Angioimmunoblastic T-cell lymphoma combined with Hodgkin's lymphoma:a case report

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Abstract

Angioimmunoblastic T-cell lymphoma (AITL) is a special subtype of peripheral T-cell lymphoma, Histopathological examination is the main basis for the diagnosis of the disease, but the diagnosis is challenging. The study has shown that combining immunohistochemistry and gene rearrangement can increase the diagnostic accuracy

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Abstract

Angioimmunoblastic T-cell lymphoma (AITL) is a special subtype of peripheral T-cell lymphoma with a poor prognosis, clinical manifestations combinationed with immunohistochemistry, gene rearrangement and so on can increase the diagnostic accuracy.

Introduction: Angioimmunoblastic T-cell lymphoma (AITL) is a special subtype of peripheral T-cell lymphoma, Histopathological examination is the main basis for the diagnosis of the disease, but due to lack of specific pathological characteristics, the diagnosis is challenging. The study has shown that combining immunohistochemistry and gene rearrangement can increase the diagnostic accuracy.

Patient Concerns: A 56-year-old male patient was admitted to the hospital due to skin redness and itching for 4 months.

Diagnoses: The patient was diagnosed with AITL with Hodgkin's lymphoma based on lymph node biopsy, immunohistochemistry, gene rearrangement and positron emission tomography computer tomography

Keywords: follicular lymphoma, myelofibrosis, immunohistochemistry, cytokines

Introduction

Angioimmunoblastic T-cell lymphoma (AITL) is a subtype of peripheral T-cell lymphoma with poor prognosis¹ accounting for 1–2% of non-Hodgkin's lymphoma and 15–20% of peripheral T-cell lymphoma. The median age is approximately 65 years. The clinical manifestations mostly include fever, weight loss, urticaria, papules, red nodules, and skin lesions² Due to the abnormal proliferation activity of B cells, AITL is often accompanied by autoimmune disorders, such as hemolytic anemia and hypergammaglobulinemia. Studies have shown the Epstein-Barr virus (EBV) to play an important role in the pathogenesis of AITL; EBV can stimulate the activation of helper T cells, thereby leading to the occurrence of tumors. While histopathological examination forms the basis for diagnosis of the disease, the latter still remains challenging due to the lack of specific pathological characteristics. The current study suggested that combination of immunohistochemistry and gene rearrangement can increase diagnostic accuracy. CD10 and CXCL13 are specifically expressed in AITL and can be used as characteristic markers for the diagnosis of AITL. The clonal rearrangement of IgH gene and TCR γ would also be of great significance in the diagnosis.

Case Report

A 56-year-old man was admitted to the hospital with Hodgkin's lymphoma. The patient received ABVD and AVD chemotherapy, and all details of unsatisfactory treatment effect were collected, wherefrom angioimmunoblastic T-cell lymphoma and focal classical Hodgkin's lymphoma (compound lymphoma) were revealed. CD21 was found to shrink and destroy the FDC network, CD20+; PAX-5+; CD3+; Ki-67+: 20 %–30%; CD10–; BCL-6+; MUM-1+; PD-1+; CXCL-13–; CD30+; CD15–. Molecular detection: TCR β DB+J β 1/2 showed monoclonal rearrangement, and V β +J β 2 showed oligoclonal rearrangement.

The patient was admitted to the hospital owing to skin redness and itching for 4 months. Physical examination revealed extensive redness, swelling, and rough skin on the head, neck, and limbs. There were multiple enlarged lymph nodes in the right armpit and bilateral groin. The largest one was approximately 4 cm in diameter, with a smooth surface, no tenderness, and good mobility. The laboratory examination results are presented in Table 1. At first, a proliferative disease of the lymphatic system was suspected; a punch biopsy was performed, whose histological diagnosis documented classic Hodgkin's lymphoma, lymphocyte-rich type, with molecular detection: EBER (+). In addition, CD3+ lymphocytes occupied 96.1% , positively expressing CD3 and CD5, whereas some expressed TCR α , and a small number expressed CD8, as per immunohistochemistry . Multiple organs with lymph node infiltration were detected using radiological imaging. Interestingly, the patient presented with skin redness. The patient completed the ABVD (doxorubicin hydrochloride liposome 40 mg ivgtt d1, 15; bleomycin 10 mg/m² iv d1, 15; vindesine 4 mg iv d1, 15; dacarbazine 375 mg/m² iv d1,15) chemotherapy, followed by AVD in the second course. However, he tended to have a poor performance status, and skin pruritus symptoms were aggravated. Immunohistochemical examination of the skin revealed CD20 +, PAX-5 +, CD3 +, Ki-67 + (20–30%), CD10–, BCL-6 +, MUM-1 +, PD-1 +, CXCL-13–, CD30 +, and CD15–(Fig. and 1,2). TCR β DB+J β 1/2 showed monoclonal rearrangement, and V β +J β 2 showed oligoclonal rearrangement upon molecular examination with PTPRD gene mutation. Pathological diagnosis was non-Hodgkin peripheral (mature) T-cell lymphoma, prone to angioimmunoblastic T-cell lymphoma. Due to the angioimmunoblastic T-cell lymphoma with Hodgkin's lymphoma, it was decided that the patient would be followed-up with EDOCH chemotherapy; however, unfortunately, he died of lung infection.

