CHAPTER 1

Introduction

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WHAT IS MULTIPLE MYELOMA?

Multiple myeloma is a B-cell neoplasm of the plasma cells. Its three hallmarks include the presence of a serum or urine monoclonal immunoglobulin, monoclonal plasmacytosis, and osteolytic lesions (Lokhorst, 2002). The clinical features of myeloma include bone pain, easy fatigability, polyuria, nausea and vomiting, recurrent infections, and neurologic symptoms, such as confusion, paraplegia, or polyneuropathy (Munshi & Anderson, 2005).

Multiple myeloma accounts for approximately 10% of all hematologic cancers (Jemal et al., 2009), with an annual incidence of 4.3 per 100,000, age-adjusted to the 2000 U.S. population (Kyle et al., 2004). In the United States, myeloma is twice as common in African Americans compared to Caucasians and is slightly more common in men than women (Jemal et al., 2009; Kyle et al., 2004).

HISTORICAL ACCOUNTS

Drs. Robert Kyle and S. Vincent Rajkumar from the Mayo Clinic in Rochester, MN, described more than 160 years of multiple myeloma and its treatment advances in a paper celebrating the 50th anniversary of the American Hematology Society (Kyle & Rajkumar, 2008). This paper began with the description of the first case of myeloma in 1844, then discussed the evolution of drug therapy and stem cell transplantation, culminating with the most recent concepts of diagnosis and therapy. According to the authors, the first few documented patients with myeloma received treatment using rhubarb pills, steel, quinine, infusion of orange peel, or the application of leeches to painful bony areas as "maintenance therapy" (Kyle & Rajkumar, 2008). No one today would think that such therapies were used, but they were. It was not until 1958 that patients started receiving the chemotherapeutic agent known as D- and L-phenylalanine mustard, otherwise called sarcolysin (Blokhin, Larionov, Perevodchikova,

Chebotareva, & Merkulova, 1958). Subsequently, it was discovered that the L-isomer of phenylalanine (melphalan) was responsible for the antimyeloma activity of sarcolysin (Munshi & Anderson, 2005). By 1962, melphalan became the first chemotherapeutic agent with a documented benefit for patients with myeloma (Bergsagel, Sprague, Austin, & Griffith, 1962).

Since the early 1960s, the need for novel therapeutic agents that could prolong and improve overall survival (OS) for patients with multiple myeloma has remained high. The median OS of 37.4 months in patients receiving conventional chemotherapies is quite dismal, with only 12% of patients making it to the fifth year compared to 52% in patients receiving high-dose chemotherapy (HDC) with autologous stem cell transplantation (ASCT) (Attal et al., 1996). These survival data were later confirmed by a meta-analysis that showed conventional chemotherapy had similar OS as treatment with melphalan and prednisone, with only 27% (age 50–64), 21% (age 65–74), and 12% (age 75 and older) of patients surviving through the fifth year, regardless of the type of chemotherapy (Myeloma Trialists' Collaborative Group, 1998).

In the 1980s, HDC with ASCT was a major breakthrough for myeloma therapy. Initial reports from phase I and II trials of HDC with ASCT showed promising clinical outcomes that led to large randomized clinical trials (Barlogie et al., 1987; McElwain & Powles, 1983; Osserman et al., 1982). By the mid-1990s to early 2000s, two large randomized, controlled studies confirmed the superiority of HDC with ASCT over conventional chemotherapies (Attal et al., 1996; Child et al., 2003), cementing HDC with ASCT as an important part of the standard frontline therapies for patients with newly diagnosed disease.

Initial reports on double (two autologous transplants) or tandem (two autologous transplants performed within a six-month period) ASCT showed OS benefits (Attal et al., 2003; Galli et al., 2005; Putkonen et al., 2005). However, other studies only showed better response rates and event-free survival, not better OS (Cavo et al., 2007; Goldschmidt, 2005). Based on these equivocal findings, large prospective, randomized, controlled studies are needed in the context of novel agents.

With the advent of novel agents such as thalidomide in 1999 (Singhal et al., 1999), bortezomib in 2003, lenalidomide in 2006, and pegylated liposomal doxorubicin in 2006, the Mayo group has reported a newly documented 50% improvement in OS in patients diagnosed during the past decade (Kumar et al., 2008). These new survival figures create "reasonable hopefulness" among patients with myeloma in achieving a better OS with a good quality of life, despite myeloma's long history of poor survivability. In the arena of HDC, the introduction of novel agents during the induction and postconditioning periods also has improved response rates and OS (Barlogie et al., 2006, 2007, 2008; Zangari et al., 2008).

