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A Case Report of Rare Presentation of Multiple Myeloma: A Case of Hepatic Amyloidosis

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Dr. Gautam M*[1], Dr. N N Anand[1], Dr. KC Kishore[1], Dr. Manoj Ravilla[1]

[1]Department of General Medicine, Sree Balaji Medical College and Hospital, Chrompet, Chennai, Tamil Nadu, India.

*** Corresponding Author: Dr. Gautam M**

Email ID: gautamsemail007@gmail.com

Keywords

Amyloidosis, Hepatic failure , Multiple myeloma

Abstract

It is uncommon for multiple myeloma (MM) to have liver involvement in a clinically documented occurrence. Approximately 15 % of MM patients have been observed to have amyloidosis, which is characterised as the clonal light-chain fibrils deposition in tissue. We documented a unique case of MM with a primary biliary system involvement and fulminant liver failure due to amyloidosis.Ascites, hepatosplenomegaly, anaemia, and hyperbilirubinemia were the patient's initial symptoms. , Thalidomide, dexamethasone , Bortezomib were used in the conventional chemotherapy regimen, and this produced a striking response. Light chain amyloidosis-related liver damage may be the first blatant manifestation of MM. When patients exhibit vague symptoms and abnormal liver function tests, infiltrative illnesses including MM and amyloidosis should be taken into account. The prognosis of patients can be directly impacted by an accurate and prompt diagnosis. There is ongoing discussion over the best strategy for handling typical situations comparable to these.

1. Introduction:

A malignant growth of plasma cells that create monoclonal immunoglobulin is what is known as multiple myeloma (MM). Up to 45% of MM patients have been observed to have pathologic liver involvement [1,2]. Massive liver invasion by plasma cells and concurrent liver failure are uncommon, nevertheless [3,4]. Amyloidosis has been identified in up to 10-15% of MM patients and is characterised as the clonal light-chain fibrils deposition in tissue [5].Rarely have certain accounts of MM patients been published who had hepatic amyloidosis infiltration as their primary clinical manifestation. [8-10]

Most documented uncommon MM manifestations have been found in autopsy series, therefore the diagnosis, clinical characteristics, treatments, and patient prognosis are still unclear[11]. Here, we documented a unique instance of a patient with multiple myeloma (MM) who first presented with hepatobiliary system involvement caused by amyloidosis and who experienced a significant response to routine chemotherapy.

2. Case Presentation:

An 61-year-old man with a history of 3-week malaise and weakness was hospitalised to the general medicine department of SBMCH, a tertiary care hospital in Chrompet, Tamil Nadu, India. Physical examination showed unnoticeable asymmetric edema in the left leg and bruises in the posterior of the left flank and thigh. He denied having ever experienced trauma or used any particular medications.

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Deep vein thrombosis was ruled out by venous-arterial colour Doppler sonography of the distal extremity, which was ordered for additional investigation. Ultrasonography examination revealed normal kidneys, bladders, and ureters but minor liver and splenic enlargement (liver diameter: 21 cm, spleen diameter:180 x59 mm).

Additionally, soft tissue ultrasonography supported the presence of a subcutaneous-intramuscular hematoma with dimensions of 80x30x40 mm and a depth of 3 cm in the rear of the proximal left thigh. The muscles in gluteal region and adductor group of muscles in left side of the pelvis were home to a sizable sub-acute hematoma, which was also detected on the contrast-free MRI.

As shown in table A, there were aberrant laboratory results at the initial evaluation for the hematologic indices and liver function indicators. Other information might be disregarded.

Table 1:

PARAMETERS	VALUES
White blood cell (WBC)	29000 cell/micL
Hemoglobin (Hg)	9.6 g/dl
Platelet (Plt)	327000 cell/micL
Aspartate transaminase (AST)	54 IU/L
Alanine transaminase (ALT)	27IU/L
Alkaline phosphatase (ALP)	1521 IU/L
Gamma-glutamyltransferase (GGT):	1556 IU/L
Bilirubin total	5.9 mg/dL
Bilirubin direct	3.0 mg/dL
Partial thromboplastin time (PTT)	31 second
International normalized ratio (INR)	1.8
Ferritin	605 ng/mL

The patient had no known prospective factors for liver disease, according to the detailed history. The modifications to the laboratory tests supported hepatic cholestasis. The gastroenterologist requested magnetic resonance cholangiopancreatography (MRCP) for additional evaluation in order to rule out any blockage, stricture, or cancer. The results of the MRCP excluded any unique biliary drainage abnormalities.

