



## Case report

## Smoldering adult T-cell leukemia complicated with pneumocystis pneumonia: A case report

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## ABSTRACT

Adult T-cell leukemia (ATL) is a tumor of CD4-positive T cells that accompanies an infection by human T-cell lymphotropic virus (HTLV-I). ATL is classified into four types—acute, lymphomatous, chronic, and smoldering. Opportunistic infections are known to occur in patients with acute or lymphomatous type ATL; however, whether patients with chronic or smoldering ATL also have a high risk of opportunistic infections is not yet known. Herein, we report a case of pneumocystis pneumonia in a patient with smoldering ATL. He was a 64-year-old man with primary complaints of cough and dyspnea on exertion. A chest radiograph showed infiltration shadows in the left lung field. He was prescribed antibiotics for pneumonia; however, his symptoms worsened, and he developed hypoxemia. White-blood cell count was 13000/ $\mu$ L, and 7% of atypical lymphocytes were found in the smears of peripheral blood cells. His serum  $\beta$ -D glucan concentration was increased to 85.9 pg/mL, and his serum tested positive for anti-HTLV-1 antibody. Chest-computed tomography revealed diffuse ground-glass opacities in the bilateral lung fields. Pneumocystis-polymerase chain reaction performed on bronchoalveolar lavage fluid confirmed pneumocystis, but atypical lymphocytes were not detected via transbronchial lung biopsy. Therefore, he was diagnosed with pneumocystis pneumonia associated with smoldering ATL. Sulfamethoxazole-trimethoprim and corticosteroid therapies were administered to treat the pneumocystis pneumonia, and his symptoms and lung shadows improved rapidly. Thus, opportunistic infections, including pneumocystis pneumonia, may be caused by smoldering ATL. In the case of atypical lymphocyte detection in peripheral-blood smears, clinicians should consider the possibility of ATL.

## 1. Introduction

Adult T-cell leukemia (ATL) is a tumor of CD4-positive T cells, accompanying retroviral infections, such as by human T-cell lymphotropic virus (HTLV-I). Approximately 10–20 million people are estimated to be infected by HTLV-I worldwide [1], and the lifetime risk of developing ATL is 1–5% [1]. ATL is diagnosed with the presence of serum anti-HTLV-1 antibodies and atypical T-cell lymphocytes in the peripheral blood and/or lymphadenopathy, skin or other organ lesions. ATL is classified into four types—acute, lymphomatous, chronic, and smoldering [2]. Acute and lymphomatous types, also called aggressive

ATL, involve hematopoietic malignant tumors with poor prognosis. Aggressive ATL is treated with potent chemotherapy and hematopoietic stem cell transplantation. Chronic and smoldering types, also called indolent ATL, have relatively mild courses and are thus followed-up without treatment if there are no symptoms. Opportunistic infections are known to occur in patients with aggressive ATL, and the immunocompromised status is mainly caused by the infection of CD4<sup>+</sup>CD25<sup>+</sup> T cells with HTLV-1 [3]. However, whether patients with indolent ATL have a high risk of opportunistic infections remains to be established [1]. Herein, we report a case of pneumocystis pneumonia in a patient with smoldering ATL.

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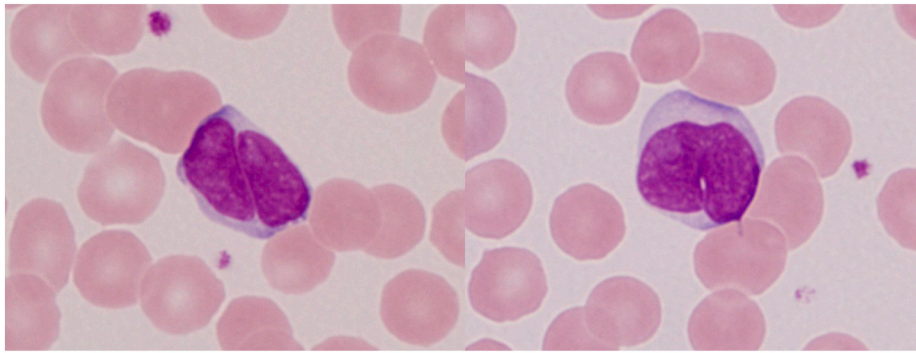


Fig. 1. Peripheral-blood smear using May–Grunwald–Giemsa (MGG) stain shows atypical lymphocytes with pale-colored cytoplasm and clefted nuclei.

