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CASE REPORT

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An unusual cause of pleural effusion

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Abstract

We describe a case of human herpes virus-8-associated primary effusion lymphoma (PEL) in a patient initially presented with fever, non-productive cough and exertional dyspnoea. Physical examination revealed oral thrush, diminished breath sounds and dullness on percussion over the left hemithorax. A thoracic computed tomography (CT) revealed left-sided massive pleural effusion without tumour masses or lymphadenopathy. The effusion was drained and cytology showed medium to large lymphoid cells, with prominent nucleoli and irregular nuclear contours. Meanwhile, his HIV was tested positive. Cell block immunostaining of the pleural effusion revealed these cells were CD45 (+), CD30 (+), MUM1 (melanoma-associated antigen [mutated] 1) (+), LANA (latency-associated nuclear antigen) (+) and EBER (Epstein–Barr virus-encoded small RNAs) in situ hybridization (−). This case highlights the learning point that PEL in the setting of HIV/AIDS should be added in the differential diagnosis of patients with unexplained oropharyngeal candidiasis and malignant lymphomatous pleural effusion without a clear primary site.

KEYWORDS
HHV-8, HIV/AIDS, oral thrush, pleural effusion, primary effusion lymphoma

INTRODUCTION

Primary effusion lymphoma (PEL) is an uncommon cause of malignant lymphomatous pleural effusion without a detectable solid tumour or lymphadenopathy. It occurs most often in immunodeficient patients and is associated with human herpes virus-8 (HHV-8). Here, we report a rare case of HHV-8-associated PEL in the setting of HIV/AIDS presenting with fever, oral thrush and malignant lymphomatous pleural effusion.

CASE REPORT

A 38-year-old man presented to our hospital with a 1-week history of fever, non-productive cough and progressive dyspnoea on exertion. On physical examination, his vital signs were as follows: temperature, 39.2°C; pulse rate, 130/min; respiratory rate, 35/min; and blood pressure, 132/88 mmHg. Oral thrush was noted on examination. The lung examination revealed dullness on percussion and decreased breath sounds over the left hemithorax. There was no lymphadenopathy or organomegaly. The laboratory studies showed white blood cell count of 7.40 × 103/μl with 54.4% neutrophils, 36.6% lymphocytes and 8.3% monocytes; haemoglobin of 10.8 g/dl; platelets of 269 × 103/μl; C-reactive protein of 21.8 mg/L; and D-dimer of 7.94 mg/L. Chest radiography showed a near-complete opacification of the left hemithorax with contralateral mediastinal shift (Figure 1A). Axial contrast-enhanced CT showed a massive left-sided pleural effusion with atelectasis and no evidence of tumour or lymphadenopathy (Figure 1B). Pleural fluid analysis revealed the following: red cell count of 35,000/μl; white cell count of 483/μl with 68% atypical cells, 22% macrophages, 7% lymphocytes and 3% neutrophils; pH of 7.68; lactate

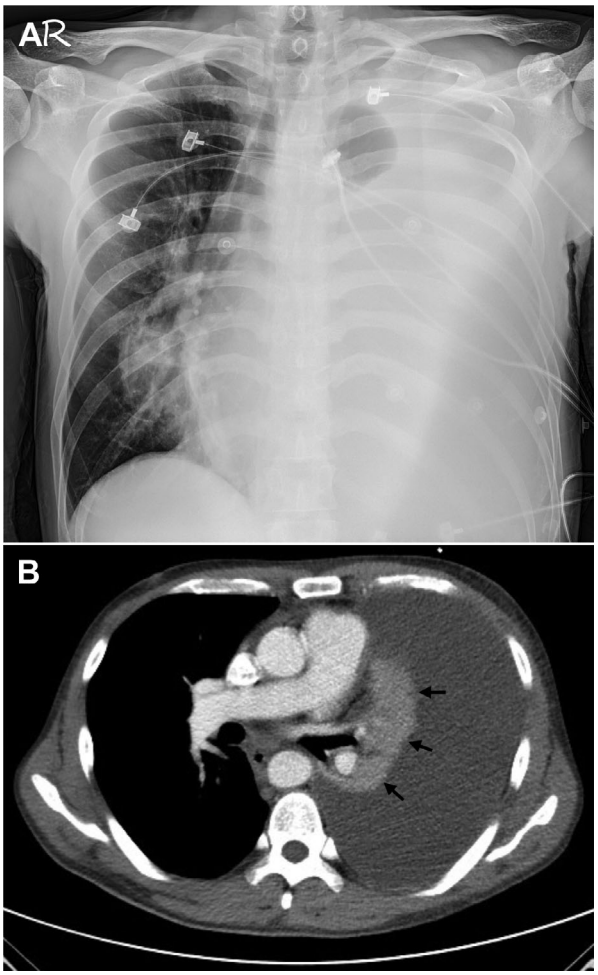

FIGURE 1 (A) Chest radiography revealed a nearly total opacification of left hemithorax with mediastinal shift towards the right. (B) Axial contrast-enhanced computed tomography demonstrated a large left-sided pleural effusion associated with compressive atelectasis (arrows) without tumour or lymphadenopathy

