The Myelodysplastic Syndromes: Challenges and Strategies for Effective Outpatient Management

At a Glance

Myelodysplastic syndromes are a category of incurable malignancies that affect mainly older adults. Cytogenetic testing and advances in targeted therapies have provided a means to extend and improve the quality of life for these patients. However, patient education and overcoming barriers, such as ageism, complex and expensive treatment regimens, and adverse events, are critical to ensuring that patients with a myelodysplastic syndrome can fully benefit from evolving therapy options.

Myelodysplastic syndromes are a class of incurable diseases that originate in the bone marrow. The disease processes are quite complex and often difficult for healthcare professionals to articulate to patients and family caregivers. Sandra E. Kurtin, RN, MS, AOCN®, ANP-C, simplified the process by comparing myelodysplastic syndromes to a "broken factory." This group of disorders is associated with the bone marrow's inability to produce healthy leukocytes, erythrocytes, and platelets. Myelodysplastic syndromes are malignant processes that can be a precursor for acute myeloid leukemia (AML). Although no complete cure is currently available, treatments are available to support patient health for months to several years after diagnosis.

Kurtin noted that nurses must embrace the fact that treatment selection for myelodysplastic syndromes is moving toward molecular-driven models. The complexity of disease and treatment can be difficult for even seasoned health professionals to grasp, which poses a challenge for patient and family education.

Cytogenetic Evaluation

Jean A. Ridgeway, MSN, APN, NP-C, AOCN®, reported that mapping the pathophysiology of this class of hematologic diseases has come a long way since they were first classified in the 1970s. Early classification models, including the French-American-British (FAB) classification in 1976 and the World Health Organization's late-1990s revision of this system focused on cell morphology and myeloblast (blast) counts. These systems describe the disease progression based on extent of refractory anemia and increase in blasts within the marrow.

Ridgeway noted that, also in the 1990s, advances in genetic research allowed clinicians to move toward a cytogenetic evaluation of myelodysplastic syndromes, and this shift in focus greatly enhanced the understanding of the disease process and treatment effects. In addition to the previously defined parameters of cell morphology, researchers discovered that these syndromes involve multiple cytogenetic defects. This discovery has allowed clinicians to use cytogenetics to drive diagnosis, prognosis, and treatment selection (Vardiman et al., 2009; Westers et al., 2011).

Conventional metaphase cytogenetic analysis is the gold standard for analyzing karyotypes associated with myelodysplastic diseases. This process uses an aspirated sample of bone marrow to examine 20 cells that are in the metaphase stage of cell division. Clinicians are then able to map the malignant defects within chromosomes. One drawback to the process is that the cells must be in active cell division because the errors are not apparent when this process is used on non-dividing cells.

Emerging technologies are overcoming limitations to metaphase cytogenetic analysis. For example, use of the single-nucleotide polymorphism (SNP, pronounced "snip") array analysis is able to identify abnormalities in non-dividing cells. In addition to helping in diagnosis and prognosis, the SNP array also can track response to treatment, particularly therapies that target the *TET2* and *TP53* genes (Garcia-Manero, 2010; Gondek et al., 2008; Graubert, 2011; Maciejewski & Mufti, 2008; Tiu, Visconte, Traina, Schwandt, & Maciejewski, 2011).

Flow cytometry is another emerging technology that may be useful in identifying prognostic features of myelodysplastic syndromes. This technology analyzes cell receptor and internal protein expression. The clinician can use this to evaluate cells from both qualitative and quantitative perspectives. Although flow cytometry has potential uses, studies indicate that standardization and refinement of quantification measures is needed (Vardiman et al., 2009; Westers et al., 2011).

Emerging technologies such as flow cytometry and SNP array analysis are helping researchers study potential targeted therapies that can be tailored to a patient's specific genetic makeup. Studies are under way to identify novel agents and targets in addition to *TET2* and *TP53* (Bejar, Levine, & Ebert, 2011; Kurtin, 2011; Tiu et al., 2011).

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Comprehensive Prognostic Indicator

The International Prognostic Scoring System (IPSS) takes variables from cytogenetic evaluation and cell morphology indicators identified by early classification systems (e.g., cytopenias and number of bone marrow blasts) to create a comprehensive score to predict survival. Patients' scores are then placed in four risk categories: low, intermediate-1, intermediate-2, and high. Low-risk patients are expected to live 5.7 years, intermediate-risk patients have a prognosis of 1.2–2.5 years, and high-risk patients are expected to live only a few months (0.4 years) (Greenberg et al., 2011).

Ridgeway noted that IPSS also serves to help clinicians to form a treatment strategy. In low-risk patients, the priorities are to manage cytopenias and their associated symptoms by administering packed red blood cells and thrombopoietin receptor agonists, as well as erythropoiesis-stimulating, immunomodulatory, and immunosuppressive agents (Ridgeway, Fechter, Murray, & Borràs, 2012). Prolonging survival is the focus of treating high-risk patients. These patients typically receive hypomethylating agents. Also, the only known "cure" for myelodysplastic syndromes is allogeneic hematopoietic stem cell transplantation; therefore, patients who fall into the high-risk category should be evaluated as potential candidates for transplantation (Ridgeway et al., 2012). Ridgeway and Kurtin both hesitated to use the word "cure" because myelodysplastic syndromes behave differently than other malignancies in that stem cell transplantation may not offer a complete response.

Complete Patient Care

Although the IPSS indicator is a handy tool that helps determine treatment strategy and risk, Kurtin noted that these prognostic categories were determined before current treatments were available. Therefore, high-risk patients have a prognosis of only a few months *without treatment*. The implications of this are that clinicians must identify and administer treatment quickly once a myelodysplastic syndrome is diagnosed.

In addition, Kurtin noted that although this is a disease that occurs in mostly older adults with the average age at diagnosis being aged 73, chronological age should not be the only indicator of treatment planning and prognosis evaluation. Performance status, frailty (failure to thrive), and comorbidities also should be considered (Balducci & Exermann, 2000; Pal, Katheria, & Hurria, 2010). Kurtin illustrated this point by noting that the average life expectancy for a 75-year-old in the United States is 12.5 years, and low-risk patients have an average time to progression to AML of 9.4 years (Greenberg et al., 1997). A diagnosis at older age does not indicate a death sentence. With proper treatment, an older adult can live an active life despite myelodysplastic diseases.

Family caregivers have an important role in ongoing care. Kurtin likes to call them her "truth squad" because family members and friends often can see things that the patient does not realize are occurring regarding the patient's health, such as cognitive problems and mood or personality changes. In addition, some patients may not want to admit certain symptoms for many reasons, including fear of disease progression or not wanting to be a burden. Family caregivers, including significant others, children, siblings, and friends, can provide an accurate assessment of daily life that clinicians are unable to observe in the brief window of an office visit (see Figure 1). Family can observe indicators of wellness, such as appetite, activity level, weakness, lack of endurances, shortness of breath, and sleeping habits (Pal et al., 2010). These indicators are important for identifying prognostic factors not included in standard laboratory or physical examinations, such as undiagnosed comorbidities, quantifying functional status, and determining frailty.

Physical
Decreased strength, decreased body organ function, altered immune response, diminished physiologic reserve, increased risk of developing concurrent illness, asthenia, exacerbation of other health conditions (e.g., CHF), dyspnea, bone pain and discomfort, malaise, fever, bleeding, weight loss, skin rash, symptoms from therapy, night sweats, and limited ability to adequately treat other conditions (e.g., hip replacement)

Social
Altered role function, diminished social interaction with friends and family, diminished economic resources, diminished social network, increased financial burden from health care, time associated with therapy, activity restrictions, planning for future, transportation challenges, altered support from family and friends, economic challenges, and alteration in sexuality

