

## Pyothorax-associated T-cell Lymphoma: a Case Report

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We present a case of pyothorax-associated T-cell lymphoma in which Epstein–Barr virus (EBV) genome is not detected in the tumor cells. An 80-year-old male came to our hospital because of a left chest pain. Chest computed tomography (CT) showed a mass at the lower-dorsal part of the pyothorax wall, which involved the adjacent chest wall. The surgical biopsy specimen showed a predominant infiltration of atypical lymphocytes. Results of immunohistochemical analysis were as follows: CD3+, CD4–, CD8+, CD20–, CD30–, CD45RO+ and CD79a–. We diagnosed this case as a type of peripheral T-cell lymphoma. *In situ* hybridization using EBV-encoded RNA-1 (EBER-1) did not reveal the positive signals in the nucleus of tumor cells. Polymerase chain reaction (PCR) analysis yielded a negative result for human herpesvirus 8 (HHV8). Radiation therapy at 54 Gy reduced the tumor size by 90%. Visual and hearing disturbances of unknown etiology developed just before the completion of radiotherapy. The symptoms progressively worsened and the patient became bedridden. He died of pneumonia 2 months after the completion of radiotherapy. Autopsy did not reveal abnormalities to which the neurological disturbances were attributable.

*Key words:* pyothorax-associated lymphoma – peripheral T-cell lymphoma – malignant lymphoma – Epstein–Barr virus

### INTRODUCTION

Pyothorax-associated lymphoma (PAL) is a rare tumor associated with long-standing tuberculous pyothorax. Most PALs are of B-cell lineage (1,2). Only two cases of T-cell PAL have been identified (2,3). The presence of the Epstein–Barr virus (EBV) genome in tumor cells has been detected in almost all of the cases tested (4,5). We report a case of PAL with T-cell immunophenotype.

### CASE REPORT

An 80-year-old man came to our hospital with a left chest pain of 6 months' duration in March 1999. At the age of 37 years, he had pulmonary tuberculosis in the left lung. He had no history of receiving an artificial pneumothorax. At the age of 55 years, he received colectomy for sigmoid colon cancer. Laboratory studies revealed a leukocyte count of 6700/ $\mu$ l, hemoglobin 14.0 g/dl, platelet count  $22.8 \times 10^4$ / $\mu$ l, LDH 749

IU/l (normal <460 IU/l), ALP 256 IU/l (normal <220 IU/l) and C-reactive protein (CRP) 0.61 mg/dl (normal <0.4 mg/l). Serum antibody for human T-lymphotropic virus type 1 (HTLV-1) was negative. A chest X-ray showed an extra-pleural mass shadow at the left side (Fig. 1). Chest computed tomography (CT) showed chronic pyothorax with calcified foci at the left side (Fig. 2). A mass was observed at the lower-dorsal part of the pyothorax wall, which involved the adjacent chest wall (Fig. 2). Surgical biopsy was performed under local anesthesia. The tumor showed a predominant infiltration of small atypical lymphocytes with pleomorphic nuclei (Fig. 3). Immunohistochemical study revealed that the proliferating cells were positive for CD3, CD8 and CD45RO but negative for CD4, CD20, CD30 and CD79a (Fig. 4). We diagnosed this case as peripheral T-cell lymphoma according to the revised WHO classification.

*In situ* hybridization using an EBV-encoded RNA-1 (EBER-1) probe did not reveal positive signals in the nucleus of the proliferating cells (Fig. 5). Polymerase chain reaction (PCR) analysis was performed by using DNA extracted from the paraffin block as described previously (6). After confirming the preservation of the extracted DNA by PCR with primers specific for a 123-bp segment of the  $\beta$ -globin gene, the case was examined for the presence of the 233-bp KS330 region of HHV8. The case was found to be negative for HHV8 (Fig. 6).

