

## CASE REPORT

# Myeloma Kidney – A Treatable Yet Often Forgotten Disease

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### ABSTRACT

Multiple myeloma is a blood dyscrasia that accounts of almost 10% of all hematological malignancy. The presentation of myeloma kidney is highly variable and it often presents as renal insufficiency, renal tubular dysfunction and proteinuria of various types. In Malaysia the true incidence of myeloma kidney is unknown. Often the diagnosis of myeloma kidney was missed out despite the patient has sought medical treatment early. A high index of suspicion is required when the middle to elderly age patients present with unexplained renal impairment and enlarged kidneys. We present here the presentation of a rare subtype of myeloma in a relatively young patient whereby the patient presented with nephrotic syndrome and azotemia.

**Keywords:** Ig D Multiple myeloma, Amyloidosis, Cast nephropathy

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### INTRODUCTION

Multiple myeloma (MM) is not a common cancer in those below 50 years of age. The trade mark of MM is overproduction of monoclonal immunoglobulin or light chains which are filtered by glomeruli. These light chains when mixed with the renal parenchymal tissue are highly nephrotoxic. Other mechanisms of renal injury include production of myeloma casts, amyloid deposition, hypercalcemia, hyperuricemia and nephrotoxic agents such as non-steroidal inflammatory drugs or contrast agent for imaging. Often the injury occurs as a combination of insults. Prompt detection and referral to both nephrologist and hematologist are crucial to ensure an excellent renal prognosis and life expectancy.

### CASE REPORT

A 47-year-old lady was referred from a secondary hospital for assessment of advanced renal impairment. She gave a history of progressive weakness, itchiness, nausea and breathlessness for 8 months. Her past medical history includes hypertension of 5 years duration in which she was prescribed perindopril 4mg once a day by her family doctor. She was also told to have normochromic normocytic anemia and was advised blood transfusion

for which she refused. No work up of anemia was ever done. On further questioning, she admitted that she has polyuria which was bothering her. She does not have any back pain or history of fracture. Physical examination revealed a normotensive state with a blood pressure of 139/73mmHg and pulse rate of 86/min. She appeared to be in pale and sallow looking. Cardiovascular, abdomen and respiratory examinations were unremarkable. Investigations revealed: Urine protein: 4+, urine RBC: 5/hpf, serum total protein: 71 g/L, serum albumin: 27 g/L, alkaline phosphatase: 85 U/L, globulin: 44 g/L; urea: 27 µmol/l, sodium: 135 mmol/l, potassium: 5.4 mmol/l, creatinine: 1252 µmol/l; calcium: 1.97 mmol/l, phosphate: 3.96 mmol/l; total white: 5.2 X 10<sup>9</sup>/L, hemoglobin: 5.7 g/dL, platelet: 282 x 10<sup>9</sup>/L; erythrocyte sedimentation rate (ESR): 124 mm/hour and 24 hours urine protein: 17.85g. Her antinuclear antibody and complements were normal. Renal ultrasound showed raised echogenicity with bipolar length of right kidney and left kidney measures 13.9cm and 12.9 cm respectively. There was no feature of amyloid related complications noted. In view of bilateral large kidneys with an unknown cause of renal impairment, a renal biopsy was carried out. Renal biopsy revealed features in keeping with myeloma cast nephropathy, moderate to severe chronic tubule-interstitial changes with concurrent peritubular amyloid deposition (Figures 1,2). Serum protein electrophoresis revealed Immunoglobulin D with Lambda light chains at 14.6 g/L. Skeletal survey revealed lytic lesions in spine, ribs, pelvic and femur bones. Bone marrow aspiration and biopsy showed diluted sample with scattered plasma cells. A diagnosis of Immunoglobulin D multiple myeloma (Ig D MM) was made. She was referred to hematologist for further

treatment. A permanent catheter was inserted and she received regular hemodialysis three times per week. Unfortunately, her renal function did not recover despite receiving full dose of chemotherapy which consisted of bortezomib, cyclophosphamide, dexamethasone and thalidomide. She had a relapsed of multiple myeloma 4 months after remission (undetectable band in electrophoresis) and succumbed due to acute coronary syndrome a few months down the road.

## DISCUSSION

The incidence of MM in Malaysia ranges from 0.4 to 0.7 per 100,000 people. The incidence ranges from 0.5 per 100,000 people for those 15 - 49 year of age to 2.6 – 3.3 per 100,000 people for those 50-60 year of age. The incidence is highest in those over 70 year of age where it is 1.8 – 5 per 100,000 people (1). The exact incidence of myeloma kidney in Malaysia is unknown. The relative young age of our patient may have contributed to the delayed diagnosis of her condition.

