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【 CASE REPORT 】

# CD56-positive Angioimmunoblastic T-cell Lymphoma Complicated by Chylothorax

Hiroki Hori[1], Yasuhiro Tanaka[1], Ryuko Nakayama[2] and Masaharu Nohgawa[1]

**Abstract:**
A 77-year-old woman presented with systemic lymphadenopathy and bilateral pleural effusion. Angioimmunoblastic T-cell lymphoma (AITL) was diagnosed based on the results of a lymph node biopsy. AITL cells expressed the aberrant antigen of CD56. The bilateral pleural effusion was attributed to chylothorax, not the infiltration of lymphoma cells into the pleura, as determined by the pleural fluid analysis. We therefore diagnosed her with CD56-positive AITL complicated by chylothorax. She achieved complete remission by multidrug chemotherapy. AITL is commonly complicated by pleural effusion, but rarely by chylothorax. This is the first case of CD56-positive AITL complicated by chylothorax.

**Key words:** angioimmunoblastic T-cell lymphoma, CD56 positivity, pleural effusion, chylothorax

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## Introduction

Angioimmunoblastic T-cell lymphoma (AITL) is a mature T- and NK-cell neoplasm characterized by multiple lymphadenopathy and hepatosplenomegaly. In AITL, the neoplastic T-cells characteristically express the immunophenotype of normal follicular helper T-cells, such as CD10, in addition to the pan-T-cell antigens. However, the aberrant expression of antigens such as CD56 is rare (1). The clinical significance of aberrant antigen expression in AITL is unclear.

AITL is occasionally complicated by pleural effusion because of the infiltration of several types of cells into the pleura. Almost all cases of pleural effusion in AITL have been cytologically proven to be malignant (2). However, rare cases of AITL complicated by chylothorax have been reported.

We encountered a case of CD56-positive AITL complicated by bilateral chylothorax at the diagnosis. Our patient achieved complete remission with multidrug chemotherapy.

## Case Report

A 77-year-old woman was transferred to our hospital for the evaluation of bilateral pleural effusion in March 2020. She had a history of uterine cancer over 20 years earlier. She had shown cerebral hemorrhaging two months previously and continued her rehabilitation at another hospital. She complained of dyspnea during rehabilitation, and chest X-ray revealed bilateral pleural effusion. At the time of admission, her body temperature was slightly elevated at 37.8 °C, blood pressure was 104/68 mmHg, heart rate was elevated at 97 beats per minute, respiratory rate was 22 breaths per minute, and oxygen saturation was 98% under 1 L nasal cannula. On a physical examination there were multiple enlarged lymph nodes palpable in the bilateral cervical and inguinal areas, and reduced breast sounds on auscultation.

A laboratory examination showed an elevated white blood cell count (WBC; 13,100/μL) and levels of lactate dehydrogenase (LDH; 708 U/L; normal range, 124-222), C-reactive protein (5.94 mg/dL), and soluble interleukin-2 receptor (sIL-2R; 4,738 U/mL; normally below 496). Her hemoglobin level was slightly decreased at 10.8 g/dL. The serum total protein and albumin levels had decreased to 5.5 and 2.6 g/dL, respectively. No hyper-gamma-globulinemia was detected. She was negative for the antibody to human T-cell leukemia virus type 1.

Computed tomography (CT) showed multiple lymphade-

[1]Department of Hematology, Japanese Red Cross Wakayama Medical Center, Japan and [2]Department of Diagnostic Pathology, Japanese Red Cross Wakayama Medical Center, Japan
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Correspondence to Dr. Yasuhiro Tanaka, yasutanaka1717@gmail.com

