

# Understanding myeloma nephropathy

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## Objectives

- Review normal bone marrow and plasma
- Review alterations to bone marrow and plasma cells in multiple myeloma
- List the risk factors for multiple myeloma
- List the signs and symptoms of a patient with multiple myeloma
- Review the process for development of cast nephropathy
- Describe the treatments available for the removal of free light chains, their advantages and limitations

## Learning Outcomes

- Have an understanding of the disease process of multiple myeloma
- Apply knowledge of the symptoms of multiple myeloma in the nursing care of patients with the disease
- Have an understanding of the tests and treatment for multiple myeloma
- Provide support and education for patients with myeloma kidney

## Introduction

Every year a small number of patients start haemodialysis because of acute renal failure secondary to multiple myeloma. Of these it is estimated that only 10-20% recovers sufficient renal function to stop haemodialysis. (Hutchison, et al, 2007). Latest ANZDATA figures show that in 2008 33 patients with multiple myeloma leading to ESRD started dialysis in Australia and 13 in New Zealand representing 1.3% of patients with ESRD starting dialysis in Australia and 2.6% in New Zealand. (ANZDATA, 2009)

## Aims

Treatment of multiple myeloma is primarily concerned with combating the malignancy, but there is increasing evidence that prompt treatment of renal failure is associated with better outcomes. The aim of this article is to give the nephrology nurse a better understanding of multiple myeloma, and the treatments available to patients.

## Pathophysiology

Plasma cells are white blood cells that produce antibodies called immunoglobulin (Ig). They leave the bone marrow as B cells and undergo terminal differentiation into plasma cells usually in the lymph nodes. A by-product of Ig (heavy chain) synthesis is free light chains; short pieces of protein that are normally filtered in the glomerulus and excreted in the urine, identifiable clinically as Bence-Jones proteinuria. (Hutchison, 2008) There are two types of free light chains: kappa and lambda.

Myeloma is a cancer of the plasma cells apparently resulting from damage to the DNA. It involves abnormal malignant proliferation of plasma cells and the development of either single or multiple plasma cell tumours within the bone marrow. The damaged myeloma plasma cells over-produce Ig resulting in a measurable spike of monoclonal protein (M-protein) on serum protein electrophoresis (SPEP) (Berenson & Casciato, 2009). In about 75% of cases, free light chains are also over-produced to levels several thousands of times higher than normal and a corresponding increase in Bence-Jones protein is measurable on urine protein electrophoresis (UPEP). (Wildes & Vij, 2008)

## Etiology

It is uncertain what causes the damage to plasma cell DNA, but there seem to be

## Key Words

myeloma, nephropathy, nursing, dialysis, renal

links to radiation exposure, environmental exposure to benzenes, autoimmune disease and human herpesvirus – 8. (Berenson & Casciato, 2009)

## Classification

The onset of myeloma is almost always gradual and patients may have a pre-symptomatic period of 5-20 years. (Thompson, 2002) During this pre-symptomatic period a small number of clonal plasma cells produce low levels of M-protein, known as 'monoclonal gammopathy of undetermined significance' (MGUS) (Kumar et al, 2009) The risk of progression to multiple myeloma is very small – approx 1% per year, but patients may be more susceptible to bacterial infections, particularly pneumonia. A further group of patients develop 'smouldering multiple myeloma' (SMM) with higher levels of malignant plasma cells and M-proteins, and with a much higher risk of progression to symptomatic myeloma at 10% per year for the first 5 years. Usually by the time of diagnosis 90% of patients have tumours at multiple sites (multiple myeloma) with lesions most commonly found in the skull, vertebrae, ribs, pelvis, and proximal long bones. (Berenson & Casciato, 2009)

## Signs and symptoms

Patients with multiple myeloma clinically present with bone pain, fatigue (due to anaemia), recurrent bacterial infections and renal insufficiency (Wildes, T. & Vij, R, 2008) The diagnosis of multiple myeloma is confirmed by bone marrow

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biopsy, although because the involvement of different bones will vary, full skeletal x-rays are required to establish the extent of the disease. (Berenson & Casciato, 2009)

**Treatments for multiple myeloma**

Many studies have been undertaken into the most effective chemotherapy treatment for multiple myeloma and indeed the efficiency of chemotherapy is of considerable importance. However a study in 2000 showed that reversibility of renal failure was a more important prognostic factor than response to chemotherapy. (Knudsen et al, 2000)

**Causes of renal insufficiency**

It has been calculated that up to 50% of patients have renal insufficiency at initial presentation, with 12-20% having acute renal failure and 10% remaining dialysis dependant. (Hutchison, 2007) Renal insufficiency may occur for several reasons including dehydration, hypercalcaemia and exposure to contrast, NSAIDs or ACE inhibitors. If proven as the cause of renal insufficiency, these are treated aggressively. The most common cause of renal insufficiency in patients with multiple myeloma, occurring in approximately 30% of patients, is cast nephropathy. (Leung, 2008).

