A Case of Adult T Cell Leukemia/Lymphoma Presenting as Severe Tracheal Stenosis

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Abstract

A 57-year-old woman was referred to our hospital for further examination of a tracheal stenosis shown on computed tomography findings. Bronchoscopy revealed multiple protruding tumors in the lumen of the trachea. Cytological findings of the cell block material from pleural effusion indicated that the T-cell lymphoma was composed of pleomorphic lymphoid cells. Serum human T-cell leukemia virus type1 antibody was positive and supported the clinical diagnosis of ATLL. Systemic chemotherapy induced the remarkable improvement of the lesions, the infiltrative lung shadow and the soft tissue neoplasm. We report a rare case of adult T cell leukemia/lymphoma (ATLL) with endobronchial involvement.

Key words: T cell lymphoma, tracheal stenosis, endobronchial involvement, ATLL

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Introduction

Adult T cell leukemia/lymphoma (ATLL) is one of the T-cell lymphomas caused by human T-cell leukemia virus type 1 (HTLV-1) (1). HTLV-1 is endemic in southwestern Japan, middle Africa, the Caribbean basin and Latin America (2). In Japan, there are 1 to 2 million carriers with HTLV-1 and 2-6% of the carriers represent ATLL (3). ATLL presents with lymph node involvement, but any site may be affected. Some cases with endobronchial involvement (EBI) have been reported, but such cases are rare (4, 5). In the present case, lymphoma cells infiltrated the trachea and pleural cavity, presenting with severe tracheal stenosis. T-cell lymphoma, suggestive for ATLL, was diagnosed by the cytological examination prepared from pleural effusion using the cell block technique, and confirmed by positive serum HTLV-1.

Case Report

A 57-year-old woman had a dry cough from July 2010. From August she felt exertional dyspnea and a sense of incongruity in her hypopharynx. Her symptoms became worse. The computed tomography (CT) on October 24th showed a stenosis of her trachea.

Therefore, she was referred to our hospital for further examination on October 27th. We could listen to the inspiratory stridor of her respiratory sound, while her SpO₂ was kept above 95% at room air. Laboratory findings on admission indicated elevated lactate dehydrogenase (LDH) 351 IU/L and soluble interleukin-2 receptor (sIL-2R) 25,620 U/mL (Table 1).

The chest X-ray and enhanced CT scan showed an infiltrative shadow in right upper lobe, soft tissue neoplasm protruding in bilateral main bronchus, all-round thickening of tracheal and bronchial wall, a wide range of stenosis in tra-
Table 1. Laboratory Data on Admission

<table>
<thead>
<tr>
<th></th>
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<th>yGTP</th>
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<tbody>
<tr>
<td>WBC</td>
<td>7600 /μL</td>
<td>25 U/L</td>
<td>HBsAg</td>
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<tr>
<td>Neu</td>
<td>66 %</td>
<td>T.bil</td>
<td>1.6 mg/dL</td>
<td>HCVAb</td>
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<tr>
<td>Lym</td>
<td>25.9 %</td>
<td>I.bil</td>
<td>1.2 mg/dL</td>
<td>HTLV-1Ab</td>
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<tr>
<td>Mon</td>
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<td>CPK</td>
<td>64 U/L</td>
<td></td>
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<tr>
<td>Eos</td>
<td>0.3 %</td>
<td>BUN</td>
<td>13 mg/dL</td>
<td>Pleural effusion</td>
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<tr>
<td>Bas</td>
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<td>Cr</td>
<td>0.4 mg/dL</td>
<td>color</td>
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<tr>
<td>RBC</td>
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<td>Na</td>
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<tr>
<td>Hb</td>
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<td>K</td>
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<td>Ht</td>
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<tr>
<td>Plt</td>
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<td>Ca</td>
<td>9.0 mg/dL</td>
<td>Alb</td>
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<tr>
<td></td>
<td></td>
<td>CRP</td>
<td>1.65 mg/dL</td>
<td>Amy</td>
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<tr>
<td></td>
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<td>Biochemical examination</td>
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<td>CA19-9</td>
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<td>Pro-GRP</td>
<td>21.4 pg/mL</td>
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<td></td>
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<td>ALT</td>
<td>14 U/L</td>
<td>SCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LDH</td>
<td>391 U/L</td>
<td>sIL-2R</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ALP</td>
<td>277 U/L</td>
<td></td>
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</table>

Figure 1. A-D: Chest X-ray and enhanced computed tomography on admission showed infiltrative shadow in right upper lobe, soft tissue neoplasm in bilateral main bronchus, all-round thickening of tracheal and bronchial wall, a wide range of stenosis in a trachea from the right side of thyroid to carina and right pleural effusion and enlarged lymph nodes in the mediastinum and cardiophrenic space.

