MULTIPLE MYELOMA AND ITS TREATMENT

Barbara Felder, RN, BSN, OCN®

CASE STUDY

In 1995, Mr. F visited an emergency room with symptoms of an upper respiratory infection and severe rib pain induced by coughing. He was diagnosed initially with pneumonia and two fractured ribs; however, further workup revealed elevated serum creatinine, calcium, and protein levels and severe anemia (hemoglobin = 4.1 mg/dl). Malignancy was suspected, and additional diagnostic test results, including a serum immunoglobulin A (IgA) level higher than 7,000 mg/dl, led to the diagnosis of stage IIIB multiple myeloma (MM).

Mr. F was treated with vincristine, doxorubicin, and dexamethasone (VAD) for one year and had a partial response to the chemotherapy. His bone pain resolved, renal function recovered, IgA level dropped to within normal limits, and hemoglobin rose to and remained greater than 10 mg/dl. He then received interferon followed by cyclophosphamide, but his disease was refractory to these agents. Mr. F underwent high-dose chemotherapy with tandem autologous stem cell transplants in March and September 1997. Disease progression was noted in January 1998 when his IgA was 3,775 mg/dl; as a result, he was started on cyclophosphamide, dexamethasone, etoposide, and cisplatin. Mr. F's disease continued to progress, and he was started again on the VAD regimen in March 1998. Prior to restarting the VAD regimen, Mr. F's cardiac ejection fraction was 65%. In July 1998, dexrazoxane was added to the VAD regimen and every 12 hours after three cycles of VAD, his IgA level dropped to 57%. In July 1998, dexrazoxane was added to the VAD regimen and in October 1998, and in January 2000, it was 66%.

Mr. F received maintenance therapy consisting of thalidomide and dexamethasone from August 1999 to May 2000. At the end of May 2000, his IgA level rose to 3,572 mg/dl and a high-grade anaplastic plasmacytoma of his right maseter muscle originating from the same cell line as his MM was diagnosed. Another cycle of dexrazoxane and VAD was administered, but Mr. F's IgA level rose to 5,960 mg/dl. He received topotecan in July and August 2000, and despite frequent transfusions, his hemoglobin level remained low. His serum creatinine level remained high, and he chose not to receive dialysis. His disease rapidly progressed, and he died in September 2000.

1. Which of the following statements best reflects current statistics regarding the incidence and death rate of MM in the United States?

A. The number of new cases of MM in 2002 approximated the number of people who died from the disease.
B. The number of people diagnosed with MM in 2002 was three times greater than the number who died from the disease.
C. The number of people who died from MM was three times greater than the number diagnosed with the disease in 2002.
D. The incidence and death rate statistics for MM are similar to rates for breast cancer, colon cancer, and lymphoma.

2. Clinical manifestations of MM result from

A. Paraproteins that block small blood vessels when the weather is cold.
B. The rationale for maintaining complete bed rest and avoiding range of motion exercises
C. Enduring expected severe pain
D. Risk of pathologic fractures and associated safety precautions

3. Dexrazoxane is thought to reduce the cytotoxic effects of anthracyclines by

A. Binding to free and bound iron.
B. Reducing left ventricular enlargement.
C. Converting to an active sulfhydryl compound.
D. Binding to derivatives of chemotherapy agents.

4. Which of the following patient-teaching topics should nurses discuss with patients with MM who have multiple lytic skeletal lesions?

A. The need for oral calcium supplementation to strengthen bone.
B. The rationale for maintaining complete bed rest and avoiding range of motion exercises.
C. Enduring expected severe pain.
D. Risk of pathologic fractures and associated safety precautions.

DISCUSSION

Question 1: The correct answer is choice A, the number of new cases of MM in 2002 approximated the number of people who died from the disease. Approximately 14,400 new cases of MM were diagnosed in 2002, and 11,200 people died of the disease (Jemal, Thomas, Taylor, & Thun, 2002). According to the MM Research Fund (2002), about 40,000 people in the United States in 2002 are living with MM.

MM is a clonal B cell disorder arising from plasma cells. The disease affects older adults,
and its etiology is unknown. Risk factors associated with MM include ethnicity (i.e., African Americans have a greater risk than Caucasians), family history of MM, high-dose ionizing radiation exposure, and occupational exposure to rubber, agricultural chemicals, chemical agents in engine exhaust, and petroleum refinery waste products (Malamed, 1999; Sonoda, Nagata, Mori, Ishida, & Imai, 2001; Speer, Semenza, Kuroski, & Anton-Culver, 2002).

