Liver Failure Caused by Light Chain Deposition Disease Associated with Multiple Myeloma

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Abstract

Acute liver failure is an unusual complication in multiple myeloma. Here, we report a case of multiple myeloma with light chain deposition disease (LCDD) that presented with progressive jaundice due to intrahepatic cholestasis. Diagnosis was made after liver biopsy that showed deposition of kappa light chains occupying perisinusoidal spaces. The patient developed encephalopathy and liver failure and died despite prompt initiation of dexamethasone therapy. The current prognosis of multiple myeloma patients with liver failure due to LCDD is dismal. New therapeutic strategies might improve this condition.

Key words: multiple myeloma, immunoglobulin light chains, liver failure

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Introduction

Acute liver failure is a rare event in multiple myeloma (MM) with a dismal prognosis as previously reported (1-9). According to autopsy reports up to 45% of patients diagnosed with multiple myeloma will have liver infiltration with malignant plasma cells (10). Only an unknown but rather small number of patients will have either a massive infiltration of plasma cells (11), light chain deposition (7) or they will develop amyloidosis (9) that causes hepatic failure. Light chain deposition disease (LCDD) is a systemic disease caused by the deposition of large quantities of a monoclonal light chain frequently involving the kidney, heart, peripheral nerves and liver. Here, we report an 81-year-old man with IgG-kappa MM with LCDD who presented with a rapidly evolving intrahepatic cholestasis that evolved into acute liver failure; he died despite high-dose dexamethasone therapy.

Case Report

An 81-year-old Caucasian man presented to his local hospital’s emergency room in March 2011 with a history of progressive jaundice, dark urine and low back pain. He had a one-month history of lassitude, intense anorexia, weight loss and inability to walk due to low back pain. He had enjoyed a healthy and autonomous lifestyle until then. On physical examination he was jaundiced and did not show signs or symptoms of encephalopathy. He had a white coated tongue but not macroglossia. No spider naevi or other chronic liver disease stigmata were present. He had no fever. Cardiovascular and respiratory examinations were strictly normal. He had no previous history of diarrhea or constipation. On neurological examination neither axonal neuropathy nor carpal tunnel syndrome were present. Laboratory studies showed: bilirubin 6.35 mg/dL (NR 0.10-1.0), aspartate aminotransferase 102 U/L (NR 5-37), alanine aminotransferase 842 U/L (NR 9-85), albumin 1.9 g/dL (NR 3.4-4.7), alkaline phosphatase 699 U/L (NR 40-129), urea 62 mg/dL (NR 10-60), creatinine 1.3 mg/dL (NR 0.7-1.2), sodium 135 mmol/L (NR 136-146), Quick time of 68% (NR 70-100%), prothrombin time 13.6 seg. (NR 11-15 seg), hemoglobin 10.9 g/dL (NR 12-16), platelets 75×10⁹/L (NR 140-470). Proteinuria was not remarkable. Hematuria or renal tubular casts were absent in urine sediment. He had an erythrocyte sedimentation rate (ESR) of 60 mm in the first hour. Serology for hepatitis A, B and C viruses, Epstein
Spine X-rays and CT scan revealed generalized reduced bone density with L1 vertebrae crushing (see Fig. 1). MRI showed neither spinal cord compression nor solid mass plasmocytoma. An abdominal ultrasound study showed hypechoic liver enlargement with hyperechoic aspect of the walls of the portal vein. No spleen enlargement was found. Serum proteins electrophoresis (Capillarys 2⡴, Sebia, Norcross, GA, USA) showed a monoclonal hypergamaglobulinemia. Immunoglobulins quantification was as shown: IgG 2,813 mg/dL with low IgA and IgM. Light chains in serum were predominantly kappa by immunofixation (Hydragel IF⡴, Sebia, Norcross, GA, USA). 90% of bone marrow cells were dysplastic plasma cells. Cytogenetics of the bone marrow cells yielded a hypodiploid clone with deletions in chromosomes 13 and 17. β-2-microglobulin was 6.47 mg/L. His disease stage was III according to the International Staging System for multiple myeloma (12). A liver biopsy was performed. Massive infiltration of a homogeneous and dense eosinophilic material that was occupying liver perisinusoidal spaces (Hematoxylin and Eosin staining ×200).

Barr virus (EBV) and cytomegalovirus (CMV) were all negative. Autoimmune antibodies were negative as well. Serum proteins electrophoresis showed increased levels of monoclonal immunoglobulin with low IgA and IgM. Light chains in serum were predominantly kappa by immunofixation (Hydragel IF⡴, Sebia, Norcross, GA, USA). 90% of bone marrow cells were dysplastic plasma cells. Cytogenetics of the bone marrow plasma cells yielded a hypodiploid clone with deletions in chromosomes 13 and 17. β-2-microglobulin was 6.47 mg/L. His disease stage was III according to the International Staging System for multiple myeloma (12). A liver biopsy was performed. Massive infiltration of a homogeneous and dense eosinophilic material that was occupying liver perisinusoidal spaces (see Fig. 2). Congo red staining was negative. Immunostaining revealed diffuse kappa light chain restriction (see Fig. 3A and 3B). The patient’s condition deteriorated rapidly during his three weeks of hospitalization. Despite high dose dexamethasone therapy he developed encephalopathy and died.

