Journal of Zhejiang University-SCIENCE B 2026 27(11):1325-1331
www.jzus.zju.edu.cn; www.springer.com/journal/11585
E-mail: jzus_b@zju.edu.cn

Correspondence

https://doi.org/10.1631/jzus.B2600224

Check for updates

Angioimmunoblastic T-cell lymphoma associated with myeloid neoplasms: a case report and literature review supporting a shared clonal origin

Yang YANG, Yi LI, Huiyao GU, Jingsong HE✉

Bone Marrow Transplantation Center, the First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310006, China

Angioimmunoblastic T-cell lymphoma (AITL) is an aggressive peripheral T-cell lymphoma derived from T-follicular helper (TFH) cells (Alaggio et al., 2022). It is characterized by a multistep oncogenic process involving recurrent mutations in epigenetic regulators such as tet methylcytosine dioxygenase 2 (*TET2*), DNA methyltransferase 3 alpha (*DNMT3A*), and isocitrate dehydrogenase 2 (*IDH2*) (Couronné et al., 2012; Chiba and Sakata-Yanagimoto, 2020). These mutations are also frequently detected in clonal hematopoiesis (CH) and myeloid neoplasms (Jaiswal and Ebert, 2019; Harland et al., 2024), suggesting a potential shared cellular origin between lymphoid and myeloid malignancies.

Myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) have occasionally been reported in patients with AITL. Historically, such cases have often been interpreted as therapy-related myeloid neoplasms arising after exposure to cytotoxic chemotherapy. However, recent genomic studies have suggested that cytotoxic treatment can sometimes accelerate the expansion of pre-existing CH clones rather than serving as the primary leukemogenic driver (Bolton et al., 2020). Several studies have demonstrated that identical CH-associated mutations can be shared between lymphoid and myeloid compartments, supporting a model of divergent clonal evolution from a common hematopoietic progenitor (Gibson et al., 2017; Tiacci et al., 2018). Nevertheless, most reported cases describe a metachronous disease course, in which MDS or AML develops months or years after AITL diagnosis or treatment. Molecular analyses made at the time of synchronous presentation remain scarce, and direct evidence for a clonal relationship at disease onset is limited.

Here, we report a patient with synchronous AITL and MDS with increased blasts 2 (MDS-IB2) and investigate the clonal relationship between the lymphoid and myeloid malignancies using targeted next-generation sequencing.

An 87-year-old male patient was admitted to the First Affiliated Hospital of the Zhejiang University School of Medicine, Hangzhou, China, for further evaluation of progressive skin lesions and unexplained cytopenia. Approximately three months prior to admission, the patient developed punctate erythematous rashes on the back accompanied by marked pruritus. Over time, the lesions gradually enlarged and coalesced into patchy erythematous plaques. The patient initially sought medical attention at a local hospital, where the lesions were suspected to represent dermatitis or eczema. Treatment with antiallergic agents and corticosteroids was initiated; however, the skin lesions showed limited improvement.

Approximately one month before admission, the patient developed poor appetite, generalized fatigue, and progressive weight loss exceeding 10% of baseline body weight. In addition, he developed dizziness, shortness of breath, and generalized weakness, prompting referral to our hospital.

Initial laboratory tests revealed pancytopenia, with a white blood cell count of 3×10^9 L^{-1}, hemoglobin of 60 g/L, and platelet count of 87×10^9 L^{-1}. Serum lactate dehydrogenase (LDH) was 230 U/L and

✉ Jingsong HE, hejingsong@zju.edu.cn
Jingsong HE, https://orcid.org/0000-0002-1190-1037
Yang YANG, https://orcid.org/0000-0001-5171-6226

Received Apr. 6, 2026; Revision accepted May 25, 2026;
Crosschecked July 27, 2026; Published online Aug. 8, 2026

© Zhejiang University Press 2026

β_2-microglobulin was 8.28 mg/L. Serum cytokine analysis showed elevated interleukin-8 (IL-8) level of 149.09 pg/mL and IL-10 level of 8.06 pg/mL.

