Multiple Myeloma Presenting with Hepatic Involvement

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ABSTRACT:
Liver involvement as space occupying lesions in multiple myeloma is very rare. Most common clinical presentation with hepatic involvement is either with primary amyloidosis or as cholestatic jaundice. In literature only few cases are reported. Clonal selection after the thalidomide treatment as one of the possibility has been hypothesized.

INTRODUCTION:
Extramedullary plasmacytoma (EP) as discrete solitary lesions at autopsy is seen in two-third of patients of multiple myeloma (MM)\(^1\). In clinical practice its incidence is less than 5%. EP is frequently seen in upper respiratory tract, lymph nodes, spleen, subcutaneous tissue and mediastinum, and less commonly in liver, testes and thyroid\(^2,3\). MM with hepatic involvement commonly presents as either primary amyloidosis or cholestatic jaundice. Also MM presenting as hepatic space occupying lesion (SOL), particularly as hyper-vascular SOL similarly as HCC (hepatocellular carcinoma) is a rare presentation. Its etiopathogenesis is still unclear but it may be related to neoangiogenesis,\(^4,6\) Clonal selection of plasma cells without CD56 adhesion molecule after the thalidomide treatment or the chemotherapy has been suggested as one of the possibility. We report two patients of MM with hepatic involvement.

CASE-1 A 60 year old male, was diagnosed to have MM, stage III-B. After monthly pulses of oral cyclophosphamide and prednisolone for a year, he achieved a complete remission and was on regular follow-up. After 1 year he had disease recurrence with increased serum LDH, positive M-spike on serum electrophoresis and absent plasma cells in peripheral blood smear. He was then treated with monthly cycles of Melphalan, Thalidomide and Dexamethasone (MDT). Two months after commencement of MDT he presented with jaundice, progressive weakness, anorexia and fatigue. On examination he had firm hepatomegaly with hard nodules, hepatic bruit and splenomegaly. Peripheral signs of the hepatic failure in form of spider naevi and palmer erythema were present. There was no previous history of jaundice, alcoholism or chronic liver disease. Ultrasonography revealed hyperechoic multiple hepatic SOLs. Biochemical investigations revealed serum bilirubin 4.2mg/dl (2.8 mg/dl direct), SGOT 210 u/l, SGPT 56 u/l, alkaline phosphatase 317 u/l, total proteins 4.9 g/dl, albumin 2.9 gm/dl, PT-INR 2.05, serum creatinine 1.7 mg/dl and blood urea 47mg/dl. HbsAg and anti-HCV were non reactive. FNAC from liver SOL was performed which revealed sheets of plasma cells suggestive of multiple myeloma. Despite adequate supportive care patient had hepatic encephalopathy and expired.

CASE-2 A 52 year old male presented with bone pains and backache was diagnosed to have multiple myeloma stage III-B. He was commenced on Melphalan (10mg/day) and Prednisolone (80mg/day). On the third day of treatment he reported to this centre. Investigations: bone marrow aspiration 90% plasma cells, positive M-spike on serum electrophoresis, raised \(\beta_2\)-microglobulin (4872 μg/l), LDH- 885 U/lt., S. Ca++ 1.11mmol/Lt and
monoclonal IgG, kappa chains on serum immunofixation. Total serum proteins 11.2 g/dl with serum albumin 3 g/dl SGOT 32 u/l, SGPT 36 u/l, alkaline phosphatase 152 u/l and total bilirubin 0.8mg/dl. Blood counts were within normal limits. MRI of whole spine revealed partial collapse of D11 vertebrae. It also revealed multiple liver lesions. CECT scan of whole abdomen showed two hypodense SOLs in right lobe of liver (Fig. 1), the larger one measuring 2.1 x 1.8 cm, which became isodense on contrast scan (Fig. 2). CT scan also revealed bilateral adrenal mass. FNAC from liver lesion showed sheets of plasma cells (Fig. 3) FNAC from adrenal mass was inconclusive. He was planned with monthly cycles of vincristine, adriamycin and dexamethasone (VAD). After one month of commencement of VAD, he was re-evaluated with USG abdomen which showed multiple hypoechoic lesions with internal septation in both lobes of liver. CT scan abdomen revealed bilateral multiple hypodense liver lesions and increase in size of adrenal masses. In view of disease progression, his chemotherapy plan was changed to three weekly bortezomib, adriamycin and dexamethasone (PAD) chemotherapy. After receiving two cycles of PAD, patient developed a single subcutaneous nodule on his scalp. FNAC from scalp nodule was positive for plasma cells. This patient disease has progressed even after two standard lines of treatment.

DISCUSSION

Most common form of liver involvement in MM is either the primary amyloidosis or the cholestatic jaundice. Only few cases have been reported of liver SOL in MM. Perez-solar et al reviewed the liver histology of 21 patients with multiple myeloma and reported the diffuse infiltration by plasma cells in 10 (47%), myeloid metaplasia in 4 (19%), amyloidosis in 2 (9%), toxic hepatitis in 2 (9%) and extrahepatic cholestasis secondary to peripancreatic tissue in 1(4.5%). Seven patients had hepatomegaly, 5 had mild elevation of liver enzymes, and 2 had portal hypertension. Jaundice was observed only in patients with hepatitis or extrahepatic cholestasis. In a study from Mayo clinic (869 patients of MM) liver was palpable in 21% of the cases, with >5cm below right sub-costal margin in only 5% cases, and 25% cases had elevation in alkaline phosphatase. In our study case no. 1 had hepatosplenomegaly, hepatic bruit and hyperdense lesions and case no. 2 had
isodense lesions on contrast CT scan suggestive of hypervascularity, mimicking hepatocellular carcinoma.10

Extradudillary involvement is usually seen in patients with advanced stage disease or in patients with relapse after allogeneic transplantation.11 The mechanism of hepatic involvement is unclear but it may be related to disease progression due to neoangiogenesis via vascular endothelial growth factor through its paracrine or an autocrine mechanism.4-6 In most cases of MM neoplastic cells strongly express CD56 at the time of primary diagnosis. Although in some cases it may be weakly expressed or absent12. In a case report of hepatic involvement in MM after thalidomide treatment, expression of CD56 was found to be positive on bone marrow but was negative in liver infiltration. This suggests that loss of adhesion molecules such as CD56 could correlate with extradudillary progression during thalidomide, probably due to a clone selection induced by the treatment.13

Etiopathogenesis of hepatic involvement in both our patients is unclear. In our study, case no. 1 had developed liver SOL after treatment with thalidomide, so possibility of clonal expansion with loss of the adhesion molecule such as CD56 is possible. In both our patients it is also possible that disease progression at extradudillary places may be due to neoangiogenesis.4,6 Prognosis of MM with hepatic involvement is worse though experience is limited.

The detection of SOL in liver, in both our patients was incidental and was confirmed by cytology. It is possible that good clinical and biochemical acumen might help in identifying more cases and at an early stage. Extradudillary manifestations though less common, should be looked for and MM should be kept as an extensive differential diagnosis of SOL of liver.

REFERENCES: