Case Report

J Korean Soc Radiol 2019;80(4):810-814
https://doi.org/10.3348/jksr.2019.80.4.810
pISSN 1738-2637 / eISSN 2288-2928

대한영상의학회지

Primary Effusion Lymphoma in a Non-Human Immunodeficiency Virus Patient: A Case Report

인간면역결핍바이러스 음성 환자에서 발견된 원발성 삼출액 림프종: 증례 보고

Beum Jin Kim, MD, Mi Sook Lee, MD*

Department of Radiology, Presybyterian Medical Center, Jeonju, Korea

Received March 9, 2018
Revised August 6, 2018
Accepted October 10, 2018

***Corresponding author**
Mi Sook Lee, MD
Department of Radiology, Presybyterian Medical Center, 365 Seowon-ro, Wansan-gu, Jeonju 54987, Korea.

Tel 82-63-230-8006
Fax 82-63-230-8387
E-mail dr.kim@hotmail.com

ORCID iDs
Mi Sook Lee
https://orcid.org/0000-0002-1488-2249
Beum Jin Kim
https://orcid.org/0000-0002-9111-5617

Primary effusion lymphoma is a large cell non-Hodgkin lymphoma exclusively presenting with effusions in body cavities in absence of solid tumor masses. It is typically associated with human herpesvirus 8 infection in immunocompromised patients with human immunodeficiency virus (HIV) infection. We report herein a case of primary effusion lymphoma in a HIV-negative patient.

Index terms Lymphoma, Primary Effusion; Lymphoma, Non-Hodgkin; HIV; Pleural Effusion; Pericardial Effusion

INTRODUCTION

Primary effusion lymphoma (PEL) is a rare large B-cell non-Hodgkin lymphoma (NHL) presenting as body cavity effusions without detectable tumor mass (1). Pleura, peritoneal or pericardium are common body cavities that are affected and typically only one body sites are involved. Patients with pleural or pericardial disease may present with dyspnea and those with peritoneal involvement present with ascites. Detection of human herpesvirus 8 (HHV-8) infection is required for definitive diagnosis (1, 2). Thus, PEL cases occur in severely immunocompromised individuals, such as in the setting of human immunodeficiency virus (HIV) or transplantation patients. Diagnosis of PEL is multidisciplinary and is based on radiology, pathology, clinical features and epidemiology. Body cavity effusions and absence of lymhpadenopathies, organomegaly, or other extracavitary masses needs to be confirmed by radiologists to make diagnosis. In the present report, we describe CT findings of PEL incidentally found in a HIV negative patient.

CASE REPORT

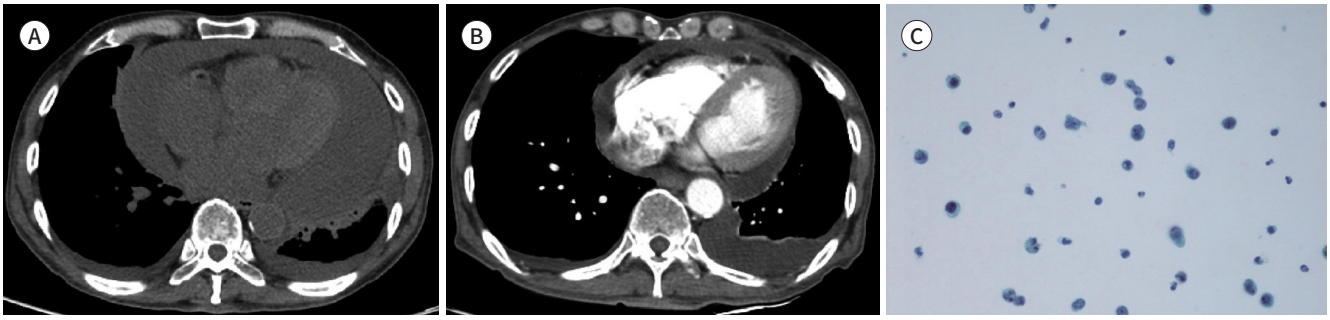
An 81-year-old male presented to our emergency department with worsening dyspnea over 5 days. Total body CT demonstrated large amount of pericardial effusion and pleural effusion with no significant pleural thickening (Fig. 1A). Pericardiocentesis was performed and patient's dyspnea improved and was discharged. HIV serology was negative and patient had no history of hepatitis, cirrhosis, transplantation or other immunodeficiency. PEL was thought to be unlikely and atypical enlarged lymphoid cells found in the pericardial effusion were assumed to be reactive inflammatory changes. Tuberculosis pericarditis was suspected but all the lab results and stains were negative. On follow up, increased amount of pericardial and pleural effusion, mild pericardial wall thickening and enhancements were noted (Fig. 1B). Thoracocentesis was performed and pleural fluid contained many atypical enlarged lymphoid cells similar to those from the pericardial effusion and lymphoid neoplasia was suspected. Entire body workup was performed. Chest CT, abdomen pelvis CT, head CT, did not reveal any abnormal masses or lymphadenopathies. Abnormal lymphocytes were positive for HHV-8 latency associated nuclear antigen stain (Fig. 1C) and diagnosis of PEL was confirmed.

