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ORIGINAL ARTICLE

A single-centre analysis of nodal peripheral T-cell lymphomas in Southern Vietnam: Insights from the WHO 2022 classification

Chi-Dung PHU[1], Ngoc-Kim-Ngan TIEU[1]*, Hoang-Thien DANG[1], Thi-Huyen-Tran LE[1], Dac-Quynh-Anh NGUYEN[2], Sy-Luan CAO[3], Thi-Ngoc-Ha HUA[1,4]

[1]Department of Pathology, Blood Transfusion Hematology Hospital, Ho Chi Minh City, Vietnam; [2]Department of Biochemistry Hematology, Blood Transfusion Hematology Hospital, Ho Chi Minh City, Vietnam; [3]Department of Molecular Cytogenetics, Blood Transfusion Hematology Hospital, Ho Chi Minh City, Vietnam; [4]Department of Pathology, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam

Abstract

Introduction: Peripheral T-cell lymphomas are rare, aggressive malignancies with significant diagnostic challenges due to their heterogeneity. *Materials and Methods:* This retrospective study analysed 43 nodal Peripheral T-cell lymphomas cases diagnosed between 2019 and 2024 at the Blood Transfusion Hematology Hospital in Southern Vietnam and reclassified them using the World Health Organization 2022 classification. *Results:* Nodal T-follicular helper cell lymphoma, angioimmunoblastic type, emerged as the most prevalent subtype (51.2%), markedly exceeding rates reported in Western (32.5%) and East Asian studies (36.2%). Despite the higher prevalence of Epstein-Barr Virus in Vietnam, the proportion of Epstein-Barr Virus positive in Peripheral T-cell lymphomas was not elevated (20%), suggesting additional genetic or environmental factors influencing lymphoma pathogenesis. *Conclusion:* These findings underscore the critical role of updated diagnostic standards and the utility of advanced markers in improving Peripheral T-cell lymphomas classification. This study provides rare insights into Peripheral T-cell lymphomas pathology in Vietnam, contributing valuable data to the global understanding of these rare lymphomas.

Keywords: Peripheral T-cell lymphoma, Nodal TFH lymphoma, Epstein-Barr virus, WHO 2022 classification, Immunohistochemistry.

INTRODUCTION

Peripheral T-cell lymphomas (PTCLs) are a rare and heterogeneous group of mature T-cell lymphomas, accounting for approximately 10-15% of non-Hodgkin lymphomas.[1] These malignancies exhibit aggressive clinical progression and are associated with poorer prognoses compared to B-cell lymphomas and Hodgkin lymphomas. PTCLs remain diagnostically challenging due to their diverse histological, immunophenotypic, and molecular characteristics. Based on the primary site of involvement, PTCLs are broadly classified into leukemic, nodal, extranodal, and cutaneous subtypes, with nodal PTCLs comprising nearly 60% of all cases.[2]

In PTCLs, lymph node architecture is typically disrupted, with an effacement of normal nodal structures and infiltration by atypical lymphoid cells. Immunohistochemical analysis commonly reveals the loss or downregulation of one or more pan-T-cell markers (CD2, CD3, CD4, CD5, CD7, and CD8). Additionally, tumour cells often express other markers such as ALK and CD30. PTCLs arising from germinal centre-derived T-follicular helper (TFH) cells typically express TFH cell markers (BCL6, CD10, ICOS, PD1, and CXCL13). Furthermore, the EBER-ISH (Epstein-Barr virus-encoded RNA in situ hybridisation) technique is used to detect the Epstein-Barr virus (EBV) in tumour tissues. EBER is a sensitive prognostic marker in PTCLs.

