

## PATHOLOGICAL ANATOMY OF ACUTE FATTY HEPATOSIS OF THE LIVER OF PREGNANT WOMEN

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### Abstract

Acute fatty liver of pregnancy (AFGP) is a rare fatal liver injury, the etiology and pathogenesis of which are not fully understood. In this work, liver morphology and immunohistochemistry were studied in AFGP cases encountered in 2005-2022. In total, in 11 cases, the diagnosis was confirmed on the basis of clinical and morphological signs characteristic of this disease, the clinical signs of some of them were based on the results of morphological examination of the liver.

**Keywords:** pregnancy, preeclampsia, liver, fatty dystrophy, HELLP-syndrome, Sudan, morphology, immunohistochemistry.

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### INTRODUCTION

Acute fatty liver of pregnancy (AFGP) is a rare fatal liver injury with poorly understood etiology and pathogenesis. Its frequency is found in 7000:1 - 16000:1 of pregnant women. AFGP in most cases develops at 32-36 weeks of pregnancy. Despite the development of modern medicine, the death rate from it reaches 23% (1,2). Accumulation of fat in liver cells is the presence of a state of liver failure due to excessive intake of free fatty acids (FFA), slow down of their  $\beta$ -oxidation, high absorption of FFA in the intestine, violation of lipoprotein synthesis and other diseases. Liver tissue normally contains up to 5% fat, and increases to 19% in AFGP. (3, 4). AFGP is not an absolute disease for pregnant women, most scientists believe that it is a form of fatty liver dystrophy, and the reasons leading to it may be as follows: toxic substances and drugs, metabolic disorders, endocrine diseases, including diabetes and other diseases. Clinically, liver damage can have the following forms: excessive recording of pregnancy, hepatic cholestasis, acute fatty liver dystrophy, preeclampsia and HELLP-syndrome. Macroscopically, the liver is slightly enlarged, pale yellow in color. Under microscopy, hepatocytes are swollen and enlarged, small and large fat droplets are detected in the cytoplasm, in which the cell nucleus is located in the center. Liver architecture is intact. The morphological specificity of this disease is the absence of necrosis in the liver tissue and the absence of inflammatory foci in its stroma, and it differs from viral hepatitis by these symptoms. (5,6).

**Purpose:** clarification of morphological and changes in the liver in acute fatty hepatitis of pregnant women.

**Material and methods.** In 2005-2022, the livers of patients with AFGP, who were found in the practice of the Republican Pathological Anatomy Center of the Ministry of Health of the Republic of Uzbekistan, were studied by macroscopic, microscopic and immunohistochemical methods. Clinical and anamnestic data were studied as a result of analysis of medical history and autopsy report. Histological sections were prepared from paraffin-embedded sections of the liver removed during autopsy and

processed with hematoxylin-eosin stain. In recent years, sections from autopsied livers have been frozen, histological sections prepared on a cryomicrotome, and stained with sudan-III. Histological preparations were studied under a binocular light microscope, and photomicrographs were taken from the necessary areas.

**Research results and their discussion.** In pregnant women with AFGP, which we studied morphologically, the diagnosis was confirmed in the clinic according to the "Swansea" criteria. According to this system, the following signs are considered, if there are 6 or more of them, the diagnosis of AFGP is made. 1. Vomiting, 2- abdominal pain, 3- polydipsia and polyuria, 4- encephalopathy, 5- transaminase increase, 6- increased bilirubin, 7- hypoglycemia, 8- increased uric acid, 9- liver dysfunction, 10- increased ammonia levels, 11- leukocytosis, 12- coagulopathy, 13- ascites, 14- microvesicular steatosis on biopsy. 7 patients diagnosed with AFGP were confirmed to have signs from 6 to 11 according to the "Swansea" system.

1- example: Patient G., 23 years old, gave birth to a boy by cesarean section on 08.05.2022. 2 days after birth, the following clinical signs were disturbing: weakness, lower abdominal pain, nausea, recording, jaundice, encephalopathy, hyperbilirubinemia, hypoglycemia, leukocytosis DIC syndrome, thrombocytopenia were observed. Based on these symptoms, a diagnosis of AFGP was made. At autopsy, it was found that the liver was macroscopically enlarged and pale yellow in color. In histology, hepatocytes were enlarged, small and large fat droplets appeared in the cytoplasm, and the nucleus of all hepatocytes was located in the center. Liver architecture is intact. The processes of necrosis and necrobiosis in the liver parenchyma, as well as the absence of inflammatory infiltrate in the interstitial tissue, were found. Based on these characteristic morphological changes, the diagnosis of AFGP was confirmed.

