An Autopsy Case of Light Chain Deposition Disease

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This report describes a case of light chain deposition disease (LCDD) with unusual findings of fibrillar structures in the deposits and marked calcification in several organs. A forty-year-old man was initially diagnosed with LCDD in 1987, and died of sepsis three and one-half-years later. Histological examination of autopsy specimens demonstrated eosinophilic amorphous materials, which differed from amyloid, in vessel walls or around parenchymal cells in almost every organ examined. Ultrastructurally, in addition to granular deposits, fibrillar structures were also seen in the deposits. Marked calcification was present in the myocardium, skeletal muscles, adrenal glands and arteries.

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Introduction

Light chain deposition disease (LCDD) is a relatively rare condition characterized by the deposition of monoclonal light chains in multiple organs (1). These deposits lack the specific properties of amyloid as they do not stain with Congo red or demonstrate apple green birefringence on polarized light. Viewed ultrastructurally, the deposits have a fine granular appearance, as opposed to a fibrillar appearance. Since the first report by Randall and colleagues in 1976 (1), over 150 cases of LCDD have been described (2). However, only a few reports have described precisely autopsy findings (3-6) and the follow-up periods have been short. We describe the three and one-half-year follow-up and subsequent postmortem findings of a patient with LCDD.

Case Report

This 40-year-old man was first admitted to our department on August 8, 1987 because of rapidly deteriorating renal function. Physical findings were unremarkable except for anemic palpebral conjunctivae and edema of the lower legs. Laboratory findings indicated normocytic anemia (red blood cells, 256\times10^6/mm^3; hemoglobin, 7.5g/dl; hematocrit, 22.2%), azotemia (serum urea nitrogen, 64 mg/dl; serum creatinine, 6.8 mg/dl), and metabolic acidosis (plasma bicarbonate, 17.3 mmol/l). Urinalysis demonstrated mild amount of protein with a sediment of 5-10 red blood cells per high power field and numerous granular casts. Serum antinuclear antibody and cryoglobulin were negative. On immunoelectrophoresis, no M-protein was detected in either the serum or urine. Ultrasonography of the kidney revealed it to be of normal size and shape with no evidence of obstruction.

The tentative diagnosis was rapidly progressive glomerulonephritis. Pulse therapy with intravenous methylprednisolone (1,000 mg/day) was instituted for 3 consecutive days followed by oral prednisolone, 40 mg/day. However, such treatment was ineffective. The patient’s condition progressed to end-stage renal disease, and maintenance hemodialysis was initiated on September 7, 1987. The dose of prednisolone was tapered gradually and was discontinued by the end of November 1987.

An open renal biopsy was performed on September 18, 1987 to determine the etiology of the renal disease. Using light microscopy, nearly all glomeruli showed nodular lesions closely resembling diabetic nodular glomerulosclerosis (Fig. 1, upper left). Thickening of the tubular basement membrane and cellular infiltrations in the interstitium were also observed. Immunofluorescence microscopy demonstrated positive staining for kappa light chain in glomerular nodules, glomerular basement membranes, Bowman’s capsules and tubular basement membranes (Fig. 1, upper right). Lambda light chain, heavy chains, including alpha, gamma and mu chains, and complements did not stain. In every specimen examined neither Congo red staining, nor apple-green birefringence under polarized light was observed. This observation indicated that the
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depicted materials differed from amyloid. Electron microscopy revealed fine granular dense deposits along the glomerular basement membrane, Bowman’s capsule and tubular basement membrane (Fig. 1, lower left). Additionally, there were fibrillar structures in the nodular lesions of the glomeruli associated with the granular deposits (Fig. 1, lower right).

These histological and immunofluorescence findings were compatible with a diagnosis of light chain deposition disease (1, 2). A bone marrow aspirate obtained from this patient revealed hypocellular marrow with a relative increase in plasma cells (12.5% of nucleated cells). Most were stained with anti-kappa light chain antibody. However, there was no morphologic evidence of plasma cell malignancy. No osteolytic lesion was seen on X-ray and no abnormal accumulation of 99m-Technetium was observed on a bone scintigram. These observations did not fulfill the criteria of myeloma (7). It was, therefore, unlikely that the LCDD was caused by myeloma.