Cast nephropathy occurs when the abnormally high levels of serum free light chains are filtered through the glomerulus. They travel through the nephron and bind with the Tamm-Horsfall protein produced in the ascending limb of the loop of Henle. They form waxy casts that block the nephron and cause interstitial inflammation (Gertz, 2005). Cast nephropathy is identifiable by renal biopsy.

**Treatment for cast nephropathy**

For many years standard therapy for cast nephropathy has been plasma exchange. Those who have nursed patients having haemodialysis for ARF related to myeloma kidney may be familiar with the regime of treatment. Haemodialysis replaces lost kidney function and is alternated with second daily plasma exchange treatments to filter off the plasma containing the excess free light chains. Despite plasma exchange being recommended in reviews

and management guidelines, its efficacy has long been in question. In a multi-centre randomised controlled trial in 2005 Clark et al demonstrated no conclusive evidence that plasma exchange improved outcomes for patients. (Clark, 2005)

More recently the development of new haemodialysis membranes has offered an alternative to plasma exchange as a method of removal of free light chains. Regular high flux haemodialysis membranes have pores of varying sizes that allow molecules of up to 10kD to pass through. The new High Cut-off (HCO) membranes have uniformly sized pores of a much larger size that allow molecules of up to 45kD through. A kappa free light chain weighs 24kD and a lambda weighs 50kD, and they are present in similar concentrations in the intravascular and extravascular compartments. Extended haemodialysis with a HCO dialyser has been shown to remove free light chains more effectively than plasma exchange, because it allows time for movement of free light chains from the extravascular into the intravascular space and thus to be removed. (Hutchison, et al, 2007)

Much work is ongoing in this field and in particular the optimal reduction in serum free light chain concentrations, and the duration of HCO dialysis required. It has been estimated that a serum FLC concentration reduction of 80-95% is associated with renal recovery, but a large multi-centre randomised controlled trial (EuLITE) is currently recruiting to gain more evidence. (Hutchison, et al, 2008)

**Implications for nursing practice**

- Patients undergoing chemotherapy have cytotoxic body fluids and nurses should take proper precautions to protect themselves and other staff from exposure.
- The most common cause of death in multiple myeloma patients is infection, particularly during chemotherapy or in the terminal stages. Nurses should be vigilant about observing and reporting any signs and symptoms of infection. Patients may be nursed in isolation, but wherever they are nurses should pay attention to basic universal precautions and hand hygiene.

- All vascular access devices, including those for plasma exchange and/or haemodialysis should be accessed under strict aseptic technique, and exit sites covered with an occlusive dressing.
- Nurses will care for patients pre and post bone marrow biopsy and renal biopsy, according to hospital policy. Both of these procedures could result in the development of infection. With renal biopsy there is a risk of bleeding, so all urine output should be tested for blood and the patient monitored for signs and symptoms of hypovolaemic shock.
- Nurses must accurately record fluid balance and daily weight. Patients who have not developed acute renal failure are encouraged to drink 2-3 litres of fluid daily to promote urinary excretion of light chains, calcium and uric acid. A diminishing urine output is a sign of worsening renal impairment that should be documented and reported. Patients with ARF who are on haemodialysis will require daily fluid assessment.
- Extended dialysis with HCO dialysers has been well tolerated in studies, but as the membrane pores are much larger, patients do suffer albumin loss that requires replacement.
- As well as receiving a highly technical and complex range of therapies, patients with multiple myeloma will require education and emotional support to help them understand what is happening to them and adjust to the implications of their diagnosis.

**Conclusion**

Multiple myeloma accounts for 1.2% of all cancers in Australia and has a mortality rate of just over 50% (AIHW, 2005). If, as the literature suggests, reversal of renal failure is of such importance to the outcome, nephrology nurses should have an understanding of the disease and of the technologies available for its treatment.

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### Questions and Activities

The following questions and activities are designed to make us think about our everyday practice and to encourage us to strive for improvements in the daily lives and health of our patients.

- Q: What happens in multiple myeloma that causes free light chains to be produced in great numbers?
- Q: How do free light chains cause ARF?
- A: Look up your unit's policy for the nursing care of a patient undergoing a renal biopsy.
- Q: Why is it important to accurately record fluid balance in a patient with multiple myeloma?
- A: Visit your hospital's plasma exchange unit and, if you are not a haemodialysis nurse, visit the haemodialysis unit too. Discuss the differences between the two therapies with the staff there.

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