Epstein–Barr Virus Positive Diffuse Large B-Cell Lymphoma Transformed Into Angioimmunoblastic T-Cell Lymphoma After Treatment: A Case Report and Literature Review

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Case Report

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Abstract

Background: Angioimmunoblastic T-cell lymphoma (AITL) is the sub-type of mature T-cell non-Hodgkin lymphoma. Compared with diffuse large B-cell lymphoma (DLBCL), AITL patients are frequently accompany with Epstein–Barr virus(EBV) infection. To date, there is no report on the subsequent development of AITL in patients with EBV-positive DLBCL. We performed a rare case of EBV-positive AITL developing one year after initial diagnosis of EBV-positive DLBCL. The patient showed poor response to the chemotherapy regimen, and poor survival.

Case presentation: A 83-year-old Chinese male presented with enlarged lymph nodes in the neck and bilateral inguinal. Immunohistochemically (IHC), the atypical cells were strongly positive for CD20, CD19, PAX-5 and MUM-1, but negative for CD3, CD5, CD10, Bcl-6, CyclinD1, CD138 and TdT. Besides, in situ hybridization for EBV-encoded small RNA (EBER) staining was also strongly positive. The patient was diagnosed with EBV-positive DLBCL, and transformed to Angioimmunoblastic T-cell lymphoma one year after initial diagnosis of EBV-positive DLBCL. Unfortunately, the patient ultimately died three months after diagnosed AITL. The overall survival time of this patient is fifteen months.

Conclusions: Transformed EBV-positive AITL is a rare type of lymphoma with high malignancy and a generally poor prognosis. The accurate diagnosis should be depended on immunophenotype and morphology.

Background

Angioimmunoblastic T-cell lymphoma (AITL) is the sub-type of mature T-cell non-Hodgkin lymphoma. Compared with diffuse large B-cell lymphoma (DLBCL), AITL patients are frequently accompany with Epstein–Barr virus(EBV) infection. To date, there is no report on the subsequent development of AITL in patients with EBV-positive DLBCL. We performed a rare case of EBV-positive AITL developing one year after initial diagnosis of EBV-positive DLBCL.

Case Presentation

In March 2019, a 83-year-old Chinese male was admitted to our hospital due to a month history of enlarged lymph nodes in the neck and bilateral inguinal without pain and fever. Computed tomography (CT) scan disclosed generalized lymphadenopathy in the mediastinum, hilum, bilateral inguinal, right lung, right kidney. However, the complete blood count, coagulation markers, albumin, lactate dehydrogenase(LDH), creatinine, β_2 -microglobulin and alanine aminotransferase(ALT) were all normal. The laboratory of EBV viral IgM-capsid antigen (VCA) and EBV-DNA were strongly positive. Then, the patient underwent biopsy of left inguinal lymph node, a large number of diffuse large sized proliferation atypical lymphoid cells can be seen under microscope. Immunohistochemically (IHC), the atypical cells were strongly positive for CD20, CD19, PAX-5 and MUM-1, but negative for CD3, CD5, CD10, Bcl-6, CyclinD1, CD138 and TdT (Fig. 1). C-myc and Bcl-2 were expressed by more than 60% and 20% of

lymphoma cells. Ki67 was expressed by more than 80% of lymphoma cells. Besides, in situ hybridization for EBV-encoded small RNA (EBER) staining was also strongly positive. Bone marrow aspiration and trephine biopsy showed no infiltration. Based on the above, a pathological diagnosis of EBV-positive DLBCL was made. After the diagnosis of EBV-positive DLBCL, the patient received eight cycles of R-miniCHOP(rituximab, cyclophamide, doxorubicin, vincristine and prednisone) therapy, but his symptoms did not disappear and PET/CT scan showed no signs of complete remission (CR) or partially remission (PR) after treatment. The disease status was stable despite the immune-chemotherapy administration.

