



Review Article

Myelodysplastic syndrome: classification and changing concept

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Keywords:

Myelodysplastic syndrome;
Refractory anemia;
Ring sideroblasts;
MDS classification

ABSTRACT

Myelodysplastic syndrome is a group of clonal disorders having wide range of outcome. Its classification and concept have been changed over time with better understanding of its prognosis and clinical significance. The first standard classification was FAB classification which came in 1982. It was based on findings on peripheral blood and bone marrow. Later in 2001, WHO incorporated clinical data into it and proposed a modified classification. The 2001 WHO classification made several criteria and entities more precise based on inputs from several studies. New terminologies (e.g., refractory cytopenia with multilineage dysplasia) and new group (e.g., myelodysplastic / myeloproliferative disorder) have been introduced and group like 'refractory anemia with excess blasts in transformation' was removed. Again in 2008, in collaboration with European Association for Haematopathology and the Society for Hematopathology, as well as considering several recommendations from a group of clinical experts, WHO published a revised and updated classification. In the latest MDS classification, the clinical implications of different groups have been given more importance and also the role of cytogenetics has been re-evaluated. Several groups were again redefined (e.g., myelodysplastic syndrome – unclassified, refractory anemia with excess blasts) or eliminated (e.g., refractory cytopenia with multilineage dysplasia and ringed sideroblasts) or newly introduced (e.g., refractory cytopenia with unilineage dysplasia). Childhood MDS was considered separately as demanded by several pediatric hematologists. It was also emphasized that the diagnosis and classification of MDS mainly require identification of dysplastic morphological features, routine stains and correlation with clinical data rather than cytogenetics which may be necessary only in rare cases.

INTRODUCTION

The diagnosis and classification of myelodysplastic syndromes (MDS) always remained a challenge over past several decades.¹ MDS can be defined as a group of several conditions characterized by clonal stem cell disorder that manifests dysplastic and ineffective blood cell production compounded by a variable risk of transformation to acute

leukemia.²⁻⁵ The standard of care ranges from amelioration of hematologic deficits with blood product transfusions and administration of recombinant growth factors to aggressive chemotherapy and stem cell transplantation for younger individuals with more aggressive disease.⁶ Although generally it arises de novo with the risk increasing proportionate to age, MDS may also occur years after exposure to mutagenic chemotherapy.^{1,7} In this study we review the evolution of different classifications of MDS and the terminologies related to it over years.

In about one-third of patients, MDS can progress to a rapidly

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growing cancer of bone marrow cells called acute myeloid leukemia. Because most patients do not get leukemia, MDS was previously classified as a disease of low malignant potential. Now that we have learned more about MDS, it is considered to be a form of cancer as it is a clonal disease typical of cancer.⁸

History

In 1938, the term 'refractory anaemia'(RA) was used by Rhoades and Barker to describe anaemic patients who were unresponsive to iron, vitamin B12 or folic acid.^{5,9} A subgroup of patients with RA was subsequently shown to have ring sideroblasts in the bone marrow.⁹ Since then the classification and nomenclature used to describe this syndrome has changed over the last 70 years. Bjorkman¹⁰ in 1956 noticed cases of RA that were associated with ringed sideroblasts in the bone marrow (BM) and coined the term refractory anemia with ringed sideroblasts (RARS). In the 1950s, it was appreciated that acute leukaemia in the elderly was often preceded by a 'pre-leukaemic' phase of peripheral blood cytopenia associated with either normal or a slightly increased percentage of bone marrow blasts.⁹ Later, in 1970s terminologies like preleukemic syndrome and Hematopoietic dysplasia and subacute myeloid leukemia came up.⁶ In 1982, the first standard classification was made as the French–American–British (FAB) group proposed a morphological classification based on the percentage of blasts and ringed sideroblasts in the bone marrow and the presence or absence of a peripheral blood monocytosis.