Zaidi and Vesole (2001) found that the initial oncogenic event that causes MM occurs 10–15 years before clinical manifestations of the disease become evident. Myeloma cells develop multiple chromosomal abnormalities, which may explain why conventional therapy often is met with resistance and why eradicating the disease is difficult (Bergsagel & Kuehl, 2001). With conventional melphalan-based chemotherapy, only 5% of patients achieve a complete response. The median duration of response remains about 18 months, and median survival is three years (Zaidi & Vesole; Zweegman & Huijgens, 2002). However, survival data are improving; complete remission rates of 25%–30% with median survival exceeding five years have been reported in recent clinical trials of high-dose chemotherapy with autologous hematopoietic stem cell transplant (Bensinger, 2002; Durie, 2001; Fassas & Tricot, 2001). Thalidomide has produced response rates of 65%–75% in previously untreated patients when administered concurrently with dexamethasone (Weber, 2002). Thalidomide also has been shown to have activity in patients with refractory MM, with response rates of 50%–60% when combined with dexamethasone, and response rates as high as 80% when combined with dexamethasone and chemotherapy (Barlogie et al., 2001). Gemcitabine has been evaluated for the treatment of MM but, in a phase II study, the drug did not produce a response to treatment, stable disease was observed in only 16 of 28 patients, and mean survival was just eight months (Weick, Crowley, Hussein, Moore, & Barlogie, 2002). Targeted therapies for MM currently are under development or being used in clinical trials examining genetic abnormalities in myeloma cells to enhance chemoradiosensitivity, dendritic cell therapy (patients with MM have been found to have functionally defective peripheral blood dendritic cells), and three types of immunotherapy (i.e., passive antibody-mediated, adoptive T cell, and active specific vaccination) (Anderson, 2001; Ratta et al., 2002; Ruffini & Kwak, 2001; Yi, Desikan, Barlogie, & Munshi, 2002).

Mr. F lived with MM for about five years. His response to treatment mirrors that of 95% of those with the disease who do not achieve complete remission with conventional chemotherapy and 65%–75% who do not respond to high-dose chemotherapy and stem cell transplant (Bensinger, 2002; Durie, 2001; Fassas & Tricot, 2001). Despite advances in its treatment, MM remains a disease with a poor prognosis.

Choices B and C are incorrect because the number of people diagnosed with MM does not greatly exceed nor is it significantly less than the number dying from the disease. Choice D is incorrect because MM’s incidence and mortality rates are approximately equal, unlike lymphoma and breast and colon cancer rates in which the number of people diagnosed far exceeds the number who died of these cancers in 2002 (Jemal et al., 2002).

**Question 2:** The correct answer is choice B, monoclonal protein production and its accumulation in the serum or urine. MM and monoclonal gammopathy of undetermined significance are the two most common causes of monoclonal protein in serum or urine. The most widely accepted major diagnostic criteria for MM include plasmacytoma confirmed by biopsy, more than 30% plasma cells in the bone marrow, a monoclonal globulin spike on serum protein electrophoresis (immunoglobulin G [IgG] > 3.5 g/dl, IgA > 2 g/dl), and the presence of light chains on urine electrophoresis (Brigden, 1999). The frequency of the various types of MM parallels the serum concentrations of the immunoglobulins in healthy individuals: The IgG subtype occurs in 60%–70%, the IgA subtype occurs in 20%, and the light chain subtype occurs in 15% of patients diagnosed with MM (MM Organization, 2001). In 75% of patients with MM, plasma cells also produce Bence Jones proteins, which are monoclonal incomplete immunoglobulin or light chains that are found in patients’ urine (MM Organization).

Common presenting signs and symptoms of MM include pain in the ribs or back, which results from accumulation of plasma cells that causes tiny fractures of the bones. Skeletal x-rays are abnormal in about 80% of patients diagnosed with MM (Kyle, 1999). Renal insufficiency, defined as serum creatinine greater than or equal to 2 mg/dl, is present in 25% of patients at diagnosis and most often is caused by “myeloma kidney” (i.e., the obstruction of the kidney tubules by casts containing Bence Jones protein) and hypercalcemia (Kyle; Sakhuja et al., 2000). Fatigue and pallor secondary to anemia and frequently recurring infections also can occur (Kyle).

