The morphometric analysis of the erythrocytes in patients with iron deficiency anemia and anemia of malignant growth

D.O. Borysenko, S.V. Vydyborets
Shupik National Medical Academy for Postgraduate Education

The article dealt with the study results of the morphometric erythrocytes changes in peripheral blood. The differential-diagnostic and prognostic importance of the morphometric erythrocytes changes in peripheral blood in patients with iron deficiency anemia and anemia of malignant growth is discussed.
Key words: anemia, erythrocytes, peripheral blood, investigations.

Морфометричний аналіз еритроцитів у хворих на залізодефіцитну анемію та анемію злоякісного новоутворення
Д.О. Борисенко, С.В. Видиборець

У статті висвітлені дані щодо клінічної ролі лабораторного визначення морфометричних змін еритроцитів у периферичній крові. Обмірковується диференційно-діагностичне і прогностичне значення морфометричних змін еритроцитів у периферичній крові при залізодефіцитній анемії та анемії злоякісного новоутворення.
Ключові слова: анемія, еритроцити, периферична кров, дослідження.

Морфометрический анализ эритроцитов у больных железодефицитной анемией и анемией злокачественного новообразования
Д.А. Борисенко, С.В. Выдыборец

Статья посвящена результатам изучения морфометрических изменений эритроцитов в периферической крови. Обсуждается дифференциально-диагностическое и прогностическое значение морфометрических изменений эритроцитов в периферической крови при железодефицитной анемии и анемии злокачественного новообразования.
Ключевые слова: анемия, эритроциты, периферическая кровь, исследования.

The anemic syndrome often occurs as a result of the development and progression of the tumor process, and cytostatic and (or) radiation therapy used to treat cancer, the presence of hemolysis, splenomegaly, hemorrhagic syndrome, hemodilution, ineffective erythropoiesis, the cascade of disorders in iron metabolism regulation in the body of the patient, whose key link is now considered to be the changes in the synthesis of hepcidin [1, 3, 6].

In the erythrocytes of a person in the course of his life changes occur due to gender, age-specific features of metabolism, hematopoiesis [8]. In the hematopoiesis system itself, when pathological conditions and disease development occur, certain functional and morphological changes appear [1, 2, 7]. Iron deficiency anemia (IDA, MKH – D50) is a disease that is accompanied by significant changes in erythropoiesis, qualitative and quantitative changes in erythrocytes, impaired functioning of organs and systems [2, 7, 8]. Fundamentally different mechanisms of formation have anemia of malignancies (malignant anemia, MKX – D63.0), which, no doubt, should affect the particular qualities of erythropoiesis [1, 3, 6]. Among malignant diseases of the urinary system stipulates the urothelial bladder cancer (UBC) [4]. In the available literature, we have not encountered data on the comparison of morphometric changes in erythrocytes in patients with IDA and patients with malignant anemia in malignant diseases of the urinary system, so it prompted us to conduct appropriate study.

The objective: is to conduct a morphometric analysis of peripheral blood erythrocytes in patients with iron deficiency anemia (IDA) and malignant anemia in urothelial bladder cancer (UBC) to identify specific changes and use them in a differential diagnostic practice.

MATERIAL AND METHODS

As the study material blood of 110 patients (58 men and 52 women) was taken. Among them 53 patients (31 women and 22 men) with IDA were examined, they formed the first (I) observation group and 57 patients (36 men and 21 women) with UBC, where the course of the underlying disease was burdened by malignant anemia second (II) observation group. The age of the patients under the survey is from 22 to 69 years. All patients were examined before any treatment was prescribed.

The diagnosis of IDA was verified based on a typical clinical picture (signs of anemic hypoxia and sideropenic syndrome), typical hematologic picture of peripheral blood and indicators of iron metabolism.

The severity of anemia was defined according to the criteria proposed by the National Cancer Institute (USA) as follows:
– mild Hb from 10 to 12 g/dL,
– moderate Hb from 8 to 10 g/dL;
– severe Hb from 6,5 g/dL to 8 g/dl,
– life-threatening Hb below 6,5 g/dL.

Among the patients with IDA, 19 were diagnosed with a mild type, 15 with a moderate, 11 with severe, and 8 with a life-threatening one. Among the patients with malignant anemia 29 were diagnosed with a mild type, 12 with moderate, 10 with severe, and 6 with life-threatening.

