

A Rare Case of Light Chain Myeloma with Amyloidosis

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Abstract

Background: Multiple myeloma is characterized by neoplastic proliferation of a single clone of plasma cells producing a monoclonal immunoglobulin. It comprises about 1% of all malignant tumours and 10-15% of haematopoietic neoplasms. Light chain myeloma accounts for up to one-fifth of all cases of myeloma and is typified by only a light chain in the serum or urine, lacking expression of the immunoglobulin heavy chain. Amyloidosis is characterized by extracellular deposition of insoluble fibrillar protein called amyloid, in various tissues and organs. Light chain (LC) amyloidosis is the most common form of systemic amyloidosis and it complicates about 10% of cases of myeloma. When multiple myeloma is complicated by LC amyloidosis, the myeloma is typically diagnosed before or around the time of the diagnosis of amyloidosis.

Case presentation: We report a rare case of an elderly patient who presented with constitutional symptoms, anaemia and renal failure with negative myeloma screen who was ultimately diagnosed with light chain myeloma with systemic amyloidosis.

Conclusion: This case highlights that it is important to perform a series of clinically directed laboratory investigations to evaluate a suspected case of myeloma even if the routine investigations of myeloma screen are negative. Even though rare light chain myeloma should be thought of in a patient, who has anaemia and renal failure, where the initial myeloma screen is negative.

Keywords: Light chain myeloma; Systemic amyloidosis

Abbreviations: LC: Light chain; AL: Amyloidosis, light chain; SPEP: Serum protein electrophoresis; ESR: Erythrocyte sedimentation rate

Background

Multiple myeloma is characterized by neoplastic proliferation of a single clone of plasma cells producing a monoclonal immunoglobulin. It comprises about 1% of all malignant tumours. One fifth of multiple myeloma produces only light chains. Amyloidosis is characterized by extracellular deposition of insoluble fibrillar protein called amyloid, in various tissues and organs. Light chain (LC) amyloidosis also named amyloidosis light chains (AL) is the most common form of systemic amyloidosis and it complicates about 10% of cases of myeloma, with most being asymptomatic [1].

Here, we report a case of light chain myeloma complicated with asymptomatic systemic amyloidosis.

Case report

Mrs. WS was a 68 year old female who presented with weakness, fatigue and loss of appetite for one years' duration. She also complained of vague lower back pain. There was no history of significant loss of weight, fever, night sweats, numbness or any bleeding manifestations. She was previously diagnosed with, and was on treatment for hypertension, diabetes mellitus, ischaemic cardiomyopathy and bronchial asthma. She had also previously been investigated for anaemia, and was being treated for Vitamin B12/folate deficiency.

On examination, she was pale and had glossitis and bilateral ankle oedema. She did not have peripheral lymphadenopathy, but on abdominal examination she had mild hepatomegaly. The rest of the system examination was normal.

Laboratory studies were performed and showed the following: Haemoglobin 5.4 g/dL with a high mean cell volume (96 fL), White blood

cell total count $6.6 \times 10^9/L$ with a neutrophil predominance, platelet count 91,000/ μL , ESR 90 mm in the first hour, leucoerythroblastic blood film with marked rouleaux formation (Figure 1), reticulocyte count 0.8%. She had normal serum calcium levels and a slightly high serum creatinine value (133 $\mu mol/L$). Her total protein level was low with a low normal albumin level (38.5 g/L) and a low globulin level (16.7 g/L). Ultrasound scan of the abdomen showed mild hepatomegaly with a prominent spleen and the skeletal survey was normal. Serum protein electrophoresis (SPE) showed evidence of hypoproteinaemia without a monoclonal band. Her urine was negative for albumin as well as for Bence Jones proteins. She had laboratory evidence of renal failure showing high serum creatinine. Bone marrow aspiration was performed and it showed a plasma cell infiltrate of more than 60% (Figure 2). The trephine biopsy confirmed this (Figure 3) and it further showed the presence of amorphous material in intertrabecular spaces which stained positively with Congo red, suggesting that it was amyloid deposition (Figure 4). Immunofixation of serum proteins was done, and it showed a small monoclonal band in the gamma region of lambda light chain type (Figure 5). A diagnosis of systemic amyloidosis was made in view of the presence of amyloid in the bone marrow. With the presence of more than 60% plasma cells in the bone marrow and a lambda light chain on serum immunofixation, the diagnosis of lambda light chain producing myeloma was also made.