A gallium scintigram showed uptake at the tumor site without any other abnormal uptake in whole body. Radiation

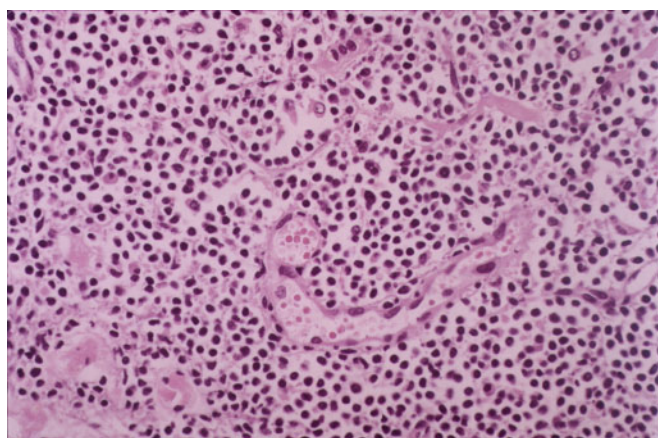
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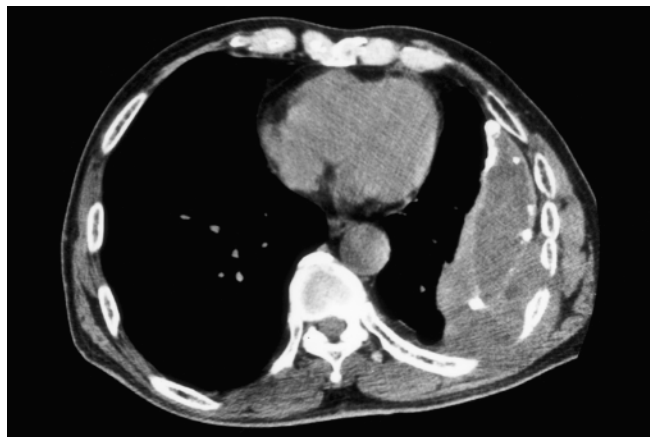


**Figure 1.** Chest X-ray showing an extra-pleural mass shadow at the left side.

therapy at 54 Gy was applied to the dorsal portion of the left thorax. A chest CT taken after the therapy showed a 90% reduction in size of the mass. Homonymous hemianopsia and hypacusia developed just before the completion of radiotherapy. The patient was suspected to have central nervous system involvement. Head magnetic resonance imaging (MRI) showed only a few small infarctions at basal ganglia. The cerebrospinal fluid obtained by lumbar puncture showed normal findings for protein level, cell count and cytological examination. The etiology of the neurological disorders could not be determined. He lost visual and hearing acuities completely and became bedridden. He died of aspiration pneumonia at the end of October 1999. Autopsy of the brain did not reveal any abnormalities, thus the etiology of the neurological disorders remains undetermined.



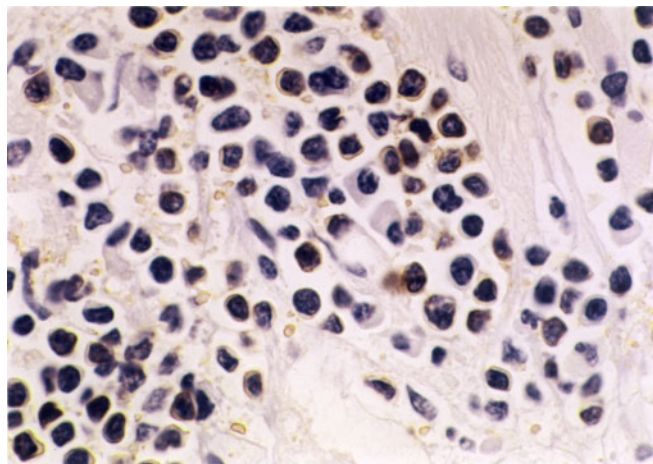
**Figure 3.** Surgical biopsy specimen showing diffuse infiltration of small atypical lymphocytes (H&E stain).