We performed a skin biopsy for histopathologic examination. Microscopic evaluation revealed hyperkeratosis and irregular epidermal hyperplasia with focal spongiosis. The dermis demonstrated a dense lymphoid infiltrate composed of atypical lymphoid cells with irregular nuclear contours and mild cytologic atypia, predominantly involving the superficial and mid dermis. Immunohistochemical staining showed that the tumor cells expressed B cell lymphoma 6 (BCL6), programmed cell death protein 1 (PD-1), and C-X-C motif chemokine ligand 13 (CXCL13), and the Ki-67 proliferation index was approximately 30%. Polymerase chain reaction (PCR) analysis demonstrated clonal T-cell receptor (*TCR*) gene rearrangement. These findings were consistent with a TFH cell phenotype and supported the diagnosis of AITL (Fig. 1). Bone-marrow aspiration and biopsy were subsequently performed to investigate the cause of pancytopenia. The bone marrow was hypercellular, with 18% myeloblasts and prominent dysplastic changes involving multiple hematopoietic lineages. Multiparameter flow cytometry identified an aberrant immature myeloid population expressing cluster of differentiation 34 (CD34), CD117, CD33, CD13, human leukocyte antigen-DR isotype (HLA-DR), and CD123, consistent with MDS-IB2.

To assess systemic involvement, we performed ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT). Imaging revealed diffuse bone-marrow hypermetabolism (SUV_{max}=5.47) and multiple hypermetabolic lymph nodes (SUV_{max}=4.70) (Fig. 2), where SUV_{max} refers to the maximum standardized uptake value, suggesting synchronous involvement by both AITL and MDS.

To further investigate the molecular relationship between the lymphoid and myeloid malignancies, we performed targeted next-generation sequencing (NGS) on paired cutaneous AITL-tissue and bone-marrow samples. Sequencing of the cutaneous lesion identified pathogenic mutations in isocitrate dehydrogenase 2 (*IDH2*; p.R140Q) and additional sex combs like-1 (*ASXL1*; p.R1415X) with variant allele frequencies (VAFs) of 7.7% and 7.5%, respectively, with additional alterations involving tumor protein p53 (*TP53*), major histocompatibility complex (MHC) class II transactivator (*CIITA*), and Notch receptor 1 (*NOTCH1*). In contrast, bone-marrow sequencing revealed the same *IDH2* and *ASXL1* mutations at markedly higher VAFs (40.24% and 39.41%, respectively), along with additional mutations involving serine/arginine-rich splicing factor 2 (*SRSF2*), stromal antigen 2 (*STAG2*), and BCL6 corepressor (*BCOR*), which were restricted to the myeloid compartment. Based on the clinicopathologic and molecular findings, the patient was diagnosed with synchronous AITL and MDS-IB2.

The patient subsequently received one cycle of azacitidine (75 mg/(m^2·d), Days 1–7) combined with

