

## Relapsed Intravascular Large B-cell Lymphoma in the Lungs

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Intravascular lymphoma (IVL) is a rare form of non-Hodgkin's lymphoma that is characterized by the preferential growth of malignant lymphocytes within blood vessels. Pulmonary presentation of IVL is uncommon, and only a few cases have been reported in Korea. Here, we report on a 59-year-old woman with relapsed intravascular large B-cell lymphoma in the lungs. She had been treated with 6 cycles of rituximab, cyclophosphamide, adriamycin, vincristine, and prednisolone (R-CHOP) combination chemotherapy for intravascular large B-cell lymphoma in the nasal cavity, and was followed up regularly with no evidence of disease recurrence. About 1 year later, her chest computed tomography showed extensive ground-glass opacity, suggesting interstitial lung disease and, interestingly, diffuse pulmonary fluorodeoxyglucose (FDG) uptake was observed in positron emission tomography (PET). We performed bronchoscopy, bronchoalveolar lavage, and transbronchial lung biopsy. Pathology revealed relapsed intravascular large B-cell lymphoma in the lungs, and she commenced ifosfamide, methotrexate, etoposide, prednisolone (IMVP-16/PD) salvage chemotherapy. After 3 cycles of chemotherapy, PET showed no abnormal FDG uptake. We suggest that a primary or relapsed pulmonary IVL should be considered in the differential diagnosis of unexplained interstitial lung disease and that PET appears be useful in evaluating pulmonary IVL. (*Korean J Hematol* 2008;43:113-117.)

**Key Words:** Intravascular lymphoma, Interstitial lung disease, Positron emission tomography

### INTRODUCTION

Intravascular lymphoma (IVL) is a rare form of non-Hodgkin's lymphoma that is characterized by proliferation of malignant lymphocytes within the lumina of small to medium-sized vessels.<sup>1)</sup> The sites most commonly involved are the central nervous system, skin, and bone marrow.<sup>2,3)</sup> Pulmonary presentation of IVL has been docu-

mented in a few cases. The major clinical symptoms include fever, cough, dyspnea, and loss of body weight, but these are not diagnostic. Most patients with pulmonary IVL show nonspecific radiological findings, including diffuse interstitial infiltrates, pleural effusion, signs of pulmonary hypertension, and tumor-like consolidation in the lungs.<sup>4-8)</sup> The usefulness of positron emission tomography (PET) in diagnosing IVL has not been established, but Odawara et al. and

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Hofman et al. suggested recently that PET is useful for evaluating IVL.<sup>9,10)</sup>

Here, we report on a 56-year-old woman with relapsed IVL in the lungs who showed extensive interstitial infiltrates in chest computed tomography (CT) and, interestingly, diffuse pulmonary high fluorodeoxyglucose (FDG) uptake in PET.

### CASE REPORT

A 59-year-old woman presented with progressive dyspnea and cough lasting several weeks. Two years previously, she had been diagnosed with IVL in the nasal cavity (Ann Arbor stage III). After 6 cycles of rituximab, cyclophosphamide, adriamycin, vincristine, and prednisolone (R-CHOP) combination chemotherapy, she had shown a complete response in her follow-up head and neck CT, and subsequent periodic head and neck CT, chest CT, and abdomen-pelvis CT showed no evidence of recurrent disease.

She was admitted for further evaluation of progressive dyspnea. On admission, her blood pressure was 120/74 mmHg, pulse 108/min, and body temperature 36.4°C. Physical examination showed the patient to be acutely ill. There were no palpable cervical lymph nodes. Her breathing sound was coarse, and dry crackle was audible at both

lung fields on auscultation. Initial laboratory findings included white blood cell count,  $3.21 \times 10^9/L$  (segmented neutrophils, 79%); hemoglobin level, 12g/dL; erythrocyte sedimentation rate, 9mm/h; serum C-reactive protein level, 0.08mg/dL; and serum lactic dehydrogenase level, 1375 IU/L. Blood chemistry and electrolytes showed no abnormal findings, but arterial blood gas drawn in room air showed PaO<sub>2</sub>, 39.2mmHg; PaCO<sub>2</sub>, 21.1mm/Hg; pH 7.50; bicarbonate, 16.2 mmol/L; and O<sub>2</sub> saturation, 81%. Tests for pneumococcal and legionella antigen in the urine were negative, and tests for mycoplasma and cytomegalovirus (CMV) serology in the serum were negative. Chest X-ray showed linear atelectasis in the right lower lung zone (Fig. 1), and chest CT revealed extensive ground-glass opacity, suggesting interstitial lung disease process in both lungs (Fig. 2).

Supplemental oxygen therapy and broad-spectrum antibiotic treatment was started on suspicion of pneumonia. We planned bronchoscopy, bronchoalveolar lavage (BAL), transbronchial lung biopsy (TBLB), and PET to evaluate further the diffuse interstitial infiltrates in both lungs. Interestingly, PET demonstrated diffuse FDG uptake



Fig. 1. Linear atelectasis in the right lower lung zone.

