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COMPARATIVE ANALYSIS OF LABORATORY PARAMETERS OF HEMATOPOIESIS AND HEMOSTATIC STATUS IN PATIENTS WITH POLYCYTHEMIA AND ESSENTIAL THROMBOCYTHEMIA.

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Relevance of the problem: Chronic myeloproliferative diseases (CMP) are a group of clonal hematological diseases that occur at the hematopoietic stem cell level and are characterized by the proliferation of one or more myelopoiesis cell lines in the bone marrow with signs of preserved terminal differentiation. The causes of chronic myeloproliferative pathologies are not reliably known. Clinicalmanifestations of this group of pathologies are usually not specific and require careful differential diagnosis with other diseases. Most often, patients complain of: rapid fatigue, weakness, chronic fatigue; unexplained weight loss; stomach discomfort; bruising; swelling of the extremities; joint pain; hearing disorders; discoloration of the skin; periodic fainting; enlarged and slightly painful liver and spleen; persistent increase in body temperature to subfebrilenumbers* intermittent lack of air; bowel disorders; increased sweating; heaviness in the hypochondrium. In addition, the time factor also has a certain value – with age, the probability of the appearance of this disease significantly increases. Patients with true polycythemiaией and эссенциальной essential thrombocythemia have a high predisposition to the development of thrombosis and bleeding, which are often found in the late stages of the disease.

Purpose of the study. The aim of the study was to determine the differences between the parameters of the general blood count and coagulogram in patients with IP and ET. These research methods are mandatory and often used in practice and in the differential diagnosis of these pathologies at the early stages.

Literature review:

Myeloproliferative diseases (MPD) are clonal diseases that occurникающие at the hematopoietic stem cell level, are characterized by proliferation of one or more myelopoiesis cell lines in the bone marrow with signs of preserved terminal

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differentiation, and are accompanied by changes in peripheral blood parameters [1, 2].

True polycythemia – IP (syn.: erythremia, Wakez's diseaseВакеза, true polycythemia red) is a clonal MPD that is characterized by proliferation of erythroid, granulocytic, megakaryocytic myelopoiesissprouts, with predominant proliferation эритроидногоof erythroid hematopoietic sprouts (panmyelosis), an increase in red blood cell counts and an increase in hemoglobin concentration, thrombocytosis, leukocytosis in the peripheral blood (pancytosis), independence of erythropoiesis from normal regulatory mechanisms. Almost all patients are carriers of the JAK2V617F mutation or another functionally similar mutation.

Essential thrombocytemia-ET (syn.: primary thrombocytosis, idiopathic thrombocytosis, hemorrhagic thrombocytemia) is a clonal MPD with uncontrolled proliferation of megakaryocytes, characterized by an increased number of large and giant megakaryocytes in the bone marrow, peripheral blood thrombocytosis (more than 450 × 109/L), and a high risk of thrombosis and/or bleeding.

The etiology of MPZ has not yet been established. The leading hypothesis is the multi-stage occurrence of the disease, where the predispositionto disease is realized under the influence of external factors that damage the genome of a normal cell and lead to its malignant transformation. Despite the fact that significant progress has been made in recent years in deciphering the molecular and genetic mechanisms of Ph-negative MPZS, the initial mutation leading to malignancy of a hematopoietic cell is unknown [3]. The discovery of the V617F mutation in the JAK2 gene in 2005 was a significant step in understanding the biological features of Ph-negative MPZS. Practically, all patients with IP have JAK2 gene mutation: in 96% of cases, JAK2V617F mutation (exon 14), and in 2% of cases, JAK2 gene mutation in econ 12 is detected [4]. The JAK2V617F mutation is detected in 55% of ET cases and is present in approximately 45-68% of PMF cases. Whereas mutation in exon 12 of the JAK2 gene is practically absent in ET and PMF [5, 6]. In addition to mutations in the JAK2 геневы-являют, mutations in other genes also occur in patients with MPD. Mutations of the MPL gene occur in 4% of cases in ET, in 8% of cases in PMF, and rarely in IP. Moreover, the most frequent mutations are MPLW515L/K in exon 10 [6, 7].The MPLS505N mutation is detected in both ET and hereditary thrombocytemia [8]. These му-тацииmutations are not strictly specific for MPZ and have a secondary genesis in the chain of genetic со-бытийevents. In 2013, data on the diagnostic significance of somatic mutations in exon 9 of the CALR gene encoding the calreticulin protein were published [9, 10]. More than 36 different types of mutations in this gene have been identified, which lead to the formation ofdefective protein. In vitro studies vitro, cells expressing the mutated genehave the ability of cytokine-independent growth in culture, which is probably

