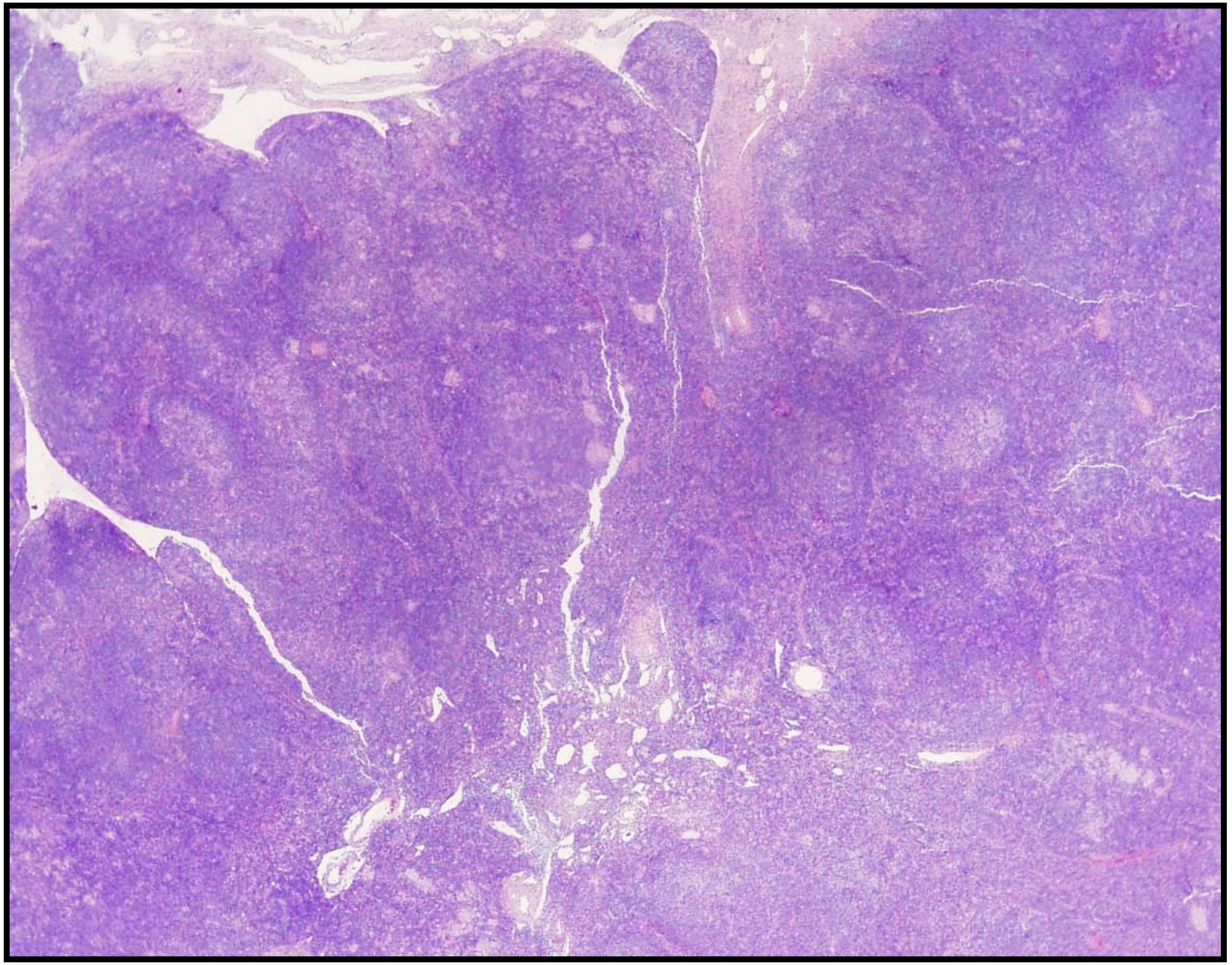
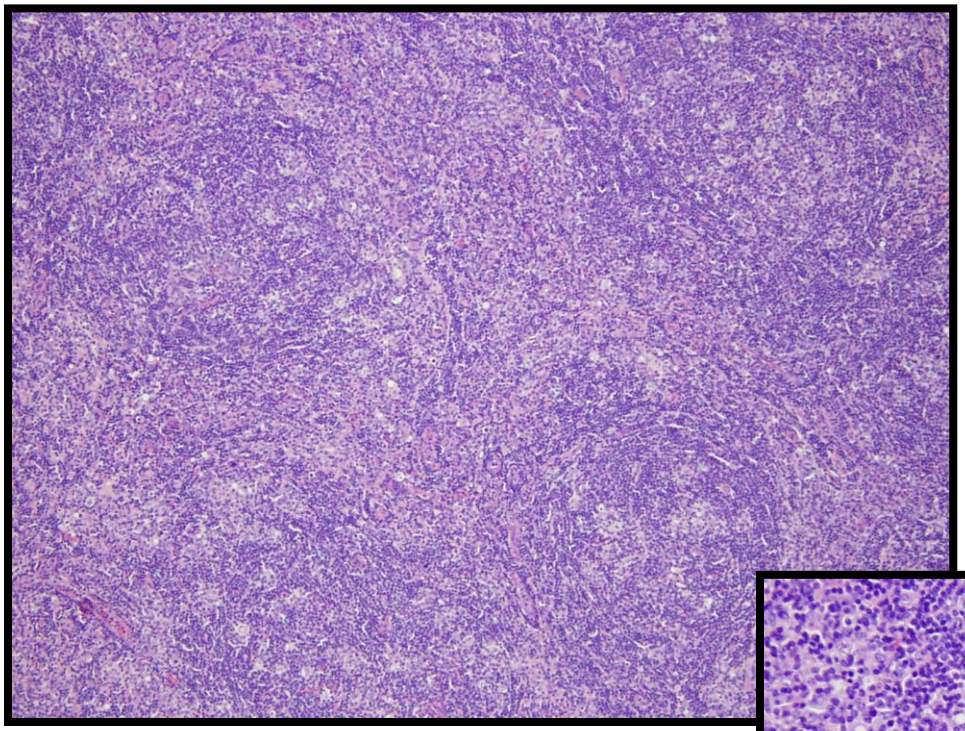
CASE 6

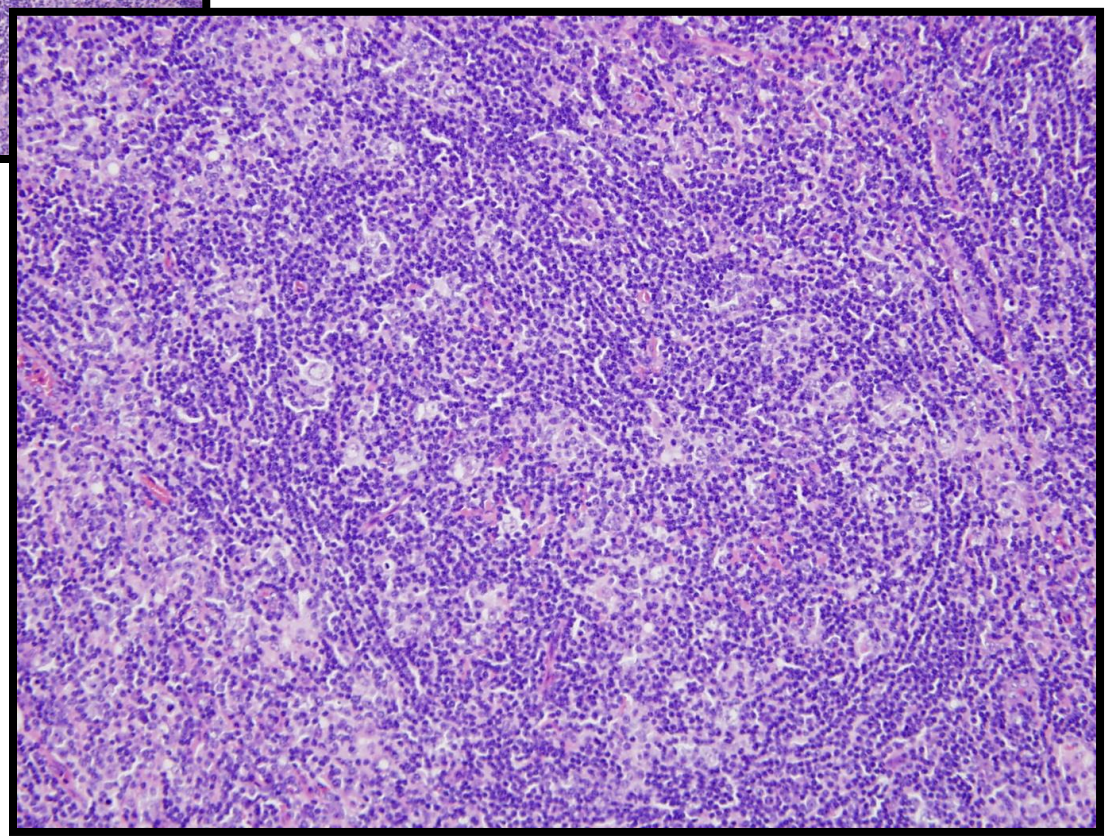
A 48-year-old man presented with palpable masses in his neck without B symptoms. Physcial examination and PET scan showed multiple left neck LNs with the largest from the submandibular region being 3.1 x 1.9 x 1.5 cm. A FNA was non-diagnostic with negative flow cytometry results. An excisional biopsy was performed.

