Case Report

A CASE OF CONCOMITANT ADULT T-CELL LEUKEMIA-LYMPHOMA LYMPHOMA TYPE AND TUBERCULOUS LYMPHADENITIS

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Abstract An 82-year-old man was diagnosed with active pulmonary tuberculosis and tuberculous lymphadenitis because *Mycobacterium tuberculosis* was detected in both the sputum and pus collected from the incision site in the neck. He was treated with a combination of isoniazid, rifampicin, and ethambutol. However, even after 2 months of treatment, the lymphadenopathy worsened with new lesions arising. The histopathological examination of cervical lymph nodes revealed T-cell non-Hodgkin lymphoma. He tested positive for anti-human T-lymphotropic virus type 1 (HTLV-1) antibody. The diagnosis of adult T-cell leukemia-lymphoma (ATL) lymphoma type was made. He was treated with supportive care alone because of his poor performance status. Approximately 2 months later he died. HTLV-1 infection, which underlies ATL, might have contributed to the development of tuberculosis in this case as HTLV-1 infection is associated with immunosuppression. When a patient does not improve after treatments, physicians should perform histological examination to avoid making a premature diagnosis and overlooking underlying serious diseases.

Key words: Adult T-cell leukemia-lymphoma, Tuberculous lymphadenitis, Human T-lymphotropic virus type 1; HTLV-1

INTRODUCTION

Tuberculosis is one of the most prevalent infectious diseases in the world causing substantial morbidity and mortality[1)]. It should be noted that tuberculosis can develop secondary to immunosuppression and human immunodeficiency virus infection is one of the most important immunosuppressive diseases which can lead to the development of tuberculosis[2)]. In addition, human T-lymphotropic virus type 1 (HTLV-1) infection may be an underrated important condition which underlies tuberculosis[3)]. Here, we present a patient who was initially diagnosed with tuberculous lymphadenitis, but was revealed to concomitantly have adult T-cell leukemia-lymphoma (ATL). There may be a relationship between the two diseases, as HTLV-1 infection, which underlies ATL, is associated with immunosuppression[3)].

CASE REPORT

An 82-year-old man was referred to our hospital owing to suspected active pulmonary tuberculosis. Approximately 4 months before the hospitalization, nurses in the day care center noticed the enlargement of his neck. One month later, the neck enlargement worsened. The neck lesion was incised to drain pus for the preliminary diagnosis of purulent lymphadenitis. However, his neck lesion did not improve after the incision and drainage, and neck computed tomography (CT) revealed multiple nodular opacifications in both the upper lungs in addition to multiple cervical lymphadenopathy. His medical history was remarkable for gastric cancer, which was treated by performing distal gastrectomy and cholecystectomy. In addition, he developed cerebral infarction that left him with permanent right hemiplegia and motor aphasia, and since then, he had been almost confined to bed. He had smoked 1 pack of cigarettes per day for approximately 30 years.

On referral, CT revealed a large low-density mass measuring approximately 6 × 5 × 3 centimeters in the left neck (Fig. 1) and multiple nodular opacities in both upper lungs (Fig. 2). No significant lymphadenopathy was detected elsewhere in the initial scan, which was not contrasted. Both the sputum and pus collected from the incision site in the neck were smear-positive for acid-fast bacilli and positive for the loop-mediated isothermal amplification (LAMP) assay. The patient was immediately admitted in our hospital with the diagnosis of active pulmonary tuberculosis and tuberculous lymphadenitis. On admission, he was afebrile and appeared well. His blood pressure was 148/74 mmHg and pulse was

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95 beats per minute; his oxygen saturation was 96% while breathing ambient air. A large firm mass was palpated in the left posterior neck. The laboratory testing on admission was unremarkable except for mild anemia, slightly elevated C-reactive protein and mild hypocalcemia (Table). Atypical lymphocytes were not detected in the peripheral blood. Cytological examination of the pus from the neck lesion showed no malignant cells. Biopsy of the lymph node lesion was not performed for histological examination. He was treated with a combination of isoniazid, rifampicin, and ethambutol. *Mycobacterium tuberculosis* was confirmed by culture of the sputum and pus from the neck lesion, and the strain was susceptible to all the administered drugs. His sputum smear and culture became negative at 2 weeks after the anti-tuberculosis therapy was started. However, even after 2 months of treatment, the lymphadenopathy worsened with new lesions arising. Contrast-enhanced CT revealed enlargement of the cervical, supraclavicular, para-aortic, and inguinal lymph nodes (Fig. 3). The small nodular opacities in the lungs were unchanged from the initial scan (not shown).