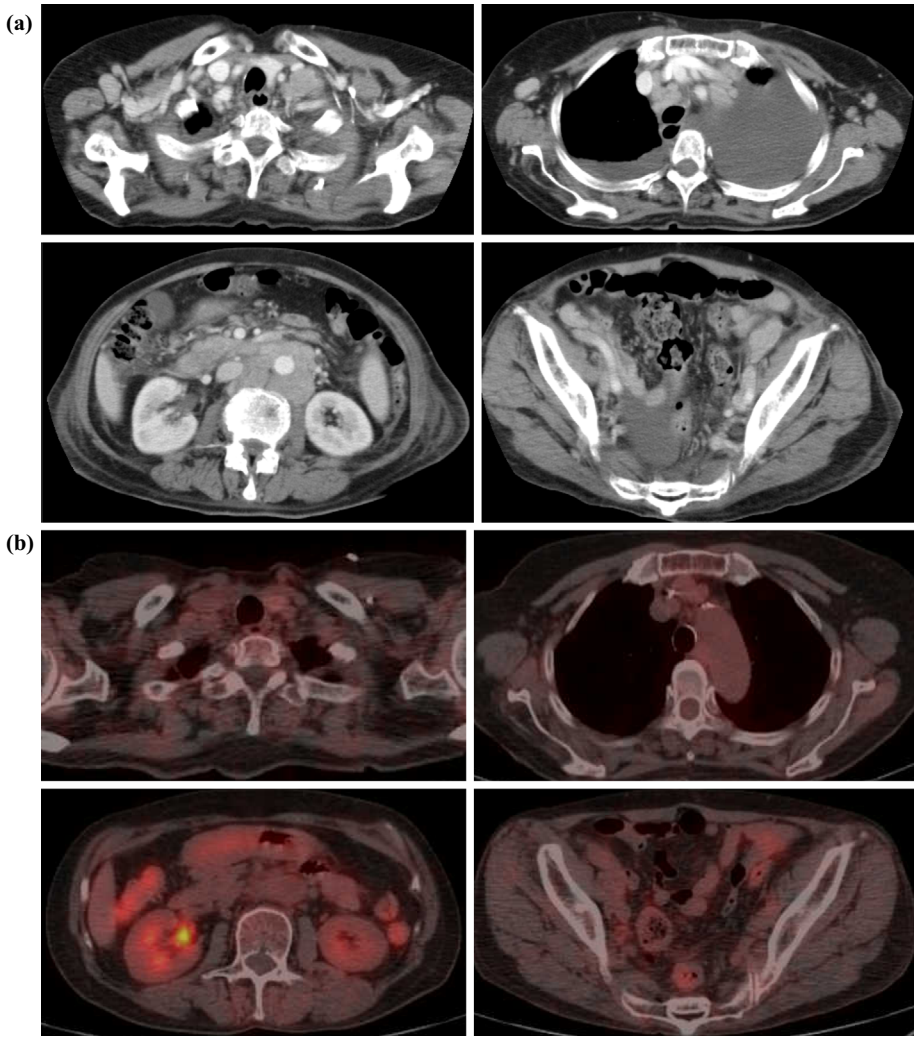


**Figure 1. CT images at the diagnosis. (a) CT shows multiple lymphadenopathy in the bilateral supraclavicular fossae, bilateral axilla, mediastinum, para-aorta, and bilateral external iliac areas as well as bilateral pleural effusion and ascites. (b) PET-CT after six courses of CHOP chemotherapy shows no abnormal accumulation of fluorodeoxyglucose in the whole body.**

nopathy involved in the bilateral supraclavicular fossae, bilateral axilla, mediastinum, para-aorta, and bilateral external iliac areas as well as bilateral pleural effusion and ascites (Fig. 1a).

A left cervical lymph node biopsy was performed on day 8 of hospitalization. A histopathological examination revealed that medium-sized abnormal lymphocytes with pale cytoplasm densely occupied the biopsied lymph node, admixed with the infiltration of eosinophils, plasma cells, and histiocytes and the proliferation of highly endothelial venules (HEVs). Large abnormal lymphocytes were few in number (Fig. 2a). An immunohistochemical analysis showed that the medium-sized abnormal lymphocytes were positive for CD3, CD4 (Fig. 2b), CD5, CD10 (Fig. 2c), CD56 (Fig. 2d), BCL2, BCL6, CXCL13 (Fig. 2e), and PD-1 (Fig. 2f), and negative for CD38, CD45RO, CD57, and granzyme B. The Ki-67 labeling index was above 80%. The large abnormal cells expressed CD20, CD30, and CD79a. CD21-positive follicular dendritic cells (FDCs) proliferated around HEVs (Fig. 2g). Epstein-Barr virus-encoded small RNA *in situ* hybridization (EBER-ISH) was positive only for large abnormal cells (Fig. 2h). A flow cytometric analysis showed that the abnormal lymphocytes were positive for CD2, CD4, CD5, CD10, and CD56, and negative for CD3, CD7, CD8, CD16, CD20, and CD30. These results led to the diagnosis of AITL in accordance with the World Health Organization (WHO) 2016 classification (1).

