

# World Journal of *Clinical Cases*

*World J Clin Cases* 2021 September 26; 9(27): 7963-8279



## Contents

Thrice Monthly Volume 9 Number 27 September 26, 2021

## EDITORIAL

7963 *Exophiala dermatitidis*
*Usuda D, Higashikawa T, Hotchi Y, Usami K, Shimozawa S, Tokunaga S, Osugi I, Katou R, Ito S, Yoshizawa T, Asako S, Mishima K, Kondo A, Mizuno K, Takami H, Komatsu T, Oba J, Nomura T, Sugita M*

## REVIEW

7973 Gastric neuroendocrine neoplasms: A review

*Köseoglu H, Duzenli T, Sezikli M*

## MINIREVIEWS

7986 Coronavirus disease 2019 and renal transplantation

*Nassar M, Nso N, Ariyaratnam J, Sandhu J, Mohamed M, Baraka B, Ibrahim A, Alfshawy M, Zheng D, Bhangoo H, Soliman KM, Li M, Rizzo V, Daoud A*

7998 Impact of COVID-19 on liver

*Su YJ, Chang CW, Chen MJ, Lai YC*

## ORIGINAL ARTICLE

## Case Control Study

8008 Association of gestational anemia with pregnancy conditions and outcomes: A nested case-control study

*Sun Y, Shen ZZ, Huang FL, Jiang Y, Wang YW, Zhang SH, Ma S, Liu JT, Zhan YL, Lin H, Chen YL, Shi YJ, Ma LK*

## Retrospective Cohort Study

8020 Clinical stages of recurrent hepatocellular carcinoma: A retrospective cohort study

*Yao SY, Liang B, Chen YY, Tang YT, Dong XF, Liu TQ*

## Retrospective Study

8027 Accuracy of ultrasonography in diagnosis of fetal central nervous system malformation

*Pang B, Pan JJ, Li Q, Zhang X*

8035 Analysis of ocular structural parameters and higher-order aberrations in Chinese children with myopia

*Li X, Hu Q, Wang QR, Feng ZQ, Yang F, Du CY*

8044 Radial nerve recovery following closed nailing of humeral shaft fractures without radial nerve exploration: A retrospective study

*Yeh KL, Liaw CK, Wu TY, Chen CP*

8051 Bridging therapy and direct mechanical thrombectomy in the treatment of cardiogenic cerebral infarction with anterior circulation macrovascular occlusion

*Ding HJ, Ma C, Ye FP, Zhang JF*

- 8061** Endu combined with concurrent chemotherapy and radiotherapy for stage IIB-IVA cervical squamous cell carcinoma patients

*Zhao FJ, Su Q, Zhang W, Yang WC, Zhao L, Gao LY*

### CASE REPORT

- 8071** Primary pancreatic paraganglioma harboring lymph node metastasis: A case report

*Jiang CN, Cheng X, Shan J, Yang M, Xiao YQ*

- 8082** Retraction of lumbar disc herniation achieved by noninvasive techniques: A case report

*Wang P, Chen C, Zhang QH, Sun GD, Wang CA, Li W*

- 8090** Mixed neuroendocrine carcinoma of the gastric stump: A case report

*Zhu H, Zhang MY, Sun WL, Chen G*

- 8097** Diploic vein as a newly treatable cause of pulsatile tinnitus: A case report

*Zhao PF, Zeng R, Qiu XY, Ding HY, Lv H, Li XS, Wang GP, Li D, Gong SS, Wang ZC*

- 8104** Acute myocardial infarction and extensive systemic thrombosis in thrombotic thrombocytopenic purpura: A case report and review of literature

*Şalaru DL, Adam CA, Marcu DTM, Şimon IV, Macovei L, Ambrosie L, Chirita E, Sascau RA, Statescu C*

- 8114** Limited thoracoplasty and free musculocutaneous flap transposition for postpneumonectomy empyema: A case report

*Huang QQ, He ZL, Wu YY, Liu ZJ*

- 8120** Paraneoplastic focal segmental glomerulosclerosis associated with gastrointestinal stromal tumor with cutaneous metastasis: A case report

*Zhou J, Yang Z, Yang CS, Lin H*

- 8127** Acute coronary syndrome with severe atherosclerotic and hyperthyroidism: A case report

*Zhu HM, Zhang Y, Tang Y, Yuan H, Li ZX, Long Y*

- 8135** Gastric cancer with calcifications: A case report

*Lin YH, Yao W, Fei Q, Wang Y*

- 8142** Value of eosinophil count in bronchoalveolar lavage fluid for diagnosis of allergic bronchopulmonary aspergillosis: A case report

*Wang WY, Wan SH, Zheng YL, Zhou LM, Zhang H, Jiang LB*

- 8147** Asymptomatic gastric adenomyoma and heterotopic pancreas in a patient with pancreatic cancer: A case report and review of the literature

*Li K, Xu Y, Liu NB, Shi BM*

- 8157** Successful treatment of gastrointestinal infection-induced septic shock using the oXiris® hemofilter: A case report

*Li Y, Ji XJ, Jing DY, Huang ZH, Duan ML*

- 8164** Streptococcal pneumonia-associated hemolytic uremic syndrome treated by T-antibody-negative plasma exchange in children: Two case reports  
*Wang XL, Du Y, Zhao CG, Wu YB, Yang N, Pei L, Wang LJ, Wang QS*
- 8171** Subclavian steal syndrome associated with Sjogren's syndrome: A case report  
*Hao LJ, Zhang J, Naveed M, Chen KY, Xiao PX*
- 8177** Metachronous mixed cellularity classical Hodgkin's lymphoma and T-cell leukemia/lymphoma: A case report  
*Dong Y, Deng LJ, Li MM*
- 8186** Duodenal perforation after organophosphorus poisoning: A case report  
*Lu YL, Hu J, Zhang LY, Cen XY, Yang DH, Yu AY*
- 8192** Surgical treatment of abnormal systemic artery to the left lower lobe: A case report  
*Zhang YY, Gu XY, Li JL, Liu Z, Lv GY*
- 8199** Madelung's disease with alcoholic liver disease and acute kidney injury: A case report  
*Wu L, Jiang T, Zhang Y, Tang AQ, Wu LH, Liu Y, Li MQ, Zhao LB*
- 8207** Anesthetic technique for awake artery malformation clipping with motor evoked potential and somatosensory evoked potential: A case report  
*Zhou HY, Chen HY, Li Y*
- 8214** Multiple hidden vessels in walled-off necrosis with high-risk bleeding: Report of two cases  
*Xu N, Zhai YQ, Li LS, Chai NL*
- 8220** Non-small-cell lung cancer with epidermal growth factor receptor L861Q-L833F compound mutation benefits from both afatinib and osimertinib: A case report  
*Zhang Y, Shen JQ, Shao L, Chen Y, Lei L, Wang JL*
- 8226** Successful removal of two magnets in the small intestine by laparoscopy and colonoscopy: A case report  
*Oh RG, Lee CG, Park YN, Lee YM*
- 8232** Acute lower extremity arterial thrombosis after intraocular foreign body removal under general anesthesia: A case report and review of literature  
*Jeon S, Hong JM, Lee HJ, Kim E, Lee H, Kim Y, Ri HS, Lee JJ*
- 8242** Low-intensity extracorporeal shock wave therapy for midshaft clavicular delayed union: A case report and review of literature  
*Yue L, Chen H, Feng TH, Wang R, Sun HL*
- 8249** Treatment of bilateral granulomatous lobular mastitis during lactation with traditional Chinese medicine: A case report  
*Li ZY, Sun XM, Li JW, Liu XF, Sun ZY, Chen HH, Dong YL, Sun XH*
- 8260** Early acute fat embolism syndrome caused by femoral fracture: A case report  
*Yang J, Cui ZN, Dong JN, Lin WB, Jin JT, Tang XJ, Guo XB, Cui SB, Sun M, Ji CC*