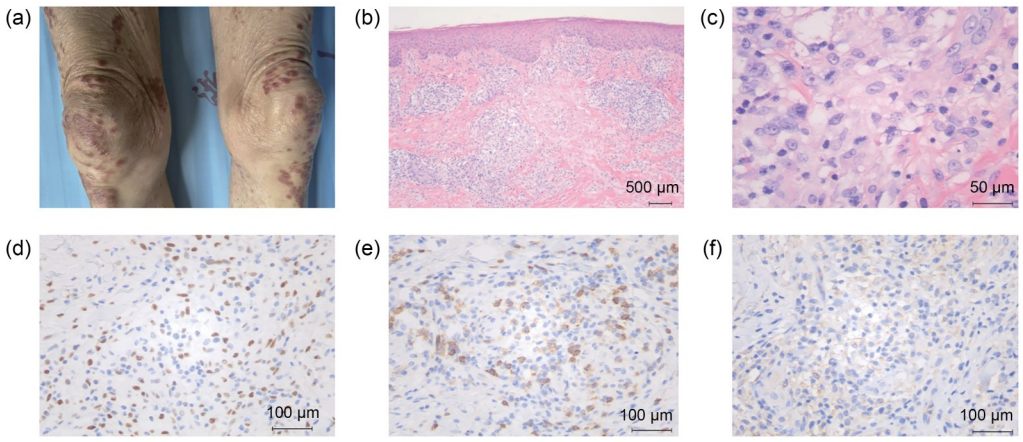


Fig. 1 Diagnostic features of angioimmunoblastic T-cell lymphoma (AITL). (a) Clinical photograph showing erythematous cutaneous lesions at presentation. (b) Skin biopsy showing a dermal infiltrate of atypical lymphoid cells with a predominantly perivascular distribution (hematoxylin and eosin). (c) Higher magnification demonstrating atypical lymphoid cells with mild cytological atypia and frequent mitotic figures (hematoxylin and eosin, ×400). (d–f) Immunohistochemistry demonstrating the expression of B cell lymphoma 6 (BCL6) (d), programmed cell death protein 1 (PD-1) (e), and C-X-C motif chemokine ligand 13 (CXCL13) (f), consistent with a T-follicular helper (TFH) cell phenotype.

