What is Myelodysplastic Syndrome?

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Normal blood cells

- Red blood cells
- White blood cells
- Platelets
Normal bone marrow

- Red cell precursors
- White cell precursors
- Platelet precursors (megakaryocytes)
Myelodysplastic syndrome definition

“Clonal bone marrow stem cell disorder characterized by ineffective blood cell production”

- **Clonal** - Arises in a single stem cell in the bone marrow.
- **Ineffective blood cell production** – Blood precursor cells are present in the bone marrow, but do not produce normal numbers of blood cells.
- **Myelodysplastic** - Bone marrow cells have an abnormal appearance.
Bone marrow stem cells
Myelodysplastic syndrome findings

One or more low blood count(s)
- Low red blood cell count/hemoglobin/hematocrit (anemia) in 85%
- Low white count cell count (neutropenia) in 50%
- Low platelet count (thrombocytopenia) in 60%
Myelodysplastic syndrome presentation

- Discovered after a blood count is drawn due to symptoms, including:
  - Fatigue, weakness, shortness of breath (anemia)
  - Infections (neutropenia)
  - Bleeding, petechiae, bruising (thrombocytopenia)
- Discovered incidentally
Myelodysplastic syndrome statistics

- 20,000 - 30,000 estimated new cases each year in the United States
- Average age 76 years
- Male > female: 4.5 vs. 2.7/100,000/year
- Acute leukemia (>20% blasts in the bone marrow) develops in 25%
- Risk factors: age, chemicals, chemotherapy, radiation, tobacco, genetic abnormalities
Age-related incidence of MDS

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Incidence Rate (per 100,000)</th>
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<tbody>
<tr>
<td>Less than 50</td>
<td>0.5</td>
</tr>
<tr>
<td>50-59</td>
<td>5.3</td>
</tr>
<tr>
<td>60-69</td>
<td>15</td>
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<tr>
<td>70-79</td>
<td>49</td>
</tr>
<tr>
<td>80 and over</td>
<td>89</td>
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Bone marrow aspirate and biopsy

**Aspirate**
- Morphology (appearance of cells under the microscope)
- Cytogenetics (chromosome analysis)
- Molecular (mutation analysis)

**Biopsy**
- Cellularity (amount of cells in the bone marrow)
Myelodysplastic syndrome diagnosis

• Adequate numbers of cells (“cellularity”) are present in the bone marrow.
• Red cell, white cell and platelet precursors (megakaryocytes) are present in the bone marrow.
• Bone marrow cells have an abnormal appearance (“dysplasia”).
Bone marrow cellularity

Decreased
Normal
Increased
Red cell, white cell and platelet precursors (megakaryocytes) are present.
Dysplasia

- Red cell precursors
- White cell precursors
- Megakaryocytes
Myeloblasts

Normal bone marrow - <5%
MDS - <20%
Acute myeloid leukemia (AML) - ≥20%
Evaluate for other causes of low blood counts and/or dysplasia

- Medications
- Vitamin B12 deficiency
- Nutrition
- Autoimmune
- Infections
- Enlarged spleen
- Alcohol
- Chemotherapy
- etc… etc… etc…
Chromosome analysis

Normal

Abnormal
Fluorescence in situ hybridization (MDS FISH)

del(5q)

+8
Mutations
# Myelodysplastic syndrome mutations

<table>
<thead>
<tr>
<th>Chromatin modification</th>
<th>DNA methylation</th>
<th>Transcripton regulation</th>
<th>RNA splicing</th>
<th>Signal transduction</th>
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</thead>
<tbody>
<tr>
<td><strong>ASXL1</strong></td>
<td><strong>TET2</strong></td>
<td><strong>RUNX1</strong></td>
<td><strong>SF3B1</strong></td>
<td><strong>NRAS</strong></td>
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<tr>
<td><strong>EZH2</strong></td>
<td><strong>DNMT3A</strong></td>
<td><strong>BcoR</strong></td>
<td><strong>U2AF1/U2AF35</strong></td>
<td><strong>JAK2</strong></td>
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<tr>
<td><strong>IDH2</strong></td>
<td><strong>IDH1</strong></td>
<td><strong>ETV6</strong></td>
<td><strong>SRSF2</strong></td>
<td><strong>CBL</strong></td>
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<tr>
<td><strong>DNA repair</strong></td>
<td><strong>DNA repair</strong></td>
<td><strong>ZRSR2</strong></td>
<td><strong>U2AF1/U2AF35</strong></td>
<td><strong>CBL</strong></td>
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<td><strong>Cohesin complex</strong></td>
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MDS Prognosis

• Number of low blood counts (hemoglobin <10, neutrophils <1800, platelets <100,000)

• Percentage of bone marrow blasts

• Chromosome abnormalities

• (Mutations)