Mr. F’s presenting signs and symptoms of MM are typical of the disease: He had severe rib pain, and multiple rib fractures were evident when the area was x-rayed. Mr. F also was in acute renal failure at the time of diagnosis and was severely anemic; his serum IgA level was more than 7,000 mg/dl (the normal range is 70–440 mg/dl).

Choice A, paraproteins that block small blood vessels when the weather is cold, causes a complication of MM known as cryoglobulinemia. Cryoglobulins are cold-precipitable immunoglobulins associated with a number of infectious, autoimmune, and neoplastic disorders (Dammacco, Sansonno, Piccoli, Tucci, & Racanelli, 2001). In cold weather, patients with MM-associated cryoglobulinemia experience numbness of the fingers and toes, which is caused by paraprotein particles blocking blood flow through small vessels. In rare instances, cryoglobulinemia can result in gangrene of the affected extremities (Cirino & Barbano, 1999; Trejo et al., 2001).

Choice C, light chain plasma cells and serum proteins that combine to form amyloid protein, causes amyloidosis. This rare complication is found most often in patients with MM whose plasma cells produce only light chains. The combination of these plasma cells with other serum proteins produces amyloid protein, which is a starch-like substance. Amyloid protein can infiltrate tissues and organs, such as the kidneys, liver, gastrointestinal tract, and heart. This protein also has the ability to infiltrate the walls of blood vessels and cause them to lose their elasticity. Therefore, symptoms of MM-associated amyloidosis include hypotension, gastrointestinal bleeding, and kidney, liver, and heart failure (Chang, Lu, Tsay, Chang, & Lee, 2001; Desikan et al., 1997; Kyle, 1999).

Choice D, high plasma viscosity, which causes the blood to become thick and sticky, is associated with hyperviscosity syndrome, a known complication of MM. This syndrome can cause dyspnea, confusion, and chest pain; however, MM-associated hyperviscosity syndrome is a reversible cause of dyspnea and should be considered in patients with MM who do not have cardiac or pulmonary impairment and become dyspneic (Coppell, 2000).

**Question 3:** The correct answer is choice A, binding to free and bound iron. Dexrazoxane is thought to reduce the cardiotoxic effects of anthracyclines by binding to free and bound iron, thereby reducing the formation of anthracycline-iron complexes and the subsequent generation of reactive oxygen molecules that are toxic to the surrounding cardiac tissue. The drug appears to offer cardiac protection regardless of preexisting cardiac risk factors and safeguards patients who have received a cumulative doxorubicin dose greater than or equal to 300 mg/m². The use of dexrazoxane allows the delivery of higher cumulative doses of anthracyclines without the expected consequence of cardiomyopathy (Hochster, 1998; Wiseman & Spencer, 1998).
Mr. F had received 450 mg/m² of doxorubicin when his ejection fraction dropped from 65% in March 1998 to 57% in June 1998. In the following 18 months, he received an additional 11 cycles of VAD chemotherapy (an added 550 mg/m² of doxorubicin) given concurrently with dexrazoxane. His ejection fraction rose to 62% in October 1998 and was 66% in January 2000, illustrating the cardioprotective effect of dexrazoxane. Choice B, reducing left ventricular enlargement, is incorrect because anthracycline-induced cardiomyopathy is characterized by global systolic dysfunction and minimal left ventricular enlargement. Mild to moderate mitral insufficiency also is usually present. Monitoring left ventricular function (not size) by assessing cardiac ejection fraction is the most reliable method of identifying anthracycline-induced cardiomyopathy (Keefe, 2001; Pai & Nahata, 2000). According to the American Society of Clinical Oncology’s clinical practice guidelines, patients receiving dexrazoxane should continue to be monitored periodically for cardiac toxicity even though they are receiving a cardioprotectant (Hensley et al., 1999).