DISCUSSION

PELs, formerly known as body cavity lymphoma, is an unusual NHL characterized by exclusive serous body cavity involvement without identifiable tumor masses. Usually pleura, peritoneum or pericardium are involved and typically only one site is involved at a time. Clinical symptoms are usually mass effects due to accumulation of the malignant effusion such as dyspnea or ascites. B symptoms such as fever, night sweats and weight loss can also be a feature (1, 2).

Infection of B-cells with HHV-8, otherwise known as Kaposi's sarcoma-associated herpesvirus is the main pathogenesis and is required for definitive diagnosis. HHV-8 viral genes are

Fig. 1. Primary effusion lymphoma in an 81-year-old male.
A. Non-enhanced chest CT showing a large amount of pericardial effusion and pleural effusion in the posterior dependent portion of both sides of the chest.
B. Follow-up enhanced chest CT performed 2 weeks after pericardiocentesis shows increased amounts of pleural effusion, especially on the left side, and recurrence of pericardial effusion.
C. Immunohistochemistry for human HHV-8–encoded LANA demonstrated positive, stippled nuclear staining in atypical pleomorphic lymphoid cells with abundant cytoplasm and prominent nucleoli (HHV-8 LANA immunostain, × 200).
HHV-8 = human herpesvirus-8, LANA = latency-associated nuclear antigen



thought to promote cellular proliferation, inhibit apoptosis and ultimately induce neoplastic transformation. Co-infection with Epstein-Barr virus (EBV) is common but EBV does not seem to play a vital role in oncogenesis (1, 2). The definitive diagnosis is based on cytological study of the involved effusion or biopsies of the tissue lining the cavity where the effusion is present. Cytologically, large neoplastic cells with abundant cytoplasm, irregular nuclei and voluminous nucleoli is a feature of PEL. HHV-8 must be detected in the malignant cells and can be done by immunohistochemical staining for latency-associated nuclear antigen. Quantitative real-time polymerase chain reaction to measure affected effusion or peripheral blood for HHV-8 is another faster option (1, 2).

The majority of cases arise in young and middle-aged homosexual or bisexual men with HIV infection. Several cases of PEL have also been reported in HIV negative patients such as transplantation, cirrhosis or those who receive systemic immunosuppression therapies (3). In our case, patient was HIV negative and did not have any immunocompromisation factors. Several literatures report that immunocompetent individuals living in HHV-8 high incidence zones such as Africa, Amazon Basin, and Mediterranean countries can develop PEL (1, 2, 4) without other risk factors. South Korea is known to have less than 5% seroprevalence (1) and is classified as low incidence area and hence in this case, old age is the only risk factor for developing PEL. A similar HIV-negative PEL case has been reported in 2014 for the first time in a 77-year-old male patient without any other risk factors except the old age (5).

Typical radiological findings of PELs have been reported to be unilateral pleural effusion occasionally accompanied with secondary ipsilateral atelectasis, pleural enhancement or thickening (1, 4-7). Ferrozzi et al. (4) reported PEL cases where CT showed solely unilateral pleural effusion in one case and another case accompanying pleural thickening. Kim et al. (1) shows a CT of PEL showing unilateral pleural effusion, passive atelectasis, and enhancing pleura. Case from Antar et al. (5) demonstrated dramatic improvement of unilateral pleural effusion with secondary atelectasis post-treatment with lenalidamide. In all of the cases, key radiological findings were effusions with negative findings of pleural nodule, pleural mass, lymphadenopathy, organomegaly and extracavitary masses. In our case, CT showed pericardial effusion with wall thickening and enhancements, recurrent bilateral pleural effusion and secondary lung atelectasis. PEL is typically known to present in unilateral fashion and involve one body cavity at a time (pericardial, pleural or peritoneal) but there have been reports about involving more than one cavity as in the case report of Nemunaitis et al. (6) where patient presented with pericardial effusion and pleural effusion simultaneously. Just like other PEL cases, whole body CT scan did not reveal any abnormal lymphadenopathies or extracavitary tumor masses.

When immunocompromised patient presents with serosal effusion, several differential diagnosis should be considered and presence of pleural nodule or mass should be carefully assessed on the CT. Kaposi's sarcoma and systemic NHL are usually accompanied by parenchymal infiltrates. Primary or secondary pleural NHL generally presents with nodular pleural thickening. HIV related lymphomatosis usually presents with pleural nodules or masses. Pyothorax associated lymphomas usually presents with calcified pleural mass and possible invasion of chest wall (1-4, 7). In this case, there was no evidence of pleural thickening, enhancement, nodules or masses. Thus all the differentials above can be excluded by radiologi-

cal evaluation.