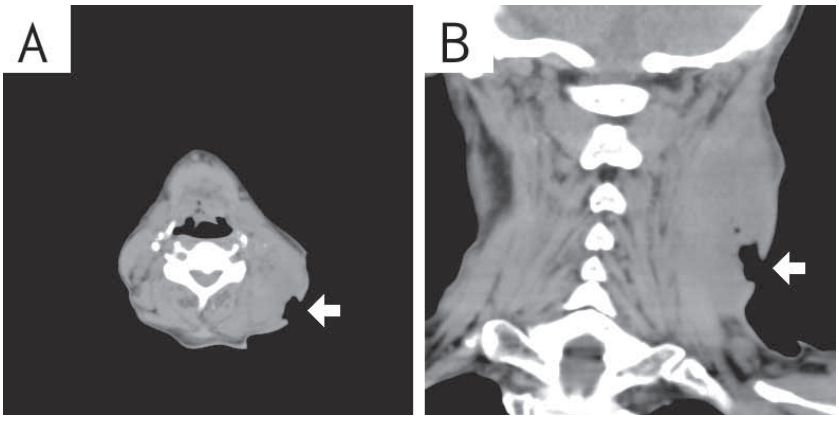

Fig. 1 (A, B) Neck computed tomography (CT) revealed large low density mass in the left neck. The arrows indicate the incision site.

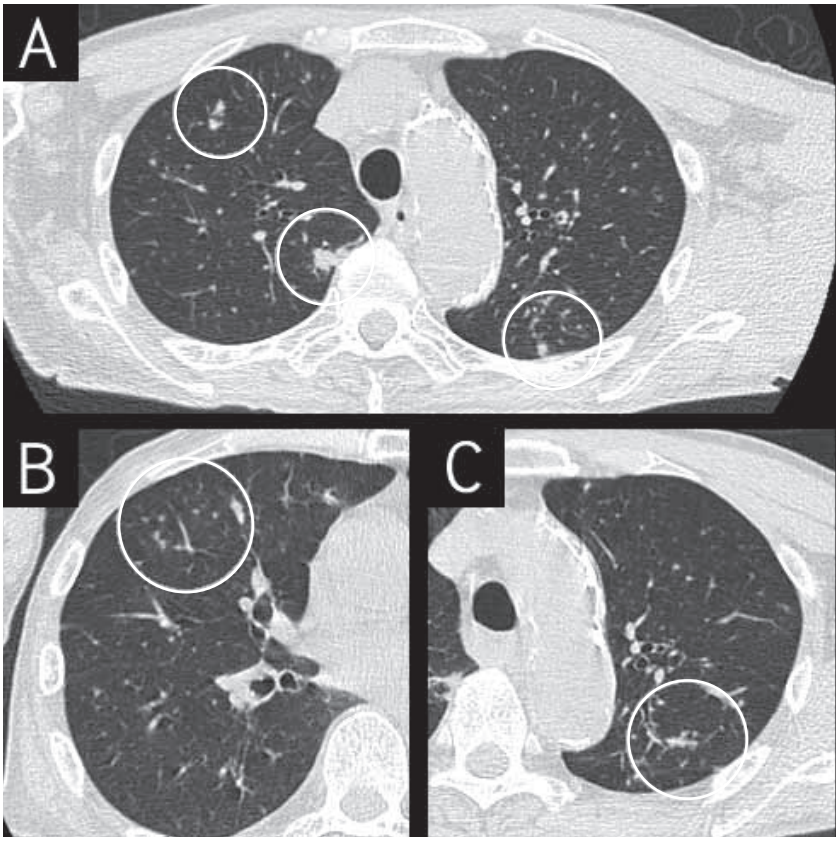

Fig. 2 (A, B, C) Chest CT revealed multiple nodular opacities in both upper lungs.

