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Efficacy of Splenectomy for Aplastic Anemia

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Abstract: ***The article presents the results of a study of 16 patients with aplastic anemia who were treated in the hematology department of the Republican Clinical Hospital for 3 years. The efficacy of immunosuppressive therapy and splenectomy in this category of patients was assessed by statistical analysis of laboratory parameters at admission and discharge. During the study, data were obtained showing that the results of treatment in the two groups of patients did not have statistically significant differences, therefore, it was determined that there are enough problems to be studied in this field in the future, and solutions to some of these problems were given.***

Keywords: aplastic, anemia, pancytopenia, splenectomy, pathophysiology, lymphocytes.

I. INTRODUCTION

Aplastic anemia is a rare blood disease and occurs with an incidence of 2.0 per 1 million population per year, varying depending on the country from 0.6 to 3.0 per 1,000,000 population per year. Aplastic anemia (AA) is a blood disease characterized by deep pancytopenia, which develops as a result of inhibition of hematopoietic germs with the replacement of bone marrow cells by adipose tissue [1]. The etiology of the disease in half of the cases consists of exposure to various medications, chemical compounds, and viral agents; in other cases, the etiology of the disease remains unclear. In this case, a diagnosis of idiopathic aplastic anemia is made. AA is a disease in which the deficiency of bone marrow hematopoiesis is clearly and fully demonstrated. In most cases, acquired AA can be pathophysiologically characterized as T-cell-mediated, organ-specific destruction of bone marrow hematopoietic cells. One of the possible mechanisms of hematopoiesis inhibition in patients with AA can be presented as follows. At the first stage, damage to hematopoietic target cells occurs through the action of ligan receptors, during the transmission of signals from cell to cell and activation of genes. Subsequently, activated cytotoxic T lymphocytes exert their damaging effects on tissue through the secretion of lymphokines (IF-γ and TNF). The latter have a regulatory effect on Fas receptors, increase the production of IL-2 and thereby lead to polyclonal expansion of T cells. Activation of Fas receptors present on T lymphocytes by Fas ligand ultimately leads to apoptosis of target cells. Some effects of IF-γ are mediated through interferon regulatory factor-1 (IRF-1), which inhibits gene transcription and cell cycle entry. As such, IF-γ is an inducer of multiple genes, including the induction of sodium oxide synthetase and the production of sodium oxide gas, which may be responsible for subsequent toxic effects. Direct intercellular effects between effector lymphocytes and target cells cannot be excluded. Patients usually present with anemic syndrome in combination with hemorrhagic syndrome of the skin and mucous membranes. Quite rarely, the first clinical signs of the disease are either only infection or an anemic syndrome. In some patients, the disease is asymptomatic and is detected incidentally during a routine peripheral blood test; in others, the course of the disease develops acutely from the very beginning. To diagnose AA, the following studies are carried out: general clinical blood test, including reticulocytes; blood smear; myelogram and trephine biopsy; cytogenetic blood test; Hem test or determination of CD55, CD59; liver function tests; viruses: hepatitis A, B, C; Ultrasound of the abdominal organs. An important and still difficult to explain complication of AA is the development of late clonal diseases, which often occur several years after successful immunosuppressive therapy. Paroxysmal nocturnal hemoglobinuria (PNH) occurs in 9% of patients. Of all the diseases that are characterized by pancytopenia, the closest relationship between AA and PNH has been identified.

II. LITERATURE REVIEW

The evolution of AA-PNH syndrome can occur in two directions: 1) PNH can debut in the form of progressive pancytopenia and failure of bone marrow hematopoiesis; 2) patients with primary AA, in whom signs of PNH manifest later [2].

To treat patients with AA, allogeneic bone marrow transplantation, combined immunosuppressive therapy (IST) is used, and one of the treatment methods is splenectomy (SE). Today, there is increasing debate about the choice of treatment method for patients with AA. According to some sources, splenectomy is not considered as a treatment for this category of patients, and the main methods of treatment are allogeneic bone marrow transplantation and combined IST [2].

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At the same time, according to other sources, the role of SE cannot be underestimated, and this surgical intervention is one of the main methods of treatment [1, 3]. Some authors associate the positive effect of splenectomy with the type of surgical intervention, namely the laparoscopic approach when removing the spleen, as less traumatic and with a lower percentage of complications in the postoperative period. Others have histological changes in the spleen, namely changes in the mass of the white pulp [4].