A chromosomal analysis using G-banding showed a normal karyotype. A T-cell receptor rearrangement analysis was not carried out. A bone marrow examination did not showed the infiltration of abnormal lymphoid cells. Pleural thoracentesis was carried out on day 1 of hospitalization. The color of the punctured pleural effusion was milky white. A laboratory examination of the pleural effusion showed an elevated WBC (1,130/μL with 61.5% lymphocytes, 23.2% neutrophils, 9.8% monocytes, and 5.8% eosinophils), LDH level (256 U/L), and triglyceride level (387 mg/dL). The level of total protein was decreased to 3.3 g/dL. These results indicated that the pleural effusion was exudative.

A cytological analysis revealed the predominance of reac-

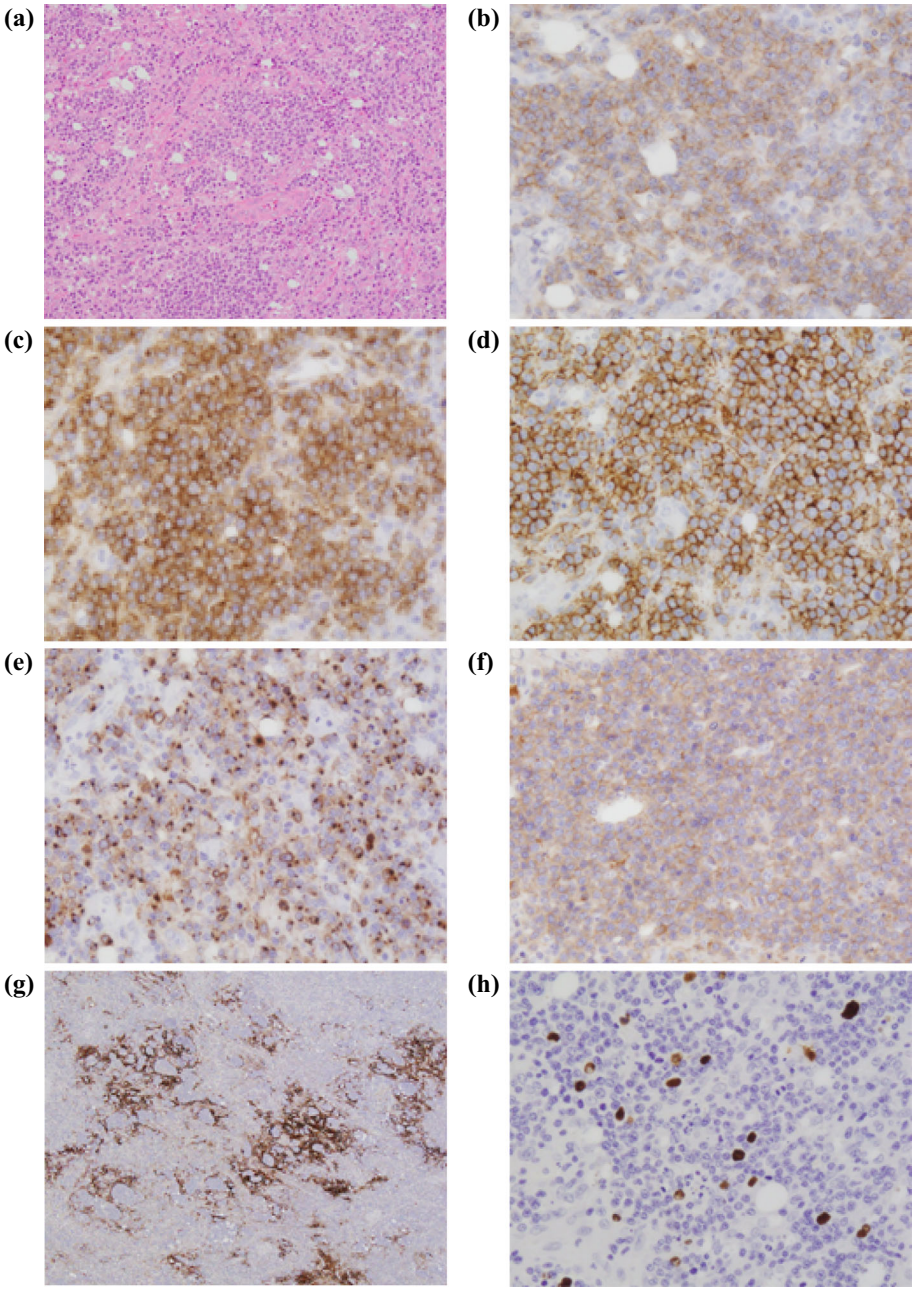


**Figure 2.** **Histopathological findings of the biopsied lymph node. (a) Medium-sized abnormal lymphocytes with pale cytoplasm densely occupied the biopsied lymph node, admixed with the infiltration of eosinophils, plasma cells, and histiocytes, and the proliferation of HEVs (Hematoxylin and Eosin staining; original magnification, ×20). An immunohistochemical analysis of the biopsied cervical lymph node showed that medium-sized abnormal cells were positive for CD4 (b), CD10 (c), CD56 (d), CXCL13 (e), and PD-1 (f) (original magnification, ×40). (g) CD21-positive FDCs proliferated around HEVs. (h) EBER-ISH was positive only for large abnormal cells.