

A Case of Primary Tracheal Lymphoma of a 65-year-old Female: Extremely Rare Primary Localization of a Diffuse Large B-cell Lymphoma

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Primary extranodal non-Hodgkin's lymphomas comprise approximately 10% of all non-Hodgkin's lymphomas. However, primary tracheal non-Hodgkin's lymphoma is extremely rare, being mainly muco-sa-associated lymphoid tissue lymphoma. A 65-year-old female has dry cough for one year. She was diagnosed as diffuse large B-cell lymphoma via bronchoscopic-guided biopsy. She was treated with four cycles of the R-CHOP regimen and adjuvant radiotherapy. After completion of the combined treatment, the treatment response was complete remission, and the disease free survival was 26 months. (*Korean J Hematol* 2007;42:439-444.)

Key Words: Primary tracheal lymphoma, Diffuse large B-cell lymphoma, R-CHOP

INTRODUCTION

Primary tumors of the trachea can be benign or malignant, and account for less than 0.1% of tumors. A majority of primary tracheal tumors are squamous cell or adenoid cystic carcinomas, while the rest are composed of adenoid cystic carcinoma, mucoepidermoid carcinoma, adenoma, and others. However, squamous cell carcinoma, the most common type of primary tumor in the

trachea, is approximately 75 times more frequent in the larynx and 140~180 times more frequent in the bronchi.^{1,2)}

Extranodal lymphoma is defined as presented or developed disease outside the traditional lymphoid tissue of the lymph nodes, spleen, thymus, tonsils, and Waldeyer's ring. Extranodal non-Hodgkin's lymphoma (NHL) is relatively common; approximately 10% to 25% of NHL cases arise in extranodal sites, and their biological be-

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havior and mode of dissemination may differ from those of nodal lymphoma.³⁾ The sites of anatomical localization of extranodal NHL vary widely. Furthermore, there is wide variation in the geographic incidence of extranodal NHL, with reports ranging from 24 percent in the USA to 13 to 48 percent in Italy.⁴⁾ The majority of extranodal lymphomas arising from the mucosa-associated lymphoid tissue are B-cell lymphomas of follicle center cell origin.⁵⁾ A few cases of extranodal NHL have been reported from Korea, but reports of primary malignant lymphoma of the trachea are extremely rare. Furthermore, no cases of primary tracheal diffuse large B-cell lymphoma have been reported from Korea.

Here, we report a case of primary tracheal diffuse large B-cell lymphoma that was successfully managed with a combination of immuno-chemotherapy and additional radiotherapy.

CASE REPORT

A 65-year-old female complained a persistent dry cough lasting for 1 year, which had been aggravated for one month. The patient also suffered from weight loss of 8kg, intermittent night sweats, and febrile sensation for 3 months. She had no other family history, nor prior medical history.

On admission, she was conscious and breathless, vital signs were stable. Physical examination revealed no any other abnormalities of lymph node, liver, and spleen. Chest radiography finding was normal.

The initial laboratory findings were: WBC 8,600/mm³ (segmented neutrophils 53.7%, lymphocytes 33%, monocytes 6.4%, eosinophils 4.4%, and basophils 0.9%), hemoglobin 12.8g/dL, hematocrit 37.0%, and platelets 327,000/mm³. Elec-

