Human herpes virus 8-unrelated primary effusion lymphoma-like lymphoma in a patient with hepatitis B virus-related liver cirrhosis: A case report

He-Bin Fan, Dong-Liang Yang, Yong Guo, An-Shen Chen, Mu-Xiu Zhou, Juan-Juan Wu, Xiao-Ju Ma, Zhi Li
Departments of Infectious Disease, Pathology, The People’s Liberation Army 161 Hospital, Department of infectious diseases, Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei Province, China

This study describes a rare case of Human Immunodeficiency Virus and Human Herpes Virus 8 (HHV-8) negative primary effusion lymphoma (PEL)-like lymphoma in a patient with hepatitis B virus-related liver cirrhosis, diagnosed in a 66-year-old male who rapidly progressed to a sense of abdominal fullness. Cytological analysis of the pleural effusion demonstrated large atypical lymphoid cells with rounded nuclei, prominent nucleoli, and abundant cytoplasm. Immunocytochemistry of the pleural effusion detected atypical CD20+ lymphoid cells. The patient was hospitalized, and died following sepsis and multi-organ failure. Our case highlights that HHV-8-unrelated PEL-like lymphoma patients have different pathogenetic mechanisms of causality at the biological level, immunophenotype, clinical behavior, and prognosis.

Key words: Hepatitis B virus, human herpes virus 8, liver cirrhosis, primary effusion lymphoma

INTRODUCTION

Primary effusion lymphoma (PEL) is a subtype of non-Hodgkin lymphoma (NHL) that is usually associated with human herpes virus 8 (HHV-8) and frequently occurs in Human Immunodeficiency Virus (HIV)-infected patients.[1] It is mainly found as a primary lymphomatous effusion in the serous body cavities without clinically identifiable tumoral masses. The malignant effusion usually involves only one body cavity: Pleural, pericardial or peritoneal.[2] Recently, a few cases of HHV-8 negative patients with similar clinical and pathological manifestations have been reported, and this condition is referred to as “HHV-8-unrelated PEL-like lymphoma”.[3-7] Distinct clinicopathological and epidemiological features characterize these patients, including the occurrence in elderly patients without gender preference, the expression of B-cells markers (i.e., CD19, CD20, and CD79a), and a more indolent clinical course.

Here, we report a case of HHV-8-unrelated PEL-like pleural lymphoma in a patient with hepatitis B virus (HBV)-related cirrhosis and ascites but HHV-8 and HIV-negative.

CASE REPORT

A 66-year-old male patient developed a rapid progressive abdominal fullness for 3 months. He had 30-year history of chronic HBV infection without family history of lymphoma and hepatitis. Three years before his hospitalization, liver cirrhosis was diagnosed through clinical, ultrasonography, and biochemical examinations. Physical inspection revealed a distended abdomen with shifting dullness. The liver and spleen were impalpable. The laboratory tests revealed impaired renal function (creatinine: 3.0 mg/dL), mild hypoalbuminemia (3.3 g/dL) and an elevated lactate dehydrogenase (LDH) serum level (750 U/L), while the liver biochemistry profile, including aminotransferases, bilirubin, and prothrombin time, were normal. Serological tests were found negative for HIV, Hepatitis C Virus (HCV) and Cytomegalovirus (CMV). Abdominal sonography confirmed the presence of cirrhosis, massive ascites, and pleural effusion. Cytological analysis of the pleural effusion demonstrated the presence of large atypical lymphoid cells with rounded nuclei, prominent nucleoli and abundant cytoplasm [Figure 1]. Immunocytochemistry recognized atypical CD20+ lymphoid cells [Figure 2]. The cells contained in the
pleural fluid were negative for HHV-8 and Epstein-Barr virus (EBV). Additionally, no evidence of lymph nodes or organ involvement was found. A comprehensive treatment strategy including diuresis, antiviral therapy, prevention of infection and maintenance of vital organ function, was adopted. The patient died on the 7th day after his hospitalization due to sepsis and multi-organ failure.

