# An Unusual Case of Chronic Hepatitis E in Haematological Malignancy

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**Abstract**

Hepatitis E is an enterically transmitted and typically self-limited infection, that is caused by the hepatitis E virus. Hepatitis E viral infection has traditionally been considered an acute. Chronic hepatitis E is rare and occurs mainly in immunosuppressed individuals such as transplant recipients, HIV patients with low CD4 count and in patients with hematological malignancies receiving chemotherapy.

## Introduction

Hepatitis E is an enterically transmitted and typically self-limited infection, that is caused by the hepatitis E virus.[1,2] It is spread by faecally contaminated water within endemic areas or through the consumption of uncooked or undercooked meat.[3,4,5] Hepatitis E viral infection has traditionally been considered an acute. However, over the past decade, zoonotic transmission and progression to chronicity in human patients has been identified, leading to progressive liver injury and cirrhosis. Chronic hepatitis E occurs mainly in immunosuppressed individuals such as transplant recipients, human immunodeficiency virus (HIV) patients with low CD4 count and in patients with hematological malignancies receiving chemotherapy.[6] Chronic hepatitis E has almost exclusively been reported with genotype 3.[7]

We describe herein a case of Chronic Hepatitis E in Acute Lymphoblastic Leukemia.

## Case Report

A 25 year old male was detected to have Acute lymphoblastic leukemia for which he was initiated on chemotherapy for ALL as per BFM protocol from February 2014 and was planned till September 2016 which comprised of initiation, consolidation and maintenance phases. The chemotherapy regimen included Prednisolone, Vincristine, Daunorubicin, L-Asparaginase, intrathecal methotrexate and methotrexate infusion, cyclophosphamide and cytarabine. The patient developed jaundice and was found to have hepatitis E (IgM antibody against Hepatitis E virus positive) in October 2014 which was self limiting. In January-2016 he developed a second episode of jaundice with deranged liver function tests and on evaluation found to have IgM antibody against Hepatitis E virus positive. 2 months later he developed ascites. For the next few months he had fluctuating bilirubin levels(reduction and elevations). The patient was referred to us in June 2016 for jaundice, splenomegaly and ascites which were confirmed on examination with no history of haematemesis, melena or encephalopathy. There was no history of alcohol intake. A differential of drug induced liver injury versus Chronic Hepatitis E was considered.USG abdomen had gross ascites with splenomegaly. A 99m-Tc phytate liver scan was suggestive of hepatocellular dysfunction likely due to acute on chronic hepatitis. A transjugular liver biopsy was done which revealed increased portal fibrosis highlighted by reticulin, small bile duct proliferation, portal lymphocytic infiltrate, ballooning degeneration of hepatocytes with intrahepatic cholestasis and bile plugs (Figures 1 and 2).Ascitic fluid analysis revealed a high SAAG and low protein ascites. Serological tests for hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus(HCV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and varicella zoster virus were all negative. The autoimmune workup was negative. Blood samples were positive for hepatitis E virus RNA levels qualitative. Since the patient was non affording, genotype testing, HEV RNA viral load and further monitoring could not be done. Laboratory investigations (Tables 1 and 2).

## Discussion

Our patient presented with history of prolonged jaundice with ascites and splenomegaly with history of repeated Acute Hepatitis E in the setting of a haematological malignancy receiving chemotherapy. A thorough diagnostic and etiological work up was performed to rule out opportunistic infections, autoimmune hepatitis and chronic hepatitis due to Hepatitis B and C viruses. Liver biopsy confirmed the diagnosis of cirrhosis. After the HEV RNA PCR was found to be positive the patient was initiated on Ribavarin in a dose of 600 mg/day. Patient`s haemoglobin was closely monitored. After a few weeks of treatment the patient`s liver function tests normalized.

### Conclusion

In conclusion, chronic Hepatitis or cirrhosis due to HEV should be considered in cases of unexplained chronic hepatitis/cirrhosis in immunocompromised hosts since it is a treatable and reversible cause.

## References

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**Table 1: Laboratory investigations**

| | 22/10/14 | 18/1/16 | 27/5/16 | 1/6/16 | 12/6/16 |
|---|---|---|---|---|---|
| T. Bilirubin (mg/dL) | 5.4 | 6.1 | 7.3 | 12.0 | 1.2 |
| D. Bilirubin (mg/dL) | 3.2 | 3.7 | 3.8 | 8.6 | 0.8 |
| I. Bilirubin (mg/dL) | 2.2 | 2.4 | 3.5 | 3.4 | 0.4 |
| SGPT (IU/L) | 149 | 92 | 132 | 161 | 44 |
| SGOT (IU/L) | 137 | 76 | 111 | 74 | 36 |
| ALP (IU/ml) | 59 | 111 | | 127 | 98 |
| GGTP (mU/mL) | | | | 108 | 90 |
| T. Proteins (g/dL) | 6 | | | 4.5 | |
| Albumin (g/dL) | 4 | | | 2.2 | |
| Globulin (g/dL) | 2 | | | 2.3 | |
| A/G ratio | 2 | | | 0.96 | |
| PT INR | | | | 1.1 | 1.0 |
| Hb (g/dL) | | | | 12.9 | |
| TLC (/mm$^{3)}$ | | | | 3900 | |
| Platelets (/mm$^{3)}$ | | | | 1.66L | |
| Creatinine (mg/dL) | | | | 0.6 | |

**Table 2: Autoimmune workup**

| | | |
|---|---|---|
| ANA | Negative | |
| AMA | Negative | |
| ASMA | Negative | |
| Serum IgG (mg/dl) | 975 | Normal<1600 (mg/dL) |

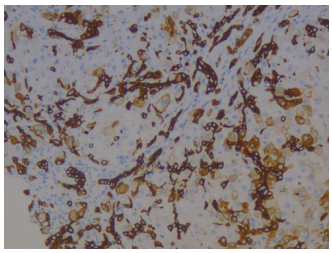

**Fig. 1: IHC marker Ck7 highlighting small bile duct proliferation**

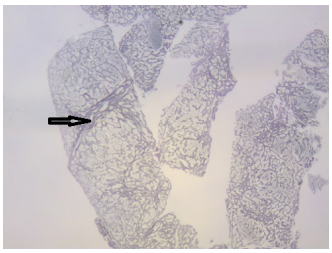

**Fig. 2: Reticulin stain. Arrow showing fibrosis**

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