Epidemiology

MDS predominantly occurs in elderly with a median age of 70 years.¹ The overall annual incidence rate is 3-4 per 100000 which increases dramatically to 20 per 100000 and 30 per 100000 in age group above 70 and 80 years.^{1,9} Males are affected approximately 1.5 times as often as females.¹¹ Case control studies of possible occupational or environmental associations have provided many insights to MDS, but none other than benzene has reached a level of scientific validity.^{12,13}

Etiology

The etiology of most cases of primary MDS remains unknown.⁹ MDS can occur as primary or de novo disorder and secondarily as therapy related disease (t-MDS).¹ Primary or de novo MDS occurs without a known history of toxic exposure and in some studies, have been linked to exposure to benzene, solvents and pesticides, and with smoking.^{1,9} However it should be remembered that dysplasia in BM can be caused secondarily by several factors which should be excluded before a diagnosis of MDS is made. It is postulated that gene polymorphism may be linked to interaction to a particular environmental factor and increased susceptibility of an individual. The t-MDS occurs with a known history of

chemotherapeutic agents, most commonly alkylating agents and radiotherapy. Rarely, inherited hematological conditions (e.g., Fanconi anemia) are associated with MDS.^{1,6}

Clinical features

Most patients present with symptoms or complication related to anemia or less commonly, neutropenia and thrombocytopenia.¹ Upto 20% cases may be detected incidentally on routine laboratory tests.⁹ Lymphadenopathy and organomegaly are rare.^{1,9} A diagnosis of MDS should be considered in any individual with unexplained persistent cytopenias or monocytosis. Diabetes insipidus, acute neutrophilic dermatosis and systemic suppurative erythematosis (SLE) like syndromes have been reported as presenting features.¹¹

Diagnosis

A diagnosis of MDS should be considered in any individual with unexplained persistent cytopenias or monocytosis. The figure 1 shows the flow chart as a diagnostic approach in MDS. Careful inspection of the peripheral blood smear (PBS) and BM is necessary to document the requisite dysplastic cytologic features in one or more hematopoietic lineages.^{5,14} PBS and BM specimens should be collected prior to any definitive therapy. A standard Wright-Giemsa or similar stain is used for smears. BM biopsy ideally should be at least 1.5 cm in length and taken at right angles to the cortical bone.¹⁵ Confirmation of dysplasia, percentage of dysplastic cells and lineages affected and in selected cases percentage of ringed sideroblasts lead to subcategorization. However, because these dysplastic findings per se may not be diagnostic of MDS, possible contributing conditions e.g., nutritional status, alcohol and drug use, occupational exposure to petrochemicals and other toxins, prior treatment with antineoplastics or radiotherapy, growth factor therapy, and risk factors for human immunodeficiency virus (HIV) must be excluded.^{1,6,15} The preponderance of macrocytic anemia in MDS necessitates exclusion of vitamin B12 and folate deficiencies. A number of medications, including valproic acid, mycophenolate mofetil, ganciclovir, and alantuzumab, have been associated with acquired dysplastic changes.⁶ In addition, copper deficiency and zinc excess may simulate myelodysplasia.⁶ Dysplastic hematopoiesis is a common finding that accompanies HIV infection.^{16,17,18} Other than these secondary causes of marrow dysplasia, diagnostic problems can arise when marrow hypocellularity or myelofibrosis obscures the underlying disease process or when BM morphologic findings do not match with PBS and laboratory findings or blast percentage is not increased in the PBS or BM.^{15,19,20}

Classifications of MDS

Dysplasia is a term that classically implies a polyclonal and, therefore, nonneoplastic process.¹¹ The choice of

