

Multiple Myeloma with Homogenous Secretion of Lambda Light Chain Immunoglobulin: A Case Report

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Authors' contributions

This work was carried out in collaboration between both authors. Author JAO designed the study, wrote the protocol and author PSO wrote the first draft of the manuscript. Authors JAO and PSO managed the literature searches. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

About 20% of people with multiple myeloma (MM) produce only light kappa chains which is produced in 80% of cases. This population of MM patients may be missed where the laboratory could not effectively detect free light chains of immunoglobulins as it is the case in most developing countries. Many reports showed that individuals with lambda light chain disease have a three times worse prognosis than kappa light chain disease. It is therefore important to improve awareness on the need to look out for light chain disease and emphasize the usefulness of a well-equipped laboratory that will fully analyze immunoglobulins of suspected multiple myeloma cases.

After reviewing the patient, main findings included paraplegia, constipation and incessant vomiting suggestive of amyloidosis, a positive urinary bence jones proteins (BJP), normal biochemical parameters, elevated lambda light chain level and reversed kappa/lambda ratio of <0.01, magnetic resonance imaging (MRI) proven osteolytic lesions restricted to the spine and histology of bone marrow sample from laminectomy, as well as bone marrow aspiration cytology showed abnormal plasmacytosis.

This is an unusual and rare presentation of MM in this environment. Free light chain (FLC)

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identification and quantitation should be carried out in all cases of suspected MM; especially in those with no monoclonal bands on serum protein electrophoresis and or immunofixation.

Keywords: Multiple myeloma; lambda light chain disease; free light chain; rare presentation; well-equipped laboratory.

1. INTRODUCTION

Multiple myeloma (MM) is a neoplastic plasma cell disorder that is characterized by clonal proliferation of malignant plasma cells in the bone marrow microenvironment. The malignant plasma cells produce excessive monoclonal (M) proteins which includes; IgG 52%, IgA 21%, Light chain 16%, Biclinal 2% and IgM 0.5%; the IgD and IgE types are very rare. On the other hand, 3% of MM patients have non-secretory myeloma [1].

Patients with light chain myeloma are more prone to developing renal failure. This monoclonal light chains may be deposited in multiple organs to form light-chain deposition disease (LCDD). LCDD is a rare disease characterized by deposition of non-amyloid immunoglobulin light chains, and they do not stain with Congo red and do not exhibit a fibrillar structure when examined ultrastructurally [2-4]. It is categorized as a "monoclonal deposition disease" in the World Health Organization (WHO) classification of tumors of hematopoietic and lymphoid tissues [5]. LCDD was first described in 1976 in two patients with end-stage renal disease as granular deposits of free light chains in multiple organs, including the kidneys, that did not stain with Congo red [6]. A single clone of plasma cells is responsible for overproduction of kappa chains and, very rarely, lambda chains [7]. A monoclonal population of plasma cells can be detected in the bone marrow, and an altered serum-free light chain ratio is present [8]. In 25% of patients, an abnormal serum free light chain ratio is noted, even without an abnormal finding with serum and or urine electrophoresis with immunofixation [9].

LCDD should also be excluded in patients who have both renal disease and a lymphoplasmaeytic disorder like macroglobulinaemia, lymphoma and chronic lymphocytic leukemia capable of producing monoclonal light chains [4].

LCDD is noted to be a disease of adults (median age 56 years, range 33-39 years which occur in association with either myeloma in 65% of cases

or monoclonal gammopathy of undetermined significance(MGUS) [10,11]. There is no evidence of sex discrimination neither is there evidence of ethnicity effect [10,11].

We hereby present this rare case of lambda light chain MM, diagnosed in our facility for the first time whereby most of the biochemical tests were normal to underscore the importance of complete immunoglobulin analysis, including FLC. Prompt bone marrow examination in every suspected case of MM should be done even in those with no monoclonal bands on serum protein electrophoresis and or immunofixation.

2. CASE REPORT

The 64 year old poultry farmer was referred to Haematology department by the neurosurgeons with a positive BJP result. He had presented to them with complaints of progressively worsened inability to walk following a fall from a height on a ladder, even though he had previously experienced a prolonged low intensity waist pains. There was associated urinary urgency, occasional urge incontinence and constipation. The review of other systems were not remarkable. There was no past history of blood transfusion.