The purpose of the study is to evaluate the effectiveness of the use of immunosuppressive therapy (IST) and splenectomy (SE) in the treatment of patients with aplastic anemia using the example of the experience of the Hematology Department of the Russian Clinical Hospital for 2012-2015.

III. MATERIAL AND RESEARCH METHODS

An analysis of 16 case histories of patients with aplastic anemia who received treatment in the hematology department of the Russian Clinical Hospital in the period from 2012 to 2015 was carried out. The study included the study of medical history, laboratory data over time, and their statistical processing using nonparametric tests (Mann-Whitney, Wilcoxon). The study was conducted in 2 groups: the main group consisted of 11 patients who received only IST. The comparison group consisted of 5 patients who, in addition to IST, underwent SE. The main group consisted of 6 men and 5 women. In the comparison group there were 2 men and 3 women. During the calculation, Fisher's exact test was 1, which indicates the comparability of the groups by gender (Fig. 1). The age of the subjects in the main group ranged from 17 to 35 years, the median age was 23 years (interquartile range (IQR) 18.5-25). In the comparison group, the age of the subjects ranged from 19 to 54 years, the median was 25 years (IQR 24-30). When comparing groups by age using the Mann-Whitney test (p=0.172), no statistically significant differences were found.

Table 1.
Comparison of the study groups according to the content of erythrocytes in peripheral blood over time

Group	Observation stage		According to Wilcoxon
	Er (*10^{12}/l) at the time of admission to the hospital	Er (*10^{12}/l) at the time of discharge	
ain (IST)	1,8 (1,5-2,1)	2,3 (1,85-2,8)	0,092
Comparisons (IST+SE)	2,4 (2,3-3,1)	2,6 (2,5-3,4)	0,715
According to Mann Whitney	0,115	0,115	-

Table 2.
Comparison of the study groups in terms of leukocyte content in peripheral blood over time

Group	Observation stage		According to Wilcoxon
	Er (*10^{12}/l) at the time of admission to the hospital	Er (*10^{12}/l) at the time of discharge	
ain (IST)	1,6 (0,8-2,4)	2,4 (1,7-2,9)	0,074
Comparisons (IST+SE)	3,1 (3,1-3,2)	1,9 (0,6-4,5)	0,138
According to Mann Whitney	0,009*	1,0	-

Note:- differences in indicators are statistically significant (p<0.05)

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Table 3.
Comparison of the study groups in terms of platelet content in peripheral blood over time

Group	Observation stage		According to Wilcoxon
	Er (*10¹²/l) at the time of admission to the hospital	Er (*10¹²/l) at the time of discharge	
ain (IST)	22,1 (16,4-49,8)	55,2 (26,6-102,5)	0,213
Comparisons (IST+SE)	33,8 (24,3-200,0)	52,6 (34,0-100,0)	0,89
According to Mann Whitney	0,145	0,661	