**Address for correspondence:* Ngoc-Kim-Ngan Tieu, Department of Pathology, Blood Transfusion Hematology Hospital, 01 Tran Huu Nghiep, Tan Kien, Binh Chanh, Ho Chi Minh City, Vietnam. Tel: +84 902 345 003; Email: *NganTNK@bth.org.vn*

PTCLs in Asia exhibit a significantly higher prevalence compared to Western countries, with notable regional variability influenced by genetic predispositions, environmental factors, and infections such as EBV. East and Southeast Asia report particularly high incidences, with PTCL subtypes such as Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), Nodal TFH cell lymphoma, angioimmunoblastic type (nTFHL-AI), and extranodal NK/T-cell lymphoma (ENKL) displaying distinct patterns.[3] Despite its high prevalence, data on PTCLs in Southeast Asia, including Vietnam, remain limited, underscoring the need for regional studies to enhance diagnostic accuracy, optimise treatment strategies, and contribute to the global understanding of PTCL.

MATERIALS AND METHODS

Study Design and Patient Selection

This retrospective study was conducted at the Blood Transfusion Hematology Hospital in Southern Vietnam, focusing on patients diagnosed with nodal PTCLs between January 2019 and June 2024. Forty-three cases were selected based on histopathological confirmation of nodal PTCLs and comprehensive clinical and pathological data availability. Patients with incomplete records or insufficient tissue samples were excluded. Although this study utilises data collected between 2019 and 2024, all cases were re-evaluated and reclassified according to the 2022 WHO classification to ensure consistency with current diagnostic standards.[4,5] This study was approved by the ethics committee of the Blood Transfusion Hematology Hospital.

Sample Preparation

Lymph nodes were processed from formalin-fixed, paraffin-embedded blocks. Sections of 2-3 µm thickness were prepared and stained using haematoxylin and eosin (H&E) for initial histological examination. Immunohistochemistry (IHC) and EBER-ISH were performed on selected sections to support diagnostic classification. H&E staining was conducted using an automated slide stainer, while IHC and EBER-ISH were performed using an automated staining system.

IHC analysis was performed using a panel of markers, including pan-T-cell markers (CD2, CD3, CD4, CD5, CD7, and CD8) and CD30 for all cases. TFH markers (CD10, CD23, ICOS, PD1, and BCL-6) were assessed in cases suspected of nTFHL. ALK-1 staining was performed in cases suspected of ALCL. The interpretation of IHC results was standardised as follows: “Positive” was defined as marker expression in at least 30% of tumour cells.[6,7] “Downregulation” indicates reduced expression compared to normal lymphoid tissues and is applicable only to pan-T-cell such as CD2, CD3, CD5, and CD7. “Negative” signifies no detectable expression. A summary of antibody characteristics is provided in Table 1.[6,7]

Statistical Analysis

All data were analysed using SPSS software (version 16.0). Descriptive statistics, such as frequencies and percentages, were used to summarise patient demographics and histopathological findings. Chi-square tests were employed to evaluate associations between categorical variables. A p-value of <0.05 was considered statistically significant.

RESULTS

Distribution

A total of 43 cases of nodal PTCLs were collected during the study period from January 2019 to June 2024. The median age of the patients was 53 years (range: 25-78 years), with a male predominance (male-to-female ratio of 2.1:1).

The WHO 2022 classification introduced significant changes in the categorisation of PTCLs, particularly by renaming TFH-related lymphoma subtypes to better reflect their cellular origin. The previous Angioimmunoblastic T-cell lymphoma (AITL) is now classified as Nodal TFH cell lymphoma, angioimmunoblastic type (nTFHL-AI), while Follicular T-cell lymphoma (FTCL) has been renamed Nodal TFH cell lymphoma, follicular type (nTFHL-F). Additionally, cases previously categorised under PTCL with TFH phenotype are now designated as Nodal TFH cell lymphoma, NOS (nTFHL-NOS). The proportions of nTFHL-AI (previously AITL) and ALCL (ALK+ and ALK−) remain unchanged between WHO 2017 and WHO 2022, indicating consistent diagnostic criteria. However, PTCL-NOS has decreased from 23.3% to 18.6%, as some cases have been reclassified under the newly introduced EBV-positive nodal T- and NK-cell lymphoma (EBV+ nTNKL). nTFHL-AI (AITL) remains the most prevalent subtype (51.2%), followed by PTCL-NOS (18.6%). A detailed comparison of PTCL