Physical examination essentially revealed chronically ill-looking man with mild pallor, normal vital signs and there was no pedal edema or lymphadenopathy. The central nervous system examination revealed sensory level of T6/T7, hyperaesthesia at T12/L1 bilaterally, reduced power of 3-4 and brisk deep tendon reflexes of lower limbs. The anal sphincter was lax. However, the examination of the respiratory, cardiovascular and gastrointestinal systems revealed no abnormal findings.

Laboratory investigations revealed, haemoglobin (Hgb) of 7 g/dl, Packed cell volume (PCV) of 22%, white blood cell count (WBC) of $11.5 \times 10^9/L$, absolute neutrophil count (ANC) of $6.87 \times 10^9/L$, platelets count of $161 \times 10^9/L$ and erythrocyte sedimentation rate (ESR) of 54 mm in 1st hour (Westergren). Tumour markers including prostate specific antigen (PSA),

carcino-embryonic antigen (CEA), and alpha-feto protein (AFP) were all within normal limits. His coagulation profile was within normal limits. Bence jones protein (BJP) was positive. The fasting blood glucose was 80 mg/dl (normal =65-110 mg/dl), blood urea of 28 mg/dl (normal =15-45 ng/dl) and serum creatinine of 1.0 mg/dl (normal = 0.5-1.5 mg/dl), serum calcium of 10.3 mg/dl (normal = 8.5-10 mg/dl) and uric acid of 5 mg/dl (normal = 2-7 mg/dl) were all within normal reference intervals.

Serum protein electrophoresis revealed a thin discrete band in the gamma globulin region. The total protein was 6.3 g/dl (normal = 6-8 g/dl), Albumin-4.3 g/dl (normal = 3.5-5), alpha 1 globulin 0.34 g/dl (normal = 0.15-0.35), albumin/globulin ratio: 2.2, alpha 2 globulin 0.64 g/dl (normal = 0.72-1.06), beta globulin 0.54 g/dl (normal = 0.74-1.06), gamma globulin 0.43 mg/dl (normal = 0.91-1.71). Serum kappa FLC-7.03 mg/dl (normal = 3.3-19.4), lambda FLC- 4,715 mg/dl (normal = 5.71-26.3) (Fig. 2), kappa/lambda ratio <0.01 (normal = 0.26-1.65) while normal Immunoglobulin levels were all low [Immunoparesis]: IgG -3.99 g/l (normal = 7.0-16.0), IgA -0.1 g/l (normal = 0.7-3.5) and IgM -0.2 g/l (normal = 0.5-2.5) (Fig. 4). Beta 2 microglobulin was markedly elevated -10.4 mg/dl (normal = 1.42-3.21).

Plain cervical spine X-ray showed minimal anterior marginal osteophytes in C4 and C5 vertebrae in keeping with early cervical spondylosis while lumbosacral spine x-ray showed decreased height of L4 and straightened lumbosacral spine. Chest X-ray revealed only unfolded aorta.

Spine magnetic resonance imaging (MRI) confirmed cervical spondylosis with multiple disc bulges at C3/4, C4/5 and C5/6 , thickened ligamentum flavum course at C4-C6, soft tissue swelling at cervico-thoracic junction posterior to the spine, osteolytic lesionns of T1 with theca and cord compression and soft tissue swelling obliterating the spinal cord behind T4. The lumbosacral spine showed osteolytic lesions at L3 and L4, and cord compression at L3/L4.

Based on the MRI findings of multi-level cord compression, the patient had a decompression laminectomy and bone marrow specimen for histology revealed nodular aggregate of malignant plasma cells with extensive bone destruction. A bone marrow aspiration cytology, carried out thereafter, revealed depression of the erythroid and myeloid cell lines with marked increase in plasma cells and plasmablasts constituting 70% and 10% of the bone marrow nucleated elements respectively.

