Medical and Research Publications
International Open Access

Case Report **Journal of MAR Oncology (Volume 4 Issue 4)**

Intrahepatic Cholestasis Due to Infiltration by Monoclonal Plasma Cells in Multiple Myeloma

Yazan Ghanameh *[1], Omar Al-Rawi [1], Aseel Al-Omari [2], Ahmad Ghanameh [3]

1. Department of Internal Medicine, Istishari Hospital, Amman, Jordan.

2. Department of Pathology and Laboratory Medicine, Istishari Hospital, Amman, Jordan.

3. University of Jordan, Faculty of Medicine, Amman, Jordan.

Corresponding Author: Yazan Ghanameh, Department of Internal Medicine, Istishari Hospital, Amman, Jordan.

Received Date: August 29, 2022

Published Date: September 05, 2022

Abstract

Clinical manifestations of liver involvement in multiple myeloma ***(****MM****)*** *are uncommon. Rare cases of MM present as intrahepatic cholestasis due to plasma cell infiltration of the liver.*

We report a case of an alcoholic 49-year-old male patient with MM who presented with painless jaundice, altered liver function test, and hepatosplenomegaly resembling a picture of alcoholic cholestatic hepatitis.

Full liver laboratory work up including viral and autoimmune studies had been done. Myeloma parameters demonstrated an immunoglobulin G kappa monoclonal protein with kappa light-chain Bence-Jones proteinuria. Bone marrow was hypercellular with 90% plasmacytosis. A liver biopsy revealed a diffuse portal and sinusoidal infiltration of monoclonal plasma cells with kappa light chain restriction along with intrahepatic cholestasis free of solid features of alcoholic hepatitis. In this report, we review the literature of intrahepatic cholestasis in MM.

Keywords: *Multiple myeloma, Intrahepatic cholestasis, Cholestatic hepatitis, Hepatic sinusoidal plasma cell infiltration.*

Introduction

Multiple myeloma is a malignant proliferation of the plasma cells that commonly involves the bone marrow. Excessive amount of production of these plasma cells can eventually lead to end organ failure. Most common clinical presentations include renal impairment, hypercalcemia, anemia and bone pain together with lytic lesions. **(**1,2**)**. Extraosseous invasion is not uncommon. Out of many organs as the spleen, kidneys or lymph nodes, hepatic involvement occurs in 25 to 40% of cases. **(**3**)**. Hepatomegaly can be found in 25 to 45 % of myeloma patients and is associated with diffuse sinusoidal infiltration in 32% of cases **(**4,5,6**)**. Intrahepatic cholestasis, hepatic amyloidosis or acute fulminant hepatitis at presentation are considered conspicuously rare cases. **(**3,7,8**)**.

Case Presentation

The patient is a 49-year-old male known case of thyrotoxicosis with a history of secondary atrial fibrillation, presented to hematology and oncology department on July 2022 complaining of generalized fatigue, back pain and abdominal pain as well for one week. Patient was previously running on Carbimazole and Beta Blockers to control his symptoms in which both were stopped two months prior to his admission. He had been smoking and drinking alcohol for the past three years. He used to drink half litre of whiskey daily. Liver function test was completely normal without any alterations as noted on his routinely check-ups records.

Upon examination, the patient was fully conscious, he looked pale, dehydrated, and in pain. Conjunctiva were yellow and hepatosplenomegaly was noted on palpation. No palpable lymph nodes detected.

His initial laboratory work up showed pancytopenia, high serum calcium 14.2 mg/dl **(**normal 8.6-10 mg/dl**)** and raised creatinine level 2.61 mg/dl **(**normal 0.7-1.2 mg/dl**)**. Inflammatory markers were also elevated. Altered liver function test was noted, alkaline phosphatase 205 U/L **(**normal 40-130 U/L**)**, Gamma Glutamyl Transferase 72 U/L **(**normal 11-44 U/L**)** raised total bilirubin 4.43 mg/dl **(**normal 0-1**)** and direct bilirubin 3.31 mg/dl **(**normal 0-0.3**)**. Liver transaminases were normal.

Serum electrophoresis showed **(**M band in gamma region**)**.

Immunofixation showed monoclonal gammopathy of the IgG type with Kappa light chain levels of 339 mg/L **(**normal 2.37-20.73 mg/L**)**. Bone marrow aspiration and biopsy was done for disease confirmation and revealed 90% involvement of the bone marrow with plasma cells.