The study was conducted in compliance with the main provisions of the Council of Europe Convention on Human Rights

Table 1

Erythrocyte indicators in the examined patients and healthy people, X±m

Indicator	Control group, n=50	I group, n=53	II group, n=57
RBC, 10^{12}/L	4,62±0,05	3,19±0,14*	3,30±0,15*
MCV, fl	86,01±0,47	80,11±0,74*	81,21±0,41*
MCP, pg	28,95±0,11	27,71±0,43	27,73±0,37
MCHC, g/dL	33,12±0,12	34,61±0,04*	34,31±0,04*
RDW, %	13,21±0,06	14,25±0,21*	13,99±0,09*

Note: * − p<0.05 compared with indicators in control group.

Table 2

Indicators of erythrocyte cytometry in patients under the observation, X±m

Indicator	Control group, n=50	I group, n=53	II group, n=57
Average diameter erythrocytes, μm^3	7,22±0,04	6,21±0,12*	6,31±0,03*
Share of micro– and schizocytes, fl	4,81±0,11	30,39±0,63*	14,21±0,23*
Anisocytosis indicator, %	4,01±0,12	17,33±0,12*	7,76±0,13*
Discocytes, %	80,91±0,47	54,29±0,15*	65,11±0,08*
Anomalous forms,%	19,07±0,52	45,71±0,14*	34,79±0,11*

Note: * − p<0.05 compared with indicators in control group.

and Biomedicine, Declaration of Helsinki Ethical Principles for Medical Research and (1964, with further additions, including 2000 version) and the Ministry of Health of Ukraine Order No. 690 dated September 23, 2009. All patients admitted to the hospital were examined with the use of clinical, laboratory, instrumental and special research methods, and were consulted by specialists of related specialties, if necessary. The examination and treatment of patients were performed in accordance with the World Medical Association Declaration of Helsinki (Seoul, 2008), and the relevant orders of the Ministry of Health of Ukraine (No. 281 from 01.11. 2000, No. 355 from 25.09.2002, No. 356 from 22.05.2009 in revision of the Ministry of Health of Ukraine Order No. 574 of 5 August 2009, No. 1118 of 21 December 2012).

The control group consisted of 50 healthy primary donors who had no history of cancer or chronic inflammatory disease. All donors were examined at the State Institution «Blood Transfusion Station of the Southwestern Railway» following the requirements of the «Procedure of medical examination of blood donors and (or) its components», approved by the Order of the Ministry of Health of Ukraine dated 01.08.2005 under No. 385 «On infectious safety of donor blood and its components».

Patients with UBC were conducted with a thorough histological examination of the drugs, taking into account the nature of the tumor margins with the surrounding tissues, the severity of infiltration, the presence of tumor cells in the vessels, the number of mitoses, including atypical ones. In addition, the cellular elements of different maturity (in %): low differentiated (LD), moderately differentiated (MD), highly differentiated (HD) cells were determined in tumors. The degree of malignancy and histologic type of the tumor were evaluated according to the generally accepted criteria.

The research materials were statistically processed according to the relevant programs [5]. The significance of the difference was assessed using the Student's Difference Factor t-test (p<0.05).

RESULTS OF THE STUDY AND DISCUSSION

When analyzing the obtained data, it was found that the erythrocyte indicators in the examined patients were as follows (Table 1):

As it is seen from the data above, significant changes in the morphometric parameters in patients with IDA and malignant anemia with UBC were found in the peripheral erythrina link. Besides, patients from group I showed a significant (p<0.01) increase in RDW compared with patients from group II. We have not found any significant changes in the above indicators depending on the sex and age of the patients from the observation groups I and II (p>0.05). Data on the erythrocyte cytometry indicators in patients under the observation is given in Table 2.

As it is seen from data in table 2, patients in both groups showed a significant increase in the number of transformed erythrocytes (stomatocytes, echinocytes, etc.), and, accordingly, a decrease in the number of normal discocytes. A more significant decrease in the average diameter of erythrocytes, an increase in the proportion of microcytes and an increase in the level of anisocytosis (p<0.05) was found in patients from a group I. In addition, a clear poikilocytosis was found in patients from group I, that showed a significant decrease in the number of discocytes, an increase in the number of echinocytes and irreversibly altered pre-hemolysed forms of erythrocytes.

