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ABSTRACT

Primary effusion lymphoma (PEL) is a large cell, non-Hodgkin lymphoma (NHL) characterized by human herpesvirus 8 (HHV8) infection, which is believed to promote oncogenic transformation. Most cases described are found in individuals who are immunocompromised, such as those with HIV or post organ transplantation. Presentation is marked by malignant body cavity lymphomatous effusions (pleural, peritoneal, or pericardial) that usually involve only one body site and are without extracavitary masses. Accounting for less than 4% of cases and possessing a median survival of 6 months, PEL represents one of the least common forms of NHL in the HIV-infected population. Currently, no standard treatment guidelines are available for PEL, and few cases report patients achieving significant remission. The aggressive nature of this malignancy and high mortality has limited longitudinal studies to prospectively observe treatment strategies and leaves clinicians to rely heavily on anecdotal evidence. Information on PEL in HIV-infected patients mostly stems from case reports or small case series, and the scarcity of guidance for relapsed PEL can make management problematic. We report the case of an HIV-infected patient who was diagnosed with PEL after presenting with pericardial tamponade and achieved remission with treatment, but then relapsed approximately two years later.

BACKGROUND

- Primary effusion lymphoma is a rare, HIV-associated, generally aggressive, large B cell lymphoma. It accounts for approximately less than 4% of AIDS-related lymphomas.¹
- Infection with HHV-8 distinguishes PEL from other lymphomas. Coinfection with Epstein-Barr virus (EBV) is common, however, its pathogenicity in PEL oncogenesis is uncertain.
- Characteristically, PEL presents as a lymphomatous effusion in a single serous cavity without a tumor mass. Cases of solid mass tumors, termed "extracavitary PEL," with the histomorphology, phenotype, and gene profiles of PEL have been described and most commonly involve the gastrointestinal tract.
- Symptomatology is dependent on the accumulation of the malignant effusion and subsequent mass effect (e.g. dyspnea, chest pain, ascites).

CASE DESCRIPTION

A 57-year-old HIV positive African American male with past medical history significant for a recent diagnosis of diffuse large B-cell lymphoma presented to the hospital with severe dyspnea and fatigue. Upon presentation, the patient was found to be in new onset atrial fibrillation with a rapid ventricular response. He converted to normal sinus rhythm with medical management alone. The following morning, electrical alternans was noted. A chest x-ray and transthoracic echocardiogram was acquired, revealing a widened mediastinum (**Figure 1**) and large pericardial effusion with clinical tamponade (**Figure 2**), respectively. An emergent pericardial window was performed with the evacuation of one liter of bloody fluid. Cytologic and immunohistochemistry evidence supported a diagnosis of PEL (including HHV-8 and Epstein-Barr virus co-infection) (**Figure 3**). Intrathecal methotrexate was initiated followed by the completion of six cycles of rituximab, cyclophosphamide, vincristine, prednisone and doxorubicin (R-CHOP). Post therapy PET (positron emission tomography) scan did not reveal any evidence of residual malignancy.

Two years later, the patient presented to his physician's office with a one month history of right lower quadrant abdominal pain. Computed tomography (CT) scan revealed bilateral ureter thickening, infiltration of the mesenteric and intra-abdominal fat, and new nonspecific lymphadenopathy (**Figure 4a**). A repeat PET scan did not find any areas of uptake for active tumor but was concerning for right ureteral obstruction. The patient underwent a cystoscopy with right ureteroscopy and stent placement. No tissue was biopsied as no suspicious lesions or masses were found. The stent was subsequently removed approximately one month later, however, within two days of removal, the patient presented to the hospital with fatigue and abdominal distension. Labs revealed the development of acute renal failure and CT demonstrated bilateral hydronephrosis, mesenteric edema, and abdominal ascites (**Figure 4b**). The patient underwent emergent cystoscopy with bilateral stent placement. Preliminary diagnostic paracentesis revealed a highly aggressive, rapidly proliferating lymphoma. The patient was begun on the MAGRATH regimen. Final pathology revealed a highly aggressive PEL (**Figure 5**) and the patient was maintained on this chemotherapeutic regimen with the addition of intrathecal cytarabine and then methotrexate.

