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Association between Hepatitis B Virus infection and risk of Acute as well as Chronic Myeloid Leukemia

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Abstract

Background: beyond the 15% of cancers in humans can be related to virus infections, which in case, Hepatitis B Virus (HBV) improves the leukemia's risk, particularly Acute Myeloid Leukemia.

Materials and Methods: This prospective study which was conducted since 2010 to 2020 in affected individuals with chronic and acute myeloid leukemia as well as the controls. Staining based on Cytochemical approach, immunophenotyping, Cytogenetic and molecular cytogenetics, Elisa, Enzyme Immuno assessment and Western Bloting, were as a main subject of lab manipulation .

Results: In a sample of control patient hepatitis B virus was diagnosed (%0.004) and four infected with leukemic patients (%3).In leukemic patients when compared with controls, differences revealed statistical significant (*P*=0.0047).

Conclusion: As a results, the prevalence of HBV infection in affected people with leukemias was higher than in patients who were as non malignant controls.We suggest that this issue warrants further investigation by large consortium studies. **Cell, Gene and Therapy, Vol.2, Number 4, Winter 1st, 2021; 126- 130**

Keywords: Hepatit B, HBV, AML, CML, Leukemia

INTRODUCTION

from the first observations of a new antigen in leukemia serum, a plethora of reports concern with increased risk of hepatitis B surface antigen (HBsAg) in patients' serum with leukemia has been shown. [1,2] HBV can rise the risk of leukemia, particularly acute myelocytic leukemia and Nearly 20-24% of cancers can be attributed to virus infection .[3,4] The attachment site of the virus has been identified in the Pre-S1 encoded protein of the virus envelope, the same position involved in hepatocyte infection[5]. HBV encoded a protein (HBX) which is thought to activate cellular signaling pathways whom are related to cell transformations and cancers.[6]

DNA methylation changes influence on the development of different kind of genetic and genomic alterations who are related with cancer , and also, some reports suggested the role of altered methylation in some tumor suppressor genes and oncogenes in the pathogenesis of viral hepatitis carcinoma can be considered.[7] The production of HBV gene detected in endothelial cells of hematopoietic cancers which can suggest that HBV has a key role in hematopoietic carcinogenesis.[8] Hepatitis B Virus is known to become

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integrated in to the host genome and undergo epigenetic changes in the host DNA.[9]

HBV can also permeate bone marrow cells and some in-vitro studies demonstrated a block of hematopoiesis by HBV, which supporting clinical observations of isolate cases of aplastic anemia related to the infection.[10] Hematopoietic malignancies comprise a drives group of neoplasms, likely with various etiologies some of which are related to Infectious agents.[11] Furthermore, HBV can activate a chronic lymphocytic inflammatory reaction in liver.[12] The main motive of this study is to analysis a frequency of a group of leukemias affected who are associated with B and C hepatitis infection.

METHODS

As part of research and project, we used these data to assess the role of infections in myeloproliferative (leukemias) malignancy. This was a cross-sectional study, during 16 years period (2010 -2020), we received Bone Marrow (BM) and Peripheral Blood (PB) specimen from AML and CML diagnosed adult patients at initial presentation from the department of medical Oncology/Hematology based hospital affiliated to Shahid Beheshti University of Medical Sciences, several private centers, Tehran, Iran and Postgraduate Institute of Medical Education and Research (PGI), Chandigarh, India. The diagnosis of acute and chronic myeloid leukemia was based on characterization of the leukemic cells, obtained from bone marrow and/ or peripheral blood, by cytochemical staining, immunophenotyping, cytogenetic and molecular cytogenetics when appropriate. All selected cases were followed according to International System for Chromosomes Nomenclature (ISCN) .[14] Cases of leukemias included in the present study were of ages 67 to 78 years at diagnosis of malignancy. The analyzed control group is made up of 265 patients, 101/ 265 females and 164/ 265 males with 21- 71 years old. The control group consisted of patients in other department specifically, the departments of dermatology, general surgery, Gynecology, Internal medicine, Ophtamology ,Orthopedics.As for the cases, only control patients with newly diagnosed were included.

Analysis of HBV-Related Antigen in The Serum

The sera of the patients was stored at -20Ċ then thawed and analyzed for HBsAg with an enzyme-linked immunoassay kit (Diapro Laboratory Diagnostics Milano-Italy).

