

CASE REPORT

AN ASSOCIATION OF HEPATITIS VIRUS INFECTION WITH RARE HEMOPOIETIC MALIGNANCIES

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ABSTRACT: Hematopoietic malignancies have a close association with viral infections which further increases secondary to immune-suppression in the post chemotherapy phase. High prevalence of HBV in cases of leukemia and relation of HCV with ALL, NHL& AML have been reported in several case series, however association of HBV with RAEB, CML, AML are reported in very few cases. We report 5 rare cases of HBV positivity in 2 cases of AML, one of which is AML M7, 1 case of RAEB and 2 cases of Aplastic anemia.

KEYWORDS: Hematopoietic malignancies, HBV.

INTRODUCTION: Relationship between hemopoietic malignancies & HBV has been established by many workers. There is worldwide increase in prevalence of hematological malignancies in HBV patients than general population⁽¹⁾. HBV reactivation is common following chemotherapy and the risk is increased in patients with nonmalignant diseases requiring continuous immunosuppressive therapy.⁽¹⁾

High prevalence of HBV in leukemia cases and HCV with ALL, NHL& AML have been reported in several case series^(2,3). However association of HBV with RAEB, CML & AML are reported in very few case.^(4,5,6,7)

Data substantiating association of hematopoietic malignancies with viral hepatitis is limited more so with subtypes. One case of AML –M7, a rare entity, was HBsAg positive in our series.

METHOD: Present study was conducted from 2009 to 2012 in Department of Pathology, Gandhi medical college, Bhopal, Madhya Pradesh to assess the relationship of HBV with hemopoietic malignancies, out of 63 hematopoietic malignancies /pre-malignant conditions diagnosed on bone marrow examination, 5 cases were found to be HBsAg positive by ELISA.

RESULTS: Out of 5 cases, 3 were males & 2 females; 1 was a child (12 years) and 2 adult (22 and 38years) & 2 elderly(50 & 55years) respectively. All were negative for HCV. Hepatosplenomegaly was present in 2, anemia in all and leucopenia in 3 cases. Platelets counts were normal in 1, decreased in 3 and increased in 1 case. Pancytopenia was present in 3 of 5 cases. Blasts were increased in 2 cases (in the range of AML). Cytoplasmic blebbing and vacuolation, nuclear clefting and platelet budding were seen in case 4 (figure 1). Auer rods were present in case 1. (figure 2) Bone marrow examination confirmed the diagnosis of AML in 2 (one of which was AML-M7), RAEB in 1 and aplastic anemia in 2 cases. Here we have included Aplastic Anemia and RAEB because it may evolve 15% and 25 % into leukemia respectively.

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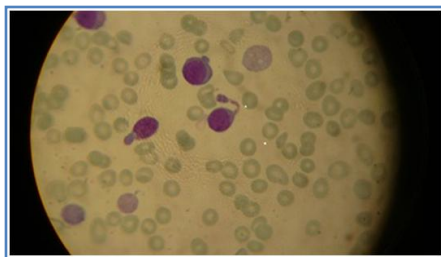


Fig. 1: Blasts showing cytoplasmic blebbing and platelet budding.

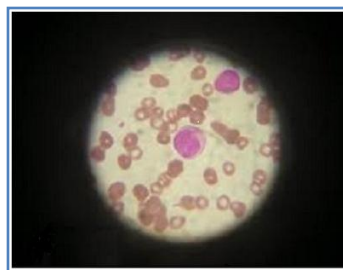


Fig.2: Blast showing auer rod

Clinico hematological profile of five HBsAg positive patients is following:

Features	Case I	Case II	Case III	Case IV	Case V
1. Age/Sex	50 yrs/M	12 Yrs/F	55 yrs/F	22Yrs/M	38yrs/M
2. Clinical features	Liver cirrhosis, Portal hypertension With ascitis	Pain abdomen, Nausea, headache	Chronic liver disease with ascites. History of jaundice 1 year back	Generalized weakness, melena	Bleeding gums, Weakness, breathlessness
3. HBsAg positive	+	+	+	+	+
4. HCV	-	-	-	-	-
4. Hepatosplenomegaly	-	+	-	-	+
5. Hb gm/dl	8.0	11.2	7.2	3.7	6
6. TLC cells/cumm	3,100	8600	2,500	4,500	1,500
7. Platelet count/cumm	50,000	1,80,000	Less than 10,000	9,00,000	20,000
8. Pancytopenia	+	-	+	-	+
9. Blasts	22	08	Nil	35	Nil
10. Morphology of blasts	-	-	-	+	-
a. Cytoplasmic Blebbing	-	-	-	+	-
b. Cytoplasmic vacuolation	-	-	-	+	-
c. Nuclear Clefing	-	-	-	+	-
d. Platelet budding	-	-	-	+	-
e. Auer rods	+	-	-	-	-
11. Bone Marrow and Final Diagnosis	Blasts 35% AML	Blasts 14% RAEB	Aplastic anemia	Blasts 55% AML M7	Aplastic anemia