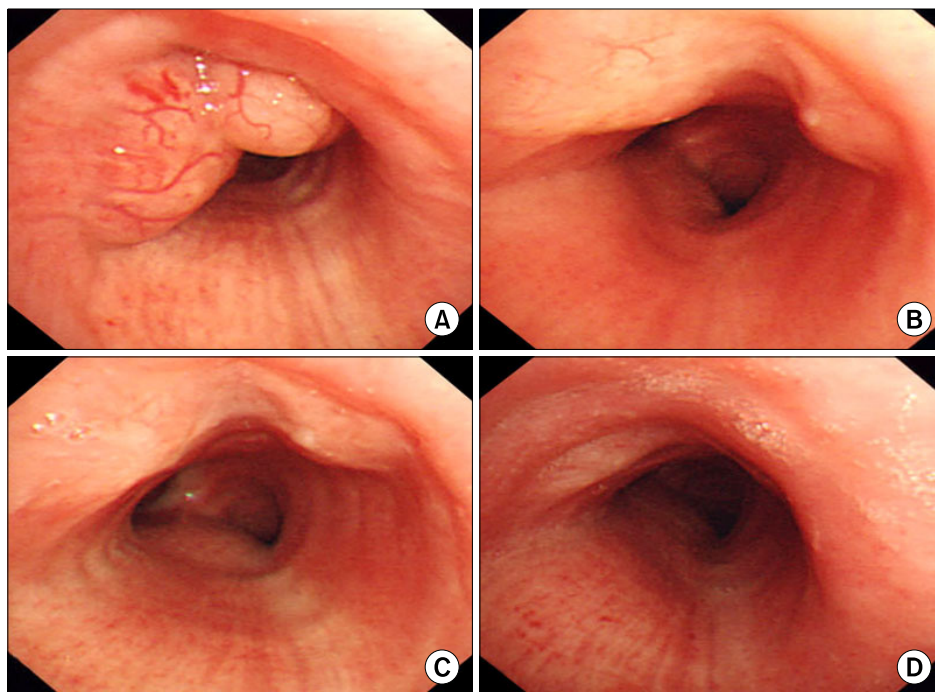


Fig. 1. Serial bronchoscopic findings. (A) At 20cm from upper incisor, multi-lobulated, multi-lobulated tumor with vascularization was seen. the tumor obstructed the tracheal lumen by about 50%. (B, C) Comparing previous bronchoscopic finding. the size of tracheal lymphoma was marked decreased at about 5cm above carina. (B) After the patient received 2 cycles of combination chemotherapy with R-CHOP regimen. (C) After the patient received 4 cycles of combination chemotherapy with R-CHOP regimen. (D) Comparing previous bronchoscopic finding. Slight flat bilobulated nodule was more decreased at about 5cm above carina after additional RT was done.

trolyte, renal function, and liver function tests were within normal limits. The lactate dehydrogenase level was 2,450U/L and the β_2 -microglobulin level was 1.6mg/L.

Fiberoptic bronchoscopy showed an intratracheal multi-lobulated polypoid lesion with the tracheal lumen narrowing. Bronchoscopic biopsy was performed to establish a pathological diagnosis (Fig. 1A).

The chest CT showed a 1.5×1.0cm sized polypoid mass lesion in the Lt anterolateral aspect of the trachea (Fig. 2).

The histological finding showed diffuse infiltration of large and globular abnormal lympho-

cytes (Fig. 3A). The malignant cells expressed CD20, indicating an increase of B-cells with a reactive response (Fig. 3B). The final diagnosis was a diffuse large B-cell lymphoma.

For the staging of the primary disease, there was no evidence of organ involvement of NHL via positron emission tomography - computed tomography (PET-CT). A whole-body combined PET-CT scan demonstrated the high uptake of ^{18}F -FDG within the 1.5×1.0cm sized polypoid mass in the middle area of the trachea. The PET-CT also revealed no increased ^{18}F -FDG uptake at adjacent or distant lymph node sites, and showed no evidence of organ involvement (Fig. 4). Thus, we concluded that the diagnosis was primary tracheal diffuse large B-cell lymphoma, stage 1BE.

Based on recent reports of the synergistic benefits of immunotherapies in combination with standard chemotherapy for diffuse large B-cell lymphoma, treatment was initiated using CHOP (cyclophosphamide, adriamycin, vincristine, and prednisone) chemotherapy with rituximab anti-CD20 monoclonal antibody immunotherapy. Four courses of combination chemotherapy with the R-CHOP regimen (rituximab 375mg/m² day 1, cyclophosphamide 750mg/m² day 1, adriamycin 50mg/m² day 1, vincristine 1.4mg/m² day 1, and prednisone 100mg/day 1 to 5, q 3 weeks) were given. After two and four courses of chemotherapy, the follow-up fiberoptic bronchoscopy



Fig. 2. The chest CT shows a polypoid mass lesion in the Lt anterolateral aspect of the trachea.