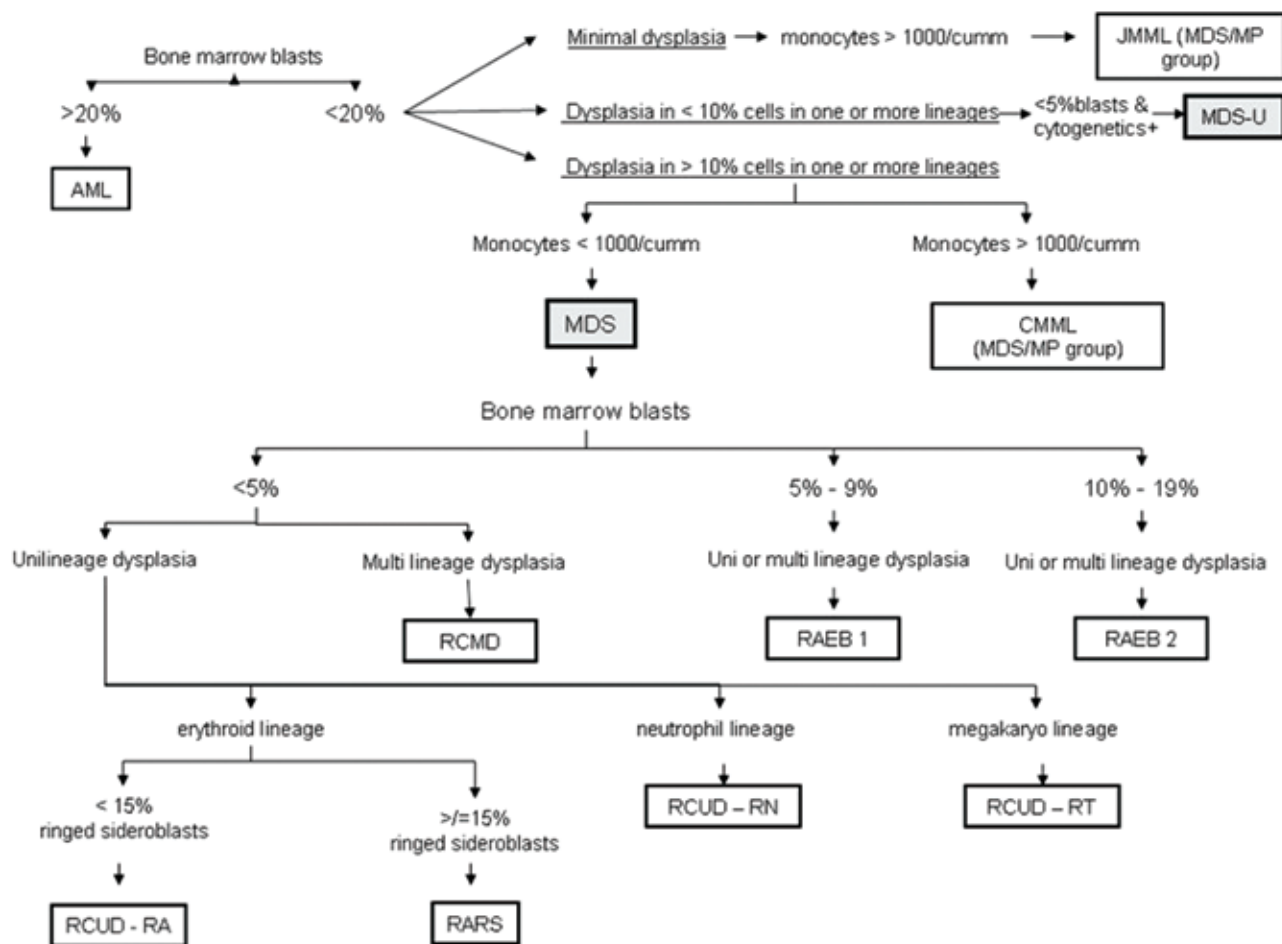


Figure 1: Flow chart showing schema of diagnostic approach in MDS

the term *myelodysplasia* to denote clonal (neoplastic) disorders was rather unfortunate because the term does not help in understanding the relationship of myelodysplasia to other clonal stem cell disorders. In addition, diseases such as idiopathic myelofibrosis can have all the features of "myelodysplasia" but are ignored in its classifications though it is widely used.¹¹