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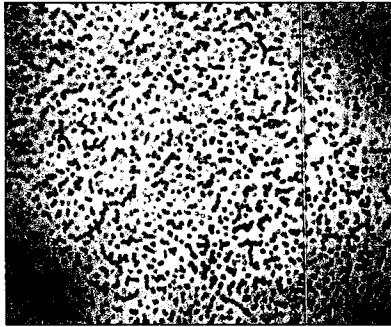


Figure 1: Blood picture with marked rouleaux formation.

- Anemia 73%
- Bone pain 58%
- Elevated creatinine 48%
- Fatigue/generalized weakness 32%
- Hypercalcemia 28%
- Weight loss 24%, one-half of whom had lost ≥ 9 kg

SPE will demonstrate a localized band or peak in 82% of patients with myeloma. The combination with serum immunofixation increases the sensitivity to 93%. If, in addition, either the serum free light chain assay or urine monoclonal protein studies (urine protein electrophoresis and urine immunofixation) are done, the sensitivity increases to 97% or more. Approximately 2% of patients with myeloma have true non-secretory disease and have no evidence of an M protein on any of the above studies (3). Among the 20% with no localized band on SPEP, hypogammaglobulinemia is seen in about one-half (due in part to suppression of normal gamma globulin production) and no apparent abnormality in the remainder.

Light chain myeloma accounts for up to 20% of myeloma and is typified by only a light chain in the serum or urine, lacking expression of the immunoglobulin heavy chain. These patients are detected readily by urine protein electrophoresis and urine immunofixation. The incidence of renal failure is much higher in light-chain myeloma, and the serum creatinine is ≥ 2 mg/dL (173 micromoles/L) in about one-third of these patients at presentation.

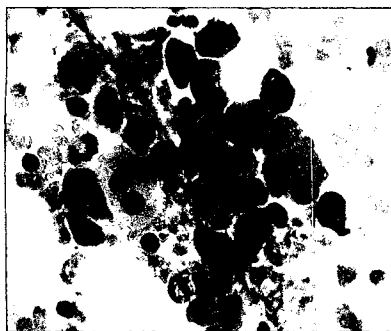


Figure 2: Bone marrow aspiration (Leishman stain) showing plasma cell infiltration.

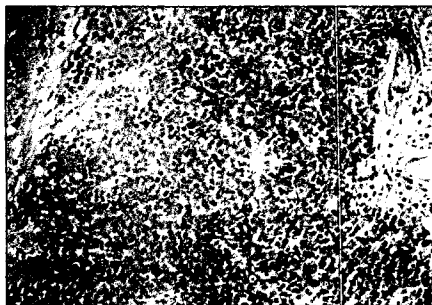


Figure 3: Bone marrow trephine biopsy (Haematoxylin and Eosin) showing plasma cell infiltration.

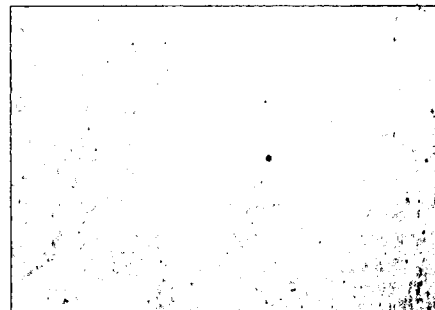


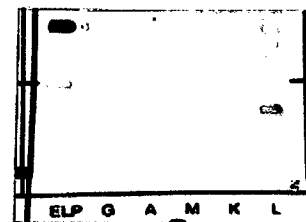
Figure 4: Bone marrow trephine biopsy showing amyloid deposition (Congo red stain).