**

tive lymphocytes without abnormal lymphoid cells. These results indicated that the pleural effusion was due to chylothorax. We therefore considered her to have CD56-positive AITL complicated by chylothorax.

Abdominal paracentesis was not performed due to the very small amount of ascites. CHOP (cyclophosphamide, 860 mg per body; doxorubicin, 60 mg per body; vincristine, 1.4 mg per body; prednisolone, 70 mg per body for five days) chemotherapy was started on day 17 and administered every 3 weeks. After one course of CHOP chemotherapy, chest X-ray showed the disappearance of bilateral pleural effusion, and she did not feel any symptoms (Fig. 3). After six courses of CHOP chemotherapy, she achieved complete metabolic remission (CMR) according to positron emission tomography - computed tomography (PET-CT) in September 2020 (Fig. 1b). At the time of this writing in June 2021, she is alive with CMR.

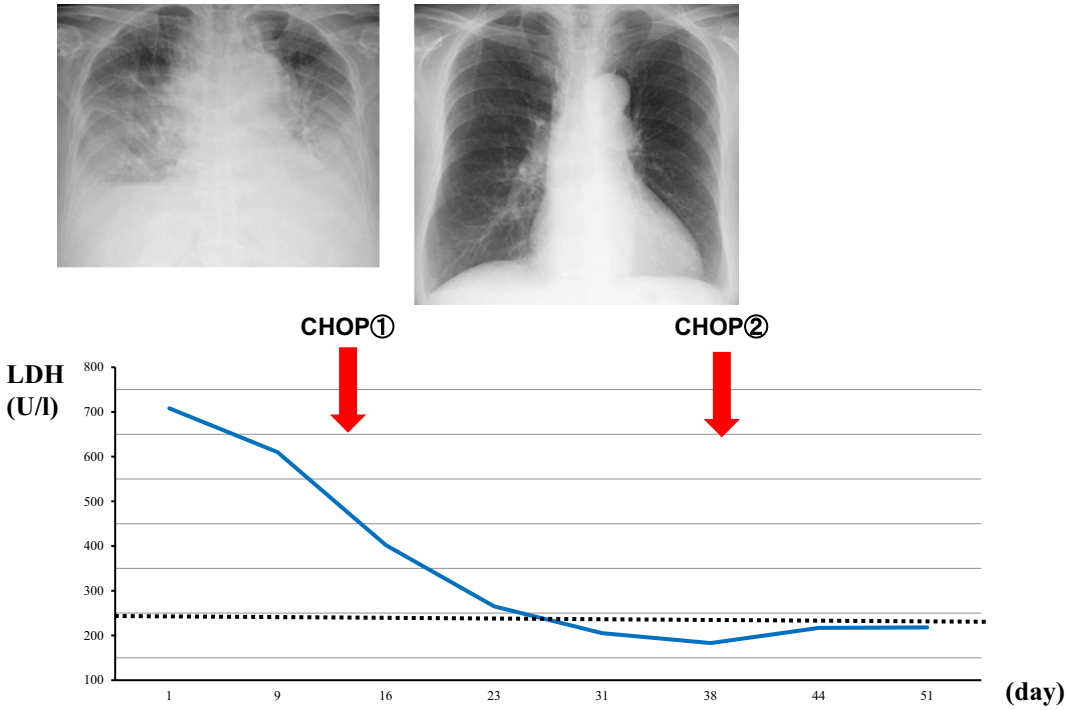


**Figure 3.** **Clinical course during hospitalization. LDH: lactate dehydrogenase, normal range, 214-222 U/L. The dotted line indicates the upper limit of LDH. CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisolone. Chest X-ray on admission showed bilateral pleural effusion. After one course of CHOP chemotherapy, chest X-ray showed the disappearance of bilateral pleural effusion.**