FAB classification

Several classification systems have been developed to subclassify MDS and to predict survival or transition to AML following MDS diagnosis. The first standard classification, the FAB system, was introduced in 1982 and is based on the percentage of blasts and morphological dysplastic features of blood and BM.^{6,14} According to this system, patients are diagnosed with MDS when PBS and BM findings of unexplained hematopoietic dysplasia in two or more lineages are present and/or myeloblasts are less than 30% of all BM cells.¹⁴ FAB classification distinguishes five morphologic subtypes of MDS namely RA, RARS, RAEB, RAEB-t and CMML (Table 1).^{6,14} However, the FAB system served as the standard for MDS classification for two decades for its easy reproducibility

and provision of considerable prognostic information.^{6,21}

Nonetheless, with time, the validity of the classification was questioned.⁶ Drawing diagnostic distinctions among different percentage of leukemic blast cells is inconsistent with the biologic behavior of the condition.^{11,22} RA in FAB is a heterogeneous group that includes patients with neutropenia and / or thrombocytopenia without anemia.⁹ In RARS, the percentage of ringed sideroblasts are more than 15%. Separation of clonal RA into two categories based on whether the anemia has greater than or less than 15 percent sideroblasts is arbitrary and is not based on the pathobiology of the two variants.¹¹ This criteria, however was taken somewhat arbitrarily. The blasts percentage in RAEB was between 5 and 19% while in RAEB-t, it is between 20% and 29%. In general, RAEB patients have more unfavorable prognosis than RARS and RAEB-t patients follows a more indolent course than AML.^{9,23} CMML in FAB classification encompasses all cases with marrow dysplasia and more than 1000/ cumm circulating monocytes. It was recognized to be heterogeneous as it includes patients with a high monocyte count and splenomegaly more typical of a myeloproliferative (MP) disorder as well as patients with a modest monocytosis

Table 1: The FAB classification of MDS 1982.^{6,9,14}

Classification	Peripheral Blood		Bone Marrow		
	Blast Cells (%)	Monocytes >1000/cumm	Blast Cells (%)	Ringed Sideroblasts (%)	Dysplasia
Refractory anaemia (RA)	<1	No	<5	<15	Yes
Refractory anaemia with ringed sideroblasts (RARS)	<1	No	<5	>15	Yes
Refractory anaemia with excess blasts (RAEB)	<5	No	5–19	Variable	Yes
Refractory anaemia with excess blasts in transformation (RAEB-t)	<5	+/-	20–29	Variable	Yes
Chronic myelomonocytic leukemia (CMML)	<5	Yes	<20	Variable	Yes

Table 2: WHO classification of MDS 20011¹

Classification	Peripheral Blood	Bone Marrow
Refractory anemia (RA)	Anemia No or rare blasts	Erythroid dysplasia only <5% blasts <15% ringed sideroblasts
Refractory anemia with ringed sideroblasts (RARS)	Anemia No blasts	>15% ringed sideroblasts <5% blasts Erythroid dysplasia only
Refractory cytopenia with multilineage dysplasia (RCMD)	Cytopenias (bicytopenia or pancytopenia) No or rare blasts No Auer rods <1 × 10 ⁹ /L monocytes	Dysplasia in ≥10% of the cells of two or more myeloid cell lines <5% blasts in the marrow No Auer rods <15% ringed sideroblasts
Refractory cytopenia with multilineage dysplasia and ringed sideroblasts (RCMD-RS)	Cytopenias (bicytopenia or pancytopenia) No or rare blasts No Auer rods <1 × 10 ⁹ /L monocytes	Dysplasia in ≥10% of the cells of two or more myeloid cell lines <5% blasts in the marrow >15% ringed sideroblasts No Auer rods
Refractory anemia with excess blasts-1 (RAEB-1)	Cytopenias <5% blasts No Auer rods <1 × 10 ⁹ /L monocytes	Unilineage or multilineage dysplasia 5–9% blasts No Auer rods
Refractory anemia with excess blasts-2 (RAEB-2)	Cytopenias 5–19% blasts Auer rods ± <1 × 10 ⁹ /L monocytes	Unilineage or multilineage dysplasia 10–19% blasts Auer rods ±
Myelodysplastic syndrome, unclassified (MDS-U)	Cytopenias No or rare blasts No Auer rods	Unilineage dysplasia: one myeloid cell line <5% blasts No Auer rods
MDS associated with isolated del(5q)	Anemia Usually normal or increased platelet count <5% blasts	Normal to increased megakaryocytes with hypolobated nuclei <5% blasts Isolated del(5q) cytogenetic abnormality No Auer rods