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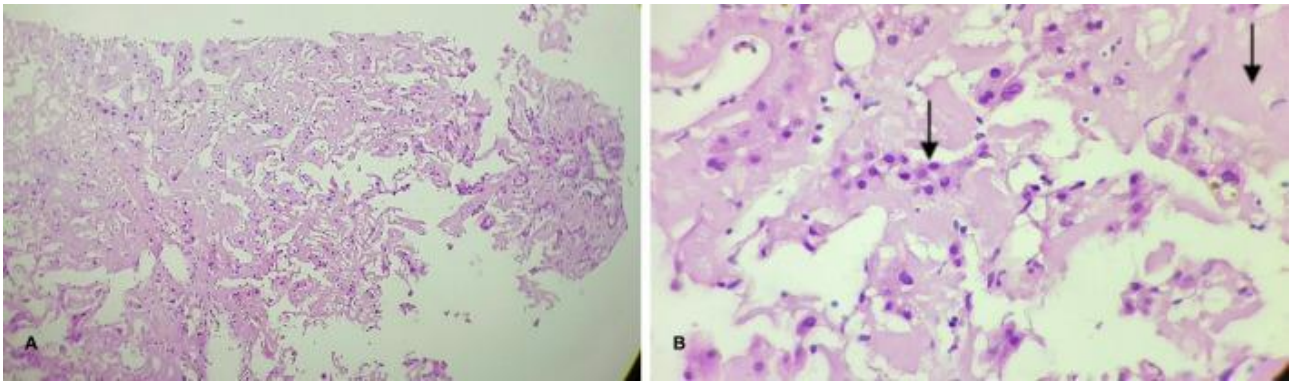
Therefore, tests for viral etiologies of hepatitis (Hep A, B, and C), HIV antibody, 2-mercaptoethanol (ME), coombs test both indirect and direct , antibody tests against leishmania , Epstein-Bar virus (EBV) and cytomegalovirus (CMV) were performed. The results of all of these tests were negative. There were many ulcers in the early and distal part of duodenum which had a clean base, ulcer in the antrum of the stomach was present and it was healed , and no dilated varices present in esophageal region, according to the endoscopic findings.

Hemotoxylin and Eosin stained biopsy was taken from the liver to determine the primary problem. The diagnosis of amyloidosis was confirmed after athe histopathologic report revealed the buildup of amyloid protein, as seen in figure A1

Figure A1:



Using a liver sample, the staining done using eosin and hematoxylin can show where amyloid protein is being deposited. The hepatocyte plates have atrophy (left arrow) and there is significant amyloid accumulation (right sided arrow mark) along the sinusoids.

The BCR-ABL P210-P190 fusion gene was also tested using RT-PCR, however the results were not positive. These were the findings from serum protein electrophoresis: albumin 48.1%, the different globulin values namely alpha1 being 7.5%, alpha 2 7.8%, beta 19.7%, gamma 18.8%, with a total of 7.3 g/dL, and ratio between albumin and globulin of 0.98.

The patients' clinical state was deteriorating, and liver enzyme levels were trending upward. The bilirubin levels were 25 mg/dl for the total and 20 mg/dl for the direct. Amyloid deposition in the liver and cholestasis caused by non obstructive etiologies were the causes of the patient's deteriorating clinical characteristics at the gastroenterologist's most recent assessment. For the escalating symptoms of anaemia, severe ascites, and high distal extremities edema, he once more recommended seeing an oncologist.

The oncologist then carried out two diagnostic procedures, an ascites paracentesis and a biopsy and aspiration from the bone marrow. Paracentesis produced transudative fluid devoid of any cancerous cells. The other finding in the bone marrow biopsy revealed monoclonality and more than 50 percent of infiltrating plasma cells. On the BMB specimen, immunophenotyping identified a population at the monocytic gate that displayed the cluster of differentiation markers 38, 138, 56, and 45, accounting for about 7% of all cells with the presence of nucleus while being devoid of the CD19 marker.

Results from serum protein electrophoresis, including total protein at 5.6, albumin to globulin ratio at 0.7, albumin at 41.8%, alpha at 7.6%, alpha 2 at 10.6%, beta at 19.8%, and gamma at 22.5%,

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were likewise consistent with tumour of plamsa cells in the bone marrow. Immunofixation testing of the serum and urine revealed the presence of monoclonal light chain especially kappa bands. Additionally, the MM diagnosis was verified. The patient, however, showed no symptoms of hypercalcemia, increased creatinine, or bone discomfort or lesions.

Immunohistochemistry analysis of the liver biopsy sample was performed, and Amyloidosis of kappa light chain variety was also confirmed. The oncologist made the quick start of the usual chemotherapy regimen for the treatment of high risk MM due to the patient's critical condition.

