnant women (AFDLPW). According to the international classification of diseases of the 10th revision (ICD-10), this pathology is classified in the K-72 heading "Liver failure, not classified elsewhere", where it is designated by the following terms: "Yellow atrophy or fatty liver dystrophy, acute fatty hepatosis, Sheehan's syndrome" [12,13]. The clinical manifestations of AFLP are diverse. There are cases with scant clinical symptoms, with and without jaundice, as well as variants of the clinical course in which the disease progresses rapidly, progresses inexorably, leading to the development of acute hepatic-renal failure, the development of DIC and the death of a pregnant woman and her child. The most typical variant of the course of the disease, in which the first signs of the disease appear most often between the 30th and

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38th week of pregnancy. However, AFLP can develop earlier [9]. As a rule, with this disease there is a preicteric period, when, against the background of sluggish preeclampsia, such signs as weakness, lethargy, nausea, vomiting, discomfort or pain in the abdomen, more often in the epigastric region, are found. At the same time, heartburn occurs, at first short-term, intermittent, then more and more prolonged and extremely intense. Heartburn is accompanied by pain along the esophagus; it increases not only when a dense food lump passing through, but also when swallowing fluid [10]. The pathological basis of this symptom, according to autopsy data, is the erosion or ulceration of the esophageal mucosa during the development of disseminated intravascular coagulation syndrome [11]. The next stage in the development of AFLP is the onset of jaundice, when the risk of severe complications for the mother and fetus increases sharply. Jaundice is usually intense but may be mild. Heartburn, reaching its maximum development, often ends with vomiting of "coffee grounds", after which temporary relief may occur. The appearance of vomiting with an admixture of hematin is an important sign, on the basis of which, it is possible to suspect this pregnancy pathology. The course of the disease may be accompanied by the development of esophagitis. About half of the patients develop ascites, apparently as a result of portal hypertension. AFLP is characterized by progressive liver failure, while encephalopathy does not lead to any prolonged loss of consciousness, stupor is replaced by complete recovery of consciousness [11]. In most cases, the disease is accompanied by leukocytosis (cases of hyperleukocytosis are described), thrombocytopenia, with the development of bleeding, the level of hemoglobin and erythrocytes decreases. Characterized by hypoproteinemia and a decrease in the prothrombin index (as a result of a sharp decrease in the protein-synthetic function of the liver), while the level of alanine aminotransferase is usually low and in the overwhelming majority does not exceed three to ten norms. AFLP, characterized by the development of hypoglycemia (due to a disturbance of the Krebs cycle), hyperammonemia (sometimes high concentrations of uric acid are found at a very early stage of the disease, before the first clinical signs appear) and metabolic acidosis. With acute gallstone disease, the kidneys are nearly always affected, thus the course of the disease is complicated by renal failure of one degree or another.

On histological examination, attention is drawn to the bright yellow color of the liver, caused by fatty degeneration of hepatocytes. Hepatocytes are swollen, with small and large drops of fat and centrally located nuclei. Hepatic architectonics is not impaired. Damage to other organs is expressed in fatty infiltration of the kidneys, pancreas and heart. Signs of a sharp disturbance of intravascular coagulation are also characteristic in the form of a pronounced hemorrhagic syndrome (hemorrhages in all organs, hemothorax, hemoperitoneum, anemia of internal organs, acute ulcers of the esophagus, stomach, etc.). The prognosis and outcomes of AFLP are very serious for both the mother and the child. Death is usually caused by disseminated intravascular coagulation syndrome, profuse bleeding, and hepatic renal failure.

The success of treatment is determined primarily by the early recognition of this disease and early delivery, as well as the improvement of intensive care methods (these measures have led to an increase in survival rates in recent decades).

As a rule, patients with AFLP are admitted to an infectious hospital with suspected viral hepatitis; therefore, the differential diagnosis is primarily carried out with acute viral hepatitis (AVH) of various etiology. With AVH, the course of the disease is also characterized by the development of the preicteric period with similar asthenovegetative and dyspeptic phenomena, but it should be noted that clinical manifestations still have a number of features. Therefore, heartburn and pain when swallowing along the esophagus are not characteristic of viral hepatitis. With a severe course of the icteric stage of viral hepatitis, the development of a kind of encephalopathy is characteristic, which, with the progression of the disease, leads to the development of coma and loss of consciousness. Acute viral hepatitis is rarely combined with preeclampsia; it is not characterized by the development of acute renal failure. Acute viral hepatitis (AVH) is not characterized by leukocytosis, thrombocytopenia and hypoproteinemia. The exclusion of AVH is a paramount task, since the therapeutic tactics in the management of pregnant women with AVH and AFLP is diametrically opposite and is aimed at maintaining pregnancy in the midst of AVH and at immediate delivery in case of AFLP.

