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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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MYELODYSPLASTIC SYNDROME: DIAGNOSIS, TREATMENT AND PROGNOSIS (LITERATURE REVIEW)

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Abstract.

Given the difficulties of diagnosis, the absence of a typical clinical picture of myelodysplastic syndrome accompanied by cytopenia, a high risk of transformation into acute myeloid leukemia, discussion of the formation, terminology, pathogenesis, classification, clinical course and principles of management of this group of tumor diseases is very relevant.

The review article discusses the issues of terminology, pathogenesis, classification and diagnosis of myelodysplastic syndrome (MDS), as well as the principles of management of this category of patients. Due to the absence of a typical clinical picture of MDS, in order to exclude other diseases accompanied by cytopenia, not only routine hematological examination methods are necessary, but also a mandatory cytogenetic examination of the bone marrow. Treatment of patients with MDS should be individualized, taking into account risk group stratification, age and physical status. To improve the quality of life of patients with MDS, epigenetic therapy with azacitidine has an advantage.

Myelodysplastic syndrome is an irreversible tumor process with a clear tendency to transform into acute leukemia. The diagnosis of MDS is always made with caution by excluding other diseases accompanied by cytopenia. To make a diagnosis, not only routine hematological examination methods are necessary, but also a mandatory cytogenetic study of the bone marrow.

The management of patients with MDS is still an unresolved problem. The approach to the treatment of MDS should be individualized and based on the patient's risk group, age, and somatic status. Epigenetic therapy has an advantage when choosing management tactics for MDS in terms of improving the quality of life of patients.

Key words. Myelodysplastic syndrome, diagnosis.

Introduction.

The review article deals with the issues of terminology, pathogenesis, classification, and diagnosis of myelodysplastic syndrome (MDS), as well as the principles of management of this category of patients. Due to the lack of a typical clinical picture of MDS, not only routine hematological examination methods are necessary to exclude other diseases accompanied by cytopenia, but also mandatory cytogenetic examination of the bone marrow.

Treatment of patients with MDS should be individualized, considering the stratification of the risk group, age, and somatic status. To improve the quality of life of patients with MDS, epigenetic therapy with azacitidine has an advantage.

Objective. To acquaint physicians of all therapeutic specialties with diagnostic criteria and principles of management of patients with myelodysplastic syndrome.

Literature review.

Myelodysplastic syndrome (MDS) is a group of heterogeneous acquired clonal hematological tumors united by a common origin from a stem hematopoietic cell with a violation of the differentiation of cells of one, two or three hematopoiesis sprouts. MDS is characterized by cytopenia, signs of dysmyelopoiesis and a high risk of transformation into acute myeloblastic leukemia (AML) [1-5].

In the general population, the prevalence of MDS is 3-15 cases per 100,000 population per year, approximately the same in men and women. The main contingent (more than 80% of patients) are people over 60 years old. Given the steady "aging" of the world's population, it is believed that the number of patients with MDS will only increase in the coming decades [1,3,4,6,7]. According to leading experts, there are currently about 2.5 thousand patients with MDS in Russia. However, there is no centralized registration of patients with MDS, and the detection of the disease remains at a low level. According to different authors, the risk of transition from MDS to acute leukemia is 30% [1,2,8].

MDS is based on various genetic changes, as well as abnormal DNA methylation, which leads to inhibition of the expression of oncosuppressor genes, which in turn leads to multiple disorders of the cell cycle and differentiation [1,6]. The most characteristic changes in chromosomes in MDS include: deletion of the long arm del 5(5q-) - in 27-30%, del 7(7q-) - in 4-10%, monosomy 7(-7) - in 15-25% , trisomy 8(+8) - detected in 20% of patients, monosomy 5(-5) - in 5-10%, del 11(11q) - in 7-11%, Y-chromosome deletion - in 5-10%, as well as translocations t(1; 3), t(1; 7), t(5; 7), t(2; 11), t(6; 9), t(11; 27), inversion of chromosome 3 [9-12].

A certain contribution to understanding the pathogenesis of MDS was made by the epigenomic concept, which describes the role of DNA hypermethylation and impaired histone acetylation in turning off the function of oncosuppressor genes [5,6,8,10-15]. Using next-generation sequencing, it has been shown that repeated somatic mutations are observed in more than 90% of patients with MDS, while the number of mutations is an independent prognostic factor [12,16]. It has been established that driver oncogenic mutations and epigenetic changes, including DNA hypermethylation, play a key role in the emergence of a pathological cell clone in MDS [10,17].

Regulatory T cells (Treg) are known to be involved in the pathogenesis of MDS, which explains the association of this disease with both autoimmune disorders and tumor transformation [9,14]. It is assumed that the weakening of the function of T-cells leads to a violation of the control over an excessive immune response and a violation of immune antitumor surveillance. This explains the fact that in most studies, poor prognosis in MDS is associated with an increase in the number of Treg [18].