Case 6

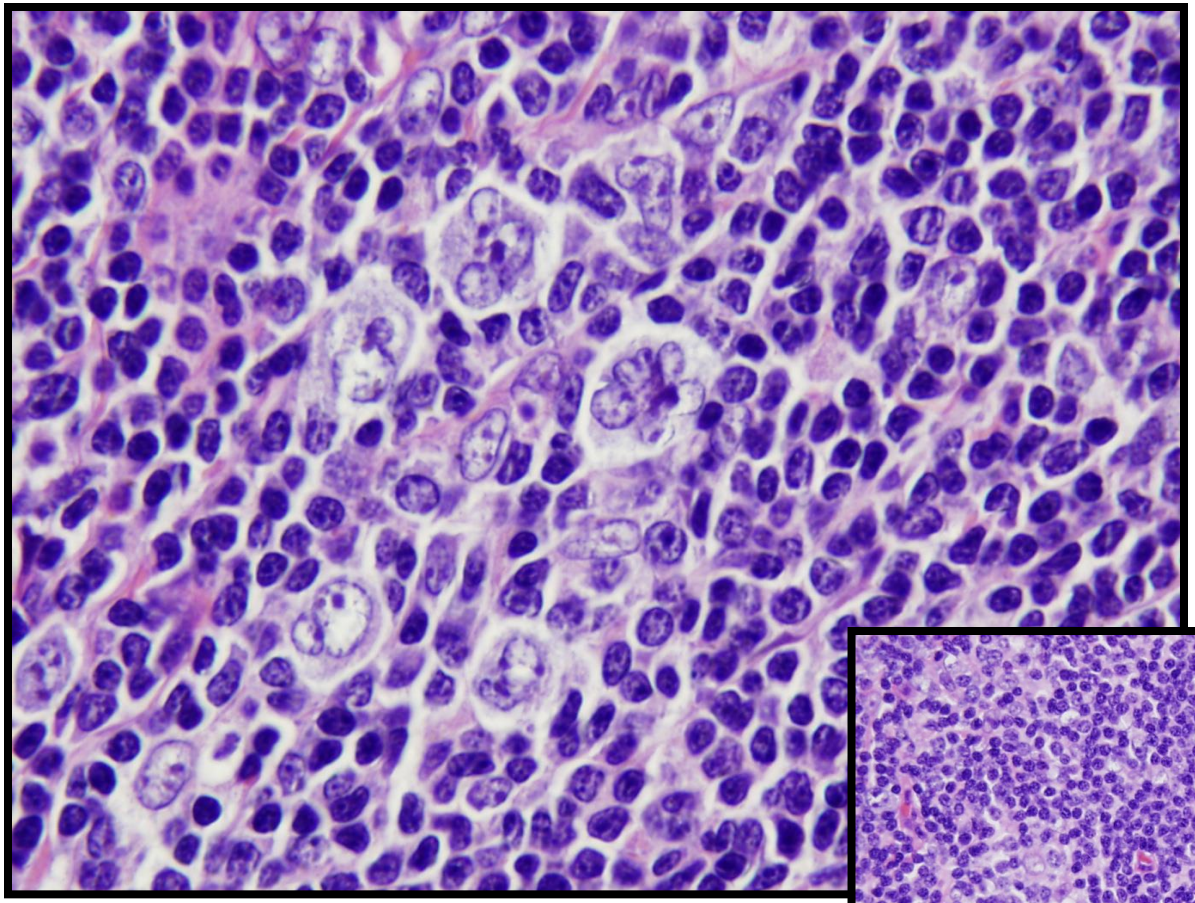


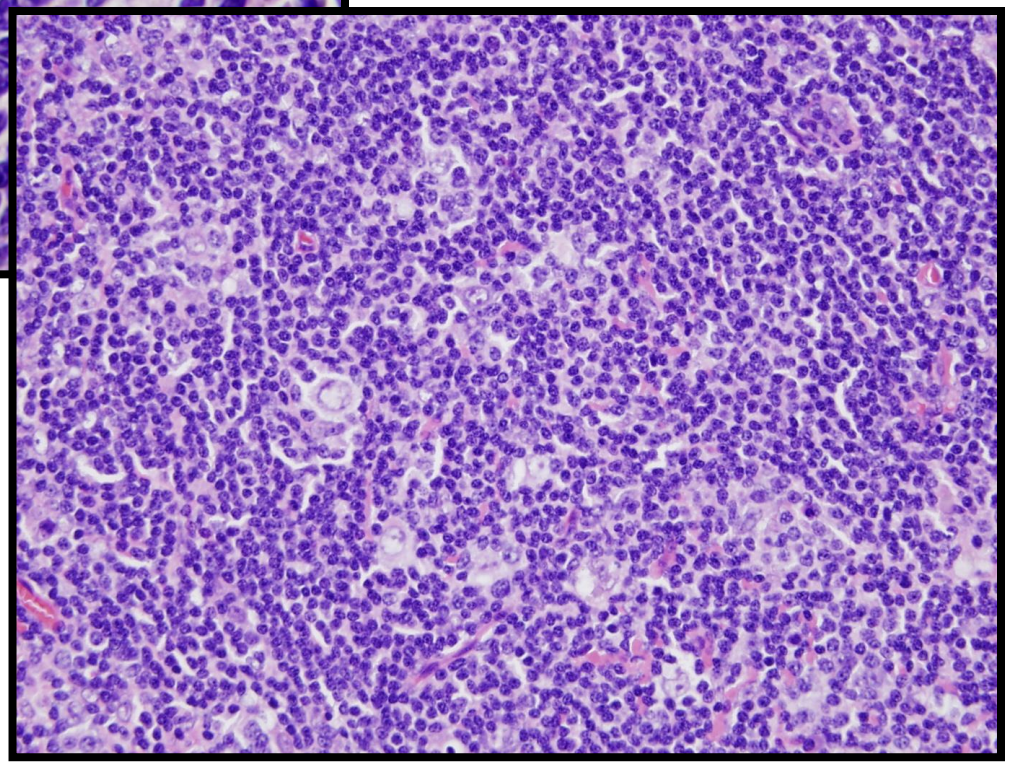
Case 6

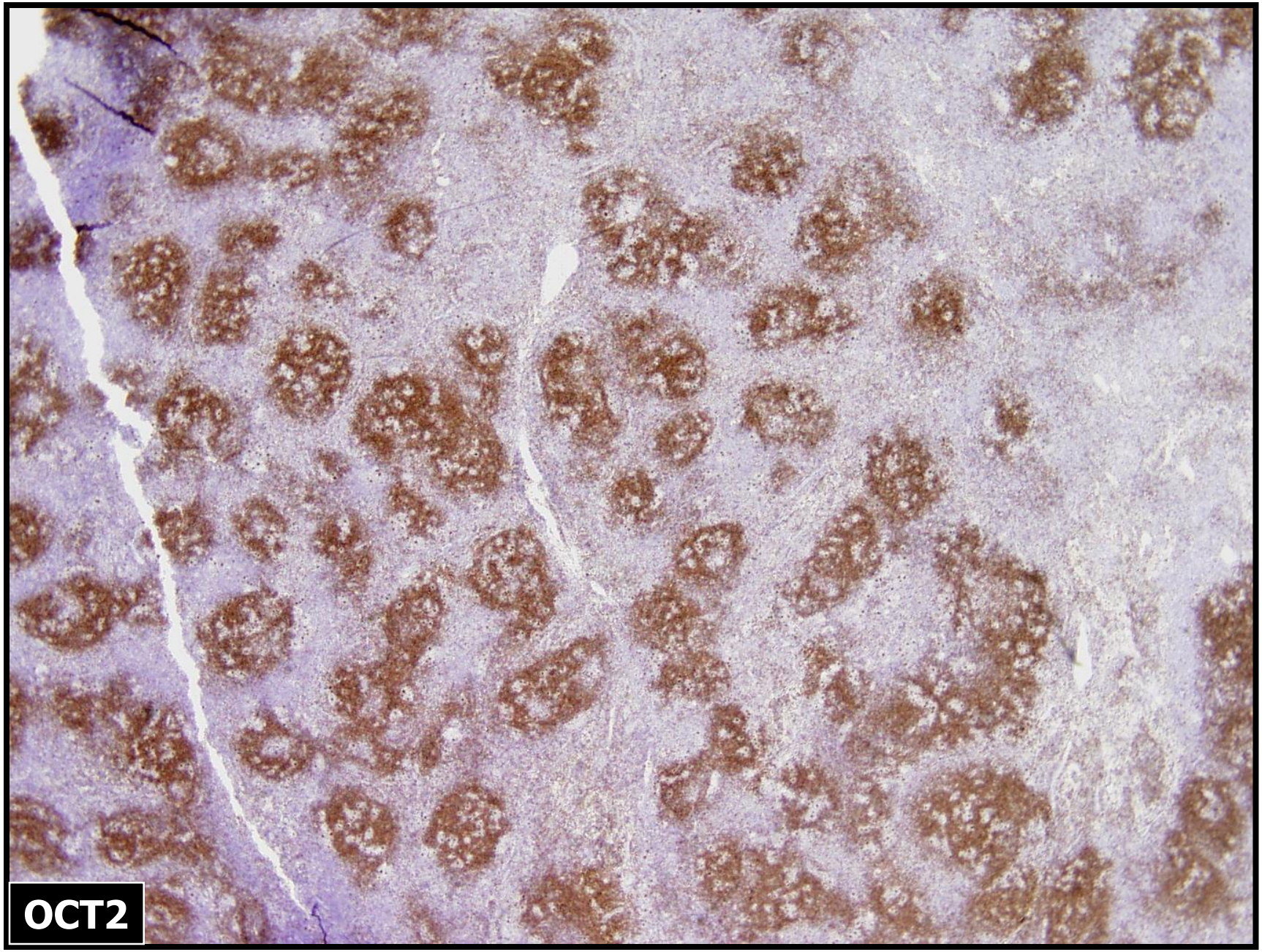


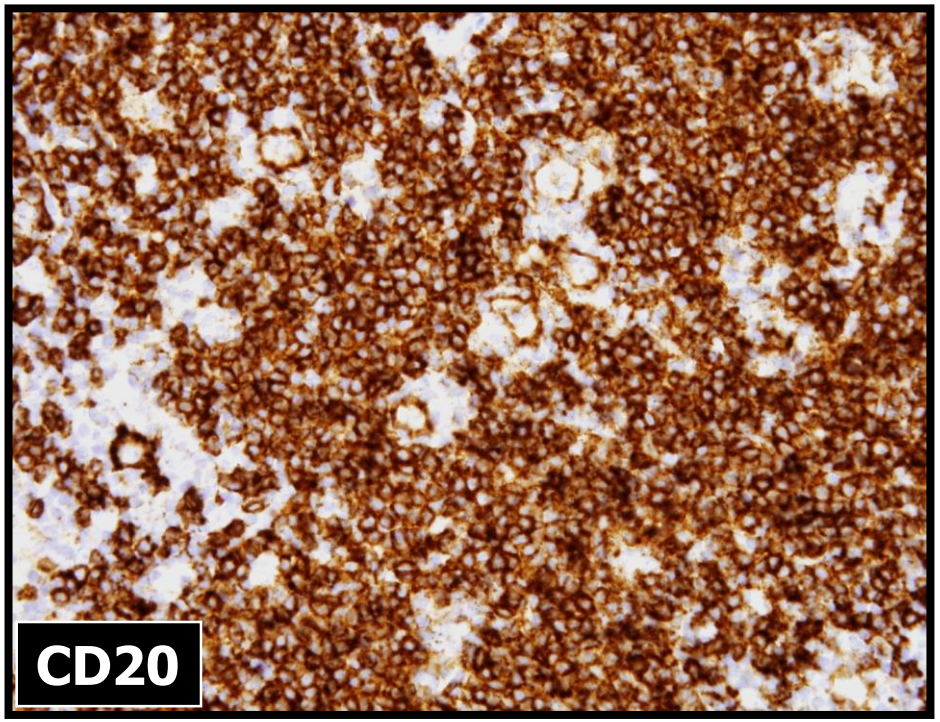


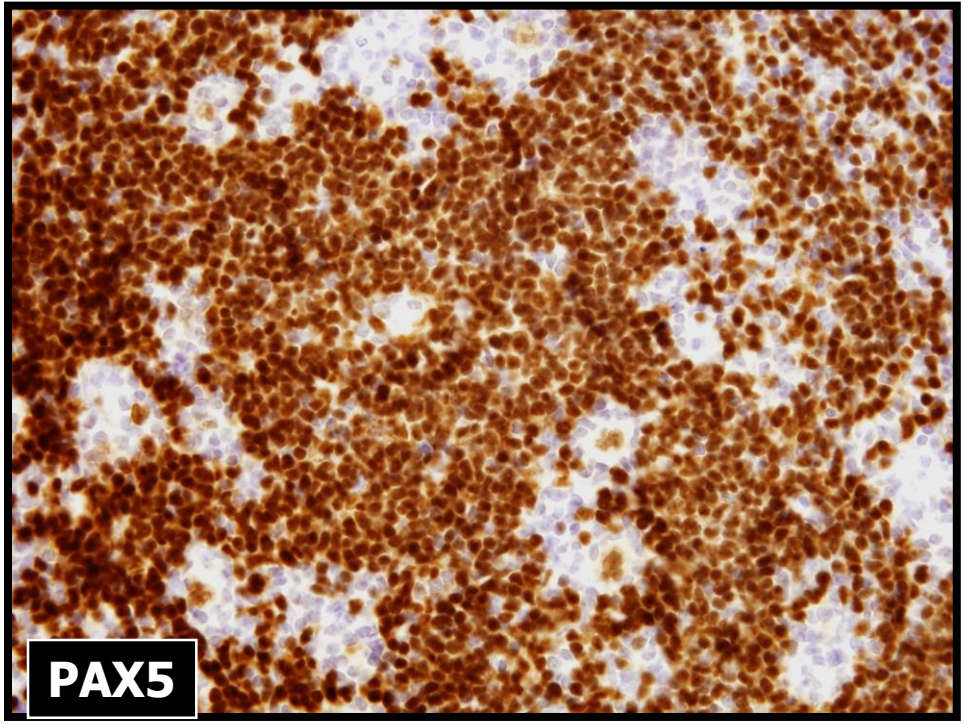
Case 6

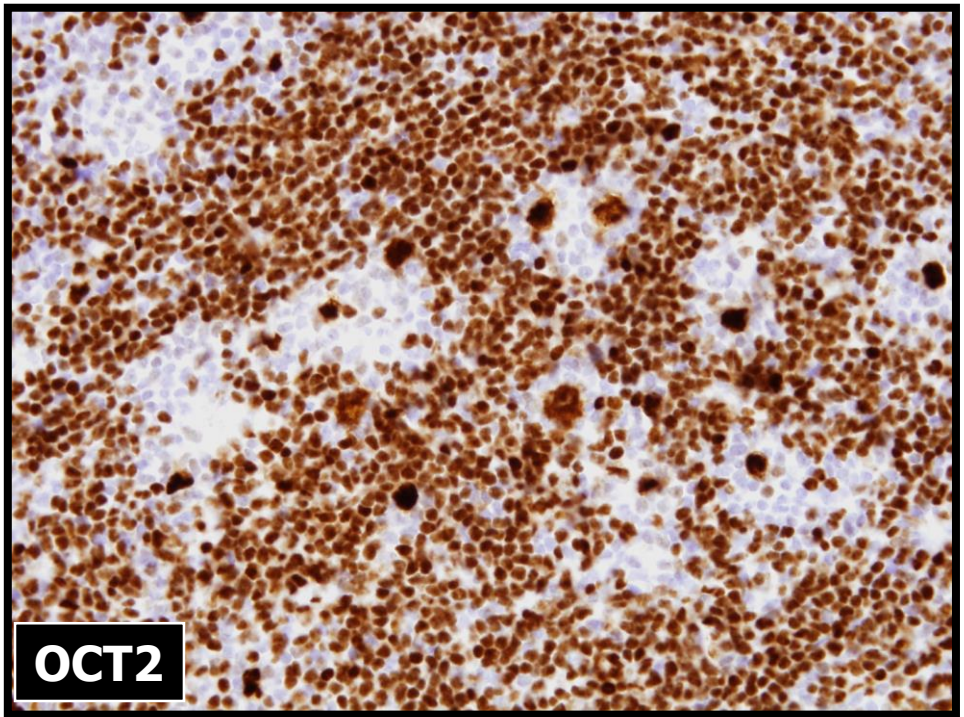




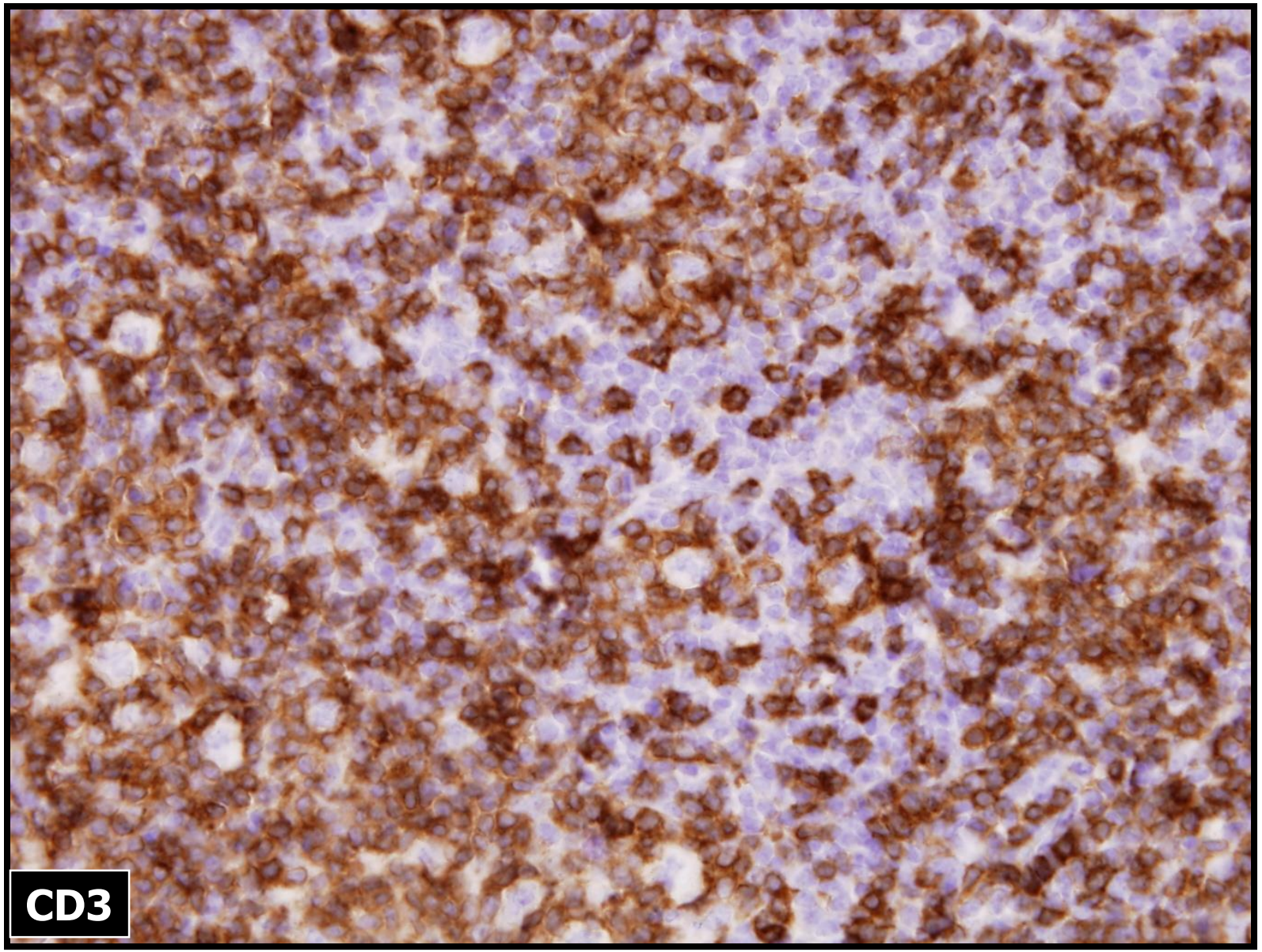

OCT2







Case 6


CD3

DIAGNOSIS (CASE 6)

Nodular lymphocyte predominant Hodgkin lymphoma

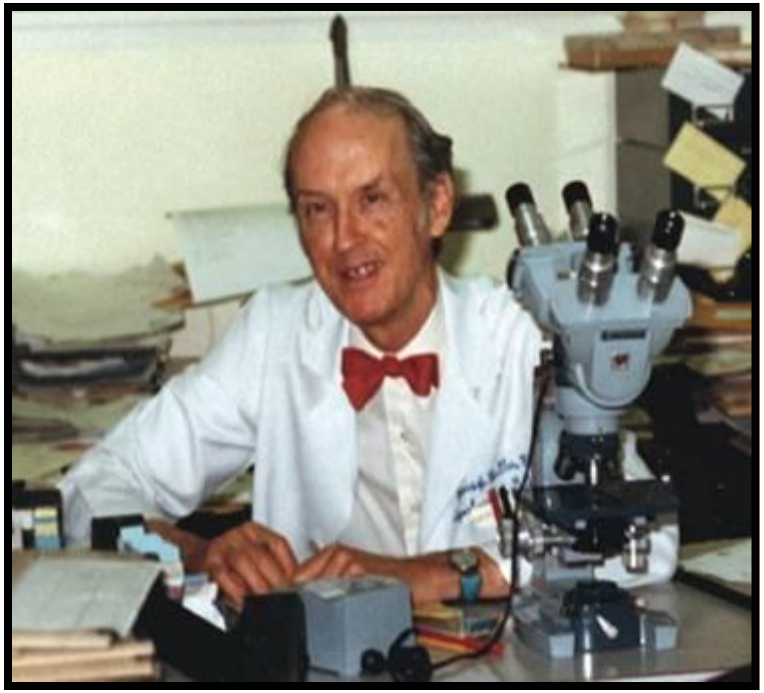
Also pattern A

The Pathology and Nomenclature of Hodgkin's Disease

ROBERT J. LUKES AND JAMES J. BUTLER

Department of Pathology, University of Southern California, School of Medicine, Los Angeles, California (R. J. L.) and Department of Pathology, M. D. Anderson Hospital, Houston, Texas (J. J. B.)

Robert J. Lukes, MD



James J. Butler, MD

Cancer Research 26; 1063, 1966

Classification of Hodgkin Lymphoma