TABLE 1: Summary of antibody characteristics

Marker	Manufacturer	Clone	Control	Cut-off	Application
CD2	VENTANA	MRQ-11	Lymph node reactive	≥30%[6,15]	Applied to all cases
CD3	VENTANA	2GV6	Lymph node reactive	≥30%[6,15]	Applied to all cases
CD5	VENTANA	SP19	Lymph node reactive	≥30%[6,15]	Applied to all cases
CD7	VENTANA	SP94	Lymph node reactive	≥30%[6,15]	Applied to all cases
CD4	VENTANA	SP35	Lymph node reactive	≥30%[6,15]	Applied to all cases
CD8	VENTANA	SP57	Lymph node reactive	≥30%[6,15]	Applied to all cases
CD20	VENTANA	L26	Lymph node reactive	Not rigid	Applied to cases when large cells are present
ALK1	VENTANA	ALK01	Known positive cases of ALCL ALK+	Not rigid	Applied to cases suspected of ALCL
CD30	VENTANA	Ber-H2	Known positive cases of ALCL	Not rigid	Applied to all cases
CD10	VENTANA	SP67	Lymph node reactive	≥20%[6,7]	Applied to cases suspected of nTFHL
BCL6	VENTANA	QI191E/A8	Lymph node reactive	≥20% [6,7]	Applied to cases suspected of nTFHL
ICOS	VENTANA	RM417	Known positive cases of nTFHL ICOS+	≥20%[6,7]	Applied to cases suspected of nTFHL
PD1	VENTANA	NAT105	Known positive cases of nTFHL PD1+	≥20%[6,7]	Applied to cases suspected of nTFHL
EBER	VENTANA	-	Known positive cases of DLBCL or HL	≥25%[8,15]	Applied to all cases

Abbreviations: ALK+ ALCL (Anaplastic Large Cell Lymphoma, ALK-positive), nTFHL (Nodal TFH cell lymphoma), DLBCL (Diffuse large B-cell lymphoma), HL (Hodgkin lymphoma).

subgroup proportions between the WHO 2017 and WHO 2022 classifications is presented in Table 2.

Immunohistochemistry

CD3 is well preserved in most cases, showing 100% positivity in nTFHL-AI and PTCL-NOS, supporting its reliability as a pan-T-cell marker. However, ALK+ ALCL exhibits significantly reduced expression (33.3%), consistent with its aberrant immunophenotype. CD2 expression is most frequently retained in nTFHL-AI (72.7%). CD5 loss is particularly common in ALCL, with 50–66.7% of cases exhibiting downregulation or complete loss of expression. In contrast, CD5 is well retained in nTFHL-AI (72.7%) and PTCL-NOS (70%). CD7 shows the highest rate of downregulation (63.4% overall), particularly in ALK− ALCL (66.7%) and PTCL-NOS (60%), reflecting its frequent loss in these subtypes.

Regarding T-cell lineage markers, CD4+/CD8- expression dominates in nTFHL-AI (81.8%), aligning with its TFH cell origin. In contrast, CD4-/CD8+ expression is relatively uncommon (12.2% overall), reflecting a minority cytotoxic T-cell phenotype. Notably, ALK+ ALCL has the highest proportion of CD4-/CD8- cases (50%), highlighting its immunophenotypic heterogeneity. The detailed proportions of each marker's expression are presented in Table 3, while

TABLE 2: Comparison of nodal Peripheral T-cell lymphomas (PTCL) classifications: WHO 2017 vs WHO 2022

WHO 2022 Classification		WHO 2017 Classification	
Subgroups	**Proportion % (n)**	**Subgroups**	**Proportion % (n)**
ALK-positive anaplastic large cell lymphoma (ALK+, ALCL)	14.0 (6)	ALK-positive anaplastic large cell lymphoma (ALK+, ALCL)	14.0 (6)
ALK-negative anaplastic large cell lymphoma (ALK-, ALCL)	7.0 (3)	ALK-negative anaplastic large cell lymphoma (ALK-, ALCL)	7.0 (3)
Nodal TFH cell lymphoma, angioimmunoblastic type (nTFHL-AI)	51.2 (22)	Angioimmunoblastic T-cell lymphoma (AITL)	51.2 (22)
Nodal TFH cell lymphoma, follicular type (nTFHL-F)	0.0 (0)	Follicular T-cell lymphoma (FTCL)	0.0 (0)
Nodal TFH cell lymphoma, NOS (nTFHL-NOS)	4.7 (2)	PTCL with TFH phenotype	4.7 (2)
Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)	18.6 (8)	Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)	23.3 (10)
EBV-positive nodal T- and NK-cell lymphoma (EBV+ nTNKL)	4.7 (2)	Not classified in WHO 2017	