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DISCUSSION: Induction of cancers by exogenous agents such as chemical, radiation and viruses have been interesting area of research.

Data of hematopoietic malignancies especially many subtypes associated with viral hepatitis is very limited.

HTLV, HCV, HBV have been assessed in relation to hemopoietic malignancies.

We have also used only one marker i.e. HBsAg to ascertain HBV infection.

Out of HBV markers like HBsAg, anti-HBsAg, anti-HBcAg, HBV, in 50 patient series, at least one marker was positive at initial diagnosis of leukemia in 68% of AML and 71% of ALL patients(4). HBsAg was positive in 12% of AML & 25 % OF ALL patients. In remission HBsAg was positive in 83% of AML and 44% of ALL patients. HBVDNA in bone marrow of AML and CML patients were found significantly increased in leukemic than normal patients⁽⁶⁾. However association of HBV with other subtypes of leukemia is uncertain.^(6,8) There is non-significant excess of HBsAg with RAEB and anti HBcAg with AML. ⁽⁵⁾

In 15% of leukemia-HBV DNA in bone marrow cells(8 out of 51) were positive. Out of these 8 one was serum HBsAg positive ⁽⁷⁾. 4 other patients developed antibody to HBV, but were negative for HBV DNA at the time of initial diagnosis. HBV DNA was positive in bone marrow in 55% of myeloid leukemia & 7% of lymphoid leukemia at the time of diagnosis.⁽⁷⁾

HBV infection was significantly associated with earlier precipitation of Diffuse large B cell lymphoma, extra nodal marginal zone B cell lymphoma, peripheral T cell lymphoma and B cell lymphoma.⁽²⁾

HBV was more common than HCV in the pathogenesis of hematological malignancies in Korea.⁽⁹⁾

Prevalence of positivity for HBsAg was 8.5% among B-NHL in contrast to 2.8 % in control⁽³⁾. Prevalence of HBV was 7.3% in NHL which was higher than in Acute Leukemia(1.7%) in contrast to the general Japanese population(1.2%).⁽¹⁰⁾

HBV reactivation is common following chemotherapy and it is associated with high mortality despite prompt antiviral treatment. Increased risk for HBV reactivation was seen more in younger males with high viral load with HBsAg /HBeAg positive lymphomas and pre-immune suppression with HBV-DNA. Hematological malignancies reported in association with hepatitis B virus reactivation are -AML, ALL, CML, CLL, NHL, Hodgkin's Disease, Multiple myeloma, Plasma cell dyscrasias, MDS and Aplastic anaemia.⁽¹⁾

In our series of 63 patients, 2 out of 4 Aplastic anemia (50%), 1 out of 3 RAEB cases (33.3%) and 2 out of 24 AML cases (8.33%, one of which was AML M7) were HbsAg positive (5 in all).

Amongst newly diagnosed cases of acute leukemias, anti HCV was found in 1.28% cases. After 1 yr of diagnosis of HCV positivity incidence rose upto 67 % in AML and 40% in ALL. ⁽⁴⁾

Lesley A. Anderson, Ruth Pfeiffer, et al (2008) have made a very interesting remark that - HCV having increased risk for AML & NHL (diffuse large B-cell lymphoma, Burkitt's lymphoma, Follicular lymphoma & marginal zone lymphoma). HCV may induce lympho proliferative malignancies through chronic immune stimulation.⁽⁸⁾ Prevalence of HCV is found in 10.1% in NHL cases, 2.9% in acute leukemias as compared with general population in Japan which was 2.6%.⁽¹⁰⁾

HCV plays a significant role in the etiology of chronic hepatitis in leukemic patients and that persistent anti-HCV activity correlates with a more severe chronic liver disease which could jeopardize the final prognosis of children cured of leukemia.⁽¹¹⁾

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These findings stress the need for identification of hepatitis virus in patients of hematopoietic malignancies.

CONCLUSION: Worldwide prevalence of HBV is more in malignant than in general population. Infection associated with a significantly earlier disease onset suggestive of possibility of HBV playing an etiological role in the induction of B-cell NHL. Overt and occult HBV pose a serious but preventable threat. HBV infection has potentially significant influence and play a major role in the process of myeloid malignancy development. However, number of cases are not big enough to draw a firm conclusion, further studies with large population of leukemic patients are needed to confirm the possibility of such an association.

Screening for HBV, HCV infection in all haemato-oncology patients pre and post chemotherapy should be practiced by all clinicians who are treating such patients.

HBV negative patients should be immunized against HBV

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REFERENCES:

1. Viral hepatitis B and C in patients with acute leukemias (Ter Arkh.1996) PubMed-NCBI
2. Gentile G, Mele A. "Hepatitis B and C viruses, human T-cell lymphotropic virus types I and II, and leukemias: a case-control study. The Italian Leukemia Study Group." *Cancer Epidemiol Biomarkers Prev.* 1996 Mar; 5(3):227-30.
3. Lesley A. Anderson, Ruth Pfeiffer, et al. "Hematopoietic Malignancies associated with Viral and Alcoholic Hepatitis". *Cancer Epidemiological Biomarkers Prev* Nov 2008 17;3069.
4. Abolfazl Movafagh, Farhad Shaveisi Zadeh, "Association of Hepatitis Virus on Acute and Chronic Myeloid Leukemias'. *Basic and clinical cancer research* 2011";3(3 &4):2-6.
5. Patrizia Pontisso MD, et al. "Detection of hepatitis B virus DNA sequences in bone marrow of children with leukemia"-Pontisso 2006-Cancer
6. Nour el deen RAA, Harfoush RA, Elgharabawy MM, Hamed NA, Morsi MG "Levels of interleukins 12 (IL-12) and 13 (IL-13), hepatitis B and C serology, and blood cultures among acute myeloid leukemia (AML) patients in Egypt." *The Journal of Venomous Animals and Toxins including Tropical Diseases*
7. Feng Wang MD, et al. "High incidence of hepatitis B virus infection in B-cell subtype non-Hodgkin lymphoma compared with other cancers"- *Cancer* Volume 109, Issue 7, pages 1360-1364, April 2007.
8. Jun Kang, Jeong Hyun Cho, Cheol Won Suh, Dae Ho Lee, et al *Ann Hematol* , vol. 90, no. 2, pp. 159-164, 2011.
9. Marcucci F, et al " High prevalence of hepatitis B virus infection in B-cell non-Hodgkin's lymphoma." *Haematologica.* 2006 Apr; 91(4):554-7.
10. Shinji Takai, Hisash, Tsurmani, Kazuki Ando. "Prevalence of hepatitis B and C virus infections in hematological malignancies and liver injury following chemotherapy". *Eur Journal of Haematol.* volume 74, issue 2, pages 158-165, Feb 2005.

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11. Lalazar G, Rund D, Shouval D. "Screening, prevention and treatment of viral hepatitis B reactivation in patients with haematological malignancies". Br J Haematol. 2007 Mar; 136(5):699-712.
12. Eric A Engels, EoRin Cho, Sun Ha Jee "Hepatitis B virus infection and risk of non-Hodgkin lymphoma in South Korea: a cohort study" Lancet, Vol.11, Issue 9, Pages 827 - 834, September 2010.
13. R-N-Chien, C -T .Yeh, P-N .Wang, M-C.Kuo, S-Y., I-y. Shih, Y-F Liaw. "Acute leukemia in chronic hepatitis B patients with lamivudine therapy, Int J Clin Pract." Volume 58, Issue 11, pages 1088-1091, November 2004.
14. A Locasciulli, G gornati, A Tagger, ML Ribero, D Cavalletto, G Masera, HM Shulman. "Hepatitis C Virus Infection and chronic liver disease in children with leukemia in long term remission" Blood, Vol78, No 6 (September 15). 1991; pp1619-1622.
15. AMERICAN CANCER SOCIETY.
16. Jeffrey A. Zonder et al., 'CLL presenting in association with aplastic anemia', Am J Hematol, Vol 71, issue 4; pp1.

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