DISCUSSION

Here we have documented a rare case of HHV-8-unrelated PEL-like lymphoma developed in a patient with chronic HBV infection and cirrhosis, characterized by ascites and pleural effusion. The primary difficulty for a clinician remains the ability to identify HHV-8-unrelated PEL-like lymphomas in cirrhotic patients due to nonspecific constitutional symptoms and laboratory abnormalities. In comparison with PEL, the HHV-8-unrelated PEL-like lymphoma appears to have a better prognosis, with a median survival of 6-10 months and a 1-year survival rate of 35%.[4,8-10] However, our patient who presented in an aggressive advanced status died after the hospital admission due to sepsis and multi-organ failure. There is no consensus regarding the optimal therapeutic approach for either PEL or HHV-8-unrelated PEL-like lymphoma due to the rarity of these diseases and the lack of appropriate studies. Furthermore, there is a compelling need of new and effective strategies to improve the prognosis of patients with PEL or HHV-8-unrelated PEL-like lymphoma.

The etiology of HHV-8-unrelated PEL-like lymphoma is indistinct. This disease occurs often in patients with immune deficiencies including HIV infection, liver cirrhosis, and solid organ transplantation.[5-7] HCV infection has been shown as a possible pathogenic factor for its high predominance (nearly, 30%-40%).[10,11] Our patient was the fourth case reported regarding PEL or HHV-8-unrelated PEL-like lymphoma related to HBV infection after a carefully review of the literature.[11] A high prevalence of HBV infection was found in patients affected by B-cell Non-Hodgkin Lymphoma (NHL).[12,13] HBV surface antigen (HBsAg) and HBV core antigen were found in B-cell NHL lymphocytes and endothelial cells.[14] We, therefore, postulated that cirrhosis related to the chronic HBV infection, as found in our patient, might be responsible to damage the host immunity, which subsequently led to the progress of HHV-8-unrelated PEL-like lymphoma.

It is known that ascites was prevalent in patients with HBV or HCV-related liver cirrhosis in Asia.[15] As it still remains difficult to recognize the true nature of the ascites, when a patient presents with cirrhosis and a rapid accumulation of large amount of ascitic fluid, irrespective of the liver biochemical abnormalities, including hypoalbuminemia, the possibility of HHV-8-unrelated PEL-like lymphoma should be considered, regardless of the patient’s HIV status. In Asiatic countries, patients with hepatitis B- and C-related cirrhosis and serious cavity effusion are relatively common. Quickly progress of pleural effusion combined with cytological examination and imaging (i.e., Positron Emission Tomography) represent the basis of the diagnostic process.[16] The pathogenesis of PEL-like lymphoma in patients with hepatitis B-related cirrhosis is still unknown. In patients with cirrhosis may be associated with a decreased immunity. Today, there was no clear standard of care established in the treatment of PEL-like lymphoma, and currently it remains the basis of PEL treatment. Pérez and Rudoy reported that a PEL patient continued in clinical remission for 13 months by using anti-CD20 monoclonal antibody.[17] Effusion drainage followed by chemotherapy containing rituximab is a potential treatment strategy for patients with HHV-8-negative PEL.[6,18]

In conclusion, HHV-8-unrelated PEL-like lymphoma patients have different pathogenic mechanisms of causality.
at the biological level, immunophenotype, clinical behavior, and prognosis. The role of chronic HBV infection in the carcinogenesis of HHV-8-unrelated PEL-like lymphoma is needed to be determined in future studies.

