STRUCTURE OF COMORBIDITY IN IDIOPATHIC THROMBOCYTOPENIC PURPLE

Abdiev Kattabek Makhmatovich*; Mamatkulova Feruza Khaydarovna; Shomirzaev Khudoyor Makhmudovich*****

*Teacher,
Department of Hematology,
Samarkand Medical University,
Samarkand, UZBEKISTAN

**Teacher,
Department of Hematology,
Samarkand Medical University,
Samarkand, UZBEKISTAN
Email id: mamatkulovaferuza11@gmail.com

**Teacher,
Department of Hematology,
Samarkand Medical University,
Samarkand, UZBEKISTAN

DOI: 10.5958/2249-7137.2022.00896.5

ABSTRACT

Idiopathicthrombocytopenicpurpura (ITP), orprimaryimmunethrombocytopenia (ITP), isanautoimmuneacquireddisease characterized by isolated thrombocytopenia with a platelet count below 100 x 109/L. It can manifest itself as a hemorrhagic symptom of varying severity - from petechial skin hemorrhages to life-threatening bleeding. Both children and adults get sick. The etiology of ITP is unknown. That's why it's called "idiopathic". Among the trigger factors, the largest group is infections, pregnancy, as well as vaccinations, and stress.

KEYWORDS: *Idiopathic Thrombocytopenic Purpura, B-Lymphocytes, T-Lymphocytes, NK Cells, Macrophages, Group Of Diseases, A Re-Examination.*

INTRODUCTION

It is known that the dominant mechanism for the development of thrombocytopenia in ITP is due to the production of autoantibodies to the structures of the platelet membrane and their precursors - megakaryocytes, which lead to increased destruction of platelets by phagocytes, mainly in the spleen, less often in the liver, and insufficient production of platelets in the bone marrow. ITP patients produce mainly IgG autoantibodies against platelet surface glycoproteins GPIIb/IIIa or GPIb/IX. The process of formation of an immune response to one's own platelets is complex, multi-stage, cyclic. It involves B-lymphocytes, T-lymphocytes, NK cells, macrophages. In addition to antibody formation, a large role in the pathogenesis of ITP is played by subpopulations of T-lymphocytes, the development of an imbalance in the T-cell link of the immune response. A relationship has been found between ITP and some candidate genes, which also indicates the presence of a genetic predisposition to ITP.

Given the associated pathology, the patient develops a certain phenotype of the disease. Thus, the pathogenesis of ITP is associated with profound disorders of the immune system. In this regard, idiopathic thrombocytopenic purpura has been renamed to primary immune thrombocytopenia of unknown etiology. Accordingly, in all other forms, immune thrombocytopenia with a known etiology will be a symptom of other autoimmune diseases – systemic lupus erythematosus (SLE), antiphospholipid syndrome (APLS), rheumatoid arthritis (RA), etc.

Currently, the search for etiopathogenetic mechanisms for the development of this rare pathology continues, which could stratify patients into risk groups for the individualization of treatment tactics.

In the literature, ITP is described as a rare, orphan disease. In the medical world there is no single definition of this group of diseases. In some countries, orphan pathologies are distinguished depending on the number of sufferers, in others – on the availability of treatment methods, in others – only chronic, life-threatening ones are classified as rare diseases.

Medicines developed for the treatment of rare diseases are also called orphan drugs and are included in the list of expensive drugs. The assignment of orphan status to diseases and any drugs is a social and political issue in many countries, as well as in Uzbekistan. Government support for rare disease research has led to breakthroughs in medicine that could not have been achieved under the previously existing funding system.

The main clinical manifestation of ITP is hemorrhagic syndrome, and the prognosis of the course of the disease depends entirely on its severity. The risk of bleeding in patients with ITP is estimated by the number of platelets in the analysis of peripheral blood. According to the registry data, in 70.0% of cases, the platelet count at the onset of the disease ranges from 3 to 30x109/l, among them, 35% have a critical level of platelets (from 3 to 10x109/l) with the risk of developing spontaneous alarming, life-threatening bleeding, which requires immediate treatment.

Hemorrhagic syndrome manifests itself in the form of: skin hemorrhages - 77% of cases; bleeding of the oral mucosa - 39%; nosebleeds - 31%; menometrorrhagia - 15% (among women); gastrointestinal bleeding - 7%; hematuria - 4%; intracerebral bleeding - 0.9%, others - 1% (retinal hemorrhage, hemorrhoidal bleeding) [4].