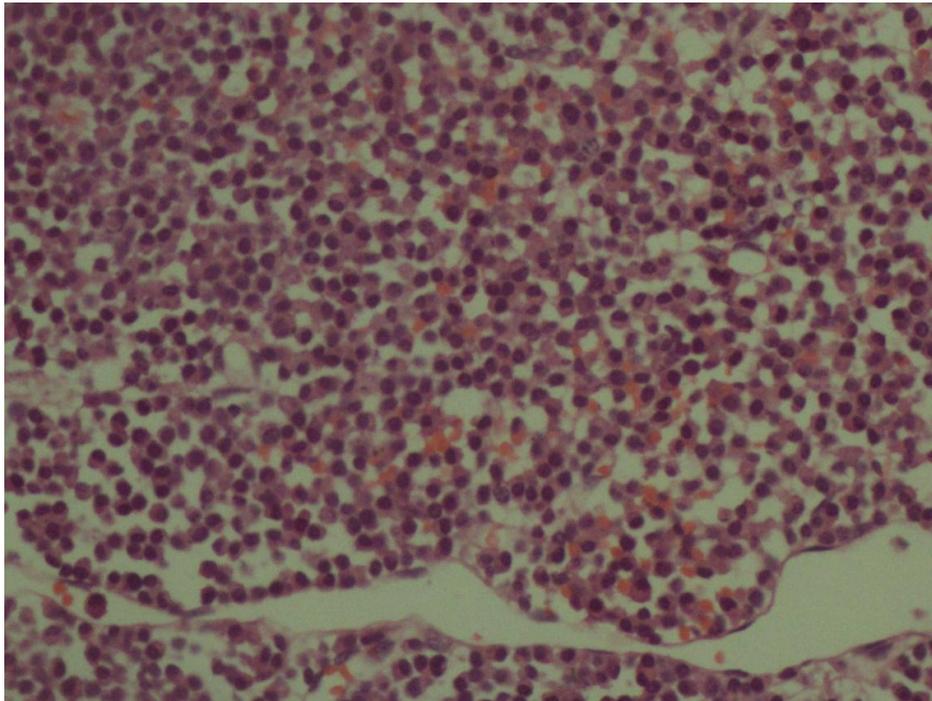


Fig. 1. Abnormal plasmacytosis in the decompression laminectomy tissue sent for histology

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REQUISITION No
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SPECIMEN:-COLL. 28/08/2015 1000 RECEIVED 28/08/2015 1100 PRINTED 22/02/2016 1001
CLINICAL DATA:- SPECIMEN TYPE: BLOOD
?MULTIPLE MYELOMA
KEEP FOR PATIENT

*** CHEMISTRY RESULTS ***

TESTS	RESULTS	FLG	REFERENCE RANGE
SERUM FREE LIGHT CHAINS			
S-KAPPA FLC	7.03		3.30-19.40 mg/L
S-LAMBDA FLC	4715.00	H	5.71-26.30 mg/L
KAPPA/LAMBDA RATIO	<0.01	L	0.26-1.65

> COMMENT:
Raised LAMBDA free light chains, with abnormal ratio. These findings are in favour of monoclonal proliferation.

Reported by Dr Younus Essack 07/09/15 1413
Abnormal serum free light chain concentrations may be associated with immune stimulation, immune suppression, monoclonal gammopathies or reduced renal clearance. An abnormal kappa/lambda ratio suggests monoclonal gammopathy. Borderline results should be repeated.

ORDERED TESTS:
IMMUNOGLOB G,A,M, 01 FREE LIGHT CHAINS, 01 BETA-2-MICROGLOB

Fig. 2. Lambda Free light chain level at diagnosis

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CLINICAL DATA:- SPECIMEN TYPE: BLOOD
MULTIPLE MYELOMA
KEEP FOR PATIENT

*** CHEMISTRY RESULTS ***

TESTS	RESULTS	FLG	REFERENCE RANGE
SERUM FREE LIGHT CHAINS			
> S-KAPPA FLC	12.43		3.30-19.40 mg/L
> S-LAMBDA FLC	477.38	H	5.71-26.30 mg/L
> KAPPA/LAMBDA RATIO	0.03	L	0.26-1.65

> COMMENT:
Raised LAMBDA free light chains, with abnormal ratio, in a patient known with previous results.