dehydrogenase of 1120 U/L; total protein of 6.5 g/dL; and glucose of 57 mg/dl. A cytology examination of pleural fluid showed a monotonous cell population formed by medium to large lymphoid cells, with prominent nucleoli and irregular nuclear contours (Figure 2A). His HIV test showed a positive result and the CD4 cell count was 18/μl. Cell block immunostaining of the pleural effusion revealed these cells were CD45 (+), CD30 (+), MUM1 (melanoma-associated antigen [mutated] 1) (+), LANA (latency-associated nuclear antigen) (+) and EBER (Epstein–Barr virus [EBV]-encoded small RNAs) in situ hybridization (−) (Figure 2B–F). The patient received sono-guided pig-tail catheter drainage for malignant pleural effusion. Whole-body F-18 fluorodeoxyglucose (FDG) positron emission tomography/CT showed diffuse and heterogeneous FDG uptake associated with pleural thickening in the left-sided pleura without other abnormal FDG-avid abnormalities. He was found to have HHV-8-associated PEL during HIV infection at the stage of AIDS with oropharyngeal candidiasis. Antifungal treatment with fluconazole 100 mg orally once a day and combined antiretroviral therapy (cART) with bictegravir/emtricitabine/tenofovir alafenamide orally once a day were prescribed for him with improvement in symptoms. He was discharged home uneventfully and prepared for further chemotherapy.

DISCUSSION

PEL is a high-grade monoclonal B-cell non-Hodgkin lymphoma (NHL) associated with HHV-8 infection characterized by lymphomatous effusions involving the serous cavities in the absence of a solid tumour.[1] Patients typically present with effusions in the pleural, pericardial or abdominal cavities, although cases of solid/extracavitary B-cell lymphoproliferative tumours with the demonstration of HHV-8 are also recognized as PEL in the literature.[2] PEL usually occurs in patients with immunocompromised states such as HIV infection, solid-organ transplants or in the elderly from HHV-8 endemic country.[3] In the present case, the patient had fever and unexplained oropharyngeal candidiasis suggesting an immunosuppression-related opportunistic fungal infection, which is often the initial manifestation of AIDS. In addition, the lymphomatous malignant pleural effusion without a localized mass and coexisting HIV/AIDS further indicates AIDS-related NHL such as PEL.

Diagnosis of PEL often relies on the cytology/histopathology and immunohistochemistry of aspiration fluid. Malignant cells reveal a monotonous cell population with large nuclei and basophilic cytoplasm. Immunohistochemistry shows positive CD45, CD30, CD38, CD138 and MUM1/IRF4.[4] HHV-8 is considered pathognomonic for PEL and demonstration of HHV-8 integration into the cell through immunohistochemical detection for HHV-8-derived gene products such as LANA is mandatory for diagnosis.[1] More than 70% of cases are also associated with EBV co-infection identified by in situ hybridizations for EBER. Although the role of EBV in pathogenesis is unknown, EBER positivity was associated with a significantly decreased risk of death .[5]

PEL carries a very poor prognosis, but treatment with cART and chemotherapy may extend the median survival to 6–10 months.[1] Standard treatment for HIV-infected PEL patients includes chemotherapy combined with cART. PEL is generally treated with chemotherapeutic regimen such as etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin (EPOCH) or cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) plus rituximab for positive CD20+.[1] cART by itself is also a reasonable option in patients with insufficient Eastern Cooperative Oncology Group status for chemotherapy and confers comparable survival benefits.