Table Results of laboratory tests on admission

Variable	Value	Normal range (in our hospital)
Hemoglobin (g/d*l*)	11.8	13.7−17.4
Hematocrit (%)	35.8	40.2−51.5
White-cell count (per mm^3)	7000	4000−8000
Differential count (%)		
Neutrophils	67.2	43.0−73.0
Lymphocytes	16.7	19.0−50.0
Monocytes	11.4	2.0−6.9
Eosinophils	4.6	0.0−3.8
Basophils	0.1	0.0−1.0
Platelet count (per mm^3)	279,000	120,000−300,000
Red-cell count (per mm^3)	4,310,000	4,310,000−5,650,000
Mean corpuscular volume (fl)	83	86−104
Sodium (mmol/liter)	136	135−147
Potassium (mmol/liter)	3.9	3.3−4.8
Chloride (mmol/liter)	100	98−108
Calcium (mg/d*l*)	8.2	8.4−10.3
Glucose (mg/d*l*)	103	70−110
Creatinine (mg/d*l*)	0.7	0.3−1.1
Urea nitrogen (mg/d*l*)	17	9−20
Protein (g/d*l*)		
Total	7.2	6.7−8.3
Albumin	3.8	3.8−5.3
Aspartate aminotransferase (U/liter)	20	8−45
Alanine aminotransferase (U/liter)	12	14−36
Alkaline phosphatase (U/liter)	243	112−355
Total bilirubin (mg/d*l*)	0.6	0.1−1.2
Uric acid (mg/d*l*)	2.8	2.8−7.5
Lactate dehydrogenase (U/liter)	202	136−240
Creatine kinase (U/liter)	63	42−207
C-reactive protein (mg/d*l*)	0.54	0.00−0.30

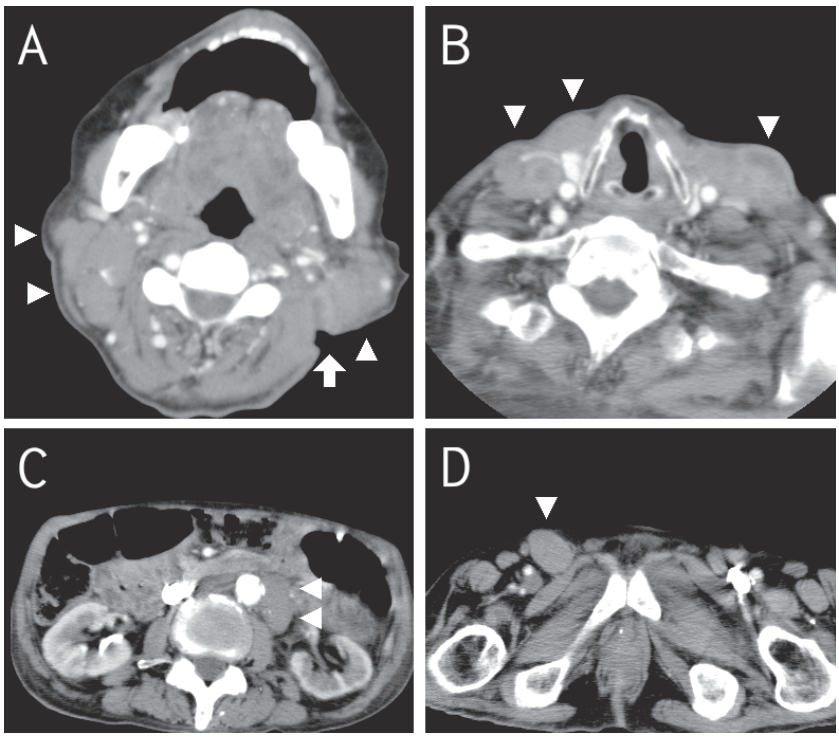

Fig. 3 Contrast-enhanced CT revealed enlargement of the cervical lymph nodes (A), supraclavicular lymph nodes (B), para-aortic lymph nodes (C) and inguinal lymph nodes (D) (arrowheads). The arrow indicates the incision site in the neck.