In March, 2020, one year after initial diagnosis of EBV-positive DLBCL, the patient was readmitted to our hospital again because of nasopharyngeal discomfort. CT scan revealed multiple enlargements of mediastinum, hilum, bilateral inguinal, right lung, right kidney lymph nodes and thickened nasopharyngeal wall. Bone marrow aspiration was normal. A left inguinal lymph node biopsy was performed, and to our surprise, it revealed ngioimmunoblastic T-cell lymphoma (AITL). Immunohistochemically, the cancer cells were positive for most pan-T cell antigens such as CD3, CD4, CD5, CD7, CD21 and T follicular helper (TFH) biomarkers including CD10, Bcl-6 and CXCL13, but negative for CD20, ALK, PD-1, EMA and Perforin (Fig. 2). Ki67 was expressed in more than 45% of lymphoma cells. EBERs showed strongly positive reaction. A diagnosis of AITL secondary to EBV-positive DLBCL was finally established. Since the patient showed poor response to the previous R-miniCHOP treatment, new strategy of therapy should be considered. So, the histone deacetylase inhibitor Chidamide and prednisolone were administered. The patient ultimately died of disease progression in July 3 2020 after three months when diagnosed AITL. The overall survival time of this patient is fifteen months.

Discussion And Conclusions

DLBCL is the most common type malignant hematological diseases and also the most common type of B-cell non-Hodgkin lymphoma[1]. Our previous retrospective study found that hepatitis B virus (HBV) is strongly associated with aggressive B cell lymphoma, especially DLBCL[2]. However, Epstein-Barr virus (EBV) associated DLBCL is relatively rare. AITL is the sub-type of mature T-cell non-Hodgkin lymphoma. Compared with DLBCL, AITL patients are frequently accompany with EBV infection, and some study found that EBV is involved in the occurrence and development of AITL.

EBV positive DLBCL patients following AITL have been reported in some case report[3–6]. EBV infection may reduce the immune function of AITL patient, and lead to B cell dysfunction. The occurrence of secondary DLBCL seems to be triggered by EBV infection. Some studies[7–8] have reported that AITL patients composite with DLBCL.

Only one case report that development of AITL after treatment of EBV-negative DLBCL[9]. This is the first report on the subsequent of AITL following DLBCL. The patient received five cycles of R-CHOP (rituximab, cyclophamide, doxorubicin, vincristine and prednisone) chemotherapy regimen, and not achieve any response. Six mouths after initial diagnosis DLBCL, the patient transformed to AITL, and ultimately died of progression disease after diagnosis AITL two months. The overall survival is only eight months.

To our knowledge, there is no report on the subsequent development of AITL in patients with EBV-positive DLBCL. Now, we performed a rare case of EBV-positive AITL developing one year after initial diagnosis of EBV-positive DLBCL. The patient showed poor response to the previous R-miniCHOP chemotherapy regimen, and then treated with Chidamide and prednisolone. Unfortunately, similar to the above case, the patient finally died three months after diagnosis secondary EBV-positive AITL. We hypothesized that EBV play an important role in the development of DLBCL transform to AITL.

In conclusion, this is a rare disease with a generally poor prognosis. However, the specific mechanism of this phenomenon is still unknown.

Abbreviations

DLBCL: Diffuse large B-cell lymphoma; AITL:Angioimmunoblastic T-cell lymphoma; EBV: Epstein-Barr virus; HBV:Hepatitis B virus; CT: Computed tomography;IHC:Immunohistochemical; EBER:EBV-encoded small RNA; LDH:Lactate dehydrogenase; ALT: Alanine aminotransferase; VCA: Viral capsid antigen; CR:Complete remission; PR: Partially remission; TFH:T follicular helper;

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from all participants. Ethical approval was obtained from the Ethics Committee of the Chongqing Key Laboratory of Translational Research for Cancer Metastasis and Individualized Treatment,Chongqing University Cancer Hospital, Chongqing, China, in accordance with the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor in-Chief of this journal.

Consent for publication

Written informed consent for publication was obtained from all participants.

Availability of data and materials

The data sets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Not applicable.

Authors' contributions

Chaoyu Wang, Yi Gong, Xiping Liang and Rui chen conceptualized and designed the study. Chaoyu Wang and Yi Gong drafted the article. All the authors approved the final version.

