Clinical Case Report

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Human herpes virus 8-unrelated primary effusion lymphoma-like lymphoma presenting with cardiac tamponade

A case report

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Abstract

Rationale: Primary effusion lymphoma (PEL) is a rare disease of lymphomatous effusion in the body cavities in the absence of detectable mass and lymphadenopathy. PEL is predominantly related to the immunosuppressed patients infected with human herpes virus 8 (HHV-8). PEL-like lymphoma is negative for HHV-8 and human immunodeficiency virus (HIV) unlike PEL. The pathogenesis and prognosis of PEL-like lymphoma are unclear and there is no established treatment yet.

Patient concerns: A 73-year-old male patient was admitted for evaluation of dyspnea on exertion with 1-week duration. His relevant examinations were completed.

Diagnoses: PEL-like lymphoma was diagnosed.

Interventions: The patient received chemotherapy including rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP), and palliative whole-brain radiotherapy, sequentially.

Outcomes: He died 3 months after the diagnosis.

Lesson: Although the prognosis of PEL-like lymphoma may be better than PEL, our case showed poor disease course despite chemotherapy.

Abbreviations: CT = computed tomography, DLBCL = diffuse large B cell lymphoma, HHV-8 = human herpes virus 8, HIV = human immunodeficiency virus, NYHA = New York Heart Association, PEL = primary effusion lymphoma, PEL-LL = PEL-like lymphoma, PET = positron emission tomography, R-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone.

Keywords: cardiac tamponade, primary effusion lymphoma, primary effusion lymphoma-like lymphoma

1. Introduction

Primary effusion lymphoma (PEL) is a rare type of non-Hodgkin lymphoma and has a unique clinical presentation in having a predilection for arising in body cavities such as the pleural space, pericardium, and peritoneum without detectable tumor masses.[1] It usually occurs in immunocompromised hosts with acquired immunodeficiency syndrome and organ transplant recipients. However, numerous cases of PEL may also occur in HIV-negative individuals who are not overtly immunosuppressed, and in the absence of HHV-8 infection. These lymphomas have correctively been reported PEL-like lymphomas (PEL-LLs). An HHV-8-unrelated PEL-LL that usually occurs in elderly individuals and follows a more indolent prognosis has been reported.[2] Here, we report a case of PEL-LL in immunocompetent patient, which showed poor disease course unlike our knowledge.

2. Case report

A 73-year-old male patient was admitted for evaluation of dyspnea on exertion of New York Heart Association (NYHA) functional class III with 1-week duration. He denied recent weight loss, night sweating, or fever. On admission, he had sinus tachycardia, and otherwise stable vital sign: blood pressure of 140/80 mm Hg, and respiratory rate of 19 min^{-1}. No heart murmur was heard, respiratory sound was decreased, fine crackles were audible, and his abdomen was distended. Dyspnea progressed gradually during the admission, and hypotension was developed on the following day. Transthoracic echocardiography (TTE) showed massive pericardial effusion with tamponade physiology (Fig. 1). Urgent percutaneous pericardiocentesis was

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HJK and SMB conceived the case report. HJK, CHY, and SMB were responsible for conducting the review of this case. KL performed pathologic examination and carried out the molecular genetic studies. HJK collected patient's data. HJK and SMB wrote the first draft of the manuscript. All authors critically revised the manuscript for important intellectual content and approved the final version of the manuscript.

The authors report no conflicts of interest.

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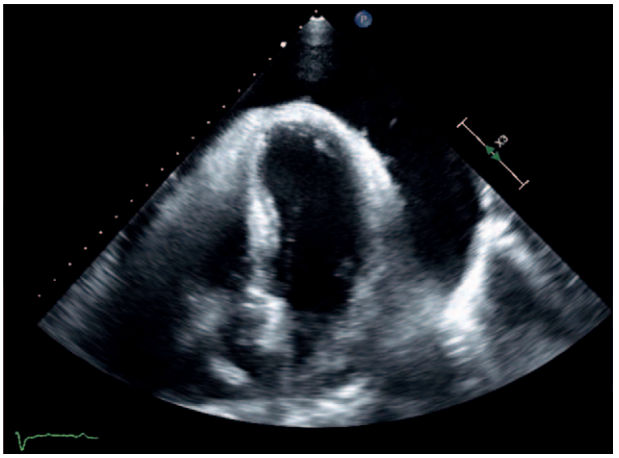