The patient was discharged from our hospital in October 1987 and appeared to be well-controlled by dialysis at an outpatient clinic. This changed in May 1989 when ultrasonography indicated the presence of hepatomegaly. The liver was palpable at 3 cm below the right costal margin in January 1990. Blood chemistry at that time indicated aspartate aminotransferase (AST) was 38 IU/l, alanine aminotransferase (ALT) 93 IU/l, a marked elevation of alkaline phosphatase (Al-p) 534 IU/l and gamma-glutamyltransferase (γ-GTP) 399 IU/l with a normal level of total bilirubin. Hepatitis B surface antigen was negative and antibody for hepatitis C virus was positive. Isoenzymes of Al-p consisted of 29.6% Al-p 1 and 70.4% Al-p 2 and 3, indicating the hepatobiliary system as the enzyme source. Ultrasonography did not demonstrate any evidence of gallstones or obstruction of the biliary system. The hepatomegaly progressed over the next 10 months, and the patient developed jaundice, muscle atrophy, hypotension, and general malaise. Since plasma cells in the bone marrow aspirate increased to 24% of nucleated cells in May 1990, prednisolone and melphalan were administered. Because of bone marrow suppression, melphalan was discontinued after 2 months without any observed effect on bone marrow plasma cells. Despite repeated examinations of serum and urine, monoclonal kappa light chain was not detected except in 2 samples of serum obtained after the initiation of chronic dialysis (December 1989, April 1990).
Hypotension, general malaise, muscle atrophy and jaundice progressed further and the patient was readmitted on October 29, 1990. At the last admission, he weighed 53.7 kg (height 163 cm), blood pressure was 72/48 mmHg, and heart rate 120 beats/min. Palpebral conjunctivae were anemic and bulbar conjunctivae were markedly icteric. Lungs and the heart were unremarkable. A firm liver was palpable at 7 cm below the right costal margin. Ascites was not present and the spleen was not palpable. Muscle atrophy predominant proximally was noted in both the legs and arms. Laboratory findings at the last admission are summarized in Table 1. Electrocardiography showed sinus tachycardia and low voltage in the limb leads. Echocardiography revealed hyperkinetic contraction of the left ventricle with an increase in thickness (14 mm in diameter). Hemodynamic parameters obtained using a Swan-Ganz thermodilution catheter indicated a cardiac index of 5.09 l/min/m² and a pulmonary capillary wedge pressure of 6 mmHg. Total peripheral vascular resistance was calculated to be 848 dynes·sec·cm⁻⁵·m² (normal, 1130±178). There was no evidence of gallstones or of biliary tract obstruction on ultrasonography or CT scan. He developed pneumonia in December 1990 and died of sepsis on January 17, 1991. Autopsy was performed 12 hours after death.

**Postmortem findings**

Many organs showed deposits of eosinophilic amorphous substances in the vessel walls or around parenchymal cells, producing atrophy of the parenchymal cells. These microscopic findings closely resembled systemic amyloidosis. However, all specimens were negative for Congo red staining and for apple-green birefringence on polarized light microscopy. The deposits did stain for kappa light chain with the peroxidase-antiperoxidase method. No staining of the lambda light chain, IgG, IgA, IgM, or complement factors was observed in the deposits.

Kidney: The right kidney weighed 140g and the left 120g. Both kidneys had a marked increase in consistency. Nearly all glomeruli were occupied by amorphous substances, and all tubular lumens were obliterated by extreme thickening of the peritubular basement membranes.

Liver: The liver weighed 2,880g and had an increased consistency. Severe perisinusoidal deposition and atrophy of liver cells were present. Pseudocholangiosis with severe bile stasis and hemosiderosis were also observed (Fig. 2).

Spleen: The spleen weighed 280g and had a marked increase in consistency. Severe deposits, chiefly around the sinusoid,

### Table 1. Laboratory Findings at the Last Admission

<table>
<thead>
<tr>
<th>Complete blood count</th>
<th>Immunological findings</th>
<th>Endocrinology</th>
<th>Blood gas analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>Anti-Nuclear antibody</td>
<td>C-PTH</td>
<td>pH</td>
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<tr>
<td>RBC</td>
<td>Anti-DNA antibody</td>
<td>Adrenaline</td>
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<tr>
<td>Hemoglobin</td>
<td>Anti-ENA antibody</td>
<td>Noradrenaline</td>
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<td>Hematocrit</td>
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<td>Dopamine</td>
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<td>Platelets</td>
<td></td>
<td>Cortisol</td>
<td></td>
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<tr>
<td>Reticulocytes</td>
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<td>PRA</td>
<td>1.3 ng/ml/h</td>
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Blood chemistry

- Total protein: 5.8 g/dl
- Albumin: 3.9 g/dl
- AST: 106 IU/l
- ALT: 33 IU/l
- LDH: 537 IU/l
- ALP: 351 IU/l
- Total Bilirubin: 9.9 mg/dl
- Direct Bilirubin: 7.6 mg/dl
- Urea Nitrogen: 47 mg/dl
- Creatinine: 8.7 mg/dl
- Sodium: 135 mEq/l
- Potassium: 3.5 mEq/l
- Chloride: 94 mEq/l
- Calcium: 12.3 mg/dl
- Phosphorus: 6.8 mg/dl
- Magnesium: 1.8 mg/dl

were observed.

