Liver Involvement in Multiple Myeloma Proven by Peritoneoscopy
—A Case Report—

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Liver involvement in multiple myeloma has been known to be common in autopsied series. However, since its clinical significance is uncertain yet, invasive procedure confirming plasma cell infiltration of the liver has been rarerly performed. We report a case with multiple myeloma which had plasma cell infiltration of a liver. A peritoneoscopic biopsy of the liver for the purpose of disclosing the nature of the aggravating liver function in a carrier of the hepatitis B virus showed infiltration of lymphoreticular cell which were identified later as λ-light chain producing primitive plasma cells by immunohistochemical stain.

Key Words: Multiple myeloma, liver, peritoneoscopy

Multiple myeloma is malignancy of plasma cell that mainly but not exclusively involves the bone and bone marrows. Tissues rich in reticuloendothelial components such as liver, spleen, and lymph nodes were the most frequently involved extraosseous sites (Hayes et al. 1952, Adams et al. 1969, Pasmanter and Azar 1969, Marsch and Gross 1978). Since liver involvement in multiple myeloma has no proven prognostic implications, invasive procedures such as liver biopsy was only rarely carried out when patients has other signs of liver disease. Therefore, previous studies on liver involvement in multiple myeloma were mainly based on postmortem studies.

We report a case with multiple myeloma who had plasma cell infiltration of the liver, which is confirmed by peritoneoscopic biopsy of the liver. Since, as we know, this is the first reported case of peritoneoscopically confirmed myelomatous involvement of the liver, we describe peritoneoscopic and histologic findings in addition to clinical manifestations.

CASE REVIEW

A 39-year-old woman was admitted to Severance Hospital because of epigastric discomfort and multiple arthralgia. She had been a carrier of the hepatitis B virus for 4 years. While she was regularly followed up at an outpatient clinic, her serum transminase levels were elevated and the prothrombin time was prolonged 2 weeks before admission. On admission she complained of easy fatigue, frothy urine, multiple bone pain and a weight loss of 3 kilograms during the last 1 week. There was a past history of the osteoarthritis on the right hip joint 16 years earlier that had been treated with surgical replacement with an artificial joint. Her family history revealed that her mother died of a hepatoma 10 years ago.

On admission the temperature was 36.4°C, the pulse rate 76/min, and the blood pressure 110/80 mmHg. On physical examination she looked chronically ill. The conjunctivae were slightly
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pale. No skin rash or lymphadenopathy was found. The lungs and heart were normal. The abdomen was soft with mild epigastric tenderness; the liver was palpated softly 4 cm below the right costal margin; no ascites was detected. No peripheral edema was found. The hemoglobin was 6.7 g/dl, hematocrit was 19.8%, and the white-cell count was 7,200/mm³ with 66% of neutrophils, 30% of lymphocytes, 4% of monocytes. The platelet count was 64,000/mm³, the reticulocyte count 2.5%, and the erythrocyte sedimentation rate 139 mm/hr. The prothrombin time was 13.5 seconds with a control of 10.7 seconds (INR 1.16); the partial thromboplastin time was 20.5 seconds (normal 21 to 35 seconds); the fibrinogen was 431 mg/dl. A test for FDP was positive in a titer of 1:5 and was negative for D-dimer. The serum iron was 25 µg/dl, total iron binding capacity 179 µg/dl, vitamin B12 421.25 µg/ml, and folic acid 3.15 ng/ml. The blood chemistry showed calcium 9.0 mg/dl, phosphorous 3.6 mg/dl, fasting blood glucose 89 mg/dl, urea nitrogen 8.4 mg/dl, creatinine 0.6 mg/dl, total protein 6.7 g/dl, albumin 2.8 g/dl, total bilirubin 0.6 mg/dl, alkaline phosphatase 91 IU/l, SGOT (AST) 131 IU/l, SGPT (ALT) 121 IU/l, LDH 273 IU/l. LDH isoenzyme pattern showed a flipped pattern with LDH1 126 IU/l, LDH2 117 IU/l, LDH3 221 IU/l, LDH4 41 IU/l and LDH5 31 IU/l. The stool gave a negative test for occult blood and the urinalysis was normal. The viral marker studies showed that HBsAg was positive, Anti-HBc negative, Anti-HBs negative, HBeAg positive, Anti-HBe negative and Anti-HCV negative. A serum protein electrophoresis showed that ß-globulin was 2.67 g/dl (normal 0.5 ~ 1.1 g/dl) and g-globulin 0.38 g/dl (normal 0.5 ~ 1.6 g/dl). The a-fetoprotein level was less than 5 ng/ml. A radionuclide liver scan revealed hepatosplenomegaly and a 2 cm x 3 cm sized equivocal cold defect in the right lower lobe (Fig. 1). But the computed tomographic scan of the abdomen revealed hepatosplenomegaly and a slight enlargement of the pancreatic shadow without evidence of a tumor mass (Fig. 2). Also ultrasonography of the abdomen showed no focal lesion.