Emotional
Anxiety, loneliness, despair, uncertainty, anger and frustration, depression, communication with the healthcare team, and patient-provider relationship

Functional
Fatigue, potential for decreased cognitive function, diminished stamina, decreased mobility, missed work associated with illness and therapy, diminished ability to perform IADLs or ADLs, diminished independence, cognitive dysfunction, and demands of illness

Spiritual
Renewed appreciation for life, renewed appreciation for relationships, enhanced faith and beliefs, hopelessness, abandonment, loss of self, and search for balance (e.g., positive and negative aspects of life)

ADL—activities of daily living; CHF—congestive heart failure; IADL—instrumental ADL

Note. Five quality-of-life domains are delineated here; however, other issues are not listed that may have a significant impact.

FIGURE 1. Quality-of-Life Issues by Domain for Patients With Myelodysplastic Syndromes

Note. From "The Importance of Quality of Life for Patients Living With Myelodysplastic Syndromes," by M.L. Thomas, N. Crisp, & K. Campbell, 2012, *Clinical Journal of Oncology Nursing, 16*(Suppl. 1), p. 48. Copyright 2012 by the Oncology Nursing Society. Adapted with permission.

Treatment Options

Unlike other cancers, such as lymphoma, where clinicians have a multitude of agents in their arsenal, Kurtin likened the treatments for myelodysplastic disorders as a tasting menu rather than an extensive buffet. Although research for novel therapies is ongoing, currently only three agents are approved by the U.S. Food and Drug Administration for treatment of myelodysplastic disorders: azacitidine, lenalidomide, and decitabine (Kurtin & Demakos, 2010). Therefore, clinicians need to adequately pace themselves so they do not run out of treatment options.

Although allogeneic stem cell transplantation offers hope for a cure, this is not an option for most patients, and not every patient who undergoes transplantation will experience a complete response (Kurtin, 2011; Kurtin & Demakos, 2010). However, stem cell transplantation does offer the benefits of stabilizing disease, improving hematologic status, and minimizing the need for transfusions.

In regard to treating older adults with myelodysplastic syndromes, treatment usually aligns with the National Comprehensive Cancer Network's approach to oncology care. This guideline provides a range of characteristics that encompass older adults who are functionally independent and are candidates for most treatment options to those with poor prognosis and functional status where the focus of treatment is supportive care and symptom management (National Comprehensive Cancer Network, 2011, 2012). However, one formula does not apply to all patients with myelodysplastic diseases, and treatment plans can change throughout the disease trajectory. Kurtin noted that treatment triggers can alert clinicians as to the need to modify therapy. These triggers include when a patient becomes dependent on transfusions, progression or increased symptom burden of cytopenias, increased blasts, and progression to high-risk disease.

Patient and Caregiver Education

Sara M. Tinsley, ARNP, AOCN®, expressed the importance of clear communication and patient and family education when treating myelodysplastic syndromes. "Patients really want clear information about what their diagnosis is. It's not like when patients with breast cancer tell their friends, and everyone knows what they have, so they don't have to go into a lot of explanation. Patients with myelodysplastic syndromes have the task of explaining what their disorder is, not only to their friends and family, but also to other healthcare providers who may not care for many patients with these syndromes."

Jayshree Shah, APN-C, AOCN®, MSN, BSN, BS, RN, CCRP, indicated that nurses are in a position to empower patients and families to be active participants in their care. Oncology nurses can directly affect outcomes by thoroughly understanding the disease state and available treatment options, educating patients and families in plain language about elements of treatment such as duration of therapy and potential adverse events, and providing strategies for how the patients can positively affect outcomes through healthy lifestyle choices (Kurtin, 2012). Shah also reminds nurses that a multidisciplinary approach to care using effective communication strategies among all healthcare professionals (e.g., specialists, primary care physicians, pharmacists, other nurses) results in better patient outcomes (Kurtin, 2012).