## Discussion

We encountered a rare case of CD56-positive AITL complicated by chylothorax. AITL cells typically show positivity for CD10, BCL6, CXCL13, and PD-1, in addition to the pan-T-cell antigens (1). In our case, CD56 expression was also detected by immunohistochemistry. CD56 is a marker for not only NK-cell neoplasms (3) but also other hematological malignancies, such as core binding factor leukemia (4), B-cell lymphoma (5), and T-cell acute lymphoblastic leukemia (6). The prognostic value of CD56 positivity differs among hematological malignancies. Among T-cell lymphomas, Suzuki et al. reported that the surface expression of CD56 is a poor prognostic factor for both anaplastic lymphoma kinase (ALK) positive anaplastic large cell lymphoma (ALCL) and ALK negative ALCL (7). Sugimoto et al. reviewed nine cases of CD56-positive adult T-cell leukemia/lymphoma (ATLL) and suggested that CD56-positive ATLL is associated with poor outcomes. These reports indicate that CD56 expression in the tumor cells may be a poor prognostic factor in T-cell lymphomas (8). To our knowledge, two cases of CD56-positive AITL have been reported. Hosoki et al. reported an 83-year-old man diagnosed with CD56-positive who AITL died of disseminated intravascular coagulation 4 months after the diagnosis (9). Sekiguchi et al. also reported a 67-year-old man diagnosed with CD56-positive AITL who relapsed 2 months after achieving CMR following 6 courses of CHOP-like chemotherapy. At the time of relapse, the neoplastic T-cells interestingly lacked CD56. They suggested that CD56 positivity might be a poor prognostic marker in patients with AITL (10). Unlike both of the patients in these previous case reports, our patient achieved CMR after six courses of CHOP chemotherapy and remained in CMR as of June 2021. The collection of further cases may clarify in which patients CD56 positivity in AITL cells would be a poor prognostic factor. AITL is occasionally complicated by pleural effusion because of lymphoma cell infiltration into the pleura. Tokunaga et al. (2) reported that among 207 cases of AITL in Japan, pleural effusion was detected in 26 cases (14%). Chylothorax has been reported as a complication of various medical conditions, such as trauma, tuberculosis, liver cirrhosis, and non-Hodgkin lymphomas (11). Among non-Hodgkin lymphomas, B-cell lymphoma, especially follicular lymphoma, is the most commonly reported as being complicated by chylothorax (12). In contrast, T-cell lymphoma is rarely complicated by chylothorax. To our knowledge, only two cases of AITL complicated by chylothorax have been reported. Iqbal et al. (13) reported a 62-year-old woman diagnosed with AITL complicated by bilateral chylothorax who received CHOP chemotherapy, and CT showed decreases in the size of enlarged lymph nodes and the volume of bilateral pleural effusion 1 month after the chemotherapy. They did not mention the outcome of this case. Willemsen et al. (14) reported a 76-year-old man presenting with systemic lymphadenopathy, generalized erythematosquamous plaques, bilateral pleural effusion, and bilateral pitting edema of the lower extremities

caused by renal failure. He was diagnosed with AITL on an autopsy. He was complicated with bilateral chylothorax and chylous ascites. In our case, the chylothorax disappeared after achieving CMR, indicating that chylothorax may not be a poor prognostic factor for AITL.

In conclusion, we reported a rare case of CD56-positive AITL complicated by chylothorax. The patient achieved CMR, and chylothorax disappeared after CHOP chemotherapy. This is the first case of CD56-positive AITL complicated by chylothorax. Clinicians should keep in mind that thoracentesis should be performed in patients with AITL complicated by pleural effusion to confirm whether pleural effusion is due to the infiltration of the neoplastic T-cells into the pleura or chylothorax.

We verbally obtained informed consent from the patient for the publication of this case report and accompanying images.

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

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