Adult T-Cell Leukemia Involving the Central Nervous System After Remission of Adult Respiratory Distress Syndrome

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We report a rare case of adult T-cell leukemia (ATL) in which the patient had an acute type of ATL involving the central nervous system (CNS) after remission of adult respiratory distress syndrome (ARDS) due to human T lymphotropic virus type 1 associated bronchopneumopathy. A 62-year-old woman was admitted to the hospital because of ARDS. Pulse therapy with methylprednisolone improved ARDS, but she fell into a coma due to ATL and CNS invasion 5 months after recovery. Although chemotherapy decreased the fraction of abnormal lymphocytes, her consciousness level did not improve and she died.

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| ATL = adult T-cell leukemia; HAB = HTLV-1-associated bronchopneumopathy; HTLV-1 = human T lymphotropic virus type 1 |

Recently, some human T lymphotropic virus type 1 (HTLV-1) associated diseases have been reported. Adult T-cell leukemia (ATL) is known to have many clinical types such as acute, chronic, and smoldering, and it can also be classified as lymphoma or leukemia. In this article, we describe a rare case of acute ATL involving the central nervous system (CNS) after remission of the adult respiratory distress syndrome (ARDS) associated with HTLV-1-associated bronchopneumopathy (HAB) in a nonendemic area for HTLV-1 in Japan.

CASE REPORT

A 62-year-old woman was admitted to the hospital because of dyspnea on November 21, 1991. She was born in Osaka and had lived in Osaka all her life. She had no medical history and no blood transfusion before her admission. At the time of hospital admission, she had a body temperature of 37.5°C, BP of 122/72 mm Hg, heart rate of 96/min, and respiratory rate of 30/min. Fine crackles were audible in both lungs. Neither organomegaly nor neurologic abnormalities were found. Cyanosis was detected on her skin.

Laboratory data on admission were as follows: WBC count elevated to 14.4 × 10⁹/μl with normal differentiation. Lactate dehydrogenase (LDH) was elevated to 1,107 IU/L and C-reactive protein (CRP) to 33.9 mg/dl. Other transaminase data were within normal levels. Arterial blood gas analysis revealed marked hypoxia (Prdo₂, 44.7 mm Hg; Praco₂, 32.9 mm Hg; pH, 7.528; and base excess, 6.1). A chest radiograph showed diffuse reticulonodular shadows (Fig 1, left) and chest computed tomography demonstrated diffusely increased concentrations with air bronchograms. Stains of sputum for tuberculosis, fungus, and Pneumocystis carinii were negative and cytologic study showed no malignant cells. Because ARDS had progressed, the patient was put on mechanical ventilation. Although we did not perform a lung biopsy because of her poor condition and the cause of ARDS was unclear, four cycles of pulse therapy with methylprednisolone at a dose of 1 g/d for 3 days was effective for ARDS. Arterial blood gas values recovered to within normal ranges and her chest radiographic finding improved remarkably (Fig 1, right). She recovered from ARDS and was discharged from the hospital on January 21, 1992. Her dose of oral prednisolone was reduced to 20 mg.

Five months after her initial hospital discharge, she complained of general malaise and of high fever and she was readmitted on June 16, 1992. She was drowsy. She had a body temperature of 38.4°C, BP of 150/94 mm Hg, and heart rate of 80/min. There were

