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Case Report

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Gamma-Delta T-Cell Acute Lymphoblastic Leukemia/ Lymphoma: Immunophenotype of Three Adult Cases

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Abstract

Gamma-delta (γδ) T-cell acute lymphoblastic leukemia/lymphoma (T-ALL) is not commonly observed in adult patients. We report three adult cases and describe their immunophenotypes. Two of these cases were diagnosed as γδ T-ALL; one was diagnosed as a mixture of T-ALL and T-cell non-Hodgkin lymphoma (T-NHL). We also discussed the differential diagnoses.

Keywords: γδ T-ALL; Immunophenotype; Diagnosis

Introduction

There are four types of gamma-delta (γδ) T-cell neoplasms, namely, γδ T-cell acute lymphoblastic leukemia/lymphoma (T-ALL), skin and mucosal γδ T-cell lymphoma, hepatosplenic T-cell lymphoma, and γδ T-cell large granular lymphocytic leukemia [1-4]. The incidence of γδ T-ALL is low [1, 2]. It is characterized by the expression of γδ T-cell antigen receptors (TCRs). Here, we report the clinical and pathological characteristics of three adult patients with γδ T-ALL.

Case Reports

As shown in Table 1, case 1 was untreated, while cases 2 and 3 were refractory.

Case 1

A 66-year-old woman with a 3-month history of gradually increasing tiredness came to our hospital. The vital signs were normal. The blood routine test was normal. Positron emission tomography/computed tomography (PET/CT) showed an irregular mediastinal mass with hypermetabolism signal. A mediastinal mass biopsy was performed. The immunohistochemistry result showed $CD99^+$, $CD5^+$, TdT^+, $CD3^+$, $CD117^+$, $CD30^+$, Ki-67^+ (90%), CK^-, $CD20^-$, and $CD15^-$. She was diagnosed as T-ALL.

Case 2

A 31-year-old woman with a 3-month history of tiredness and low fever presented to another hospital. The vital sign showed the heart rate of 110 beats per minute (bpm). The hemoglobin was 99 g/L, and platelet was 79×10^9/L. The bone marrow (BM) film showed plenty of abnormal lymphoblasts (84%). The immunophenotype of the BM specimen showed $CD7^+$, cytoplasmic (c) and surface (s) $CD3^+$, and $cTdT^+$. She was diagnosed as T-ALL. The chemotherapy regimens were cyclophosphamide, vindesine, doxorubicin, and dexamethasone (CHOP), methotrexate and pegaspargase in time sequence. After two cycles of chemotherapy, the patient presented to our hospital. The BM aspirate showed lymphoblasts (17%) this time.

Case 3

A 29-year-old man with a 1-month history of cough and enlargement of cervical lymph nodes was admitted to another hospital. He had generalized cervical lymphadenopathy. Platelet was 69×10^9/L. The CT showed lymphadenopathy in multiple superficial lymph nodes. A cervical lymph node biopsy was performed. The immunohistochemistry result showed $CD3^+$, $CD5^+$, TdT^+, and Ki-67^+ (80%). The BM film showed plenty of abnormal lymphoblasts (41%). He was diagnosed as T-ALL. The chemotherapy regimen was vincristine, daunorubicin, cyclophosphamide, and prednisone (VDCP) for one cycle. Then the patient presented to our hospital. The BM aspirate showed abnormal lymphoblasts (25%).

BM specimens of all patients were collected. A total of 5×10^5 nucleated cells per tube were incubated with 0.1% bovine serum albumin solution and then stained with monoclonal antibodies (mAbs). Samples were stained as described before [5]. All samples were detected by BD FACSCalibur and analyzed by Cell Quest (all are from BD).

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Table 1. Clinical Presentations

Case No.	Sex	Age	Status	Bone marrow involvement	Mediastinal involvement	Lymphadenopathy	Hepatosplenomegaly	Skin involvement
1	Female	66	Untreated	+	+	-	-	-
2	Female	31	Refractory	+	-	-	-	-
3	Male	29	Refractory	+	-	+	-	-

The gating strategy was as follows: live cells were gated on the forward scatter/side scatter (FSC/SSC) dot plot. Then, each cellular population was delineated on the SSC/CD45 dot plot. Abnormal γδ T cells were gated on the CD45/TCR γδ or CD45/CD3 dot plot. The definitions of the expression of a certain marker were described previously [6].

