Introduction

Multiple myeloma **(MM)** is a haematopoietic malignancy of terminal differentiated clonal plasma cells. The clinical symptoms are caused by diffuse or multilocular infiltration of the bone marrow with osteolysis and suppression of the normal haematopoesis, as well as by the production of monoclonal immunoglobulins or fragments **(**light chains or heavy chains**)**. The incidence is approximately **3-4/100 000**/year. **MM** is a disease of the elderly. Approximately **15%** of patients are aged **60** years or younger and a further **15%** between **60** and **65** years. Fewer than **2%** of the patients are younger than **40** years at diagnosis. ***(Marion and Dietrich, 2006)***

Multiple myeloma is a malignant disease characterized by plasmacytosis, paraprotein production, bone lesions, hypercalcemia, susceptibility to infections, and renal impairment. The underlying pathophysiologic phenomena of the clinical features include suppression of humoral- and cell-mediated immunity, elevation of **IL-6**, abnormalities of the bone marrow microenvironment, and increased osteoclastic activity. ***(Seema and Jayesh, 2006)***

Patients with multiple myeloma often present with vague, common symptoms such as back pain, bony pain, fatigue, and anemia. These symptoms may be treated as separate medical conditions if physicians fail to include multiple myeloma in their differential diagnosis. ***(Dvorak, 2006)***

The presenting features include symptoms of bone disease, typically unexplained backache and sometimes fractures, anaemia, renal insufficiency of different degrees, oedema **(**caused by a nephrotic syndrome and/or cardiac failure**)**, hypercalcaemia, severe bacterial infections and bleeding abnormalities **(**less frequently leucopenia/ thrombocytopenia**)**, peripheral neuropathy and symptoms from hyperviscosity. ***(Marion and Dietrich, 2006)***

Complications of multiple myeloma include renal insufficiency, hematologic complications **(**anemia, bone marrow failure, bleeding disorders) infections, bone complications **(**pathologic fractures, spinal cord compression, hyercalcemia) and neurologic complications **(**spinal cord and nerve root compression, intracranial plasmacytomas, leptomeningeal involvement, among others**)**. ***(Blade and Rosinol,2007)***

Kidney involvement is seen in **50%** of the patients, but completely different diseases are found. Moreover, more than one renal manifestation is often seen in a single patient. ***(Marion and Dietrich, 2006)***

Most of the kidney disorders associated with myeloma are caused by the excess production of monoclonal light chains and renal involvement is almost always accompanied by light chain proteinuria. Light chains have variable effects on the kidney; some are more toxic than others and different light chains affect different structures in the kidney. ***(Batuman, 2007)***

Proximal tubule injury is the most common mode of renal involvement and it can manifest in a variety of ways. In early stages of myeloma, light chain nephrotoxicity often presents with proximal tubular functional abnormalities. If These proximal tubule alterations often progress to a severe tubulointerstitial kidney disease, the most common type of kidney involvement responsible for endstage renal failure seen in myeloma patients. ***(Batuman, 2007)***

The diagnosis of **MM** is confirmed by demonstration of a monoclonal protein in the serum and/or urine and/or lytic lesions on **X**-ray together with an increased number of plasma cells in the bone marrow **(**bone marrow aspirate, trephine biopsy showing more than **10%** clonal plasma cells**)**. ***(Marion and Dietrich, 2006)***

The treatment of myeloma comprises disease-specific therapy and supportive care. The general principle is to reserve disease-specific therapy for active disease. Definitive therapy is required when the patient is symptomatic or when organ dysfunction is present or impending. There is no evidence that

starting definitive therapy in patients with smoldering or indolent myeloma improves survival. ***(Seema and Jayesh, 2006)***

Advances in therapy have resulted in improvement in the survival of patients with myeloma over the years. Without therapy, the median survival of a patient with active myeloma is approximately **6 mo**. With oral melphalan prcdnisonc **(MP)** therapy, median survival improves to **3** yr. High-dosage therapy with **HSCT** further improves median survival to **5** yr, making this the current standard therapy for myeloma. Tandem autologous transplantation is superior to single in selected patients. Now the newer agents, such as thalidomide, raise a possible challenge to the established approach of evermore aggressive dose escalation. ***(Seema and Jayesh, 2006)***

Supportive therapy comprises management of hypercalcemia, skeletal complications, anemia, infections, and pain. Regular administration of bisphosphonates such as pamidronate **(90 mg** once a month**)** or zoledronate **(4 mg** once a month**)** in patients with skeletal lesions is important. Any symptoms that involve the jaw should be investigated carefully, and a careful dental evaluation and corrective work should be performed before starting bisphosphonates or early in the course of therapy. ***(Seema and Jayesh, 2006)***

Rapid reduction, or removal of light chains by aggressive chemotherapy/**HDT** and/or **TPE** could prevent irreversible renal failure or reduce the risk of renal damage. In cases where renal failure proves to be irreversible, maintenance dialysis should be considered in virtually all patients in whom continuing myeloma treatment is warranted. ***(Hartmut et al., 2001)***

Factors affecting renal function recovery are the degree of renal failure, the presence of hypercalcemia, and amount of proteinuria. Effective and causative treatment of renal failure in combination of myeloma therapy has been proven to prolong event-free and overall survival of **MM** patients. ***(Hartmut et al.,2001)***

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The impact of high dose dexamethasone containing regimens with or without the novel agents thalidomide and bortezomib on the reversal of renal failure **(RF)** was evaluated. **RF** was reversed in **73%** of all patients within a median of **1.9** months in patients treated with dexamethasone and novel agents **(**thalidomide and/or bortezomib**)** the reversibility rate was **80%** within a median of **0.8** months. Severe **RF** and significant Bence Jones proteinuria were associated with a lower probability of **RF** reversal. Patients who responded to treatment achieved **RF** reversal more often than in those who did not. In conclusion, **RF** is reversible in the majority of newly diagnosed **MM** patients treated with high-dose dexamethasone containing regimens. The addition of novel agents induces a more rapid **RF** reversal. ***(Efstathios et al.,2007)***