An increase in the number of echinocytes is always accompanied by an increase in blood viscosity. Moreover, rigid erythrocyte forms, due to their loose contact with the vessel wall, cannot fully participate in a gas exchange, which enhances tissue hypoxic processes. The movement of these cells in the total volume of capillary blood flow slows down, which can create a favorable background for the formation of microtubules. If we take into account that these processes occur in the vessel crease, where pathophysiological and pathobiochemical shifts occur, the significance of these disorders in the formation of anemic hypoxia syndrome in the examined patients of both groups will become more obvious. In the erythrocyte formula in patients from group I, against the background of a decrease in the average size of erythrocyte cell diameter and an increase in anisocytosis due to an increase in the number of microcytes we observed a significant decrease (p<0.01) in the number of discocytes, an increase in the number of echinocytes and irreversibly changed prehemolized erythrocyte forms, that can obviously affect the life span of erythrocytes.

CONCLUSIONS

1. Malignant anemia is an urgent problem in the modern oncology clinic since anemic syndrome is one of the common complications of cancer. Instead, the number of studies

highlighting this problem in cancer of the urinary system is limited. Also, the issues of secondary metabolic disorders in anemic hypoxia in combination with tumor intoxication are insufficiently covered.

2. Malignant anemia at UBC is accompanied by significant changes in the morphometric characteristics of erythrocytes, which is manifested by a decrease in the proportion of discocytes, an increase in the proportion of echinocytes and irreversibly altered prehemolytic forms of erythrocytes.

3. The changes that we have detected in the erythrocyte link of peripheral blood, on the one hand, is a reflection of the peculiarities of hematopoiesis and, in particular, erythropoiesis, and on the other, evidence of deeper pathophysiological disorders in people with malignant anemia while UBC.

4. IDA is characterized by changes in morphometric parameters: a decrease in the average diameter of erythrocytes, an increase in the number of microcytes and an increase in the level of anisocytosis, clear poikilocytosis, which showed a significant decrease in the number of discocytes, an increase in the number of echinocytes and irreversibly changed prehemolized erythrocyte forms.

5. Further study of the pathophysiological and biochemical changes in the erythrocyte link of hematopoiesis with IDA and malignant anemia is a promising area of scientific research. Its implementation will allow optimizing diagnostics, differential diagnosis and pathogenetic treatment regimens in these categories of patients, which, in the end, will obviously lead to an improvement in their quality of life.

Сведения об авторах

Борисенко Дмитрий Александрович – Национальная медицинская академия последипломного образования имени П.Л. Шупика, 04112, г. Киев, ул. Дорогожицкая, 9; тел.: (044) 483-16-61

Выдыборец Станислав Владимирович – Национальная медицинская академия последипломного образования имени П.Л. Шупика, 04112, г. Киев, ул. Дорогожицкая, 9; тел.: (044) 483-16-61

REFERENCES

1. Andriyaka AA. (2018) Anemia of malignant neoplasm: peculiarities of patient management. Hematology. Transfusiology. Eastern Europe. 4 (2): 223–229.

2. Vidiborets S.V., Andriyaka A.O. (2017) The physiological role of hepcidin as a central regulator of iron metabolism (literature review). Family medicine. 1 (69): 154–157.

3. Matlan V.L. (2015) Anemia in malignancies: differential diagnosis and treatment features. Health of Ukraine; October: 26–27.

4. Titov E.V. (2018) Modern methods for the diagnosis and prognosis of urothelial bladder cancers. Problems of uninterrupted medical education and science. 2 (29): 86–91.

5. Khalafyan A.A. (2014) Modern statistical methods of medical research: monograph. M., 320 p.

6. Shparik Y.V. (2015) Anemia in solid tumors. The health of Ukraine. October: 10.

7. Atanasiu V., Manolesku B., Stoian I. (2007) Hepsidin – central regulator of iron metabolism. E.J.Haematol. 78(1): 3–10.

8. Green JP, Arber DA, Glader B. (eds.) (2014) Wintrobe's clinical hematology. Philadelphia: Lippincott Williams&Wilkins. 2278 p.

Статья поступила в редакцию 19.12.2019