



Research Article

LIGHT CHAIN MULTIPLE MYELOMA: A CASE REPORT

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ABSTRACT

Light chain multiple myeloma (LCMM) initiates approximately 15 percentage of patients with multiple myeloma (MM). It has a lower prognosis when compared with the variant immunoglobulin (Ig) G or IgA. We report a rare case on Light chain multiple myeloma in 49-year-old male patient who presented with acute kidney injury, hypercalcemia. histopathology examination was found to be plasmacytoma, kappa restricted; and free kappa lamda chain in urine and serum was found to be greater. Bone pain and renal dysfunction were the most common prevalent initial signs and symptoms while extramedullary disease (EMD) was later acquired during disease. Bortezomib demonstrated superior efficacy over nonbortezomib in LCMM patients.

Key words: Light chain multiple myeloma, monoclonal, non- amyloid, plasmacytoma

INTRODUCTION

Multiple myeloma (MM) comprises 10% of all haematological malignancies and 1% of all malignancies.^{1,2} This is a malignant disorder characterized by irregular plasma cells proliferation and monoclonal immunoglobulins or free light chains (FLC). The annual occurrence of multiple myeloma (MM) is 7.74 per 100,000 population while the annual number of deaths due to Multiple myeloma is 3.52 per 100,000 population.^{3,4}

Immunoglobulin (Ig) G followed by IgA is the most common form of M-protein found in multiple myeloma.^{5,6} In patients with light chain multiple myeloma, renal failure, bone disease, and systemic light chain AL amyloidosis tend to be more common. In contrast to the IgG or IgA version, LCMM has an earlier average age of onset and tends to have a worse prognosis.^{3,5} Plasma cells exhibit rearrangements in immunoglobulin heavy chains (IgH) at the level of DNA in patients with light chain multiple myeloma, thereby resulting in an inability to generate IgH. In most instances, one IgH allele has a germline configuration (for the D, J, and C domains), while a second allele is involved in a translocation. This results contrast with classical MM where one allele has a functional rearrangement, whereas the second allele is usually involved in a translocation.⁷

Diagnostic criteria of multiple myeloma

10% clonal bone marrow plasma cells or biopsy-proven bony or extramedullary plasmacytoma and myelomas are identified by either or more of the following events:

Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:

- Hypercalcemia: serum calcium >0.25 mmol/L (>1 mg/dL) greater than the normal upper limit or >2.75 mmol/L (>11 mg/dL)

- Renal insufficiency: creatinine clearance <40 mL per min or serum creatinine >177 μ mol/L (>2 mg/dL)
- Anemia: hemoglobin value of >20 g/L lower than acceptable limit, or hemoglobin, <100 g/L
- Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT

Any one or more of the following biomarkers of malignancy:

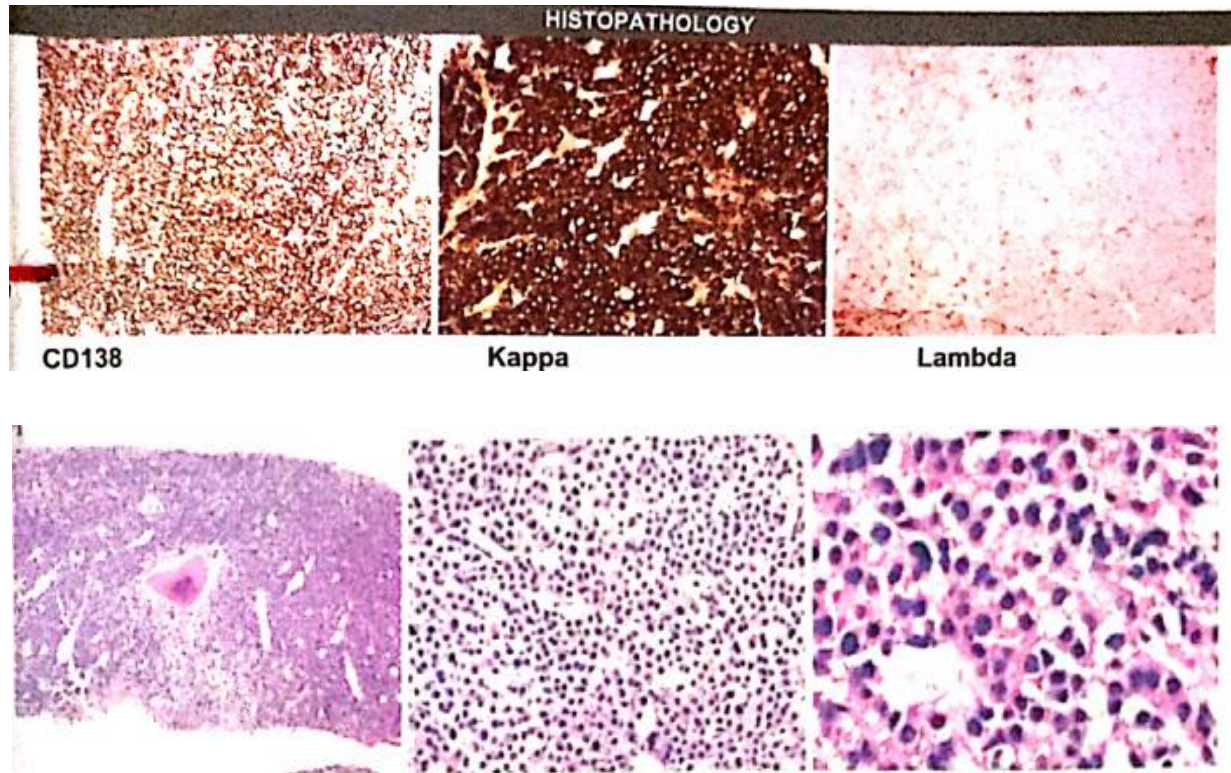
- Clonal bone marrow plasma cell percentage $\geq$ 60%
- Involved: uninvolved serum free light chain ratio $\geq$ 100
- >1 focal lesion on MRI studies

CASE PRESENTATION

A 49-year-old male known case of type II diabetic mellitus, admitted with complaints of Low back ache in the past 10 days, associated with occasional vomiting, pain over ribs, pedal edema. His CT showed multiple vertebral lesions. CT guided biopsy from sacrum revealed plasmacytoma, kappa restricted. His physical examination revealed, BP: 150/80mmHg, PR:88/mt, bilateral pedal oedema. He had mild pallor. Rest of the systemic examination was unremarkable. Initial laboratory work up revealed haemoglobin 5.5gm/dl, PCV 15.6%, total count: 3.500cells, hypercalcemia 11.2mg/dl, AKI (S.Cr:2.47mg/dl), LDH:363, Phosphorous:6.0mg/dl, uric acid:2.8mg/dl. Routine urine examination showed albumin 4+, sugar 3+. Urine bence jones protein was positive. Hypercalcemia corrected with hydration. He was also managed with 2-unit PRBC transfusion, antibiotics, PPI'S, analgesics and other supportive medications. Ultrasonogram of KUB showed bilateral increased renal cortical echotexture with accentuated CMD- AKI, Moderate ascites, bilateral moderate pleural effusion, and mild prostatic enlargement.

Bone marrow aspiration and biopsy study showed markedly hypercellular marrow with marked plasmacytosis (90%) consistent with multiple myeloma shown in below.

Histopathology examination showed that plasmacytoma, kappa restricted.



In kappa and lambda- free light chain, urine analysis showed increased free kappa light chain >13600mg/l normal value (1.35-24.19) while free lambda light chain was normal. Serum, protein electrophoresis showed increased Alpha1 globulin (0.56gm/dl), increased beta 2 globulin (0.71gm/dl). On immunofixation-quantitative serum showed that a band in kappa region.

In immunoglobulin profile IgG, IgM and IgA serum shows that less total IgG (422MG/DL) less total IgA (20mg/dl) and less total IgM(15mg/dl). Serum beta-2 microglobulin was increased 10700 ng/ml. kappa and lambda- free light chain serum shows high free kappa(light chain), in serum accounting for 13600 mg/dl which is significantly higher than normal (3.3-19.4) and lower level of free lambda (light chain) in serum accounting for 1.94mg/l which is very low compared to the normal range (5.71- 26.3). In serum, beta-2 microglobulin was increased to 10700ng/l (Normal range:670-2143)

He was treated with 4 doses of dexamethasone 20mg, he was noted to have dexamethasone induced bradycardia, hence dexamethasone was withheld. Metaproterenol Sulfate, T. deriphyllin 100 mg TID was given in view of bradycardia, stopped once heart rate become normal.