On the 6th hospital day peritoneoscopic examination of the liver with biopsy was performed because we suspected chronic liver disease associated with the hepatitis B virus. On gross examination, both lobes of the liver were enlarged; the edge was blunted; the surface

![Fig. 1](image1.png)

**Fig. 1.** Liver scan using ¹ⁱ⁵I-sulfur colloid shows enlarged liver especially of the left lobe with equivocal cold defect in the right lower lobe, and an increased uptake in the spleen.

![Fig. 2](image2.png)

**Fig. 2.** Computed tomography of the abdomen reveals hepatosplenomegaly and enlarged pancreas suggesting chronic pancreatitis, but the mass shadow observed in the liver scan is not visible.

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... showed a waxy, yellowish tint and coarse granularity intermingling with various fine nodules; the vascularity of the surface was normal without red spots but some lymphatic blebs were seen; the consistency was slightly firm; no ascites was observed (Fig. 3). Although these peritoneoscopic findings were not a usual pattern of the hepatitis B virus associated with chronic liver disease, liver biopsy was performed to find the cause of liver dysfunction. Microscopic examination of the biopsied specimen revealed some ground glass cells scattered throughout the lobule with minimal parenchymal necroinflammatory activity suggesting an inactive carrier state of hepatitis B (Fig. 4). It also showed massive infiltration of atypical lymphoreticular cells into portal tracts (Fig. 5) and less into sinusoids (Fig. 6). Immunohistochemical stains were done to confirm the exact nature of the atypical mononuclear cells, and a positive reaction for MB (B-cell marker) was revealed; subsequent studies disclosed that the infiltrated cells showed light chain restriction demonstrated by an exclusive positive reaction for λ-light...
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**Fig. 5.** Microscopic examination of the liver shows dense infiltration of atypical mononuclear lymphoreticular cells in portal tracts (P) and through the sinusoids (SIH&E, ×200).

**Fig. 6.** Microscopic examination of liver shows atypical mononuclear cells predominantly in portal tracts (P) and less in sinusoids (SIH&E, ×400).
Fig. 7. Immunohistochemical stain shows strong positivity for λ-light chain in the infiltrated mononuclear cells (immunohistochemistry, λ-light chain, ×200).

Fig. 8. Bone marrow aspiration smear shows markedly increased cellularity with predominant primitive plasma cells (Wright-Giemsa stain, ×1000).
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chain (Fig. 7). These findings suggested \(\lambda\)-light chain producing plasma cell infiltration of the liver parenchyma. On the 10th hospital day, bone marrow examination was done to confirm the diagnosis of plasma cell dyscrasia. The cellularity was more than 90% and immature plasma cells were more than 80% of all the nucleated cells (Fig. 8). Serum immunoelectrophoresis showed abnormal precipitation arcs on the zones of the IgD and \(\lambda\)-light chain. The serum level of \(\lambda\)-light chain was 700 \(\mu\)g/dl, but the IgD level was too low to be quantified. Urine immunoelectrophoresis showed abnormal precipitation arc on the zone of the \(\lambda\)-light chain but its quantification was impossible. A test for urine Bence-Jones protein was negative. The serum \(\beta\)-microglobulin level was 4.76 mg/ml. X-ray films of the chest and skull showed no osteolytic lesions, but radionuclide bone scanning disclosed multiple hot uptakes on the lower ribs, cervical and mid thoracic vertebrae and the shaft of the right humerus. From these findings, all we concluded was that this case is a stage III, multiple myeloma of IgD-\(\lambda\) type, which infiltrated the liver parenchyma. After the patient was treated with melphalan and steroid for 4 days, her symptoms such as multiple bone pain and constipation steadily improved with shrinkage of the liver size. She was discharged on the 21st hospital day without complication. The hemogram on the discharge day showed that hemoglobin was 8.4 g/dl, hematocrit 25.4\%, white-cell count 4900/mm\(^3\) with 49\% of neutrophils, 44\% of lymphocytes and 7\% of monocytes, and platelet 142,000/mm\(^3\). Recently she was in good health, was followed up at an outpatient clinic and continued to receive chemotherapy with MP (melphalan and steroid) regimen every 6 weeks.