Figures 1 and 2 provide illustrative examples of T-cell marker expression levels.

nTFHL-AI has the highest proportion of cases with all markers preserved (40.9%), suggesting a more intact T-cell phenotype compared to other subtypes. In contrast, ALK+ and ALK- ALCL exhibit extensive marker loss, with up to 33.3% of ALK- ALCL cases completely lacking all four markers. PTCL-NOS shows intermediate variability, with 30% of cases losing one marker, 40% of cases losing two markers and 20% losing three markers, reflecting its heterogeneity. Notably, no cases of nTFHL-AI or PTCL-NOS exhibit total pan-T cell marker loss, reinforcing their stronger lineage preservation. Detailed proportions are provided in Table 4.

nTFHL-AI exhibits the highest expression of TFH markers, particularly PD1 (77.8%) and ICOS (94.4%). In contrast, CD10 (40.9%) and BCL6 (36.4%) show lower positivity. nTFHL-NOS demonstrates moderate TFH marker expression, with 50% positivity for CD10,

TABLE 3: Combined analysis of T-cell marker expression

Diagnosis	Marker expression (%)											
	CD2		CD3		CD5		CD7		CD4+/ CD8+	CD4+/ CD8-	CD4-/ CD8+	CD4-/ CD8-
	P	D/N	P	D/N	P	D/N	P	D/N				
PTCL-NOS	60.0	30.0	100.0	0.0	30.0	70.0	40.0	60.0	30.0	20.0	20.0	30.0
ALK+ ALCL	33.3	66.7	33.3	66.7	50.0	50.0	16.7	83.3	0.0	50.0	33.3	16.7
ALK- ALCL	66.7	33.3	33.3	66.7	33.3	66.7	33.3	66.7	0.0	66.7	33.3	0.0
nTFHL-AI	72.7	27.8	100.0	0.0	72.7	27.8	40.9	59.1	18.2	81.8	0.0	0.0
Total	63.4	36.6	85.4	14.6	56.1	43.9	36.6	63.4	17.1	61.0	12.2	9.8

Abbreviations: "P" indicates positive expression, and "D/N" represents downregulated or negative expression. PTCL-NOS (Peripheral T-cell Lymphoma, Not Otherwise Specified), ALK+ ALCL (Anaplastic Large Cell Lymphoma, ALK-positive), ALK-ALCL (Anaplastic Large Cell Lymphoma, ALK-negative), and nTFHL-AI (Nodal TFH cell lymphoma, angioimmunoblastic type).