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Figures

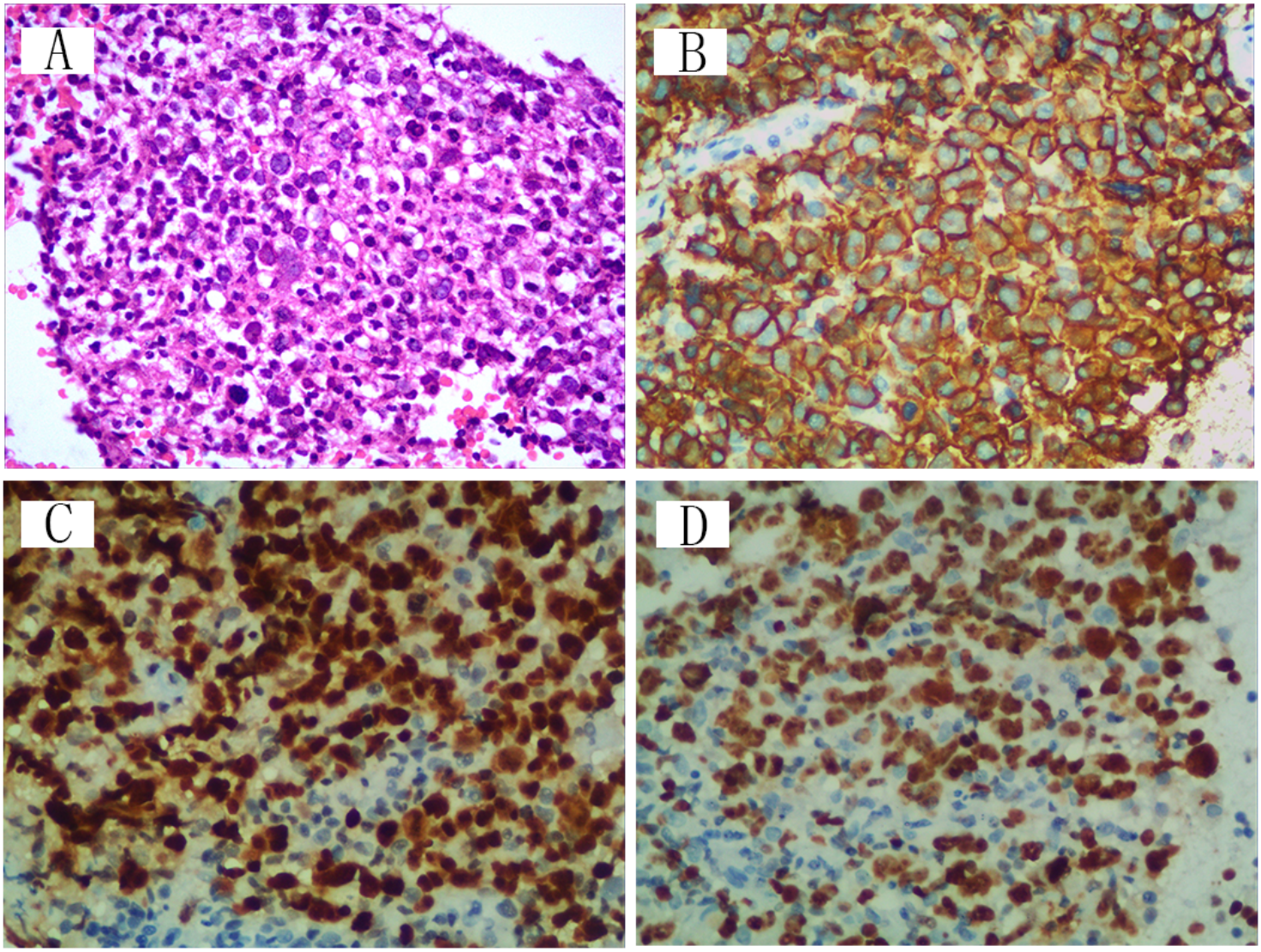

Figure 1

The left inguinal lymph node biopsy of initial diagnosis showing morphological (A,×200) and immunohistochemistry staining with positivity for CD20 (B,×200), PAX-5 (C,×200) and Ki-67(D,×200).