Little Change Over Time

Lukes & Butler	Rye	WHO - 2017
Lymphocytic and/or histiocytic Nodular Diffuse	Lymphocytic predominance	Nodular lymphocyte predominant HL Lymphocyte-rich classic HL
Nodular sclerosis	Nodular sclerosis	Nodular sclerosis classic HL
Mixed	Mixed cellularity	Mixed cellularity classic HL
Diffuse fibrosis Reticular	Lymphocytic depletion	Lymphocyte-depleted classic HL

Mercedes Benz

Same name – different cars

Criteria for HL Diagnosis

Criteria have shifted from purely histologic to histologic and immunophenotypic

Reclassification of disease

Change in disease frequencies

Change in criteria for diagnosis of HL overall

Hodgkin Lymphomas
Frequency

HL ~ 10% lymphomas in USA (~8,830 cases/yr)

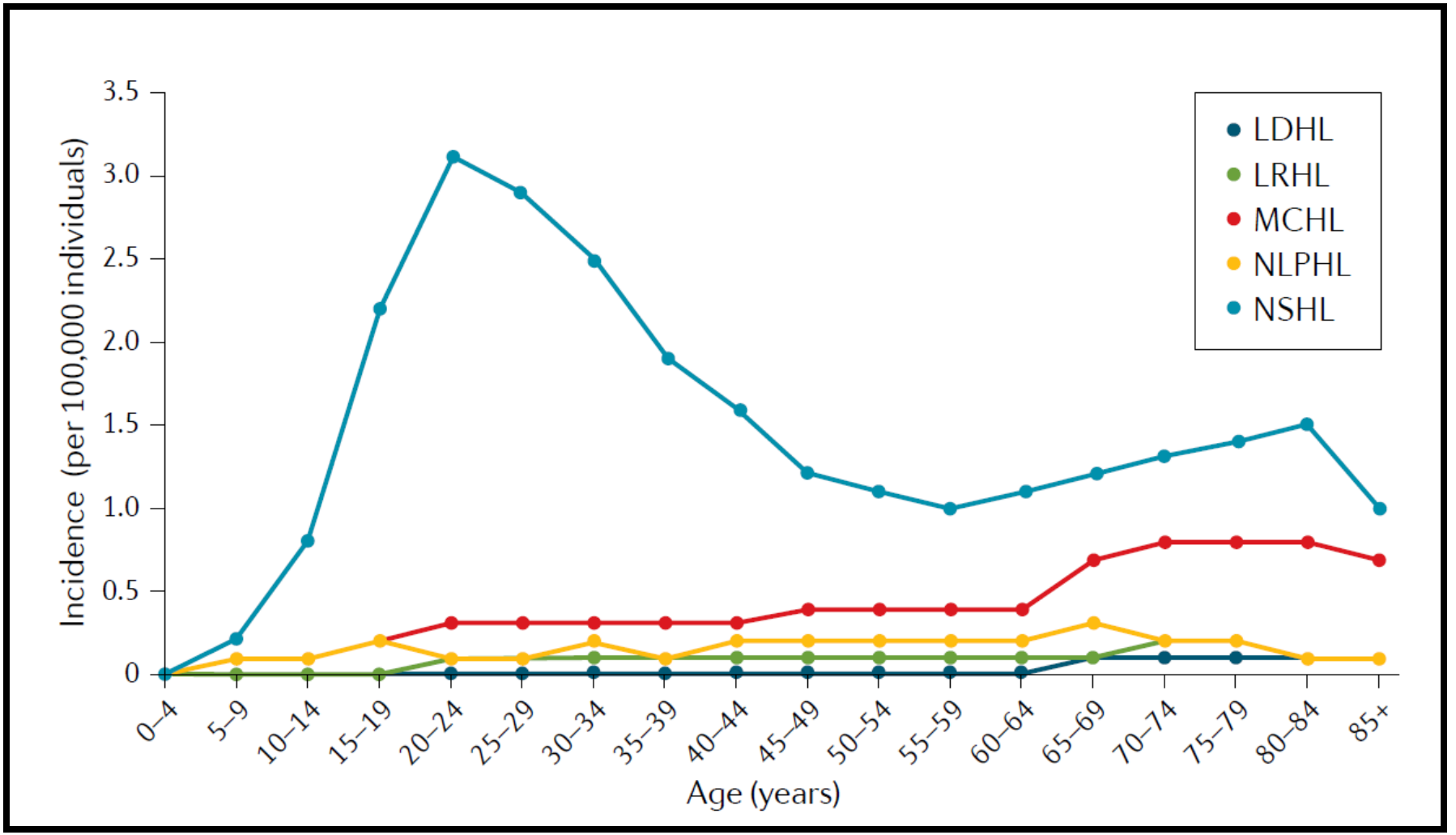
Nodular sclerosis	62%
Mixed cellularity	27%
Nodular lymphocyte predominant	5%
Lymphocyte-rich classical	4%
Lymphocyte depleted	1%