![Figure 1. Left (a), Chest radiograph revealing diffuse reticulonodular shadows. Right (b), The chest radiograph improved remarkably after pulse therapy with prednisolone.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21678/)
no other physical abnormalities except for the disturbed consciousness. Laboratory findings on her second hospital admission were as follows: WBC count elevated to 19.9 × 10^6/μL with 33.0 percent atypical lymphocytes. The LDH was 475 IU/L, alkaline phosphatase (ALP) was 1512 IU/L, CRP was 4.8 mg/dl, and calcium was 11.2 mg/dl. Lumbar puncture revealed a marked increase in lymphocytes (1,494/μL) and an elevated intrathecal pressure at 150 mm H₂O. Neither bacteria nor fungus was detected. Flower-like hypersegmented atypical lymphocytes were observed both in peripheral blood and cerebrospinal fluid (Fig. 2). The surface marker for these lymphocytes was positive in CD3, 4, 5, and negative in CD8. Bone marrow puncture revealed 3.4 percent atypical lymphocytes similar to those seen in the peripheral blood and cerebrospinal fluid. Anti-HTLV-1 antibody was detected at a titer of 256 by the passive agglutination method and at a titer of 5 by the fluorescence antibody method in serum. Anti-HTLV-1 antibody in cerebrospinal fluid was also detected at a titer of 5 by the passive agglutination method. A chest radiograph showed no change after the remission of HAB. A brain computed tomographic scan showed neither a mass nor hemorrhage, but an enhanced gyrus was observed. Magnetic resonance imaging of the brain showed multiple high-intensity small tumors in the T₂-weighted image. We diagnosed her as having ATL in the CNS. Treatment with VCPA (vincristine, 1.5 mg; cyclophosphamide [Endoxan], 500 mg; prednisolone, 40 mg; and doxorubicin [Adriamycin], 60 mg) and the intrathecal administration of methotrexate (20 mg), cytarabine (40 mg), and prednisolone (20 mg) markedly decreased the levels of serum LDH, ALP, calcium, and abnormal lymphocytes in both peripheral blood and cerebrospinal fluid. However, her consciousness level did not improve and she died of respiratory failure. An autopsy could not be performed.

**DISCUSSION**

Human T lymphotropic virus type 1 associated bronchopneumopathy is one of the HTLV-1-associated diseases and was first reported in 1988 by Maruyama et al. HAB includes different kinds of lung disease such as P carinii pneumonia, lymphoma cell invasion, and noninfectious pneumonia, and it varies in seriousness from asymptomatic to very severe, resulting in a so-called destroyed lung. In this case, we did not realize that the initial respiratory failure was associated with HAB until ATL became overt with CNS involvement. There are no reports (to our knowledge) about severe noninfectious pneumonia that presents with acute respiratory failure as in ARDS and that requires mechanical ventilation support. Moreover, the patient responded well to steroid therapy and recovered from respiratory failure. This suggests that the immunologic disorder caused by HTLV-1 was associated with the pathogenesis of HAB. Therefore, we must keep in mind that HAB is one of the manifestations of noninfectious pneumonia even in a nonendemic area in Japan and that HAB may respond to steroid therapy.

Adult T-cell leukemia is known to invade various organs such as skin, lymph nodes, liver, spleen, bone marrow, and brain. Some reports have been described ATL with CNS involvement. Consciousness disturbance in HTLV-1 carriers caused by meningeal invasion and opportunistic infection such as with Cryptococcus meningitis is not unusual. In this case it is obvious that ATL cells invaded the meninges and the enhanced computed tomographic findings are compatible with the report of ATL in the CNS. However, we do not know whether the brain tumors detected by magnetic resonance imaging were due to ATL invasion or disseminated necrotizing leukoencephalopathy that may be caused by intrathecal methotrexate.

It is reported that about one of every thousand HTLV-1 carriers develops overt ATL each year in Japan, but the reason why ATL becomes overt remains unclear. It is not clear in this case whether the large dose of prednisolone promoted the development of overtly acute ATL bypassing the smoldering stage in a healthy carrier.

This is a rare case of ATL, presenting CNS involvement after remission of ARDS due to HAB.

**REFERENCES**

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**FIGURE 2. Top (a), Atypical lymphocytes with convoluted nuclei in peripheral blood (×500). Bottom (b), Atypical lymphocytes in cerebrospinal fluid (×500).**
with HTLV-1 infection. Jpn J Thorac Dis 1992; 30:780-86

Gaucher’s Disease*
An Unusual Cause of Intrathoracic Extramedullary Hematopoiesis

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A thoracic paravertebral mass in an asymptomatic woman with type 1 Gaucher’s disease proved to be due to extramedullary hematopoiesis. This is, to our knowledge, the first case of intrathoracic extramedullary hematopoiesis reported with Gaucher’s disease.