The appearance of the term "Myelodysplastic Syndrome" dates back to 1982, when the first generally accepted classification of this disease, developed by the Franco-American-British Group (FAB), was presented. For decades, scientists have described this disease under various names. It is known that since 1923 it has changed many names: from Di Guglielmo's syndrome to refractory anemia, dysmyelopoietic syndrome, etc. eventually leading to acute leukemia.

The word "odo-leukemia" means "way", "road" and R. Chevallier chose this term to emphasize the high predisposition of patients with this disease to leukemia with a high risk of developing acute leukemia. Later, in 1949, the term "preleukemic anemia" appeared to describe anemia refractory to therapy and associated with further leukemia. Other authors also reported on the connection of anemia with the final development of leukemia. So, in 1953, researchers at the University of Chicago School of Medicine first called this condition preleukemia. This name was used to describe MDS until 1976, and this is no coincidence: a third of patients with MDS are at risk of transforming the disease into acute myeloid leukemia, a life-threatening disease characterized by an urgent course and an unfavorable outcome.

In 2017, the current MDS classification was presented for the first time. Below, in accordance with the WHO criteria, MDS variants are listed [19]:

1. MDS with linear (unilinear) dysplasia (LD)
2. MDS with multilinear dysplasia (MDS-MD)
3. MDS with ringed sideroblasts (MDS-KS)

– MDS with ringed sideroblasts and linear dysplasia (MDS-KS-LD). – MDS with ringed sideroblasts and multilinear dysplasia (MDS-KS-MD).

4.MDS with an isolated deletion of the long arm of the 5th chromosome (MDS-5q-)

5. MDS with excess blasts:

– MDS with excess blasts-1 (MDS-IB-1)
– MDS with excess blasts-2 (MDS-IB-2)

6. MDS unclassified (MDS-N).

The main clinical manifestations of MDS are nonspecific and are most often caused by both quantitative and qualitative changes in the hematopoietic system: cytopenic syndrome (anemic and hemorrhagic syndromes, leukopenia), infectious complications, symptoms of intoxication, splenomegaly. Autoimmune manifestations in 10% of cases of MDS manifest from an autoimmune process: systemic vasculitis, necrotizing panniculitis, seronegative arthritis, polymyalgia rheumatica, Coombs-positive hemolytic anemia, pericarditis, pleurisy [4,7].

Difficulties in detecting MDS are associated with the absence of a typical clinical picture and with the complex diagnosis of the disease, which, in addition to the usual clinical examination performed in case of suspicion of any oncohematological disease, includes a mandatory morphological analysis and cytogenetic examination of the bone marrow (BM) [1,3,7,9,14,20].

Diagnosis of MDS is based on the presence of persistent (more than 6 months) cytopenia, expressed in a decrease in hemoglobin < 100 g/l, absolute neutrophil count < 1.8 × 109/l and/or platelet count < 100 × 109/l, signs of dysplasia CM, characteristic cytogenetic changes in blast cells in the absence of other hematological and non-hematological diseases that can explain these cytopenias [2,4]. Cytogenetic aberrations in MDS can be detected in 20-50% of cases, with the most common abnormalities being del(5q), trisomy 8 pairs, -Y, del(20q) and monosomy 7 chromosomes. A major chromosomal anomaly in MDS is the loss of a part of the long 23 arm of chromosome 5 - del (5q), which, according to the WHO classification, is classified as a separate type of MDS and occupies about 30% of all cytogenetic rearrangements in primary cases of the disease.

To verify the diagnosis of MDS, a set of necessary and decisive criteria should be considered.

1. **Required criteria:** stable cytopenia in 1 or more shoots for ≥4 months, in particular: hemoglobin level <110 g/l, neutrophil count <1.8×10 9/l, platelets <100×10 9/l .

2. **Decisive criteria:** dysplasia ≥10% of all erythroid and/or granulocytic and/or megakaryocytic sprouts, identified during the morphological study of BM; ≥15% ring sideroblasts (CS) or ≥5% CS in combination with an SF3B1 mutation; 5–19% blast cells in BM or 2–19% blast cells in peripheral blood. Typical karyotype anomalies (–7, 5q–, etc.) detected by standard cytogenetic study or by FISH.

3. **Additional criteria:** if the necessary criteria are present, but there are no decisive criteria, there is a clinical picture presented by macrocytic anemia and transfusion dependence, then the diagnosis can be confirmed by: an atypical immunophenotype of BM cells with multiple MDS-associated aberrations, detected by immunophenotyping and confirming a monoclonal population erythroid and myeloid cells; changes in the histological picture of CM, including immunohistochemical studies, confirming MDS [2,6,21].