960 (~11%) deaths per year

J Clin Oncol 23: 5739, 2005
CA Cancer J Clin 71: 7, 2021

Hodgkin Lymphomas

Incidence



Nat Rev Dis Primers 6: 61, 2020

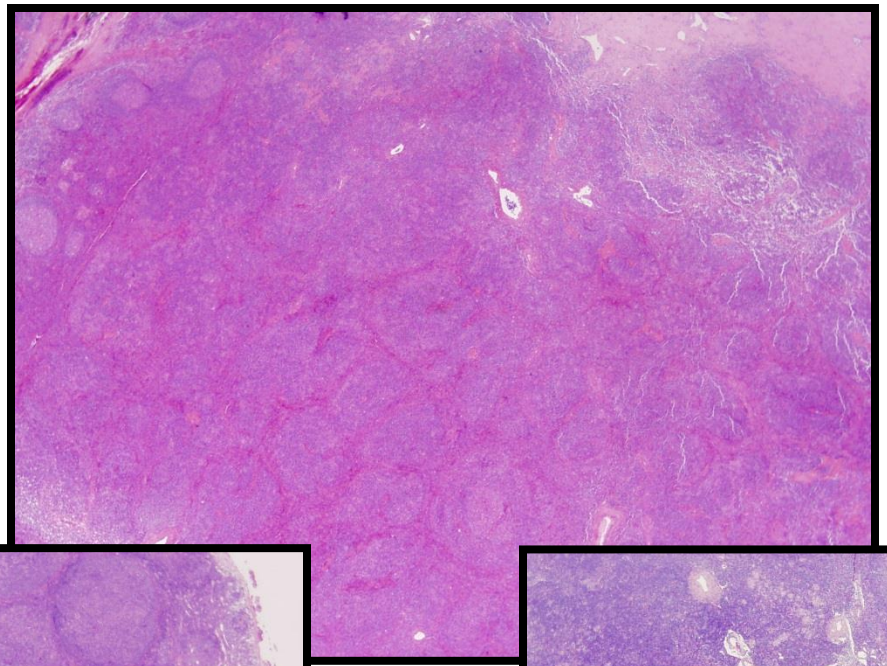
Nodular Lymphocyte Predominant HL

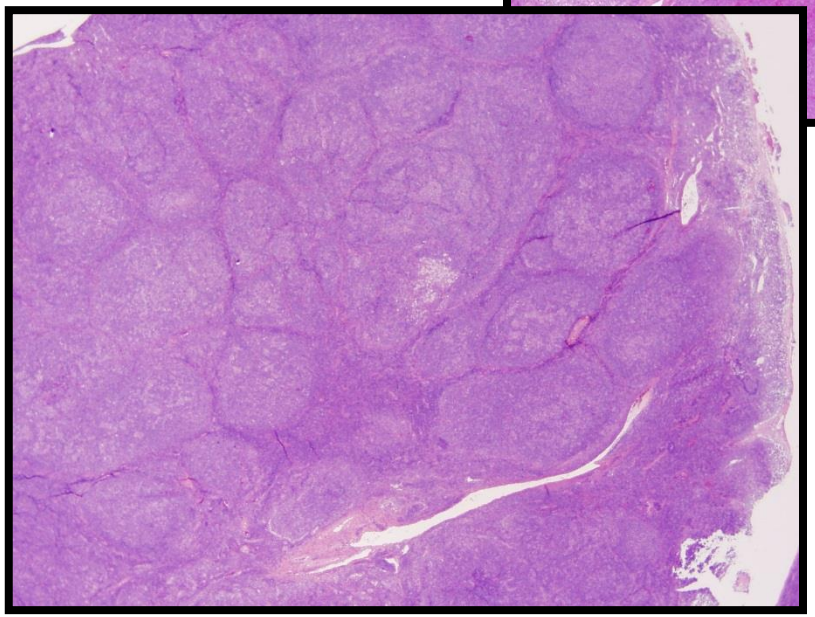
- Male predominance
- Peak incidence 30-50 years age group
- Localized peripheral LNs (cervical #1)
- B-symptoms unusual
- Mediastinum, spleen and bone marrow rarely involved
- Frequent relapses (late)