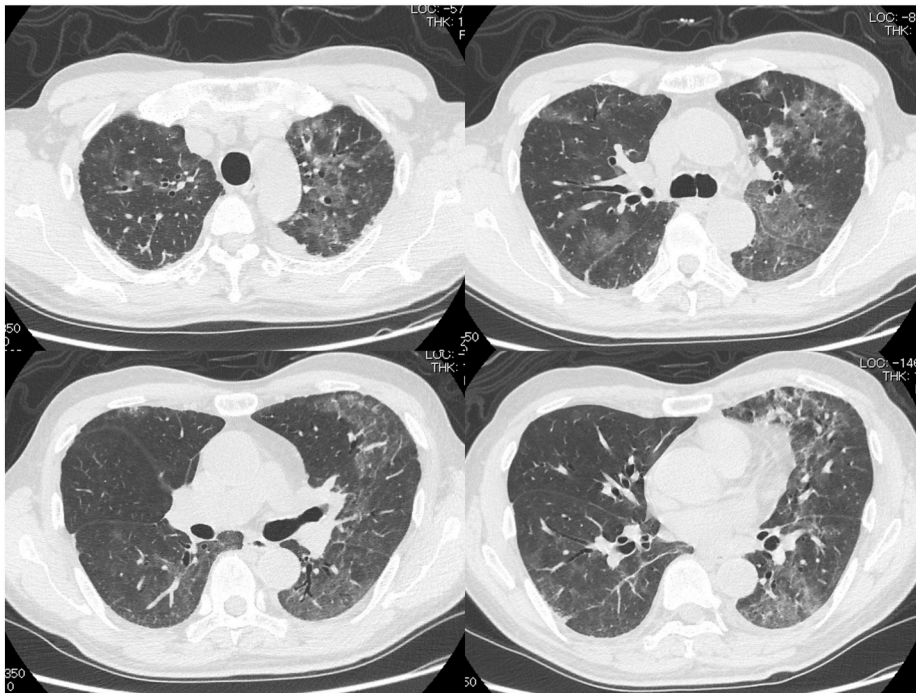


Fig. 2. Chest-computed tomography scan, obtained on admission, shows infiltration and diffuse ground-glass opacity in the bilateral lung fields.

## 2. Case report

A 64-year-old man presented to a nearby hospital with primary complaints of cough and dyspnea on exertion. He had neither pertinent medical history, including pulmonary, renal, or immunocompromising diseases nor family medical history involving ATL. Chest radiography showed infiltration shadows in the left lung field. Left-lung pneumonia was considered, and antibiotics were administered accordingly; however, the symptoms worsened and led to hypoxemia, and he was subsequently referred to our department on the next day. His body temperature was increased to 38 °C, and his oxygen saturation was 92% in ambient air. His white-blood cell count was 13000/ $\mu$ L, of which 20% were lymphocytes; in addition, 7% of atypical lymphocytes were found in the peripheral-blood smears (Fig. 1). His serum  $\beta$ -D glucan concentration was increased to 85.9 pg/mL, and his serum tested positive for anti-HTLV-1 antibodies. Bone-marrow aspiration was performed; atypical lymphocytes were not detected, but clonal T-cell receptor gene rearrangements were confirmed. In addition, HTLV-I proviral DNA was detected in the peripheral-blood lymphocytes. Chest-computed tomography (CT) revealed diffuse ground-glass opacities in the bilateral lung fields (Fig. 2). Pneumocystis-polymerase chain reaction performed on