IV. DISCUSSION AND RESULTS

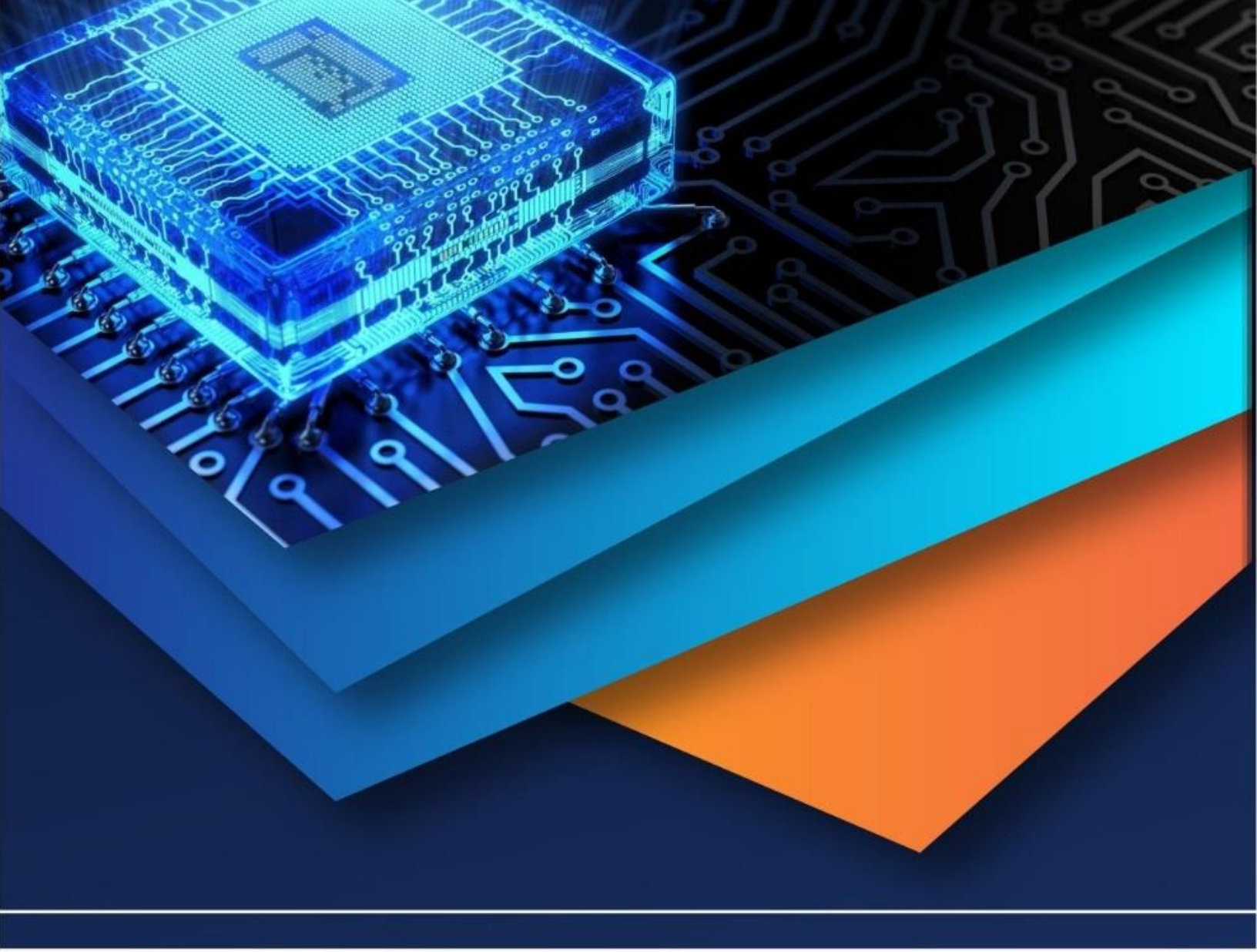
At the first stage of the study, laboratory test data were compared over time. The values were recorded at the time of admission to the hospital and at the time of discharge. As a result, the following data were obtained (Table 1). In both groups there was a trend towards an increase in the number of red blood cells (Er). According to the Wilcoxon test, changes in this indicator are not statistically significant, although for the main group the criterion is very close to the critical level of significance. It should be noted that the dynamics are more pronounced in the main group. When comparing Er levels at discharge, the two groups showed comparable values. The next indicator for which the comparison was made the level of leukocytes (Leu) (Table 2). According to the Wilcoxon test, the differences in Leu indicators over time are not statistically significant, although in the main group the criterion is close to the critical significance value. At the same time, we can observe pronounced positive dynamics in the main group, given that initially the Leu level was statistically significantly lower, which is confirmed by the Mann test
— Whitney (p=0.009). Taking this into account, comparable values of the indicator were achieved at the discharge stage.
The last indicator for which comparison was made was the level of platelets (Thr) (Table 3). According to the Wilcoxon test, the differences in these indicators are not statistically significant, although in the main group the criterion is closer to the critical value than in the comparison group. According to this table, we can observe more pronounced dynamics in the main group of patients with an initial low Thr level. When comparing the Thr level at the time of discharge in the two study groups, the indicators were comparable.
At the second stage of the study, we analyzed the survival of patients with AA depending on the use of SE using the Cox regression method. The resulting graph shows that the risk of death in patients with SE is slightly higher than in patients who did not undergo SE. However, these results turned out to be statistically insignificant, which is confirmed by the Mann-Whitney value (p = 0.736).

V. CONCLUSION

Thus, as a result of statistical processing using nonparametric criteria of laboratory test data (Er, Leu, Thr) over time, the following conclusion can be drawn: when compared at the time of discharge, laboratory test indicators do not have statistically significant differences. According to the results of an analysis of the survival of patients with AA, depending on SE, the risk of death does not have statistically significant differences. The results of treatment of patients with AA using IST+SE and using IST alone do not have statistically significant differences. Based on this, the question that becomes relevant in the future is whether splenectomy should be performed in this category of patients.

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