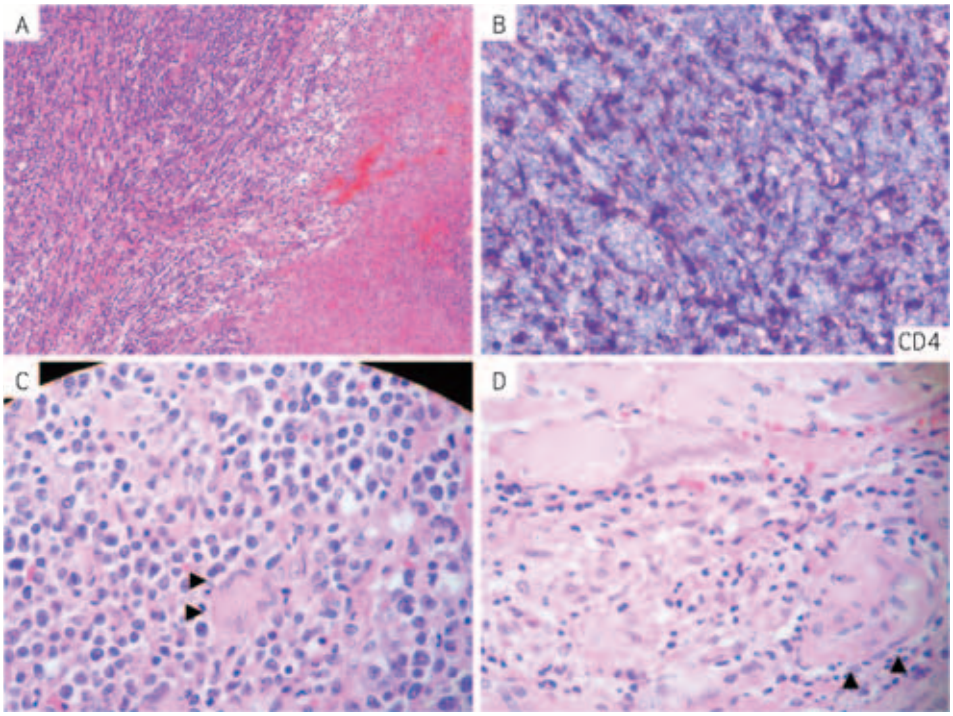

Fig. 4 Histopathological examination of cervical lymph nodes revealed T-cell non-Hodgkin lymphoma. (A) Hematoxylin-eosin staining. (B) CD4 stain. (C) Langhans giant cell was seen surrounded by lymphoma cells. (D) Epithelioid granuloma was seen in intramuscular connective tissue adjacent to the lymph node lesion.

