Modern Diagnostic and Treatment Methods for Myelodysplastic Syndromes

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Abstract: Myelodysplastic syndromes are clonal diseases of hematopoietic stem cells characterized by ineffective hematopoiesis, peripheral cytopenias, and a risk of transformation into acute myeloid leukemia. In recent years, significant advances in molecular genetics, cytogenetics, and targeted therapy have fundamentally altered the principles of MDS diagnosis and treatment. This article analyzes the pathogenesis of MDS, modern diagnostic algorithms, the importance of molecular biomarkers, and the innovative treatment methods currently being used.

Keywords: myelodysplastic syndrome, hematopoiesis, cytopenia, NGS, IPSS-M, azacitidine, luspatercept, transplantation.

Introduction

Myelodysplastic syndromes are clonal neoplastic diseases of hematopoietic stem cells in the bone marrow. They are characterized by ineffective hematopoiesis, dysplastic changes, and blood cell deficiencies [1].

Although MDS was first identified as a distinct nosological entity in the second half of the 20th century, its genetic basis has been extensively studied in recent decades. Today, MDS is considered not only a morphological but also a molecular and cytogenetic disease [2].

Methodlogy

The disease primarily occurs in the elderly population. In European countries, there are 4–5 new cases per 100,000 people, while among the population over 70 years of age, this rate increases to 20–50 cases.

Etiology and Risk Factors
The etiology of MDS is multifactorial.
Primary MDS
In 80–90% of patients, the disease develops de novo.
Secondary MDS
It can be associated with the following factors:
Alkylating chemotherapeutic agents;
Topoisomerase II inhibitors;
Radiation therapy;
Benzene;

Pesticides;
Ionizing radiation.
Therapy-related MDS typically has a poor prognosis.
Pathogenesis
According to modern views, MDS develops as a result of a genetic mutation in the hematopoietic stem cell.
Main pathogenetic mechanisms:
clonal hematopoiesis;
impaired gene expression;
increased apoptosis;
immune dysregulation;
changes in the microenvironment.
Common mutations in MDS:
Gene Frequency
TET2 20-30
SF3B1 20-30
ASXL1 15-20
DNMT3A 10-15
SRSF2 10-15
RUNX1 10
TP53 5-10
In particular, the TP53 mutation is associated with a high-risk course and a short lifespan.

RESULTS AND DISCUSSION

Classification

According to the World Health Organization classification:
MDS is divided into the following main types [3]:
MDS with low blasts
MDS with ring sideroblasts
MDS with isolated del
MDS with biallelic TP53 inactivation
MDS with excess blasts
MDS, not otherwise specified
Clinical Signs
The clinical presentation depends on the degree of cytopenia [4].
Signs of Anemia
fatigue; decreased work capacity; dizziness; tachycardia; shortness of breath .
Signs of Neutropenia: frequent infections; pneumonia; septic complications.
Signs of Thrombocytopenia: petechiae, purpura, nosebleeds, bleeding gums.

Modern Diagnostic Algorithm

Stage 1: Laboratory Tests
Complete Blood Count
Hemoglobin
Leukocytes
Neutrophils
Platelets[5]
Biochemical Analysis:
Ferritin
Vitamin B12
Folate

- LDH
- Erythropoietin

Stage 2: Bone Marrow Examination

Aspiration

Assessed:

- Dysplasia
- Blast count
- Sideroblasts

Trepanobiopsy

Determined:

- Cellularity
- Fibrosis
- Architectural changes [6]

Stage 3: Immunophenotyping

Via Flow Cytometry:

- CD34
- CD117
- HLA-DR
- CD13
- CD33

expression is assessed [7].

Stage 4: Cytogenetic Analysis

The most significant aberrations:

- del (5q)
- -7
- del (7q)
- +8
- del (20q)
- Complex karyotype

Stage 5: Molecular Diagnostics

NGS Technology

It is now considered a part of standard diagnostics [8].

Checked:

- TP53
- TET2
- ASXL1
- SF3B1
- RUNX1
- DNMT3A
- EZH2

Molecular analysis is of great importance for prognosis and therapy selection.

Modern Prognostic Assessment

IPSS-R

5 risk groups:

- Very low
- Low
- Intermediate
- High
- Very high

IPSS-M
Introduced in 2022.
It simultaneously takes into account:
- 31 gene mutations
- Cytogenetics
- Laboratory parameters

This system has significantly increased prognostic accuracy.
This system significantly increased the accuracy of the forecast [9].

Modern Treatment Methods
Supportive Therapy
Transfusion Support
- Packed red blood cells;
- Platelet concentrate [10].

Iron Chelators
- Deferasirox
- Deferoxamine

Treatment of Low-Risk MDS
Erythropoiesis-Stimulating Agents
Epoetin alfa
Darbepoetin alfa
Efficacy is observed in 40–60% of cases.
Lenalidomide
In del syndrome, it provides:
- transfusion independence;
- cytogenetic remission [11].

Luspatercept
In patients with SF3B1 mutations, it:
- increases hemoglobin;
- reduces the need for transfusion.

Imetelstat
A new-generation drug used for transfusion-dependent anemia.
Treatment of High-Risk MDS
Azacitidine
Currently considered the first-line standard of care.
Advantages:
- increases overall survival;
- delays transformation to AML [12].

Decitabine
An alternative hypomethylating agent.
Combination Therapy
Current clinical trials are studying regimens such as:
- azacitidine + venetoclax;
- azacitidine + magrolimab;
- azacitidine + sabatolimab.

New combinations are particularly promising for patients with TP53 mutations.
Allogeneic Hematopoietic Stem Cell Transplantation
The only potentially curative method for MDS [13].
Indications:

high-risk MDS;
young patients;
good functional status.

Modern technologies:

high-resolution HLA typing;
haploidentical transplantation;
reduced-intensity conditioning.

The 5-year survival rate after transplantation can reach 40–70% [14].

Future Prospects

Current research is being conducted in the following areas:

TP53-targeted therapy;
immune checkpoint inhibitors;
bispecific antibodies;
CAR-T therapy;
gene editing technologies;
personalized medicine.
gene editing technologies;
personalized medicine [15].

Conclusion

Myelodysplastic syndromes are one of the most pressing issues in modern hematology. The development of molecular genetics has fundamentally changed our understanding of MDS. Currently, diagnosis is based on morphology, cytogenetics, and NGS technologies. Treatment primarily involves a risk-stratified approach, hypomethylating agents, targeted therapy, and allogeneic transplantation. In the near future, genetic and immunological technologies are expected to further enhance the effectiveness of MDS treatment.

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