TCR rearrangements were detected by the ABI 7500 Fast Real-Time PCR System (Applied Biosystems, Foster City, CA, USA). The methods have been previously described [7].

The abnormal T cells in all cases were highly positive for CD7 and CD99, and positive for TCR γδ, CD45, and c/sCD3. For other pan-T-cell markers, all cases were positive for CD5; case 2 was dimly positive for CD8; case 3 was positive for CD2 and partially positive for CD8 (75.4%). For markers of immature cells, a fraction of abnormal T cells in cases 1 and 2 was positive for CD34 (22.9% and 46.1%, respectively); the abnormal T cells in case 1 were dimly positive for cTdT; a fraction of abnormal T cells in case 1 was positive for CD1a (15.47%); and a fraction of abnormal T cells in case 2 and case 3 was dimly positive for cTdT (75.2% and 24.6%, respectively). For the other markers, the abnormal T cells were negative for cMPO, CD11c, CD14, CD64, DR, CD13, CD15, CD33, cCD22, cCD79a, CD16, CD56, and CD57. The results of flow cytometry and PCR are presented in Table 2 and Figure 1.

Discussion

Generally, T-ALL lacks TCR expression, and only rare cases are positive for TCR γδ. The diagnosis of T-ALL is based on the immunophenotype, that is simultaneous positivity for c/sCD3 and blastic markers (cTdT, CD34, or CD1a) [8]. First, we defined the lineage of these abnormal cells, and the three cases were all positive for cCD3 and sCD3 and negative for cMPO, CD11c, CD14, CD64, CD19, CD10, cCD22, and cCD79a. Therefore, these cells were definitely T cells. Second, we needed to clarify the maturation stage. Based on the expression of sCD3 and CD1a, the World Health Organization (WHO) separates T-ALL into three categories: early T-ALL ($CD1a^-$, $sCD3^-$), thymic T-ALL ($CD1a^+$, $sCD3^-$), and mature T-ALL ($CD1a^-$, $sCD3^+$). T-ALL cells in case 1 dimly expressed cTdT, and some cells also expressed CD34 (22.9%) and CD1a (32.1%). A fraction of T-ALL cells in case 2 expressed CD34 (46.1%) and dimly expressed cTdT (75.2%). In case 3, some of these cells dimly expressed cTdT (24.6%). All these data show that these abnormal T cells are immature. Considering these data, case 1 was diagnosed as thymic T-ALL, while the other two as mature T-ALL.

The diagnosis of case 3 is worthy of being discussed in more detail. All the abnormal T cells expressed sCD3. Approximately 25% of the abnormal T cells dimly expressed cTdT, while approximately 75% of the abnormal T cells expressed CD8. These data suggest that there were two abnormal T-cell populations in this sample, and the majority of abnormal T cells were more mature than others. Based on the developmental stage, T cells can be divided into four types: pro-T, pre-T, cortical-T, and mature-T [9]. Therefore, in case 3, the majority of abnormal T cells were in the mature T-cell stage, while the minority were somewhere between the cortical T-cell stage

Table 2. Immunophenotype and TCR Rearrangement

Case No.	Percentage of abnormal T cells %[a]	Immunophenotype				TCRγδ rearrangement
		High	Positive[b]	Dim[b]	Negative	
1	20.1	CD7, CD99	cCD3, sCD3, TCRγδ, CD45, CD5, CD34 (22.9%), CD1a (32.1%), CD117 (54.97%), CD10 (15.47%)	cTdT	cMPO, CD11b, CD13, CD15, CD33, CD11c, CD14, CD64, DR, CD19, cCD22, cCD79a, TCRαβ, CD2, CD4, CD8, CD16, CD57, CD56	Positive
2	19.6	CD7, CD99	cCD3, sCD3, TCRγδ, CD45, CD34 (46.1%), CD5, CD10 (83.8%)	CD8, cTdT (75.2%)	cMPO, CD117, CD11B, CD13, CD15, CD33, CD11c, CD14, CD64, DR, CD19, cCD22, cCD79a, TCRαβ, CD1a, CD2, CD4, CD16, CD57, CD56	Positive
3	27.7%	CD7, CD99	cCD3, sCD3, TCRγδ, CD45, CD5, CD2	cTdT (24.6%), CD10 (9.4%), CD8 (75.4%)	cMPO, CD117, CD11b, CD13, CD15, CD33, CD11c, CD14, CD64, DR, CD19, cCD22, cCD79a, TCRαβ, CD1a, CD4,CD16, CD57, CD56, CD34	Positive

TCR: T-cell antigen receptor. [a]The percentage of abnormal T cells in the bone marrow nucleated cells. [b]The percentage of cells in the abnormal T cells.