Figure 1. TTE performed on second day of the hospitalization. The image confirmed presence of large pericardial effusion. TTE = transthoracic echocardiography.

performed to relieve symptom and to establish diagnosis. Pericardial effusion was grossly bloody, and laboratory test indicated exudate. Lactate dehydrogenase of pericardial fluid was high (>4000 IU/L). The fluid contained 750,000 red blood cells/mm^3 and 1200 white blood cells/mm^3 (granulocytes 16%, lymphocytes 18%, and other cells 66%). Microbiological studies found no bacteria, fungus, or acid-fast organisms. Cytology revealed cellular population compatible with diffuse large B cell lymphoma (DLBCL). Immunohistochemistry confirmed these large atypical cells positive for CD20, CD79a, and MUM-1 with a small subset expressing PAX-5 with weak-to-moderate intensity (Fig. 2A and B). The Ki-67 proliferating index was approximately 90% (Fig. 2C). Stainings for human herpes virus (HHV)-8 (Cell Marque Corp.; Rocklin, CA, USA) by immunohistochemistry and for EBV by in situ hybridization were negative (Fig. 2D). The patient's serology was positive only for HBsAg, and negative for EBV (IgM), hepatitis C virus, HHV-8, and human immunodeficiency virus (HIV). Especially, the serum sample was analyzed for HHV-8 by the CMV HHV-6, 7, 8 RgeneTM kit (Argene, Varilhes, France) and the result was negative for HHV-8.

Thorough imaging studies were followed to identify anatomical extent of the lymphoma. Computed tomography (CT) of the chest showed massive pericardial effusion, and pericardial thickening (Fig. 1). However, no lymphadenopathy, organ involvement, or extracavitary malignancy was identified on any imaging modalities such as chest CT, abdomen-and-pelvis CT, and whole body positron emission tomography (PET)-CT scan. Esophagogastroduodenoscopy, colonoscopy, and the bilateral bone marrow biopsy were all negative.

Thus, final diagnosis of HHV-8-unrelated primary effusion lymphoma-like lymphoma (PEL-LL) in an immunocompetent host was established. The patient received chemotherapy including rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP). However, despite the 2 cycles of R-CHOP brain metastasis including multiple embolic infarctions was detected. Metastatic brain lesions showed diffuse proliferation of large anaplastic cells with atypical mitosis, which were positive for CD20, MUM-1 but negative for CD10, EBV on immunostaining (Fig. 3). He received the palliative whole brain radiotherapy but died 3 months after the diagnosis.

3. Discussion

PEL is a rare type of non-Hodgkin lymphoma confined to lymphomatous effusion in a body cavity without detectable tumor masses.[1] PEL is usually found in HIV-positive immunocompromised patients and positive for HHV-8 infection.[3] PEL has very