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Gaucher’s disease is an uncommon familial disorder characterized by deficiency of beta-glucosidase, a lysosomal enzyme responsible for the degradation of glucosyl ceramide (glucocerebroside). This biochemical defect leads to glucocerebroside-laden histiocytes (Gaucher cells) which assume distinctive morphologic features in systemic organs. Deposits of Gaucher cells typically accumulate in the spleen, liver, bone marrow, lymph nodes, and in some cases, the brain and lung. While Gaucher cells may infiltrate the lung and extramedullary hematopoiesis invariably involves the spleen and liver, intrathoracic extramedullary hematopoiesis has not been previously described in Gaucher’s disease.

CASE REPORT

A 74-year-old woman presented with a one-month history of dry cough recently productive of a small amount of white sputum. She denied fever, chills, weight loss, and dyspnea. Gaucher’s disease had been diagnosed on bone marrow aspirate ten years earlier when she presented with a prolonged bleeding time, thrombocytopenia, and purpura. She had no other signs or symptoms referable to this disorder except for transient elevation of liver enzymes and mild splenomegaly discovered 2 years prior. Other past medical history included stage Ia ovarian adenocarcinoma 11 years earlier, without evidence of recurrence following hysterectomy and bilateral salpingo-oophorectomy.

Physical examination revealed a well-appearing woman with

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FIGURE 1. A 74-year-old asymptomatic woman with type 1 Gaucher’s disease: computed tomography scan showing a right paraspinal mass.

normal vital signs and in no apparent discomfort. The lung examination was normal, and there was no detectable lymhadenopathy or abdominal organomegaly. Examination of her skin disclosed a few purpuric lesions and petechiae.

Laboratory data including hematocrit value, erythrocyte indices, and morphologic findings, white blood cell and platelet counts, and liver enzyme levels were within the normal range. Pulmonary function tests showed mild reversible airways dysfunction but normal lung volumes and diffusing capacity for carbon monoxide. The chest radiograph showed a new, discrete 2-cm paraspinal mass at the level of the ninth thoracic vertebra which was confirmed by computed tomography (Fig 1). No parenchymal lung disease or lymphadenopathy was present. Percutaneous computed tomography-guided fine needle aspiration of the paravertebral mass showed Gaucher cells as well as megakaryocytes and immature red blood cells, findings representing extramedullary hematopoiesis (Fig 2). The patient’s cough responded to inhaled bronchodilators.

DISCUSSION

Gaucher’s disease is an inborn error of metabolism with several genetically distinct clinical types. At least three forms are described, and all may demonstrate lung parenchymal abnormalities. The adult form (type 1, chronic nonneuronopathic type) may present in infancy or adulthood, typically showing anemia, thrombocytopenia, splenomegaly, and bone lesions. Although somewhat variable, the course is relatively benign. The present case depicts this form. The rarer infantile form (type 2, acute neuronopathic type) is malignant, demonstrating progressive neurologic symptoms and death from respiratory infection by age 2 years. An intermediate juvenile form (type 3, subacute neuronopathic type) consists of a heterogeneous patient group demonstrating reticulendothelial involvement as well as progressive neurologic deterioration characteristic of the infantile form. This type also exhibits an aggressive course resulting in hepatosplenomegaly and early death.

Intrathoracic Gaucher’s disease typically affects the lung and is characterized histologically by extensive infiltration of interlobular septa, alveolar spaces, and terminal bronchioles by iron-laden Gaucher cells. It correlates roentgenographically with a diffuse reticulonodular or miliary parenchymal pattern. The diffuse pulmonary infiltration, absent in the present case, affects a small minority of patients. We could find no documentation in the literature of a discrete intrathoracic mass due to Gaucher’s disease, except for a