After 2 cycles, progression of the lymphoma was noted on peripheral smear and the patient was switched to bortezomib, dexamethasone, and lenolidamide. The patient's course was complicated by the development of severe orthostatic hypotension and peripheral neuropathy, hence, the patient was switched to carfilizomib. Unfortunately, the patient's health continued to decline and he ultimately succumbed to his underlying malignancy.

DISCUSSION

- PEL is a rare non Hodgkin lymphoma of HIV. Malignant pericardial effusion is cited as the effusion site in only 5% of PEL cases.²
- Establishing a diagnosis of PEL requires demonstration of HHV-8 infection.
 - HHV-8 positivity narrows the differential of likely NHLs
- Infection with HHV-8 promotes oncogenesis, the exact mechanism to cause such is an area of investigation.
 - EBV co-infection is common (70%) in HIV-associated PEL but the role it may play in malignant transformation remains uncertain.³
- The optimal therapy for PEL is unknown. There are limited longitudinal studies to prospectively observe treatment strategies which leaves clinicians to rely heavily on anecdotal evidence.
- The relapse rate after achieving an initial remission is not well defined in the literature as overall reports are scarce.
 - Successful eradication of relapsed PEL has been observed in HIV-negative patient with high-dose chemotherapy & autologous stem cell transplantation.³⁻⁵
 - There is no specific guidance for treating relapse in HIV-associated PEL
- Irregardless of a primary or relapse presentation, the diagnosis of PEL carries a high mortality

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FIGURES



Figure 1: AP chest X-ray of pericardial effusion resulting in widening of the cardiac silhouette

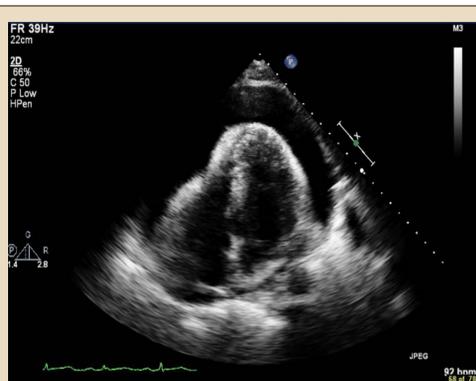


Figure 2: Echocardiogram revealing a large pericardial effusion and left ventricular collapse during diastole

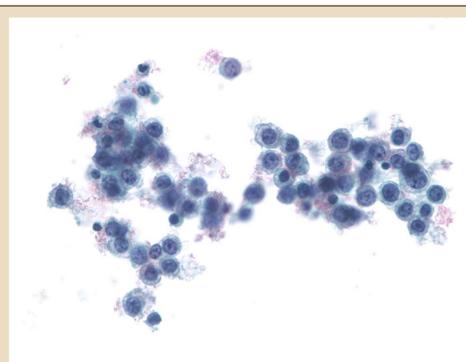


Figure 3: Pericardial fluid microscopic examination demonstrating immunoblastic cells with abundant basophilic cytoplasm with prominent nuclei. (H&E, 400x)



Figure 4a: CT abdomen of ureteral thickening and nonspecific lymphadenopathy located at the lateral aspect of the right psoas muscle

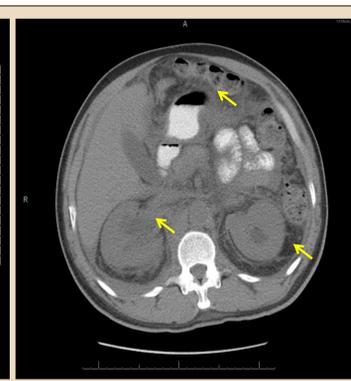


Figure 4b: CT abdomen with moderate ascites, right hydronephrosis, mesenteric edema, and perinephric fluid

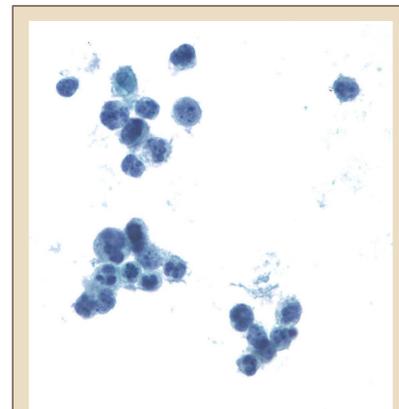


Figure 5: Peritoneal fluid microscopic examination revealing recurrent PEL. (H&E, 400x)