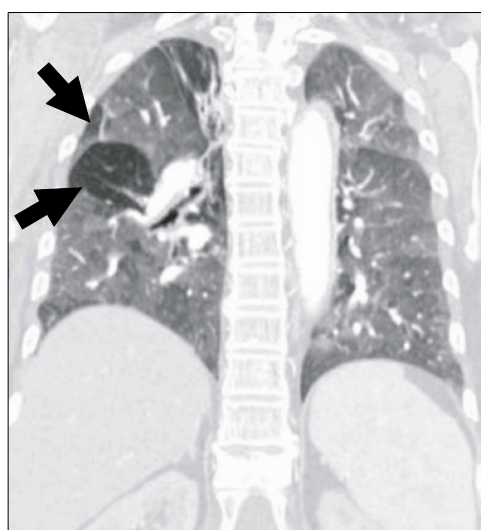
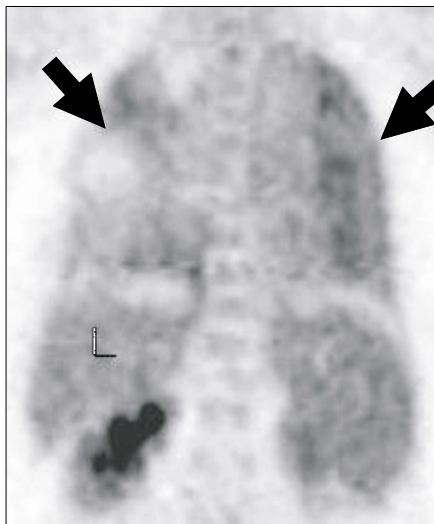
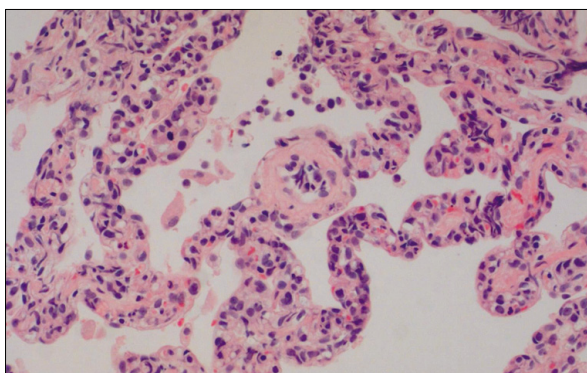


Fig. 2. Lung window of a coronal reformatted CT scan shows extensive ground-glass opacity in both lungs except for some areas (arrows). Ground-glass opacity lesions suggest the presence of interstitial disease process.

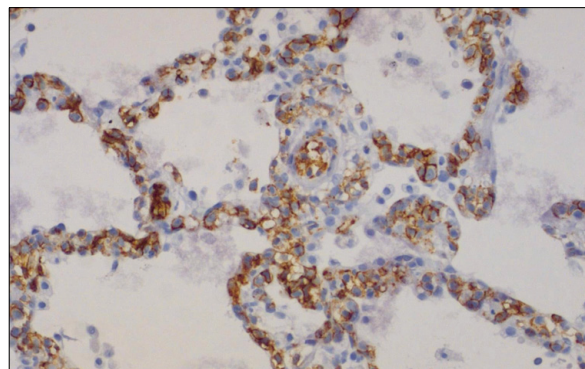


**Fig. 3.** Maximum intensity projection image of PET demonstrates diffuse FDG uptake in both lungs (arrows). Abbreviation: L, liver.

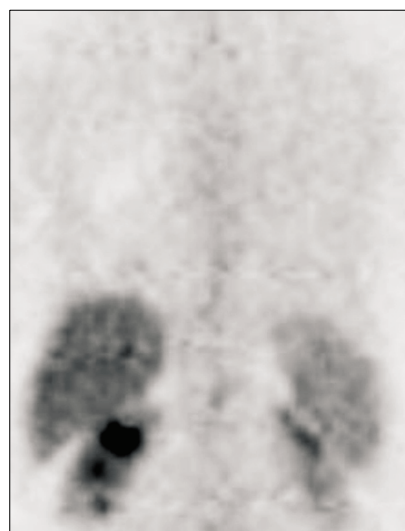


**Fig. 4.** Small and medium-sized blood vessels of the lung filled with intravascular lymphoma cells. Hematoxylin and eosin staining,  $\times 400$ .

in both lungs (Fig. 3). She was transferred to the medical ICU for bronchoscopy, BAL, and TBLB. The bronchoscopic examination showed no endobronchial lesion, and BAL was performed in the right middle lobe and TBLB in the right lower lobe, laterobasal segment. Gram stain and culture, Acid-fast bacilli stain and culture, and viral cultures for herpes simplex virus, cytomegalovirus, respiratory syncytial virus, adenovirus, and influenza virus in the BAL fluid were negative. Finally, TBLB pathology showed atypical lymphocyte proliferation in the small and medium-sized blood vessels (Fig. 4); the lympho-



**Fig. 5.** Immunohistochemical staining for CD20 in neoplastic cells,  $\times 400$ .



**Fig. 6.** Follow-up PET scan shows reduced lung lesions with nearly complete disappearance of FDG.

cytes were positive for CD20 in immunohistochemistry (Fig. 5). The final diagnosis was consistent with relapsed IVL in the lungs. Bone marrow examination also showed intravascular large B-cell lymphoma involvement.