- 8268** Combined fascia iliaca compartment block and monitored anesthesia care for geriatric patients with hip fracture: Two case reports  
*Zhan L, Zhang YJ, Wang JX*
- 8274** Bell's palsy after inactivated COVID-19 vaccination in a patient with history of recurrent Bell's palsy: A case report  
*Yu BY, Cen LS, Chen T, Yang TH*

**ABOUT COVER**

Editorial Board Member of *World Journal of Clinical Cases*, Sunil Kumar Gupta, MBBS, MD, Reader (Associate Professor), Department of Dermatology, Venereology and Leprology, All India Institute of Medical Sciences, Gorakhpur, Gorakhpur 273008, Uttar Pradesh, India. dr.sunil\_30@yahoo.co.in

**AIMS AND SCOPE**

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

**INDEXING/ABSTRACTING**

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJCC as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Ji-Hong Lin; Production Department Director: Xiang Li; Editorial Office Director: Jin-Lai Wang.

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Thrice Monthly

**EDITORS-IN-CHIEF**

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**PUBLICATION DATE**

September 26, 2021

**COPYRIGHT**

© 2021 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/gerinfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/gerinfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/gerinfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

# Metachronous mixed cellularity classical Hodgkin's lymphoma and T-cell leukemia/lymphoma: A case report

Yang Dong, Lai-Jun Deng, Mi-Mi Li

**ORCID number:** Yang Dong 0000-0001-2345-6789; Lai-Jun Deng 0000-0002-2513-4991; Mi-Mi Li 0000-0002-6947-9705.

**Author contributions:** Dong Y designed the research study; Deng LJ performed the research and wrote the manuscript; Li MM analyzed the data; all authors have read and approve the final manuscript.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** The authors do not have any possible conflicts of interest.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build

**Yang Dong,** Department of Clinical Pharmacy, Weifang Hospital of Traditional Chinese Medicine, Weifang 261000, Shandong Province, China

**Lai-Jun Deng,** Department of Hematology, Weifang Hospital of Traditional Chinese Medicine, Weifang 261000, Shandong Province, China

**Mi-Mi Li,** Department of Pathology, Weifang Hospital of Traditional Chinese Medicine, Weifang 261000, Shandong Province, China

**Corresponding author:** Lai-Jun Deng, MS, Staff Physician, Department of Hematology, Weifang Hospital of Traditional Chinese Medicine, No. 1055 Weizhou Road, Kuiwen District, Weifang 261000, Shandong Province, China. [denglaijun1982@163.com](mailto:denglaijun1982@163.com)

## Abstract

### BACKGROUND

The development of peripheral T-cell lymphoma (PTCL) after chemotherapy for Hodgkin's lymphoma (HL) is rare, and highly aggressive TCL/leukemia has not been reported to date. The relationship between HL and PTCL needs further exploration to understand the pathogenesis of metachronous lymphoma (ML) and find effective treatment options. We report a patient with ML, whose biopsy of a right cervical lymph node initially confirmed classical HL (CHL).

### CASE SUMMARY

We report a patient with ML, whose biopsy of a right cervical lymph node initially confirmed CHL, with typical reed-sternberg cells expressing CD30 and PAX-5. T-cell leukemia/lymphoma occurred 3 years after treatment, and a lymph node biopsy at the onset confirmed PTCL, nonspecific type, expressing CD3, CD4 and CD8. The patient was treated with standard doses of chemotherapy, programmed cell death-ligand 1 monoclonal antibody, and chidamide, all of which failed to achieve complete remission. The patient was diagnosed with refractory state, and eventually died of leukocyte stasis.

### CONCLUSION

The accuracy of the diagnosis needs to be confirmed when chemotherapeutic drugs are not effective.

**Key Words:** Classical Hodgkin's lymphoma; T-cell lymphoma/leukemia; Bone marrow; Chemotherapy; Drug resistance; Case report

upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Unsolicited manuscript

**Specialty type:** Medicine, research and experimental

**Country/Territory of origin:** China

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**Received:** April 12, 2021

**Peer-review started:** April 20, 2021

**First decision:** July 5, 2021

**Revised:** July 13, 2021

**Accepted:** August 23, 2021

**Article in press:** August 23, 2021

**Published online:** September 26, 2021

**P-Reviewer:** Watanabe T

**S-Editor:** Gong SS

**L-Editor:** A

**P-Editor:** Liu JH



©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** We report a patient with metachronous lymphoma. The development of peripheral T-cell lymphoma (TCL) after chemotherapy for Hodgkin's lymphoma is rare, and highly aggressive TCL/leukemia has not been reported to date. We reviewed the literature and discussed whether immunodeficiency and malignant transformation of reactive T-cells may be major factors contributing to the development of TCL/leukemia.