He was admitted for treatment of hypercalcemia and acute kidney injury, and chemotherapy was considered after stabilizing the patient. During hospitalization, the patient was noted to become progressively increasingly jaundiced. Repeated investigations showed high total bilirubin 7.08 mg/dl **(**normal 0-1 mg/dl**)** and direct bilirubin 6.35 mg/dl **(**normal 0-0.3 mg/dl**)**. ALP 172 U/L **(**normal 40-130 U/L**)**. ALT 50 U/L **(**normal 0-40 U/L**)**, AST 82 U/L **(**normal 0-37 U/L**)**.

Abdominal ultrasound declared hepatosplenomegaly, patent portal system and unremarkable biliary system and CBD. **(**figure2,3**)**

Due to his unexplained liver condition, we decided to proceed to liver biopsy which was done after platelets correction.

Histopathology report disclosed diffuse involvement of portal triads and hepatic sinusoids by monoclonal plasma cells with Kappa light chain restriction, consistent with involvement of the liver by multiple myeloma along with moderate to marked intrahepatic cholestasis, free of features of alcoholic or autoimmune hepatitis. **(**Figure 1**)**

The Patient was started on Methylprednisolone in addition to other supportive measures **(**IVF, blood products, antibiotics**)**. 8 days later, there was significant reduction in bilirubin serum levels and liver enzymes.

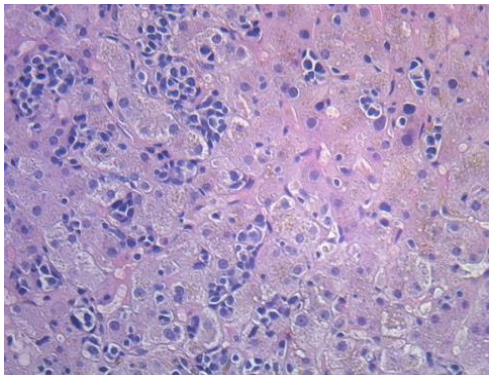

Figure 1: Liver parenchyma showing extensive sinusoidal neoplastic plasma cell infiltration and cholestasis **(**hematoxylin and eisin stain, 400x**)**.

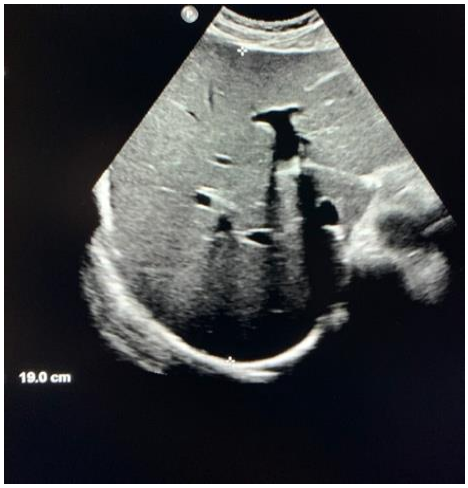

Figure 2: Enlarged liver measuring about 19cm in craniocaudal dimension, with congested echo texture, with no evidence of focal masses.

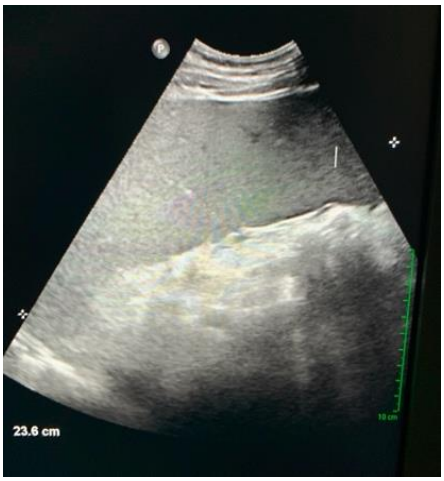

Figure 3: Hugely enlarged spleen measuring about 24cm in length.

Discussion

Multiple myeloma is a neoplasm of monoclonal plasma cells that involves the bone and bone marrow. Extramedullary infiltration usually occurs in tissues abundant with reticuloendothelial components such as liver, spleen and lymph nodes **(**7**)**. Infiltration of the liver sinusoids with plasma cell account for 32% of cases **(**4,7**)**. Altered liver enzymes are common on presentation, yet jaundice could happen with rapid surprising frequency **(**8**)**.

Our study shows the correlation between multiple myeloma and liver infiltration, with presenting cholestasis. In our knowledge, few cases have been reported in literature describing acute cholestasis in multiple myeloma away from acute cholestatic hepatitis which presents with high transaminases. **(**9,10,11**)**.

In our case, the explanation of the acute cholestasis together with altered liver enzymes was quite challenging, taking into account the medical history of the excessive alcohol intake, the disease its self and its treatment.

