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Additional information on myelodysplastic syndrome

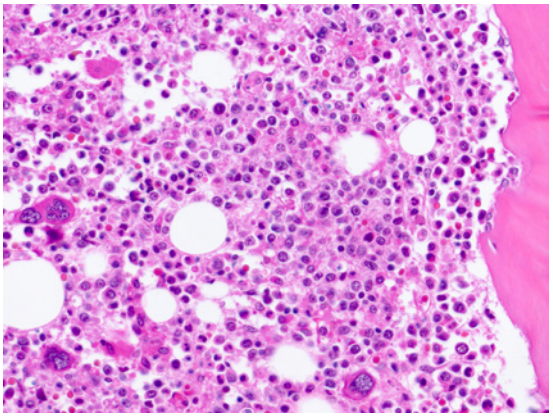
Epidemiology

The myelodysplastic syndromes (MDS) are a group of clonal malignant diseases of the bone marrow stem cells. MDS results in abnormal morphology and quantitative changes in one or more blood cell and bone marrow elements, for example red cells, white cells and/or platelets.[1-4] In Australia the incidence of MDS is approximately four to five per 100,000, which increases to 20-50 per 100,000 in the over 60s.[2] Over 90% of patients diagnosed with MDS are above the age of 60.[5] It is more common in older men[2] and Caucasians. Up to 10% of adults over 70 years-of-age, without symptoms, have *clonal haematopoiesis* of indeterminate potential (CHIP) which is associated with an MDS-associated mutation. CHIP may be the first indication that a patient may develop MDS.

In 90% of cases there is no identified cause; however, age appears to be a risk factor as more mutations are acquired as we grow older. For some patients MDS can be linked to previous exposure to chemotherapy, radiotherapy or exposure to high levels of environmental toxins like benzene, petroleum products or tobacco smoking.[1,4,6]

Common presenting features include:[2]

- dysplastic changes in red cells, white cells or platelets on blood film morphology
- cytopenias presenting as anaemia (low red cell count), infections (associated with low numbers of white cells) or bleeding and bruising (associated with the low numbers of platelets) or low cell counts of all three cell types. Rare MDS patients, associated with specific mutations, may have a high platelet count[1,6]
- substantial risk of disease transformation to acute myeloid leukaemia for most subtypes.



Bone marrow aspirate of a patient with myelodysplastic syndrome. Marrow is hypercellular.

Diagnosis

The diagnosis is generally suspected based upon the abnormal full blood count and peripheral blood film appearances. Clinical history and laboratory testing to exclude other possible causes of these abnormalities such as nutritional deficiencies (vitamin B_{12}, folate or copper deficiency), zinc excess, excessive alcohol intake, HIV infection, certain medication and chemotherapy is important.

Bone marrow biopsy and other associated tests are necessary to confirm the diagnosis, and category type, and help determine prognosis.[4] The bone marrow usually has a hypercellular appearance despite the patient's cytopenia(s), but occasionally is normal or decreased.

Risk stratification

The clinical course of MDS is variable and can depend on several factors.

There are many scoring tools used for MDS, with one of the most commonly used being the International Prognostic Scoring System (IPSS) and revised IPSS (IPSS-R) that stratifies patients by risk based upon:[1,4]

- percentage of blasts in the bone marrow
- presence of cytogenetic abnormalities
- number of cell lines affected by cytopenia.

Revised international prognostic scoring system (IPSS-R) in myelodysplastic syndrome

Prognostic variable	Score						
	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics*	Very good		Good		Intermediate	Poor	Very poor
Bone marrow blast (percent)	≤2		>2 to <5		5 to 10	>10	
Haemoglobin (g/L)	≥100		80 to <100	<80			
Platelets 10^9/L	≥100	50 to 100	<50				
Absolute neutrophil count 10^9/L	≥0.8	<0.8					

This scoring system was applied to an initial group of 7012 patients with primary MDS by the French-American-British classification who had at least two months of stable blood counts, ≤30 percent bone marrow blasts and ≤19 percent peripheral blood blasts, and who were observed until progression to AML transformation or death (did not receive disease-modifying agents for MDS). Patients could be stratified into five groups with the following estimated overall survival and progression to AML.

* Cytogenetic definitions:
Very good: –Y, del(11q)
Good: Normal, del(5q), del(12p), del(20q), double including del(5q)
Intermediate: del(7q), +8, +19, i(17q), any other single, double not including del(5q) or –7/del(7q), or independent clones
Poor: –7, inv(3)/t(3q)/del(3q), double including –7/del(7q), complex: 3 abnormalities.
Very poor: Complex: >3 abnormalities.

The IPSS-R assessment, can be found at *https://www.mds-foundation.org/ipss-r-calculator/*

Treatment

The nature of treatment will depend upon factors including the type and rate of progression of the disease together with the patient's age and other comorbidities. Risk stratification is important for guiding treatment choices and timing.[7]

Treatment options include:

- supportive therapies - including red cell or platelet transfusions to alleviate symptoms and antibiotics to treat infections
- low intensity therapies - including azacitidine, decitabine or lenalidomide
- high intensity therapies - including intensive combination chemotherapy and allogeneic stem cell transplant.

Outcomes

MDS is a heterogeneous disease and therefore, the course and outcome of MDS differs, but most patients will die because of the consequences of their bone marrow failure, rather than progression to acute myeloid leukaemia.

Median survival (in years) in myelodysplastic syndrome according to International Prognostic Scoring System (IPSS) and age

Risk group	IPSS-R score	Median overall survival (years)	Median time to 25 percent AML evolution (years)
Very low	≤1.5	8.8	>14.5
Low	>1.5 to 3.0	5.3	10.8
Intermediate	>3 to 4.5	3.0	3.2
High	>4.5 to 6	1.6	1.4
Very high	>6	0.8	0.7

The prognostic value of the IPSS-R was validated in an external cohort of 200 patients with MDS

Glossary terms

Hypocellular	Contains less than the normal number of cells.
AML	Acute myeloid leukemia.

References

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