Renal disease in myeloma most often presents as renal impairment and proteinuria. Severe renal impairment is expected in one fifth of the cases (2). Proteinuria is observed in over 80% of cases and it consists mostly

of light chains. Light-chain proteinuria can be massive (> 10 g/d) but yet cannot be detected by conventional dipstick or urinalysis. Fewer than 15 to 25% of patients with myeloma actually develop the classical nephrotic syndrome with conventional albuminuria. This often is the results of amyloid deposition or monoclonal Ig G deposition disease (MIDD). The renal pathology of myeloma cast nephropathy, MIDD and amyloidosis is complex and diverse. However in each occasion, it is preceded by the production in the bone marrow of an abnormal immunoglobulin fragment (usually a light chain) by a clone of neoplastic plasma cells. Other causes that can contribute to the renal impairment include obstructive uropathy, hyperviscosity syndrome, hyperuricemia, volume depletion and the use of nephrotoxic agents such as non-steroidal anti-inflammatory drugs or contrast agents. A kidney biopsy is required to establish the diagnosis.

Our patient suffered from IgD MM which is an extremely rare form of MM. It accounts for almost 2% of all myeloma cases (3). It is associated with extremely advanced disease at diagnosis, an increased frequency of undetectable or small monoclonal (M)-protein levels on electrophoresis; osteolytic lesions; extramedullary involvement; amyloidosis; a lambda light chain predilection; renal impairment and hypercalcemia.

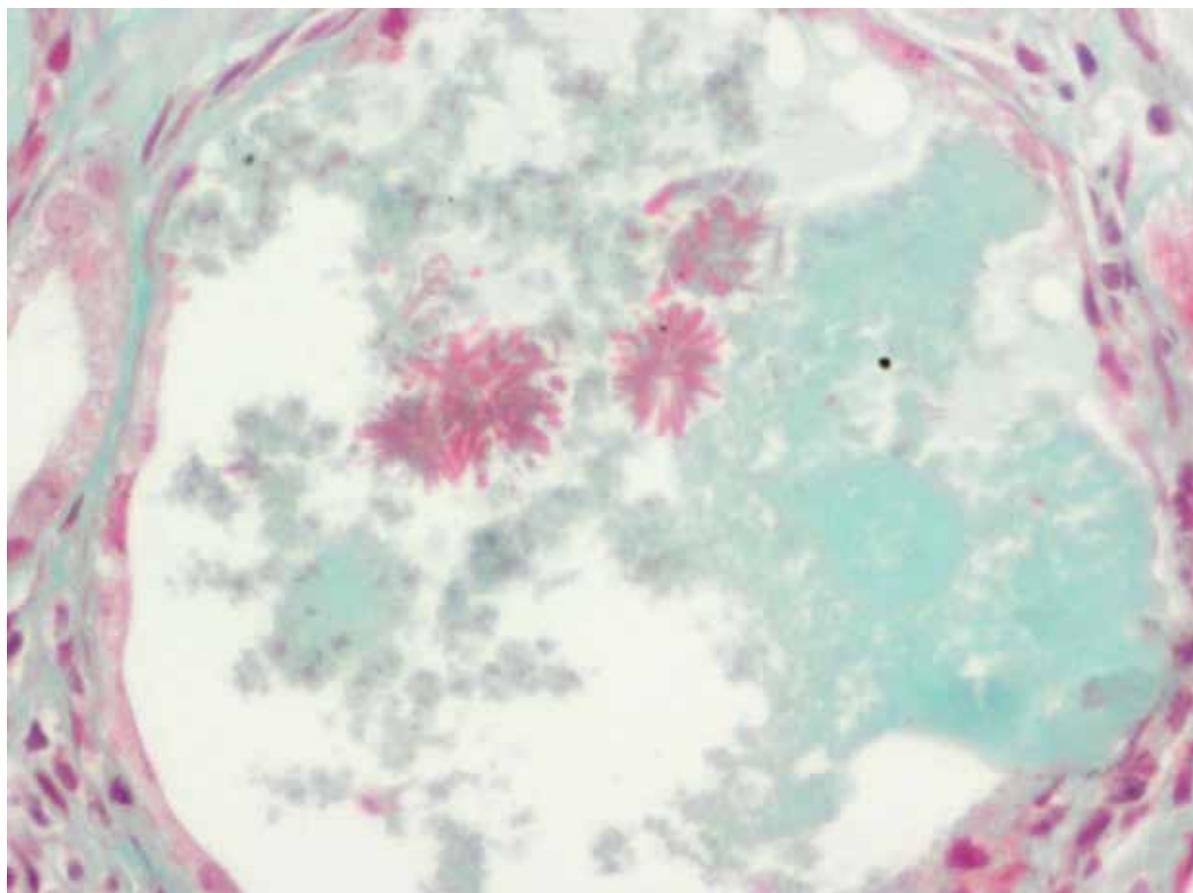


Fig. 1. Masson trichrome statining showing non-polarizing crystals inside the tubules

