A Case of Light Chain Deposition Disease (LCDD) in a Young Patient

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Abstract Light chain disease is a variant of multiple myeloma in which the malignant population of marrow cells produces free monoclonal light chains but no heavy chain or complete immunoglobulin. The monoclonal light chains are small enough to be freely filtered by the kidneys and become Bence–Jones protein. Light chain disease comprises about 18% of multiple myeloma patients. Here we present a case report of a 38-year-old man who initially presented with complaints of pain in back and low grade fever off and on. He was found to have collapse of D9 and D12 vertebrae along with ascites and right pleural effusion and massive proteinuria. Multiple myeloma was considered as a differential diagnosis based on the investigations but eventually the patient was lost to follow up. This case is reported here as the light chain variant of multiple myeloma leading to deposition disease is less commonly reported and presents considerable difficulties in diagnosis.

Keywords Multiple myeloma · Light chain disease · Bence–Jones protein

Introduction

Light chain disease (LCD) is a variant of multiple myeloma in which the malignant plasma cells of the bone marrow produce free monoclonal light chains [1]. These light chains can be deposited in many organs leading to light chain deposition disease [2]. Renal involvement is most

frequent and it manifests as nephrotic range proteinuria and renal insufficiency. Light chain deposition disease is found in 5% of the myeloma patients at autopsy. The monoclonal light chains are small enough to be freely filtered by the kidneys and become Bence–Jones protein. The clinical features [3] include:

1. A more malignant course as compared to classical myeloma.
2. Extremely rapid doubling time.
3. Tendency for more osteolytic lesions.
4. Increased hypercalcemia.
5. Higher incidence of renal failure (including azotemia at presentation) as compared to other patients with multiple myeloma.
6. Higher incidence of amyloidosis and plasma cell leukaemia in the terminal stages of the disease. Renal failure is the principle cause of death in these patients.

Here we report a variant of multiple myeloma manifesting as excess kappa light chain production leading to extramedullary involvement in the form of hepatosplenomegaly, ascites, pleural effusion and renal failure.

Case Report

A 38-year-old male presented to the hospital with complaints of back ache for 2 months associated with low grade fever off and on. There were no complaints of bowel and bladder. He admitted to having a decreased appetite associated with weight loss. There was no history of any trauma or swelling in any part of the body.

Clinical examination of the abdomen revealed hepatosplenomegaly and presence of free fluid. On CNS examination power was 4/5 in bilateral lower limbs. B/L Plantars

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were flexor. The deep tendon reflexes were normal. Upper limb power was normal. Tenderness was elicited at the level of lumbar vertebrae. Higher mental functions were normal.

On routine examination his complete blood count revealed anaemia with a haemoglobin cont of 5.8 g/dl. His total leukocyte count was 4,500 cells/mm³. Platelet count was normal. His biochemical investigations revealed an elevated blood urea of 108 mg/dl and creatinine of 3.9 mg/dl. His lipid profile and liver function tests were normal except for total protein and albumin levels. The total protein was low at 5.1 g/dl and albumin was 2.7 g/dl. There was hypercalcemia with a serum calcium of 12.8 mg/dl and hyperphosphatemia with a serum phosphorus of 6.9 mg/dl. Urine revealed albuminuria of 3+. On quantitative estimation of total protein loss in urine, the patient was found to have massive proteinuria of 9.8 g/24 h. His thyroid function test was normal. Immunoglobulin G (IgG) and Immunoglobulin M (IgM) for mycobacterium tuberculosis were found to be negative by ELISA.

His radiological investigations revealed patchy opacity in right lung field with relative sparing of right upper zone. Right sided pleural effusion was present. Left lung field was clear. X-ray of dorso-lumbar spine revealed collapse of D9 and D12 vertebrae. Ultrasonography of abdomen and pelvis revealed presence of ascites and evidence of medical renal disease. There was evidence of bilateral nephropathy with ascites and mild splenomegaly. MRI of dorso-lumbar spine revealed evidence suggestive of marrow infiltrative disorder with multiple vertebral collapse, subchondral fracture at D9 and D12 vertebrae and posterior convex bulge in D5 vertebra causing marked thecal compression at this level. Hepatosplenomegaly, ascites and right sided pleural effusion was also reported.

A bone marrow aspiration was done where RBCs were found to be normocytic and normochromic. Large macro-ovalocytes were present. The bone marrow was hypercellular, replaced by sheets of plasma cells which constituted 90% of marrow cells. There was marked paucity of erythroid and megakaryocytes. Majority of the plasma cells were mature and few immature forms were seen. Few binucleated, multinucleated plasma cells and flame cells were seen.