DISCUSSION

Multiple myeloma is a disease of malignant proliferation of plasma cells. It mainly involves the bone and bone marrows but extramedullary involvement is also known to be relatively common (Churg and Gordon 1950; Hayes et al. 1952; Pasmantier and Azar 1969; Marsch and Gross 1978; Kapadia 1980). These studies showed that tissues rich in reticuloendothelial elements such as liver, spleen, lymph nodes and kidney were the most frequently involved sites (Hayes et al. 1952; Pasmantier and Azar 1969; Edwards and Zawadzki 1967; Marsch and Gross 1978).

In a series of postmortem and biopsy studies, liver infiltration by plasma cells was observed in 26\% to 47\% of the cases with multiple myeloma, among which nodular, sinusoidal, portal and mixed patterns of involvement were found (Churg and Gordon 1950; Hayes et al. 1952; Pasmantier and Azar 1969; Thomas et al. 1973, Kapadia 1980). Hepatic involvement reported by most authors was similar in that plasma cells appeared more often in the sinusoids than in portal spaces, and there was no clinical difference according to the patterns of plasma cell infiltration (Hayes et al. 1952; Thomas et al. 1973; Kapadia 1980; Perez-Soler et al. 1985). In this case, portal infiltration was dominant with less infiltration into sinusoids. The origin of the plasma cell in the liver is obscure, whether from bone marrows or from reticuloendothelial cells within the liver. In a review of liver involvement in multiple myeloma, histologic studies were available in only twenty one out of 128 cases (Perez-Soler et al. 1985). Among them, biopsies were performed in only five patients; in three patients who were already diagnosed of multiple myeloma because of persistent elevation of serum transaminases and in two patients because of hepatomegaly or hepatosplenomegaly of unknown origin. In sporadic cases, liver biopsy was performed due to space-occupying lesions in the liver (Voet et al. 1983; Garfinkel et al. 1985; Thiruvengadam et al. 1990). Other reported histologic findings of the liver in cases with multiple myeloma include amyloidosis (Kaye and Bayrd 1961), myeloid metaplasia (Ujodi and Pemmaraju 1973; Ujodi and Krohn 1977) and extrahepatic cholestasis (Bark 1967; Matuchansky et al. 1979).

Of patients with hepatic infiltration by plasma cells, 70\% had hepatomegaly and 50\% to 70\% showed mild elevation of serum transaminases (Thomas et al. 1973; Perez-Soler et al. 1985). However, plasma cell infiltration of the liver was also found without clinical or biological signs of the liver involvement (Thomas et al. 1973; Perez-Soler et al. 1985). Clinical signs of
the liver involvement in multiple myeloma are known to be hepatomegalgy, splenomegalgy, ascites and jaundice. The hepatomegaly, usually defined as palpable liver more than 4 cm to 6 cm below the costal margin, has been documented in 13% to 63% (Thomas et al. 1973; Kyle 1975; Kapadia 1980; Perez-Soler et al. 1985), hepatosplenomegaly in about 9% to 22% and splenomegaly in 25% of the cases (Adams et al. 1969; Thomas et al. 1973). The splenomegaly usually coexisted with the hepatomegaly (Thomas et al. 1973). The jaundice and ascites were documented in 14% and 14%, respectively (Bark 1967; Thomas et al. 1973). A higher incidence of hepatomegaly may occur in patients with POEMS syndrome i.e., myeloma, polyneuropathy, organomegaly, endocrinopathy and skin changes (Bardwick et al. 1980). This case does not present any other associated findings with this syndrome. In patients with hepatomegaly, extensive plasma cell infiltration of the liver was confirmed in 46% to 70% by autopsy studies (Thomas et al. 1973; Kapadia 1980) and elevation of serum transaminases were observed in 64% (Perez-Soler et al. 1985). However, bilirubin level was not elevated in most of the cases (Perez-Soler et al. 1985).

