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

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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

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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 clinico-pathological 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

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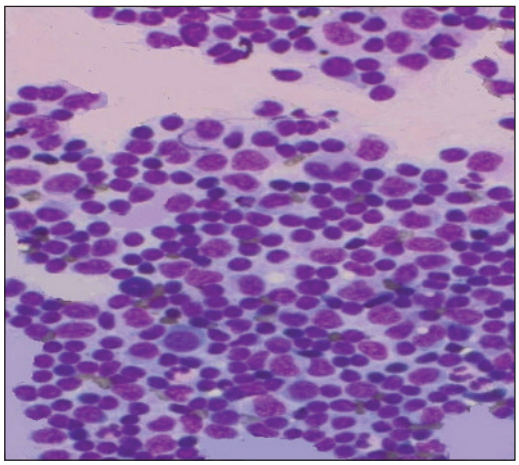

Figure 1: Pleural effusion sediment analysis shows atypical large lymphoid cells with irregular and lobulated nuclei (H and E staining, original magnification ×200)

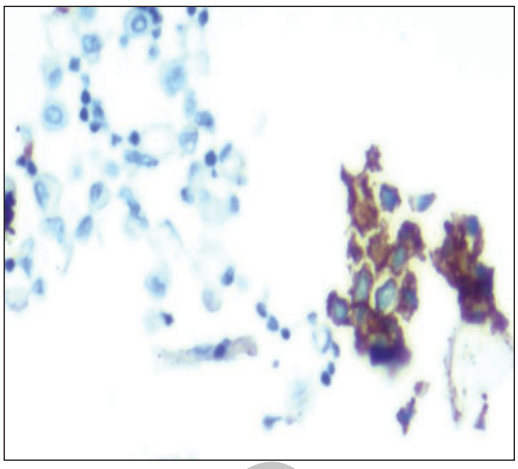

Figure 2: Immunocytochemistry of the pleural effusion shows CD20 reactivity in the cytoplasm of atypical lymphoid cells (original magnification, ×200)

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.[3-7] 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.

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