

# Synchronous diffuse large B-cell lymphoma and squamous cell lung carcinoma

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## Keywords

18F-fluorodeoxyglucose positron emission tomography, diffuse large B-cell lymphoma, squamous cell lung carcinoma, staging, synchronous.

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## Abstract

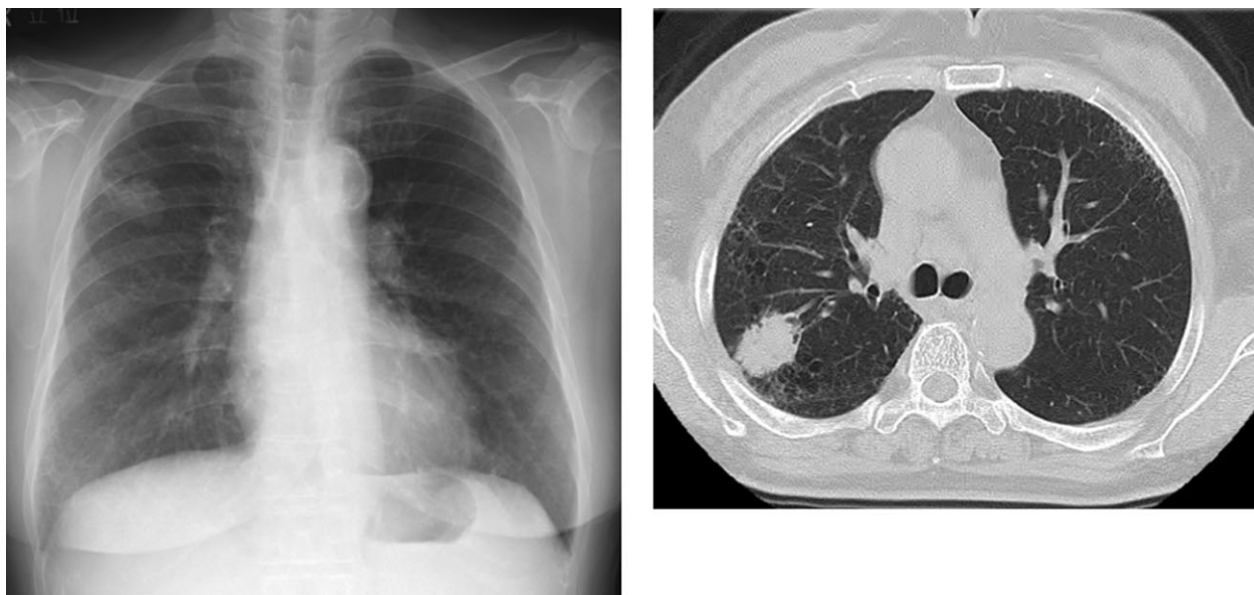
A 68-year-old woman was referred for a nodule in the right lung and hilar and mediastinal lymphadenopathy. Physical examination revealed left cervical lymphadenopathy. 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) images revealed radiotracer uptake in the pulmonary nodule and multiple lymph nodes of the truncus. Biopsies confirmed the diagnosis of synchronous diffuse large B-cell lymphoma and squamous cell lung carcinoma. Because the etiology of hilar and mediastinal lymphadenopathy was unknown, the staging of lung cancer could not be determined. We performed therapy for malignant lymphoma earlier than lung cancer. After therapy, FDG-PET showed that uptake in the lymph nodes due to lymphoma had disappeared, whereas uptake in the pulmonary nodule and right hilar lymph node remained or had increased. Based on these findings, the staging of lung cancer was determined and radical surgery was performed successfully. This rare case of synchronous malignancy illustrates the limitation of initial single testing of FDG-PET.

## Introduction

Synchronous occurrence of multiple neoplasms is a rare condition. It is often difficult to assess the staging of each neoplasm and to determine optimal treatment according to the state of each disease. Non-Hodgkin's lymphoma (NHL) is one of the most common neoplasms. Thoracic involvement occurs in up to 43% of patients with NHL [1]. When lung cancer is complicated with NHL, it is difficult to determine the stage of lung cancer since both neoplasms can invade the mediastinal and hilar lymph nodes. Here, we report a unique case of synchronous advanced diffuse large B-cell lymphoma (DLBCL), a subtype of NHL, and squamous cell lung carcinoma, indicating the limitation of initial single testing of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) for staging examination.

## Case Report

A 68-year-old woman visited our hospital for the investigation of abnormal shadows on a chest X-ray at her annual medical examination. She was a current smoker (29 pack-years) with a history of hypertension and cholelithotomy. A physical examination revealed left cervical elastic hard lymphadenopathy. The chest X-ray and computerized tomography scan showed a well-defined nodule (3.0 cm × 1.4 cm in diameter) in the right upper lobe and hilar and mediastinal lymphadenopathy (Fig. 1). Laboratory data on the first visit revealed serum carcinoembryonic antigen (CEA) of 7.6 ng/mL (normal range <5.0 ng/mL) and soluble interleukin-2 receptor (sIL-2R) of 4500 U/mL (normal range <519 U/mL). CEA and sIL-2R are the most commonly used tumor markers in patients suspected of having lung cancer or malignant lymphoma in our