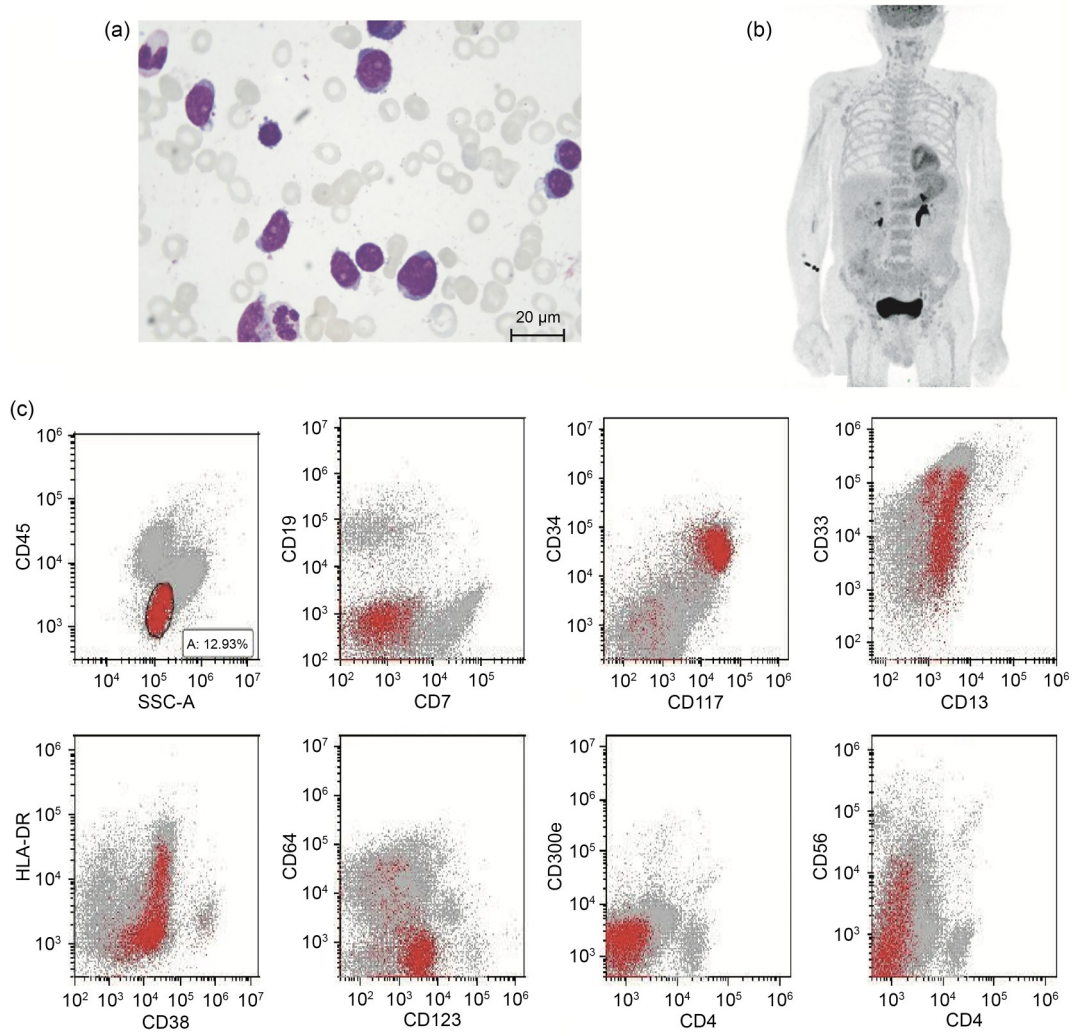


Fig. 2 Diagnostic features of angioimmunoblastic T-cell lymphoma (AITL) and myelodysplastic syndrome with increased blasts 2 (MDS-IB2). (a) Bone-marrow aspirate smear showing hypercellularity with increased myeloblasts and dysplastic features (Wright-Giemsa stain). (b) ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) demonstrating diffuse bone-marrow hypermetabolism and generalized lymphadenopathy. (c) Flow cytometry demonstrating an aberrant immature myeloid population expressing CD34, CD117, CD33, CD13, human leukocyte antigen-DR isotype (HLA-DR), and CD123. CD: cluster of differentiation; SSC-A: side scatter area.

chidamide (20 mg twice weekly). However, the clinical course was complicated by *Candida tropicalis* infection. Due to clinical deterioration, the family declined further treatment, and the patient died one month after discharge.

Following the diagnosis of our patient, we systematically reviewed previously reported cases of AITL associated with myeloid neoplasms which had clinical and molecular data; these are summarized in Table 1. In most published reports, the two malignancies occurred in a metachronous pattern, with MDS or AML developing months to years after the initial diagnosis of AITL (Huang et al., 2016; Shang et al., 2018; Tiacci et al., 2018). The reverse sequence, in which AITL develops following a prior myeloid neoplasm, is rarely reported (Iturrate et al., 2020). Several case reports have described AML emerging during treatment or after disease relapse, frequently following exposure to cytotoxic chemotherapy or autologous stem-cell transplantation. In these patients, the interval between AITL and AML ranged from several months to several years, and the prognosis after development of AML was generally poor. Because many patients had received intensive chemotherapy before the onset of AML, early reports often interpreted these cases as therapy-related myeloid neoplasms, particularly given

Table 1 Summary cases of AML secondary to AITL

No.	Age (years)/ sex	Timing of AML/MDS	AML/MDS subtype	Gene detection in AITL	Gene detection in AML/MDS	Outcome/notes	Reference
1	77/F	7 months after AITL	AML-M5b	Not reported	Not reported	Died 5 d after diagnosis of AML; OS 7 months	Chunli and Liqun, 2022
2	63/F	32.4 months after AITL	AML	*TET2*, *DNMT3A*, *ARID1B*, *DDX3X*, *NFE2*, and *ROBO1*	*TET2*, *DNMT3A*, and *RUNX1*	Died after diagnosis of AML; OS 33 months	Lewis et al., 2020
3	71/M	43.2 months after AITL	MDS-IB1→ AML	*TET2* and *DNMT3A*	*TET2* and *DNMT3A*	Died after diagnosis of AML; OS 56 months	Lewis et al., 2020
4	58/F	16 months after AITL	AML-M5b	Not reported	Not reported	Not reported	Huang et al., 2016
5	65/M	9.5 months after AITL	AML-M2	Not reported	Not reported	Died 10 months after diagnosis of AML; OS 20 months	Shang et al., 2018
6	70/M	14 months after AITL	AML-M2	Not reported	Not reported	Died 11 months after diagnosis of AML; OS 27 months	Shang et al., 2018
7	64/M	14 months after AITL	AML-M3	Not reported	Not reported	Not reported	Shang et al., 2018
8	45/M	12 months after AITL	AML	*TET2*, *ASXL1*, and *RHOA*	*TET2*, *ASXL1*, *NPM1*, and *KRAS*	Died five months after diagnosis of AML; OS 17 months	Tiacci et al., 2018