Healthcare professionals also can help by considering lifestyle factors, such as older adults who are able to drive but need to schedule appointments in the daytime because they have poor night vision. Although some older adults are retired, many still may need to schedule treatments around work schedules or social commitments. Offering this flexibility will not only allow patients to maintain active lifestyles but also will help motivate them to stick with the treatment schedule.

Nurses should frequently remind patients that treatment is "a marathon, not a sprint."

Kurtin said that it is important for patients and families to understand that, unlike many cancers that have a definitive beginning and end to treatment, myelodysplastic syndromes are chronic illnesses that require management for the remainder of the patient's life span. Patients may express frustration with this, and nurses should frequently remind them that treatment is "a marathon, not a sprint."

Although life-sustaining, treatment for myelodysplastic syndromes is difficult and time intensive. Patients can be subjected to many transfusions over the course of their lifetime. "Unfortunately, cytopenias are expected to become worse before they get better because treatment cleans the marrow to allow for the new growth of healthy cells," Kurtin explained. Worsening cytopenias will naturally lead to a more intense symptom experience. In addition, treatments also will suppress patients' immune systems, thus requiring them to take extra precautions to avoid infections. Kurtin stressed that patients and families need to thoroughly understand this trajectory at the outset of treatment so that they avoid frustration and discouragement. Patients who understand the disease process and that they need to "get to the other side of the [cytopenias] ravine" before their condition can improve are more likely to comply with the treatment regimen.

In addition to the effects of immunosuppressive therapies and worsening cytopenias, patients also will have to deal with toxicities related to multiple transfusions. Shah noted that healthcare professionals should be aware of the potential for iron overload because each unit of packed red blood cells that a patient receives contains 25 mg of inextricable iron. This extra iron cumulates in the heart, liver, and endocrine system, which can lead to toxicities in these organs. Iron chelation therapy can correct this, but Shah warns that this is not without side effects. Patients who undergo chelation therapy can experience pancytopenia, high-frequency hearing loss, and ocular disorders, such as cataracts and increased pressure (Jabbour, Garcia-Manero, Taher, & Kantarjian, 2009; Kurtin, 2007; Malcovati et al., 2005).

Reliable Resources for Patients

Shah noted that the International Nursing Leadership Board of the Myelodysplastic Syndromes Foundation has created a patient education tool called *Building Blocks of Hope: A Patient and Care Giver Guide for LIVING With MDS.* The guide answers questions about the syndromes and their treatment options, and offers suggestions about how patients can adopt healthy strategies and be an active part of the treatment team. The guide encourages patients to continue with usual activities while using common sense to avoid illnesses associated with suppressed immunity.

Tinsley suggested that, in addition to information nurses can provide during appointments, a wealth of resources are available on the Internet from many organizations, such as the Myelodysplastic Syndromes Foundation (www.mds-foundation.org), the Leukemia and Lymphoma Society (www.lls.org), and the American Cancer Society (www.cancer.org). These sites offer patient-specific information written in clear language that helps to cut through medical jargon. Some sites offer access to support groups, message boards, and clinical trial information.

Summary

To effectively manage myelodysplastic syndromes, clinicians must have a thorough grasp of the disease state, treatment trajectory, and expected side effects. In addition, effective communication, both through patient education and among multidisciplinary team members, will help improve treatment compliance and patient outcomes.

Kurtin stressed that continued treatment provides the best opportunity for positive responses. She noted that barriers to treatment, including clinicians' ageism toward patients, patients' and caregivers' perceptions of lack of treatment benefit, treatment noncompliance, and toxicities and adverse events, can be overcome by clear expectations and care plans, rapid identification and management of side effects and adverse events, and a partnership with the patient and family (Eliasson, Clifford, Barber, & Marin, 2011). Overcoming these barriers can help to ensure that patients with myelodysplastic syndromes can live full, active lives despite their illness.

—Reporting by Laura J. Pinchot, BA

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