and a clinical course similar to that seen in RA or RAEB.⁹ Nonetheless, in different studies over time, it was revealed that the clinical outcomes of patients assigned to the same MDS subgroup in FAB remained too variable to accurately predict survival or transformation to AML in individual patients.²¹

WHO classification 2001

In 2001, the WHO proposed a revision of the FAB morphological approach and incorporated more recent clinical and genetic data.^{9,21} Table 2 shows the subcategories and their respective diagnostic criteria and Table 3 shows a

comparison between FAB and WHO 2001 classifications. The WHO classification recognizes the prognostic importance of the percentage of BM blasts in MDS and includes myeloblasts, monoblasts, promonocytes and megakaryoblasts, but not erythroblasts.^{1,15}

Removed from MDS

The revisions included lowering the threshold for the percentage of blasts for the diagnosis of AML from 30% to 20%, thus elimination of the MDS subcategory RAEB-t. All cases with more than 20% blasts and dysplasia in more than 50% of cells in at least 2 lines have been classified as AML with multilineage dysplasia, and it may occur either de novo or following MDS or a myelodysplastic / myeloproliferative disorder (MDS/MP).¹ In addition, CMML was reclassified from the subcategory of MDS to a new subcategory of MDS/MP.

New terms

It was noted that patients with less than 5% marrow blasts had a poorer prognosis if they had multilineage dysplasia. In WHO 2001 classification, RA and RARS are confined to patients with unilineage erythroid dysplasia and new terms, RCMD and RCMD-RS have been introduced for cases with bi- or pancytopenia and dysplastic features in more than 10% of cells in two or more myeloid lineages (Table 2, Table 3).^{1,6,9}

RAEB has been divided into 2 subcategories viz RAEB-1 and RAEB-2 based on the observation that higher number blasts in PBS or BM denoted poorer prognoses.¹ Moreover though the significance of Auer rods within blast cells remained uncertain in classifying MDS, but any patients in whom Auer rods are seen are categorized as having RAEB-2.⁹

A new subgroup of MDS unclassified (MDS-U) has also been introduced specifically for patients with unilineage, myeloid or megakaryocytic dysplasia and not as a waste basket group for inadequately investigated cases.

Similarly, another new subgroup has been introduced i.e; MDS with isolated 5q deletion, based on the uniformity of clinical and laboratory features of cases.¹ Majority of these patients were elderly women with a macrocytic anaemia, normal white cell count and a normal or raised platelet count.^{1,9} BM of these patients show erythroid hypoplasia and large mono- or binuclear megakaryocytes.⁹

Progression to other group

It was also described that though some patients may remain within a single WHO subgroup, others may progress through two or more subgroups during the course of their disease.^{1,9}

Recommendation for follow up

Patients with unilineage erythroid dysplasia, or in whom dysplasia is seen in < 10% of cells are not diagnosed as “MDS” in the absence of a clonal karyotypic abnormality. It is recommended that such patients be re-evaluated after 6 months.^{1,9}

WHO classification 2008

In 2008, WHO in collaboration with the European Association for Haematopathology and the Society for Hematopathology, published a revised and updated edition of the WHO Classification of Tumors of the Hematopoietic and Lymphoid Tissues. While developing the classification system, a Clinical Advisory Committee of 30 renowned clinical experts of relevant fields met with Pathology Committee and made several recommendations.^{15,21} It was decided that the definition of subgroups of MDS should be more clearly redefined with precise clinical relevance and also the diagnostic role of cytogenetics and flow cytometry be clarified and re-evaluated.^{15,21}