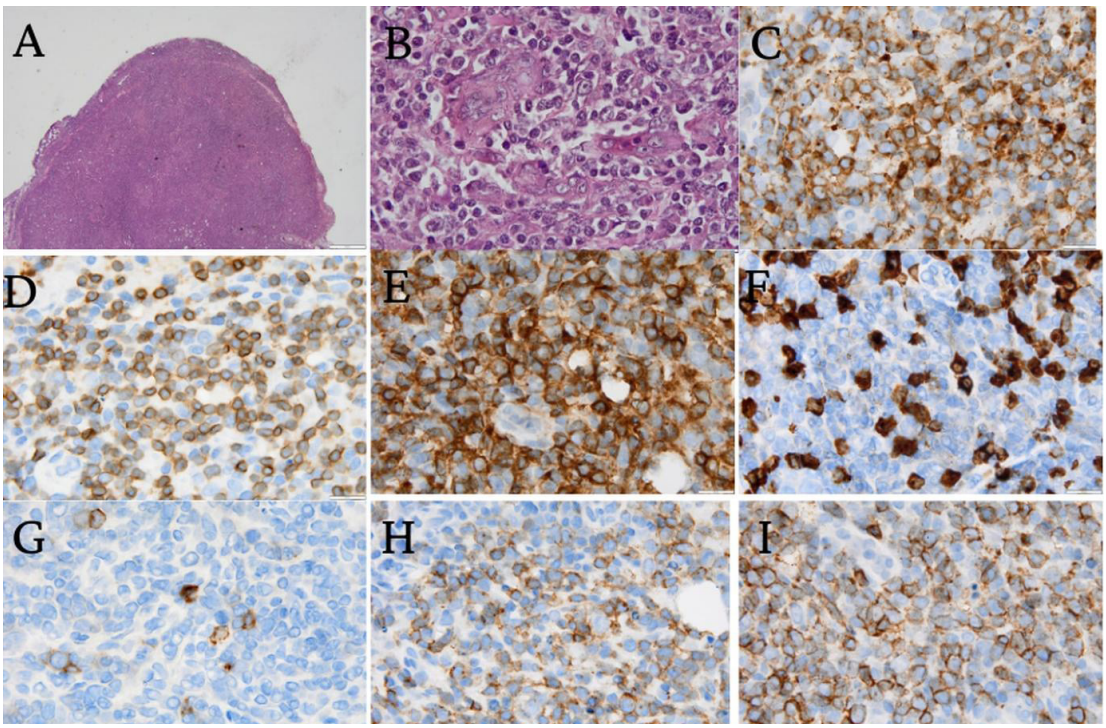

FIG 1. Histological and immunohistochemical features of a case of Nodal TFH cell lymphoma, angioimmunoblastic type (nTFH-AI) (magnification ×1000). (A) H&E staining at ×100 demonstrating an expanded paracortex. (B) H&E staining at ×1000 showing medium-sized clear cells, increased high endothelial venules (HEVs), and scattered immunoblasts. (C) CD2 positive (×1000). (D) CD3 positive (×1000). (E) CD4 positive (×1000). (F) CD8 negative (×1000). (G) CD30 positive in immunoblasts (×1000). (H, I) PD-1 and ICOS positive (×1000).

BCL6, PD1, and ICOS. PTCL-NOS, lacking a clear TFH signature, shows minimal expression of TFH markers, with CD10 and BCL6 completely absent (0%), PD1 undetectable (0%), and ICOS expressed in only 12.5% of cases. The strong association of PD1 and ICOS with nTFHL-AI supports their utility as diagnostic markers, helping to differentiate TFH-derived lymphomas from PTCL-NOS. The detailed marker expression is presented in Table 5.

Incorporating a 25% tumour cell cut-off, EBER positivity was detected in 20% of PTCL cases, leading to their reclassification as EBV+ nTNKL, a newly recognised entity. The EBER-ISH positivity is illustrated in Figure 2, demonstrating strong nuclear staining in tumour cells, confirming EBV association.

DISCUSSION

Distribution

The median age of patients in our study was 53 years, aligning with the findings of Liang *et al*.[9] and Lin *et al*.[10] (57 and 62 years, respectively) but lower than that reported by Yagi *et al*.[11] (70 years). Primary nodal PTCLs predominantly occur in older patients and exhibit a slight male predominance, with a male-to-female ratio of 2.1, consistent with previous studies reporting ratio ranging from 1.6 to 2.3.[9-11]

ALCL was observed in 21.0% of cases, consistent with Yagi's study (18.7%).[11] Among these, ALK+ ALCL (14.0%) was more prevalent than ALK−ALCL (7.0%), consistent with findings from other studies where ALK+ ALCL generally predominates.[3] Rare subtypes, including nTFHL-NOS (4.7%) and EBV+ nTNKL (4.7%), were also identified, emphasising their low prevalence.