Thus, at the time of diagnosis, about 1/3 of patients have hemorrhagic manifestations corresponding to a severe form of ITP (3-4th degree of bleeding according to the WHO classification). ITP is not a genetic disease, but usually accompanies the patient throughout his life and is incurable. The course of the disease is further complicated by the fact that in 60–70% of patients, after 12 months (chronic phase), the disease becomes chronic, recurrent, and again.

ITP is not a genetic disease, but usually accompanies the patient throughout his life and is incurable. The course of the disease is further complicated by the fact that in 60–70% of patients after 12 months (chronic phase) the disease becomes chronic, relapsing, and hemorrhagic syndrome reappears, requiring an anti-relapse course of therapy.

The diagnosis of "ITP" is a diagnosis of exclusion, i.e., to date, there is no specific test for the disease. Thrombocytopenias of various origins are recorded in a wide range of hematological, non-hematological and congenital diseases, in which isolated thrombocytopenia can be the dominant clinical symptom for a long time. Therefore, to establish the true causes of

thrombocytopenia, it is necessary to conduct an extended diagnostic search at the onset of the disease [5].

The initial approach to diagnosing the causes of thrombocytopenia is based on the patient's history (his underlying medical conditions and previous drug therapy), his objective physical examination, and protocol examination. The protocol for the differential diagnosis of thrombocytopenia developed by us is included in the National Clinical Guidelines for ITP [1]. Most importantly, all the proposed laboratory and instrumental studies exist in routine practice and are mandatory for all patients with suspected ITP.

After excluding other causes of thrombocytopenia, the diagnosis of ITP is based on the following criteria:

- Isolated thrombocytopenia less than 100.0x109/l, registered in at least two consecutive blood tests;
- Absence of morphological and functional anomalies of platelets;
- Absence of pathology of lymphocytes, granulocytes and erythrocytes;
- Normal indicators of hemoglobin, erythrocytes and reticulocytes, if there was no significant blood loss;
- Increased or normal number of megakaryocytes in the myelogram;
- Normal size of the spleen.

It is important to keep in mind: corticosteroids are often prescribed for quick relief of hemorrhagic syndrome without examination according to the protocol, which blurs the true clinical picture of secondary immune thrombocytopenia and affects the true results of immunological tests. According to our department, up to 15–20% of cases in dynamics during a re-examination according to the protocol, the diagnosis of ITP is replaced by another one. The picture of the disease can change over time, in this regard, it is necessary to constantly update data on the patient's condition, differential diagnostics should be carried out at each stage of observation/treatment of ITP. Thus, it is very important to make a differential diagnosis between primary and secondary thrombocytopenia, not only at the onset of the disease, but also with relapse of thrombocytopenia.

Rituximab, another drug for the treatment of ITP, has recently appeared in clinical practice, which was developed for the treatment of hematological malignancies. Rituximab is currently used to treat patients with ITP who are resistant to other therapies. Its use in chronic ITP is based on the removal of autoreactive B-lymphocytes. Rituximab is included as 3rd line therapy. There is about a 60% chance of getting a primary response. But in Russia it is not registered for the treatment of ITP, so the decision is made individually by the medical commission.

In 2018, the US Food and Drug Administration (FDA) approved a new oral drug, a selective small molecule splenic tyrosine kinase inhibitor, fostamatinib, for medical use in patients with resistant ITP. And in 2019, a bioavailable thrombopoietin small molecule receptor agonist for the treatment of adult patients with chronic ITP who had an inadequate response to previous therapy. Both drugs are not registered in Russia for the treatment of ITP. This is perspective.

If different therapy options are unsuccessful in subsequent lines of therapy, it is recommended to use a non-realizing method or conduct complex therapy using immunosuppressants.

As a rule, modern methods of therapy still make it possible to achieve remission of various durations or a state of clinical compensation. But clear prognostic criteria for the course of the disease, response to therapy and outcomes of the disease have not yet been developed due to the nature and unpredictability of the course of the disease.

When starting therapy for chronic, recurrent ITP, it must be remembered that the choice of therapy should be aimed at stopping bleeding of any localization, improving the quality of life of the patient, and not at normalizing the number of platelets at any cost.

In clinical practice, it is important to remember that therapy should always be selected individually for a particular patient, taking into account his age, comorbidity, comorbidities, and also take into account patient preferences. But our practice often collides with the objective realities of life.