1st cycle of chemotherapy was started with inj. bortezomib 2mg IV push over 5sec flush with 10ml NS. inj. zoledronic acid 3mg in 100ml NS over 30 minutes was also administered. 2nd cycle treatment was started after 1 week of 1st cycle with inj. bortezomib 2mg S/C stat and 1-unit PRBC over 3 hours was also administered. His renal function improved and his serum creatinine level stabilised. Hypercalcemia become normal with hydration. At present patient symptomatically improved with treatment, and advised to follow up in OPD basis.

DISCUSSION

While most cases of multiple myeloma (MM) are characterized by the presence of monoclonal serum immunoglobulin, about 15 % of patients have only light chains of immunoglobulin found either in the urine or in the serum, or both. The most common signs and symptoms at presentation of the disease in patients diagnosed with LCMM were bone pain, fatigue and renal failure. The symptoms observed as the disease progressed were lytic bone lesions, pleural effusion, EMD, anaemia, and hypercalcemia.

An unusual but very severe comorbidity of LCMM is AL amyloidosis in the systemic light chain. It is only observed in 5% -10% of LCMM cases.⁸ Significant quantities of plasma cell-produced monoclonal light chains accumulate in tissues in the form of insoluble amyloid-forming fibrils. Using Congo red stain, homogeneous red deposits are usually seen under a light microscope which produce apple-green birefringence under polarised light. Any organ except brain may be involved in patients with AL amyloidosis, but the most commonly involved organs are the heart and kidney. Especially painful skin changes on the extremities occur only in 25 per cent of patients.

Other rare clinical manifestations in LCMM patients include a hepatic plasmacytoma presenting in the right hypochondrium as nodular lesion, jaundice, and pain .Single or multiple spatially occurring lesions, hepatomegaly, extrahepatic biliary obstruction, and ascites may be seen with an aggressive disease associated with very poor outcome, including aggressive management.⁹ Another rare event is an epidural plasmacytoid tumour in the history of LCMM that poses back pain, pathological vertebral fracture and weight loss.¹⁰

Multiple myeloma and associated diseases are generally detected using serum protein electrophoresis. Based on their physical properties, electrophoresis is a method of distinguishing proteins and the pattern relies on the fractions of two protein types: albumin and globulin (alpha 1, alpha 2, beta and gamma). In this patient, alpha 1 globulin was high, beta 2 globulin and gamma globulin were low. 'M' BAND (0.39GMS%) seen in BETA-2 region.

Serum creatinine level greater than 4 mg/dl is a poor prognosis sign for future progression to end stage renal disease in this disease¹¹. A timely diagnosis is important in order to initiate early treatment regimens to rapidly reduce FLC concentrations in patients with myeloma kidney. Such early FLC reductions are associated with improved survival⁶. The use of protocols including bortezomib followed or not by autologous stem cell transplantation have induced hematological responses and improvement of renal injury.¹²

Treatment which include Stem cell transplantation can produce durable responses in patients with LCMM. Stem cells are mobilized using granulocyte colony-stimulating factor (G-CSF), (filgrastim) and high-dose chemotherapy with melphalan is given. To decrease morbidity the dosage of melphalan is tailored to the renal function. A long-term analysis of 6 patients with LCMM who underwent ASCT demonstrated that this is an effective therapy for patients with renal dysfunction due to LCD. Proteinuria was reduced by 92%, and the glomerular filtration rate was improved by 95% in these patients. The drug Bortezomib inhibits the NFκB pathway, and decreases cytokine production, decreases collagen production. Bortezomib interrupts the downstream cascade, which prevents the rapid progression of glomerulosclerosis and proteinuria and improves renal function.

Bortezomib has been used in patients with LCMM as induction therapy. In one series 3 patients have been treated as induction therapy with bortezomib. After an average of 2 cycles, this led to a rapid hematologic response based on a decrease in serum free light-chain levels. Some patients with end-stage renal disease LCD (ESRD) underwent renal transplantation. Patients with LCMM having visible light chains in urine or serum have worse results, with early recurrences despite treatment with pretransplantation.

CONCLUSION

Multiple myeloma is a haematological malignancy characterized by the invasion of the hematopoietic bone marrow by monoclonal plasmocytic proliferation. Light chain multiple myeloma is an aggressive subset of multiple myeloma. LCMM response to Bortezomib based induction therapy.

INFORMED CONSENT

Informed consent was taken from the subject prior to participation in study.

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