Update on Myelodysplastic Syndromes Classification and Prognosis

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KEYWORDS

- Myelodysplastic syndromes (MDS) • Cytogenetics • Dysplasia • Cytopenia
- Idiopathic cytopenia of uncertain significance (ICUS)

KEY POINTS

- MDS is a collection of cytogenetically heterogeneous clonal BM failure disorders derived from aberrant hematopoietic stem cells in the setting of an aberrant hematopoietic stem cell niche.
- The 2008 WHO classification of MDS incorporates peripheral blood and bone marrow morphologic findings, blast percentage, cytogenetics, and history of chemotherapy/radiation.
- Benign mimics of MDS include vitamin/micronutrient deficiencies, infections, drugs/toxins, autoimmune/rheumatologic disease and congenital syndromes.
- The Revised International Prognostic Scoring System (IPSS-R) incorporates a new blast count threshold of 2% in the marrow, necessitating careful quantification of blast counts below 5%.

ABSTRACT

Myelodysplastic syndromes (MDS) are a collection of cytogenetically heterogeneous clonal bone marrow (BM) failure disorders derived from aberrant hematopoietic stem cells in the setting of an aberrant hematopoietic stem cell niche. Patients suffer from variably progressive and symptomatic bone marrow failure with a risk of leukemic transformation. Diagnosis of MDS has long been based on morphologic assessment and blast percentage as in the original French-American-British classification. The recently developed Revised International Prognostic Scoring System provides improved prognostication using more refined cytogenetic, marrow blast, and cytopenia parameters. With the advent of deep sequencing technologies, dozens of molecular abnormalities have been identified in MDS.

OVERVIEW

MDS is an umbrella term for a clinically and cytogenetically heterogeneous collection of clonal BM failure disorders. The pathophysiology of MDS is shaped by its clonal origin from aberrant hematopoietic stem cells[1] in the setting of an aberrant hematopoietic stem cell niche.[2] Patients with MDS can have a relatively stable clinical course, may suffer from the complications of refractory cytopenias, or may develop acute myeloid leukemia. MDS is diagnosed in more than 10,000 patients a year in the United States and fewer than 50% of patients with MDS are alive 3 years from diagnosis. More than 80% of patients with MDS are over 60 years old at diagnosis, and their cytopenias and transfusion dependence interact with other age-related comorbidities to increase both patient morbidity and mortality[3] and at significant cost to the U.S. health care system.[4] Diagnosis of MDS has long been based on morphologic assessment and blast percentage as in the original French-American-British (FAB) classification.[5] More recently, refined histology and cytogenetic abnormalities have been added to the diagnostic algorithm in the world health organization (WHO) diagnostic schema,[6,7] although diagnosis remains problematic in patients with borderline morphologic abnormalities and normal

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Acronyms and Abbreviations for MDS

ALIP	Abnormal localization of immature precursors
AML	Acute myeloid leukemia
AML-MRC	AML with myelodysplasia-related changes
ANC	Absolute neutrophil count
BM	Bone marrow
CGH	Comparative genomic hybridization
CMML	Chronic myelomonocytic leukemia
del	Deletion
FAB	French-American-British (classification scheme preceding WHO)
FISH	Fluorescence in situ hybridization
G-CSF	Granulocyte colony stimulation factor
GM-CSF	Granulocyte-macrophage colony-stimulating factor
Hg	Hemoglobin
HHV	Human herpesvirus
HIV	Human immunodeficiency virus
ICUS	Idiopathic cytopenias of uncertain significance
IDUS	Idiopathic dysplasia of uncertain significance
IPSS	International Prognostic Scoring System
IPSS-R	Revised IPSS
IWG-PM	International Working Group for Prognosis in MDS
IWGM-MDS	International Working Group on Morphology of Myelodysplastic Syndrome
LDH	Lactate dehydrogenase
MDS	Myelodysplastic syndrome
MDS-U	MDS, unclassified
MMF	Mycophenolate mofetil
MonoMAC	Monocytopenia with Mycobacterium Avium Complex susceptibility
NCCN	National Comprehensive Cancer Network
NK	Natural killer
PB	Peripheral blood
RA	Refractory anemia
RAEB	RA with excess blasts
RAEB-T	RAEB in transformation
RARS	RA with ring sideroblasts
RCC	Refractory cytopenia of childhood
RN	Refractory neutropenia
RS	Ring sideroblasts
RT	Refractory thrombocytopenia
SM-AHNMD	Systemic mastocytosis with associated clonal hematologic non–mast cell lineage disease
SNP	Single-nucleotide polymorphism
WHO	World health organization

cytogenetics. With the advent of deep sequencing technologies, dozens of molecular abnormalities have been identified in MDS,[8] and a subset of these may soon become part of the standard clinicopathologic evaluation in known or suspected MDS.

GROSS FEATURES

MDS are diagnosed exclusively based on features of the peripheral blood (PB) and BM. Gross diagnosis is not applicable.

MICROSCOPIC FEATURES OF MDS

Examination of a high-quality PB smear and BM aspirate smear, iron stain, and core biopsy are crucial for accurate determination of blast count and morphologic dysplasi, as well as to identify or exclude alternate causes of cytopenias, such as hemolysis or lymphoproliferative disorders.

Red blood cell abnormalities include anemia, oval macrocytes, and poikilocytosis (**Fig. 1**A).