T-Cell Prolymphocytic Leukemia Accompanied by Plural M-Proteins with Myelodysplastic Syndrome in a Nonagenarian

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Abstract

T-cell Pro-Lymphocytic Leukemia (T-PLL) is a rare disease caused by malignancy of mature post-thymic T-cell. Myelodysplastic Syndrome (MDS) is caused by abnormal differentiation of myeloid lineage cells resulting in myeloid leukemia. Both of these hematological disorders are frequently diagnosed in elderly persons. Myeloid lineage is believed to be situated at the position far from lymphoid one as it is regarded on a tree diagram about the blood cell maturation. We reported herein a rare case of T-PLL accompanied by plural M-proteins with MDS a nonagenarian. The 96 years old patient was admitted to our hospital because of lymphocytosis and abnormal lymphocytes. From the bone marrow aspirate, biopsy and hematological findings, abnormalities were observed in cells of three different lineages, namely, (i) neutrophils with hypersegmented-nuclei (ii) erythroblasts with nuclear division, large platelets and megakaryoblastic cells, and (iii) reticulum cells with phagocytosed iron in their cytoplasm. Lymphocytes showed CD3 (+), CD4 (+), CD5 (+), CD8 (+), CD10 (+), CD56 (-) and CD57 (-). Mast cells and large lymphocytic cells with nuclear pockets were also seen. Anti-HTLV-1 antibody was negative. Soluble IL-2 receptor was significantly elevated to 7910 U/ml. Both IgGλ and IgGκM-protein were detected. No Bence-Jones protein was detected in the urine. Chromosomal abnormality of 45 (X, 0) or loss of Y chromosome was also demonstrated. Due to his high age, it was difficult to classify his condition according to the conventional classification. Thus, what we had experienced is truly a rare case that coincidentally showed T-PLL and MDS with plural M-proteins.

Keywords: M-protein; Myelodysplastic syndrome; T-prolymphocytic leukemia

Introduction

T-cell prolymphocytic leukemia (T-PLL), which is commonly accompanied by splenomegaly, is a mature post-thymic T-cell malignancy with an aggressive clinical course. It is an extremely rare disorder accounting for the lowest number of all the lymphocytic leukemia [1]. This disease was previously known as T-cell chronic lymphocytic leukemia but has now been reclassified as T-PLL based on the post-thymic T-cell markers [2]. T-PLL is frequently diagnosed in elderly people [3].

Myelodysplastic syndrome (MDS) is a hematological disease caused by abnormal differentiation of myeloid lineage cells in which some patients will develop to several forms of myeloid leukemia [4]. MDS is also commonly seen in elderly persons [5]. Whatever the cause of both T-PLL and MDS, it is still a mystery that both of these hematological disorders are frequently diagnosed in elderly persons [3,5].

Although there have been some reports showing concurrent lymphoid malignancies with MDS, almost all cases of these lymphoid malignancies associated with the MDS were of the B-cell type, which developed after therapy with drugs such as alkylating agents [6].

We present an oldest patient ever of T-PLL accompanied by plural M-proteins with MDS, without any previous chemotherapy.

Case Report

Patient Y.S, a 96-yr-old Japanese male, was referred from a practicing physician to our Nemuro city hospital because of a WBC count of 26.6 × 10⁹/L with 75% lymphocytes. He was admitted to our hospital for a detailed examination of bone marrow aspiration and biopsy to make a definitive diagnosis of lymphocytic leukemia. He did not show any abnormal physical findings such as skin lesion nor lymphadenopathy on admission, except for splenomegaly.

His hematological data were as follows; Red Blood Cell count (RBC) 3.40 × 10¹²/L, Hemoglobin (Hb) 10.7 g/l, Hematocrit (Ht) 32.3%, White Blood Cell count (WBC) 132 × 10⁹/L with 87% lymphocytes and Platelet count 72 × 10⁹/L. By light microscopy, the lymphocytes in the peripheral blood smear were seen as small-sized lymphocyte with an irregular nuclear outline and condensed chromatin. Their cytoplasm was scant, non-granular and basophilic by May-Grünwald-Giemsa stain (Figure 1a). Free cells in aspirated bone marrow consisted of 82.8% lymphocyte and 0.2% plasma cell. In the biopsy specimens, the lymphocytes showed CD3 (+), CD4 (+), CD5 (+), CD8 (+), CD10 (+), CD56 (-) and CD57 (-). Mast cells and large lymphocytic cells with nuclear pockets were also seen. Anti-HTLV-1 antibody was negative. Soluble IL-2 receptor was significantly elevated to 7910 U/ml. Both IgGλ and IgGκM-protein were detected. No Bence-Jones protein was detected in the urine. Chromosomal abnormality of 45 (X, 0) or loss of Y chromosome was also demonstrated. Due to his high age, it was difficult to classify his condition according to the conventional classification. Thus, what we had experienced is truly a rare case that coincidentally showed T-PLL and MDS with plural M-proteins.

