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CYTOMORPHOLOGICAL CHARACTERISTICS OF BONE MARROW IN PATIENTS WITH LIVER CIRRHOSIS

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Summary: *the liver cirrhosis of* HCV etiology was accompanied by more significant changes in the process of hemopoiesis of all germs in the bone marrow, in contrast of the liver cirrhosis HBV etiology. There is hyperplasia of the red bone marrow germs, depression of the megakaryocytic germ and inhibition of cells of the granulocyte series.

Keywords: *liver cirrhosis, bone marrow.*

Introduction. Hemostasis is a function of the body that, on the one hand, ensures the preservation of blood in the bloodstream in a liquid state, and on the other hand, stops bleeding and prevents blood loss in case of damage to blood vessels. The hemostasis system actively responds to various exogenous and endogenous influences, it may have congenital and acquired functional disorders - "diseases of the hemostasis system" [1].

The liver plays a central role in maintaining hemostasis, since most of the coagulation factors, anticoagulant proteins, components of the fibrinolysis system,

and thrombopoiesis stimulators are synthesized by hepatocytes. A decrease in the production of blood coagulation factors by liver cells plays a key role in changes in hemostasis and the occurrence of hemorrhagic syndrome in liver diseases. In the occurrence of hemostasis disorders in liver diseases, complex mechanisms of interaction between platelets, coagulation factors, and the fibrinolysis system are involved [5].

Consequently, chronic or acute liver diseases often have a profound effect on the hemostasis system. Violation of the delicate balance of blood coagulation factors is associated with the development of bleeding [4, 6].

Bleeding that occurs in patients with liver cirrhosis (LC), bleeding from varicose veins of the esophagus, hematomas, hemorrhagic purpura, epistaxis, bleeding from the gums, menorrhagia are an urgent clinical problem [3]. The addition of coagulopathy, vascular endothelial dysfunction and platelet disorders in liver pathologies leads to a decrease in the hemostatic reserve of the liver and worsens the course of the disease. This is manifested by a decrease in the concentration of fibrinogen, a prolongation of the active partial thromboplastin time, and a violation of the adhesive and aggregation properties of platelets [2].

Purpose of the study: cytomorphological characteristics of the bone marrow in patients with liver cirrhosis of viral etiology.

Materials and methods. Clinical studies were carried out in the department of hepatobiliary pathology of the 1st clinic of the Tashkent Medical Academy during 2018. The study included 29 patients with liver cirrhosis of viral etiology who did not receive antiviral therapy. When establishing the diagnosis of liver

cirrhosis of viral etiology, anamnesis data, characteristic clinical syndromes, and data from laboratory and instrumental studies were taken into account. Mandatory was the detection of hepatitis virus markers by ELISA, PCR blood tests, determination of hepatitis B virus (HBV) DNA and hepatitis C virus (HCV) RNA. The diagnosis of liver cirrhosis and the degree of hepatocellular insufficiency was established according to the Child-Pugh classification based on diagnostic criteria.

Group I consisted of 15 patients with liver cirrhosis HBV etiology, group II - 14 patients with liver cirrhosis HCV etiology, Child-Pugh class B, in the stage of decompensation. Among the 29 patients included in the study, there were 17 (58.6%) men and 12 (41.4%) women. The age of the patients ranged from 21 to 60 years, the average age of the examined was 48.2 ± 12.1 years. Among patients, people of working age accounted for 43.97%.

The control group included 11 apparently healthy individuals with no history of liver damage and fatty hepatosis, with negative results for markers of hepatitis B and C.

Bone marrow was obtained by sternal puncture according to the Arinkin method using a Kassirsky needle. A smear was prepared from the resulting smear and a cytological examination of the bone marrow was performed, counting the number of cells of all hematopoietic lineages.

Main results. When studying the myelogram parameters of various groups of liver cirrhosis of viral etiology, noticeable changes were revealed in the myelogram parameters of groups I and II compared with the control. In group I, a pronounced increase in the number of immature erythrocyte precursors was noted

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in the red bone marrow - the total number of erythroid cells exceeded the control values by almost 16.68%. At the same time, the number of polychromatophilic normoblasts with delayed maturation at this stage was increased, which indicated a violation of the maturation of erythroid cells at the stage of polychromatophilic normoblasts.

In group II, a pronounced increase in the number of immature erythrocyte precursors was noted in the red bone marrow - the total number of erythroid cells exceeded the control values by 18.88%. At the same time, against the background of a significant decrease in the number of oxyphilic normoblasts, a 3-5-fold increase in the number of pronormoblasts and basophilic normoblasts was observed. This indicated that there was a pronounced inhibition of the maturation of erythroid cells at the stage of pronormoblasts and basophilic normoblasts (table 1).

Table 1.

Cytological analysis of red bone marrow germ of patients with liver cirrhosis of viral etiology.

Bone marrow cells	**Control group,(n=11)**	**Group I (n=15)**	**II group (n=14)**
All erythroid cells, %	23,22 ± 2,2	39,9±3,7***	42,1±2,7***
Erythroblasts, %	1,43 ± 0,23	2,70±0,27***	3,81±0,28***
Pronormoblasts, %	1,77 ± 0,12	3,72±0,31***	10,24±0,34***
Basof. normoblasts, %	4,73 ± 0,08	6,25±0,22***	14,42±0,65***
Polychromatophilic normoblasts, %	9,25 ± 0,8	19,65 ± 0,41***	11,22±0,38*
Oxyphilic normoblasts,%	6,04 ± 0,13	7,58 ±0,36***	2,41±0,12***
maturation index	0,66 ±0,007	0,68±0,003*	0,28±0,002***

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Note: *-P<0.05, ***-P<0.001 significant in relation to the control group.

