Multiple Myeloma: Most Common End-Organ Damage and Management

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Key Words
Multiple myeloma, vertebral fractures, bisphosphonates, kyphoplasty, infections, renal failure

Abstract
End-organ damage is the factor that differentiates plasma cell dyscrasia requiring therapy (active multiple myeloma [MM]) from disease that does not require therapy (monoclonal gammopathy of undetermined significance and smoldering [asymptomatic] MM). Progressive skeletal destruction is the hallmark of MM and responsible for principle morbidity in the disease. The spine is the most afflicted skeletal organ, and vertebral fractures have significantly contributed to its poor prognosis. Early mortality in MM is usually attributed to the combined effects of active disease and comorbid factors. Infection and renal failure are the main direct causes of early mortality. Using bisphosphonates to manage skeletal events mainly by preventing or slowing the destructive process has become an important adjunctive treatment in MM. Advances in minimally invasive surgical techniques, such as percutaneous vertebroplasty and kyphoplasty, offer these patients less-invasive options for treating vertebral collapse and restoring function. The aggressive management of other complications of the disease through more effective and less toxic therapy that targets the primary disease, in addition to supportive care, is resulting in patients experiencing less morbidity and probably lower mortality. This article reviews recent advances in the understanding of bone disease in MM, the role of bisphosphonates in preventing skeletal events, and available data on percutaneous vertebroplasty and kyphoplasty, and discusses the management of infection and renal failure, which seem to be responsible for high initial mortality and thereby compromise the current advances in therapy. (JNCCN 2007;5:170–178)

Multiple myeloma (MM) is a malignancy of plasma cells (B-cell origin) that accounts for 10% of all the hematologic malignancies diagnosed in the United States. In 2005, almost 16,000 new cases of MM and more than 11,000 deaths from the disease were expected. Early mortality in MM is usually attributed to the combined effects of active disease and comorbid factors. Infection and renal failure are the main direct causes of early mortality. Median survival is expected to range from 8 to 10 years with the incorporation of novel agents and treatment strategies for current management. End-organ damage is the defining factor that differentiates plasma cell dyscrasia requiring therapy (active MM) from disease that does not require therapy (monoclonal gammopathy of undetermined significance and inactive MM).

The management of active MM could be divided into managing the disease, managing complications related to the disease (end-organ damage), and preventing and interacting with complications related to the applied therapy. This article focuses on management of the most common end organs affected. Clinically, the disease manifests itself with the signs or symptoms of end-organ damage as evidenced by renal failure, anemia, hypercalcemia, and skeletal destruction. This article reviews recent advances in the understanding of bone disease in MM, the role of bisphosphonates in preventing skeletal events, and available data on percutaneous vertebroplasty and kyphoplasty, and discusses the management of infection and renal failure, which seem to be responsible for high initial mortality and thereby compromise the current advances in therapy.

Organ Damage

Skeletal System
Damage to the skeletal organ is responsible for significant morbidity in the disease and has contributed...
End-Organ Damage and Management of Multiple Myeloma

considerably to its poor prognosis. Conventional radiographs show abnormalities consisting of lytic lesions, osteoporosis, or fractures in 79% of patients with MM at diagnosis. More than 50% of patients in the Mayo study presented with vertebral fractures, making the spine the most commonly affected skeletal organ in patients with MM. In a recent review of 1027 patients with MM, plain radiograph showed that almost 80% had abnormal radiographs at diagnosis (metastatic bone survey). Osteolytic destruction of the spine is common because of diffuse involvement of bone marrow with malignant plasma cells, which results in painful progressive vertebral compression fractures at multiple levels. These vertebral body compression fractures can compromise the spinal cord and the patients' height and stature. As the vertebral bodies collapse, angulation of the spine increases pressure on the sternum, eventually resulting in sternal fractures and making restoration of stature almost impossible. In addition to the traditional symptoms associated with vertebral compression fractures, compromised pulmonary capacity is a serious complication wherein a 9% loss in predicted forced vital capacity is associated with each vertebral fracture. Chronic sequelae, such as deconditioning, deformity, insomnia, and depression, can occur and result in substantial physical, functional, and psychosocial impairment. Because of the improved survival and predicted improvement in survival of patients with MM, accompanied by the inability of bisphosphonates or active therapy to totally reverse the skeletal process, morbidity and possibly mortality from spinal disease will be on the rise. Therefore effective management of MM-associated bone disease is essential to prevent permanent disability and improve quality of life.