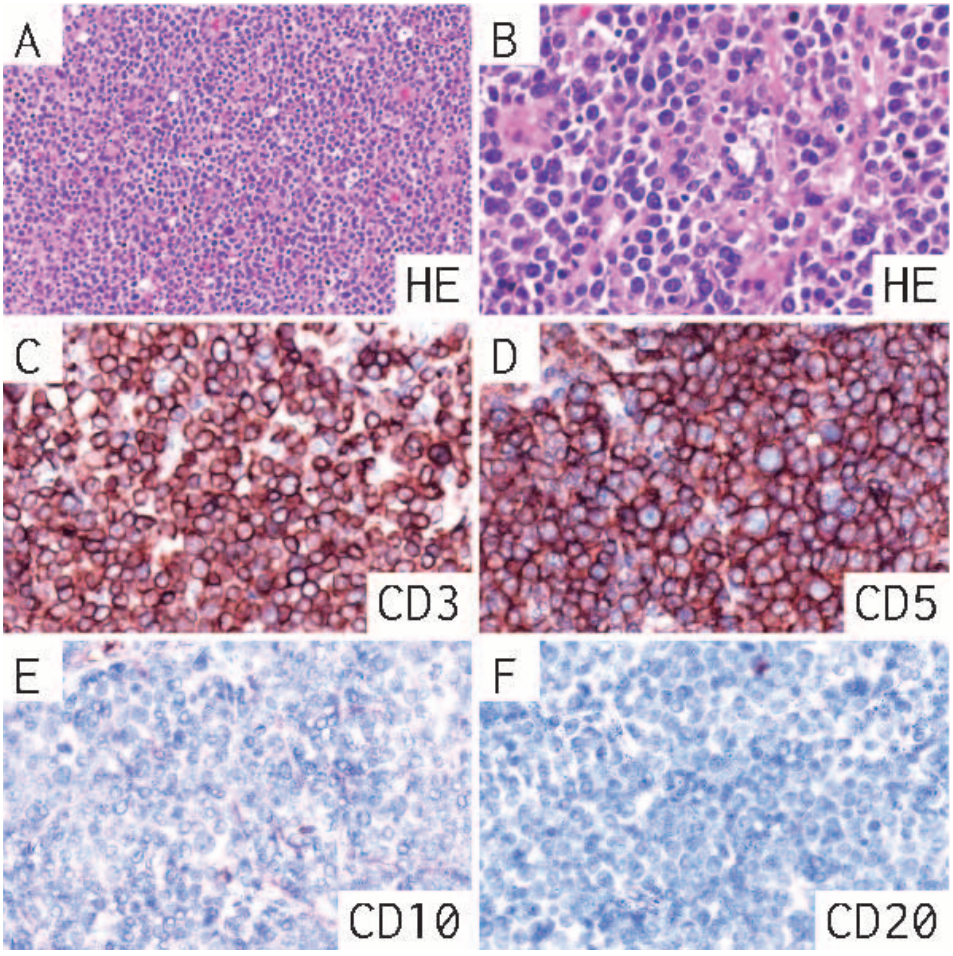

Fig. 5 Histopathological examination of cervical lymph nodes revealed T-cell non-Hodgkin lymphoma. (A, B) Hematoxylin-eosin staining. (C) CD3 stain. (D) CD5 stain. (E) CD10 stain. (F) CD 20 stain.

The cervical lymph nodes were surgically resected and histological examination revealed CD4-positive atypical cells inside and around the lymph node lesions (Fig. 4). They were medium- to large-sized mononuclear cells, which were CD3- and CD5-positive, and CD10- and CD20-negative (Fig. 5). These findings suggested the pathological diagnosis of T-cell non-Hodgkin lymphoma. Epithelioid granulomas and Langhans giant cells were also seen in the resected specimens (Fig. 4). The patient tested positive for anti-HTLV-1 antibody. The serum soluble interleukin (IL)-2 receptor and serum lactate dehydrogenase levels were 52,900 units per milliliter and 248 international units per liter, respectively. He used to live in the Kyushu region (southern part of Japan), where HTLV-1 is prevalent. The diagnosis of ATL lymphoma type was made and he was treated with supportive care alone because of his poor performance status.

In the following month, his condition deteriorated. His oral intake decreased and he received intravenous fluids and nutritional supplementation. Although it was difficult to understand his complaints because of his aphasia, he appeared unpleasant. Atypical lymphocytes appeared in the peripheral blood. The serum soluble IL-2 receptor and serum lactate dehydrogenase levels were elevated to 154,000 units per milliliter and 504 international units per liter, respectively. He died approximately 2 months after the diagnosis of ATL.

Fig. 6 shows the patient's clinical course.

DISCUSSION

HTLV-1 infection, which underlies ATL, might have contributed to the development of tuberculosis in this case. As HTLV-1 predominantly infects CD4-positive T-lymphocytes, HTLV-1 infection has been reported to be associated with susceptibility to opportunistic pathogens such as strongyloidiasis, tuberculosis, leprosy, and Norwegian scabies[3)4)]. A previous study on 11 patients with ATL showed a high frequency of opportunistic infections, which included *Pneumocystis jirovecii* pneumonia (previously termed *P. carinii* pneumonia), cryptococcal meningitis, candida sepsis, and bacterial lung abscess[5)].

As T-cell-mediated immunity via CD4-positive T-cells plays a crucial role in the host immune response to tuberculosis, HTLV-1 infection can be associated with the increased risk of developing tuberculosis[3)]. It has been well established that HTLV-1 infection is associated with reduced delayed-type hypersensitivity reactions to purified protein-derivative tuberculin[6)–8)]. A recent study conducted by Grassi et al.[9)] suggested that this perturbation in the immune response to *M. tuberculosis* can actually lead to clinically significant susceptibility to tuberculosis. They retrospectively investigated a cohort of 6,495 individuals, out of whom 1,711 had HTLV-1 infection, and showed that the incidence of tuberculosis was higher in those with HTLV-1 infection as compared to those without (3.3 vs. 1.1 cases per 1,000 person-years, respectively) and the relative risk of developing tuberculosis was 2.6 (95% confidence interval [CI] 1.6–4.2).