**Citation:** Dong Y, Deng LJ, Li MM. Metachronous mixed cellularity classical Hodgkin's lymphoma and T-cell leukemia/lymphoma: A case report. *World J Clin Cases* 2021; 9(27): 8177-8185

**URL:** <https://www.wjgnet.com/2307-8960/full/v9/i27/8177.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v9.i27.8177>

## INTRODUCTION

In 1954, Custer first proposed the term composite lymphoma (CL) to describe a "lymphoma in which more than one histological form occurs in the patient" [1]. In 1982, the "Non-Hodgkin lymphoma Work Program" defined CL as "two completely different types of non-Hodgkin's lymphoma (NHL) or, rarely, a combination of NHL and Hodgkin's lymphoma (HL) in a single organ or tissue". The two histological subtypes of CL include two different types of NHL or a combination of HL and NHL. Different combinations are named differently. When HL or NHL appears before the other, it is called metachronous lymphoma (ML), two histological forms of HL or NHL appearing together is referred to as synchronous lymphoma. However, CL refers to both histological types of synchronous lymphoma that occur in the same anatomical site [2]. In this article, we report a patient with ML, whose biopsy of a right cervical lymph node initially confirmed classical HL (CHL), with typical reed-sternberg (RS) cells expressing CD30 and PAX-5. T-cell leukemia (TCL)/lymphoma occurred 3 years after treatment, and a lymph node biopsy at the onset confirmed peripheral TCL (PTCL), nonspecific type, expressing CD3, CD4 and CD8. A bone marrow biopsy revealed abnormal T-cell proliferation (25.5%) and immunophenotyping. *T-cell receptor variable (TCRV) β* (1-24) subfamily analysis, and *TCR beta (TCRβ)* and gamma (*TCRγ*) gene rearrangement all confirmed a large number of malignant T-cell infiltrated in the bone marrow.

## CASE PRESENTATION

### Chief complaints

The patient was a 59-year-old man who presented with right neck swelling and was diagnosed with enlarged lymph nodes in March 2017.

### History of present illness

The patient was diagnosed with enlarged lymph nodes in March 2017. Subsequent computed tomography scans confirmed the nodes at multiple sites (bilateral neck, axilla, and abdomen), with a maximum cervical lymph node of approximately 3.8 cm × 2.4 cm and an enlarged spleen of approximately 15 cm in diameter. The patient had no other feeling of discomfort.

### History of past illness

Five years before the discovery of the enlarged lymph nodes he suffered from allergic purpura (simple skin type); however, the symptoms disappeared after treatment and did not recur.

### Personal and family history

He was a non-smoking non-drinking patient and had no history of other major



diseases nor any significant family history of disease.

### Physical examination

The rest of physical examination was normal.

### Laboratory examinations

The laboratory tests showed white blood cells  $4.10 \times 10^9/\text{L}$ , hemoglobin 120 g/L, and platelets  $115 \times 10^9/\text{L}$ . Polymerase chain reaction (PCR) was used to detect Epstein-Barr virus (EBV) DNA in peripheral blood mononuclear cells at  $6.66 \times 10^4$  cells/mL (reference range:  $< 5.0 \times 10^2$  cells/mL).

### Imaging examinations

Imaging examinations were normal.

## FINAL DIAGNOSIS

The pathology of the right cervical lymph node excision showed popcorn-like RS cell morphology, with abundant blood vessels, CD30 and PAX-5 expression, EBER<sup>+</sup> and Ki67 proliferation index of approximately 20%, and negative for CD3, CD5, CD20 and CD21 (Figure 1). Biopsy of the right cervical lymph node initially confirmed CHL. In the subsequent 3 years of clinical observation after prophase treatment, the patient did not experience discomfort; only occasional weakness. The cervical lymph node lesion occurred in September 2020 and we excised both lymph nodes. The diagnosis of TCL/leukemia was confirmed.

## TREATMENT

After pathological diagnosis of CHL, the patient was given eight courses of ABVD [adriamycin 40 mg intravenous injection (iv) d1, 15; bleomycin 15 mg iv d1, 15; vincristine 4 mg iv d1, 15; dacarbazine 0.5 g iv d1 and 15]. The systemic lymph nodes and spleen shrank and he was classified as partial remission according to the response evaluation criteria for lymphoma[3]. After 6 mo, bone marrow and lymph node biopsies were re-evaluated and the diagnosis remained unchanged. Programmed cell death-ligand 1 (PD-1) monoclonal antibody (sugemalimab, 1200 mg iv q21d) was administered eight times, and was discontinued due to a significant decrease in platelets. The cervical lymph node lesion occurred in September 2020 and we excised both lymph nodes. The pathology showed diffuse consistent T-cells with abundant blood vessels, expressing CD3 (diffuse), CD4 (little) and CD8 (little), but not CD20, CD79 $\alpha$ , CD56, PD-1, Bcl-6 or CD10; Ki67 index was 60%–70%, and EBER. The diagnosis was PTCL, nonspecific type (Figure 1). Because the peripheral blood lymphocytes were as high as  $85.87 \times 10^9/\text{L}$ , we considered the possibility of leukemia. Further cytomorphological testing was performed and a significantly higher percentage of lymphocytes (63%) could be seen in the bone marrow, with abundant atypical lymphocytes. Bone marrow biopsy with hematoxylin and eosin and periodic-acid-Schiff staining revealed proliferation of bone marrow with diffuse abnormal lymphocytes (Figure 2). Flow cytometry (FCM) was performed and the results were analyzed using CD45/side scattering gating procedure, with bone marrow immunophenotyping expressing CD3, CD2, CD5, TCR $\alpha\beta$  and CD45RO (Figure 3), weakly expressing perforin, and no expression of CD7, CD4, CD8, CD10, CD30, CD57, CD16, CD56, CD19, CD20, TCR $\gamma\beta$ , CD45RA, CD25, CD26, CD or GranzymeB. FCM detected 24 TCRV $\beta$  subfamilies, of which  $\nu\beta 14$  was 91.55% (Table 1). A TCR cloning assay (Invivo Scribe Technologies, San Diego, CA, United States) was performed and a positive TCR $\beta$  and TCR $\gamma$  gene rearrangement was detected by extracting total DNA from bone marrow mononuclear cells and PCR amplification of the target fragment (Figure 4). No abnormal chromosomal results. The diagnosis of TCL/leukemia was confirmed. He was treated with eight courses of cyclophosphamide, vincristine, adriamycin, dexamethasone, cisplatin and chidamide; all of which failed to achieve remission.