Jaundice in pregnant women in hospitals of any level and qualifications is often regarded as

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a manifestation of viral hepatitis and causes a "transfer reflex", which inevitably delays the process of diagnosis and making a responsible decision.

In a number of cases, AFLP has a not quite typical course, when there are clinical and laboratory signs that allow reasonably suggesting acute viral hepatitis. Therefore, in some patients, the course of AFLP differed in a number of features that made it difficult to timely diagnose this serious disease. These include, in particular, the absence of heartburn and vivid jaundice even at the height of the development of AFLP, a quite favorable response to conservative therapy on the second day of hospitalization, a relatively high ALT level reaching 16 norms, a slight decrease in prothrombin index, the absence of thrombocytopenia and hypoglycemia. The listed factors made it difficult to diagnose AFLP, and therefore the decision to terminate the pregnancy was made with a delay. At the same time, the onset of the disease against the background of signs of preeclampsia with the appearance of characteristic complaints, the course of the disease was accompanied by the phenomena of encephalopathy, there was a "flapping" tremor, the patient was quickly exhausted, at times was loaded, but the coma did not develop (in the intervals between the urge to vomit, the patient's consciousness remained clear, she was oriented in place and time).A characteristic sign of AFLP in the observed patient was a progressive increase in leukocytosis, anemia, hypoproteinemia, as well as oligoanuria and increased levels of creatinine and urea [2].

In those cases when patients have expressed nausea and vomiting, but there is no jaundice yet, it is often assumed at the prehospital stage that a pregnant woman has food toxic infection.

Increased weakness, lethargy, nausea and vomiting in the absence of other signs of foodborne toxicity infection (fever, loose stools, abdominal pain, etc.), as well as the appearance of an admixture of hematin in the vomit (vomiting of "coffee grounds") and other manifestations of the initial stage of DIC-syndrome made it possible to exclude foodborne toxic infection and to undertake urgent delivery in connection with AFLP. In this case, the delivery, carried out at the very beginning of the disease, contributed to the successful outcome of the disease. The difficulty in diagnosing AFLP at the prehospital stage is that pregnant women are hospitalized with a wide variety of diagnoses: cholecystopancreatitis, influenza, ARVI, preeclampsia, foodborne toxicity [7]. DIC syndrome develops in many severe pathological processes, especially rapidly in pregnant women; it cannot be considered pathognomonic only for AFLP. However, in combination with other symptoms of the initial stage of blood clotting disorders, it will be possible to suspect AFLP with a sufficient degree of probability. Many cases of AFLP developed at first as a sluggish preeclampsia, which often occurs in a pregnant woman in the third trimester, but only with AFLP, this process acquires a completely different quality. Masquerading as viral hepatitis, Foodborne toxic infection, and other diseases, AFLP leaves too little time for differential diagnosis [12, 13]. Due to objective reasons, laboratory tests often "do not have time" by the time it is necessary to make a decision on the choice of obstetric tactics. In addition, clinical medicine does not have tests that could confirm the development of AFLP; tests can rather indicate the absence of other diseases with which it has to be differentiated. A quick and accurate answer to all questions could be given by a puncture biopsy of the liver, which many researchers recommend to carry out in order to establish a diagnosis [4]. However, the threat of bleeding in developing DIC syndrome limits the use of puncture biopsy, in addition, this technique is not routine in all obstetric and infectious diseases clinics [8,11].

Thus, knowledge of the peculiarities of the course of this formidable complication of the third trimester of pregnancy should contribute to improving the tactics of treating AFLP, the main element of which is the fastest and most careful delivery with the subsequent complex of therapeutic measures aimed at correcting existing disorders of various organs and systems, which can reduce the incidence of obstetric pathology, indicators of perinatal morbidity and mortality, reduce the number of embryo and fetopathies and ensure the birth of healthy children.

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