A Rare Case of Adult T Cell Leukemia/Lymphoma: Clinicopathological Correlation with Autopsy Confirmation

M. G. Manoj · J. Kotwal · V. Dutta

Received: 23 April 2012 / Accepted: 22 October 2012 / Published online: 21 November 2012
© Indian Society of Haematology & Transfusion Medicine 2012

Abstract Adult T cell leukaemia/lymphoma (ATLL) is a rare T lymphoproliferative disorder which is etiologically linked with human T cell lymphotropic virus type-1 (HTLV-1). HTLV-1 is endemic in Japan, Caribbean and Africa. The highest incidence of ATLL is in Japan although sporadic cases have been reported elsewhere in the world. We describe a case of ATLL with an unusual presentation with clinic-pathological correlation and autopsy confirmation. A 56 year old male was referred to Command Hospital (Southern Command) for an incidental finding of lymphocytosis on a routine Hemogram. Clinical examination did not reveal hepatosplenomegaly, lymphadenopathy, jaundice or skin lesions. Laboratory investigations showed lymphocytosis with predominance of atypical lymphomonocytoid cells. Immunophenotyping of the bone marrow mononuclear cells showed positivity for CD45, CD2, CD3, CD4, CD5 and negative for CD7, CD8, CD13, CD33, CD19, which is characteristic of ATLL phenotype. Clonality was confirmed by PCR for TCR gene rearrangement on post mortem tissue. He succumbed to his illness after 40 days of initial presentation and 16 days of being diagnosed as ATLL. Here, we discuss the pathogenesis and characteristics of ATLL with clinico-pathological correlation and autopsy confirmation.

Keywords Adult T cell leukemia/lymphoma · Autopsy · Immunophenotyping · PCR

Introduction

Adult T cell leukemia/lymphoma (ATLL) is a rare T lymphoproliferative disorder which is etiologically linked with human T cell lymphotropic virus type-1 (HTLV-1). HTLV-1 is endemic in Japan, the Caribbean and parts of Africa [1]. ATLL was first described as a distinct clinical entity in Kyoto, Japan in 1977 [2, 3]. It occurs in about 5 % of asymptomatic carriers of HTLV-1 after a long latency period of more than 30 years.

The clinical picture of ATLL is diverse and can be classified into four categories: acute, lymphoma, chronic and smoldering types [4]. ATLL cells originate from the CD4-positive subset of peripheral T cells. It is believed that the HTLV-1 provirus becomes clonally integrated in these affected helper T cells [5]. The appearance of one or more prevalent T cell clones carrying the HTLV genome represent an increased risk of developing full blown disease. The highest number of reported cases of ATLL is in Japan although sporadic cases have been reported elsewhere in the world. Here, we describe a case of A Rare Case of Adult T Cell Leukemia/Lymphoma with autopsy confirmation.

Case report

A 56 year old male, serving officer was detected to have asymptomatic leucocytosis of 40,000/cumm with a monocytosis of 40 % and Hb of 14.8 gm % on a routine Hemogram, during his annual medical examination. On examination, no hepatosplenomegaly, lymphadenopathy,

M. G. Manoj (✉) · J. Kotwal · V. Dutta
Department of Pathology, Armed Forces Medical College,
Sholapur Road, Wanowarie, Pune 411040, India
e-mail: manoj.gopal@gmail.com

J. Kotwal
e-mail: atuljyot@hotmail.com

V. Dutta
e-mail: vdajat@rediffmail.com

jaundice or skin lesions were seen. Patient was evaluated for various causes of monocytosis, at a peripheral hospital, before transferring him to the nearest tertiary care Army hospital.