AITL: angioimmunoblastic T-cell lymphoma; AML: acute myeloid leukemia; *ARID1B*: AT-rich interaction domain 1B; *ASXL1*: additional sex combs-like 1; *DDX3X*: DEAD-box helicase 3 X-linked; IB1: increased blasts 1; F: female; *KRAS*: Kirsten rat sarcoma viral oncogene homolog; M: male; MDS: myelodysplastic syndrome; *NFE2*: nuclear factor, erythroid 2; *NPM1*: nucleophosmin 1; OS: overall survival; *RHOA*: Ras homolog family member A; *ROBO1*: roundabout guidance receptor 1; *RUNX1*: Runt-related transcription factor 1; *TET2*: tet methylcytosine dioxygenase 2; *DNMT3A*: DNA methyltransferase 3 alpha. OS indicates the time from AITL diagnosis to the date of death.

the known leukemogenic effects of alkylating agents and topoisomerase II inhibitors commonly used in lymphoma treatment.

However, accumulating molecular evidence suggests that the relationship between AITL and myeloid neoplasms extends beyond a purely therapy-related process. CH arises at the level of hematopoietic stem cells and is increasingly recognized as an early event in AITL pathogenesis. In addition to its role in lymphomagenesis, CH has been associated with adverse clinical features, including increased systemic inflammation, worse treatment response, and inferior progression-free survival (Wei et al., 2026). Consistent with this model, recurrent mutations in epigenetic regulators such as *TET2* and *DNMT3A* are frequently shared between lymphoid and myeloid compartments (Quivoron et al., 2011; Odejide et al., 2014). Lewis et al. (2020) demonstrated that identical CH-associated mutations can be detected in both the neoplastic T-cell compartment and the myeloid lineage in a substantial proportion of patients. In some cases, subsequent myeloid neoplasms shared these mutations with the original AITL clone, supporting a shared clonal origin.

Further molecular evidence for this relationship has been reported in individual case studies. Tiacci et al. (2018) described a patient who developed AITL followed by nucleophosmin 1 (*NPM1*)-mutated AML arising from a common clone harboring *TET2* and *ASXL1* mutations. VAF analysis indicated that these mutations were present at the level of hematopoietic progenitor cells prior to the development of either malignancy. In this case, the AITL clone acquired an *RHOA* mutation, while the AML clone developed *NPM1* and *KRAS* mutations, illustrating lineage-specific divergence from a shared ancestral clone.

A schematic model summarizing the potential clonal relationship between AITL and myeloid neoplasms is shown in Fig. 3. In this framework, early CH-associated mutations arising in hematopoietic progenitor cells may give rise to both TFH-lineage malignant cells and myeloid progeny, with subsequent acquisition of lineage-restricted secondary mutations driving