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observed (Figure 1b-1e). They were (i) the neutrophils, most of which have hypersegmented nuclei and with few cytoplasmic granules, (ii) the erythroblasts with nuclear division, the large platelets and the abnormal megakaryoblastic cells, and (iii) the reticulum cells which possessed iron in their cytoplasm. This is despite that the serum iron concentration, unsaturated iron binding capacity, total iron binding capacity and serum ferritin were found to be 29 μg/dl, 174 μg/dl, 203μg/dl and 122 ng/ml, respectively (the normal range being 60–157, 190–269, 290–355, 13–215, respectively) (Figure 1f). Mast cells were also frequently observed (Figure1g). Large lymphocytic cells with nuclear pockets were also seen (Figure 1h). Chromosomal abnormality of 45 (X, 0) or loss of Y chromosome (in 4/20 analyzed cells) was also demonstrated. Serum Immunoglobulin (Ig) consisting of IgG at 2490 mg/dl, IgA at 439 mg/dl, IgM at 154 mg/dl, IgE at 753 IU/ml and IgD at 2.3 mg/dl (the normal range of the 5 classes of aforementioned serum Ig are 870–1700, 110–470, 23–250, 0–170, < 9, respectively) were observed. Serum IgG containing IgGκM-protein was slightly elevated. No Bence-Jones protein was detected in the urine. IgGA was faintly detected by immuno-electrophoresis (Figure 3). The C-reactive protein, anti-nuclear antibody titer and rheumatoid arthritis test were 0.35 mg/dl, × 80 and negative, respectively.

Since the measurements of his blood sedimentation test, D-dimer and Thrombin/Anti-Thrombin III (TAT) complex were 9 mm/hour, 3.2 μg/ml and 6.5 ng/ml, respectively, coupled with low platelet count on admission, the patient was regarded as having a disseminated intravascular coagulation by leukemic cells, and needs to be administered nafamostat. While under a mild chemotherapy using a small amount of etoposide and prednisolone, he was supervened by acute pneumonia and died on the 42nd day of his admission.

**Discussion**

The phenotype of the lymphocytic cells seen in our case was considered to be of the mature post-thymic stage T-cell and come under the category of the leukemic cells in T-cell prolymphocytic leukemia (T-PLL) because anti-HTLV-1 antibody could not be detected in the serum [7]. Although the leukemic cells of T-PLL generally show CD4 (+) and CD8 (-) [8], those of our case were CD4 (+) and CD8 (+). Therefore, the cells seen in our case were considered to belong to a rare group in T-PLL. CD7, which is known to be positive in T-PLL [8], has also been reportedly detected on myeloid cells [9]. However, due to the relatively high cost of testing for CD7, we examined CD10 instead. The phenotype of the lymphocytic cells seen in our case was considered to be of the mature post-thymic stage T-cell and come under the category of the leukemic cells in T-cell prolymphocytic leukemia (T-PLL) because anti-HTLV-1 antibody could not be detected in the serum [7]. Although the leukemic cells of T-PLL generally show CD4 (+) and CD8 (-) [8], those of our case were CD4 (+) and CD8 (+). Therefore, the cells seen in our case were considered to belong to a rare group in T-PLL. CD7, which is known to be positive in T-PLL [8], has also been reportedly detected on myeloid cells [9]. However, due to the relatively high cost of testing for CD7, we examined CD10 instead. The clinical course of T-PLL is progressively fast, and death usually occurs within one year [10]. In our case, the patient died at about 6 months after the practicing physician became aware of his lymphocytosis.

Several decades ago, T-PLL has been classified as one of the chronic T-cell leukemia, based on morphological, cytochemical and immunological evidences. However, the short survival time of this type of leukemia contradicts its characterization as being “chronic”. Therefore, this type of leukemia is presently called T-PLL and thought
to be a distinct pathophysiological entity because of recent evidences provided, such as cellular immunophenotyping [11,12].

Soluble IL-2 receptor has been demonstrated to be able to activate B-cells or T-cells [13], especially the CD8 (+) T-cells [14]. The elevated IL-2 receptor seen in our case might have been the trigger for the proliferation of the leukemic cells belonging to CD8 (+), after his admission into our hospital.

Interestingly, this case also showed morphological abnormality in three cellular lineages coupled with chromosomal abnormality of 45 (X, Y), and the presence of plural M-proteins such as IgGk and IgGλ. Previously, we have reported an MDS case with B-cell abnormality [15]. Since the leukemic cells in our present case were also positive for CD10, a marker which is also detected on immature B-cells, it is rational to implicate that certain kind of MDS cases might be related to B-cell disorder.

Since our patient in the present case was 96 years old, the morphological abnormalities seen in the three cellular lineages suggested that he might already have had the MDS disease long before the discovery of his T-PLL. Abnormality in 45 (X, 0) chromosome and the loss of Y chromosome, has been reportedly seen not only in MDS cases but also in normal elderly person [16,17]. Thus, our patient’s chromosomal abnormality could not be determined as being due to MDS-related abnormality or to the high age-related one. However, he was suggested to have come down with MDS. A serum M-protein has been reportedly detected in elderly persons as well as in diseases other than B-cell malignancies [18-20]. Plural M-proteins observed in our elderly case with non-B cell leukemia would probably have come from his high age. The large lymphocytic cells with nuclear pockets seen in the bone marrow smears would not be capable of differentiating into leukemia-related cells associated with MDS, despite that abnormal cells with nuclear pockets had been observed in MDS-bone marrow cells in certain instances [15].

Several mast cells were found sporadically among the free cells from bone marrow in our case. His IgE was slightly elevated. Mast cells are well recognized as one of key effector cells in IgE-associated immune responses [21]. In addition, GATA-1 secreted from mast cells are known to influence erythropoiesis [22], megakaryopoiesis [23], and immune responses [21]. In addition, GATA-1 secreted from mast cells are well recognized as one of key effector cells in IgE-associated immune responses. Nat Immunol 6: 135-142.

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It is generally regarded that MDS serve as a precursor phase leading to “myeloid” leukemia. What we had experienced here is truly a rare case that coincidentally showed T-PLL and MDS with plural M-proteins.

References