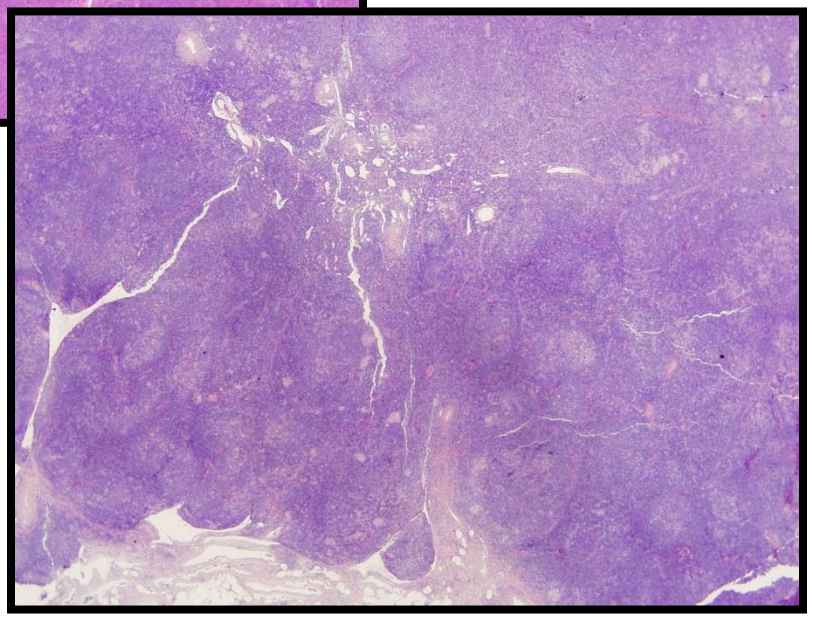
Nodular LPHL

Vaguely Nodular Pattern

3 cases

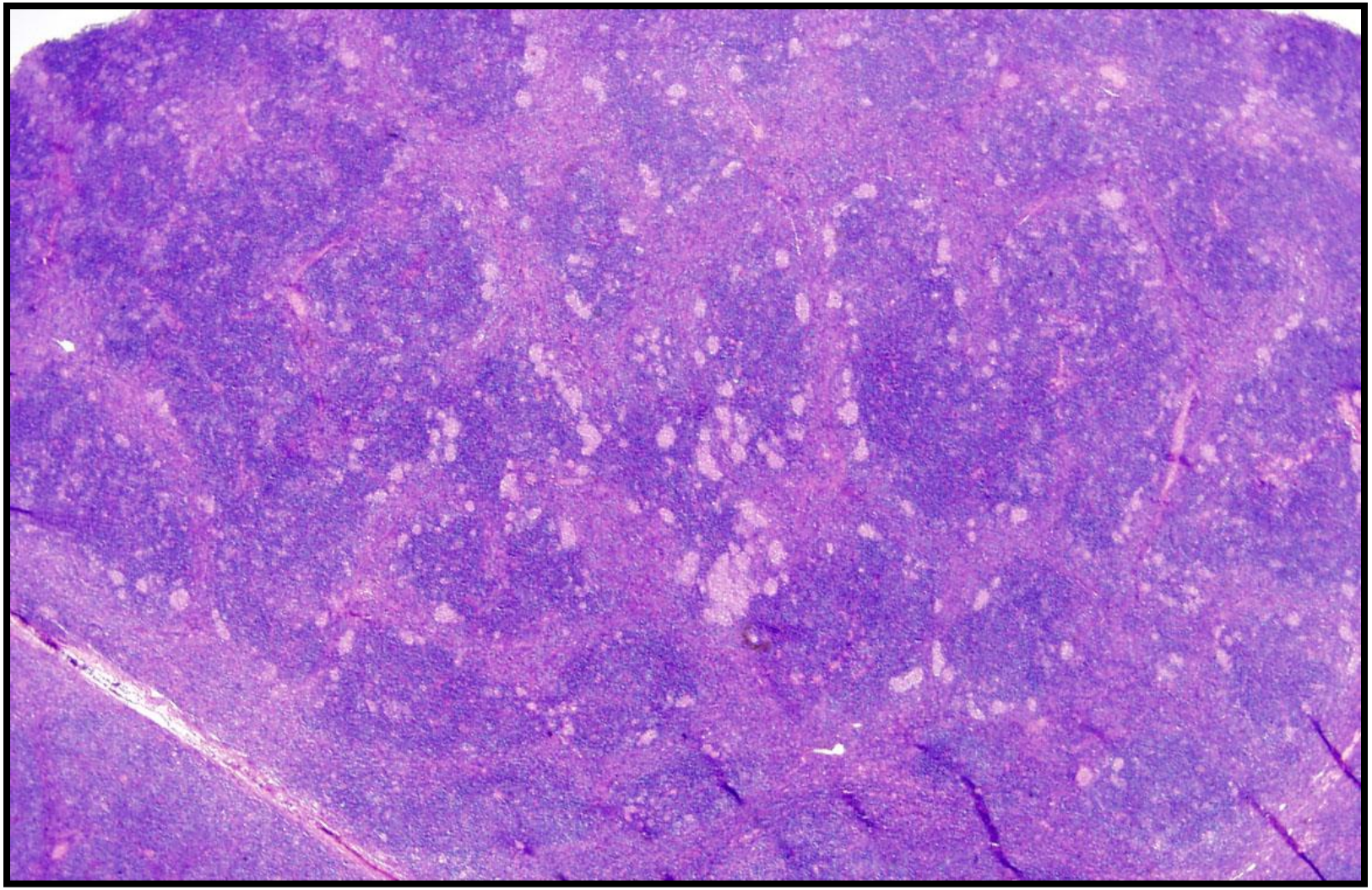






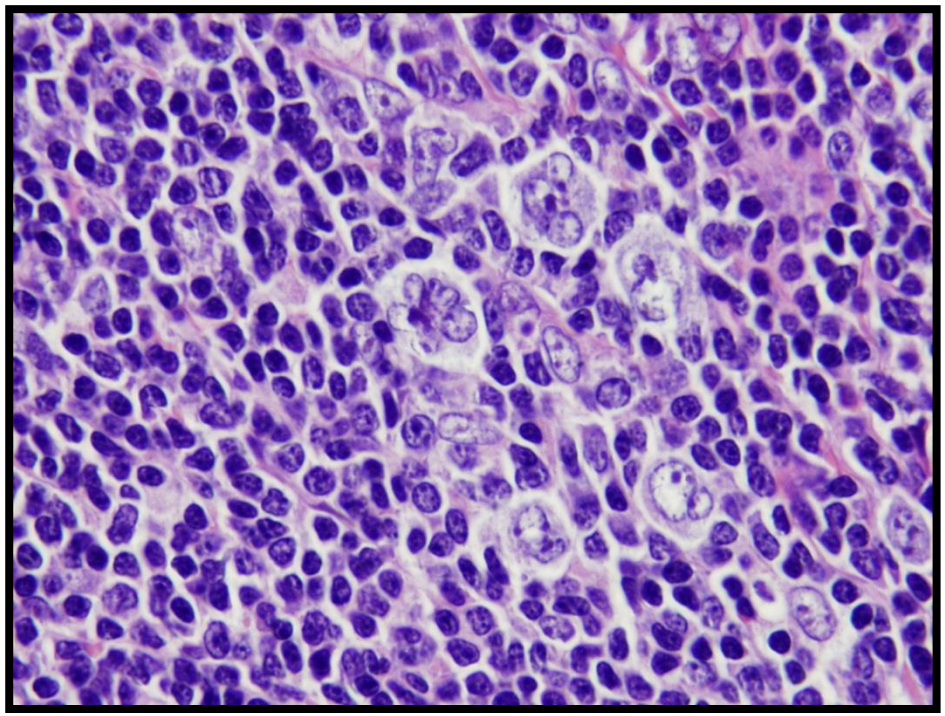
Nodular LPHL

Epithelioid Histiocytes

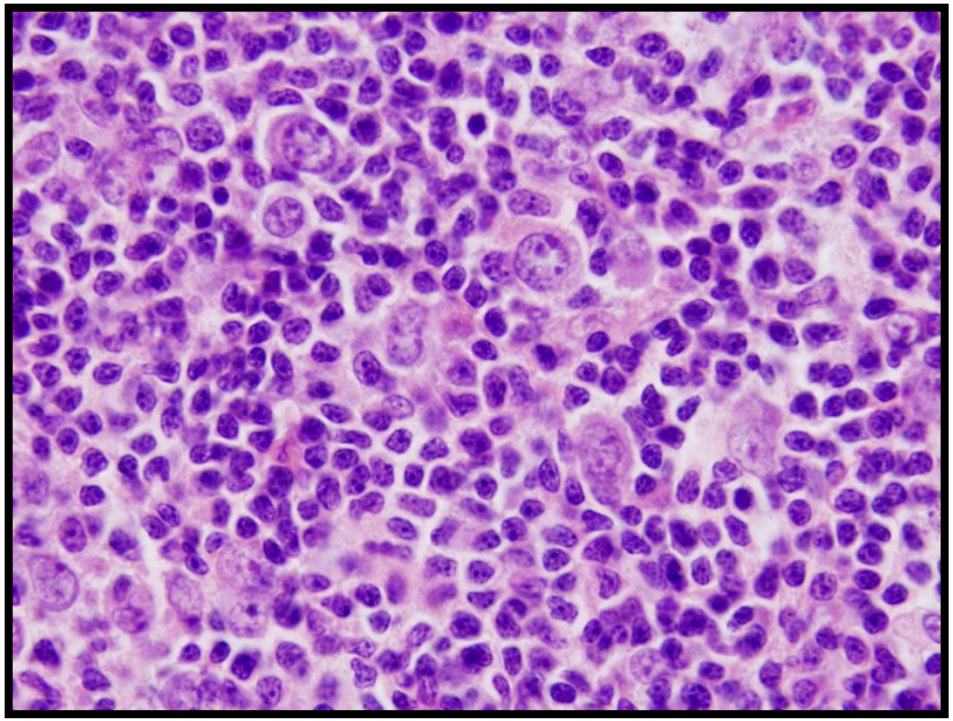


Nodular LPHL

LP (Popcorn) Cells



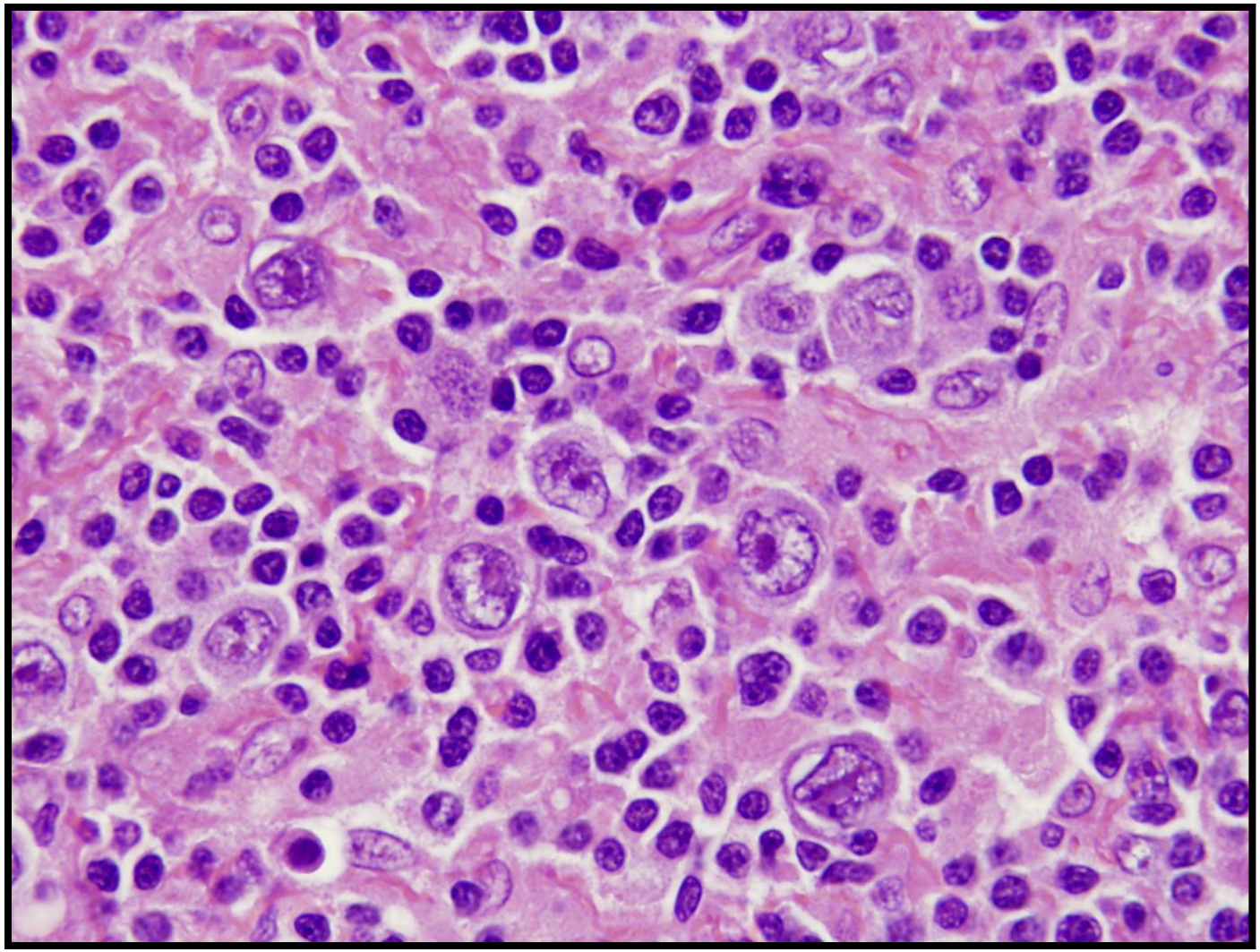
Popped



Unpopped

Nodular LPHL

Atypical LP Cells (Classic-like)



Lab Invest. 1986 Apr;54(4):457-61.

Nodular lymphocyte predominance type of Hodgkin's disease is a germinal center lymphoma

W Timens, L Visser, S Poppema

PMID: 3083157

7 cases assessed by frozen section immunohistochemistry

Small lymphocytes

Polytypic B-cells, IgM+, IgD+

Large L&H cells

B-cell antigens+

Sibrand Poppema, MD, PhD

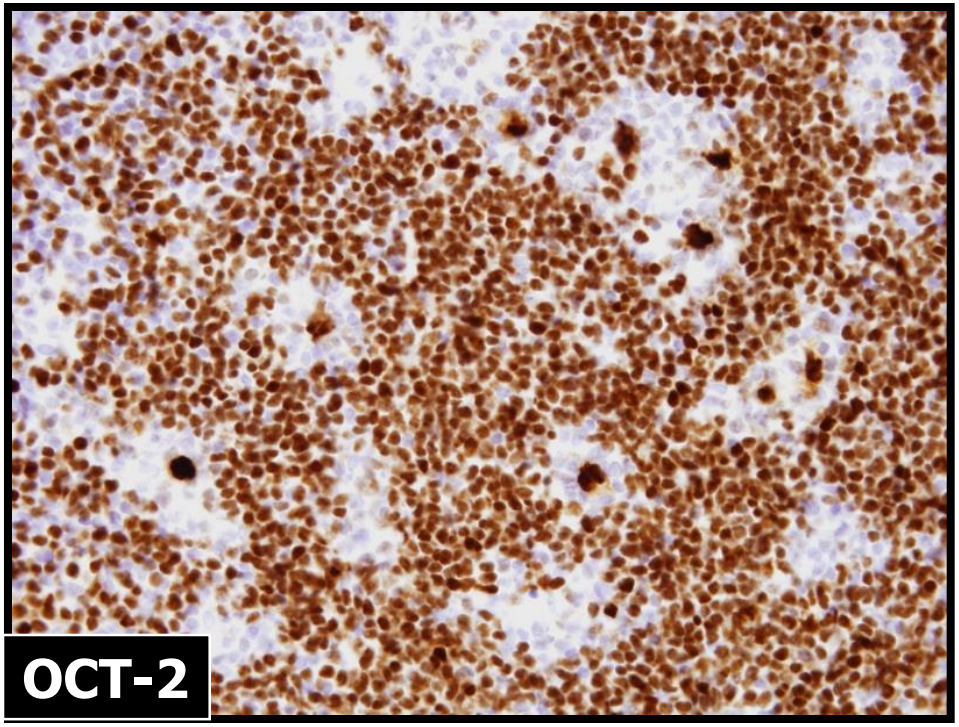
Immunophenotype of Neoplastic Cells in HL

	Classic HRS Cells	NLP LP Cells
T-cell	-	-
CD15	+/-	-
CD20	-/+	++
CD30	+	-
CD45/LCA	-	+
PAX-5	+ dim	+
OCT-2	-	+
BCL-2	+/-	-
BCL-6	-/+	+
EBV	+/-	-

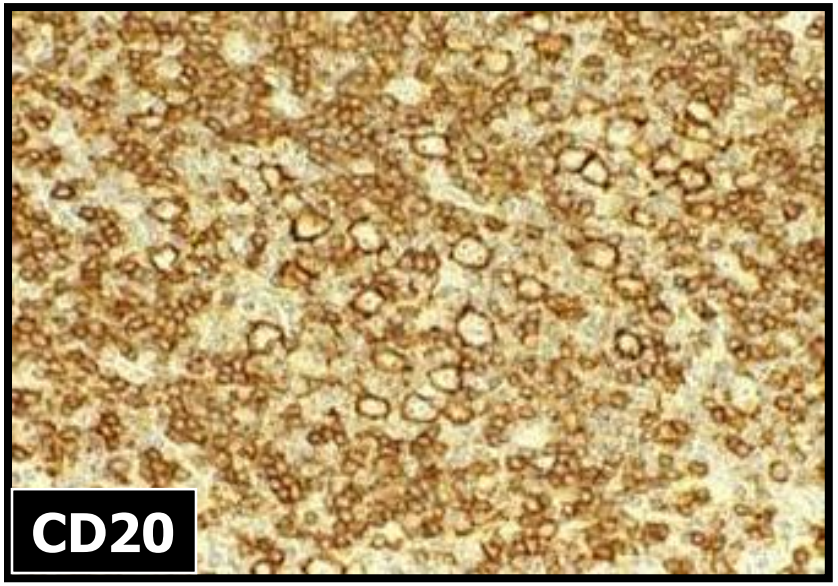
CD20-	3%
CD45-	5%
CD15+	6%
CD30+	10%

Nodular LPHL

LP Cells Are B Cells



Many reactive cells are also B-cells

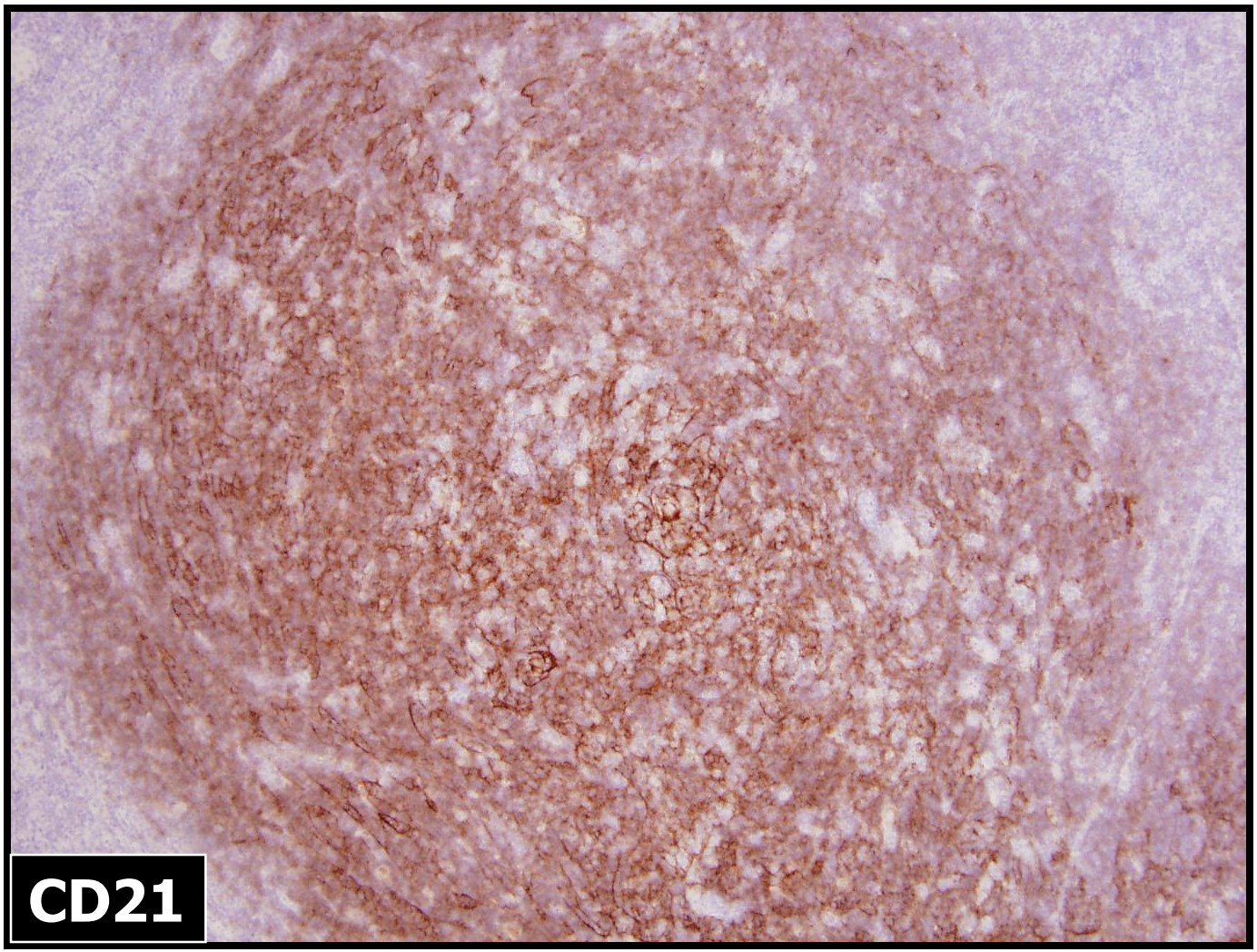


OCT2 is very helpful

We use Leica (catalog # PA0532)