The basic minimal criteria for diagnosis of MDS remains same i.e., at least 10% cells in one or more cell line must show unequivocal dysplastic features. It is again re-emphasized that before a diagnosis of MDS is made, all secondary causes and congenital abnormalities should be excluded.^{8,15}

Table 4 shows the WHO classification 2008 while in Tables 5 and 6 we have summarized the basic approach in diagnosis based on PBS and BM findings. Table 7 shows the older terminologies of FAB and WHO 2001 and their current counterparts.

New group

The group MDS-U of WHO2001 has been re-evaluated. Refractory cytopenia with unilineage dysplasia (RCUD) has been expanded to include any unilineage dysplasia with less than 5% blasts in marrow irrespective of uni or bi-cytopenia in PBS.^{8,15,24,25} Thus new entities RCUD–RN and RCUD–RT have evolved. On the other hand, patients with pancytopenia and unilineage morphologic dysplasia are classified as having MDS-U, because of the uncertain clinical significance of such findings.

New definition

The definition of RAEB-1 and -2 have been redefined to emphasize blasts percentage in PBS.^{15,24,25} RAEB-1 includes patients with 2-4% blasts in PB even if BM blasts is <5%. RAEB-2 includes patients with 5-19% blasts in PBS or 10-19% blasts in BM. So, cases of RAEB-2 may have <10% blasts in the marrow but may be diagnosed by other 2 findings; 5% to 19% blasts in the blood and/or Auer rod.^{15,24,25}

Table 3: Relationship between the FAB and WHO classification 2001⁹

FAB	WHO 2001
RA	RA (unilineage) RCMD 5q- syndrome
RARS	RARS (unilineage) RCMD-RS
RAEB	RAEB-1 RAEB-2
RAEBt	AML with multilineage dysplasia AML and MDS, therapy related
CMML	Myelodysplastic/myeloproliferative diseases
--	New Terminology - RCMD , RCMD-RS , RAEB1, RAEB2 , MDS-U, 5q- syndrome
	New Group - MDS/MP

Table 5: Peripheral blood approach in diagnosis of MDS

Peripheral blood findings		Possible diagnosis (under MDS)
Cytopenia(s) <1000/cumm monocytes	No or rare blasts (<1%) No Auer rods	RCUD – RA/ RN / RT RARS RCMD MDS – U 5q- (platelet normal / increased)
	<1000/ cumm monocytes	RAEB- 1
	5%-19% blasts Auer rods +/-	RAEB- 2
> 1000 / cumm monocytes	< 20% blasts	CMML (chronic myelomonocytic leukemia) JMML (Juvenile myelomonocytic leukemia) (both come under MDS/MPD group)

Table 4: WHO classification of MDS 2008¹⁵

Disease	Blood findings	BM findings
Refractory cytopenia with unilineage dysplasia (RCUD): -Refractory anemia -RA -Refractory neutropenia -RN -Refractory thrombocytopenia - RT	Unicytopenia or bicytopenia No or rare blasts (<1%)	Unilineage dysplasia >10% of the cells in one myeloid lineage < 5% blasts <15% of erythroid precursors are ring sideroblasts
Refractory anemia with ring sideroblasts (RARS)	Anemia No blasts	Erythroid dysplasia only <5% blasts ≥ 15% of erythroid precursors are ring sideroblasts
Refractory cytopenia with multilineage dysplasia (RCMD)	Cytopenia(s) No or rare blasts (<1%) No Auer rods <1000/cumm monocytes	Dysplasia in >10% of the cells in ≥ 2 myeloid lineages (neutrophil and/or erythroid precursors and/or megakaryocytes) <5% blasts in marrow No Auer rods +/- 15% ring sideroblasts
Refractory anemia with excess blasts-1 (RAEB-1)	Cytopenia(s) < 5% blasts No Auer rods <1000/cumm monocytes	Unilineage or multilineage dysplasia 5%-9% blasts No Auer rods
Refractory anemia with excess blasts-2 (RAEB-2)	Cytopenia(s) 5%-19% blasts Auer rods +/- <1000/cumm monocytes	Unilineage or multilineage dysplasia 10%-19% blasts Auer rods+/-
Myelodysplastic syndrome—unclassified (MDS-U)	Cytopenias <1% blasts	Unequivocal dysplasia in <10% of cells in one or more myeloid lineages when accompanied by a cytogenetic abnormality considered as presumptive evidence for a diagnosis of MDS < 5% blasts
MDS associated with isolated del(5q)	Anemia Usually normal or increased platelet count No or rare blasts (<1%)	Normal to increased megakaryocytes with hypolobated nuclei < 5% blasts Isolated del(5q) cytogenetic abnormality No Auer rods