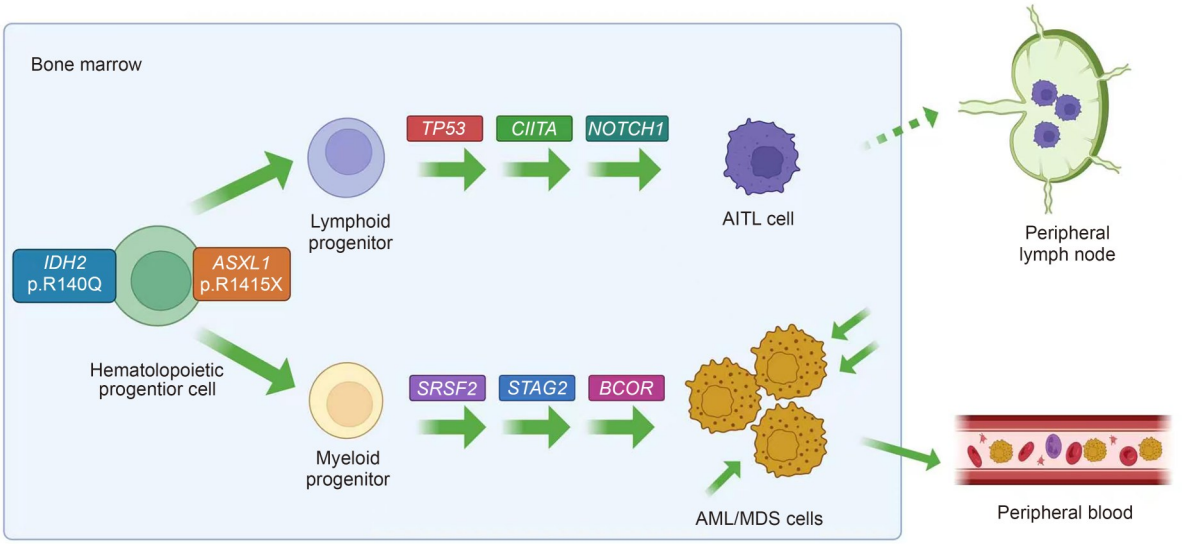


Fig. 3 Divergent clonal evolution linking angioimmunoblastic T-cell lymphoma (AITL) and myeloid neoplasms. Schematic representation of divergent clonal evolution from a shared ancestral hematopoietic progenitor clone harboring early clonal hematopoiesis (CH)-associated mutations. Lineage-specific genetic events give rise to T-follicular helper (TFH) cell-derived AITL or myeloid neoplasms (MDS/AML). MDS: myelodysplastic syndrome; AML: acute myeloid leukemia; *IDH2*: isocitrate dehydrogenase 2; *ASXL1*: additional sex combs like 1; *TP53*: tumor protein p53; *CIITA*: major histocompatibility complex (MHC) class II transactivator; *NOTCH1*: Notch receptor 1; *SRSF2*: serine/arginine-rich splicing factor 2; *STAG2*: stromal antigen 2; *BCOR*: B cell lymphoma 6 corepressor. Figure created using BioRender (https://biorender.com) with institutional subscription license.

the development of AITL and myeloid neoplasms such as MDS or AML.

These observations highlight the central role of epigenetic dysregulation in AITL pathogenesis and suggest a potential therapeutic vulnerability. Although the combination of azacitidine and chidamide is not a standard therapy for AITL according to international guidelines, we selected it here as an epigenetically targeted approach, supported by studies showing meaningful clinical activity in AITL and other PTCL subtypes, particularly in patients with mutations in epigenetic regulators (Falchi et al., 2021; Ruan et al., 2023). However, the clinical course was complicated by *C. tropicalis* infection, underscoring the need to balance therapeutic efficacy with treatment-related toxicity.

Consistent with this epigenetically driven model, targeted NGS identified identical *IDH2* and *ASXL1* mutations in both cutaneous AITL tissue and bone-marrow samples, whereas additional mutations, including *SRSF2*, *STAG2*, and *BCOR*, were confined to the myeloid compartment. The higher VAFs of the shared mutations in bone marrow are consistent with a CH-derived origin. *IDH2* mutations contribute to epigenetic dysregulation in AITL (Cairns et al., 2012), most commonly involving the R172 hotspot (Wang et al., 2015). In contrast, the $IDH2^{R140Q}$ mutation identified in our case, which is more frequently reported in myeloid neoplasms, provides additional support for a CH-related origin with subsequent divergent evolution into lymphoid and myeloid lineages (Kunadt et al., 2022). A limitation of our study is that NGS was performed on bulk tissue/aspirate, which does not permit mutation assignment to individual cell populations; future single-cell sequencing studies will be required to validate these findings.

