Case Report

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Acute myeloid leukemia with T lymphoblastic lymphoma: a case report and literature review

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Abstract

Acute myeloid leukemia (AML) with T lymphoblastic lymphoma (T-LBL) is a hematologic tumor of two origins, myeloid and lymphoblastic, and is relatively rare in the same patient. We report a rare case of AML with T-LBL. After the patient was diagnosed, he received standard chemotherapy, which decreased the primitive bone marrow cell percentage from 84% to 5%; however, the enlarged superficial lymph nodes showed no obvious change in size. Immunohistochemistry revealed the following: cluster of differentiation (CD)3 (+), CD5 (+), CD7 (+), transmission disequilibrium test (TDT) (+), myeloperoxidase (MPO) (−), and lysozyme (Lys) (−). The lymph node morphology and immunohistochemical results indicated T-LBL. Therefore, the final diagnosis was AML with T-LBL, with both diseases occurring independently and concurrently.

Keywords

Acute myeloid leukemia, T lymphoblastic lymphoma, case report, lymph node biopsy, myeloid protocell, immunohistochemistry

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Introduction

Clinically, both acute myelocytic leukemia (AML) and T-lymphoblastic lymphoma (T-LBL) are common hematological malignancies.[1,2] Because AML and T-LBL have different cell origins, their onsets are usually

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isolated, and it is rare for both diseases to develop concurrently in the same patient.[3,4] We report an AML patient complicated with T-LBL, and we describe the patient's disease evolution, with a literature review.

Case presentation

General information and physical examination findings

The patient was a 54-year-old man who first visited our hospital on 30 November 2016 because of "fatigue for 2 months and fever for 1 week". Physical examination revealed signs of anemia and five enlarged lymph nodes in the left submandibular region and left posterior triangle of the neck. The maximum lymph node diameter was 3 cm, and the nodes were firm but not tender. The patient had poor range of motion in his neck, and no tenderness in the sternum, and the liver and spleen were not palpable below his ribs.

Laboratory testing, and imaging and immunophenotyping findings

Peripheral blood evaluation revealed the following: white blood cell (WBC) count: 3.9×10^9 cells/L, neutrophil (NEU) count: 0.07×10^9 cells/L, hemoglobin (Hb): 83.00 g/L, and platelet (PLT) count: 77.00×10^9cells/L. Computed tomography (CT) revealed small lymph nodes in bilateral axillae, and multiple enlarged retroperitoneal lymph nodes were noted. The lymph nodes were obviously enlarged in the bilateral iliac vessel distribution areas. Bone marrow cell morphology revealed that archeocytes accounted for 84% of the cells. Immunophenotyping revealed expression of myeloperoxidase (MPO), cluster of differentiation (CD)34, CD38, CD33, and CD7; CD13 and CD117 were weakly expressed, and CD3 was not expressed. Bone marrow biopsy revealed hyperreactivity (>90%) and diffusely hyperplastic immature cells. Immunohistochemistry revealed CD34 (+), CD117 (+), transmission disequilibrium test (TDT) (+), PAX5 (−), CD3 (−), slight MPO (+), lysozyme (Lys) (−), and CD10 (+). Bone marrow gene tests for platelet-derived growth factor receptor-alpha (PDGFRA), platelet-derived growth factor receptor-beta (PDGFRB), platelet-derived growth factor-1 (PDGF1), and Janus kinase-2 (JAK2) were negative. The patient's chromosome number was 46 (XY), and the leukemia fusion genes, retinoic acid receptor alpha (RARA), eight-twenty-one (ETO), MYH11, nucleophosmin (NPM), and mixed-lineage leukemia (MLL) were negative. Leukemia mutation gene WT1 quantification was 8.53%, and C-KIT and FMS-like tyrosine kinase 3 (FLT3) were negative.

The patient was initially diagnosed with acute myelocytic leukemia (WT1 positive). On 1 December 2016, the standard-dose cytarabine + idarubicin (IA) regimen was given as induction chemotherapy. After 4 weeks of chemotherapy, bone marrow evaluation revealed obvious hyperplasia, with 5% archeocytes. However, no significant changes were found in the enlarged lymph nodes on repeat imaging; therefore, left cervical lymph node biopsy was performed on 14 January 2017. Histopathology showed that the lymph node structure was destroyed, and that tumor cells were densely infiltrated in the lymph node capsule and parenchyma. The cell volume was medium to large, with scant cytoplasm and no obvious cytoplasmic inclusions (Figure 1). Immunohistochemistry revealed CD3 (+), CD34 (+), MPO (−), Ki-67 (+) and approximately 80%, TDT (+), CD5 partially (+), PAX5 (−), and CD7 (+).