The combination of three drugs including targeted therapy, Immunotherapy and a steroid **(**Bortezomib, Lenalidomide, Dexamethasone**)** based on the National Comprehensive Cancer Center Network **(**NCCN**)** guidelines for multiple myeloma treatment was initially considered, however the patient clinical picture, hospitalization course, and according to a cited study describing the association between Lenalidomide

and it's conceivable intrahepatic cholestasis, Lenalidomide was excluded from the management plan and replaced by cyclophosphamide, to prevent any possible acute events (12,13,14).

Here it's worth mentioning that the patient showed good response after administration of prednisolone. Same results were documented in other similar study (3).

Conclusion

Infiltration of the liver by monoclonal plasma cells can happen in multiple myeloma, but clinical presentation with acute cholestasis is rare. Such patients present with hyperbilirubinemia and altered liver enzymes. Individuals showed good response to steroids which is something to consider in such cases.

References

1. Perez-Soler, R., Esteban, R., Allende, E., Saloma, C. T., Julia, A., & Guardia, J. (1985). Liver involvement in multiple myeloma. American journal of hematology, 20(1), 25-29.

2. Kiss, S., Gede, N., Soós, A., Hegyi, P., Nagy, B., Imrei, M., ... & Alizadeh, H. (2021). Efficacy of first-line treatment options in transplant-ineligible multiple myeloma: A network meta-analysis. Critical Reviews in Oncology/Hematology, 168, 103504.

3. Barth, C., Bosse, A., & Andus, T. (2005). Severe acute cholestatic hepatitis by infiltration of monoclonal plasma cells in multiple myeloma. Zeitschrift für Gastroenterologie, 43(10), 1129-1132.

4. Walz-Mattmüller, R., Horny, H. P., Ruck, P., & Kaiserling, E. (1998). Incidence and pattern of liver involvement in haematological malignancies. Pathology-Research and Practice, 194(11), 781-789.

5. Bhandari, M. S., Mazumder, A., & Vesole, D. H. (2007). Liver involvement in multiple myeloma. Clinical Lymphoma and Myeloma, 7(8), 538-540.

6. Thomas, F. B., Clausen, K. P., & Greenberger, N. J. (1973). Liver disease in multiple myeloma. Archives of Internal Medicine, 132(2), 195-202.

7. Yamamoto, T., Maeda, N., & Kawasaki, H. (1995). Hepatic failure in a case of multiple myeloma-associated amyloidosis (k-AL). Journal of gastroenterology, 30(3), 393-397.

8. Ales, N. C., Daniels, J. T., Frizell, E. R., Koff, J. M., Kaplan, K. J., & Wortmann, G. W. (2001). Multiple myeloma-associated amyloidosis manifesting as fulminant hepatic failure. SOUTHERN MEDICAL JOURNAL-BIRMINGHAM ALABAMA-, 94(10), 1036-1038.

9. Vella, F. S., Simone, B., Giannelli, G., Pesolo, M., Ingravallo, G., Gentile, A., & Antonaci, S. (2003). Case of multiple myeloma mimicking an infectious disease with fever, intrahepatic cholestasis, renal failure, and pulmonary insufficiency. American journal of hematology, 72(1), 38-42.

10. Mena-Durán, A., Vicente, E. M., Llorens, G. P., & Cervera, J. S. (2012). Liver failure caused by light chain deposition disease associated with multiple myeloma. Internal Medicine, 51(7), 773-776.

11. Taarit, C., Ajlani, H., Fareh, F., Zermani, R., Jilani, S. B., Gharbi, W., ... & Khedher, A. (2007). Multiple myeloma of the liver presenting as non-obstructive jaundice. Annals of Hematology, 86(7), 529-530.

12. Jena, R. K., Swain, T. R., Kansurkar, S. S., & Swain, M. (2012). Lenalidomide induced intrahepatic cholestasis in newly diagnosed patients of multiple myeloma. European journal of clinical pharmacology, 68(5), 881-884.

13. Nojkov, B., Signori, C., Konda, A., & Fontana, R. J. (2012). Lenalidomide-associated hepatotoxicity–a case report and literature review. Anticancer research, 32(9), 4117-4119.

14. Callander, N. S., Baljevic, M., Adekola, K., Anderson, L. D., Campagnaro, E., Castillo, J. J., ... & Kumar, S. K. (2022). NCCN Guidelines® Insights: Multiple Myeloma, Version 3.2022: Featured Updates to the NCCN Guidelines. Journal of the National Comprehensive Cancer Network, 20(1), 8-19., https://www.nccn.org/patients/guidelines/content/PDF/myeloma-patient.pdf