**Table 1 Proportion of CD3<sup>+</sup>CD4<sup>+</sup>CD8 to 24 T-cell receptor variable  $\beta$  subfamilies in T-cells, with a significant increase in v $\beta$ 14 (91.55%)**

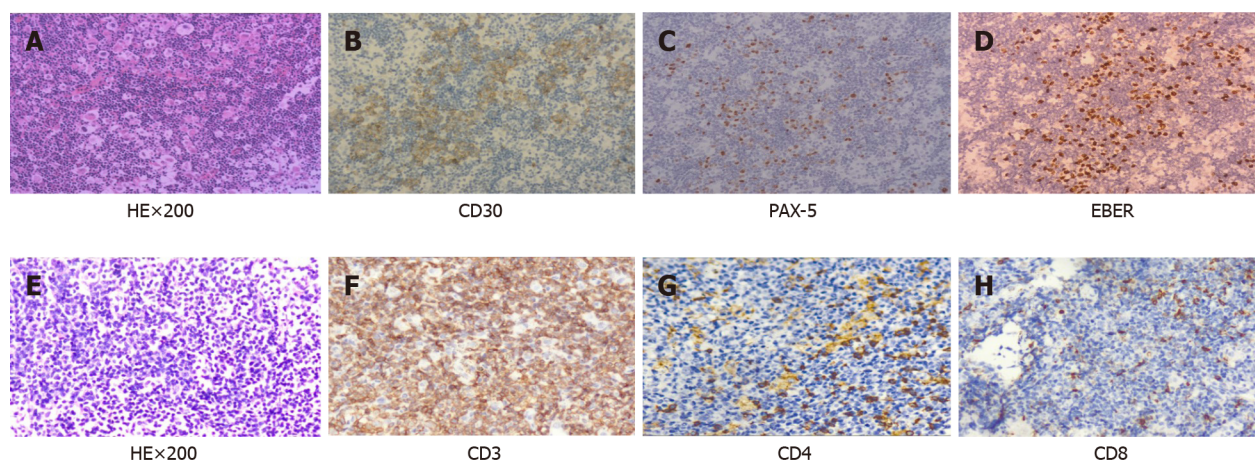
No	Name	Results	CD3 <sup>+</sup>	Biological reference interval of CD3 <sup>+</sup> CD4 <sup>+</sup>	CD3 <sup>+</sup> CD8 <sup>+</sup>	Unit
1	V $\beta$ 5.3	0.19	0.37-2.98	0.36-2.10	0.32-2.64	%
2	V $\beta$ 7.1	0.34	0.64-20.01	0.59-3.80	0.87-7.14	%
3	V $\beta$ 3	0.59	0.52-15.71	0.66-10.04	0.32-13.80	%
4	V $\beta$ 9	0.38	1.10-9.30	0.78-8.24	1.16-7.67	%
5	V $\beta$ 17	0.36	2.28-12.61	3.12-8.32	1.83-11.18	%
6	V $\beta$ 16	0.15	0.42-1.90	0.34-1.80	0.02-2.24	%
7	V $\beta$ 18	0.03	0.58-5.23	0.72-3.35	0.02-2.76	%
8	V $\beta$ 5.1	0.45	3.19-14.93	4.67-10.94	1.12-8.92	%
9	V $\beta$ 20	0.07	0-9.73	0.04-5.30	0.08-5.61	%
10	V $\beta$ 13.1	0.36	1.62-8.16	1.93-7.70	0.41-5.35	%
11	V $\beta$ 13.6	0.30	0.84-8.80	0.86-3.40	0.47-4.56	%
12	V $\beta$ 8	0.46	2.26-29.47	2.94-6.73	0.86-11.43	%
13	V $\beta$ 5.2	0.15	0.49-4.98	0.50-2.87	0.18-3.53	%
14	V $\beta$ 2	1.25	4.03-23.48	5.43-12.84	1.65-12.42	%
15	V $\beta$ 12	0.24	1-4.76	1.08-2.80	0.33-3.33	%
16	V $\beta$ 23	0.02	0.28-4.76	0.13-1.90	0.04-5.13	%
17	V $\beta$ 1	0.49	1.89-11.70	1.62-14.20	1.40-8.21	%
18	V $\beta$ 21.3	0.23	1.08-5.97	1.53-4.7	0.54-4.93	%
19	V $\beta$ 11	0.05	0.25-5.11	0.30-1.90	0.14-2.25	%
20	V $\beta$ 22	0.23	1.99-9.89	1.98-8.48	0.54-6.47	%
21	V $\beta$ 14	91.55	1.33-8.03	1.57-4.68	1.50-14.3	%
22	V $\beta$ 13.2	0.39	0.80-5.28	0.72-7.27	0.96-9.62	%
23	V $\beta$ 4	0.04	0.79-3.26	1.20-2.83	0.61-4.34	%
24	V $\beta$ 7.2	0.06	0.05-5.45	0.00-3.10	0.01-12.10	%
25	The sum of the 24 subfamilies	98.38	69.95	72.25	66.58	%

## OUTCOME AND FOLLOW-UP

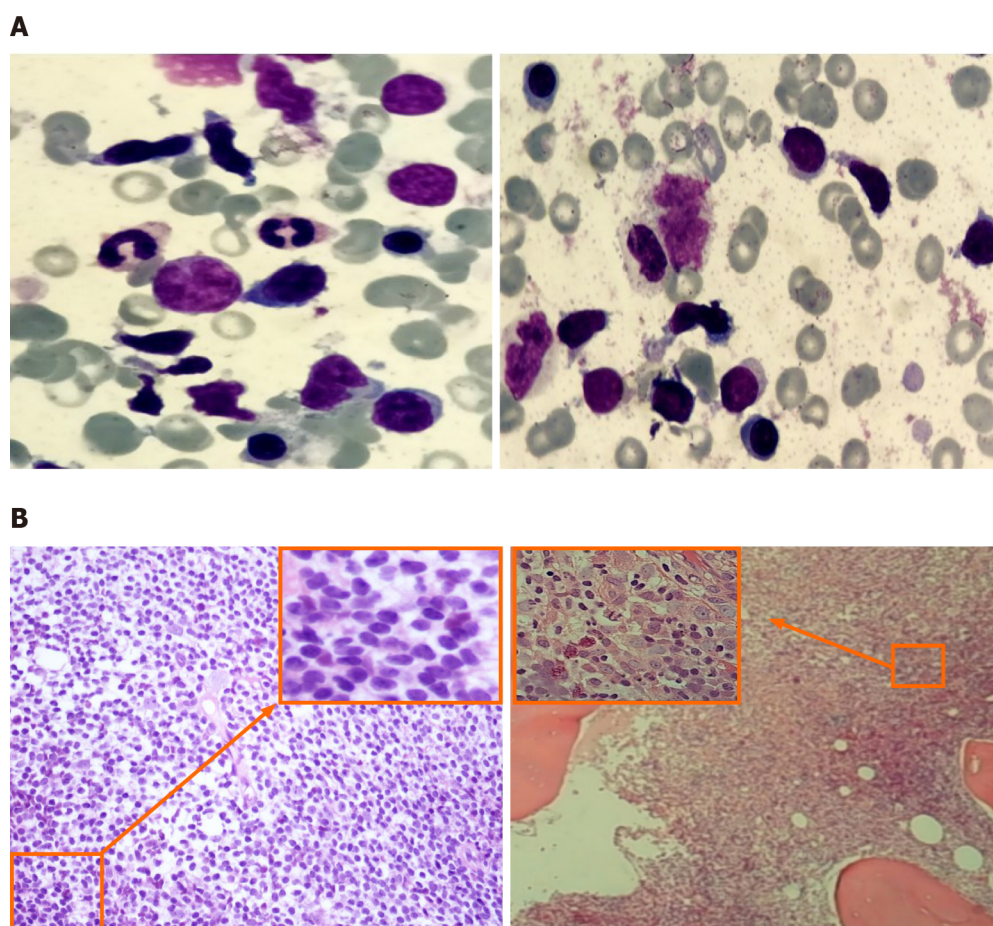
The patient was diagnosed with refractory state, and eventually died of leukocyte stasis syndrome.