Mechanism of Bone Destruction in MM
The principal underlying pathologic mechanism causing bone disease in MM is a shift in the balance of bone formation and resorption towards bone resorption, and later in the disease course a dissociation between the 2 processes.

Osteoclastic activation is mainly controlled by the receptor activator of nuclear factor-κB (RANK), the receptor activator of nuclear factor-κB ligand (RANKL) for RANK, and osteoprotegerin, which is a decoy receptor for RANKL. Interactions between RANK expressed on the surface of the osteoclasts lineage cells and RANKL expressed on stromal cells play a key role in the development and activation of osteoclasts, whereas osteoprotegerin, secreted from stromal cells, inhibits RANKL–RANK signaling. MM cells stimulate osteoclastogenesis by triggering a coordinated increase in RANKL and decrease in osteoprotegerin in bone marrow stromal cells. Direct contact of stromal cells with the malignant plasma cells results in either secretion by the malignant cells or induction of the stromal cell to produce multiple cytokines, such as interleukin (IL)-1β, IL-6, tumor necrosis factor beta (TNF-β), and insulin-like growth factor (IGF). These mediators change the bone marrow microenvironment by up-regulating RANKL expression and secretion by stromal cells and osteoblasts and causing bone destruction, which then causes further release of these cytokines, thus perpetuating the cycle. Osteoprotegerin levels are decreased in MM and are inversely proportional to the extent of bone destruction. A gene dickkopf 1 (DKK1) and its associated protein DKK1, a soluble inhibitor of Wnt pathway, play an important role in osteoblastic activation. The Wnt signaling pathway is important for the growth and differentiation of osteoblasts, and mutations and alterations in the gene regulating the pathway are known to cause osteoporosis and osteopenia in animal models. The increased expression of DKK1 and the associated DKK1 protein seem to play an important role in osteoblastic inhibition. Disruption of these processes seems to be responsible for the bony manifestations of MM.

Evaluation of Spine Disease in Patients with MM
Diagnostic assessment for patients with MM should include a baseline complete skeletal survey, including plain radiographs of skull, ribs, spine, pelvis, and long bones. The most common vertebral bodies to experience compression are the lower thoracic (T11–12) and the upper lumbar. Traditional treatment of osteolytic vertebral collapse without cord compression includes bed rest, analgesics, and bracing. This type of medical treatment, however, fails to restore spinal alignment, and the lack of mobility can result in secondary complications, including worsening osteoporosis, atelectasis, pneumonia, deep vein thrombosis, decubitus ulcer, and pulmonary embolism.

Prevention of Skeletal-Related Events
Medical Management: Bisphosphonates are a rediscovered class of agents that have been shown in various studies to reduce bony complications associated with MM. During the past decade, bisphosphonates
became an important adjunctive treatment for patients with MM and bone disease. Chemically, bisphosphonates are synthetic analogues of endogenous pyrophosphate; variation of their side chains contributes to the different relative potency of bisphosphonates. Although worldwide 7 bisphosphonates are available for various conditions, only 2 intravenous forms (pamidronate and zoledronic acid) are approved in the United States for treating bone disease in MM. Clodronate, which is available in intravenous and oral forms, is not available in the United States. Clinical benefits of intravenous pamidronate, zoledronic acid, and oral clodronate were proven in randomized trials and are summarized in Table 1. Berenson et al. ran- domized 392 patients with stage III myeloma with at least 1 lytic lesion to undergo treatment with either placebo or pamidronate 90 mg intravenously, administered as a 4-hour infusion monthly for 21 cycles. After 21 cycles, the proportion of patients who developed a skeletal event was lower in the pamidronate group ($P = .015$). The mean number of skeletal events per year was also less in the pamidronate arm (1.3) than the placebo arm (2.2; $P = .008$). In a noninferiority randomized trial, zoledronic acid was compared with pamidronate in 1648 patients with either stage III MM or advanced breast cancer and at least 1 bone lesion. The proportion of patients experiencing at least one skeletal-related event and the median time to first skeletal-related event were similar in all treatment groups. Patients treated with 4 mg of zoledronic acid over a 15-minute infusion had a similar incidence of renal impairment to patients treated with pamidronate. 