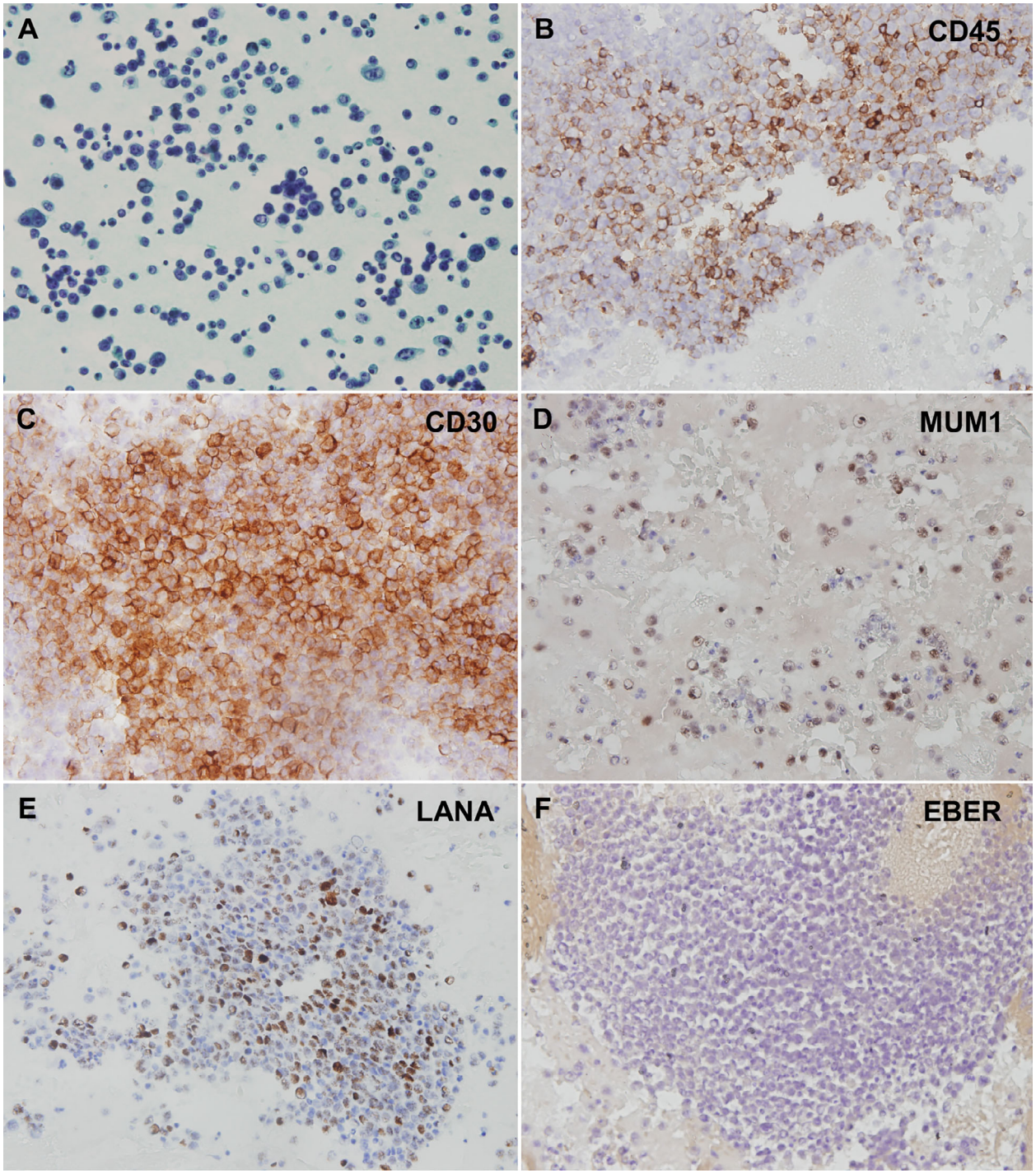

FIGURE 2 (A) Cytological smear of pleural fluid showed a malignant monotonous cell population with irregular nuclear contours and prominent nucleoli (Papanicolaou stain, ×400). (B–F) Pleural fluid cell block immunocytochemistry showed CD45 (+), CD30 (+), MUM1 (+), LANA (+) and EBER in situ hybridization (−). EBER, Epstein–Barr virus-encoded small RNAs; LANA, latency-associated nuclear antigen; MUM1, melanoma-associated antigen (mutated) 1

This case highlights the fact that PEL in the setting of HIV/AIDS should be considered in patients with unexplained oropharyngeal candidiasis and malignant lymphomatous pleural effusion without a clear primary site. Early diagnosis and prompt treatment of PEL are crucial to prevent delayed diagnosis associated poor prognosis and improve clinical outcome.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Chi-Wei Shih and Chia-Hsin Liu wrote the manuscript. Yi-Jia Lin, Hung-Yi Yang and Chia-Hsin Liu performed collection, analysis and interpretation of data.

ETHICS STATEMENT

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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