The laboratory results (including HBsAg and Anti-HCV antibody by enzyme immunoassay) that were performed at the time of diagnosis. For having a strong confirmation, all of HBV-Ab and HCV-Ab positive samples were confirmed by western blot and positive testes were considered as hepatitis B infections. Patients who were positive for HBsAg were considered to have chronic hepatitis B virus. Patients with post –transplant lymphoproliferative disorder, human immunodeficiency virus –positive lymphomas , and chronic Epstein –Barr virus infection associated lymphoproliferative disorders were excluded from this study. Statistical analysis was done by applying SPSS.

Results

We initially enrolled 1124 patients with different types of hematological malignancies, but we selected 136 leukemias cases and 389 controls, due to repeated sampling, this corresponds to 265 unique control patients. Serological results for HBsAg were available for four cases, and one match controls (selected by random sampling). Leukemic patients were HBsAg positive before and at the time of malignant diagnosis. One hundred thirty six patients with leukemias were studied. Sixty two patients had acute myeloid leukemia. A substantial number of 74 CML patients in different phases of disease (60 patients in CP, 5 patients in AP, 9 patients in BC) were the subject of cytogenetic investigation for this study. Four patients, three with AML and one with CML- CP had HBsAg positive before and at the time of leukemia diagnosis. The results of the present study also indicates that HBV is associated with leukemia, particularly with acute myeloid leukemia (Table 1). The leukemic patients were statistically significant when compared with control (P=0.0047). There was

Table 1 . Distribution of HBV among leukemic patients and corresponding controls

Hepatitis HBV	Leukemias 4(**3**%)	Other disease 1(0.004%)	Total 5
Non Hepatitis HBV	132(97%)	264(99.6%)	396
	136	265	401

no significant differences in the age of the patients in the two groups (P>0.05).

DISCUSSION

A highly prevalence of HBV marker has been found in patients with leukemia compared to the general population, and also numerous previous limited studies have cleared a strong correlation between leukemia and HBV.[13,14] These reports are in an accordance with the present investigation. On the other hands, another study reported non-significant association of HBV and leukemia, indeed, HBV was not associated to any lymphoid or myeloid malignancies.[15] Further investigationa concern with consequence of HBV in myeloproliferative malignancies is required in order to solve such conflicting findings.

Some myeloid leukemia cases were more frequently positive for HBV- DNA in bone marrow, which indicates hematopoietic cells are susceptible to infection with hepatitis B virus and stimulate new interest in to the relation of HBV infection to progress some forms of leukemia.[16] The results of our study also suggest that HBV have a strong relevance to leukemia, especially acute myeloid leukemia (AML), but that association of HBV to other leukemia subtypes is uncertain.

Sequences of HBV-DNA have been detected in the bone marrow of different patients who were affected by leukemia.[17] The wast number of Mutations was distributed in exons 5 to 8 of gene P^{53} in hepatocarcinogene patients which reported in a specific study in Taiwan and other nations.[18,19,20] Different patterns of methylation in selected tumor suppressor genes and oncogenes have been associated with cancers in different populations.[21,22]

The existence of HBV gene products in endothelial cells suggests a role for HBV infection in the development of certain hematopoietic tumors, possibly though activation of cytokines or growth factors, which may stimulated cell proliferation.[23] Taking all this data together, this might be probably that endothelial cells' HBV infections, can considere as a trigger for expression, production, or release of hematopoetic tumor growth factors, which would stimulate cell proliferation.[24,25,26] Establishing the causality of virus-associated tumorogenesis and detecting cofactors for intervention, these are important goals.[27] HBV infection can increases the malignancy risk in lymphoma, which is include NK/Tcell and Hodgkin lymphoma.[28]

The primary data which explained in this study shows that HBV infection may have a critical role in development of leukemias malignancy. In this study, the prevalence of such infection in patients with leukemia was higher than the control group. This observations and results can be considered as another piece of evidence in in order to uphold the association between HBV infection and enhanced risk of leukemias. However, leukemic patients group were not large enough to draw confirm conclusion. Therefore, further studies and investigation in large populations of leukemic patients are necessary to confirm the validity and reliability of such a correlation.

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