On 11 February 2017, repeat bone marrow evaluation revealed 20.5% archeocytes; CD33, CD34, CD7, and human leukocyte antigen DR (HLA-DR) were

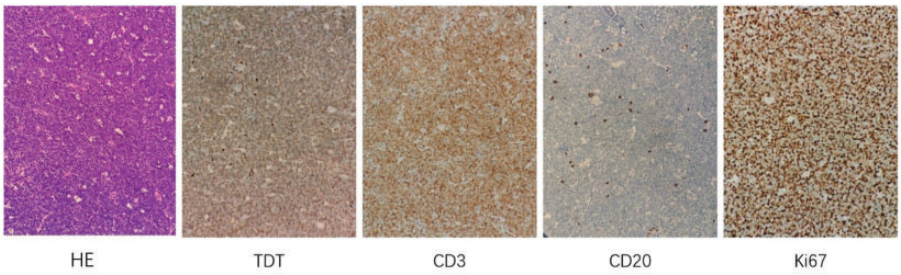

Figure 1. Histology of the lymph node biopsy.

expressed, while MPO, CD3, CD19, CD10, CD10, and CD79a were not expressed. Combined with the bone marrow examination findings at the first visit, the patient was finally diagnosed with AML complicated with T-LBL.

Treatment regimen

After the final diagnosis of AML complicated with T-LBL, the IA + vinovelbine, cyclophosphamide, pegaspargase, and prednisone (VCLP) regimen was initiated as induction therapy on 15 February 2017. The lymph nodes shrank significantly after this chemotherapy, and repeat bone marrow evaluation revealed 1.5% archeocytes. The previous regimen (IA+VCLP regimen) was given as consolidation chemotherapy on 24 March 2017. Post-chemotherapy imaging revealed that the enlarged lymph nodes had disappeared, and WT1 was 0.21%. High-dose cytarabine (3 g every 12 hours on days 1, 3, and 5) + pegaspargase was given for four courses as consolidation chemotherapy.

Clinical follow-up

At the end of the chemotherapy, bone marrow evaluation revealed 6% archeocytes, and CT revealed multiple enlarged lymph nodes in the neck, axillae, and mediastinum, indicating recurrent disease. Chemotherapy with cyclophosphamide, vinorelbine, prednisone, etoposide, pegaspargase, and idarubicin (COPEL + IDA) and cyclophosphamide, vinorelbine, prednisone, etoposide, pegaspargase, and mitoxantrone (COPEL + MTZ) were given on 31 October 2017 and 30 November 2017, respectively. Bone marrow evaluation on 8 January 2018 revealed 15.5% archeocytes, and immunophenotyping revealed that HLA-DR, CD7, CD38, CD33, and CD11b were expressed, cytoplasmic (cy)MPO was weakly expressed, and CD117, CD13, CD64, CD14, CD3, and CD79a were not expressed.

Positron emission tomography (PET)-CT revealed that multiple superficial and deep lymph nodes were enlarged, and the maximum standardized uptake value (SUV_{max}) was approximately 13.3. Cervical lymph node biopsy was repeated and revealed destruction of the normal structure and diffuse immature cell proliferation. Immunohistochemistry revealed the following: CD5 (+), CD7 (+), TDT partial (+), CD99 (+), CD33 (+), CD117 partial (+), B cell chronic lymphocytic leukemia/lymphoma-2 (Bcl-2) (+), and CD3 partial weak (+); TCR$\gamma\delta$ gene rearrangement was positive. Following decitabine + cyclophosphamide + vindesine (HOAP) chemotherapy and two courses of gemcitabine, dexamethasone, and cisplatin (GDP) + hyaluronic acid (HA), the enlarged lymph nodes disappeared. In June 2018, bone marrow evaluation revealed 38% archeocytes, and

immunophenotyping revealed two groups of abnormal archeocytes, accounting for 34.2% of all cells; 24.1% of these cells expressed CD3, CD5, CD7, and CD34, and 10.1% of the cells expressed CD34dim, CD7, CD5, and CD38. The following were not expressed: CD33, cyMPO, CD3, CD79a, CD13, and HLA-DR. The patient underwent successive fludarabine + cytarabine + recombinant human granulocyte colony-stimulating factor (G-CSF) (FLAG) and HOAP chemotherapy regimens, after which, bone marrow evaluation revealed 47% archeocytes. Immunophenotyping revealed CD34 (+), CD38 (+), CD7 (+), and CD45dim (+), and weak expression of CD33, CD3, and CD79a. Subsequently, three courses of chemotherapy with vincristine, cyclophosphamide, daunorubicin/idarubicin, and prednisone (VDCP) was administered. In addition, the patient's lactate level fluctuated between 10.0 and 20.0 mmol/L from 30 January 2018. During the treatment, the patient's condition continued to progress, and he died in January 2019.

Discussion

We reported a rare case of AML complicated with T-LBL. According to the flow cytometry and bone marrow biopsy results at the first visit, the patient was confirmed as having single myeloid clones instead of mixed-phenotype acute leukemia (MPAL) in accordance with the 1998 Immunologic Classification of Leukemias (EGIL) diagnostic score system[5] and the 2016 diagnostic classification standard of the World Health Organization (WHO).[6] The confirmation of AML was clear in our patient; however, because there was no significant change in the superficial and deep lymph nodes, we performed lymph node biopsy, and the morphological and immunohistochemical results indicated T-LBL. Hence, we diagnosed AML complicated with T-LBL.