An expert panel from the American Society of Clinical Oncology (ASCO) recommends that patients with MM who have lytic destruction of bone on plain radiograph undergo treatment with intravenous pamidronate, 90 mg, delivered over at least 2 hours or zoledronic acid, 4 mg, delivered over 15 minutes every 3 to 4 weeks. Initiating intravenous bisphosphonates in MM patients experiencing osteopenia, but with no evidence of lytic bone disease, is probably a reasonable approach.

Adverse events noted more frequently than placebo include renal dysfunction (albuminuria or azotemia), transient myalgias, arthralgias, and flu-like symptoms with fever. However, therapies were rarely discontinued because of adverse effects and most were either mild or reversible. More recently, osteonecrosis of the jaw has been associated with the use of pamidronate and zoledronic acid and has become a serious issue that might not be related to dental adverse events. 

### Table 1 Selected Randomized Trials Evaluating the Efficacy of Bisphosphonates

<table>
<thead>
<tr>
<th>Bisphosphonate Treatment</th>
<th>Pamidronate, 90 mg IV, Over 4 Hours Every 4 Weeks for 12 Months</th>
<th>Pamidronate, 90 mg IV, Over 4 Hours Every 4 Weeks for 21 Months</th>
<th>Zoledronic Acid, 4 or 8 mg, Every 3–4 Weeks for 12 Months vs. Pamidronate, 90 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>392</td>
<td>392</td>
<td>1648 (513 myeloma)</td>
</tr>
<tr>
<td>Pain score decline</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, equal to P</td>
</tr>
<tr>
<td>Time to first skeletal-related event</td>
<td>−12 vs. 21 m</td>
<td>−12 vs. 21 m</td>
<td>12.3 m Z vs. 12.0 m P (median)</td>
</tr>
<tr>
<td>Skeletal-related events/year</td>
<td>28% vs. 44%</td>
<td>38% vs. 51%</td>
<td>47% Z vs. 49% P</td>
</tr>
<tr>
<td>Vertebral fractures, people</td>
<td>16% vs. 27%</td>
<td>16% vs. 27%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Relative risk ratio</td>
<td>36.4%</td>
<td>25.4%</td>
<td>29.50%</td>
</tr>
<tr>
<td>NNT avoid one event</td>
<td>6.2</td>
<td>7.7</td>
<td>15.3 all patients; 5.2 N/A with x-rays</td>
</tr>
</tbody>
</table>

*Continuation of Brenson et al., trial to 21 months of treatment.

Abbreviations: ITT, intention to treat; IV, intravenous; N/A, not applicable; NNT, number needed to treat; P, pamidronate; Z, zoledronic acid.
procedures in patients undergoing long-term bisphosphonates therapy. One series suggested that the process is related to decreased immunity and susceptibility to infections, especially in patients with plasma cell dyscrasia. A recent study that assessed 202 patients with MM who were treated with bisphosphonates from April 1995 to July 2003 found that 15 patients (7.4%) developed osteonecrosis of the jaw. The median time of exposure to bisphosphonates was 39 months for patients with osteonecrosis of the jaw compared with 28 months \( (P = .048) \) for patients without. The cumulative hazard of developing osteonecrosis of the jaw was significantly higher in patients treated with zoledronic acid alone than in those sequentially treated with pamidronate alone, pamidronate + zoledronic acid, and zoledronic acid + ibandronate (1% at 1 year and 15% at 4 years vs. 0% and 5%, respectively; \( P = .003 \)). The authors concluded that risk for osteonecrosis of the jaw increases with time of exposure and probably with the use of zoledronic acid.

**Physical Management:** Increasing activities in a controlled manner is important to improve patients’ mobility with the least amount of impact on the spine. Clinicians usually recommend that patients initiate a swimming program and, as their mobility and stature improve, proceed with more involved physical therapy.

**Spinal Disease in MM**

**Operative Management of Spine Disease in MM**

Surgical intervention for skeletal disease in MM can be divided into minimally invasive and standard surgical procedures. A critical role of surgical intervention is to prevent pathologic fractures. Preventive procedures are easier to perform and carry less morbidity than procedures that are performed after the pathologic fracture. The role of preventive procedures in the management of long bones is relatively well established. For vertebral bodies, however, the process is in development because risk criteria for compression fractures are not clear. Historically, the only alternative to nonoperative treatment for symptomatic osteolytic vertebral fractures was open surgical decompression (anterior or posterior decompression and stabilization through internal fixation hardware and bone grafting), which was usually reserved for patients (< 0.5%) with gross spinal deformity or neurologic impairment.