When the livers of women who died of acute fatty liver of pregnancy were stained with Sudan-III, it was found that the histographic architecture of the liver was not disturbed. In the liver tissue, the central vein and portal triad vessels are well defined, they consist of connective tissue cells and fibers that make up the usual vessel wall and the surrounding stroma. Signs of inflammation, that is, lymphohistiocytic cells, are not detected in them. Only the walls of blood vessels are slightly thickened due to edema and dystrophy. Liver parenchyma is slightly swollen due to swelling, sinusoids and space of Disse are enlarged. The main changes, i.e. liver cells positively stained with sudan, are well defined mainly in the 3rd morphofunctional area of the lobules, in the centrolobular area (Fig. 1). When studied under a microscope lens, it is found that the cytoplasm of liver cells is filled with sudan substance, which is stained yellow (Fig. 2). However, although the cytoplasm is affected by parenchymatous fatty dystrophy, it is determined that the nuclei of hepatocytes are located in the center of the cell, and this sign is a characteristic sign of acute fatty hepatitis of the liver. In addition, the absence of signs of inflammation in the liver tissue, that is, stroma-blood vessels, confirms the disease of acute fatty dystrophy.

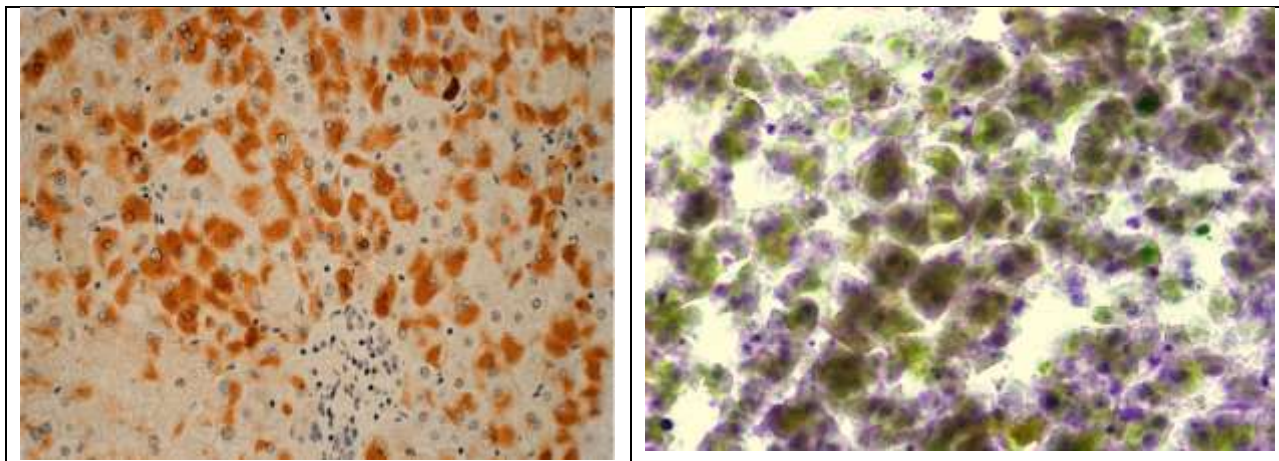


Figure 1. AFGP, parenchymatous fatty dystrophy of liver lobe 3-morphofunctional area. Paint: sudan-III. X: 10x10.

Figure 2. AFGP, cytoplasm of hepatocytes is stained yellow with water dye. Paint: sudan-III. X: 10x40.

Example 2: Patient N, 32 years old, gave birth to a boy by cesarean section on 24.10.2019. Immediately after childbirth, the following clinical symptoms began to bother. Symptoms of preeclampsia, namely hypertension, headache, visual impairment, epigastric pain, nausea, vomiting, jaundice, blood hemolysis, thrombocytopenia, DIC syndrome were observed. Based on these clinical signs, the following diagnosis was made: HELLP-syndrome, acute fatty dystrophy of the liver. Morphologically, the jaw is enlarged, pale yellow in color, and the edges are blunt. In histology, hepatocytes are swollen with vacuolation, fatty dystrophy with small droplets in their cytoplasm. Liver tissue contains small foci and large massive foci of hemorrhage. Based on these characteristic morphological changes, the diagnosis of HELLP-syndrome and AFGP was confirmed.