Our study observed a higher prevalence of nTFHL-AI (51.2%) compared to PTCL-NOS (32.5%), which differs from previous studies. According to the International T-Cell Project, nTFHL-AI accounted for 32.5% of nodal PTCL cases, while PTCL-NOS accounted for 45.6%, making it the most common subtype in this group.[12] In the study by Park *et al*.[3] the prevalence of nTFHL-AI was 36.2%, lower than that of PTCL-NOS (45.3%). The Southeast

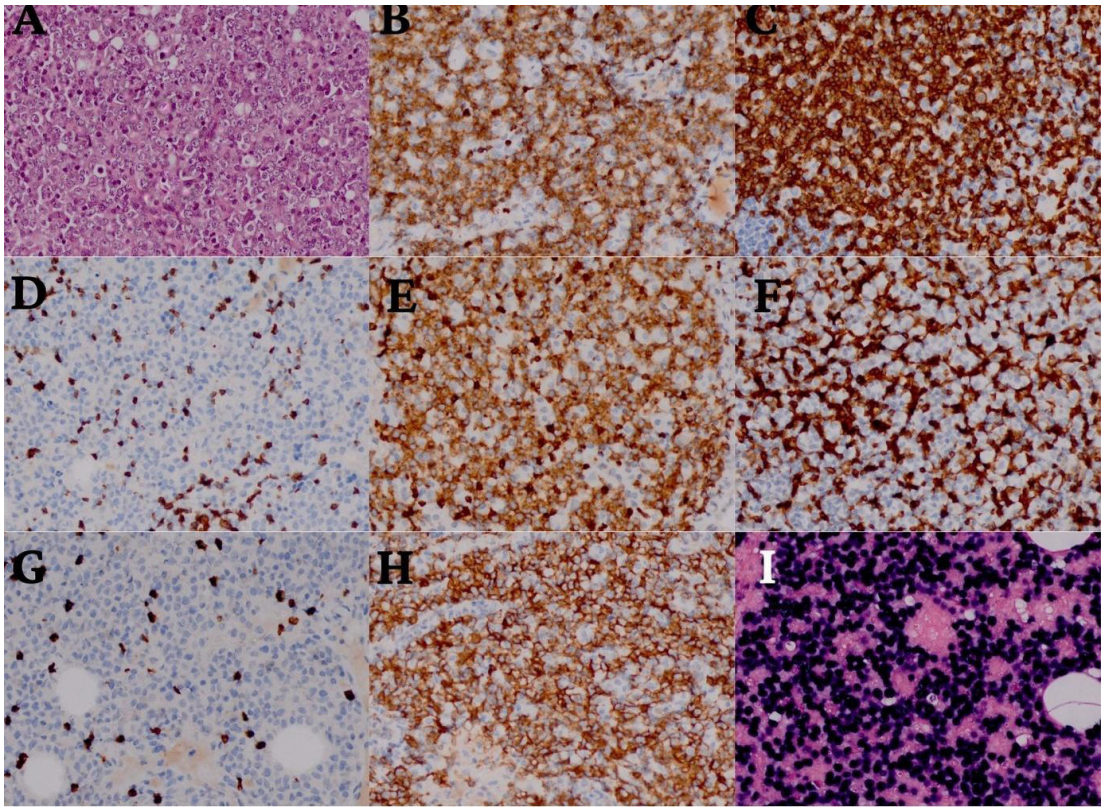

FIG. 2. Histological and immunohistochemical features of EBV-positive nodal T- and NK-cell lymphoma (EBV+ nTNKL). (A) H&E staining shows diffuse medium-sized lymphoid cells (×400). (B) CD2 positive (×400). (C) CD3 positive (×400). (D) CD5 negative (×400). (E) CD7 positive (×400). (F) CD4 negative (×400). (G) CD8 negative (×400). (H) CD56 positive (×400). (I) Epstein-Barr virus-encoded RNA in situ hybridisation (EBER-ISH) positive (×400).