Notably, AITL and MDS-IB2 were diagnosed synchronously in this patient. Unlike most reported cases in which myeloid neoplasms develop during disease progression or after treatment, both malignancies were identified at initial presentation. Although such synchronous presentations are uncommon, they support the possibility of parallel evolution of lymphoid and myeloid neoplasms.

Overall, this case provides additional evidence supporting a shared clonal origin between AITL and myeloid neoplasms. Careful bone-marrow evaluation and molecular profiling may therefore be warranted in patients with AITL presenting with unexplained cytopenias.

Data availability statement

Data sharing is not applicable to this article as all the data are already listed in this paper.

Acknowledgments

This work was supported by the Zhejiang Provincial Natural Science Foundation (No. MS26H080020). We thank Dr. Xiaoping SUN from the University of Texas MD Anderson Cancer Center (Houston, TX, USA) for editing.

Author contributions

Yang YANG designed the study and drafted the manuscript. Yi LI contributed to clinical and pathological data collection. Huiyao GU performed molecular analyses. Jingsong HE supervised the study and revised the manuscript. All authors have read and approved the final manuscript, and therefore, have full access to all the data in the study and take responsibility for the integrity and security of the data.

Compliance with ethics guidelines

Yang YANG, Yi LI, Huiyao GU, and Jingsong HE declare that they have no conflicts of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient for being included in the study. The study protocol was approved by the Research Ethics Committee of the First Affiliated Hospital, School of Medicine, Zhejiang University (Approval No. IIT20240469B-R1).

Declaration on the use of generative AI tools

No generative AI tools were employed during the whole process of this manuscript.

References

Alaggio R, Amador C, Anagnostopoulos I, et al., 2022. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. *Leukemia*, 36(7):1720-1748. https://doi.org/10.1038/s41375-022-01620-2

Bolton KL, Ptashkin RN, Gao T, et al., 2020. Cancer therapy shapes the fitness landscape of clonal hematopoiesis. *Nat Genet*, 52(11):1219-1226. https://doi.org/10.1038/s41588-020-00710-0

Cairns RA, Iqbal J, Lemonnier F, et al., 2012. *IDH2* mutations are frequent in angioimmunoblastic T-cell lymphoma. *Blood*, 119(8):1901-1903. https://doi.org/10.1182/blood-2011-11-391748

Chiba S, Sakata-Yanagimoto M, 2020. Advances in understanding of angioimmunoblastic T-cell lymphoma. *Leukemia*, 34(10):2592-2606. https://doi.org/10.1038/s41375-020-0990-y

Chunli Y, Liqun Z, 2022. Acute monocytic leukemia secondary to angioimmunoblastic T-cell lymphoma: a case report and literature review. *Ann Clin Case Rep*, 7:2281.

Couronné L, Bastard C, Bernard OA, 2012. *TET2* and *DNMT3A* mutations in human T-cell lymphoma. *N Engl J Med*, 366(1):95-96. https://doi.org/10.1056/NEJMc1111708

Falchi L, Ma H, Klein S, et al., 2021. Combined oral 5-azacytidine and romidepsin are highly effective in patients with PTCL: a multicenter phase 2 study. *Blood*, 137(16):2161-2170. https://doi.org/10.1182/blood.2020009004

Gibson CJ, Lindsley RC, Tchekmedyian V, et al., 2017. Clonal hematopoiesis associated with adverse outcomes after autologous stem-cell transplantation for lymphoma. *J Clin Oncol*, 35(14):1598-1605. https://doi.org/10.1200/JCO.2016.71.6712

