Lecture 13 in hematology by Dr.Alaa Fadhil Alwan

Myelodysplastic syndromes

Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal disorders characterized by one or more peripheral blood cytopenias and dysplasia of at least one lineage (classically three lineages) in the bone marrow. The approximate incidence is two to four cases for a population of 100,000 annually.

ETIOLOGY

Etiology is poorly understood. MDS occurs infrequently before the age of 50 but its incidence increases rapidly thereafter. Prior exposure to chemotherapeutic agents, ionizing radiation, or benzene are risk factors .

PATHOPHYSIOLOGY

The vast majority of MDS cases are acquired. The development of MDS is due to accumulated DNA damage in the hematopoietic stem cell. This damage may take the form of chromosomal gains or losses, translocations, or point mutations..

CLINICAL AND LABORATORY MANIFESTATIONS

Patients commonly present with symptoms of fatigue and decreased exercise tolerance due to anemia. Less often, patients will have bleeding, easy bruisability, or recurrent bacterial infections as an initial complaint.

Physical examination may reveal pallor, peripheral edema, and if the anemia is severe, evidence of heart failure. Petechiae may be present on the lower extremities or the buccal mucosa if severe thrombocytopenia is present (i.e., the platelet count is less than 20,000/L); ecchymoses may be observed. Splenomegaly may be present, especially in patients with chronic myelomonocytic leukemia (CMML). Laboratory tests may reveal an isolated decrease of one peripheral blood count or multiple cytopenias. The anemia may be microcytic, normocytic, or macrocytic. An. Thrombocytopenia may be present, although the platelet count may be elevated in patients with refractory anemia (RA) and an isolated 5q- abnormality, or in some cases of RARS. The peripheral blood smear often demonstrates cellular morphological abnormalites. The neutrophils may be hypogranular, and the nucleus may have a bilobed appearance (pseudo-Pelger-Huet abnormality).. Chemistry tests typically are normal except the lactate dehydrogenase, which is elevated as a result of increased rate of cell death in the bone marrow.

The bone marrow biopsy usually is hypercellular for the age of the patient. However, approx 15% of patients have a hypocellular marrow (cellularity <25%). The hallmark of MDS is the presence of tri-lineage dysplasia in the marrow. The erythroid series usually is megaloblastic in appearance, with prominent nuclear-cytoplasmic asynchrony. The erythroid cells may have additional abnormalities including bi-nuclearity or nuclear budding. Ringed sideroblasts, erythroid precursors with iron-laden mitochondria surrounding the nucleus, may be increased and they exceed 15% of the nucleated bone marrow cells in patients with RARS. Megakaryocytes frequently are small (micromegakaryocytes) with decreased nuclear ploidy (mono- or binucleated). The myeloid series usually is left-shifted and increased myeloblasts are present in more advance stages.

Classification of Myelodysplastic Syndromes:

A. FAB Classification of Myelodysplastic Syndromes

Subtype	Blood myeloblasts	BM myeloblasts	Other features
RA	<1%	<5%	
RA with RS	<1%	<5%	RS > 15% BM cells
RAEB	<5%	5–20%	
CMML	< 5%	< 20%	AMC > 1000/mL

B. WHO Classification of Myelodysplastic Syndromes

Myelodysplastic Syndromes	
RA with or without RS	Erythroid-only dysplasia (<5% blasts)
Refractory cytopenia with multi-lineage dysplasia	Two or three lineage dysplasia (<5% blasts)
RAEB-1	Blasts 5–9%
RAEB-2	Blasts 10–19%
5q- syndrome	<5% blasts
Myelodysplastic syndromes, unclassifiable	Dysplasia, not meeting above criteria
Myelodysplastic/myeloproliferative syndromes	
CMML	
Atypical chronic myelogenous leukemia	
JMML	

TREATMENT

supportive care is the treatment of choice for many patients. Blood transfusions frequently are required for symptomatic anemia and antibiotics are administered for bacterial infections. Chronic red blood cell transfusions lead to iron overload. In patients who will require ongoing transfusional support, iron chelation should be considered after 20 U of packed red cells have been administered or when the serum ferritin level exceeds 1000 ng/mL. Platelet transfusions typically are reserved for individuals who are actively bleeding or those who have experienced life-threatening bleeding below a certain platelet count. Hematopoietic growth factors may benefit a minority of patients with MDS. Allogeneic stem cell transplantation (SCT) is the only curative modality for MDS,