Differential diagnosis is particularly important for patients with these diseases concurrently. Wang *et al.*[7] reported an AML patient with T-LBL who was finally diagnosed with MPAL according to in-depth examination. Therefore, it was proposed that full attention should be given to immunohistochemical examination for patients whose bone marrow immunophenotypes are inconsistent with peripheral tissues at the preliminary diagnosis. Evaluating myeloid markers, such as CD117, CD33, Lys, and MPO, should be performed with lymph node biopsy. We repeatedly evaluated our patient's recurrently enlarged lymph nodes compared with the initial diagnosis, and also evaluated myeloid molecular markers. Our findings confirmed a clear diagnosis of T-LBL. In addition to MPAL, myeloid and T-lymphoid expression often occurs simultaneously in early T-cell precursor-acute lymphoblastic leukemia (ETP-ALL). ETP-ALL is a new tentative T-ALL/LBL subtype added in the 2016 WHO classification.[6] ETPs are derived from bone marrow and thymus precursor cells; therefore, ETP-ALL may present with myeloid/T-lymphoid expression. However, the important point differentiating ETP-ALL from AML and MPAL is that patients with ETP-ALL are MPO-negative. Hence, ETP-ALL was also excluded in our patient. Furthermore, myeloid/lymphoid leukemia with eosinophils and abnormalities in PDGFRA, PDGFRB, PDGF1, or pericentriolar material 1 (PCM1)-JAK2 are also present with ETP-ALL. Eosinophil counts were not increased in our patient, and bone marrow gene testing for PDGFRA, PDGFRB, PDGF1, and JAK2 were negative. Therefore, a diagnosis of myeloid/lymphoid leukemia was excluded.

The most remarkable feature in the present case is the clonal evolution of marrow

archeocytes during the disease course. In the early stage of the disease, the bone marrow had a single myeloid clone and expression. In later stages, two groups of abnormal cells appeared; one group expressed early myeloid markers, while the other group expressed T-lymphoid markers. By the end of the disease course, all bone marrow archeocytes had evolved lymphoid expression. The clinical incidence of this cell line transformation is very low. Rossi *et al.*[8] statistically analyzed 1482 children with acute leukemia; only nine (0.6%) had line transformation. Furthermore, seven of nine patients had 11q23 chromosome/MLL genetic abnormalities. Therefore, we consider that an abnormal 11q23 chromosome/MLL gene may be correlated with the clone transformation in our patient.

Pedigree transformation is rarer in adult patients.[9] In the present case, there was a clonal evolution in the later course of the disease; abnormal cells were transformed from myeloid to lymphoid. We assumed that this immune phenotype was unstable and suggests that the abnormal cells in these patients originate from more primitive hemopoietic progenitor cells, even from the pluripotent stem cell phase. However, this hypothesis requires more clinical cases for further analysis.

Another characteristic of the present case was the persistent hyperlactatemia late in the disease course. This was considered a clinical manifestation of aggravation of the primary disease. Hyperlactatemia is more common in solid tumors and malignant hematopathy, although this has been reported only in single cases.[10–12] The mechanism of hyperlactatemia is considered overexpression of hexokinase and insulin-like growth factors (IGFs) in tumor cells. Hexokinase catalyzes the initial rate-limiting steps in glycolysis. IGFs are an activator of hexokinase, which can promote glycolysis metabolism[13] even in the presence of oxygen, when both compounds are present at high concentrations. During later treatment, our patient's lactate levels always decreased after chemotherapy, and subsequently increased. The characteristics of our case show that hyperlactatemia is correlated with hematologic tumors.

The treatment plan for AML with T-LBL is still being researched (Table 1).[14–16] In the present case, the IA regimen was introduced as the initial treatment. Bone marrow findings improved, but the lymph nodes did not shrink. The patient had short-term recurrence, but he responded to the combination VCLP + IA regimen. A variety of combined regimens were used during the second recurrence, but all failed to achieve remission, suggesting that the prognosis of AML with T-LBL is poor, and patients are prone to relapse. Currently, allogeneic hematopoietic stem cell therapy (allo-HSCT) may be the only option to cure this disease. Considering that the present study was a case report

Table 1. Literature review of the treatment regimens for patients with AML complicated with T-LBL

First author	Year	Journal	Treatment regimen
Chen[14]	2015	J Clin Hematol	IA regimen, which failed and was changed to the FLAG + aclacinomycin
Chang[15]	2012	Diagn Pathol	DA + dexamethasone; complete remission was achieved. Then, allo-HSCT
Ly[16]	2014	Pediatr Blood Cancer	allo-HSCT

AML, acute myeloid leukemia; T-LBL, T lymphoblastic lymphoma; IA, standard-dose cytarabine + idarubicin; FLAG, fludarabine + cytarabine + recombinant human granulocyte colony-stimulating factor (G-CSF); DA, standard-dose cytarabine + daunorubicin; allo-HSCT, allogeneic hematopoietic stem cell transplantation.

without a control group, our conclusions would be more robust if supported in multicenter clinical research.

Conclusion

There is currently no treatment regimen recommended for AML with T-LBL. Allo-HSCT may be the only option to cure this disease.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics statement

This study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of our hospital. The patient described in this study provided verbal informed consent.

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