Choice C, converting to an active sulphydryl compound, and choice D, binding to derivatives of chemotherapy agents, describe the action of another chemoprotectant—amifostine. Amifostine is a prodrug converted by alkaline phosphatase to an active sulphydryl compound that protects normal cells by scavenging free radicals, depleting oxygen, and binding to active derivatives of chemotherapy agents. Amifostine is used in conjunction with cisplatin to reduce cumulative renal toxicity, as well as xerostomia secondary to radiation therapy to the head and neck (Foster-Nora & Siden, 1997; Links & Lewis, 1999).

Question 4: The correct answer is choice D, risk of pathologic fractures and associated safety precautions. Patients with MM require nursing care to manage problems and symptoms associated with the disease, which may include pain, impaired physical mobility, fatigue, bleeding, infection, and fluid and electrolyte imbalances (Malamed, 1999; Rice & Sheridan, 2001). Many patients with MM have lytic lesions at multiple sites in the axial skeleton, which place them at high risk for pathologic fractures. Nurses must inform patients of this risk and teach safety precautions, which include instructions to use good body mechanics, change position gradually, avoid moving or lifting heavy objects, and ensure a safe hospital and home environment (e.g., implement strategies to reduce falls). Nurses also need to consult with physical therapists (PTs) regarding strengthening exercises and the need for assistive devices (e.g., back braces) and continually assess for the presence of pain (Holley, 2002; Malamed). Pamidronate often is used to treat lytic bone involvement associated with MM (Berenson, 2001). Recently, the safety and efficacy of kyphoplasty (i.e., the introduction of inflatable bone tamps into the vertebral body) in treating osteolytic vertebral compression fractures resulting from MM has been reported (Dudeny, Lieberman, Reinhardt, & Hussein, 2002).

Choice A, the need for oral calcium supplementation to strengthen bone, is incorrect because patients with MM typically present with elevated serum calcium levels, usually caused by lytic bone disease and immobility. Oral calcium supplementation would not strengthen bone; instead, it would compound patients’ already elevated calcium levels. Nurses must be alert for signs and symptoms of hypercalcemia when caring for patients with MM. Symptoms vary depending on the calcium level and rapidity with which the elevation occurs and include nausea, vomiting, constipation, lethargy, drowsiness, mood changes, muscle weakness, bradycardia, polyuria, and polydipsia (Malamed, 1999).

The rationale for maintaining complete bed rest and avoiding range of motion exercises, choice B, is incorrect because promoting and preserving patients’ mobility is a key goal in caring for patients with MM. Promoting, not restricting, activity has many benefits. Skeletal strength is enhanced, muscle strength can be maintained, fatigue may be reduced, and quality of life may be improved. Activity also is helpful in reducing MM-induced hypercalcemia (Malamed, 1999). Nurses should consult with PTs to develop individualized exercise prescriptions for patients with MM. Patients with lytic disease may require the use of assistive devices and may need PT-assisted exercise and monitoring. Choice C, enduring expected severe pain, is incorrect because although pain is associated with lytic disease, this pain can be managed effectively if appropriately assessed and treated. Metastatic bone pain has been found to interfere with work, social activities, and relationships (Coward & Wilkie, 2000). In a study of 206 patients with MM, 29% reported experiencing moderate to severe pain (Poulos, Gertz, Pankratz, & Post-White, 2001).

Undertreatment of cancer-related pain remains fairly common, and nurses play an important role in advocating for pain relief. Pain should be assessed using a standardized tool (e.g., a 0–10 scale), and trends in pain intensity, location, duration, and contributing and alleviating factors should be examined. Patients must be informed that persistent localized pain may signal a pathologic fracture and should be reported. Steadily increasing pain in the back area must be reported immediately as it may be an early sign of impending spinal cord compression. Patients’ pain management regimens should be assessed frequently and should include pharmacologic, as well as nonpharmacologic, measures. Opiates may be required to control pain. Nonsteroidal anti-inflammatory agents must be used with caution because they are associated with a higher incidence of renal failure in patients with MM.

Summary

Mr. F received several different treatment regimens for MM. He required a cardioprotectant, dexrazoxane, to continue treatment with the VAD regimen. He received interferon, high-dose chemotherapy with tandem stem cell transplants, and newer agents used in the treatment of MM, such as thalidomide and topotecan. However, as illustrated by Mr. F’s case study, MM remains an incurable disease despite advances in its treatment.

Author Contact: Barbara Felder, RN, BSN, OCN®, can be reached at barbaraefelder@cs.com.

References