Traditional surgical procedures of the spine in patients with MM have higher morbidity and mortality because of comorbid conditions related to age and end-organ damage inflicted by the disease.

**Back Pain and Height Loss Associated with Vertebral Compression Fractures and Minimally Invasive Procedures**

**Percutaneous Vertebroplasty:** One method to manage osteolytic vertebral collapse involves the percutaneous injection of low-viscosity liquid bone cement (poly-methylmethacrylate [PMMA]), in the vertebral body. Percutaneous vertebroplasty was first described in French literature in 1987, and resulted in early appreciable pain relief and a low complication rate. However, vertebroplasty typically does not restore lost vertebral body height and therefore does not correct altered biomechanics. Another complication is related to the uncontrolled pressure while introducing the cement material, resulting in higher incidence of leakage and possible vertebral body shattering more likely to occur in patients with MM because of diffuse bone loss. Opacified PMMA is injected through a transpedicular or paravertebral approach under continuous fluoroscopic guidance to obtain adequate filling and avoid PMMA leakage. In routine cases, vertebroplasty can be performed using local anesthesia with slight sedation in less than 1 hour. Vertebroplasty produced good results with osteoporotic fracture, with infrequent clinically significant complications (0%–10%). Experience with vertebroplasty in MM literature is limited. In a study of 40 vertebroplasty procedures, 30 were performed in patients with metastatic carcinoma and 10 in patients with MM. Pain control was 97% (70 % significantly improved), although leakage of cement outside the vertebral body occurred in 29 patients (72.5%). Two of 8 foraminal leaks produced nerve root compression that required decompressive surgery, and 1 of 21 paravertebral leaks produced transitory femoral neuropathy. The PMMA bone filler has associated problems, including epidural leakage, thermal necrosis, inability to integrate with bone, handling difficulties, and toxicity to patient and operator. Overall, the risk for complications that carry clinical significance after vertebroplasty for vertebral fracture is 1% to 3%, and most potential complications can be avoided with good technique.

**Kyphoplasty:** Kyphoplasty is a new technique that has evolved from a marriage of vertebroplasty with balloon angioplasty. It has numerous potential advantages, including lower risk for cement extravasation and
better restoration of vertebral body height. A cannula is introduced into the vertebral body through a transpedicular or extrapedicular route, followed by the insertion of an inflatable bone tamp that, when deployed, reduces the compression fracture and restores the vertebral body toward its original height. This then creates a cavity to be filled with bone cement.

The cement augmentation can be completed with more control into the low-pressure environment of the preformed cavity using viscous, partially cured cement. Using a cannula for bone filler with a steel stylet as a plunger enables the operator to apply cement at a considerably higher viscosity than is possible with injection through a 5-cc syringe and 11-gauge needle. The higher cement viscosity and lower-pressure injection reduce the risk for cement extravasation. Filling is done using continuous lateral fluoroscopic guidance similar to vertebroplasty. The procedure can be performed using general anesthesia or local with intravenous sedation. Some patients are able to return home the day of procedure. Dudeney et al. reported prospective experience with 55 consecutive kyphoplasty procedures performed in 18 patients with osteolytic vertebral compression fractures resulting from MM. Early objective analysis was made by comparing preoperative and latest Short Form (SF) 36 Health Survey scores. No major complications were directly related to this technique, and an average of 34% of lost height (range, 0%–100%) was restored. Asymptomatic cement leakage occurred at 2 (4%) of 55 levels. Significant improvement in SF-36 scores occurred for bodily pain (23.2–55.4; P = .0008), physical function (21.3–50.6; P = .0010), vitality (31.3–47.5; P = .0010), and social functioning (40.6–64.8; P = .014). Recently, the authors’ experience was extended to 52 myeloma patients with 242 treated vertebral levels. In this group, no symptomatic cement leaks occurred and asymptomatic leaks were less than 5%. Statistically significant improvement in SF-36 scores occurred for bodily pain (28.33–47.56; P = .0003); physical function (24.48–47.17; P < .0001); visual analogue pain scale score (6.18–2.84; P < .0001); and Oswestry disability index score (46.7–30.33; P = .0001).