## DISCUSSION

Incongruent lymphoma is a rare solid tumor characterized by the appearance of two different types of lymphoma at different anatomic sites, which may manifest clinically as concurrent or sequential disease. ML refers to the appearance of either HL or NHL before the other. The appearance of B-cell lymphoma after CHL can be explained by the clonal progression of malignant B cells. Such more-aggressive and higher-grade B-cell lymphoma originates from RS cells in CHL, as RS cells are thought to originate from B-cells[4]. The reason for the presence of both B- and TCL at different anatomical sites is unclear and there are several explanations[5]. First, the presence of two unrelated clones leads to the presence of two different types of lymphomas. Second, the presence of a typical pluripotent tumor stem cells can differentiate into precursor cells containing both types of lymphoma. Third, secondary lymphomas are a transformation of primary lymphomas, and in clinical practice, it is more common for indolent lymphomas to transform into aggressive lymphomas.



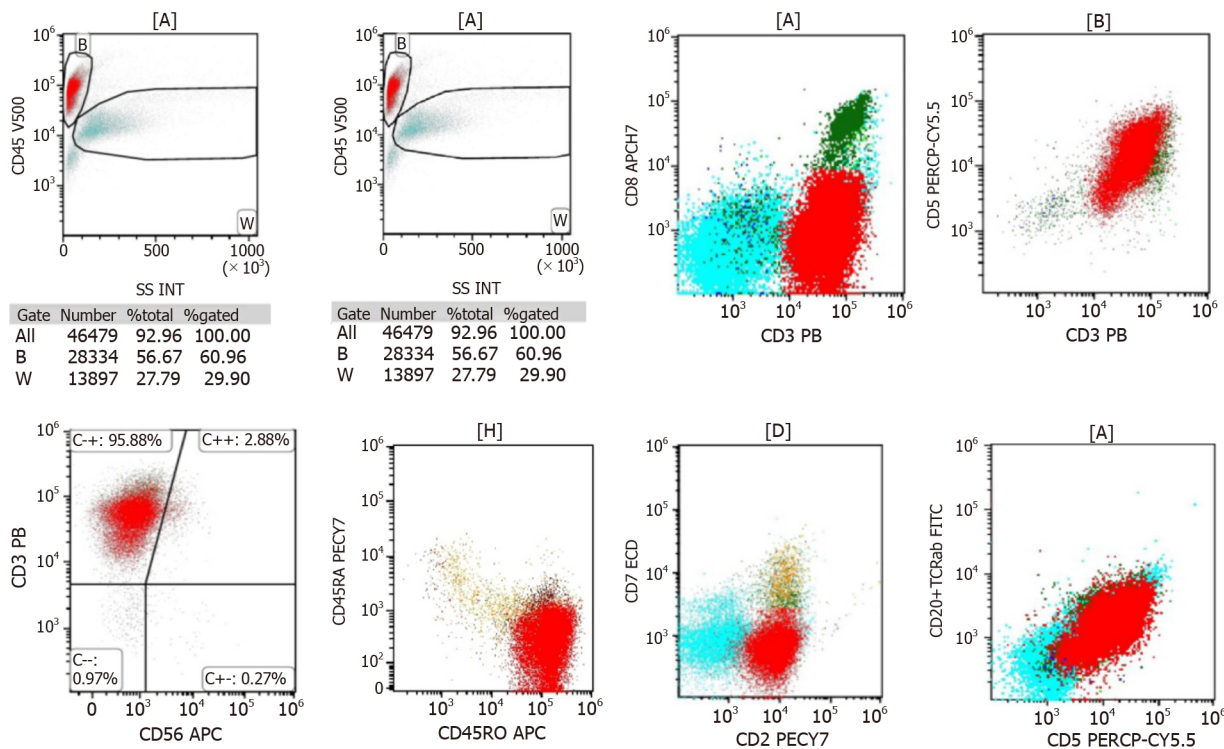
**Figure 1** Pathological findings of Hodgkin's lymphoma and the peripheral T-cell lymphoma. A-D: Pathological findings of Hodgkin's lymphoma; the lymph node structure was disrupted, and a large number of small lymphocytes and popcorn-like cells were observed, with abundant blood vessels (HE,  $\times 200$ ) (A), positive expression of CD30 (B) and PAX-5 (C) in reed-sternberg (RS) cells, EBER<sup>+</sup> expression in RS cells (D); E-H: Pathological findings of the peripheral T-cell lymphoma; the lymph node structure was disrupted, and diffuse consistent T-cells were observed, with abundant blood vessels (HE,  $\times 200$ ) (E), CD3<sup>+</sup> T-cells (F), CD4<sup>+</sup> (G) and CD8<sup>+</sup> T-cells (few) (H).



**Figure 2** Morphological and biopsy results of peripheral T-cell lymphoma bone marrow. A: Atypical lymphocytes, with irregular, spindle-shaped, small to medium morphology, visible pseudopods and cytoplasmic granules, and no reed-sternberg cells observed ( $\times 100$ ); B: The lymphoma cells were diffusely proliferating, with small cytosol, low cytoplasmic volume, irregular nuclei, and coarse chromatin (HE/periodic acid-schiff,  $\times 40$  and  $\times 400$ ).