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associated with the activation of proteins of the STAT (signal transducer and activator of transcription) signaling pathway. In patients without mutations in the JAK2 and MPL genes, mutations in this gene were detected in 67% of cases in ET and 88% in PMF. Other authors also found an extremely вы-high frequency of CALR gene mutations in patients with MPD (in 70-84% of cases in the absence of JAK2 gene mutation). At the same time, CALR mutations were detected in 8% of cases in myelodysplastic синдposyndrome (MDS) and in isolated cases in other myeloid neoplasms. It is important that in no case of non-myeloid diseases, мутациимutations in this gene were detected [9, 10].Mutations in the JAK2, MPL, and CALR genes have important diagnostic significance. Their detection indicates the clonal nature of the disease and helps in the differential diagnosis of IP, ET, PMF from a number of other myeloid neoplasms, as well as secondary erythrocytosis and thrombocytosis. Along with this, the significance of these mutations in the prognosis of MPZ is actively studied. Despite a number прове-денныхof studies conducted, it is not possible to draw an unambiguous conclusion about the prognostic significance of the JAK2V617F allele load in IP, ET, and PMF. The question of the impact ал-of allelic load on survival or progression IP and ET with outcome in myelofibrosis also need to be studied [11]. Other mutations are also detected in IP, ET, and PMF: TET2, IDH1 / 2, ASXL1, DNMT3A, and others [3]. None of them is specific for classical Ph-negative MPZS, and their pathogenetic significance is being investigated. Molecular genetic disorders in Ph-negative MPZS lead to activation of the JAK-STAT signaling pathway. This results яв-ляетсяin increased proliferation and an increase in thenumber of red blood cells, white blood cells, and peripheral blood platelets in IP, or isolated thrombocytosisin ET. The pathogenesis of PMF is complex and consists of a chain of events, the primary of which is the appearance of a pathological clone. Итвестноis known that monocytes and megakaryocytes in patients with PMF activelyproduce many cytokines (TGF-β, FGF, VEGF, ANG1, OPG, BMP4), the excess of which stimulates fibrosis, neoangiogenesis and leads to osteosclerosis. Along with this, the connection of stem cells with the microenvironment is disrupted, which contributes to the appearance of extramedullary оча-говfoci of hematopoiesis, primarily in the spleen and liver. Massive cytokine release is one of the causes of tumor intoxication symptoms, which leads to a significant deterioration in the quality of life of patients with PMF [12]. Clonal proliferation of myeloid cells in Ph-negative MPZS can also сопровобе accompanied by secondary inflammation with changes in the bone marrow stroma and abnormal выра-боткойcytokine production. миелофиброза, как первичного, так и вторичного, остеосклероза и ан-гиогенезаTransforming growth factor beta (TGF-β) of myeloid progenitors-ков, ростовой фактор вырабатываемый , platelet-derived growth factor (PDGFR), and endothelial

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vascular growth factor (VEGF) are involved in the development of both primary and secondary myelofibrosis, osteosclerosis, and angiogenesis [13]. Abnormal production of cytokines, chemokines, and metalloproteinases can be involved in the pathological intercellular interaction of neutrophils, monocytes, and megakaryocytes, leading to the release of CD34+ myeloid пред-precursors and endothelial cells into the peripheral blood [14]. Ph-CMP is considereda rare neoplasm with a cumulative annual incidence of less than 6 per 100,000 people. According to reports, the annual incidence of IP is between 0.4 and 2.8 per 100,000 people, and the corresponding ET rates are 0.38-1.7 per year for ET.

Research material and methods:

1. Material: 35 patients with true polycythemia(n=20) and эссенциальнаяessential thrombocythemia (n=15) located in the 2nd hematology department of the Republican Specialized Scientific-and Practical Medical Center of Hematology (RSNPMCH), medical history, venous blood.

2. Methods: statistical analysis of laboratory data: ototal blood count (hemoglobin, red blood cells, white blood cells, platelets, ESR), coagulogram (activated partial thromboplastin time [APTT], thrombin time [TV], international normalized ratio [INR], fibrinogen at the risk of thrombotic or hemorrhagic complications);

Interpretation of the results:

In 35 patients with ET and IP, the following results were obtained in the UAC(Table.1) In patients with IP(177.4) , the hemoglobin level was significantly higher than in patients with ET(153.1875). The indicators of red blood cells ofакthe same type significantly differed 7.69 and 6.57, respectively. The platelet count was higher in patients with ET(853.5) compared to that in patients with IP(621.5). В показателях No significant differences were foundin the coagulogram parameters.(Table 2)

Indicators	ET(15)	IP (20)
Hemoglobin	153.1875	177.4
Erythrocytes	6.574688	7.69
Leukocytes	23.58563	20.23
Platelets	853.5323	621.5
Segmented cores	Segmenton uclear 71.05938	69.25
Eosinophils	2.679844	2.58
Lymphocytes	16.47469	18.5
Monocytes	3.392656	2.165

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ESR	9.495313	4.54

Table 1

Table 2

Indicators	**ET indicators**	**IP**
APTT	44,19355	43,83929
PTV	83,11111	83,96795
TPKG	12,4425	12,91912
FP	4,339655	4,215192
FA	219,0909	227,8125

Conclusions: 1.On the basis of the study, it was revealed that in MPD, significant changes in the UAC and coagulogram of patients are determined in comparison with normal indicators. In patients with true polycythemia, hemoglobin and red blood cell counts are higher , and platelets are higher in patients with essential polycythemia. It was found that there were no clear differences in the coagulogram parameters in patients with IP and ET нет.

2.Making conclusions, it should be noted that changes in the UAC and coagulogram make возможностіt possible to assume the presence of IP or ET. For differential diagnosis between ET and IP, the UAC and coagulogram data are not sufficient anda number of in-depth studies are necessary .

Early differential diagnosis and the correct treatment plan contribute to a shorter recovery time.

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