The use of kyphoplasty should be considered in patients with back pain where the clinical findings correlate with radiologic findings. Patients with asymptomatic fractures appearing to compromise the spinal structure should be pursued for kyphoplasty to avoid further deterioration and symptom development leading to significant morbidity. Patients who present with fractures that are less than 6 months old have a better chance of restoring a large percentage of lost height. When doubting whether to perform the procedure (usually in patients who are minimally symptomatic or when baseline radiologic studies show only severe osteoporosis or minimal compression of the vertebral bodies), follow-up with spinal x-rays and magnetic resonance imaging (MRI) should be considered. Clinical or radiologic worsening of the symptoms or signs should guide the decision. Using kyphoplasty to prevent vulnerable vertebral bodies from fracturing is not well established, because no objective criterion identifies which patients are at risk.

Because of its good success rates in pain relief, height restoration, and stabilization of the spinal structure, which improve quality of life with minimal complications, kyphoplasty is the preferred procedure, especially as it becomes more widely available with increasing awareness and specialized training.

**Cord Compression:** Patients who have with MM with pain in the spine, pelvis, or extremities, and those who develop neurologic symptoms, require careful evaluation to monitor for spinal cord compression and pathologic fractures. MRI of the spine should be considered for symptomatic patients, especially if spinal cord compression is suspected and probably should be performed as a baseline in all MM patients at diagnosis. Spinal cord compression and pathologic fractures require emergent intervention either to relieve the pressure on the spinal cord or to control the pain, respectively. Patients should be evaluated for emergent radiotherapy or surgical decompression in acute cord compression. Steroids help decrease edema associated with cord compromise and can improve pain control and neurologic complications.

**Radiotherapy:** The role of radiotherapy in managing MM has become more restricted as experts have realized that back pain is not necessarily related to a myeloma lesion. However, in most patients, back pain is secondary to skeletal structural damage, and radiation does not offer any benefit. On the other hand, radiotherapy to the spine could be detrimental to bone marrow function, resulting in inadequate stem cell collection for subsequent autologous bone marrow transplantation or cytopenias with chemotherapy. Uncontrolled localized pain secondary to a myeloma lesion and spinal cord compression are the most common indications in treating bone metastases with...
radiotherapy. The goal of palliative radiation is to relieve symptoms, restore function, and prevent complications related to disease progression.

Infections and Plasma Cell Dyscrasias

Recurrent bacterial infections are a major cause of illness and are the most frequent cause of death in patients with advanced myeloma. Infections result primarily from the marked depression of production of normal immunoglobulins that occur in more than 90% of patients. *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most common pathogens in untreated patients with myeloma and in non-neutropenic patients whose disease responds to chemotherapy. However, in patients with neutropenia and those with refractory disease, *Staphylococcus aureus* and Gram-negative bacteria are the predominant organisms. Pneumococcal vaccination is worth trying; however, most patients with MM experience poor response to bacterial antigenic stimulation. Patients with plateau-phase MM have an increased risk for life-threatening bacterial infections and polyclonal humoral immune suppression.

Preventive Measures for Infectious Complications

A double-blind, placebo-controlled, multicenter trial of intravenous immunoglobulin (IV Ig) as prophylaxis against infection was conducted to evaluate the role of IV Ig in patients with myeloma. Eighty-two patients with stable MM were treated with monthly infusions of IV Ig at 0.4 g/kg body weight or an equivalent volume of placebo (0.4% albumin) intravenously for 1 year. Other interventions, including chemotherapy, were not affected; no patient was treated with prophylactic antibiotics. No differences in clinical or laboratory variables occurred between patients in the 2 groups at entry or on study. No episodes of septicemia or pneumonia occurred in patients treated with IV Ig compared with 10 in patients treated with placebo (P = .002). In this trial, 57 serious infections occurred, 38 of which occurred during 470 patient-months on placebo, compared with 19 in 449 patient-months on IV Ig (P = .019). IV Ig also protected against recurrent infections (P = .021) in 60 patients who completed a year of treatment. Before treatment, 54 patients were immunized with pneumococcal vaccine polyvalent and their specific IgG responses were measured. A poor pneumococcal IgG antibody response (less than twofold increase) identified patients who experienced a maximum benefit from IV Ig. Mild adverse reactions were noted in 12% of patients given IV Ig infusions and 5% of those given placebo infusions.