Metachronous CHL and PTCL are uncommon in the literature, and the pathogenesis is difficult to explain. Overall, persistent immune dysregulation and chemotherapeutic injury are key factors for the occurrence of lymphoma, which may allow aggressive lesions in atypical lymphoproliferative disease. When CHL occurs, persistent immune dysregulation, chemotherapy induction, tumor biology, and RS



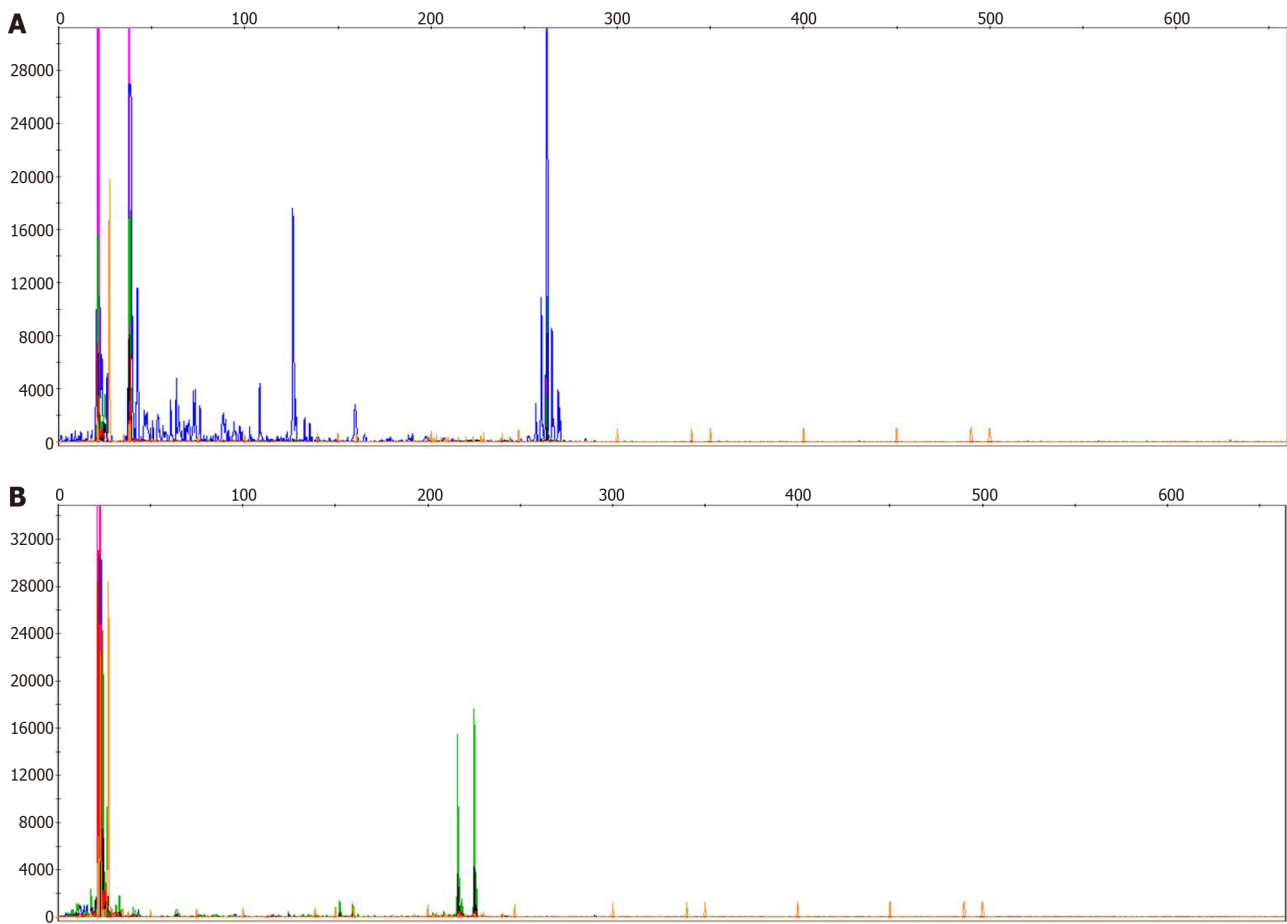


**Figure 3 Immunophenotyping of T/natural killer lymphoma through 8-color flow cytometry.** Abnormal T lymphocytes accounted for 57.8% of the nucleated cells and expressed CD3+, CD2+, CD5+, TCRαβ, and CD45RO.

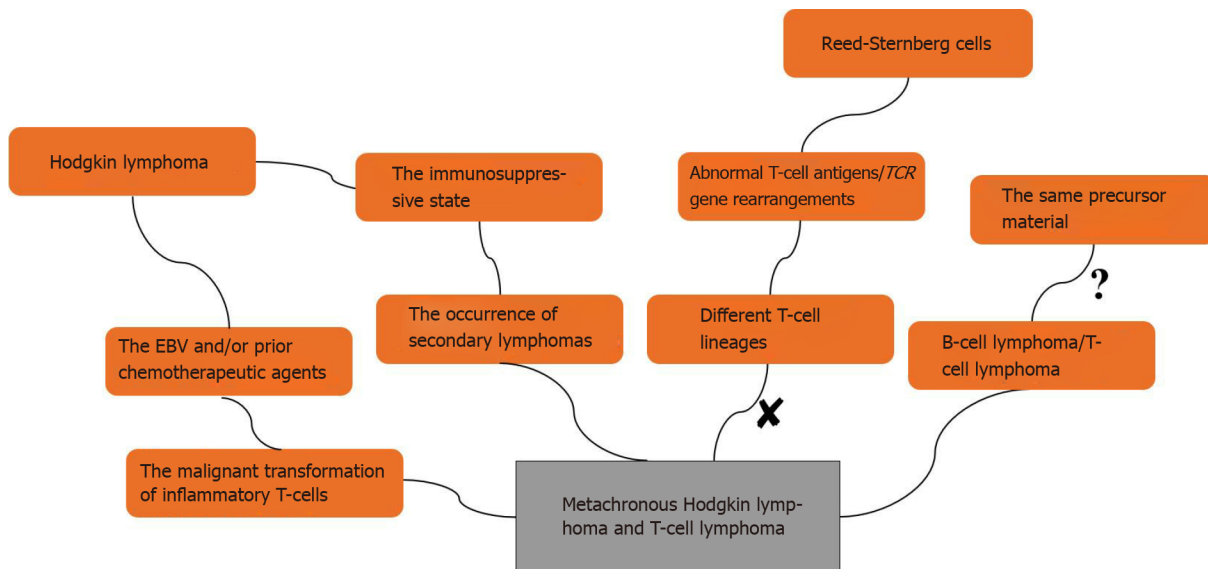
cells can regulate T-cell growth by expressing multiple cytokines[6], and promoting the occurrence of PTCL in case of immunodeficiency and malignant transformation of cells.