Thus, idiopathic thrombocytopenic purpura (ITP) is a rare (orphan) chronic, relapsing disease that significantly impairs the health and quality of life of patients according to assessments of physical, social functioning, and mental state. Bleeding causes fear, anxiety and depression in them with a short-term effect of the therapy and side effects of drugs against the background of long-term treatment with corticosteroids, immunosuppressants.

ITP cannot be completely cured, but can be effectively contained. Modern drugs (thrombopoietin receptor agonists) that have appeared in recent years, with an adequate choice of dose and control of the course of the disease, make it possible to quickly stop the hemorrhagic syndrome, achieve remission of various durations or a state of clinical compensation, prevent the development of severe side effects of treatment, improve the prognosis of the disease, which, naturally, not only increases the life expectancy of patients with orphan diseases, but also its quality. Therefore, it is very important to include them in the therapy of all patients who need it. Today, this equal accessibility is possible only if ITP is included in the federal program for financing high-cost nosology.

REFERENCES

1. Neunert C, Terrell Dr, Arnold Dm, Et Al. American Society Of Hematology 2019 Guidelines For Immune Thrombocytopenia. 2019;3(23):3829–3866. Doi:10.1182/Bloodadvances.201900096
2. Provan D, Arnold Dm, Bussel Jb, Et Al. Updated International Consensus Report On The Investigation And Management Of Primary Immune Thrombocytopenia. Blood Adv. 2019;3(22):3780–3817. Doi:10.1182/Bloodadvances.2019000812
3. Меликян А.Л., Пустовая Е.И., Егорова Е.К., Калинина М.В., Колошейнова Т.И., Суборцева И.Н., Гилязитдинова Е.А., Двирнык В.Н. Дифференциальная Диагностика Тромбоцитопений // Онкогематология. 2017;12(1):78–87. Https://Doi.Org/10.17650/1818-8346-2017-12-1-78-87
4. Меликян А.Л., Пустовая Е.И., Егорова Е.К., Калинина М.В., Колошейнова Т.И., Суборцева И.Н., Гилязитдинова Е.А., Двирнык В.Н. Дифференциальная Диагностика Тромбоцитопений // Онкогематология. 2017;12(1):78–87. Https://Doi.Org/10.17650/1818-8346-2017-12-1-78-87

5. Черников М.В., Куликов С.М., М. А. Русинов М.А. И Соавт. Мультинозологический Регистр Заболеваний Системы Крови. Состав, Структура, Итоги Опытной Эксплуатации // Гематология И Трансфузиология. Т. 59, № 1, 2014, С.

6. Comparative Evaluation Of New Treatments For Immune Thrombocytopeniakm Abdiev, M Ozoda G, On Ruziboeva, Km Shomirzaevnatural Volatiles And Essential Oils (Nveo) 8 (5:), 10160 - 10166

7. Modern Methods Of Treatment Of Hemorrhagic Syndrome At An Early Stage In Patients With Idiopathic Thrombocytopenic Purpurakm Abdiev, Ag Madasheva, Fk Mamatkulovaученый Xxi Века, 41-44

8. Ud Dadajonov, Km Abdiev, Fx Mamatkulova. Innovative Methods Of Treatment Of Immune Thrombocytopenic Purpura In Young Peoplesociety And Innovations, 52-56

9. Км Абдиев, Хх Хамраев Современные Аспекты Диагностики, Лечении, Тактики, Ведения Родов У Беременных С Идиопатической Тромбоцитопенической Пурпурой (Обзор). 2021..Journal Of Reproductive Health And Uro-Nephrology Research, 5-10.

10. Mamatkulova F. X. Mamatova N. T. Ruziboeva.O. N. Prevention Of Anemia In Patients With Tuberculosis. The American Journal Of Medical Sciences And Pharmaceutical Research, 2(11), 62–65.

11. Dadajanov U. D., Mamatkulova F. X., Ruziboeva O. N. Features Of Thrombophilia In Covid-19. European Journal Of Molecular & Clinical Medicine Issn 2515-8260 Volume 07, Issue 03, 202

12. L. S. Makhmonov., F. Kh. Mamatkulova., M. B. Berdiyarova. , K.E. Shomurodov.The Main Causes Of Anemia In Iron And Vitamin B 12 Deficiency Associated With Helicobacter Pylori

13. Makhmonov L. S., Mamatkulova F. Kh., Kholturaeva D. F., Muyiddinov Z. Z.Importance Of Detection Of Hepsidine And Interleukins In Iron Deficiency Anemia. Asian Journal Of Multidimensional Research Issn: 2278-4853 Vol. 11, Issue 4, April 2022