IV Ig can be given safely to patients with plateau-phase myeloma. It protects against life-threatening infections and significantly reduces risk for recurrent infections. Individuals who benefit most can be identified prospectively by measuring IgG antibody responses to pneumococcal immunization. Patients with active MM are at an increased risk for bacterial infection. During the first 2 months of initial chemotherapy, the rate of infection is twice that experienced during the remainder of the disease course. As many as one third of these early infections could be fatal and could compromise adequate administration of chemotherapy.

Oken et al. performed a study to determine whether the morbidity and mortality of early infection can be prevented by prophylactic administration of trimethoprim-sulfamethoxazole (TMP-SMX). Patients eligible to start chemotherapy for MM were randomly assigned to treatment with prophylaxis for 2 months or no prophylaxis (control). Antibiotic prophylaxis consisted of TMP-SMX, 160/800 mg orally, every 12 hours for the first 2 months of initial chemotherapy. All patients were observed for infection for 3 months after the start of chemotherapy. Of 57 patients entered in the study, 54 were evaluable, representing 13.1 patient-years of observation. The 28 patients treated with TMP-SMX and 26 control patients were comparable in chemotherapy regimens, age, gender, stage, and bone marrow function. Bacterial infection during the 3-month study period occurred in 11 control patients, but only in 2 patients assigned to treatment with TMP-SMX (P = .004). Eight severe infections occurred in controls compared with 1 in patients treated with TMP-SMX (P = .010), leading to 4 and 1 deaths from infection, respectively (P = not significant). Severe infections included 5 pneumonias (3 with sepsis), 2 urinary tract infections with complicating pneumococcal or sepsis, 1 diverticulitis with perforation, and 1 staphylococcal scalded skin syndrome. None of the 4 nonbacterial infections was severe. The rate of bacterial infection was 2.43 per patient-year for controls and 0.29 per patient-year for the TMP-SMX group (P = .001). Toxicity (skin rash, 6 patients; nausea, 1 patient) was not life-threatening but required discontinuation of TMP-SMX in 25%
of patients. Administering TMP-SMX for the first 2 months of initial chemotherapy is effective, inexpensive prophylaxis for early bacterial infection in MM.52

Renal Failure in MM

A large review of 204 cases with MM admitted over a 10-year period to this tertiary care center evaluated the incidence and pathology of renal failure.53 Renal involvement occurred in 55 cases (27%), most of which (94.5%) presented with renal failure, and 7.3% had nephrotic syndrome. Oliguria was seen in 23.6% and two thirds of patients required dialysis. Factors precipitating renal failure were identified in 53% and included dehydration (33%), hypercalcemia (24%), nephrotoxic drugs (16%), sepsis (9%), recent surgery (5%), and contrast media (2%). Patients with renal involvement were more likely to have a high tumor burden. The myeloma was the light-chain type in 68% of patients with renal involvement, whereas IgG myeloma was the most common (57%) in patients without evidence of renal disease. Renal histology was studied in 27 cases, with myeloma cast nephropathy seen in more than 60%. Tubulointerstitial nephritis was seen in 14% of cases, 11% of cases had amyloidosis, 7% had acute tubular necrosis, and 3.6% each had nodular glomerulosclerosis and plasma cell infiltration. Renal function improved in 33% cases. Cast nephropathy associated with renal failure may not occur in the presence of a large amount of monoclonal protein is present; cases of cast nephropathy have been reported in nonsecretory MM. Plasma cell dyscrasias patients should be encouraged to increase fluid intake and avoid nonsteroidal anti-inflammatory drugs.54

Management of MM Renal Failure

The key to the management of renal failure in this patient population is timely action to correct any event that precipitated renal damage. Because most cases of renal failure are secondary to cast nephropathy, hydration is crucial in management. Although some clinicians advocate alkalization, this has to be performed cautiously to avoid overloading with sodium, which has a negative impact by promoting further cast formation. Correcting hypercalcemia is critical. Although the use of plasmaphoresis continues to be controversial, it should be considered early until definitive studies have shown that the procedure is not worthy.55,56 These supportive care measures are critical in supplementing aggressive active therapy for MM.

Summary

MM continues to be an incurable disease, and end-organ damage is the marker for initiation of therapy. Appropriate management of these events not only improves patients’ quality of life but also will probably improve survival.

References