In addition, this case teaches us an important lesson: even when *M. tuberculosis* is detected in the pus from a lymph node, histological examination should be considered for possibilities other than tuberculous lymphadenitis. Premature diagnoses can be dangerous. However, when *M. tuberculosis* is detected in the pus from a lymph node, physicians may be reluctant to perform histological examination to confirm the

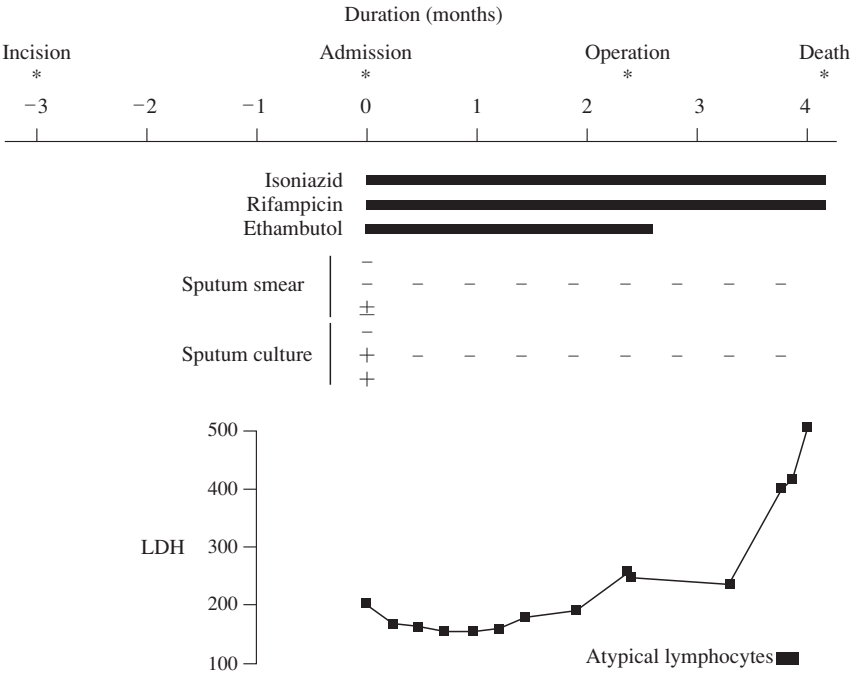

Fig. 6 Schematic presentation of the patient's clinical course

diagnosis of tuberculous lymphadenitis and rule out other possibilities.

In conclusion, when physicians treat a patient with tuberculosis, physicians should always be aware of the possibilities of underlying diseases associated with immunosuppression. In addition, when a patient does not improve after treatments, they should perform histological examination to avoid making a premature diagnosis and overlooking underlying serious diseases.

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Conflicts of interest: None to declare.

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成人T細胞白血病・リンパ腫 リンパ腫型と結核性頸部リンパ節炎が併存した1例

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要旨：症例は82歳男性。喀痰および頸部リンパ節病変切開部位の膿から結核菌が検出されたため活動性肺結核および結核性頸部リンパ節炎と診断した。イソニアジド（INH），リファンピシン（RFP），エタンブトール（EB）で治療を開始した。しかし，治療開始後2カ月が経過してもリンパ節病変は増大し新規病変の出現も認めた。外科的に切除したリンパ節病変の病理診断は非ホジキンT細胞リンパ腫であった。さらに抗ヒトT細胞白血病ウイルス1型（HTLV-1）抗体陽性であったため，成人T細胞白血病・リンパ腫（ATL）リンパ腫型と診断した。Performance Status不良であったため緩和治療のみが行われた。成人T細胞リンパ腫の診断から約2カ月後に死亡した。ATLの原因であるHTLV-1感染症は免疫不全を引き起こしうるため，活動性結核発病の要因になった可能性がある。また，治療が奏功しない場合は重大な疾患を見逃さないためにも，組織診断による正確な診断が重要と考えられた。

キーワーズ：成人T細胞白血病・リンパ腫，結核性頸部リンパ節炎，ヒトT細胞白血病ウイルス1型，HTLV-1