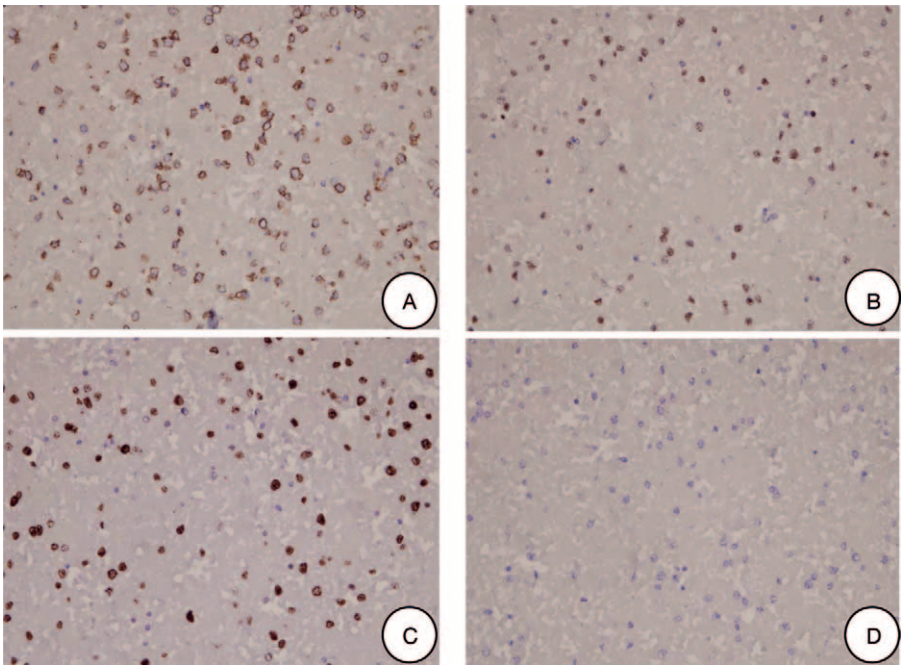

Figure 2. Immunophenotypic findings of PEL-LL: large pleomorhpic cells are frequently noted in cell block preparation. (A) Positive staining on lymphoid cells to brown color for CD20, a B-cell marker (immunohistochemical stain, 200×), (B) weak to moderate positivity in PAX-5 staining (IHC stain, 200×), (C) immunostaining for Ki-67 proliferating index showed strong positive reaction (IHC stain, 200×), (D) negative reaction with human herpesvirus 8 (HHV8) (IHC stain, ×200). PEL-LL = primary effusion lymphoma-like lymphoma.

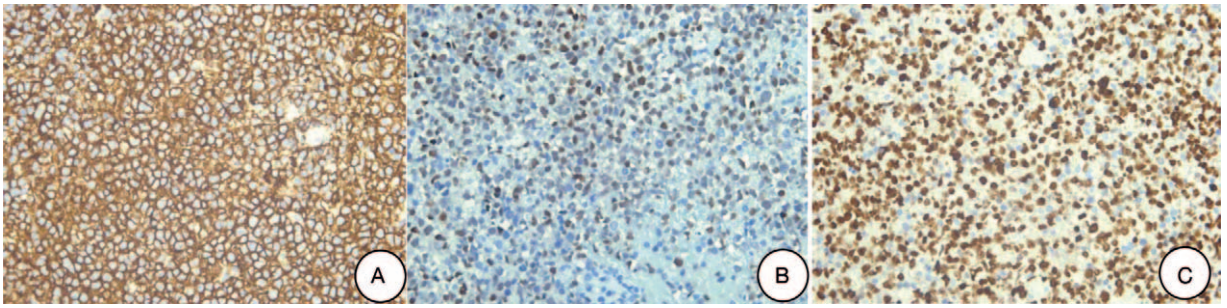

Figure 3. Microscopic finding of PEL-LL: brain lesion showing diffuse proliferation of large anaplastic cells with atypical mitosis, which were positive for CD20, MUM-1 but negative for CD10, EBV on immunostaining. (A) Positive reaction with immunostaining for CD20 (IHC stain, 200×). (B) Positive reaction with immunostaining for MUM-1 (IHC stain, 200×). (C) Immunostaining for Ki-67 proliferating index showed high and strong positive reaction (IHC stain, 200×). PEL-LL = primary effusion lymphoma-like lymphoma.

poor prognosis and yet no standard treatment exists. 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 (PEL-LL)." Since PEL-LL was first described in 2001,[4] approximately 50 cases have been reported in the literature. Compared with PELs, the majority of PEL-LLs are older with median age of 70 years versus 44 years.[2] Most cases were negative for HHV-8 and HIV, and a small percentage were EBV and HCV infection (20–40% of cases).[5,6] The median survival of PEL is 4 months, whereas the prognosis of PEL-like lymphoma has been reported to be better than that.[7]

In contrast to previous reports, this case has several distinguishing features. First, this patient had small tumor burden at presentation but showed poor response to chemotherapy and an aggressive clinical course. The mean survival of previous PEL-LL case reports was 10 months when treated with conventional CHOP or R-CHOP.[2] Second, literatures reviewed that PEL-LL showed frequent involvement of the peritoneum[6] but our case was presented with cardiac tamponade. According to the several published studies, cardiac tamponade is generally associated with extremely poor prognosis and recognized as a pre-terminal event.[8] Third, the PEL-LL may be associated with hepatitis C or EBV infection, and is often seen in individuals with underlying medical conditions that lead to fluid overload such as liver cirrhosis and congestive heart failure.[9] However, the presented case showed no evidence of infection with HCV or EBV. Although HBsAg was positive, his liver function was good and showed no cirrhotic features.

In conclusion, we describe the first case report of PEL-LL showed poor disease course despite immune-chemotherapy unlike the previous articles. This is one of PEL-LL case for EBV and HCV negative. We intend to report this PEL-LL, which appeared with very rare first symptom of cardiac tamponade at presentation, revealing an underlying malignancy.[10] Further research is needed to understand the pathophysiology of PEL-LL.

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