Asian study by Yoon *et al*.[13] reported that nTFHL-AI accounted for 39.5% of nodal PTCL cases, whereas PTCL-NOS accounted for only 33.3%, with nTFHL-AI surpassing PTCL-NOS in prevalence within the nodal PTCL group. The significantly higher prevalence of nTFH-AI (51.2%) compared to Western studies (32.5%) may reflect indirect effects of chronic immune activation associated with EBV infection or regional immune responses.[14]

Although the prevalence of EBV infection is higher in Southeast Asia compared to Western countries, the proportion of EBV-positive PTCL-NOS cases in this study (20%) is similar to that reported in Western cohorts. This suggests that EBV is not the primary driver of PTCL-NOS pathogenesis in this region.

Immunohistochemistry

CD2 was positive in 63.4% of PTCL cases in this study, with 60% positivity in PTCL-NOS and 72.7% in nTFHL-AI, compared to the Went *et al*.[15] higher rates of 70% and 100%, respectively. CD3 emerged as the most commonly expressed marker, with an overall positivity of 85.4%, reaching 100% in both PTCL-NOS and nTFHL-AI.[15] This aligns with the Patel *et al*.[6] findings of 93% positivity in PTCL-NOS and 100% in nTFHL-AI, and Went's rates of 86% and 96%.[6,15] However, in ALCL, CD3 was absent in 66.7% of cases, highlighting potential diagnostic challenges. CD5 showed variable positivity, detected in 30% of PTCL-NOS and 72.7% of nTFHL-AI cases, compared to Patel's[6] higher rates of 96% and 88%. Similarly, CD7 exhibited loss or reduced expression in 63.4% of PTCLs in this study, consistent with Patel's[6] report of 87% CD7 loss. However, CD7 loss requires careful interpretation, as it can occur in reactive conditions or appear weak in normal tissues. Overall, CD2 and CD3 showed high positivity and remain reliable markers for identifying PTCLs.[16,17] In contrast, CD5 and CD7 exhibited significant variability, reflecting their diverse

TABLE 4: Percentage of patients in relation to the number of downregulated or negative pan-T-cell markers

Number of D/N	PTCL-NOS % (n)	nTFH-AI % (n)	ALK+ ALCL % (n)	ALK- ALCL % (n)	Total % (n)
0	10.0 (1)	40.9 (9)	0.0 (0)	33.3 (1)	26.8 (11)
1	30.0 (2)	18.2 (4)	16.7 (1)	0.0 (0)	19.5 (8)
2	40.0 (3)	22.7 (5)	16.7 (1)	0.0 (0)	24.4 (10)
3	20.0 (2)	18.2 (4)	50.0 (3)	33.3 (1)	24.4 (10)
4	0.0 (0)	0.0 (0)	16.7 (1)	33.3 (1)	4.9 (2)

Abbreviations:"P" indicates positive expression, and "D/N" represents downregulated or negative expression. The four pan-T cell markers include CD2, CD3, CD5 and CD7. PTCL-NOS (Peripheral T-cell Lymphoma, Not Otherwise Specified), ALK+ALCL (Anaplastic Large Cell Lymphoma, ALK-positive), ALK- ALCL (Anaplastic Large Cell Lymphoma, ALK-negative), and nTFHL-AI (Nodal TFH cell lymphoma, angioimmunoblastic type).

expression patterns in different PTCL subtypes.

In PTCL-NOS, 30% of cases in this study lose one marker, 40% lose two markers, and 20% lose three markers, whereas Patel *et al*.[6] report 61% losing one marker, 24% losing two markers, and 10% losing three markers. Additionally, the proportion of cases retaining all markers is slightly different—10% in this study compared to 5% in Patel's[6] cohort. These findings indicate that while a small subset of PTCL-NOS cases may retain all pan-T cell markers, the vast majority exhibit some degree of downregulation. For nTFHL-AI, a significant difference is observed—40.9% of nTFHL-AI cases in this study retain all markers, whereas Patel *et al*.[6] do not report any AITL cases with full marker preservation.

