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March 2011 (updated May 2015)

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A program of the Hartford Geriatric Nursing Initiative

Myelodysplastic Syndrome: A Primer for Geriatric Clinicians

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What is Myelodysplastic Syndrome (MDS)?

MDS encompasses a group of disorders in which hematopoietic stem cells have impaired differentiation and accelerated cell death. Despite one or more peripheral-blood cytopenias (anemia, neutropenia, and/or thrombocytopenia), patients with MDS usually have hypercellular bone marrow, often with dysplastic features.

Most cases of MDS are primary (*de novo*) and of unknown cause. In 10-20% of cases, however, the condition is secondary and follows treatments with radiation or chemotherapeutic agents, particularly alkylating agents. Both primary and secondary MDS can progress to marrow failure or evolve into acute myeloid leukemia (AML). Secondary MDS has an inherently poor prognosis, with a high risk of evolution to AML.

The risk of MDS increases with age and most cases occur in elders. Indeed, more than 80% of patients with MDS are over age 60 at the time of diagnosis.

Clinical Presentation

Anemia (often macrocytic) is the most frequent cytopenia in MDS. Symptoms of dyspnea and fatigue may result from decreased hemoglobin levels and tissue hypoxia. Patients with neutropenia develop infections, and infections account for most deaths in MDS. Thrombocytopenia can cause petechiae, purpura, or other bleeding manifestations.

In a recent survey, MDS patients reported many symptoms, including fatigue, bruising, bleeding, fevers, recurrent infections, unintentional weight loss, and various other factors affecting quality of life. As a result of these MDS-related symptoms, 30% of the survey participants were unable to work, and 5% had other types of disability.

Diagnosis

MDS should be included in the differential diagnosis whenever anemia, leukopenia, neutropenia and/or thrombocytopenia are found in an older adult. As these hematological abnormalities are nonspecific, other causes must also be considered, including (but not limited to) nutritional deficiencies, anemia of chronic disease, hemolysis, aplastic anemia, myeloproliferative diseases, human immunodeficiency virus infection, and copper deficiency. Table 1 lists a recommended initial evaluation of cytopenia.

Table 1. Initial Evaluation of Patients with Cytopenia

Detailed history:

- Types and severities of other medical conditions
- Medication, both prescription and over-the-counter
- Dietary, including supplements
- Environmental exposures (hydrocarbons, pesticides, etc)
- Exposure to previous chemotherapy or radiation

Laboratory tests:

- Complete blood count including differential white count
- Reticulocyte count
- Review of peripheral blood smear
- Serum ferritin, iron, and total iron binding capacity
- Erythrocyte folate level
- Serum vitamin B12 level
- Serum erythropoietin level (if patient has anemia)

When your evaluation yields no explanation for a patient's anemia or other cytopenias, hematology consultation should be obtained. The definitive diagnosis of MDS will require a bone marrow aspirate and biopsy.

Prognosis

The Myelodysplastic Syndrome International Prognostic Scoring System (IPSS) uses several clinical characteristics (percentage of bone marrow blasts, presence of various chromosomal abnormalities, and number of cytopenias) to predict survival and the risk of transformation to AML in patients with *de novo* MDS. Several IPSS calculators can be found with a simple Internet search.

TIPS FOR DEALING WITH MYELODYSPLASTIC SYNDROME (MDS)

- Always consider MDS when older adults present with anemia, neutropenia, leukopenia, and/or thrombocytopenia.
- When an older adult has a cytopenia, initiate the evaluation outlined in Table 1.
- If the cause of cytopenia is not evident from the results of the evaluation, consider referral to a hematologist for bone marrow aspirate and biopsy.
- For patients with confirmed MDS, predict prognosis using the International Prognostic Scoring System.

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Management

Optimal management of patients with MDS reflects a constructive collaboration between primary care clinicians and hematologists. Objectives of treatment depend on the stage of the disease, patient's age and performance status, presence and severity of other medical conditions, and the patient's ability and willingness to undergo treatment and tolerate its side effects. The focus is on monitoring, medical support, treatment of infections, dealing with patients at high risk of progression to AML, and providing psychosocial support to patients and their families.

Monitoring Periodic monitoring of blood counts allows assessment of the trends and severity of MDS. This allows identification of individuals at risk for progression to AML.

Medical Support Standard supportive care involves maintaining and improving quality of life through transfusions of red blood cells and/or platelets, and administration of cytokines (erythropoiesis stimulating agents, granulocyte colony-stimulating factor). Patients who require frequent red cell transfusions can develop iron overload and need monitoring of ferritin levels; such patients may require chelation therapy with deferoxamine or deferasirox.

Treating Infections Bacterial, viral, and fungal infections, sometimes life-threatening in nature, can develop in neutropenic patients. Antimicrobial therapy is appropriate for treating such infections, particularly bacterial infections, which can progress rapidly to sepsis. Antibiotics must be used judiciously, however, to minimize emergence of antibiotic-resistant organisms.

Approach to High-Risk Patients Patients at high risk of developing AML, such as those exposed to radiation or alkylating agents, or those with specific cytogenetic abnormalities like deletion of the long arm of chromosome 5 (known as "5q-"), should be considered for treatment with azacitidine, decitabine or lenalidomide. These medications (especially lenalidomide), can have an impressive response rate, but they can cause myelosuppression, especially during the initial phase of treatment.

Patients with MDS should also consider participation in clinical trials of novel agents or hematopoietic stem cell transplantation. Currently, hematopoietic stem cell transplantation from an HLA-compatible related or unrelated donor is the only potentially curative treatment for MDS.

Psychosocial Support Patients with MDS require frequent medical appointments and transfusions, develop infections, and in some cases have frequent hospitalizations. As a result, many patients become depressed. Their families are also affected, as they provide transportation and financial support for the patients. As a results, patients and their families need ongoing psychosocial support.

Table 2. Key Facts About MDS
MDS is a disorder of hematopoietic stem cells that causes ineffective hematopoiesis, leading to one or more peripheral blood cytopenias.
MDS is primarily a disorder of older adults. More than 80% of patients are age 60 or older at diagnosis.
Anemia is the most common presenting cytopenia in MDS.
A detailed history and physical examination and basic laboratory testing is essential to rule out other more common causes of cytopenias.
Patients with unexplained cytopenias should be referred to a hematologist for further evaluation, including bone marrow aspiration and biopsy.
MDS in many patients evolves into marrow failure or acute myeloid leukemia (AML).
The risk of developing AML can be predicted with on-line calculators.

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Supported by: Donald W. Reynolds Foundation, Arizona Geriatric Education Center and Arizona Center on Aging

This project was supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number UB4HP19047, Arizona Geriatric Education Center. This information or content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S. Government.