The patient started on a chemotherapy course that included bortezomib thalidomide and dexamethasone. Bortezomib's recommended dosage was 1 mg/m2 intravenously given on day one, four , eight , eleven of treatment, followed by a 20-day rest period. The administration of this schedule lasted for 8 cycles. Dexamethasone was prescribed as an initiation treatment of 40 mg daily once on days 1 through 4, 9–12, and 17–20 in conjunction with bortezomib. Thalidomide was prescribed at a dose of 100 mg per day for 8 (21-day) cycles. Once every week on days 1, 8, and 15 of every 28 days, this was modified to 40 mg.

The patient reacted to the medication after two months, and all hepatic symptoms, including ascites and icterus (with total bilirubin level of 1.0 mg/dl and direct bilirubin levels of 0.3 mg/dl, respectively), vanished. With gamma globulin at 1.7 g/dL, total protein at 6.3 g/dL, and the ratio of albumin to globulin at 0.79, the assessment of M protein in the serum and urine fell within an acceptable range. By using an immunofixation technique, in the urine and serum it was found that the light chain was decreased to undetectable levels. As a result, complete remission was shown by just under 5% plasma cell characteristic in BMA/BMB. Thalidomide, 100 mg daily, was given to preserve the medical response, and after 30 months of follow-up, the cancer continued to be under control. Unrelated, the patient agreed to the distribution of the specific information by signing a consent form.

3. Discussion:

The most common histological patterns for liver involvement in MM are Disease involving deposition of light chains and amyloid , extramedullary tumour of plasma cells , participation of sinusoids or disease pattern infiltrating diffusely . In our case, hepatic involvement most likely resulted from diffuse sinusoidal flooding, which has a tendency to harm the liver parenchyma.

Primary amyloidosis and multiple myeloma are commonly detected at the same time. Less frequently, though, myeloma appears more than 6 months after an amyloidosis diagnosis (delayed progression). 47 patients (1.1%) out of a total of 4319 myeloma patients who attended the Mayo between 1990 and 2008 also had a primary amyloidosis diagnosis that came at least six months after the myeloMayo between Although liver failure was our patient's primary symptom, the BMA/BMB assessment completed criteria that was required to diagnose MM, and the discovery of a plasmacytoma in the bone marrow was followed by high gamma globulin levels in tests involving electrophoresis of serum at the time of amyloidosis identification.

It has been established that primary amyloidosis presenting in a patient with multiple myeloma has a worse prognosis than MM alone. 8,9,13,14 et al described a lady of 46 years of age Caucasian lady who was diagnosed with concurrent MM with involvement of bone marrow and amyloid accumulation in the liver biopsy. In a case comparable to this, Yamamoto et al. described a 79-year-old Japanese woman who was diagnosed with multiple myeloma of the IgG-K subtype and severe hepatic failure brought on by kappa-AL amyloidosis. Due to severe liver damage in both cases, the patients passed quite quickly 14. The consequences present in the presentation were controlled by modern chemotherapy medications as compared to similar situations in the past.

Although our patient experienced severe jaundice symptoms and liver enzyme levels that were substantially raised, suggesting a dismal prognosis for the future, he exhibited an extreme response to the chemotherapy regimen and showed no signs of

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recurrence or liver complications after 30 months of follow-up.13

The malfunction of the hepatic and biliary systems in our case was caused by the buildup of precursors of amyloid in liver cells. Additionally, a more accurate diagnostic examination should be carried out for MM patients who exhibit non-routine symptoms such CRAB (high levels of calcium, kidney failure, anaemia, or bone deficiency).12

Additionally, it can be difficult to treat MM patients who have hepatic impairment. Most chemotherapy drugs would require dose modification. For new anti-cancer drugs like bortezomib, decrease in dosage has been advised. 5 As a result, we increased the bortezomib dosage to 1 mg/m2.

Bortezomib, thalidomide, and steroids like dexamethasone were used as part of the conventional chemotherapy regimen, and after just two months of treatment, the principal signs and symptoms, including such ascitic fluid collection and bilirubinemia, had completely vanished. The case history is distinctive and vulnerability-reporting due to the predominate response to the conventional chemotherapy regimen as well as the atypical primordial clinical appearance.

4. Conclusion:

The earliest severe manifestation of MM may be liver damage without any traditional clinical indication caused by light chain amyloidosis. The diagnosis of a patient who is this intricate needs to be given more consideration. When patients report with vague symptoms and abnormal liver function tests, it is vital to take infiltrative illnesses like amyloid deposition and multiple myeloma into consideration. The outcome of patients can be directly impacted by an accurate and prompt diagnosis. There is still room for discussion regarding the best strategy for managing typical cases that are comparable.

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ETHICAL CONSENT :

Informed consent was taken from the patient regarding this study .

FUNDING :

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CONFLICT OF INTEREST :

The authors declare that there was no conflict of interest.

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