Discussion

AITL is a special subtype of peripheral T-cell lymphoma that originates from follicular helper T cells (TFH), often with fever, night sweats, weight loss, lymphadenopathy, skin rash, and other clinical manifestations³

Skin involvement is one of the most common extranodal manifestations of the disease⁴ Due to the heterogeneity of AITL, most cases do not get diagnosed until weeks or months after the onset of symptoms.

While the diagnosis of AITL relies on lymph node biopsy, some patients may be diagnosed after 2–3 lymph node biopsies. The pathological features include the destruction of lymph node structure, the tumor cells being mainly of medium size, the cytoplasm being lightly stained or transparent, the nucleus being generally round or oval, and the cell being atypical. In the background of inflammatory cells, such as eosinophils, lymphocytes, and plasma cells, large cells of varying numbers are scattered. The TFH phenotype is positive for CD3, CD4, and CD10⁵ Most CD5 and CD7 expression are absent⁶ CD30 is found in 20% of patients⁷ Cytoplasmic CXCL13 is almost uniformly expressed, and is specific for AITL⁸ TFH expression of PD-1, ICOS, BCL-6, and CD200 can be distinguished from that in benign lymphoproliferative diseases and PTCL subtypes. Approximately 60% of patients have TCR gene rearrangements, as seen in TC β , TCD, and TCG rearrangements, whereas some patients have IgH gene rearrangements. In recent years, with advanced research on genomics, AITL has been found to have higher TET2, RHOA, IDH2, and DNMT3A mutations, especially TET2 mutations, which are related to poor prognosis⁹ However, AITL currently lacks a systematic method of identification, and hence its diagnosis is still challenging.

The occurrence of AITL is highly correlated with EBV infection. EBV-infected B cells can transmit EBV protein signals on their surface to T cells through major histocompatibility complex II (MHCII) molecules when TFH cells interact with B cells. Cells up-regulate the expression of CD ligands, provide antigen and costimulatory signals for T cell activation, and promote the secretion of chemokine CXCL13¹⁰ which subsequently leads to B cell activation. Laforga et al¹¹ had proposed the hypothesis that EBV promotes the proliferation of B cells in AITL. They believed that due to the effect of EBV, CD8-positive T cells are immunosuppressed, leading to oversight of EBV-positive B cells. EBV-infected B cells lose control and may be polyclonal, oligoclonal, or monoclonal. If the immunoglobulin structure is broken, B cells can have three outcomes: 1. proliferation resembling that of RS cells; 2. proliferation resembling that in CHL; or 3. it might develop into CHL.

In the 2008 edition of the ‘WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues’, RS-like cells were mentioned, for the first time, to be seen in early AITL¹²; AITL and CHL also have lymph node structure destruction, and plasma cell, tissue cell, and other inflammatory cell infiltration, in addition to a correlation with EBV infection¹³ thereby confirming the dependence of AITL and CHL on immunophenotypes only. The immunophenotype of CHL includes CD15+, CD30+, PAX-5 weakly positive, CD3-, CD20- (mainly), CD45-, and CD79a-, which combined with RS cells, help in the diagnosis^{14,15} CHL and AITL are two types of lymphoma with extremely different prognoses. While CHL has good prognosis, with a 5-year overall survival (OS) rate > 80%¹⁶ AITL has poor prognosis. A retrospective analysis had found (after CHOP chemotherapy in elderly patients with AITL) the CR rate to be 25%, and the median OS to be only 14.9 months. At present, ABVD is the first-line treatment for CHL, and most patients benefit from it. However, AITL progresses rapidly with high mortality rate. Therefore, patients with newly diagnosed lymphoma should be verified based on clinical phenotype, pathological morphology, and immunohistochemistry for better and successful.

The Key Clinical Message

Clinical manifestations combinationed with immunohistochemistry, gene rearrangement can increase the diagnostic accuracy of lymphoma.

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Conflict of Interest Statement

The authors report no conflict of interest

Author Contributions

Xiao-han Gao, Jing Li, Lin Kang, Qiang Wei, Jie Li, Jie Yang and Hongling Hao: collected and recorded the clinical data.

Xiao-han Gao and Yan Li: analyzed the case, wrote the manuscript and performed the critical revision.

Ethics Statement

Written consent was obtained from the patient’s relatives ahead of submission.

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Table 1. The laboratory findings

CBC	WBC	15.00×10 ⁹ /L
	LY	5.12×10 ⁹ /L

	HGB	151g/L
	PLT	$292 \times 10^9/L$
β2-Microglobulin	β2-MG	4.288ug/mL
Biochemistry	TP	53.5g/L
	GLO	22.3g/L
	LDH	323.9U/L
	HBDH	222.4U/L
	TG	1.84mmol/L
Coombs test	Direct Coombs test	negative
	Indirect Coombs test	negative
Tumor Marker	CA 125	125.100U/mL
	VEGF	178.4pg/mL

CBC:complete blood count;WBC:white blood cell;LY:lymphocyte cell; HGB:hemoglobin; PLT:plate;TP:Total protein;GLO:Globulins;LDH:Lactate dehydrogenase;HBDH:GHB dehydrogenase TG:Triglyceride;VEGF:Vascular endothelial growth factor

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Zhang-figures.pdf available at <https://authorea.com/users/431237/articles/534744-angioimmunoblastic-t-cell-lymphoma-combined-with-hodgkin-s-lymphoma-a-case-report>