REFERENCES

1. Nador RG, Cesaran E, Chadburn A, Dawson DB, Ansari MQ, Knowles DM. Primary effusion lymphoma: A distinct clinicopathologic entity associated with the Kaposi's sarcoma-associated herpes virus. Blood 1996;88:645-56.
2. Boulanger E, Agbalika F, Maarek O, Daniel MT, Grollet L, Molina JM, et al. A clinical, molecular and cytogenetic study of 12 cases of human herpes virus 8 associated primary effusion lymphoma in HIV-infected patients. Hematol J 2001;2:172-9.
3. Carbone A, Gloghini A. PEL and HHV8-unrelated effusion lymphomas: Classification and diagnosis. Cancer 2008;114:225-7.
4. Adiguzel C, Bozkurt SU, Kaygusuz I, Uzay A, Tecimer T, Bayik M. Human herpes virus 8-unrelated primary effusion lymphoma-like lymphoma: Report of a rare case and review of the literature. APMIS 2009;117:222-9.
5. Takahashi T, Hangaiishi A, Yamamoto G, Ichikawa M, Imai Y, Kurokawa M. HIV-negative, HHV-8-unrelated primary effusion lymphoma-like lymphoma: Report of two cases. Am J Hematol 2010;85:85-7.
6. Terasaki Y, Yamamoto H, Kiyokawa H, Okumura H, Saito K, Ichinohasama R, et al. Disappearance of malignant cells by effusion drainage alone in two patients with HHV-8-unrelated HIV-negative primary effusion lymphoma-like lymphoma. Int J Hematol 2011;94:279-84.
7. Kim KH, Lee JH, Jeong HC, Kim GW, Song SH, Jung SY, et al. A case of human herpes virus-8 unrelated primary effusion lymphoma-like lymphoma presented as pleural effusion. Tuberc Respir Dis (Seoul) 2012;73:336-41.
8. Boulanger E, Gérard L, Gabarre J, Molina JM, Rapp C, Abino JF, et al. Prognostic factors and outcome of human herpesvirus 8-associated primary effusion lymphoma in patients with AIDS. J Clin Oncol 2003;21:4372-80.
9. Simonelli C, Spina M, Cinelli R, Talamini R, Tedeschi R, Gloghini A, et al. Clinical features and outcome of primary effusion lymphoma in HIV-infected patients: A single-institution study. J Clin Oncol 2003;21:3948-54.
10. Kobayashi Y, Kamitsuji Y, Kuroda J, Tsunoda S, Uoshima N, Kimura S, et al. Comparison of human herpes virus 8 related primary effusion lymphoma with human herpes virus 8 unrelated primary effusion lymphoma-like lymphoma on the basis of HIV. Report of 2 cases and review of 212 cases in the literature. Acta Haematol 2007;117:132-44.
11. Wu SJ, Hung CC, Chen CH, Tien HF. Primary effusion lymphoma in three patients with chronic hepatitis B infection. J Clin Virol 2009;44:81-3.
12. Wang F, Xu RH, Han B, Shi YX, Luo HY, Jiang WQ, et al. High incidence of hepatitis B virus infection in B-cell subtype non-Hodgkin lymphoma compared with other cancers. Cancer 2007;109:1360-4.
13. Ulcickas Yood M, Quesenberry CP Jr, Guo D, Caldwell C, Wells K, Shan J, et al. Incidence of non-Hodgkin's lymphoma among individuals with chronic hepatitis B virus infection. Hepatology 2007;46:107-12.
14. Wang F, Yuan S, Teng KY, Garcia-Prieto C, Luo HY, Zeng MS, et al. High hepatitis B virus infection in B-cell lymphoma tissue and its potential clinical relevance. Eur J Cancer Prev 2012;21:261-7.
15. Michitaka K, Nishiguchi S, Aoyagi Y, Hiasa Y, Tokumoto Y, Onji M, et al. Japan etiology of liver cirrhosis study group. Etiology of liver cirrhosis in Japan: A national survey. J Gastroenterol 2010;45:86-94.
16. Makis W, Stern J. Hepatitis C-related primary effusion lymphoma of the pleura and peritoneum, imaged with F-18 FDG PET/CT. Clin Nucl Med 2010;35:797-9.
17. Perez CL, Rudoy S. Anti-CD20 monoclonal antibody treatment of human herpesvirus 8-associated, body cavity-based lymphoma with an unusual phenotype in a human immunodeficiency virus-negative patient. Clin Diagn Lab Immunol 2001;8:993-6.
18. Terasaki Y, Okumura H, Saito K, Sato Y, Yoshino T, Ichinohasama R, et al. HHV-8/KSHV-negative and CD20-positive primary effusion lymphoma successfully treated by pleural drainage followed by chemotherapy containing rituximab. Intern Med 2008;47:2175-8.

Source of Support: Nil. Conflict of Interest: None declared.