The improvements in OS and event-free survival can also be attributed to some of the major advances seen in the management of patients with multiple myeloma in the past decade. Recent discoveries and advances in imag-

ing, immunology, cytogenetics, molecular biology, stem cell transplantation, tumor microenvironment, and gene microarray expression profiling have contributed to a better understanding of the disease and improvement in its management and outcomes (Braggio, Sebag, & Fonseca, 2008; Mulligan et al., 2007; Raab & Anderson, 2008; Shaughnessy, Zhan, Barlogie, & Stewart, 2005; Shaughnessy et al., 2007). Lastly, the refinement in the delivery of HDC with growth factor support with or without stem cell transplantation, the use of bisphosphonates, and the use of supportive care also have significantly improved patient outcomes (Kyle et al., 2007; Mehta & Singhal, 2007, 2008; Tariman & Faiman, 2010).

NURSING CONTRIBUTIONS TO MYELOMA CARE

Oncology nurses are key healthcare team members during early recognition of disease complications and management of treatment-related toxicities (Bertolotti et al., 2008). They provide patient and family education regarding the disease, review conventional and novel treatment options, and assess signs and symptoms of disease or treatment complications. Oncology nurses play an important role not only as direct caregivers but also as patient advocates and educators. Nursing research demonstrates that specific nursing interventions contribute to patients' quality of life and perhaps affect event-free survival and OS of patients with myeloma (Coleman, Coon, et al., 2003; Coleman et al., 2008; Coleman, Hall-Barrow, Coon, & Stewart, 2003; Coon & Coleman, 2004a, 2004b; Poulos, Gertz, Pankratz, & Post-White, 2001). However, more nursing studies are direly needed to strengthen evidence-based nursing care.

COLLABORATION AND PARTNERSHIP

The International Myeloma Foundation (IMF), a nonprofit organization dedicated to improving the lives of patients diagnosed with multiple myeloma, has recognized the need for collaboration and partnership with oncology nurses. With the leadership of Susie Novis, IMF's president and cofounder, the Nurse Leadership Board (NLB) was created to develop guidelines in managing the side effects associated with novel therapies (Durie, 2008). This is the first major collaboration and partnership between professional nurses and a patient advocacy group in the area of myeloma care. Through the support of IMF, the NLB successfully published nursing guidelines for the management of peripheral neuropathy (Tariman, Love, McCullagh, & Sandifer, 2008), myelosuppression (Miceli, Colson, Gavino, & Lilleby, 2008), deep vein thrombosis (Rome, Doss, Miller, & Westphal, 2008), steroid-related side effects (Faiman, Bilotti, Mangan, & Rogers, 2008), and gastrointestinal side effects (Smith, Bertolotti, Curran, & Jenkins, 2008). These guidelines have been disseminated through national and regional oncology nursing conferences and in several

continuing nursing education programs across the United States. The NLB is developing several other projects for future implementation, including survivorship care and long-term care guidelines.

FORGING AHEAD

Moving onward, the therapeutic options for patients with myeloma have significantly increased, patient outcomes have improved, and further insight has been gained into the biology and genetics of the disease (Barlogie et al., 2004). It has been suggested that a stepwise approach in targeting not only myeloma cells but also its microenvironment, using novel biologically based therapeutic agents alone or in combination with conventional chemotherapy, can overcome drug resistance and may further improve survival (Anderson, 2003; Barlogie et al., 2004). ASCT using high-dose melphalan as the conditioning regimen is now considered standard therapy for myeloma, at least for younger patients or those age 70 and younger with no significant comorbidities (Attal et al., 1996; Barlogie et al., 2004; Child et al., 2003; Harousseau, 2008; Mehta & Singhal, 2007).

Researchers continue to heavily investigate the role of immunotherapy in multiple myeloma, and future immune strategies will eventually lead to improved OS (Qian et al., 2005; Wang et al., 2006; Yi, 2003). The systematic application of cytogenetics and molecular genetics, especially gene expression profiling, has led to biology-based classification and staging of myeloma; wide clinical utilization of this new classification and staging needs to continue to increase among community-based healthcare providers (Chng & Bergsagel, 2008). The major challenge for clinicians is to maximize the therapeutic benefits of every novel agent. Translating all these advances to better patient care that could lead to longer OS accompanied with a good quality of life remains a big challenge in clinical practice.

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