In our study, nTFHL-AI cases showed high expression of PD1 (77.8%) and ICOS (94.4%), with lower rates for CD10 (40.9%) and BCL6 (36.4%). The Basha *et al*.[7] study reported PD1 positivity at 95% and ICOS at 91% in AITL cases, similar to our findings. According to Basha's study, the sensitivity and specificity of the five TFH markers (CD10, BCL6, PD-1, ICOS) are as follows: PD-1 shows a sensitivity of 97% and specificity of 71%; ICOS demonstrates a sensitivity of 94% and specificity of 82%; CD10 has a sensitivity of 44% and specificity of 100%; while BCL6 has the lowest sensitivity at 29% but the highest specificity at 100%.[7] Several questions remain unanswered, including whether the expression of only the two markers with the lowest specificity (PD-1 and ICOS) is sufficient to assign a TFH phenotype and make an accurate diagnosis. This highlights the necessity of carefully evaluating the markers within the clinical and histopathological context to ensure diagnostic accuracy.[18]

EBV plays a critical role in the pathogenesis of certain PTCL subtypes, where reported EBV positivity ranges from 5-31%, depending on the threshold for EBER-positive neoplastic cells. The WHO 2022 classification introduces EBV-positive nodal T/NK-cell lymphoma (EBV+ TNKL) as a distinct entity but does not define a fixed EBER-ISH positivity cut-off, instead recommending a flexible range (≥10% to ≥70%).[8,19-21] We applied a ≥25% cut-off for EBER-ISH, leading to the reclassification of 20% of PTCL-NOS cases as EBV+ TNKL.[8,15] This entity is particularly important due to its aggressive clinical course, distinct molecular mechanisms, and poor response to conventional therapies. Despite higher EBV seroprevalence in Southeast Asia, the proportion of EBV-positive PTCL-NOS cases is not proportionally high.

TABLE 5: Expression of follicular helper T cell (TFH) markers

Diagnosis	CD10 % (n)	BCL6 % (n)	PD1 % (n)	ICOS % (n)
PTCL-NOS (n = 8)	0.0 (0)	0.0 (0)	0.0 (0)	12.5 (1)
nTFHL-NOS (n = 2)	50.0 (1)	50.0 (1)	50.0 (1)	50.0 (1)
nTFHL-AI (n = 22)	40.9 (9)	36.4 (8)	77.8 (17)	94.4 (21)

Abbreviations: TFH (Follicular helper T cell) markers, PTCL-NOS (Peripheral T-cell Lymphoma, Not Otherwise Specified), nTFHL-NOS (Nodal TFH cell lymphoma, NOS) and nTFHL-AI (Nodal TFH cell lymphoma, angioimmunoblastic type).

Limitations
Small sample size and retrospective design limit generalisability. Lack of genetic profiling, which could provide deeper insights into pathogenesis. Future research should focus on larger, multicentre studies to validate regional trends, comprehensive genetic profiling to refine classification.

CONCLUSION

This study provides data on PTCLs in Vietnam, highlighting nTFH-AI as the most prevalent subtype (51.2%), exceeding rates in Western and East Asian studies. Despite high EBV prevalence in Asia, the proportion of EBER-positive PTCLs was not elevated, suggesting additional environmental or regional factors in pathogenesis. Aberrations in pan T-cell markers (CD2, CD3, CD5, CD7) were just observed in 59.1% of nTFH-AI cases, underscoring diagnostic challenges. These findings emphasise the need for multicentre studies to validate regional trends and improve understanding of PTCLs in Southeast Asia.

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Informed Consent Statement: Not applicable, this retrospective study analysed clinical and pathological data from PTCL patients who performed pathological routine testing.

Authors' contributions: Conceptualisation, Chi-Dung PHU, Ngoc-Kim-Ngan TIEU, Hoang-Thien DANG; formal analysis, Chi-Dung PHU, Ngoc-Kim-Ngan TIEU, Hoang-Thien DANG, Thi-Huyen-Tran LE, Dac-Quynh-Anh NGUYEN, Thi-Ngoc-Ha HUA; writing, Chi-Dung PHU, Ngoc-Kim-Ngan TIEU; review and editing, Ngoc-Kim-Ngan TIEU, Sy-Luan CAO, Thi-Ngoc-Ha HUA; supervision, Hoang-Thien DANG; final approval of the manuscript, Ngoc-Kim-Ngan TIEU. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

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