During the course in the hospital, patient developed sudden acute respiratory symptoms. Swine flu (H1N1) was

Fig. 1 Peripheral blood smear showing atypical lymphomonocytoid cells with convoluted nucleus (Leishman-Giemsa stain)

Fig. 2 Flow cytometry pattern showing cells which are CD4+, CD5+, CD7– and CD20–

considered, as during that time, Pune was having an outbreak of the disease. However, the thorax swab sent to National Institute of Virology was reported as negative for the virus. The peripheral smear was reviewed by the hematopathologist which showed lymphocytosis with predominance of atypical lymphomonocytoid cells (Fig. 1). These cells were NSE positive (both dot and diffuse). Platelets were adequate on smear. A differential diagnosis of Chronic reactive monocytosis/Chronic myelomonocytic leukemia and T cell Leukemia/lymphoma were considered. BMA and Flowcytometry studies were advised.

Bone marrow aspirate showed atypical lymphomonocytoid cells with polylobated cells with no convoluted atypical nuclei. A differential diagnosis of Adult T cell lymphoma/leukemia (ATLL) and Peripheral T cell lymphoma spill were considered.

Flow cytometry showed the cells to be positive for CD45, CD2, CD3, CD4, CD5 and negative for CD7, CD8, CD13, CD33, CD19 (Fig. 2). The presence of CD4 and absence of CD8 suggested monoclonality. In view of the clinical features, peripheral blood smear and bone marrow aspiration findings in conjunction with Flow cytometry was confirmatory for ATLL. The biochemical parameters showed a Serum Calcium of 12 mg/dl and Lactate dehydrogenase of 650 IU/L respectively.

Fig. 3 **a** Gross photograph of lungs with shaggy, lusterless pleural surface with fibrinous adhesions. Focal areas of consolidation present in both upper lobes. **b** Gross of liver, pancreas and spleen block showing an enlarged liver and spleen

The patient continued having respiratory distress. With this diagnosis the lung lesions were suspected to be fungal pneumonia. Chemotherapy consisting of CHOP regimen (Cyclophosphamide, Doxorubicin, Vincristine and Dexamethasone), antibiotics (Inj Piperacillin-Tazobactam 4.5 gm IV 6th hourly) and antifungals (Inj Voriconazole 4 mg/kg 12th hourly) were started. He succumbed to his illness after 40 days of initial presentation and 16 days of being diagnosed as ATLL.

The salient gross autopsy findings included; areas of consolidation in the right and left lower and upper lobes, hepatomegaly ($14 \times 16 \times 7$ cm and weighing 1,800 gm), splenomegaly ($13 \times 8 \times 5$ cm and weighing 300 gm) and multiple small paraortic and paratracheal lymphnodes, which had become apparent during the course of the illness (Fig. 3).

The salient histopathological autopsy findings included; bilateral microabscesses (composed chiefly of atypical cells) in right upper lobe, right lower lobe, left upper lobe and left lower lobe. The alveolar wall showed hyaline membrane and diffuse infiltration by the atypical cells with convoluted and polylobated nucleus. The paraaortic and paratracheal lymph nodes showed diffuse effacement of the architecture with similar cells (Fig. 4). Both kidneys showed features of acute tubular necrosis. Spleen showed diffuse effacement of the architecture by infiltration of similar cells (Fig. 5).

Monoclonality was determined by performing PCR for TCR- γ gene rearrangement on postmortem tissue (Fig. 6).

Clinicopathological correlation of autopsy findings revealed the typical features of lung and reticuloendothelial system involvement in ATLL, which was not picked antemortem was picked up on autopsy. Thus confirming the complete presentation of ATLL (Acute variant).