A, B, C, D: Trans-tracheal aspiration cytology from the middle tracheal tumor was performed. The cytological diagnosis was malignant non-epithelial cells, suspicious for malignancy.

Chea from the right side of thyroid to carina, right pleural effusion and enlarged lymph nodes in the mediastinum and cardiophrenic space (Fig. 1A-D). Abdominal CT scan showed a soft tissue neoplasm in the head of pancreas (data not shown). On radiological findings, neither HTLV-1 associated bronchopneumopathy (HAB) nor HTLV-1 associated bronchiolo-alveolar disorder (HABA) was seen in the peripheral lung fields (data not shown). It was difficult to perform spirometry because of dyspnea.

Bronchoscopy revealed all-round stenosis in the lumen of the trachea extending from under vocal cord to the carina and multiple protruding tumors with hyperemic mucosal change extending from the middle trachea to the carina (Fig. 2A-D). Trans-tracheal aspiration cytology from the middle tracheal tumor was performed. The cytological diagnosis was malignant non-epithelial cells, suspicious for malignancy.
Figure 2. A: Bronchoscopy on admission revealed all-round stenosis in the lumen of trachea extending from under vocal code to the carina. B, C: Protruding tumors with hyperemic mucosal changes were found in the middle of trachea. D: A smooth protruding tumor from the anterior trachea caused stenosis in the carina.

The right pleural effusion was aspirated and cytologically examined. Cytospin preparations and cell block material revealed malignant cells, medium-sized to large lymphoid cells with irregular nuclei, intermingled with cerebriform giant cells (Fig. 3A). The nuclear chromatin was coarsely clumped with distinct nucleoli. Blast-like cells with dispersed chromatin were present. Giant cells with many nuclear convolutions and lobules, which have been described as “flower cells” were noted. Immunocytochemical study, performed on the cell block sections, revealed that the atypical cells were positive for leukocyte common antigen (LCA), CD3 and CD5 and negative for CD20 (Fig. 3). The cytological diagnosis was T-cell lymphoma composed of highly pleomorphic lymphoid cells, suggestive for ATLL. At the time, we needed to start the medication as soon as possible because the stenosis of her trachea was rapidly progressing. We could not determine HTLV-1 proviral DNA by the Southern blotting method in the absence of fresh samples. We confirmed the diagnosis as clinical ATLL (Ann-Arbor stage IV) based on the serum HTLV-1 antibody positivity and clinical data.

She was treated with two cycles of VCAP-AMP-VECP therapy (vincristine 1 mg/m², cyclophosphamide 350 mg/m², adriamycin 40 mg/m², prednisolone 40 mg/m²: day1, adriamycin 30 mg/m², ranimustine 60 mg/m², prednisolone 40 mg/m²: day8, vindesine 2.4 mg/m², carboplatin 100 mg/m²: day15, etoposide 100 mg/m², prednisolone 40 mg/m²: day 15~17). After the treatment, sIL-2R level decreased to 729 U/mL. CT and bronchoscopic findings after the chemotherapy showed remarkable improvement in all of the lesions; in particular, there was disappearance of infiltrative lung shadow, reduction in the size of the soft tissue neoplasm, and opening of lumen in her trachea (Fig. 4). We are currently planning bone marrow transplantation after the completion of four cycles of chemotherapy.

Discussion

ATLL is a hematologic malignancy with a poor prognosis that commonly involves leukemic infiltrates in a variety of organs. ATLL is also known to show a variety of types of broncho-pulmonary involvement in the distal respiratory tract, while those in the more proximal tracts including in the trachea and larger size of bronchi are rare. In a retrospective review of 87 ATLL patients, abnormal findings on CT were seen in 60 patients, ground-glass attenuation in 37, centrilobular nodules in 25, consolidations in 13, thickening of bronchovascular bundles in 22, enlarged lymph nodes in 27 and pleural effusion in 22 (6). However, there was no case which showed EBI.