Ifosfamide, methotrexate, etoposide, and prednisolone (IMVP-16/PD) salvage chemotherapy was started, and her dyspnea was gradually alleviated. The patient was discharged after chemotherapy and supportive care of neutropenia. At the time of discharge, her dyspnea had been dramatically reduced and there was no need for supplemental oxygen therapy. We performed 3 cycles of IMVP-16/PD chemotherapy and reevaluated

using PET. The follow-up PET showed no abnormal FDG uptake in either lung, and both lungs showed a complete metabolic response (Fig. 6).

## DISCUSSION

IVL is a rare form of non-Hodgkin's lymphoma that is characterized by the presence of lymphoma cells within the lumina of small to medium-sized vessels, and it has a highly variable end-organ involvement and clinical presentation.<sup>1)</sup> IVL is aggressive and often takes a fatal clinical course.<sup>11,12)</sup> The B-cell immunotype is most common, although cases with T-cell lineage have been reported.<sup>13,14)</sup>

IVL patients diagnosed in Western countries show a relatively high frequency of central nervous system and skin involvement,<sup>2)</sup> whereas patients in Asian countries are more likely to show hemophagocytic syndrome, bone marrow involvement, fever, hepatosplenomegaly, and thrombocytopenia.<sup>3)</sup> Pulmonary involvement of IVL is also rare. Only a few cases have been reported in Korea, and these have involved nonspecific radiological findings, including diffuse interstitial infiltrates, pleural effusion, signs of pulmonary hypertension, and tumor-like consolidation in the lungs.<sup>4-8)</sup> No PET images of pulmonary IVL have been reported. Interestingly, two recent reports suggest that PET is useful for evaluating IVL.<sup>9,10)</sup> Odawara et al. reported a patient with disseminated IVL and high FDG uptake throughout the entire body on PET. Their patient received R-CHOP combination chemotherapy and showed a complete metabolic response on the follow-up PET.<sup>9)</sup> Hofman et al. also showed that PET was useful in the early diagnosis of relapsed meningeal IVL, and the early diagnosis allowed prompt salvage chemotherapy.<sup>10)</sup> Our patient is the first reported case of relapsed pulmonary IVL showing diffuse pulmonary FDG uptake on PET and a complete metabolic response after IMVP-16/PD combination chemotherapy.

In conclusion, we suggest that primary or re-

lapsed pulmonary IVL should be considered in the differential diagnosis of unexplained interstitial lung disease, and that PET could be useful in the diagnosis, staging, and early diagnosis of disease recurrence in pulmonary IVL.

## 요 약

혈관내 림프종은 비호지킨 림프종의 드문 한 종류로 혈관내 악성 림프구의 증식을 특징으로 한다. 현재까지 한국에서 혈관내 림프종의 폐 침범은 매우 드물게 보고되었다. 저자들은 혈관내 B 대세포 림프종이 폐로 재발한 59세 여자환자의 증례를 보고한다. 환자는 비강에 발생한 혈관내 B 대세포 림프종에 대하여 6차례의 cyclophosphamide, adriamycin, vincristine, prednisolone (R-CHOP) 복합항암요법 후 완전관해로 추적관찰 중이었다. 항암치료 1년 경과 후 시행한 추적관찰 흉부 전산화 단층촬영에서 간질성 폐질환을 시사하는 간유리 혼탁화 소견이 보이고, 양전자방출단층촬영술에서 미만성 폐섭취가 나타났다. 기관지 내시경, 폐 세척술, 경 기관지 폐생검을 시행하였다. 폐조직검사 결과에서 재발성 혈관내 B 대세포 림프종이 진단되었으며, 3차례의 ifosfamide, methotrexate, etoposide, prednisolone (IMVP-16/PD) 구제 항암요법을 시행하였다. 구제항암요법 후 양전자방출단층촬영술에서 관찰되었던 미만성 폐섭취는 완전히 소실되었다. 저자들은 원인불명의 간질성 폐질환의 감별진단으로 원발성 혹은 재발성 혈관내 B 대세포 림프종이 포함되어야 하며, 폐에 발생하는 혈관내 림프종을 평가하는데 양전자방출단층촬영술이 유용할 수 있음을 제안한다.

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