Table 6: Bone marrow approach in diagnosis of MDS

BONE MARROW ASPIRATION AND BIOPSY MORPHOLOGY								
DYSPLASIA	Dysplasia in more than 10% cell in one or more lineage							Dysplasia in less than 10% cell in one or more lineage
BLAST%	<5% blasts					5-9% blasts	10-19% blasts Auer rods +	<5% blasts
LINEAGE with dysplasia	Unilineage		Unilineage	Unilineage	multi lineage	Uni or multi lineage	Uni or multi lineage	Cytogenetic findings present
	Only erythroid lineage dysplasia		Only neutrophil lineage dysplasia	Only megakaryocyte lineage dysplasia				
DIAGNOSIS	< 15% ringed sideroblasts RCUD - RA	>=15% ringed sideroblasts RARS	RCUD – RN	RCUD – RT	RCMD	RAEB1	RAEB2	MDS-U

Elimination of group

A separate group RCMD-RS of WHO2001 classification has been eliminated in 2008 classification and is incorporated under RCMD.^{15,24,25}

Cytogenetics

Fifty percent of patients with a primary myelodysplastic syndrome have a normal karyotype; hence, the current classification system is still largely based on morphology.²⁶

Nonetheless, in WHO2008, a list of specific chromosomal abnormalities has been published. It was decided that Patients with refractory cytopenia(s) suspected to have MDS, but who lack diagnostic morphologic features may be considered to have presumptive evidence of MDS if they have specific MDS related cytogenetic abnormalities. Patients with pancytopenia and less than 10% dysplasia can be categorized under MDS-U if they show specific cytogenetic abnormalities. It might also be of significance in unusual presentations like hypocellular or fibrotic marrow. Very recently, in 2011, Bejar R et al found that somatic point mutations are common in myelodysplastic syndromes and are associated with specific clinical features and prognosis.^{26,27}

Flow cytometry and phenotypic abnormality

Though there are several studies demonstrating phenotypic abnormalities in flow cytometry in MDS cases, it has not been considered as “definite” diagnostic evidence due to

inadequate data.^{15,24,25} In absence of morphological and/or cytological features, if a case has 3 or more phenotypic abnormality in flow cytometry, it can be reported as “suggestive of MDS” (rather than “MDS”) and should be followed up.^{15,24,25}

MDS with unusual presentation

It was noted that some cases of MDS present with hypocellular marrow or myelofibrosis.^{15,24} It was further commented that hypocellular cases may show macrocytes in PB mimicking aplastic anemia and myelofibrosis cases may mimic AML-M7 and Idiopathic myelofibrosis (under myeloproliferative diseases). However; the clinical significance of these types of MDS are yet to be defined and so they are not categorized under any separate group. It was suggested that these cases should be subtyped as per MDS criteria with “hypoplastic” or “myelofibrosis” as prefix or suffix (e.g., RCMD with myelofibrosis). In cases with difficulty, immunohistochemical stains and cytogenetics would be helpful.^{19,28,29} Usually myelofibrosis cases show increased CD34+ blasts and hypoplastic cases are of lower grade.^{15,24}