However, in a literature review of the association with a category of non-Hodgkin lymphoma beyond ATLL, reports of EBI are accumulating. Related case reports in the 1980s were written without awareness of ATLL since the concept of the disease had only just been established (7-10). In 1992 Tanigawa et al reported 47 cases of non-Hodgkin’s lymphomas with EBI who had been encountered by 1990, but no
Figure 3. Cell block sections from pleural effusion. A: The infiltrate consisted of medium-sized to large lymphoid cells with irregular nuclei, intermingled with cerebriform giant cells (arrow) (Hematoxylin and Eosin staining). B: Leukocyte common antigen (LCA) staining showed the positivity of the neoplastic cells, indicates malignant lymphoma. C: CD3 staining, Neoplastic cells were positive. D: CD20 staining. Neoplastic cells were negative whereas reactive small B-lymphocytes positive.

Figure 4. CT scan and bronchoscopic findings after the treatment showed the remarkable improvement of the lesions including the disappearance of infiltrative lung shadow, enlarged patency of the carina, reduction in the size of soft tissue neoplasm, and opening of lumen in her trachea.

case of ATLL was included (5). Ninety-six cases who had been encountered in Japan between 1990 and 2007 revealed only a few patients with ATLL (11, 12). Thus, ATLL with EBI is very rare in the literature.
Rose et al. classified the EBI of non-Hodgkin’s lymphoma into 2 types; the Type 1 pattern is characterized by diffuse submucosal infiltrates occurring in the presence of intra- and extrathoracic lymphoma (10). In the Type 2 pattern, the central airway is involved by a solitary mass in the absence of clinically apparent systemic lymphoma. Moreover, there is a modified classification in a Japanese report, which adds diffuse submucosal infiltration to the two patterns previously described (5).

In the present case, the bronchoscopy on admission showed all-round bronchial wall thickening, protruding elastic and hemorrhagic tumors, hyperemic mucosal changes and disappear of bronchial cartilaginous rings. Thus, we considered that these lesions represented submucosal diffuse lymphomatous involvement of the airways. In addition, the bronchoscopy after two cycles of chemotherapy revealed reduced multiple submucosal nodules even in the peripheral bronchus, suggesting that the EBI was a type 1 pattern in this case.

In the type 1 pattern, most patients had the initial and advanced disease (Ann-Arbor stage IV), and these radiological findings of parenchymal infiltration were frequently seen (5, 10). The features of the present case corresponded with these characteristics. In fact there are only a few reported data of this classification, therefore, it is difficult to estimate her prognosis.

Various mechanisms have been suggested as being responsible for the development of the endobronchial lesion in patients with lymphoma: (i) direct invasion from an adjacent mediastinal lymph node, (ii) direct invasion from a parenchymal lesion, (iii) lymphatic dissemination to the peribronchial tissues, and (iv) hematogenous dissemination (8). In the present case, all-round thickening of tracheal and bronchial wall and submucosal infiltration without paratracheal lymphadenopathy suggest that the lymphatic dissemination to the peritracheal tissues was involved in the lesion formation.

In the present case, we were unable to determine the monoclonal HTLV-1 pro-virus in the bone marrow aspirate. Because her tracheal stenosis was so severe, we could not afford to wait for surgical biopsy. The cytological examination, by the cell block technique and immunocytochemical study, prepared from pleural effusion, lead to the diagnosis of ATLL (13).

For chemotherapy, the recent review in ATLL treatment by Tsukasaki et al. (14) suggested that VCAP-AMP-VECP regimen is superior to biweekly cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). The rate of complete response (CR) was higher in the therapy compared to the biweekly CHOP therapy (40%-25%, respectively p=0.02). The overall survival (OS) at 3 years was 24% in the VCAP-AMP-VECP therapy and 13% in the CHOP therapy (p=0.085) (14). For the present case, we introduced the VCAP-AMP-VECP regimen, which induced a partial response (PR). Later, we will do an allogeneic hematopoietic stem cell transplantation (allo-HSCT).

The authors state that they have no Conflict of Interest (COI).

References