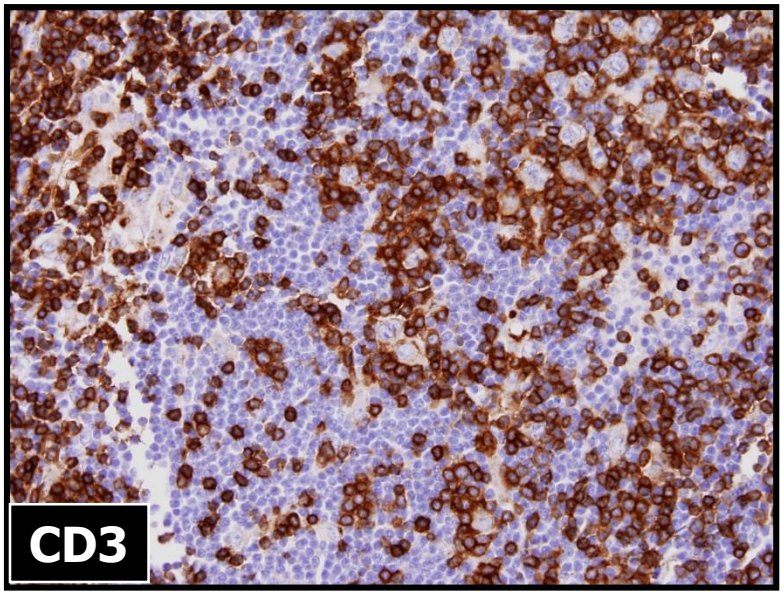
Nodular LPHL

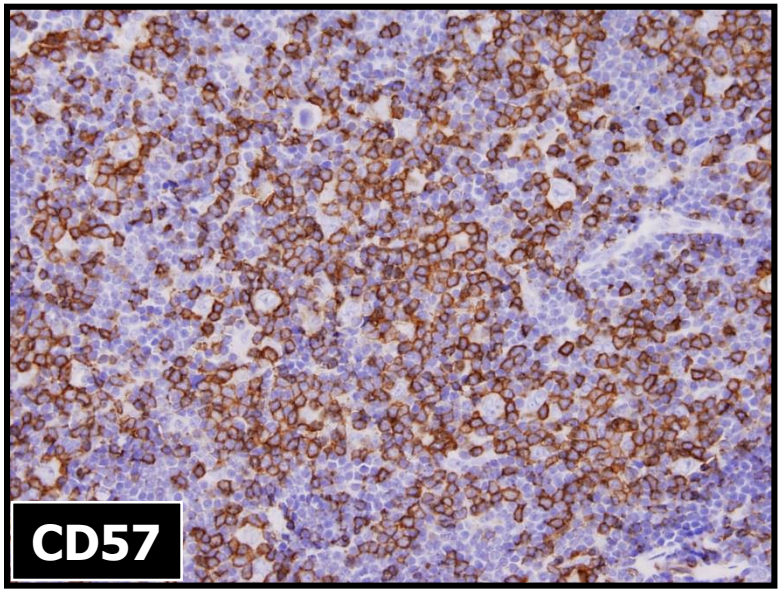
A Tumor Based in Follicles

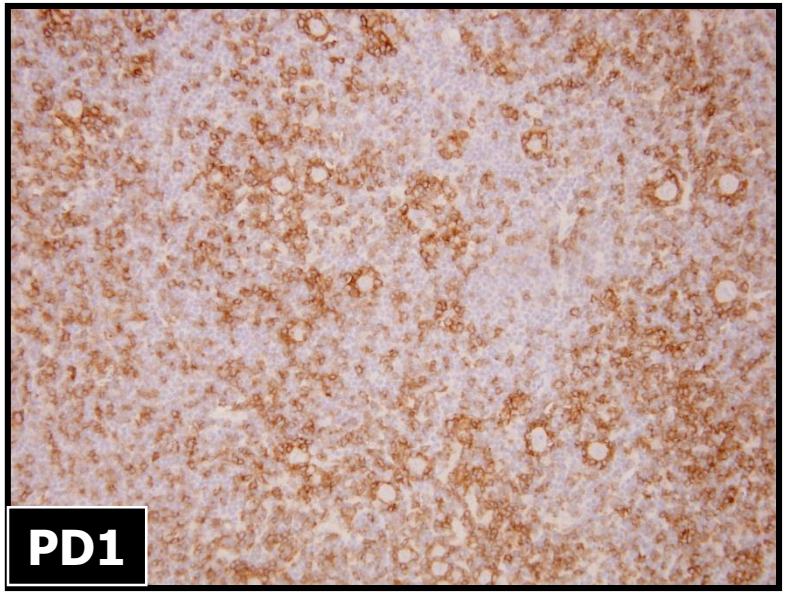


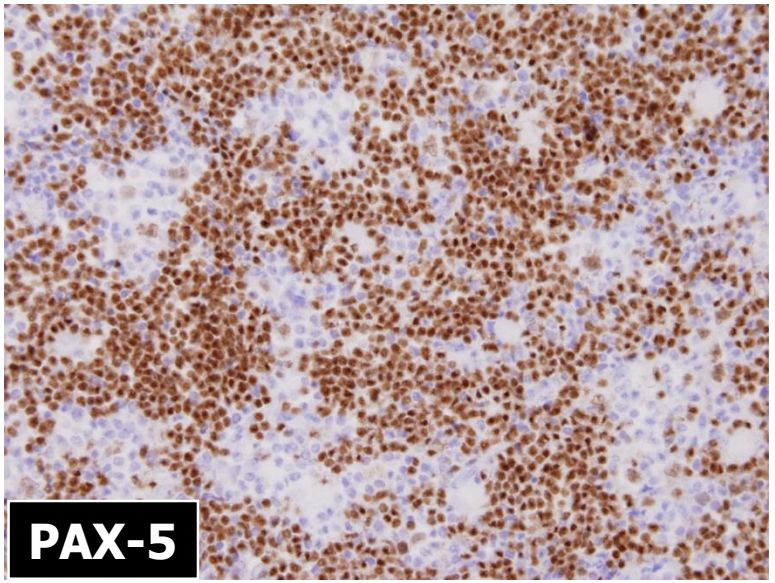
Nodular LPHL

Rosettes





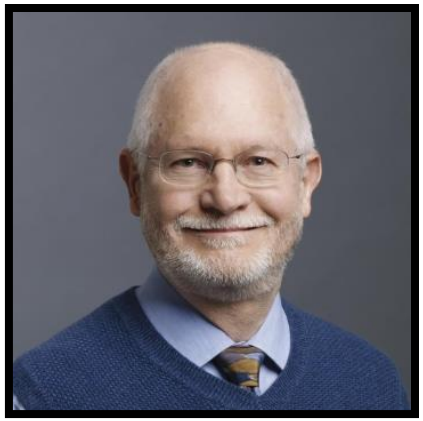




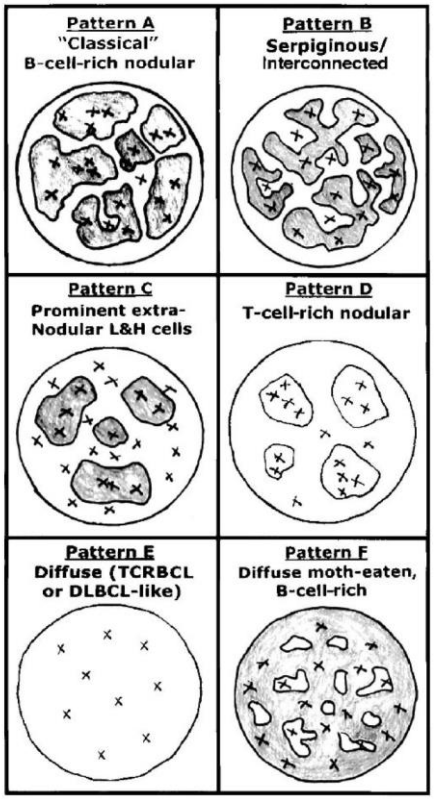
Characterization of Variant Patterns of Nodular Lymphocyte Predominant Hodgkin Lymphoma with Immunohistologic and Clinical Correlation

Zhen Fan, MD, Yasodha Natkunam, MD, PhD, Eric Bair, BS, MS, Robert Tibshirani, PhD, and Roger A. Warnke, MD

Y. Natkunam, MD

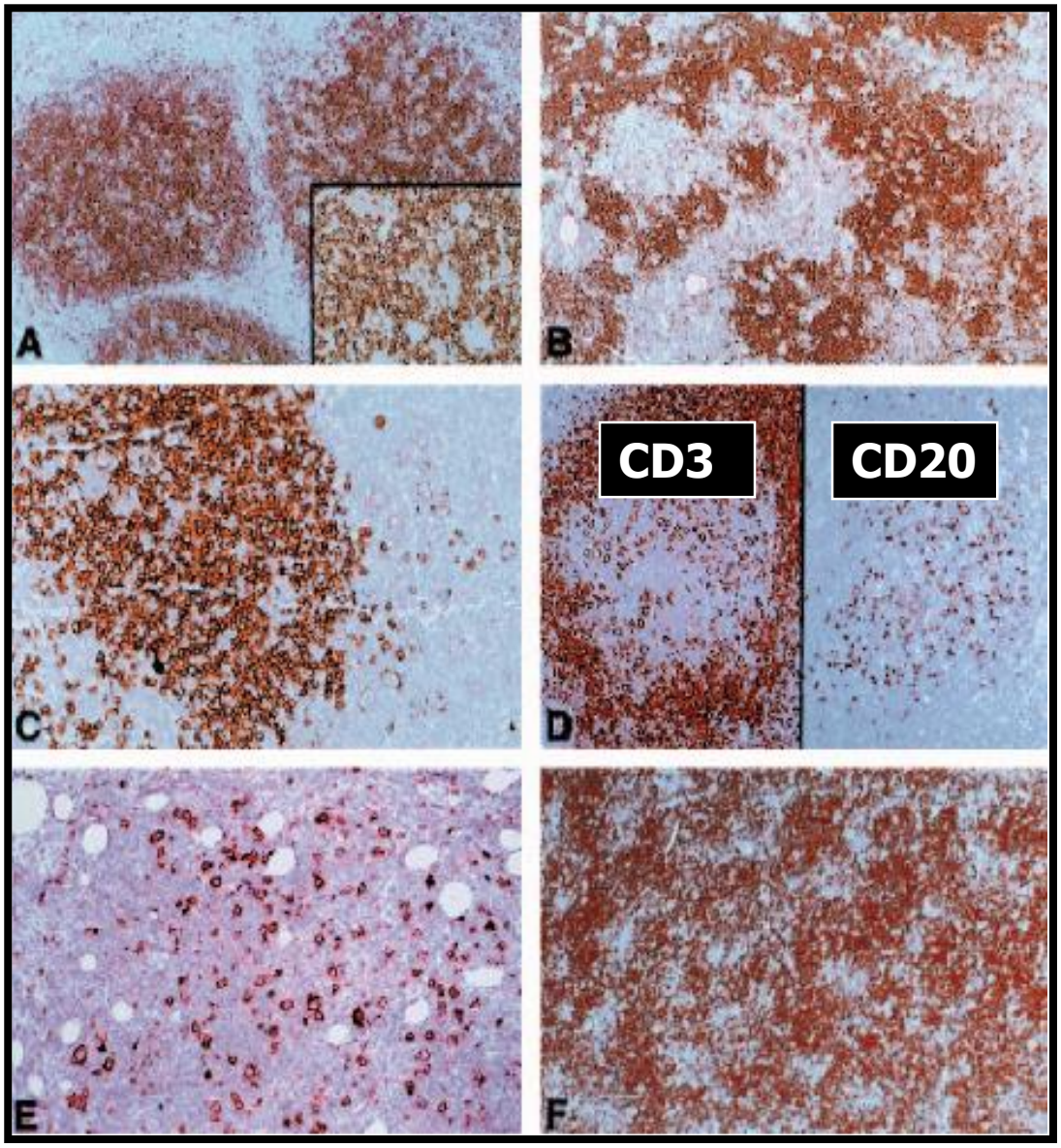


R. Warnke, MD



Am J Surg Pathol 27: 1346, 2003

NLPHL Patterns - CD20



A. B-cell rich nodular
B. Serpiginous nodular
C. Nodular with extranodular LP cells
D. T-cell rich nodular
E. Diffuse T-cell-rich (TCRBCL-like)
F. Diffuse moth-eaten