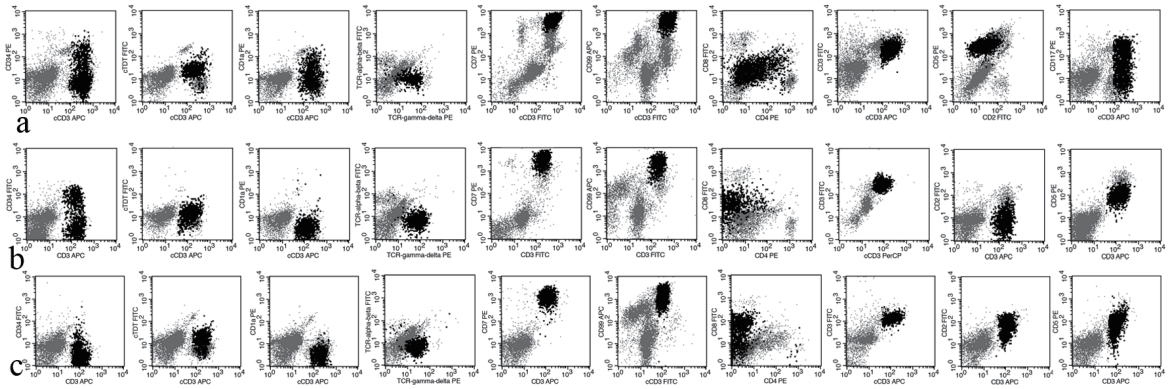

Figure 1. The expression profile of T-ALL cells in cases 1, 2, and 3. T-ALL: T-cell acute lymphoblastic leukemia/lymphoma.

and mature T-cell stage.

Early T-cell precursor T-ALL (ETP-ALL) is a subtype of T-ALL [10]. These cells deriving from hematopoietic stem cells migrate from the BM to the thymus [11]. Approximately 54% of T-ALL cells in case 1 expressed CD117, and thus we need to distinguish it from ETP-ALL. We have pieces of evidence to support the diagnosis of γδ T-ALL. First, the abnormal T cells were positive for CD5 (100% of blasts) and sCD3. Second, some abnormal T cells were positive for CD1a. Third, these T cells lacked the expression of other myeloid or stem cell markers. Fourth, CD117 can rarely be detected in T-NHL and T-ALL (2.2% and 11.4%, respectively) [8]. The immunophenotype shows that these T-ALL cells were more mature than ETP-ALL cells. Therefore, we excluded the diagnosis of ETP-ALL [10-12].

We were also interested in other immunophenotypic characteristics of these γδ T-ALL cases. CD7 and CD99 are universally highly expressed in all cases. For the other pan-T-cell markers, at least some T-ALL cells positively or dimly express CD2, CD5, or CD8. Although normal γδ T cells are double negative for CD4 and CD8, some γδ T-ALLs express CD4, CD8, or both [2]. These findings suggest that γδ T-ALL exhibits asynchronous antigen expression. In addition, CD10 is a common marker of lineage infidelity, the same finding in αβ T-ALL.

Here, we report three cases of γδ T-ALL. More studies are needed to clarify the unique clinical and laboratory characteristics.

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Financial Disclosure

None to declare.

Conflict of Interest

All authors have no conflict of interest to disclose.

Informed Consent

All the data and specimens were collected with informed consent.

Author Contributions

WW wrote the manuscript and analyzed the results of flow cytometry; YL performed the flow cytometry; MOY, MZ, LZ, JL, YZ, and WH treated the patients, and provided clinical information and other lab results; BJ treated the patients and revised the manuscript.

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