Discussion

Multiple myeloma is a bone marrow-based, multifocal plasma cell neoplasm associated with an M-protein in serum and/or urine. It comprises about 1% of all malignant tumours, 10-15% of haematopoietic neoplasms and is the cause for 20% of deaths due to a haematological malignancy. Myeloma is a disease of older adults, with the median age at diagnosis being 70 years [1].

Most patients with myeloma present with symptoms or signs related to the infiltration of plasma cells into bone or other organs or to renal damage from excess light chains. As an example, a retrospective analysis of 1027 sequential patients diagnosed with multiple myeloma at a single institution, revealed the following symptoms and signs at presentation [2].

Immunofixation / Bence Jones



Comment:

The small monoclonal band seen in the gamma region is Lambda light chain type.

Figure 5: Immunofixation of serum proteins showing a monoclonal band of lambda light chain type.

According to the 2014 update on Multiple Myeloma in the American Journal of Haematology [3], multiple myeloma is defined as follows:

- Clonal bone marrow plasma cells $\geq 10\%$ or biopsy proven plasmacytoma, and
- Evidence of end-organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically
 - Hypercalcaemia: serum calcium >11.5 mg/dL or
 - Renal insufficiency: serum creatinine >173 micromoles/l (or >2 mg/dL) or estimated creatinine clearance <40 mL/min
 - Anaemia: normochromic normocytic with a haemoglobin value of >2 g/dL below the lower limit of normal or a haemoglobin value of <10 g/dL
 - Bone lesions: lytic lesions, severe osteopenia or pathologic fractures
- In the absence of end-organ damage: Clonal bone marrow plasma cells $\geq 60\%$
- Amyloidosis is characterized by extracellular deposition of insoluble fibrillar protein called amyloid, in various tissues and organs. Light chain amyloidosis (AL) is the most common form of systemic amyloidosis and complicates about 10% of multiple myeloma cases. A diagnosis of systemic AL is defined as [3]:
 - Presence of an amyloid-related systemic syndrome (such as renal, liver, heart, gastrointestinal tract or peripheral nerve involvement)
 - Positive amyloid staining by Congo red in any tissue (e.g.: fat aspirate, bone marrow or organ biopsy)
 - Evidence that amyloid is light-chain related established by direct examination of the amyloid using Mass Spectrometry-based proteomic analysis or immunoelectron microscopy, and
 - Evidence of a monoclonal plasma cell proliferative disorder (serum or urine M-protein, abnormal free light chain ratio or clonal plasma cells in the bone marrow)
- When multiple myeloma and AL are diagnosed in the same patient, the myeloma is typically diagnosed before or around the time of the diagnosis of amyloidosis. Less commonly, myeloma develops more than six months after the diagnosis of amyloid (delayed progression) [4].

There are several case reports published on presentations of light chain myeloma and its prognosis [5-7]. The index patient presented with long term constitutional symptoms, anaemia and a degree of renal impairment without hypercalcaemia or lytic bone lesions. Her bone marrow showed more than 60% of plasma cells with evidence of amyloidosis. The type of amyloid was not further defined due to limitations with available investigations. Our patient had no evidence

of other system involvement. Her serum immunofixation revealed a monoclonal band of lambda light chain type in the gamma region, being compatible with the diagnosis of light chain myeloma.

Our patient belongs to a rare group of patients who present with light chain myeloma with co-existing systemic AL. This case emphasizes the importance of a high degree of clinical suspicion and the importance of using clinically directed laboratory evaluation to increase the sensitivity of the diagnosis of multiple myeloma.

Declarations

Consent to collect data and for publication: Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests: There are no competing financial or non-financial interests from any part from the principal and the co-author of this case report. There was no finding involved from external sources for this publication.

Authors' contribution: Data collection and initial writing up of the case report was done by Dr. SK and the final designing, drafting of the manuscript and revising it critically and the intellectual input was given by the principal author of the paper Dr. DG.

The final approval for publication was given by DG.

Availability of data and materials: I wish to share the data of the study.

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