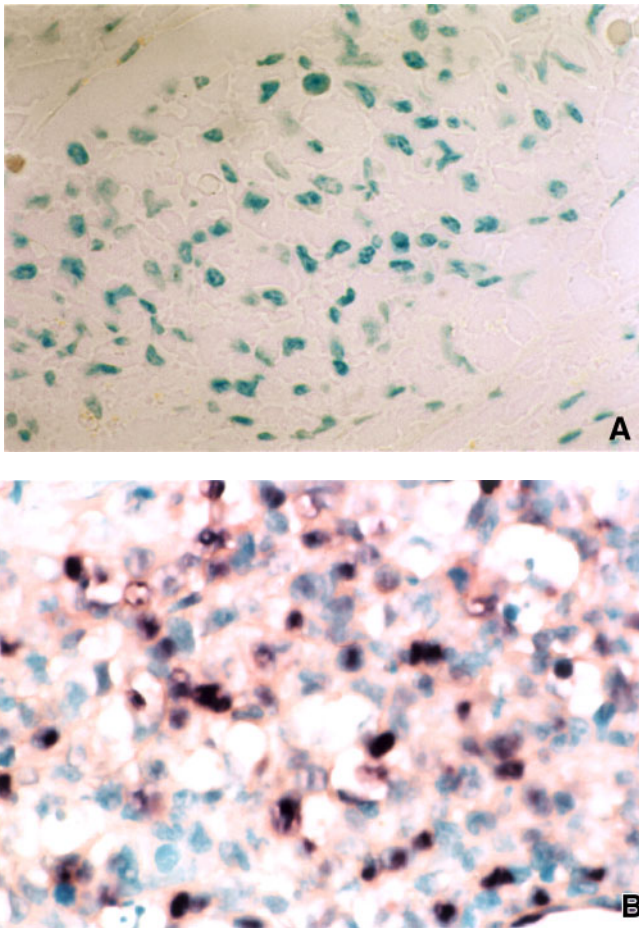
**Figure 2.** Chest CT showing a mass at the lower-dorsal part of the pyothorax wall, which involved the adjacent chest wall.

## DISCUSSION

Pyothorax-associated lymphoma (PAL) is relatively rare even in Japan. The incidence of PAL is reported to be 2.2% among patients with long-standing pyothorax in Japan (1). The histological subtype of PAL is usually B-cell lymphoma of diffuse, large cell or immunoblastic type. Only two cases of T-cell lymphomas have been identified (2,3). The presence of the Epstein-Barr virus (EBV) genome in PAL cells has been detected in almost all of the cases tested, with a constant expression of two latent membrane proteins: latent membrane protein (LMP)-1 and EBV-associated nuclear antigen (EBNA)-2 (4). Nakamura et al. reported the first case of T-cell PAL in which EBV genome was detected (3). This was a case of T-cell PAL without EBV association. Human herpesvirus 8 (HHV8) has recently been reported in association with body cavity-based lymphomas and this has led to speculation regarding its involvement in PALs (7). Cesarman et al. did not detect HHV8 in 14 cases of PAL (8). On the other hand, Ascani et al. (9) and Donovan et al. (10) identified HHV8 in PALs. In the present case, PCR analysis showed the absence of HHV8



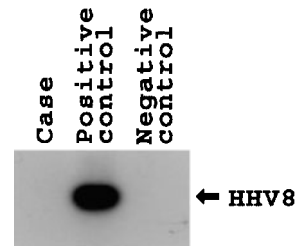
**Figure 4.** The tumor cells are stained with UCHL-1 (anti-CD45RO antibody).



**Figure 5.** (A) EBER-1 *in situ* hybridization showing negative signals in the nucleus of the tumor cells. (B) Positive signals in the nucleus of the Raji cells (positive control).

in the tumor cells. An association between PAL and HHV8 remains controversial. Recently, different mechanisms from EBV association for the development of PAL have also been proposed (5). Aozasa (11) detected p53 mutations at dipyrimidine sites in PAL. This finding suggests that long-term radiation during the artificial pneumothorax or specific drug exposure may have caused specific mutations in the p53 gene. Chronic inflammation may also induce the secretion of cytokines such as IL-6, which could play a role in the proliferation of EBV-infected cells (5).

The prognosis of PAL is poor and the optimum management of PAL remains unresolved. A relatively good response of PAL to chemotherapy has been reported sporadically. In locally limited disease, Nakajima et al. reported an excellent result for pleuropneumectomy with or without radiation therapy (12). In the present case, we applied radiotherapy because the patient was aged and the disease was locally limited. The radiotherapy was successful but progressive neurological disorders of unknown etiology brought an unfavorable outcome. Autopsy did not reveal abnormalities relevant to the disorders



**Figure 6.** PCR analysis of HHV8. The case was negative for HHV8. Positive control: HHV8-positive pulmonary effusion lymphoma.

in the central nervous system except for some small infarctions. The etiology of the neurological disorders remains unresolved.

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