Reported by Dr Esme Hitchcock 19/02/16 1101

ORDERED TESTS:
01 FREE LIGHT CHAINS

Fig. 3. Post chemotherapy Labda Free light chain level

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CLINICAL DATA:- SPECIMEN TYPE: BLOOD			
?MULTIPLE MYELOMA KEEP FOR PATIENT			
* * * CHEMISTRY RESULTS * * *			
TESTS		RESULTS FLG	REFERENCE RANGE
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IMMUNOGLOBULINS			
IMMUNOGLOBULIN G (IgG)	3.99	*L	7.00-16.00 g/L
IMMUNOGLOBULIN A (IgA)	0.10	*L	0.70-3.50 g/L
IMMUNOGLOBULIN M (IgM)	0.21	L	0.50-2.50 g/L
ORDERED TESTS: IMMUNOGLOB G,A,M, 01 FREE LIGHT CHAINS, 01 BETA-2-MICROGLOB			

Fig. 4. Level of immunoparesis at diagnosis

Patient was diagnosed as a case of lambda light chain multiple myeloma and was commenced on combination therapy comprising mephalan, thalidomide and prednisolone and this later changed to bortezomib, dexamethasone and thalidomide (VTD) after 2 cycles of the former.

The lower limb power has improved to grade 5 and he is currently ambulating without support after 5 cycles of VTD. The lambda light chain has reduced to 477 mg/dl from 4,715 mg/dl at diagnosis and his renal profile remain normal (Figs. 2 and 3).

3. DISCUSSION

Multiple myeloma (MM) is a malignant neoplasm of the plasma cells [11]. The malignant cells arise from post-germinal center of lymph nodes and home back to the bone marrow [12,13].

MM was first documented in 1844 [14]. The annual incidence is 4 per 100 000 and it represents approximately 1% of all malignancies, 10% of all haematological malignancies and second most common after non Non-Hodgkin's lymphoma [15,16]. MM has been reported to be

twice commoner in blacks than in white and has a M: F of 1.4:1 [17]. The median age at diagnosis is 65-70 years and only 15% and 2% of the patients are younger than 50 and 40 years respectively [1].

Aside from elevated free light chain of 4,715 mg/dl (normal range: 5-71-26.3) and severely low reduced kappa:lambda ratio of <0.01 (normal range: 0-26-1.65); other main findings include anaemia, moderately raised ESR of 54 mm in 1st hr, immunoparesis and abnormal plasmacytosis in bone marrow aspiration cytology as well as the marrow sample at decompression laminectomy sent for histology (Fig. 1). However, we found normal renal profile and normal calcium and phosphate levels. This is of importance because hypercalcaemia often occur in MM and renal impairment is frequently expected in lambda-type LCDD.

The presence of only a light chain monoclonal protein is seen in approximately 20% of MM cases, more often kappa light chain (in 80%) and the condition is known as light chain myeloma [18]. In this index case, amyloid light-chain (AL) – amyloidosis consisting predominantly of lambda

light chains is expected but kappa light chains are predominantly involved in LCDD. Electron microscopy is known to be helpful in distinguishing between these two lesions.

The diagnosis of light chain disease depends on the availability of specific antisera against the five known classes of immunoglobulins and against free and bound light chains. In MM, there is increased concentration of monoclonal protein, which is an abnormal immunoglobulin produced by the malignant plasma cells, along with normal or reduced concentration of other normal immunoglobulins.

In the analysis of serum protein electrophoretic pattern reported locally [19] in the 19 cases of MM in a five year review, non-secretory MM was found in 16%. These so called "non-secretory" may include undiagnosed light chain myeloma because of the unavailability of specific antisera for the free light chains in plasma or in urine at the time of diagnosis.

Determination of SFLC ratio is important not only for diagnosis, it is also important for the monitoring of the disease. It is a very sensitive indicator in the evaluation of early response and also of early relapse. Its determination also gives valuable information on MGUS.

Plasma cell neoplasms secreting only kappa or lambda light chains were not previously diagnosed in our facility even though we received and treated an average of 4.2 cases of MM per year[19].

4. CONCLUSION

This case report highlights the fact that light chain myeloma might have been previously overlooked because of poor awareness and the non-availability of required monoclonal antisera against light chains of immunoglobulins. It has also shown that diverse variation of MM exists even in our environment and that a well-equipped laboratory capable of providing all necessary monoclonal antibodies to analyze immunoglobulin subtypes in each of our facilities will improve diagnostic accuracy and proper prognostication of our MM cases.

CONSENT

All authors declare that 'written informed consent was obtained from the patient for publication of this paper and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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