His serum protein electrophoresis revealed a suspicious discrete band in γ globulin region which was not conventionally placed as an M band (Fig. 1). It was faint in appearance and not very sharply localised. A serum immuno fixation was carried out which revealed the presence of a sharply localised discrete kappa band corresponding to the level of the M band in the electrophoresis lane (Fig. 2). Urine Bence–Jones was positive and urine sample was subjected to electrophoresis after concentration. This revealed a sharp, densely staining discrete band

Fig. 1 Serum protein electrophoresis; arrow corresponds to M band

Fig. 2 Serum immunofixation depicting Ig kappa

Fig. 3 Urine protein electrophoresis; arrow corresponds to M band

Fig. 4 Urine immunofixation depicting light chain Kappa

in the gamma globulin region (Fig. 3). Other protein fractions were stained very lightly. Urine immuno fixation electrophoresis revealed presence of kappa band (Fig. 4). These findings confirmed monoclonal gammopathy involving production of only kappa light chains. Thus the diagnosis of LCD multiple myeloma with extramedullary involvement was made.

Discussion

Light chains (molecular weight 22,000 D) are polypeptides synthesized by plasma cells and assembled with heavy chains to form the various classes of immunoglobulins, for example, IgG, IgM, and IgA. Plasma cells normally produce a slight excess of light chains that are either excreted or catabolized by the kidney [4].

Light chains are divided into two major classes based on the amino acid sequence in the constant portion of the polypeptide chain and are designated as kappa and lambda. These are further divided into at least ten subtypes (four kappa and six lambda) based on the amino acid sequence in the variable region of the polypeptide chain. Individual immunoglobulins have either kappa or lambda light chains, but not both.

Kappa light chains usually exist as monomers (22,000 D) and are therefore small enough to be filtered through the glomerulus, but they may exist as dimers. Lambda light chains usually exist as dimers (44,000 D) and, therefore, are less likely to be filtered and appear in urine. At times, light chains of either kappa or lambda type may form tetramers (88,000 D), which are not filtered, and a patient may have light chain proteinemia without light chain proteinuria.

The kidney is the major site of metabolism of light chain proteins. The filtered light chain proteins, reabsorbed by the proximal tubular cells via the tandem megalin/cubilin receptors, are catabolized by lysosomal enzymes. This process is exceedingly efficient, and only a minute amount of light chain protein normally appears in the urine. Metabolism (catabolism) of these filtered light chain proteins depends on normal proximal tubular cell function, and damage to these cells can result in increased excretion of light chain proteins in the urine. Hence, light chain proteins appear in urine in high concentration either when the production of light chain proteins is markedly increased or when the ability of the proximal tubules to reabsorb all the filtered protein is exceeded.

Structural gene loss involving the deletion of the J–H segment of the heavy chain locus (situated on chromosome 14) is the most probable cause leading to isolated production of light chains in the disease.

Light chains cause rapid decline of renal function and early onset of clinical deterioration in LCD. Renal damage caused by the freely filtered light chains affects every segment of the nephron.

1. In the glomerulus, they can cause a non fibrillary glomerulopathy involving deposition of light chains as

well as fibrillary glomerulopathy characterised by amyloidosis.

2. In the proximal tubules, reabsorption leads to formation of toxic metabolites and an acquired Fanconi syndrome.
3. The distal tubules suffer what has been termed “cast nephropathy” as a result of epithelial damage due to cast formation in the lumina. Proteinaceous casts are prominent in the distal convoluted tubules and collecting ducts. Some of the casts are surrounded by multinucleated giant cells derived from fusion of infiltrating macrophages.

The laboratory features of LCD are different from classical myeloma and hence present considerable challenge to diagnosis [5]. The serum total protein is normal to low. Hypogammaglobulinemia is commonly encountered as opposed to hypergammaglobulinemia seen in classical multiple myeloma. This is because of the fact that only light chains are produced which because of their low molecular weight are easily filtered out by the kidneys. 100% of the patients show evidence of Bence–Jones protein. Many patients do not have a serum M (monoclonal) component on electrophoresis as most light chains are quickly filtered by the kidneys. Urine electrophoresis therefore becomes an important test in such cases. Urine immuno fixation electrophoresis reveals the type of monoclonal component present in case it is not detected by serum. The usual picture in the disease population reveals kappa: lambda ratio of 2:1. This distinction is important because lambda LCD has a three times worse prognosis than kappa LCD.

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