Positron emission tomography (PET) with 2-Fluoro-2-deoxy-D-glucose (FDG) can be considered in PEL evaluation (8). Increased radiotracer uptakes and metabolic activity in the effusion or along the body cavity lining may be seen in PEL (8, 9). PET-CT also is more effective in excluding tumor masses as it may reveal small lymphoma that was not visible on the CT. By definition, all cases of PEL are Stage IV, and thus Ann Arbor staging for PEL seems insignificant (2). FDG-PET scan should be considered especially if HHV-8 stain is negative which suggests different diagnosis rather than PEL (9).

PEL is notorious to have extremely poor prognosis with median survival time less than 6 months and most patients die within 1 year of diagnosis (1, 10). The most frequent causes of death are opportunistic infection, HIV-related complications, and progression of lymphoma (1, 2). Generally combination of antiretroviral therapy and chemotherapy are used but optimal treatment for PEL has not been established yet. However since this patient is HIV negative, we can assume lower risk for opportunistic infections or other HIV related complication which are major cause of death and may suggest better prognosis than HIV positive groups (10). There also has been a case report about using Lenalidomide, an immunomodulatory drug that is known for multiple myeloma treatment, was effective in treating a PEL patient with HIV seronegativity, achieving complete remission (5). Use of Lenalidomide should be considered as one of treatment option for this patient.

In conclusion, radiologists play a vital role in diagnosis of PEL, detecting effusions in body cavities and excluding existence of solitary masses or pleural nodules or masses, ultimately narrowing down the differential diagnoses. Despite its rarity, radiologists should consider possibility of PEL as one of differential diagnosis when encountered with recurrent body cavity effusions without any extra-cavitary solid masses.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

REFERENCES

1. Kim Y, Park CJ, Roh J, Huh J. Current concepts in primary effusion lymphoma and other effusion-based lymphomas. *Korean J Pathol* 2014;48:81-90
2. Chen YB, Rahemtullah A, Hochberg E. Primary effusion lymphoma. *Oncologist* 2007;12:569-576
3. Nepka C, Kanakis D, Samara M, Kapsoritakis A, Potamianos S, Karantana M, et al. An unusual case of primary effusion lymphoma with aberrant T-cell phenotype in a HIV-negative, HBV -positive, cirrhotic patient, and review of the literature. *Cytojournal* 2012;9:16
4. Ferrozzi F, Tognini G, Mulonzia NW, Bova D, Pavone P. Primary effusion lymphomas in AIDS: CT findings in two cases. *Eur Radiol* 2001;11:623-625
5. Antar A, El Hajj H, Jabbour M, Khalifeh I, El-Merhi F, Mahfouz R, et al. Primary effusion lymphoma in an elderly patient effectively treated by lenalidomide: case report and review of literature. *Blood Cancer J* 2014;4:e190
6. Nemunaitis MC, Schussler JM, Shiller SM, Sloan LM, Mennel RG. Primary effusion lymphoma diagnosed by pericardiocentesis. *Proc (Bayl Univ Med Cent)* 2009;22:77-80
7. De Paoli L, Quaia E, Poillucci G, Gennari A, Cova MA. Imaging characteristics of pleural tumours. *Insights Imaging* 2015;6:729-740
8. Bhargava P, Glass E, Brown J, Eapen E, Ames E. FDG PET in primary effusion lymphoma (PEL) of the pericardium. *Clin Nucl Med* 2016;31:18-19

9. Patil VV, Sideras P, Machac J. PET/CT presentation of primary effusion lymphoma-like lymphoma unrelated to human herpes virus 8, a rare NHL subtype. *Indian J Nucl Med* 2014;29:182-184
10. Okada S, Goto H, Yotsumoto M. Current status of treatment for primary effusion lymphoma. *Intractable Rare Dis Res* 2014;3:65-74

인간면역결핍바이러스 음성 환자에서 발견된 원발성 삼출액 림프종: 증례 보고

김범진 · 이미숙*

원발성 삼출액 림프종은 비호치킨 림프종의 일종으로 다른 종괴가 없이 몸 안 내막들에 삼출액으로만 나타나는 것이 특징이다. 사람헤르페스바이러스8과 관련이 되어있으며 인간면역결핍바이러스 환자들 같은 면역력이 저하된 환자들에서 흔히 발생한다. 우리는 인간면역결핍바이러스 음성인 환자에서 발견된 원발성 삼출액 림프종 증례를 보고하자고 한다.

예수병원 영상의학과