The pathological substrate of HL is RS cells; some of which express abnormal T-cell antigens, as demonstrated by molecular studies with 15%–20% clonal *TCR* gene rearrangements[7]. Davis *et al*[8] reported a patient with HL and cutaneous TCL in 2014, which was confirmed by PCR as a single T-cell clone, suggesting that HL and TCL may originate from the same precursor material. A direct clonal relationship between HL and PTCL has rarely been examined, as only a few RS cells that express aberrant T-cell antigens have clonal *TCR* gene rearrangements and are of different T-cell lineages[9,10]. One hypothesis is that the immunosuppressive state of HL may promote the occurrence of secondary lymphomas, including PTCL. Another hypothesis is the malignant transformation of a pre-existing inflammatory T-cell population in patients with HL. Brown *et al*[11] studied a patient with metachronous HL and anaplastic large cell lymphoma, and suggested that the malignant transformation of T-cells originated from an oligoclonal population of reactive T-cells that developed through sustained clonal expansion. Oligoclonal T-cell expansion may arise from genetic alterations such as those caused by continuous stimulation of EBV and/or prior chemotherapeutic agents. Although EBV is a B-lymphotropic virus that does not infect the T-cell lineage *in vivo* as part of its natural life cycle, alterations in the immune microenvironment result in malignant transformation of inflammatory T-cells [12]. The possible mechanisms of metachronous B-cell lymphoma and TCL are shown in Figure 5.

Our patient was diagnosed with PTCL 3 years after the first lymph nodes were detected, but it could not be determined whether there was synchronous lymphoma at the time of the CHL diagnosis. We only obtained a lymph node biopsy of the neck, and after the appearance of secondary PTCL, we subjected a sample of the bone marrow collected at the beginning of the disease to FCM, which revealed some reactive T-cells. Furthermore, EBER<sup>+</sup> RS cells at the beginning of the disease and EBER<sup>+</sup> PTCL cells both supported the possibility of sequential occurrence of CHL and PTCL. Thus, the PTCL that emerged after CHL may have been due to chemotherapy-induced immunodeficiency. T-cell genetic damage, due to chemotherapeutic drugs, induced clonal proliferation and transformation into malignant cells, and EBV was involved in the alteration of the immune microenvironment, as demonstrated by EBER<sup>+</sup> PTCL cells.



**Figure 4** Identification of the T-cell receptor clone gene rearrangement by applying BIOMED-2 primer system. A: *TCRβ* gene rearrangement were detected; B: *TCRγ* gene rearrangement were detected.



**Figure 5** The possible mechanisms of metachronous B-cell lymphoma and T-cell lymphoma. EBV: Epstein-Barr virus.

## CONCLUSION

The occurrence of ML is rare and the diagnostic accuracy needs to be confirmed. We should be alerted to the occurrence of secondary lymphoma when chemotherapeutic drugs are not effective. In addition, the eight patients reported had a poor prognosis, short survival time, and high incidence of bone marrow infiltration (identified in three

**Table 2** Previously reported and current cases of classical metachronous Hodgkin lymphoma and peripheral T-cell lymphoma

Age, y/sex	One (EBV)	Therapy for one	Other (EBV)	Therapy for other	Interval (mo)	BM infiltration	Outcome	Ref.
32/M	CHL (+)	ABVD	PTCL (-)	Unknown	24	Unknown	Unknown	Brown <i>et al</i> [11], 2004
77/F	PTCL (nd)	CHOP	CHL (nd)	Radiation therapy	48	Unknown	Unknown	Brown <i>et al</i> [11], 2004
34/F	CHL (?)	ABVD	PTCL (+)	CHOP, IVE, intermediate-dose MTX, ASCT, BV	47	No	Died after 26 mo	Meconi <i>et al</i> [12], 2020
54/M	CHL (nd)	MOPP, ABVD	PTCL (nd)	Unknown	24	No	Unknown	Wlodarsk <i>et al</i> [13], 1993
76/F	CHL (+)	ABVD	PTCL (+)	CHOP	108	No	Died after 5 mo	Oka <i>et al</i> [14], 2011
37/M	PTCL (nd)	IVAM, BEAM, ASCT	CHL (+)	ABVD	60	Yes	Died after 17 mo	Park <i>et al</i> [15], 2013
64/F	CHL (-)	ABVD	PTCL (-)	Etoposide, <i>etc</i>	15	Yes	Died after 9 mo	Chang and Lee [16], 2015
59/M	CHL (+)	ABVD, PDL-1	PTCL (-)	E-CHOP, DICE, chidamide	42	Yes	Died after 7 mo	Present study

EBV: Epstein-Barr virus; CHL: Classical metachronous hodgkin lymphoma; PTCL: Peripheral T-cell lymphoma. Nd: Not done; +: Positive; -: Negative; MOPP/ABVD: Mechlorethamine, vincristine, procarbazine, prednisone/doxorubicin, bleomycin, vinblastine, dacarbazine; CHOP: Cyclophosphamide, doxorubicin, vincristine, prednisone; IVAM: Ifosfamide, etoposide, cytarabine, methotrexate; BEAM: Bendamustine, etoposide, cytarabine, melphalan; ASCT: Autologous peripheral blood stem cell transplant; IVE: Icyctophosphamide epirubicin etoposide; MTX: Methotrexate; BV: Brentuximab vedotin; E-CHOP: Etoposide CHOP; DICE: Icyctophosphamide, etoposide, cisplatin, dexamethasone; M: Male; F: Female.

patients), as shown in Table 2. The patient we studied matched the diagnosis of TCL/leukemia, which has not been examined before. The staging and diagnosis of TCL are complex, and although our understanding of the molecular pathogenesis of TCL/leukemia cases is increasing, first-line therapies have not progressed proportionately, and the effectiveness of such treatments is limited. The relationship between HL and PTCL needs further exploration to understand the pathogenesis of metachronous T-cell NHL and find effective treatment options.