Analysis of the bone marrow megakaryocytic series showed that in group I, the number of megakaryocytes in the bone marrow was increased, which had a compensatory character for producing more platelets and maintaining their number in the blood. In the II group of patients with HCV cirrhosis, the number of megakaryocytes was normal. At the same time, in group I of HBV etiology, platelet-containing and platelet-lacing active megakaryocytes prevailed in the bone marrow, which indicated the normal production of platelets by megakaryocytes. In group II, in the bone marrow, bare-nuclear megakaryocytes were more than 2 times and inactive megakaryocytes 1.5 times more than in the control group. At the same time, the number of platelet-containing megakaryocytes and megakaryocytes with platelet lacing was reduced by almost 2 times. These data indicate a significant impairment of platelet production in the bone marrow in HCV cirrhosis of etiology (Table 2).

Table 2.

Analysis of the megakaryocytic row of the bone marrow

Megakaryocytes	**Control group**	**I group**	**II group**
Naked megakaryocytes,%	12,3±1,1	19,6±1,3***	27,2±0,8***
Inactive megakaryocytes,%	24,1±1,6	24,5±1,5	36,4±0,9***
Platelet containing megakaryocytes,%	33,3±1,8	26,5±1,9	19,8±0,6***
Megakaryocytes with platelet	30,3±1,7	29,9±2,1	16,6±0,5***

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lacing,%			

Note: ***-P<0.001 significant in relation to the control group.

This indicated that in the first group of patients, platelet production in the bone marrow was not impaired, and in HCV cirrhosis of etiology, there is a pronounced inhibition of platelet production in the bone marrow with a compensatory increase in the number of inactive megakaryocytes.

Cytological analysis of the leukocyte series showed that in group I the total number of neutrophilic granulocytes was reduced and was lower than the control group by 6.39%. At the same time, the number of stab and segmented neutrophils decreased especially significantly, which, respectively, turned out to be lower by 6.43% and 3.78% lower than the control figures.

In group II, the total number of neutrophilic granulocytes also decreased, and was lower by 13.57% of the control values. At the same time, as in group I, the number of stab and segmented neutrophils significantly decreased, which were respectively lower by 7.43% and 4.18% of the control figures (table 3).

Table 3

Leukocyte series of the bone marrow of patients with liver cirrhosis of viral etiology

Cells	**Control group (n=15)**	**Group I (n=15)**	**Group III (n=14)**
Blasts, %	1,55 ± 0,12	1,51±0,09	1,34± 0,11
All neutrophils, %	54,86±0,30	43,47±3,1**	39,29±4,4**
Promyelocytes, %	3,87 ± 0,16	3,26 ±0,11**	3,22 ± 0,14**
Myelocytes, %	10,53 ± 0,19	9,65 ± 0,15**	8,58 ± 0,17***
Metamyelocytes,%	14,05 ± 0,88	14,36 ± 0,97	12,29 ± 0,65

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Stab,%	16,88 ± 0,27	10,45 ±1,5***	9,85 ± 1,2***
Segmented,%	9,53 ± 0,21	5,75 ±2,3***	5,35 ± 0,31***
maturation index	0,93 ±0,008	0,50±0,005***	0,58±0,009***
Eosinophilic cells,%	1,52 ± 0,19	1,13 ± 0,12	1,50 ± 1,7
Basophilic cells, %	0,53 ± 0,07	0,42 ± 0,08	0,37 ± 0,6
Lymphocytes, %	10,30 ± 0,29	6,30 ± 016***	7,44 ± 1,5***
Monocytes, %	6,02 ± 0,18	5,19 ± 0,54	5,77 ± 0,46
Plasma cells,%	0,57 ± 0,11	0,39 ± 0,11	0,62 ± 0,14
Reticular cells, %	1,43 ± 0,26	1,69 ± 0,32	1,57 ± 0,24

Note: **-P<0.01,***-P<0.001 is significant in relation to the control group.

The foregoing suggests that in liver cirrhosis, not only a violation of the process of maturation of erythroid cells takes place, but neutrophilic granulocytopoiesis also suffers to a large extent, which manifests itself in the form of inhibition of the differentiation of neutrophilic cells, which is more pronounced in liver cirrhosis of HCV etiology. It should be noted that during this period, the quantitative indicators of lymphocytes, megakaryocytes, eosinophilic and basophilic granulocytes did not significantly differ from the control figures. On smears of red bone marrow, large macrophages were often detected, in the cytoplasm of which there were remains of destructive cells. Reticular cells were relatively rare, and their average number did not differ significantly from the control.

It should be noted that in response to the delay in granulocyte differentiation, a compensatory increase in the number of mitoses of granulocytic germ cells was observed, which exceeded the control data by almost 30%. The number of eosinophilic and basophilic granulocytes remained without significant changes.

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Findings:

1. Cirrhosis of the liver of HCV etiology was accompanied by more significant changes in the process of hemocytopoiesis of all germs in the red bone marrow, in contrast to cirrhosis of the liver of HBV etiology.
2. In liver cirrhosis of HCV etiology, there is hyperplasia of the erythroid germ of the bone marrow, due to a delay in the process of differentiation of these cells at the level of pronormoblasts and basophilic normoblasts. In liver cirrhosis of HBV etiology, hyperplasia of bone marrow erythroid cells occurs on more mature cells, due to a delay in the differentiation process at the level of polychromatophilic normoblasts.
3. Analysis of the bone marrow megakaryocytic series showed that in viral etiology liver cirrhosis, depression of this germ is observed, which is more pronounced in HCV cirrhosis.
4. With cirrhosis of the liver, neutrophilic granulocytopoiesis also suffers, which manifests itself in the form of inhibition of the differentiation of neutrophilic cells, which is more pronounced in liver cirrhosis of HCV etiology.

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