Human T-cell Lymphotrophic Virus Type-1 (HTLV-1)-associated Bronchioloalveolar Disorder Presenting with Mosaic Perfusion

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Abstract

Human T-cell lymphotropic virus type-1 (HTLV-1)-associated bronchioloalveolar disorder (HABA) is a specific state with chronic and progressive respiratory symptoms caused by bronchiolar or alveolar disorder characterized by smoldering adult T-cell leukemia or the HTLV-I carrier state. We herein report a rare case of HABA with an initial presentation of mosaic perfusion in the lung. The diagnosis was made according to the results of a flow cytometry analysis of the bronchoalveolar lavage fluid and pathological findings. Clinicians must be careful to recognize that mosaic perfusion may be a radiological finding of HABA.

Key words: human T-cell lymphotropic virus type-1 associated bronchioloalveolar disorder, mosaic perfusion, air trapping, flow cytometry

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Introduction

Human T-cell lymphotropic virus type-1 (HTLV-1) infection is endemic in tropical areas and in southwestern Japan and has now been identified in the United States and some European countries (1). HTLV-1 is an etiological retrovirus of adult T-cell leukemia/lymphoma (ATLL) and is also associated with a nonmalignant neurological disorder termed HTLV-1-associated myelopathy (HAM) (2). The lung is a preferential site for HTLV-1 infection. Pulmonary computed tomography (CT) findings in HTLV-1 carriers mainly demonstrate centrilobular nodules, ground-glass opacities, and thickening of the bronchovascular bundles (3). We herein report our experience with a rare case of HTLV-1-associated bronchioloalveolar disorder (HABA) presenting with mosaic perfusion in the lung.

Case Report

The patient was a 63-year-old Japanese non-smoking woman in whom an obstructive ventilatory impairment had been noted during a medical examination in 2011. In October 2013, she complained of sensory disturbance of her lower limbs and underwent neurology consultation at another hospital. Because she was positive for HTLV-1 antibody in her serum and cerebrospinal fluid, the patient was suspected of having HAM. However, her symptoms improved with only symptomatic treatment over a 2-month period. Therefore, she was diagnosed as having degenerative lumbar spondylosis, and not HAM. Afterwards, the patient complained of slight dyspnea on exertion, and abnormal shadows were noted on chest CT in January 2014. Because these abnormalities did not improve, she was referred to our

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At this admission, the physical examination did not reveal Raynaud’s phenomenon, any eruptions or swelling of any joints, or dry eyes or mouth. Clubbing was not evident. The patient had a normal respiratory rate (15 breaths per minute), normal heart rate (76 beats per minute) with a blood pressure of 128/80 mmHg, and body temperature of 36.4°C. Chest auscultation revealed no abnormal findings. The laboratory data on admission included an arterial blood gas analysis at room air, which showed a partial pressure of oxygen of 91.5 Torr, partial pressure of carbon dioxide of 38.7 Torr, and pH of 7.388. Her white blood cell count was 6,000/μL. No abnormal cells were detected in a peripheral blood smear. The lactate dehydrogenase (LDH) level was 192 IU/L, and soluble IL-2 receptor was 454 U/mL (within the normal range). Anti-nuclear antibody was 40 titers according to immunofluorescence testing; however, no other autoantibodies including anti-DNA, anti-Sm, anti-Scl 70, anti-SS-A, anti SS-B, and anti-Jo-1 antibody were detected. Brain natriuretic peptide was slightly elevated at 26.8 pg/mL. Her HTLV-1 antibody was elevated at 4,096 titers using the particle agglutination method, and no monoclonal integration of proviral DNA using the Southern blotting method was found. Therefore, the patient was diagnosed as being an HTLV-1 carrier.

A chest CT scan in the expiratory phase revealed inhomogeneous lung attenuation, compared with the inspiratory phase (A-C). The vessel size in the areas of lower attenuation is only slightly reduced, thus indicating mosaic perfusion as a cause of inhomogeneous lung attenuation.
the lung was performed from the right S6 for the diagnosis. Thereafter, a thoracoscopic biopsy of infected lymphocytes resulted in an inflammatory response. Therefore, we speculated that the accumulation of HTLV-1-eral blood and compared with healthy subjects (4) (Table). The percentages of CD4+ cells (83.1%), CD25+ cells (40.7%), and CD4+CD25+ cells (39.0%) were significantly higher in the BALF than in CD4+cells (53.0%), CD25+ cells (27.6%), and CD4+CD25+ cells (26.0%) in the peripheral blood. Histologically, the biopsied lesion incorporated a part of the dilation from the bronchiole to the alveoli, and slight lymphoid cell infiltration around the bronchiole (Hematoxylin and Eosin staining 25x) (A). Stenosis of the bronchiolar lumen was not seen [elastic-van gieson (EVG) stain 25x] (B). Moreover, no atypical lymphocyte cells or foamy macrophages were present.

Table. Lymphocyte Subsets in BALF and Peripheral Blood of the Patient and Healthy Subjects.

