We report a case of 77-year-old woman suffering from breathlessness on exertion and dry cough. Chest computed tomography (CT) showed diffuse ground-glass shadows. A video-assisted thoracoscopic lung biopsy resulted in the diagnosis of diffuse large B-cell lymphoma (DLBCL). Gene rearrangement analysis using polymerase chain reaction (PCR) technique was performed on the cells in bronchoalveolar lavage (BAL) fluid, and showed the clonality of the immunoglobulin heavy chain (IgH) gene, supporting the diagnosis. DLBCL should be considered in the differential diagnosis of diffuse ground-glass shadows in the chest CT, and gene rearrangement analysis may have an impact on the diagnosis of pulmonary DLBCL.

Keywords: primary pulmonary lymphoma (PPL), diffuse ground-glass shadows, immunoglobulin heavy chain gene rearrangement
infection, but the patient had no improvement. Bronchoscopic examination with the specimens of transbronchial biopsy was performed, and there was no significant finding. BAL revealed a increase in lymphocytes (61%) of total cells, and showed some atypical lymphocytes, but these results were not conclusive. Flow cytometry of peripheral blood was normal findings. A video-assisted thoracoscopic lung biopsy was performed to confirm the diagnosis, and the pathological examination of the biopsied specimen revealed that large-sized polygonal atypical lymphoid cells proliferate diffusely in widened alveolar interstitium (Fig. 2a and 2b). The features were suggestive of large cell lymphoma. Immunohistochemical examination was undertaken which was positive for B cell markers (CD20 and CD79a), and negative for T cell markers (CD3 and UCHL-1), which proved conclusively the lesion to be as a B-cell lymphoma (Fig. 2c and 2d). Bone marrow biopsy, abdominal and neck CT scan, and magnetic resonance imaging (MRI) of the brain did not reveal any abnormality excluding splenomegaly, indicating primary pulmonary lymphoma. In addition, we performed gene rearrangement analysis using polymerase chain reaction (PCR) technique of the cells in the BAL fluid. The clonality of the V-D-J region of the immunoglobulin (Ig)
heavy chain gene was detected, supporting our diagnosis (Fig. 3). She received chemotherapy with rituximab / cyclo-phosphamide / doxorubicin / vincristine / prednisolone (R-CHOP) regimen, and got improvement of her symptoms and marked clearing of multiple areas of consolidation and ground-glass shadows.

Discussion

We described a case of primary pulmonary diffuse large B-cell lymphoma (DLBCL) that showed ground-glass shadows on chest radiographs and the clonal rearrangement of immunoglobulin heavy chain (IgH) gene in BAL fluid specimen.

PPL are representing less than 1% of lung cancers, fewer than 1% of malignant lymphomas. The typical radiographic findings in PPL are single or multiple nodular shadows that may occupy one or both lungs, and well-defined infiltrates containing air-bronchograms are also frequently observed. Nodal involvement is seen in around 30% of cases. The present case showed diffuse ground-glass shadows, and it is rare for this disease. Therefore it was difficult to differentiate malignant lymphoma from other diseases.

Radiological differential diagnoses of PPL are lymphocytic interstitial pneumonia (LIP), bronchioloalveolar carcinoma, cryptogenic organizing pneumonia, pulmonary infection and pulmonary metastases. Regarding LIP, Honda et al. reported the difference between LIP and malignant lymphoma on High-resolution CT. Cysts and small nodules are common findings in patients with LIP. On the other hands, air-space consolidation, large nodules (11-30 mm in diameter) and pleural effusion are more commonly seen in patients with malignant lymphoma. In the present case, chest CT showed ground-glass shadows and thickening of peribronchovascular interstitium without nodule and pleural effusion.

The diagnosis of this disease is often made at the time of surgery because of non-specific radiographic signs and a low diagnostic yield in bronchoscopy. BAL appears to be particularly valuable if it shows lymphocytic alveolitis (lymphocyte >20% of total cells), such as our case, which is found in about two-thirds of patients with PPL. This lymphocytosis, which is usually composed principally of T cells, is only specific sign when >10% of B lymphocytes are present. In the present case, >10% of B lymphocytes were observed. Furthermore, B-cell alveolitis is particularly valuable when its clonal nature can be demonstrated by the detection of IgH gene clonal rearrangements using molecular biology-based methods (Southern blot or reverse transcriptase-polymerase chain reaction). Such rearrangements were found only in B-cell neoplasm but not reactive lymphoid process and non-B-cell neoplasm. In the current case, immunoglobuline gene rearrangement have been studied by Southern blot analysis, which has a relatively low sensitivity and requires large amount of DNA. More recently, polymerase chain reaction (PCR) technique has been used to determine the clonality of lymphoid infiltrates, and has the advantage of requiring a much smaller amount of DNA, such as the amount obtained needle aspirates, cytologic samples or BAL samples. In the present case, we showed the
clonal rearrangement of IgH gene based on PCR analysis in BAL fluid, strongly suggesting of neoplastic disease. Although PCR analysis will not replace histological diagnosis as the gold standard, it may be efficient to diagnoses this disease for clinical decisions.

We reported a case of DLBCL diagnosed by histopathological study and the presence of IgH gene rearrangements. We conclude that DLBCL should be considered in the differential diagnosis of diffuse ground-glass shadows in the chest radiographs, and gene rearrangement of IgH gene based on PCR analysis may be useful for the diagnosis of pulmonary DLBCL.

Reference