Differential diagnosis of MDS is carried out with macrocytic B^{-12} and folate deficiency anemia, acute leukemia, and aplastic anemia. In B^{-12} and folate deficiency anemias, there is macrocytosis in the peripheral blood and megaloblastoidity in the BM, and in patients with MDS, the number of blast cells and / or monocytes in the peripheral blood may be increased and often a normal or elevated platelet level. In MDS, various non-accidental lesions of the hematopoietic karyotype are detected, and patients do not respond to treatment with vitamin B-12 and folic acid. In aplastic anemia, the presence of hypoplasia or even an empty BM in the trepan biopsy is decisive; there are no signs of dysplasia and chromosomal changes. In MDS, an increase in the expression of the WT1 gene, which is uncharacteristic of aplastic anemia, is detected, the diagnostic and prognostic significance of which in the management of patients with MDS is undeniable [1]. In acute leukemias, in addition to the acute debut of the disease and a vivid clinical picture, the main difference is the presence of more than 20% of blast cells in the BM or in the peripheral blood.

Once the diagnosis of MDS has been verified, it is important to accurately assess the prognosis in order to decide on treatment. For this purpose, the International Prognostic Scoring System (IPSS), which takes into account the number of blast cells in BM, cytogenetic abnormalities, and the severity of peripheral cytopenias in MDS, has been proposed [7,22].

Due to the lack of a universal prognostic scale that would include all the parameters that are significant for MDS, when

deciding on the choice of therapy, it is possible to assess the prognosis using several scales at once (IPSS, IPSS-R, WPSS) [16,18].

Using the above prognostic score scales, all patients with MDS were divided into 5 cytogenetic prognostic risk groups, taking into account data on the karyotype, blast content and severity of certain types of cytopenias: 1) very good (-Y, del(11q); 2) good (normal, del(5q), del(20q), del(12p); 3) intermediate (trisomy 8, del(7q)); 4) poor (chromosome 7 monosomy, inv3, complex karyotype with 3 abnormalities) and 5) very poor (complex karyotype with more than 3 abnormalities).

It should be noted that the threshold values for the number of blast cells in BM used in IPSS-R, namely, less than 2, more than 2, but less than 5, are difficult to determine in practice. A serious limitation of the use of IPSS, WPSS and IPSS-R in clinical practice is that these scales were developed exclusively for patients with newly diagnosed MDS. For patients with a karyotype that has not been assessed due to technical reasons, when choosing a therapeutic regimen, one should take into account the morphological variant of MDS according to the WHO classification, the number of blast cells in the BM and the dynamics of their change, BM cellularity, and the severity of cytopenias [1,6].

The choice of therapy depends on the patient's age, MDS variant, belonging to a risk group, the presence and severity of concomitant pathology, and the presence of an HLA-compatible donor.

In the treatment of MDS, taking into account the peculiarities of the pathogenesis and heterogeneity of the disease, there are several directions, however, the most effective and recognized throughout the world are:

- symptomatic therapy: replacement therapy with blood components, chelation therapy, hemopoiesis stimulants, antibiotic therapy.
- cytostatic therapy: PCT for AML treatment programs, low-dose chemotherapy, hypomethylating drugs.
- immunosuppressive and immunomodulatory therapy: antithymocyte globulin (ATG), cyclosporine-A (CSA), lenalidomide, splenectomy.
– allogeneic transplantation of hematopoietic stem cells (allo-HSCT).

The only treatment for patients with MDS is allogeneic hematopoietic stem cell transplantation (allo-HSCT) [15].

Unfortunately, the use of this method is limited by relapses of the disease and a large number of complications directly related to the transplantation procedure, including acute and chronic graft-versus-host disease, which often leads to death [1,6]. At the same time, patients with MDS aged 55-60 years and older, as a rule, are not considered as candidates for transplantation at all. In these and other cases, when allo-HSCT is impossible for some reason, epigenetic therapy acts as a standard, and the main drugs for it are decitabine (5-aza-2′-deoxycytidine) and azacitidine (5-azacytidine), belonging to the class of hypomethylating agents or inhibitors of the DNA methyltransferase enzyme [17,22].

Decitabin can be used in 2 modes of administration: 20 mg/m^2 as a 60-minute infusion once a day on days 1–5 every 28–35 days or 15 mg/m^2 3 times a day as a 3-hour intravenous infusion on days 1–5 3 days, every 6 weeks.

Azacitidine is prescribed in several regimens: 75 mg/m^2 subcutaneously 1 time per day for 1–7 days every 28 days or 75 mg/m^2 subcutaneously 1 time per day (the drug is administered on days 1–5 and 8–9 of the course, 6th and the 7th day - a break) every 28 days - this mode can be used for treatment in a day hospital.