Follow up recommended

The following conditions are not classified as MDS and careful follow up is advised to monitor development of any features of MDS.¹⁵

- Patients with refractory cytopenia but lacking morphologic or specific cytogenetic abnormality

- b. “Suggestive of MDS” cases, i.e., with 3 or more phenotypical abnormalities only
- c. Unilineage dysplasia present in BM but no increase in blasts and ringed sideroblasts are <15% and no cytogenetic abnormality

Childhood MDS

In WHO 2008 classification, childhood MDS was considered separately as demanded by several pediatric hematologists.^{15,24,25} A provisional entity, “refractory cytopenia of childhood” (RCC), has been added to include children with cytopenia(s) with less than 2% blasts in the peripheral blood and less than 5% in the bone marrow and evidence of dysplasia in 2 or more lineages (Table 8).¹⁵ They usually present with refractory anemia, initially associated with thrombocytopenia and/or neutropenia and hypocellular BM.^{15,24,25,30} Sometimes, the distinction between RCC and aplastic anemia or congenital bone marrow failure syndromes may be very difficult on morphological ground and cytogenetic abnormalities may be needed. For children with 2% to 19% blasts in the blood and/or 5% to 19% in the bone marrow, the MDS subclassification should be made using the same criteria used for adults.¹⁵

RARS-T

“Refractory anemia with ring sideroblasts and thrombocytosis” (RARS-T) does not come under MDS. (Please note that T stands for “thrombocytosis” and not “in

transformation” like RAEB-t) It is a “provisional entity” kept under MDS/MP group with CMML and JMML. It includes cases with refractory anemia, thrombocytosis > 450000/cumm in PB and BM showing dyserythropoiesis, ringed sideroblasts >15% and megakaryocytes with features resembling those in primary myelofibrosis or essential thrombocythemia.¹⁵

CONCLUSION

No clinical features are specifically associated with MDS to differentiate it from other pancytopenic states. In 50% of patients, diagnosis depends on the process of elimination. Observation time and repeated BM studies may be necessary. It is to re-emphasize that diagnosis and classification of MDS mainly requires identification of dysplastic morphological features, routine stains and correlation with clinical data. Cytogenetics are necessary only in cases with inadequate morphological evidence which are rare. However very recently some studies show prognostic implications of point mutations

ACKNOWLEDGMENT

The author is very grateful to Prof. OP Talwar, Dr. D Ghartimagar, N Nepal and R Narasimhan for their tremendous help.

Table 7: Comparison between older nomenclatures (FAB and WHO 2001) and WHO classification 2008

Older nomenclatures (FAB and WHO 2001)	Current nomenclatures
RA (FAB, WHO 2001)	RCUD – RA , new entity (In RCUD other entities are RN and RT)
RARS (FAB, WHO 2001)	In RARS – a new provisional entity is RARS –thrombocytosis (RARS-t) , which is under MDS / MPD and usually has a JAK2 mutation
RCMD –RS (WHO 2001)	A separate RCMD – RS has been removed and has been included under RCMD
RAEB (FAB)	Divided into RAEB-1 and RAEB-2
RAEB – t (FAB)	Eliminated , comes under Acute leukemia
CMML (FAB)	Removed from MDS and put under MDS/MP
MDS-U (WHO 2001)	Several cases have been included in RCUD-RN and RCUD-RT
	<u>New terminologies</u>
	a)RCUD-RA, RCUD-RN, RCUD-RT
	b)Refractory cytopenia of childhood (RCC)
	c)RARS-t (under MDS/MP group)

Table 8: Marrow dysplasia in children^{15,24,25}

Peripheral blood	Bone marrow	Diagnosis
<2% blasts	< 5% blasts	Refractory cytopenia of childhood RCC
2-19% blasts	5-19% blasts	Classify as MDS with criteria for adults

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