Harland L, Borgmann V, Otto F, et al., 2024. Clonal hematopoiesis and bone marrow infiltration in patients with follicular helper T-cell lymphoma of angioimmunoblastic type. *Mod Pathol*, 37(7):100519. https://doi.org/10.1016/j.modpat.2024.100519

Huang WJ, Wang L, Fan L, et al., 2016. Acute myeloid leukemia secondary to autologous hematopoietic stem cell transplant of angioimmunoblastic T-cell lymphoma: one case report and literatures review. *Chin J Hematol*, 37(7):620-622 (in Chinese). https://doi.org/10.3760/cma.j.issn.0253-2727.2016.07.017

Iturrate I, Loscertales J, Fernández-Ruiz E, et al., 2020. Angioimmunoblastic T-cell lymphoma after acute myeloid leukemia: alleged common pathogenesis. A case report and literature review. *Clin Case Rep*, 8(12):3493-3496. https://doi.org/10.1002/ccr3.3430

Jaiswal S, Ebert BL, 2019. Clonal hematopoiesis in human aging and disease. *Science*, 366(6465):eaan4673. https://doi.org/10.1126/science.aan4673

Kunadt D, Stasik S, Metzeler KH, et al., 2022. Impact of *IDH1* and *IDH2* mutational subgroups in AML patients after allogeneic stem cell transplantation. *J Hematol Oncol*, 15:126. https://doi.org/10.1186/s13045-022-01339-8

Lewis NE, Petrova-Drus K, Huet S, et al., 2020. Clonal hematopoiesis in angioimmunoblastic T-cell lymphoma with divergent evolution to myeloid neoplasms. *Blood Adv*, 4(10):2261-2271. https://doi.org/10.1182/bloodadvances.2020001636

Odejide O, Weigert O, Lane AA, et al., 2014. A targeted mutational landscape of angioimmunoblastic T-cell lymphoma. *Blood*, 123(9):1293-1296. https://doi.org/10.1182/blood-2013-10-531509

Quivoron C, Couronné L, Della Valle V, et al., 2011. TET2 inactivation results in pleiotropic hematopoietic abnormalities in mouse and is a recurrent event during human lymphomagenesis. *Cancer Cell*, 20(1):25-38. https://doi.org/10.1016/j.ccr.2011.06.003

Ruan J, Moskowitz A, Mehta-Shah N, et al., 2023. Multicenter

phase 2 study of oral azacitidine (CC-486) plus CHOP as initial treatment for PTCL. *Blood*, 141(18):2194-2205. https://doi.org/10.1182/blood.2022018254

Shang YF, Fu XR, Zhang L, et al., 2018. Acute myeloid leukemia secondary to angioimmunoblastic T-cell lymphoma: report of three cases and review of literature. *J Leuk Lymphoma*, 27(3):164-167 (in Chinese). https://doi.org/10.3760/cma.j.issn.1009-9921.2018.03.009

Tiacci E, Venanzi A, Ascani S, et al., 2018. High-risk clonal hematopoiesis as the origin of AITL and *NPM1*-mutated AML. *N Engl J Med*, 379(10):981-984. https://doi.org/10.1056/NEJMc1806413

Wang C, McKeithan TW, Gong Q, et al., 2015. *IDH2*^{R172} mutations define a unique subgroup of patients with angioimmunoblastic T-cell lymphoma. *Blood*, 126(15): 1741-1752. https://doi.org/10.1182/blood-2015-05-644591

Wei C, Zhang Y, Zhao DQ, et al., 2026. Clonal haematopoiesis in T-follicular helper cell lymphoma: a prognostic biomarker and early event in lymphoma evolution. *Br J Haematol*, 208(4):1223-1231. https://doi.org/10.1111/bjh.70363