Abnormal liver function is also known to be common in patients with multiple myeloma. Increased retention of bromosulphophthalein, hypoprothrombinemia and hypoalbuminemia are the most frequent abnormalities, each found in 39% to 88%, 63%, and 52% to 69% of the patients, respectively (Thomas et al. 1973; Kyle 1975). Prothrombin time prolongation may not necessarily reflect the presence of decompensated liver disease in myeloma since prolonged prothrombin time may be a result of interactions between the abnormal M-protein and prothrombin (Turino 1968). Hypoalbuminemia as an index of liver function is mitigated because there was a profound renal loss of protein in myeloma patients and also there was no correlation between serum albumin level and hepatic histologic abnormalities (Thomas et al. 1973). A review study showed that elevation of serum transaminases such as aspartate aminotransferase (SGOT) and alanine aminotransferase (SGPT) were mild; SGOT less than 140 units/dl was found in 57% and SGPT less than 100 units/dl in 62%. Serum alkaline phosphatase was reported to be elevated in 25% to 85% of the cases with extensive plasma cell infiltration of the liver (Thomas et al. 1973; Kyle 1975; Perez-Soler et al. 1985) and is suggested by one report to be the only test of liver function that correlates well with the presence of plasma cell infiltration (Thomas et al. 1973). But in this case, the serum alkaline phosphatase was normal. The relation between the types of immunoglobulins and extramedullary manifestation is uncertain (Marsch and Gross 1978). Also, it is accepted that there is no correlation between the immunoglobulin class with alteration of the liver function (Perez-soler et al. 1985). One review study showed that radionuclide liver scan showed uneven distribution of the radioactivity without cold areas in all of the four patients with hepatic infiltration (Perez-Soler et al. 1985).

According to the above studies, in the absence of a previous chronic liver disease, plasma cell infiltration of the liver should be suspected in patients with multiple myeloma who have hepatomegaly with or without signs of portal hypertension or mild elevation of liver transaminases. Plasma cell infiltration of the liver is not always a terminal event but may be already present at the time of diagnosis (Thomas et al. 1973; Perez-Soler et al. 1985). The impact of plasma cell infiltration of the liver at diagnosis on the response to the therapy and the prognosis of the disease cannot be ascertained yet because signs of liver dysfunction are not part of the classical clinical picture of multiple myeloma. Therefore invasive procedures such as liver biopsy were undertaken rarely, and the prospective study was not possible. One report said that the chemotherapy did not seem to reduce the incidence of myelomatous involvement of the liver significantly because the frequency of abnormal liver function tests was similar before and after chemotherapy for multiple myeloma (Thomas et al. 1973). However, there were some pitfalls because they didn’t perform liver biopsy after chemotherapy.

For this case of an already known hepatitis B viral carrier, the nonspecific general symptoms, hepatomegaly, and liver function abnormalities suggested chronically progressed liver disease from a healthy carrier. But the monoclonal β-globulin peak on the serum protein electrophoresis is not only compatible with such liver disease, but also with the usual electrophoretic abnormalities observed in multiple myeloma.
Although peritoneoscopic liver biopsy gave the clue to the diagnosis, it was confirmed later by bone marrow study and the serum immunoelectrophoresis. In the context of these clinical findings, this is an unusual pattern of presentation of multiple myeloma, and as we know, this is the first report that the peritoneoscopy with liver biopsy was performed in a patient with multiple myeloma. Because the information about the clinical and prognostic implication of liver involvement in multiple myeloma is insufficient yet, some prospective study for the relation between liver involvement and therapeutic response should be considered.

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