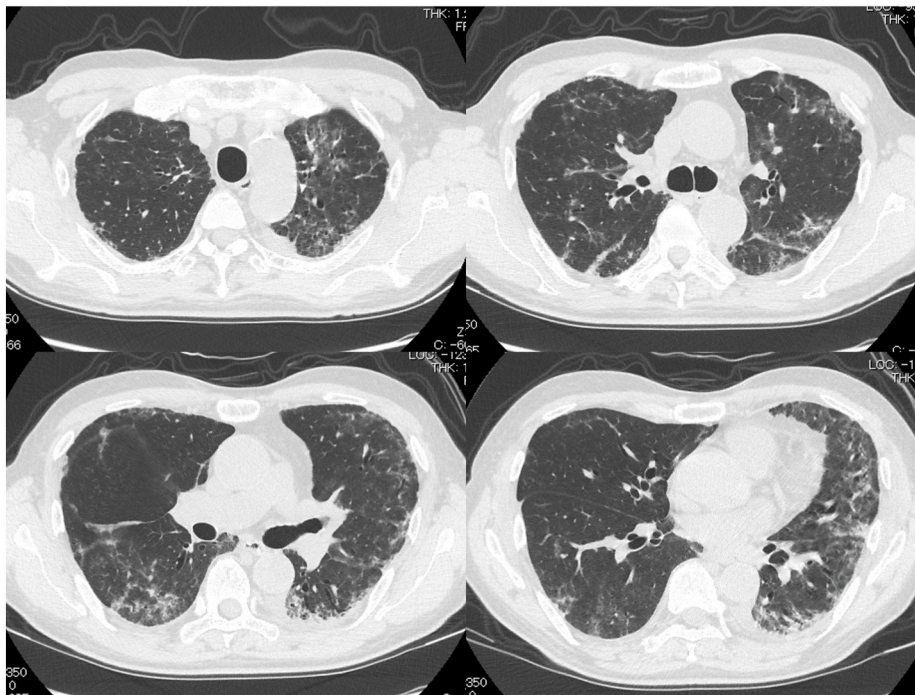
bronchoalveolar lavage fluid confirmed pneumocystis, but ATL cells were not detected via transbronchial lung biopsy. Therefore, he was diagnosed with pneumocystis pneumonia associated with smoldering ATL. Sulfamethoxazole-trimethoprim and corticosteroid therapies were started to treat pneumocystis pneumonia, after which his symptoms and lung shadows improved rapidly (Fig. 3). Fourteen months later, he contracted cryptococcal meningitis but recovered after treatment with antifungal agents. The patient is still alive after 3 years.

Informed written consent was obtained from the patient for publication of this case report and accompanying images.

## 3. Discussion

In this case report, we present two important clinical observations. First, smoldering ATL may cause opportunistic infection, including pneumocystis pneumonia. Previously, some cases of opportunistic infections, mainly pneumocystis pneumonia and cryptococcosis, have been reported in HTLV-I carriers or patients with smoldering ATL [3,4]. These studies suggested that HTLV-I infection or smoldering ATL may reduce the cell-mediated immunity. High frequency of FoxP3-positive cells among CD4<sup>+</sup> T cells has previously been reported in patients





**Fig. 3.** The findings from chest-computed tomography scan after 3 weeks of sulfamethoxazole-trimethoprim and corticosteroid therapies. The diffuse ground-glass opacity in the bilateral lung fields improved.

with ATL as well as asymptomatic HTLV-I carriers with high proviral load [5]. FoxP3 is a specific marker of CD4<sup>+</sup>CD25<sup>+</sup> regulatory T cells with immunosuppressive properties [6]. The findings of the present study may support the status of cell-mediated immunosuppression in patients with smoldering ATL.

Second, atypical lymphocytes in peripheral-blood smears may lead to the diagnosis of smoldering ATL. To diagnose ATL, detection of ATL cells in peripheral blood is required [7]. Typical ATL cells have highly lobulated and clefted nuclei, with homogenous and condensed chromatin, small or absent nucleoli, and agranular and basophilic cytoplasm; they are also called “flower cells.” However, ATL cells have been recognized and reported to be morphologically diverse [8,9]. Peripheral-blood atypical lymphocytes also appear in several viral infections. However, if lymphocytes show unusual morphology, clinicians should consider the possibility of ATL as well, and additional examination, such as bone-marrow aspiration and polymerase chain reaction for HTLV-I proviral DNA should be performed.

Pulmonary complications are common in patients with ATL; approximately half of these complications are related to ATL-cell infiltration and the other half to infections. Even in the cases of chronic and smoldering types, pulmonary infiltration of ATL cells is detected [10]; and, bronchoscopic examinations play a key role in the diagnosis. Patients with both ATL and pulmonary complications demonstrate several abnormal findings on chest CT, such as ground-glass attenuation, centrilobular nodules, thickening of bronchovascular bundles, and consolidation [11]. If chest radiography reveals abnormal findings in patients with ATL, bronchoscopic examination should be considered to confirm whether the lesions correspond to infiltration of ATL cells.

In conclusion, we reported a case of pneumocystis pneumonia in a patient with smoldering ATL. Opportunistic infections, including pneumocystis pneumonia, may be caused by smoldering ATL. If atypical lymphocytes are detected in peripheral-blood smears, clinicians should consider the possibility of ATL.

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The authors have no ethical conflicts to disclose.

#### Declaration of competing interest

The authors of this work have no conflict to disclose.

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