HHV-8/KSHV-Negative and CD20-Positive Primary Effusion Lymphoma Successfully Treated by Pleural Drainage Followed by Chemotherapy Containing Rituximab

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Abstract

The present patient was diagnosed as having human herpes virus-8 (HHV-8)/Kaposi sarcoma herpes virus (KSHV)-negative and CD20-positive primary effusion lymphoma (PEL) of the right-sided pleural effusion. After pleural drainage, malignant cells disappeared spontaneously in a small amount of the remaining pleural effusion without chemotherapy. The patient was treated with six cycles of chemotherapy consisting of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone. He has been in complete remission for more than 22 months. It is suggested that effusion drainage followed by chemotherapy containing rituximab is a potential treatment strategy for patients with HHV-8/KSHV-negative and CD20-positive PEL.

Key words: primary effusion lymphoma, pleural effusion drainage, rituximab


Introduction

Primary effusion lymphoma (PEL) is a rare type of non-Hodgkin lymphoma that involves only body cavities without detectable tumor masses. According to the World Health Organization (WHO) classification of hematopoietic malignancies, PEL is classified as a subtype of diffuse large B-cell lymphoma and is closely associated with human herpes virus-8 (HHV-8)/Kaposi sarcoma herpes virus (KSHV), Epstein-Barr virus (EBV), and human immunodeficiency virus (HIV) (1). The malignant cells are usually negative for B-cell markers, such as CD19, CD20, and CD79a, but are positive for activation and plasma cell-related markers, such as CD30, CD38, and CD138. The median survival of patients with HHV-8/KSHV-positive PEL is less than 6 months (1). On the other hand, it has been reported that patients with HHV-8/KSHV-negative and HIV-negative PEL that highly express B-cell markers are sensitive to rituximab (2, 3). It has been reported that the malignant cells of HHV-8/KSHV-negative and CD20-positive PEL patients disappear spontaneously without treatment after the serous effusion is aspirated (4, 5). We report a case of HHV-8/KSHV-negative and CD20-positive PEL in whom no malignant cells were present after pleural effusion drainage.

Case Report

A 68-year-old man who had no previous history of tuberculosis or pyothorax was admitted to our hospital due to the rapid progression of dyspnea in August 2006. On physical examination, breath sounds were absent on the right side. There was no lymphadenopathy or hepatosplenomegaly. The chest X-ray and chest computed tomography (CT) scan showed a massive, right-sided pleural effusion (Fig. 1). Soon after admission, the patient was treated with continuous drainage of the right-sided pleural effusion. On initial cytological examination of the pleural effusion, large atypical...
lymphoid cells were observed with both Giemsa and Papanicolaou staining (Fig. 2A, B). In addition, the cells were positive for CD20 and CD79a (Fig. 2C, D), but negative for CD3 and CD45RO. The hemogram was normal. The serum and pleural effusion lactate dehydrogenase (LDH) levels were 230 IU/L (normal range, 110-210 IU/L) and 2,178 IU/L, respectively. Tests for hepatitis C virus (HCV) and HIV antibody were negative. Whole peripheral blood tests for HHV-8/KSHV and EBV using the polymerase chain reaction (PCR) method (BML, Tokyo, Japan) were also negative. The pleural effusion disappeared almost completely after pleural drainage. After pleural drainage, the second cytological examination with a small amount of the remaining pleural effusion showed no lymphoma cells, and the pleural effusion LDH level had decreased to 105 IU/L from 2,178 IU/L. Moreover, after drainage, no CD19- or CD20-positive cells were detected in the pleural effusion by flow cytometry, tests for HHV-8/KSHV sequences using the PCR primers specific for HHV-8/KSHV were negative, and no chromosomal abnormalities were detected on G-band study. Evidence of B-lineage cell clonal proliferation was detected in DNA extracted from the ethanol-fixed cells of the pleural effusion before drainage using the PCR method involving primers for the immunoglobulin heavy chain (IgH) gene (Mitsubishi Chemical Medience Corp, Tokyo, Japan). Cytological analysis with interphase fluorescence in situ hybridi-
zation (FISH) detected no translocation of the c-MYC gene in tumor cells before drainage. On the other hand, using the DNA extracted from the ethanol-fixed cells after drainage, IgH gene rearrangement was judged to be practically negative by at least two kinds of PCR (FR3 and DH7); however, examinations for the three other sets of PCR (FR1, FR2 and DH1-6) failed, probably due to highly degraded DNA.

No masses or lymphoma cells were detected on whole body CT scan, gastrointestinal and total colonic fiberoscopy, bone marrow aspiration, and bone marrow biopsy. The patient was diagnosed as having HHV-8/KSHV-negative and CD20-positive PEL, and malignant cells disappeared spontaneously in a small amount of the remaining pleural effusion without chemotherapy after drainage.

The patient was treated with 6 cycles of chemotherapy consisting of intravenous rituximab at a dose of 375 mg/m²/day on day 1, cyclophosphamide 750 mg/m²/day, doxorubicin 50 mg/m²/day, and vincristine 1.4 mg/m²/day on day 2, and oral prednisone 100 mg/day on days 2 to 6 (R-CHOP). After 6 cycles of R-CHOP, the pleural effusion disappeared completely (Fig. 3). The patient has continued to be in complete remission for more than 22 months.

Discussion

PEL is considered to be one of the virus-associated non-Hodgkin lymphomas. It is typically associated with HHV-8/KSHV and HIV. The PEL tumor cell is generally negative for B-cell markers, such as CD19, C20, and CD79a, however, PEL is classified as a mature B-cell neoplasm because of the presence of immunoglobulin rearrangements. On the other hand, HHV-8/KSHV- and HIV-negative PEL cells highly express B-cell markers; most of these cases have been reported from Japan (2-10). Ichinohasama et al reported that PEL could be classified into three types according to the HHV-8/KSHV and c-MYC gene expression patterns (4). Type I PEL is characterized by HHV-8/KSHV infection and germ line configurations of the c-MYC gene, type II PEL is characterized by HHV-8/KSHV negativity and rearrangements of the c-MYC gene, and type III PEL is characterized by HHV-8/KSHV negativity and germ line configurations of the c-MYC gene. Thus, the present case was classified as type III PEL.

Two cases of HHV-8/KSHV-negative PEL with spontaneous regression of the malignant cells without any treatment after aspirations of the serous effusion have been reported from Japan (4, 5). In the present patient, no lymphoma cells were identified on cytological examination of the pleural effusion after drainage. In addition, IgH gene rearrangement was judged to be practically negative by at least two kinds of PCR. The patient was considered to have achieved complete remission after drainage of the pleural effusion. This observation suggests that sufficient drainage of the serous effusion may alone induce cytogenetic complete remission in patients with HHV-8/KSHV-negative PEL. Most cases of HHV-8/KSHV-negative PEL are positive for CD20, unlike HHV-8/KSHV-positive PEL; therefore, rituximab treatment is considered to be effective for patients with HHV-8/KSHV-negative PEL (2, 3). The present patient was given R-CHOP because the tumor cells were CD20 positive. After 6 cycles of R-CHOP, the patient has remained in complete remission for more than 22 months. Effusion drainage followed by chemotherapy containing rituximab is a potential treatment strategy for patients with HHV-8/KSHV-negative and CD20-positive PEL.

References


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