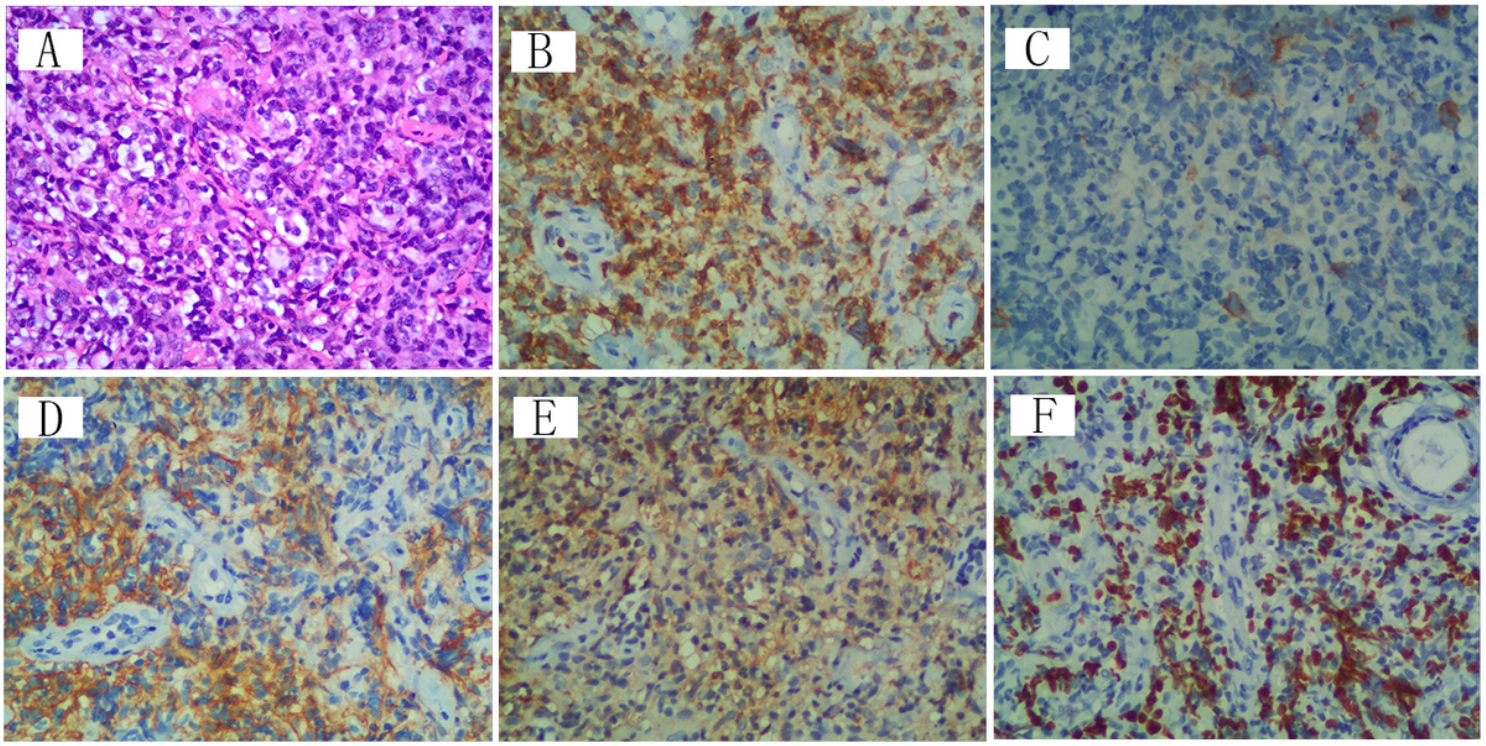

Figure 2

The biopsy of left inguinal lymph node one year after initial diagnosis showing morphological (A,×200) and immunohistochemical finding with negativity for CD20 (C,×200), positivity for CD5 (B,×200), CD21(D,×200), CXCL13 (E,×200), Ki-67 (F,×200).

Supplementary Files

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