According to the latest data from the literature, despite the longer experience with decitabine, azacitidine is considered as a hypomethylating drug of choice for the treatment of MDS, especially in elderly patients with a high risk of transformation to acute leukemia [22]. However, overall survival with hypomethylation therapy, even in standard cases, does not exceed 10-17 months. [1,6,13,14].

Replacement therapy with blood components is the main method for correcting refractory anemia in MDS and often causes post-transfusion iron overload in this category of patients. Thus, all patients with symptoms of hypoxemia (with Hb <85–80 g/l) and thrombocytopenia (<10–20×10 9/l) undergo blood transfusion therapy with erythrocyte mass, platelet concentrate to relieve anemia and hemorrhagic syndrome [1,6,23].

The clinician often has to face such difficulties as anemia with transfusion dependence, transfusion iron overload with the development of secondary hemosiderosis, alloimmunization with transfusion refractoriness, and progression of the disease with transformation into AML. Proliferation of the blast cell pool and disturbance of the cellular composition of the bone marrow in MDS are controlled by a number of autocrine and paracrine signaling cascades that can largely modulate their malignant phenotype and lead to disease progression. Studies have shown that the survival rate of "transfusion-dependent" patients with MDS is reduced if ferritin is more than 1000 ng/ml [5,11,12,15].

Note that observed in patients with MDS from increased and intermediate-1 IPSS risk and very high and increased IPSS-R risk with asymptomatic cytopenia, specific treatment is not recommended, the manifestation of dynamic monitoring is a tactic called "watch and wait"» for the purpose of disease control [1,6,8,13,14].

In patients with MDS, there is a tendency to increase iron absorption against the background of ineffective erythropoiesis. Due to the deposition of excess iron in the liver, myocardium and other organs, post-transfusion hemosiderosis develops. Chelation therapy with deferasirox is one of the key methods of accompanying therapy for patients receiving a large number of blood transfusions [13,22,24]. It is known that each dose of erythrocyte mass transfused to a patient contains 200–250 mg of iron, and there are no mechanisms for removing it from the body.

The life expectancy of patients with MDS and hemosiderosis who received chelation therapy significantly exceeds the life expectancy of patients who did not receive such therapy. Iron chelators are prescribed to patients with an increase in ferritin levels above 1000 ng / ml or after transfusion of more than 20 doses of erythrocyte suspension. With regard to low-risk MDS (very low, low, and intermediate risk according to IPSS-R), one of the methods for treating refractory anemia is

the administration of erythropoietin preparations (darbepoetin alfa, epoetin alfa) [6,13,14,21,22,24].

The response rate to erythropoietins in MDS is about 20%. Response predictors are the level of endogenous erythropoietin ≤500 mU/ml and the absence of high blood transfusion dependence. Of the methods of drug therapy for patients with anemia, the anabolic steroid danazol is used.

For patients with MDS who fail treatment with erythropoietin monotherapy, it is recommended to add colony-stimulating factors to increase the effectiveness [3,4,14,18,15].

Immunosuppressive therapy (IST) with antithymocyte globulin and cyclosporine A may be effective in patients younger than 60 years of age with high levels of endogenous erythropoietin (>500 mU / ml), hypocellular bone marrow and in the case of HLA-DR15 antigen expression or the detection of a paroxysmal nocturnal hemoglobinuria clone. It is in cases of hypoplastic forms of MDS that IST is particularly important. Lenalidomide is a drug that has found its use in patients with MDS with an isolated deletion of the long arm of the 5th chromosome (MDS with 5q–) and with the impossibility or ineffectiveness of therapy with erythropoietin drugs is lenalidomide [1,25-27].

Activators of the TGF-beta/SMAD signaling pathway have become promising new drugs in clinical trials of blood transfusion-dependent anemia. These include the TGFbeta-agonists sotatercept (ACE-011) and luspatercept (ACE-536). Sotatercept is a type IIA receptor activator that promotes the release of mature red blood cells into the circulation. The results of a phase 2 study of sotatercept administered to 54 patients with low and intermediate-1 risk MDS and transfusion-dependent anemia showed that 21 (40%) of 53 evaluable patients showed hematological improvement [1,2,6,14,28] .

The last decade has seen significant progress in understanding the molecular genetic events in the pathogenesis of MDS. Currently, these molecular discoveries are being appropriately used to improve the approach to diagnosis, prognosis, and therapy.

Conclusion.

Myelodysplastic syndrome is an irreversible tumor process with a clear tendency to transform into acute leukemia.

The diagnosis of MDS is always made with caution by excluding other diseases accompanied by cytopenia. To make a diagnosis, not only routine hematological examination methods are necessary, but also a mandatory cytogenetic study of the bone marrow. The management of patients with MDS is still an unresolved problem. The approach to the treatment of MDS should be individualized and based on the patient's risk group, age, and somatic status. Epigenetic therapy has an advantage when choosing management tactics for MDS in terms of improving the quality of life of patients.

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