<table>
<thead>
<tr>
<th>Positive rate</th>
<th>BALF (%)</th>
<th>Peripheral blood (%)</th>
<th>BALF in healthy subjects (%) (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD 2</td>
<td>98.2</td>
<td>89.0</td>
<td></td>
</tr>
<tr>
<td>CD 3</td>
<td>87.8</td>
<td>69.1</td>
<td>72±8</td>
</tr>
<tr>
<td>CD 4</td>
<td>83.1</td>
<td>53.0</td>
<td>42±6</td>
</tr>
<tr>
<td>CD 8</td>
<td>13.3</td>
<td>20.3</td>
<td>36±11</td>
</tr>
<tr>
<td>CD 25</td>
<td>40.7</td>
<td>27.6</td>
<td></td>
</tr>
</tbody>
</table>

BALF: bronchoalveolar lavage fluid, CD: cluster of differentiation

Discussion

We herein describe the rare case of a patient with HABA presenting with mosaic perfusion in the lung. HABA is a specific state with chronic and progressive respiratory symptoms caused by bronchiolar or alveolar disorder characterized by smoldering adult T-cell leukemia or the HTLV-I carrier state (5). Patients with HAM and HTLV-1-associated uveitis who are in the carrier state, as shown with polyclonal integration of proviral DNA, have frequent pulmonary complications characterized by T-lymphocytic alveolitis (6). However, unlike patients with ATLL, neither leukemic cells nor pathogens associated with opportunistic infections are found in the lungs of carriers of HTLV-1. Surprisingly, a similar pulmonary involvement has been observed in asym-
tomatic carriers of HTLV-1. These reports suggest the possibility that the lung is the preferential site for HTLV-1 infection and that this peculiar tropism is responsible for the high incidence of pulmonary involvement (3).

The HTLV-1 proviral load in the BALF appeared to be related to the proportion of lymphocytes in the BALF of HTLV-1 carriers, as reported previously (7). Seki et al. reported that a significantly higher number of total cells, percentage, and absolute number of lymphocytes were present in the BALF of HTLV-1 carriers, together with a significantly lower percentage of alveolar macrophages, compared with these values in healthy controls (8). Furthermore, in HTLV-1 carriers, the percentages of CD3+ and CD3+CD25+ cells are significantly higher in the BALF than in peripheral blood (9). The results of these studies have suggested that HTLV-1 infection could induce chronic inflammation in the lung through immunologic mechanisms. In our patient, the BALF was analyzed using flow cytometry, and nearly identical results were obtained. Therefore, we speculate that the accumulation of HTLV-1-infected lymphocytes resulted in a particular lung inflammatory response.

Pathological findings with chronic pulmonary diseases associated with HTLV-1 were found in chronic bronchiolitis (43.8%), diffuse panbronchiolitis (28.1%), chronic fibrosing interstitial pneumonia (15.6%), ATLL invasion (9.4%), and lymphoproliferative disease (3.1%) (10). Our patient was diagnosed as having chronic bronchiolitis, and according to the results of the flow cytometry analysis of the BALF and the histological findings, the diagnosis of HABA was compatible.

Radiological findings of HTLV-1 carriers consist mainly of centrilobular nodules (97.0%), thickening of the bronchovascular bundles (56.0%), ground-glass opacities (52.0%), and bronchiectasis (51.0%) (3). In our patient, slight thickening of the bronchovascular bundles was found, but no existence of centrilobular nodules, and interestingly, mosaic perfusion was conspicuous. Mosaic perfusion may be present in patients who have airway obstruction with reflex vasoconstriction or in patients with vascular obstruction, such as that occurring in pulmonary embolism. In many patients, a distinction may be made between airway and vascular obstruction as a cause of mosaic perfusion using expiratory scans (11). Because air trapping is commonly present in patients with mosaic perfusion related to airway disease, we therefore suspected our patient to have BO. In our case, although lymphoid cell infiltration around the bronchiole and the dilation from the bronchiole to the alveoli were confirmed, stenosis and destruction of the bronchioles were not observed. Her pathological findings were not compatible with BO, and thus the patient was ultimately diagnosed as having HABA. Furthermore, we speculate that chronic lymphoid infiltration around the bronchiole leads to hypoventilation and secondary vasoconstriction. This vasoconstriction can be observed as areas of decreased attenuation. In the uninvolved segments of the lung with normal ventilation, there is normal or increased perfusion, which results in normal to increased attenuation on chest CT images. This combination of low attenuation changes in the involved regions with higher attenuation areas in the uninvolved regions is referred to as mosaic perfusion.

To the best of our knowledge, only one case of HABA presenting with mosaic perfusion case has been reported previously (12). In this case, diffuse centrilobular nodules were found at diagnosis, and 7 years later, mosaic perfusion manifested with progressive stenosis of the bronchioles. In contrast, our patient was initially found to have mosaic perfusion. We propose two possible explanations for this discrepancy. First, bronchiolitis is commonly seen as centrilobular nodules, thus we presumed that the lymphoid cell infiltration around the bronchioles was slight in our patient. Therefore, nodules may not have been found, reflecting an early stage of the lesion. Second, although our patient’s pathological findings were not necessarily BO, these regions may be an early stage or subtype of BO. Hartman et al. reported that the radiological findings of centrilobular nodules are direct signs. On the other hand, these regions are an uncommon finding of BO (13). Because the disease concepts of HABA have been obscure, it may present various patterns of radiological and pathological findings.

The treatment of HABA has not yet been clearly established, however, Kadota et al. reported that some patients received a positive long-term effect with the use of macrolides (14). Further studies are needed to clarify the efficacy of this therapeutic regimen for the management of HABA.

In conclusion, we herein reported a rare radiological case of HABA with an initial presentation of mosaic perfusion in the lung. The diagnosis was made according to the results of the flow cytometry analysis in the BALF, which was a useful strategy for the diagnosis of HABA. Case reports on HABA presenting with mosaic perfusion are rare, and thus, this educational case is worth reporting.

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

References