The results of microscopic examination of the liver showed that when HELLP-syndrome and AFGP were combined, the main changes were developed in blood vessels and interstitial tissue. In this case, the central vein and sinusoids are sharply expanded, full, the walls of most of them are cracked, and blood is poured around them. That is, when the liver is viewed under a microscope, it is determined that erythrocytic lakes have appeared in the center of the lobes as a result of massive hemorrhages (Fig. 3). As a result, it is observed that the interstitium of the liver tissue has expanded, swelling, plasma and erythrocytes have appeared in its contents. At the periphery of the lobes, that is, in the periportal area, the liver columns are deformed, some of them are broken, and fat droplets are detected in the cytoplasm of hepatocytes. When viewed through a large lens of a microscope, it is observed that columns of liver cells are broken, and hepatocytes are located separately. This morphological sign is a histological change that develops in the liver in a state of shock and is also called a shock liver. In this case, hepatocytes break their desmasomal connections, each one is located separately, and necrobiotic changes develop in its cytoplasm. Due to the combination of HELLP-syndrome and AFGP, it is determined that in the liver parenchyma, that is, in the cytoplasm of hepatocytes in a state of shock, there are fat deposits stained with Sudan yellow color (Fig. 4). In this case, it is determined that fat drops occupy the cytoplasm of some hepatocytes completely, while in other hepatocytes they are located in a part of the cytoplasm. The nuclei of hepatocytes are located in the center of the cell and most of them are enlarged and hyperchromic.

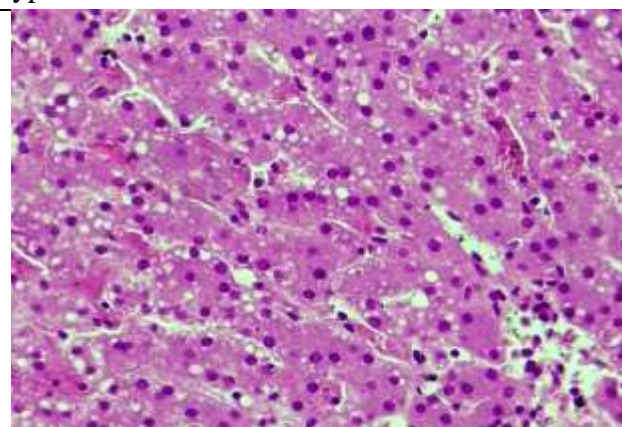


Figure 3. A case where HELLP-syndrome and AFGP are combined. There are massive hemorrhages in the center of the liver lobes. Paint: G-E. X: 10x10.

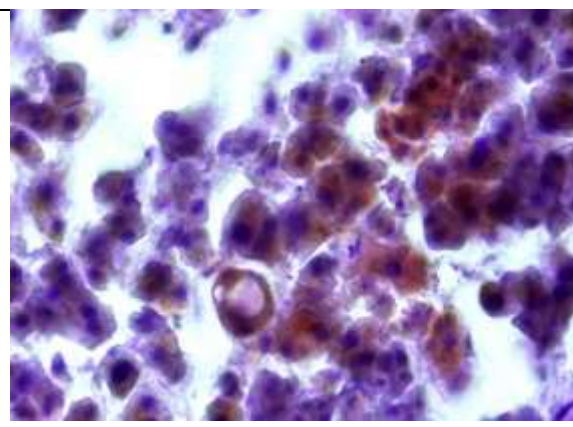


Figure 4. A case where HELLP-syndrome and AFGP are combined. Oil droplets in the cytoplasm of hepatocytes are stained yellow with Sudan. Paint: sudan-III. X: 10x40.



### Summary

In the medical records of pregnant women who died of liver failure, the presence of 6 or more clinical signs, indicated by the “Swansea” system, confirmed acute fatty liver disease.

If the liver is macroscopically slightly enlarged, pale yellow in color, microscopically, hepatocytes are swollen and enlarged, there are small and large fat droplets in the cytoplasm, the nucleus of hepatocytes is located in the center, the architecture of the liver is intact, and there are no necrosis and inflammatory foci in the stroma, it is considered a AFGP disease.

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