**Discussion**

Light chain deposition disease (LCDD) has been rarely reported as a cause of acute liver failure and death (7, 13, 14). LCDD is a systemic disease caused by the deposition of large quantities of a monoclonal light chain frequently involving kidney, heart, peripheral nerves and liver. This monoclonal light chain is produced by neoplastic plasma cells in multiple myeloma or lymphoplasmacytic-B cell diseases. Only 5% of multiple myeloma patients will have a LCDD (15). Unlike AL-amyloidosis these deposits are PAS-positive after diastase digestion, and usually kappa restricted, they do not fold into β-sheets, do not stain with Congo red, do not stain for anti-AL protein, do not stain for anti-P component antiserum and show a granular pattern in histology sections. As in the present case, liver involvement is often described as the deposition of this amorphous proteinaeous material in the perisinusoidal space. It has been reported that 15-20% of LCDD have lambda light chain deposition and a combination of light and heavy chain deposition has been described in less than 10% of reported cases.
cases (1, 15). Also cases of combined AL-type amyloidosis and LCDD have been reported in the same or different organs (14, 23). Although a common pathogenesis has been suggested for both LCDD and AL-amyloidosis, it is currently unknown why LCDD and AL-amyloidosis proteinaceous material have different morphological features.

Liver is the second most common organ affected by LCDD. Most patients remain asymptomatic or merely feature mild to moderate alterations in liver function tests, cholestasis or portal hypertension. Only a few will develop liver failure. Most MM patients presenting with liver failure are AL-amyloidosis (1-3, 8, 9) but massive plasma cell infiltration (11) or LCDD (7) may also lead to liver dysfunction. Liver involvement in other forms of amyloidosis, particularly familial amyloidosis, can be severe and lead to liver failure and the necessity for transplantation (16). The prognosis is grim once liver failure is established (7, 13). The clinical picture of these patients (i.e. progressive jaundice, encephalopathy, coagulopathy) is not different from other causes of liver failure regardless of the mechanism of liver infiltration. Diagnosis can be a tough challenge. Hyperbilirubinemia in patients with MM may have many different causes like chemotherapy toxicity (i.e. vincristine, Adriamycin and dexamethasone, VAD scheme), viral infection, obstruction of the biliary tree by enlarged lymph nodes or the aforementioned histological patterns of MM liver infiltration. In the present case the diagnosis was not immediately obvious but the patient complained of intense low back pain: spine CT-scan, elevated ESR, absence of biliary tree dilatation and serum monoclonal hypergammaglobulinemia prompted us to perform a percutaneous liver biopsy and the diagnosis was made. As previously reported by Michopoulos et al (7) and Faa et al (14) our patient showed abnormal liver tests of intrahepatic cholestasis (i.e. elevated alkaline phosphatase and gamma-glutamyltranspeptidase) with only a slight elevation in ALT or AST serum levels. They also reported prolonged prothrombin times in these patients. The present patient did not have remarkable abnormalities in coagulation times and had no hemorrhages. The kidney is the most frequent organ affected by LCDD (90%) and it is the main clinical problem affecting most of these patients. LCDD with renal involvement will present with nephrotic syndrome and renal failure. Microscopic hematuria is present in 20% of cases. Excretion of hydrogen ion and potassium will be impaired if the light chain deposits involves the tubules (17). Kidney function prognosis in MM patients with LCDD is dismal despite reports showing a reduction of proteinuria and stabilization of renal function in several uncontrolled studies and case reports (18-20). Most such cases end up rapidly developing end-stage renal disease (ESRD). Hemodialysis and kidney transplantation are the available treatment options at this stage but light chain deposition with renal impairment has been also described in the transplanted organ (21). Interestingly the present patient’s serum or urine analysis parameters for kidney function were strictly normal. To our knowledge only four other cases with LCDD without overt kidney failure have been reported (7, 14, 22, 23). We did not perform a kidney biopsy in our patient because his kidney function was spared. Autopsy was not done after the rapid fatal outcome.

Treatment with melphalan-prednisone and bortezomib is of limited value in most patients with LCDD liver involvement (24, 25). Moreover Samanez et al reported a liver failure with rapid fatal outcome that debuted after the first cycle of VAD (26). Newer approaches like high-dose melphalan therapy followed by autologous transplantation may improve the prognosis especially in younger patients (27).

In conclusion we report an unusual case of IgG kappa MM LCDD presenting with rapid fatal acute liver failure without renal disease. Despite recent efforts to improve therapy LCDD presenting as liver failure has an ominous prognosis according to the limited number of cases reported. Optimal approach in LCDD management can only be standardized after a large prospective trial but this seems unrealistic due to the low prevalence of this disease.

The authors state that they have no Conflict of Interest (COI).

References