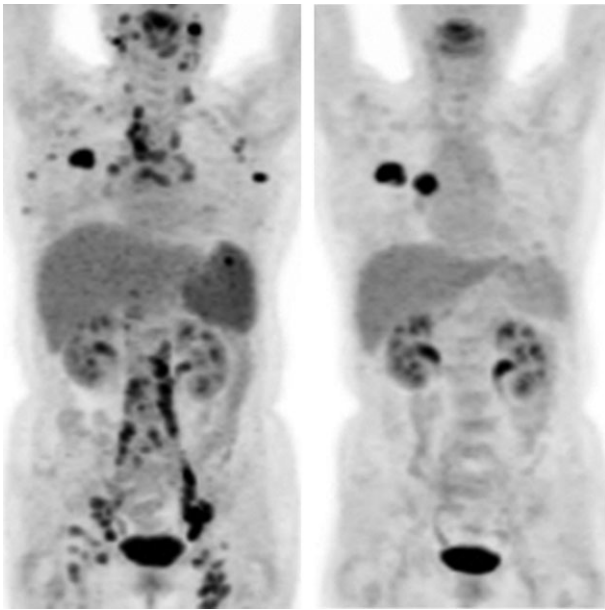
**Figure 1.** Chest X-ray and computerized tomography (CT) findings on the first visit showing a nodule in the right upper lobe and hilar and mediastinal lymphadenopathy.

hospital. FDG-PET images revealed radiotracer uptake in the pulmonary nodule (the maximum standardized uptake values, 10.1) and multiple lymph nodes, including cervical, submandibular, hilar, mediastinal, axillar, paraaortic, intrapelvic, and inguinal lymph nodes, and the spleen (Fig. 2, left). Since the patient had a history of heavy smoking and elevated serum CEA, the differential diagnosis included not only malignant lymphoma but also lung cancer. An excisional biopsy and immunohistochemical analysis of the left cervical lymph node revealed DLBCL, and a transbronchial lung biopsy of the nodule showed squamous cell carcinoma, leading to the diagnosis of synchronous malignant neoplasms. The staging of primary lung cancer could not be determined because it was unknown whether hilar and mediastinal lymphadenopathy were due to the metastases of lung cancer or extranodal invasion of malignant lymphoma. Evaluation of regional lymph node involvement is indispensable for determining if surgery is possible for lung cancer, and studies have indicated that DLBCL is responsive to recent standard regimens [2]. Thus, we decided to perform three courses of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) therapy for malignant lymphoma before assessing the staging of lung cancer. After R-CHOP therapy, FDG images showed that FDG accumulation in multiple lymph nodes and the spleen due to DLBCL had disappeared, whereas uptake to the pulmonary nodule and right hilar lymph node remained or had increased (Fig. 2, right). Based on these findings, the staging of lung cancer was determined clinically as T2aN1M0 and radical surgery

was performed successfully. Surgical pathology specimens revealed only squamous cell carcinoma but not lymphoma with the same staging between pre- and post-operation. Based on consultations with hematologists, we estimated that the risk of recurrence due to chemotherapy interruptions for lymphoma would be higher than that due to lack of adjuvant chemotherapy or irradiation for lung cancer. Thus, three more courses of R-CHOP were added and DLBCL went into complete remission. Laboratory data at this time revealed serum CEA of 2.9 ng/mL and sIL-2R of 413 U/mL.

## Discussion

DLBCL is the most common histologic subtype of NHL, accounting for approximately 30% of all new diagnoses. It is an aggressive NHL in which survival without treatment is measured in months. The addition of rituximab to CHOP chemotherapy has resulted in a marked improvement in outcomes for patients with DLBCL [2]. Squamous cell lung carcinoma mostly develops in smokers. Patients with stage I, II, or III non-small-cell lung carcinoma are generally treated with curative intent using surgery or radiation therapy, sometimes combined with concurrent or adjuvant chemotherapy. In contrast, palliative systemic therapy is appropriate for patients who have stage IV disease. In the present case, since the treatment procedure for lung cancer could not be determined, the patient was treated initially with R-CHOP. Fortunately, this therapy was effective; however, the outcome would not have been



**Figure 2.** 18F-fluorodeoxyglucose (FDG) positron emission tomographs before (left) and after (right) three courses of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone therapy. After therapy, FDG accumulation in the nodule in the right upper lobe remained, whereas accumulation in the right hilar lymph node had increased. Other accumulations had disappeared completely.

as favorable had the remaining hilar lymph node after chemotherapy showed residual lymphoma or there had been more than one hypermetabolic lymph node remaining after chemotherapy. Thus, this case indicates the importance of evaluating the feasibility of restaging. As curative resection varies from patient to patient, restaging for possible curative resection should be considered and revisited on treatment.

The advantage of FDG-PET over conventional imaging techniques is its ability to distinguish between viable

tumors and necrosis or fibrosis in residual masses often present after treatment [3]. DLBCL is classified into routinely FDG-avid lymphoma and FDG-PET is recommended to assess effectiveness after medical treatment [4]. As we expected in the present case, FDG accumulation in the lymphoma lesions disappeared after R-CHOP therapy, whereas accumulation in the pulmonary nodule and hilar lymph node remained or increased, thereby enabling determination of the staging and subsequent radical surgery for squamous cell lung carcinoma.

In conclusion, in this particular patient with synchronous DLBCL and squamous cell carcinoma of lung, FDG-PET becomes useful only after chemotherapy for DLBCL.

### Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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