Am J Surg Pathol 27: 1350, 2003

Helpful Tidbits from the Fan et al paper

Small reactive follicles within or outside nodules in ~15%

Sclerosis in ~20% (can be prominent in ~5%)

Pattern C predicted subsequent development of pattern E

Pattern E correlated with recurrence

Characterization of Variant Patterns of Nodular Lymphocyte Predominant Hodgkin Lymphoma with Immunohistologic and Clinical Correlation

Zhen Fan, MD, Yasodha Natkunam, MD, PhD, Eric Bair, BS, MS, Robert Tibshirani, PhD, and Roger A. Warnke, MD

Am J Surg Pathol 27: 1350, 2003

Pattern is Prognostic in NLPHL

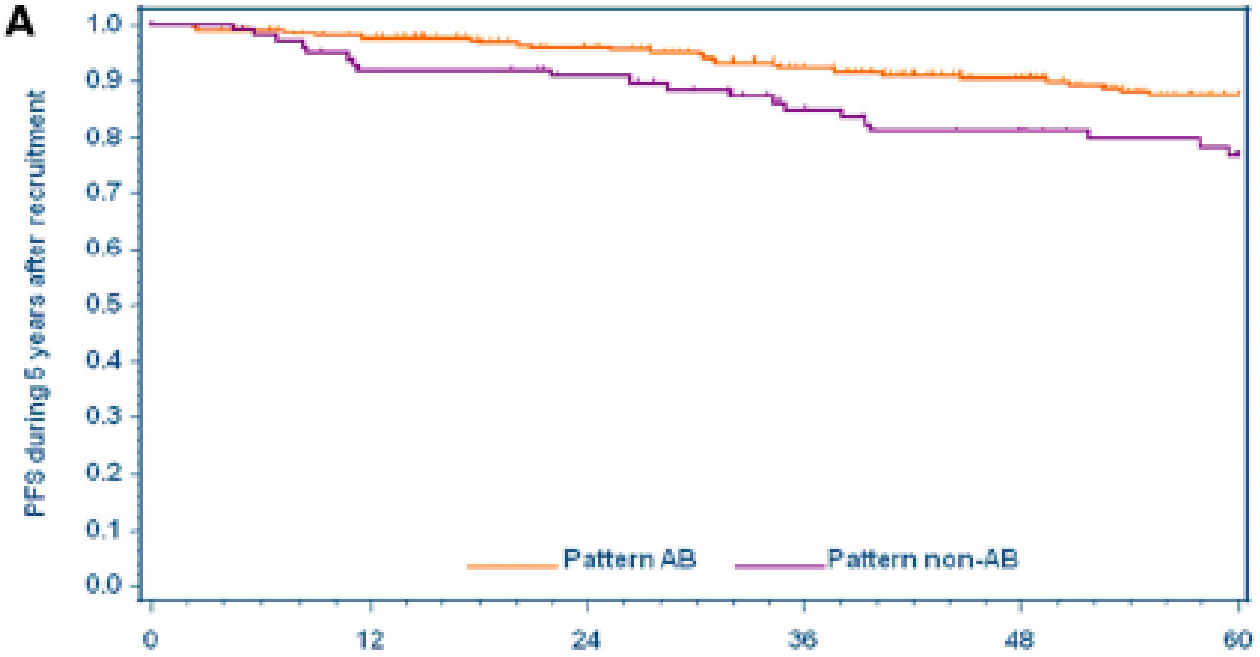
The prognostic impact of variant histology in nodular lymphocyte-predominant Hodgkin lymphoma: a report from the German Hodgkin Study Group (GHSG)

Sylvia Hartmann,[1] Dennis A. Eichenauer,[2,3] Annette Plütschow,[2,3] Anja Mottok,[4] Roshanak Bob,[5] Karoline Koch,[6] Heinz-Wolfram Bernd,[7] Sergio Cogliatti,[8] Michael Hummel,[9] Alfred C. Feller,[7] German Ott,[10] Peter Möller,[11] Andreas Rosenwald,[4] Harald Stein,[5] Martin-Leo Hansmann,[1] Andreas Engert,[2,3] and Wolfram Klapper[6]

[1]Dr. Senckenberg Institute of Pathology, Goethe University, Frankfurt am Main, Germany; [2]First Department of Internal Medicine and [3]German Hodgkin Study Group, University Hospital of Cologne, Germany; [4]Institute of Pathology, University of Würzburg and Comprehensive Cancer Center (CCC) Mainfranken, Germany; [5]Pathodiagnostic Berlin, Berlin Reference Center for Lymphoma and Hematopathology, Berlin, Germany; [6]Institute of Pathology, Haematopathology Section and Lymph Node Registry, Universitätsklinikum Schleswig-Holstein, Campus Kiel, Germany; [7]Institute of Pathology, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Germany; [8]Institute of Pathology, Kantonsspital St. Gallen, Switzerland; [9]Institute of Pathology, Charité University Hospital, Berlin, Germany; [10]Department of Clinical Pathology, Robert-Bosch-Krankenhaus and Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany; and [11]Institute of Pathology, University Hospital Ulm, Germany

Blood 122: 4246, 2013

Sylvia Hartmann, MD



bjh short report

Histopathological growth patterns in patients with advanced nodular lymphocyte-predominant Hodgkin lymphoma treated within the randomized HD18 study: a report from the German Hodgkin Study Group

Dennis A. Eichenauer,[1,2] Ina Bühnen,[1,2] Stefanie Kreissl,[1,2] Helen Goergen,[1,2] Michael Fuchs,[1,2] Bastian von Tresckow,[2,3] Andreas Rosenwald,[4] Wolfram Klapper,[5] Martin-Leo Hansmann,[6] Peter Möller,[7] Heinz-Wolfram Bernd,[8] Alfred C. Feller,[8] Andreas Engert,[1,2] Peter Borchmann[1,2] and Sylvia Hartmann[6]

Atypical growth patterns correlate with

Stage IV disease

Splenic involvement

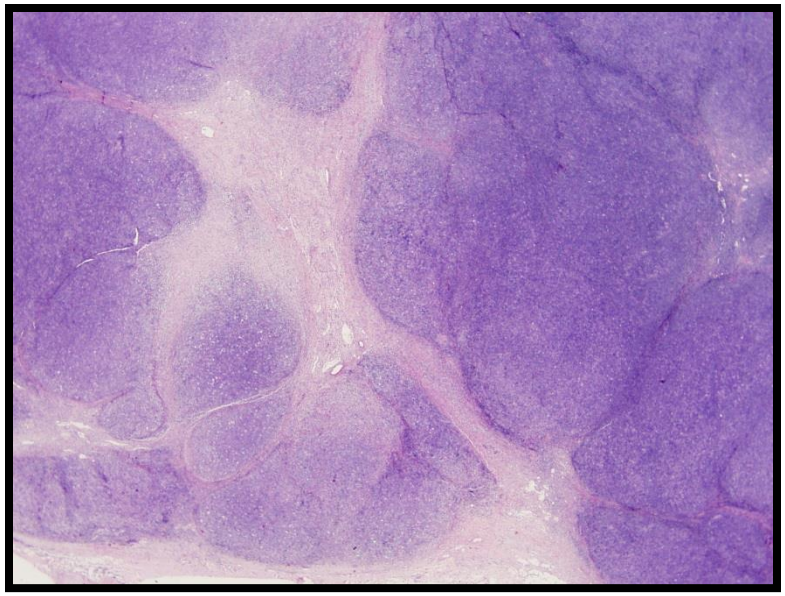
Persistent disease after 2 cycles of BEACOPP

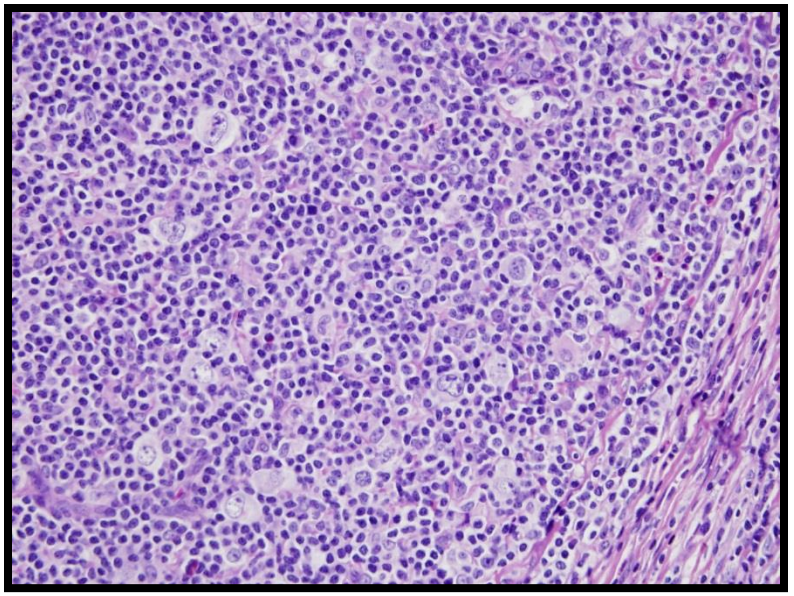
Atypical patterns do not have prognostic impact if treated with escalated BEACOPP