Fig. 4 Section from lymph node showing large atypical giant cells scattered singly. (Hematoxylin and Eosin stain)

Fig. 5 Section from spleen showing large atypical giant cells scattered singly. (Hematoxylin and Eosin stain)

Fig. 6 Monoclonality delineated by PCR for TCR- γ gene rearrangement

Discussion

ATLL is a mature T cell neoplasm that occurs in a small percentage of people infected with HTLV-1 predominantly in endemic areas. ATLL has a long latency period and is associated with exposure to the virus very early in life. The main mechanisms of transmission are vertical transmission during pregnancy, breastfeeding, sexual intercourse, blood products transfusion and intravenous drug use [1]. Several host and viral factors contribute to HTLV-I associated disease pathogenesis such as human leukocyte antigen (HLA) haplotype, viral strain, route of infection and immune response to HTLV-1 [5]. MHC class I molecules that predispose to ATLL are HLA-A*26, HLAB*4002, HLAB*4006, and HLA-B*4801. One of the important viral factors is the tax protein encoded by the pX region of the HTLV-1 virus. This protein induces the expression of several cytokines and anti-apoptotic genes which are critical in the proliferation of infected T-lymphocytes. There are four recognized clinical presentations of ATLL. Of these, the chronic and smoldering forms are relatively indolent whereas the acute and lymphomatous forms are more aggressive (Table 1). Our patient fits into the acute subtype [5] based on his clinical presentation as well as laboratory findings: absolute lymphocytosis, lymphadenopathy, hepatosplenomegaly, presence of abnormal ATLL cells with an increased serum LDH. The diagnosis of ATLL in this patient was initially suspected from the immunophenotyping results which showed an ATLL phenotype although with pathognomonic flower cells were seen in the peripheral blood film. The patient also had no known

Table 1 Diagnostic criteria for subtypes of ATLL

Parameter	Smoldering	Chronic	Acute
Lymphocytosis	No	Increased	Increased
Abnormal Lymphocytes	>5%	Increased	Increased
LDH	Normal	Increased	Increased
Calcium	Normal	Normal	Variable
Skin Rash	Erythema	Variable	Variable
Lymphadenopathy	No	Mild	Variable
Hepatosplenomegaly	No	No	Variable
BM infiltration	No	No	Variable

Lymphomatous variant is characterized by prominent lymphadenopathy but without peripheral blood involvement

risk factors for acquiring HTLV-1 infection. This highlights the need for a high index of suspicion for patients with typical immunophenotypic findings of ATLL in areas which are non-endemic for HTLV-1 virus. Detection of TCR rearrangement by PCR helped to confirm the diagnosis in this patient. Serological testing for anti-HTLV-1 was not performed. Indian literature also emphasizes that ATLL can be seen in non endemic area like India and the diagnosis should be based on clinicopathological features and demonstration of circulating antibodies towards HTLV-1 (if available) [6].

In conclusion, ATLL is a rare disease and in the absence of classical morphological findings, the diagnosis of ATLL can only be made by having a high index of suspicion, characteristic immunophenotyping features and detection of TCR rearrangement by PCR.

References

1. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW (eds) (2008) WHO Classification of tumours of haematopoietic and lymphoid tissues. IARC, Lyon
2. Takatsuki K, Uchiyama T, Sagawa K, Yodoi J (1977) Adult T cell leukaemia in Japan. In: Seno S, Takaku F, Irino S (eds) Topics in haematology. Excerpta Medica, Amsterdam, pp 73–77
3. Chihara D, Ito H, Katanoda K et al (2012) Increase in incidence of adult T-cell leukemia/lymphoma in non-endemic areas of Japan and the United States. Cancer Sci. doi:10.1111/j.1349-7006.2012.02373.x
4. Shimoyama M (1991) Diagnostic criteria and classification of clinical subtypes of adult T cell leukemia/lymphoma. A report from the lymphoma study group (1984–1978). Br J Haematol 79: 428–437
5. Matsuoka M (2005) Human T-cell leukemia virus type 1 (HTLV-1) infection and the onset of adult T-cell leukaemia (ATL). Retrovirology 2:27–39
6. Ahmed F, Murthy SS, Mohan MK, Rajappa SJ (2012) HTLV 1 associated adult T cell lymphoma/leukemia a clinicopathologic, immunophenotypic tale of three cases from non-endemic region of south India. Indian J Pathol Microbiol 55:92–96