## REFERENCES

- Custer R. Pitfalls in the diagnosis of lymphoma and leukemia from the pathologist's point of view. New York: American Cancer Society, 1954: 35-37
- Geladari E, Dimopoulou G, Margellou E, Paraskevas A, Kafetzis G, Rontogianni D, Vadiaka M. Coexistence of Hodgkin and Non-Hodgkin Lymphoma; Composite Lymphoma [CL] in a Patient Presenting with Waxing and Waning Lymphadenopathy. *Cardiovasc Hematol Disord Drug Targets* 2020; **20**: 160-163 [PMID: 31633478 DOI: 10.2174/1871529X19666191014111118]
- Younes A, Hilden P, Coiffier B, Hagenbeek A, Salles G, Wilson W, Seymour JF, Kelly K, Gribben J, Pfreundschuh M, Morschhauser F, Schoder H, Zelenetz AD, Rademaker J, Advani R, Valente N, Fortpie C, Witzig TE, Sehn LH, Engert A, Fisher RI, Zinzani PL, Federico M, Hutchings M, Bollard C, Trneny M, Elsayed YA, Tobinai K, Abramson JS, Fowler N, Goy A, Smith M, Ansell S, Kuruvilla J, Dreyling M, Thieblemont C, Little RF, Auer I, Van Oers MHJ, Takeshita K, Gopal A, Rule S, de Vos S, Kloos I, Kaminski MS, Meignan M, Schwartz LH, Leonard JP, Schuster SJ, Seshan VE. International Working Group consensus response evaluation criteria in lymphoma (RECIL 2017). *Ann Oncol* 2017; **28**: 1436-1447 [PMID: 28379322 DOI: 10.1093/annonc/mdx097]
- Wang HW, Balakrishna JP, Pittaluga S, Jaffe ES. Diagnosis of Hodgkin lymphoma in the modern era. *Br J Haematol* 2019; **184**: 45-59 [PMID: 30407610 DOI: 10.1111/bjh.15614]
- Boyer DF, Lindeman NI, Harris NL, Ferry JA. Peripheral T-cell lymphomas with cytotoxic phenotype in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma. *Am J Surg Pathol* 2014; **38**: 279-288 [PMID: 24418862 DOI: 10.1097/PAS.0000000000000140]
- Aoki T, Chong LC, Takata K, Milne K, Hav M, Colombo A, Chavez EA, Nissen M, Wang X, Miyata-Takata T, Lam V, Viganò E, Woolcock BW, Telenius A, Li MY, Healy S, Ghesquiere C, Kos D, Goodyear T, Veldman J, Zhang AW, Kim J, Saberi S, Ding J, Farinha P, Weng AP, Savage KJ, Scott DW, Krystal G, Nelson BH, Mottok A, Merchant A, Shah SP, Steidl C. Single-Cell Transcriptome Analysis Reveals Disease-Defining T-cell Subsets in the Tumor Microenvironment of

- Classic Hodgkin Lymphoma. *Cancer Discov* 2020; **10**: 406-421 [PMID: [31857391](#) DOI: [10.1158/2159-8290.CD-19-0680](#)]
- 7 **Seitz V**, Hummel M, Marafioti T, Anagnostopoulos I, Assaf C, Stein H. Detection of clonal T-cell receptor gamma-chain gene rearrangements in Reed-Sternberg cells of classic Hodgkin disease. *Blood* 2000; **95**: 3020-3024 [PMID: [10807764](#)]
  - 8 **Davis TH**, Morton CC, Miller-Cassman R, Balk SP, Kadin ME. Hodgkin's disease, lymphomatoid papulosis, and cutaneous T-cell lymphoma derived from a common T-cell clone. *N Engl J Med* 1992; **326**: 1115-1122 [PMID: [1532439](#) DOI: [10.1056/NEJM199204233261704](#)]
  - 9 **Hummel M**, Marafioti T, Ziemann K, Stein H. Ig rearrangements in isolated Reed-Sternberg cells: conclusions from four different studies. *Ann Oncol* 1996; **7** Suppl 4: 31-33 [PMID: [8836406](#) DOI: [10.1093/annonc/7.suppl\\_4.s31](#)]
  - 10 **Küppers R**, Schwering I, Bräuninger A, Rajewsky K, Hansmann ML. Biology of Hodgkin's lymphoma. *Ann Oncol* 2002; **13** Suppl 1: 11-18 [PMID: [12078890](#) DOI: [10.1093/annonc/13.s1.11](#)]
  - 11 **Brown JR**, Weng AP, Freedman AS. Hodgkin disease associated with T-cell non-Hodgkin lymphomas: case reports and review of the literature. *Am J Clin Pathol* 2004; **121**: 701-708 [PMID: [15151210](#) DOI: [10.1309/W1GW-43HT-793U-F86R](#)]
  - 12 **Meconi F**, Provenzano I, Nasso D, Mariotti B, Pupo L, Secchi R, Cerretti R, Lucia A, Arcese W, Cantonetti M. A case of metachronous peripheral T-Cell non-Hodgkin lymphoma following chemotherapy for Hodgkin disease successfully treated with brentuximab vedotin. *Clin Case Rep* 2020; **8**: 1353-1356 [PMID: [32884752](#) DOI: [10.1002/ccr3.2898](#)]
  - 13 **Wlodarska I**, Delabie J, De Wolf-Peters C, Mecucci C, Stul M, Verhoef G, Cassiman JJ, Van den Berghe H. T-cell lymphoma developing in Hodgkin's disease: evidence for two clones. *J Pathol* 1993; **170**: 239-248 [PMID: [8133397](#) DOI: [10.1002/path.1711700305](#)]
  - 14 **Oka K**, Nagayama R, Iijima S, Yonekawa N, Hirose K, Yatabe Y, Mori N. Epstein-Barr virus-associated lymphoproliferative disorder presenting with classical Hodgkin lymphoma and developing as peripheral T-cell lymphoma 9 years later: a case report of composite lymphoma. *Pathol Int* 2011; **61**: 752-755 [PMID: [22126384](#) DOI: [10.1111/j.1440-1827.2011.02723.x](#)]
  - 15 **Park J**, Lee JE, Kim M, Lim J, Kim Y, Han K, Park G, Jung YH, Roh SY, Hong YS. Discordant lymphocyte-depleted classical Hodgkin's and peripheral T-cell lymphoma arising in a patient 11 years after diagnosis of multicentric Castleman's disease. *Int J Hematol* 2013; **98**: 114-121 [PMID: [23733446](#) DOI: [10.1007/s12185-013-1358-0](#)]
  - 16 **Chang SH**, Lee HR. Peripheral T Cell Non-Hodgkin's Lymphoma following Treatment of Hodgkin's Lymphoma. *Case Rep Oncol Med* 2015; **2015**: 438385 [PMID: [25664194](#) DOI: [10.1155/2015/438385](#)]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