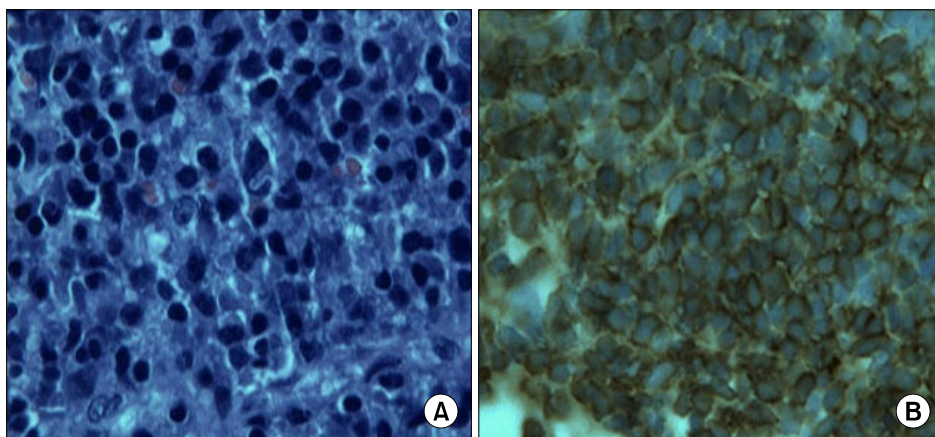


Fig. 3. Pathologic findings. (A) Large, globular abnormal lymphocytes are observed (H&E stain, ×1,000). (B) Strongly stained tumor cell (CD20 stain, ×1,000).

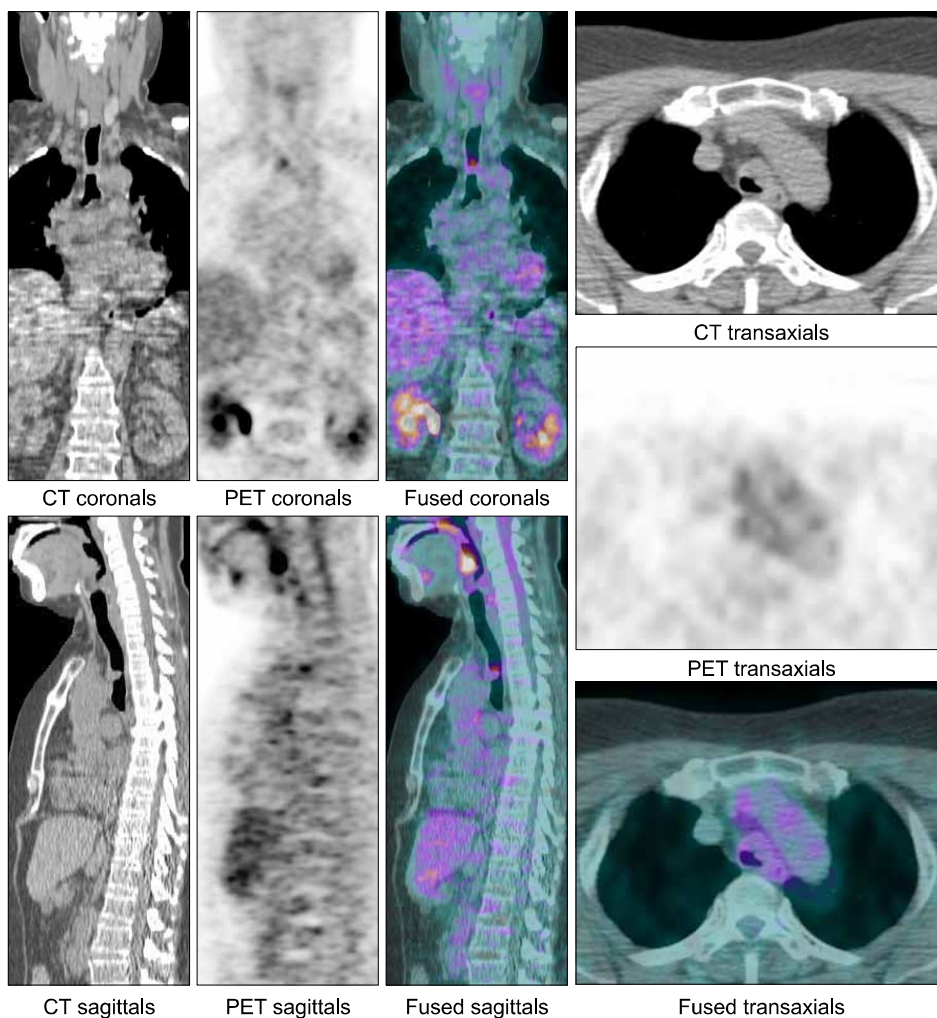


Fig. 4. PET-CT shows a 1.5×1.0cm sized polypoid mass lesion in trachea.

was performed. The follow-up bronchoscopic exam demonstrated that the size of the tracheal mass became reduced, thus indicating partial remission (Fig. 1B, C).

We performed the additional irradiation as adjuvant therapy. The patient received a total of 3,960cGy in twenty 198cGy fractions. Complete remission was confirmed by bronchoscopic exam (Fig. 1D). Currently, the patient was found to be in complete remission and has been alive for 26 months after initial diagnosis.