Heart: The heart weighed 430g and was mildly enlarged. The left ventricle wall was 13 mm thick. Substantial pericellular deposits were observed. Occasional calcification of myocardial fibers was also observed (Fig. 3).

Bone marrow: Specimens of bone marrow from the femur, sternum and vertebral bodies were examined. There was no cluster, aggregate, or infiltrate of plasma cells at any site of the bone marrow examined. No plasma cell atypia was noted. These findings indicated that the present case was not complicated by myeloma.

Other organs: The adrenal glands exhibited marked deposits of amorphous material with marked calcification. Skeletal muscles demonstrated such deposits with calcification of degenerated lesions. Deposits of moderate to marked severity were present in the pituitary, the thyroid, and the gastrointestinal mucosa. Mild deposits were found in the parathyroid glands. The lungs showed mild deposits and calcification of the small branches of the pulmonary arteries. There was evidence of severe focal bronchopneumonia and an abscess in the left lower lobe.

Ultrastructural studies: Formalin-fixed, paraffin-embedded specimens of the kidney, liver, spleen, and heart were examined ultrastructurally. Electron microscopy demonstrated fine, granular electron-dense deposits in all organs examined. Fibrillar structures (diameter 10 nm) were also associated with the granular deposits in these organs (Fig. 4).
Ultrastructurally, the deposits in LCDD demonstrate a fine granular pattern (13). In addition to the granular deposits, we also observed fibrillar structures in the kidney, liver, spleen, and heart deposits of approximately 10 nm in diameter which resembled amyloid fibrils. These arrangements, however, were parallel rather than randomly oriented networks of amyloid fibrils. Fibrillar structures in the deposits (5, 6, 14–16), or coexistence of granular light chain deposits and amyloid (2–4, 17–21) have been reported in some patients with LCDD. Although the pathogenesis and the clinical significance of the fibrils observed in LCDD remain obscure, three interpretations are proposed: [a] fibrils are synthesized as a host reaction to the materials deposited (13), [b] the fibrils are an intrinsic structure in the mesangium (14) or [c] the coexistence of fibrillar and granular deposits is an intermediate stage in the transition from LCDD to amyloidosis (19). In the present case, fibrillar structures were seen in the heart, spleen, and liver as well as in the kidney. Furthermore, there is no evidence that during the follow-up period of three and one-half-years light chain deposits changed their structure from nonamyloid to amyloid. Therefore, the latter two possibilities seem to be unlikely. Solomon and colleagues (22), by working with mice, demonstrated that the kidney lesions such as tubular basement membrane precipitates, casts, crystals, or fibrils produced by Bence-Jones protein mimicked those changes found in the kidney of the patient who provided the protein. This finding suggests that particular Bence-Jones proteins are primarily responsible for producing the distinctive types of protein deposits in the kidney.

Another striking finding at the postmortem examination was calcification at specific sites such as the myocardium, skeletal muscles, pulmonary arteries, and adrenal glands. Pathologic calcification is classified as either dystrophic, where calcification occurs in injured and necrotic tissues, or metastatic, signifying mineral deposits in essentially normal tissues (23). To our knowledge, there has been no previous report describing significant tissue calcification in LCDD. On the other hand, soft tissue calcification is common in patients undergoing long-term dialysis (24). In these cases, the calcification is considered to be metastatic and the calcified areas include the lung, heart, liver and blood vessels. Several mechanisms have been postulated for the soft tissue calcification seen in dialyzed patients, i.e., the presence of a high calcium-phosphorus (Ca-P) product, hyperparathyroidism, local and systemic alkalosis (25), and hyperoxalemia (26). The present subject did not demonstrate secondary hyperparathyroidism or persistent alkalosis but did have a high serum Ca-P product. From January 1990 to the last admission, control of serum calcium and phosphorus had been poor, with a Ca-P product of 60–86. Histologically, calcification in the present case was noted predominantly in degenerated cells. This finding suggests that the occurrence of soft tissue calcification in the present patient may have resulted from a combination of tissue injury produced by light chain deposition and a high Ca-P product in the serum.

In conclusion, we report the three and one-half-year follow-up and subsequent postmortem findings of a case of LCDD. Light chain deposition was observed in the vessel walls or...
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around parenchymal cells in every organ examined which caused the parenchymal cells to atrophy. Unusual findings in the present case included the presence of fibrillar structures in the deposits and substantial calcification in the myocardium, skeletal muscles, pulmonary arteries and adrenal glands.

References