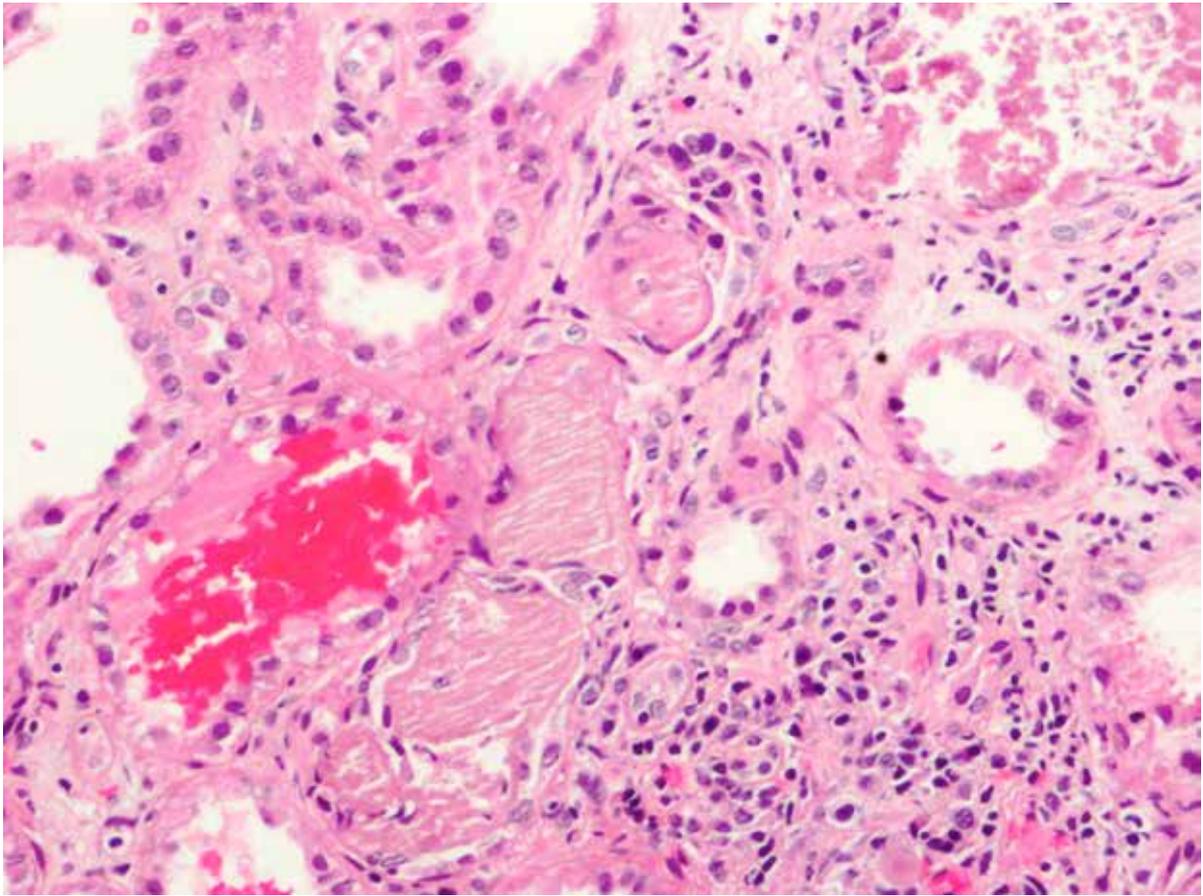


Fig. 2. Hematoxylin and eosin stain showing tubules show irregularly fragmented cast with cellular debris admixed with red cell cast

Although survival of patients with IgD MM or IgE MM is shorter in comparison to those with immunoglobulin G (IgG) MM or immunoglobulin A (IgA) MM, the outcome for patients with IgD and IgE subtypes is improving with the use of novel agents and autologous transplantation (3). Unfortunately our patient however has declined autologous transplantation when offered by the hematologist. Her outcome was guarded in view of the advance renal impairment, low hemoglobin level level and multiple areas of the bone destroyed by the cancer.

The management of myeloma kidney involves anti-myeloma therapy with bortezomib based chemotherapy with high dose dexamethasone (4). Chemotherapy should be initiated as rapidly as possible to decrease light chain production. All potentially nephrotoxic agents should be discontinued. Unless contraindicated, intravenous fluid therapy with the goal of attaining a positive daily urine output of at least three liters, should be provided to all patients to reduce light chain precipitation, hypercalcemia and hyperuricemia. Dialysis should be initiated as per normal indications while the use of extracorporeal methods remains controversial.

The case highlighted the importance of being vigilance in cases of acute renal impairment of unknown origin with enlarged kidneys as myeloma kidney remains a distinct possibility. Prompt detection and referral to both nephrology and hematologist are crucial to ensure an excellent renal prognosis and life expectancy.

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