DISCUSSION

Primary tumors of the trachea are rare, and are usually malignant in adults and benign in children. Primary cancers of the upper respiratory

tract account for more than 1% of malignant diseases, but the frequency of tumors is not consistent throughout the upper respiratory tract. Although the supraglottis is affected in 1.3 per 100,000 people and the glottis is affected in 2.3 per 100,000 people, fewer than 0.04 of 100,000 people have tumors in the subglottis or trachea.¹⁾

About 33% of NHL cases arise in tissues other than the lymph nodes, spleen, Waldeyer's ring, and thymus, and these are referred to as primary extranodal NHL. Rosenberg et al. reported on 1,269 cases of primary extranodal non-Hodgkin's lymphoma. This study showed that the most common site of anatomical localization was skin, followed by tonsil, bone, stomach, and others. Furthermore, diffuse large B-cell lymphoma is a subtype of lymphoma that commonly has extra-

nodal presentation.⁶⁾

Primary tracheal tumors account for 0.1~0.4% of malignant diseases, with 2.6 new cases arising per million people every year.¹⁾ Fidiias P et al. described primary tracheal lymphoma in only six cases in a review study published in 1999.⁴⁾ Furthermore, from 1989 to 2005, only three cases of primary tracheal non-Hodgkin's lymphoma were reported with literature review in Medline.⁷⁾

In histological classification of primary tracheal lymphoma, the more common types are lymphoblastic lymphoma and mucosa-associated lymphoid tissue lymphoma.⁸⁾ The most frequently presenting symptom/sign was cough (49%), followed by dyspnea (44%), hemoptysis (44%), wheeziness (33%), stridor (20%), hoarseness (10%), and others.²⁾ In Korea, the most common site of primary extranodal non-Hodgkin's lymphoma was the stomach, followed by the intestine. Low incidence was found in the skin and bone. There were no reported cases for primary tracheal lymphoma.⁹⁾ In this patient, the symptoms is dry cough, weight loss, intermittent night sweats, and febrile sensation.

Furthermore, a tendency for extranodal lymphomas to remain localized for long periods of time is attributed to the migration of circulating mucosal B-lymphocytes back to their sites of origin, thus rendering the lymphomas amenable to local therapy. In addition, the observation that extranodal lymphoma often disseminates to other mucosal sites rather than peripheral lymphoid tissue is attributed to the homing properties of the mucosal B-lymphocytes to other mucosal sites. These extranodal recurrences are frequently responsive to local treatment, even when the patient is in Stage III or IV of the disease.^{3,5)}

Therefore, the combination R-CHOP regimen, consisting of rituximab plus CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), is now considered as the standard treatment for treating young and elderly patients with diffuse large B-cell lymphoma.¹⁰⁾

Although CT remains the gold standard for the

staging and follow-up of malignant lymphomas, ¹⁸F-FDG PET has a potential role in the accurate staging of disease and in predicting the response to therapy. This role has the potential to affect both the initial choice of chemotherapy and the decision to alter management based on the initial response to therapy.¹¹⁾

As mentioned in reviews by Malik E. Juweid et al., IV contrast-enhanced PET/CT likely provides at least equal information to that provided by the sum of the PET plus a separately performed contrast-enhanced CT, and therefore represents an adequate alternative. In addition, if hepatic or splenic involvement was demonstrated at initial staging, PET-CT performed without IV contrast appears to be adequate for response assessment of lymphomatous involvement of nodes or other extralymphatic organs that may not be detectable by PET. It was recommended that investigators should note that only PET or PET-CT systems, and not coincidence imaging, should be used for response assessment of lymphoma. In relation to bone marrow involvement, it was noted that bone marrow biopsy remains the standard procedure for assessment of bone marrow because of poor clinical correlation.¹²⁾

We diagnosed primary tracheal diffuse large B-cell lymphoma, that is actually extremely rare. After R-CHOP based chemoradiotherapy, complete remission was obtained. We reported primary tracheal diffuse large B-cell lymphoma with literature review.

요 약

비호지킨 림프종은 약 10% 정도는 림프절 외의 조직에서도 일어난다. 기관에서 원발성으로 발생하는 경우는 국제적으로도 극히 드문 것으로 보고되고 있으며, 대부분은 점막 관련 림프 조직 림프종으로 알려져 있다. 본 저자들은 건성 기침을 주소로 내원한 65세 여자 환자에서 기관지 내시경을 이용하여 조직학적으로 미만성 거대 B세포 림프종을 확진하였다. 환자는 이후 4 cycle의 R-CHOP과 adjuvant RT 시행 이후 완전관해를 유도하였으며, 26개월간 완전 관해 상태가 유지되고 있

다.

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