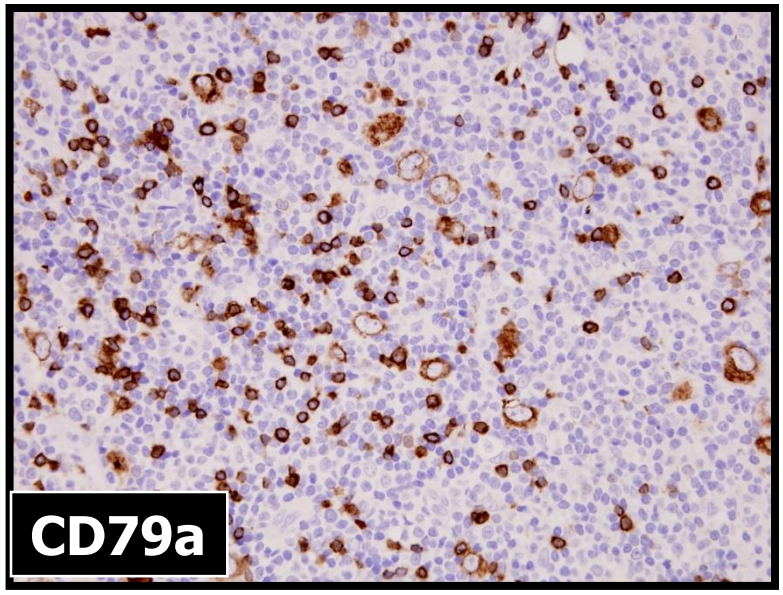
Br J Haematol 196: 99, 2021

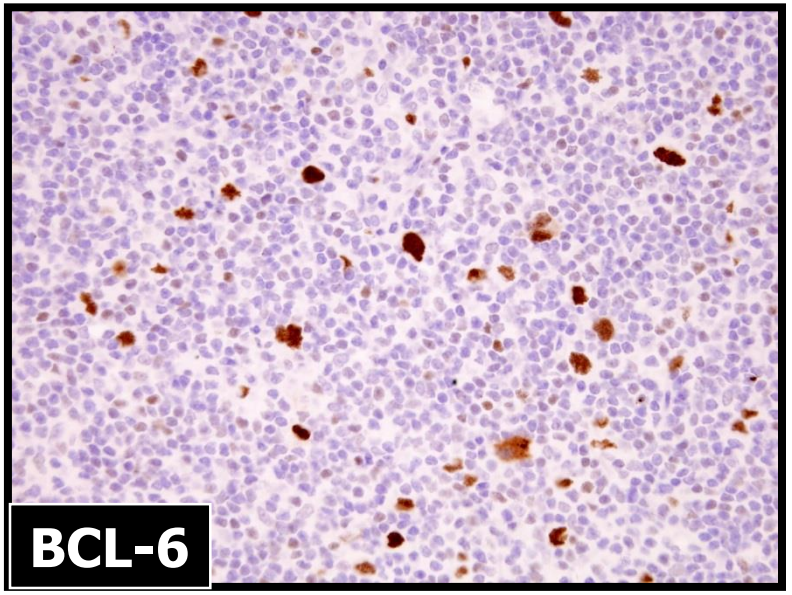
Nodular LPHL

Nodular Sclerosis-like Pattern









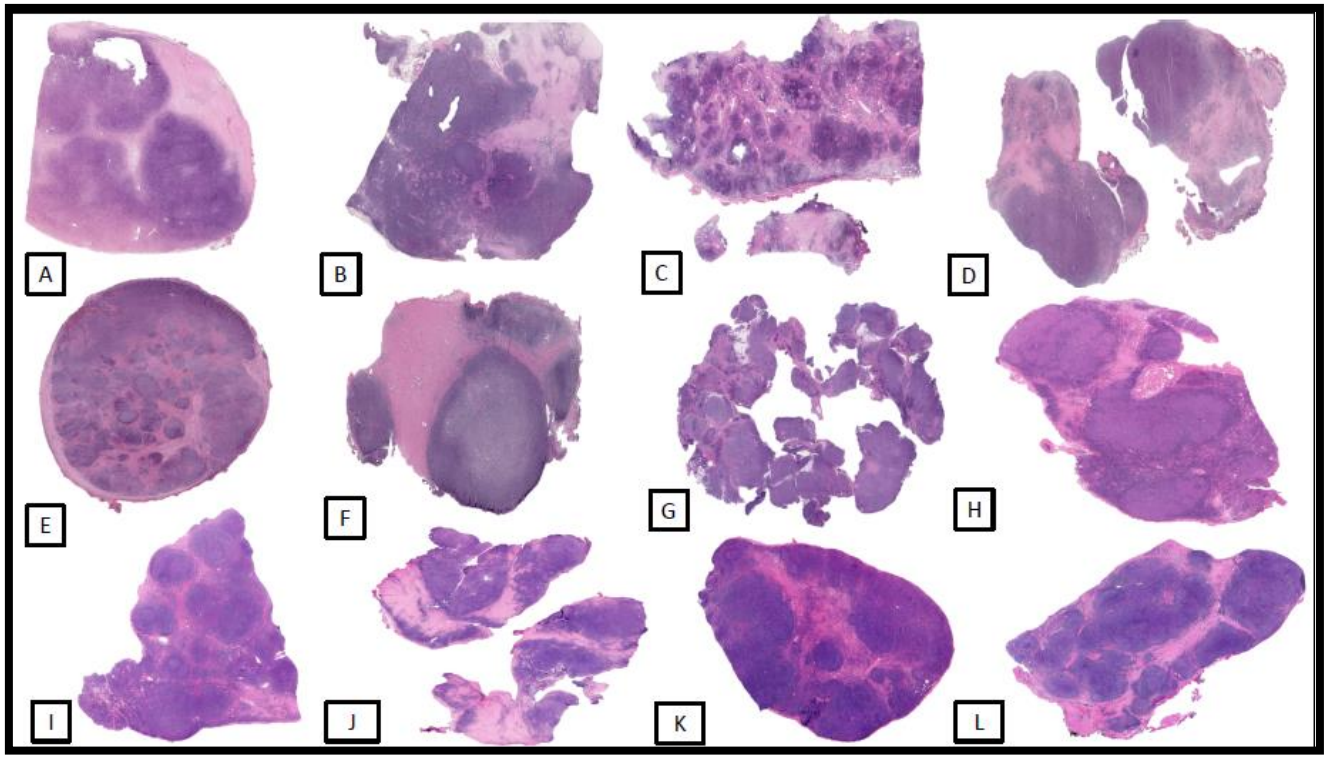
Nodular Lymphocyte Predominant Hodgkin Lymphoma with Nodular Sclerosis-Like Features:

An Underrecognized Variant Associated with Pattern D

Siba El Hussein[1,2†], Xiaoqiong Wang[2], Hong Fang[2], Fatima Zahra Jelloul[2], Wei Wang[2], Sanam Loghavi[2], Francisco Vega[2], Roberto N. Miranda[2], Tariq Muzzafar[2], John T. Manning, Jr[2], Joseph D. Khoury[2], W. Richard Burack[1], Andrew G. Evans[1], L. Jeffrey Medeiros[2]

Am J Surg Pathol (in press)

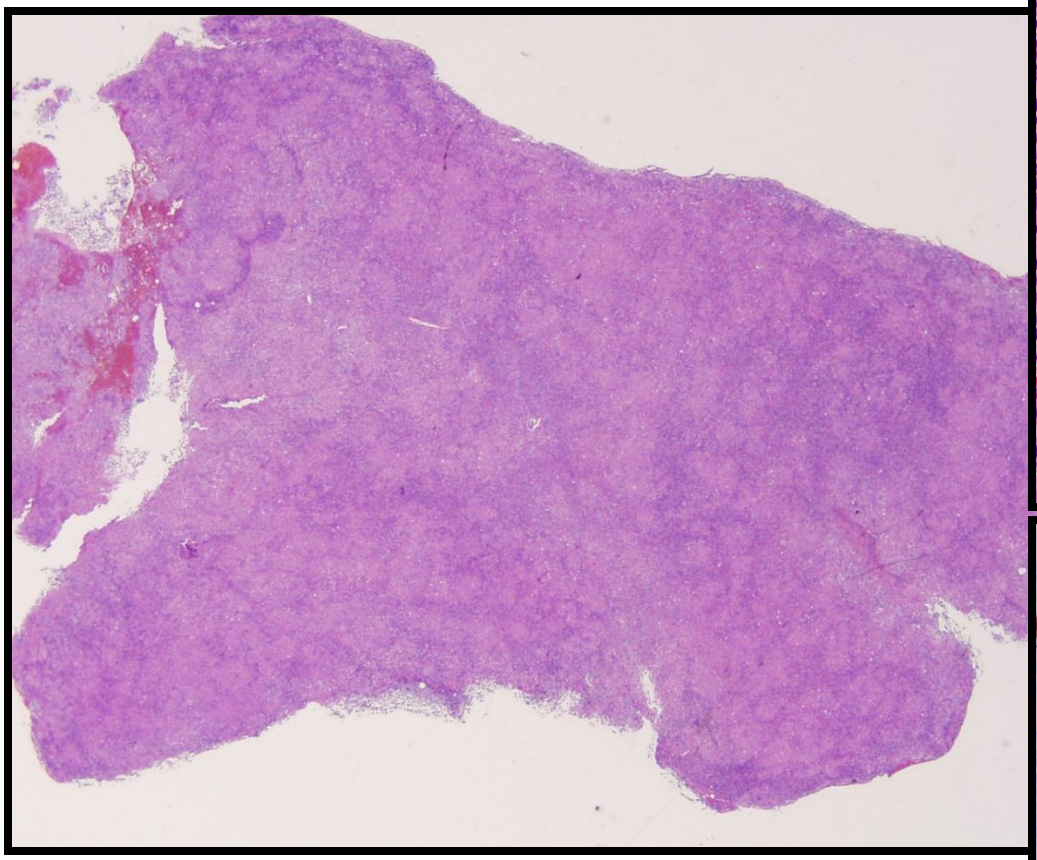
Siba El Hussein, MD

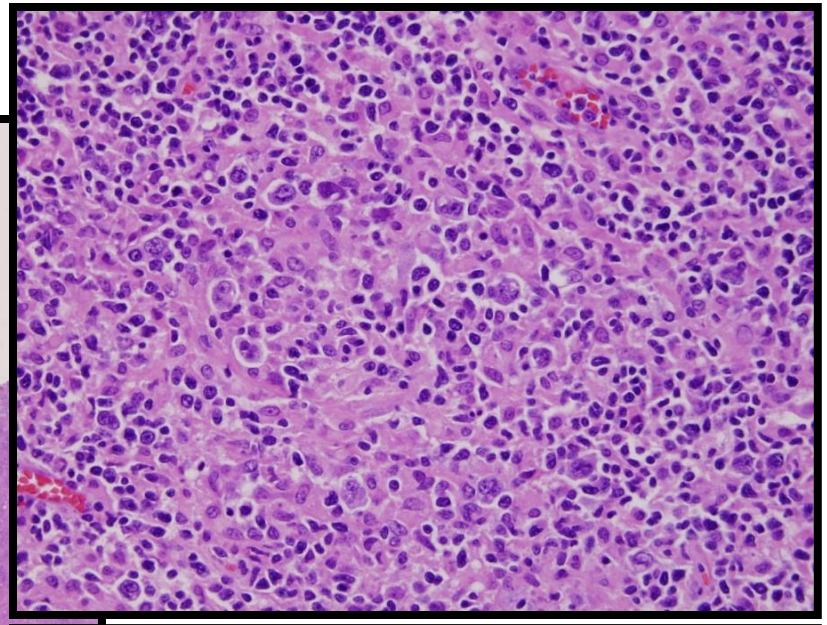


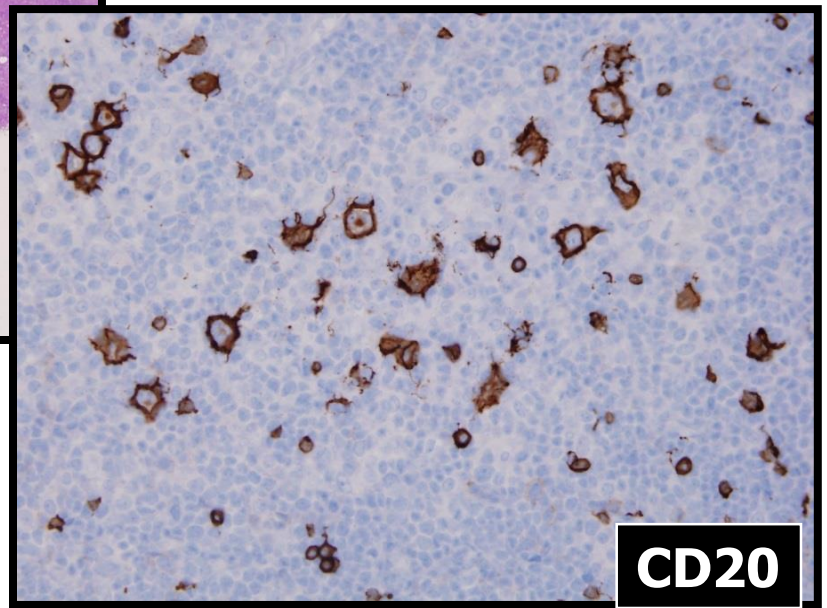
12 cases in study

10-15% of cases of NLPHL show prominent sclerosis
Often associated with patterns D and/or E
No prior therapy in this cohort

NLPHL Pattern E







NLPHL Pattern E

Nodular areas are required to recognize pattern E in NLPHL

Is pattern E = T-cell/histiocyte rich large B-cell lymphoma ?

No good criteria to distinguish pattern E from THRLBCL

I use clinical criteria in this differential

- **B symptoms**
- **Bone lesions, BM involvement**
- **Hepatosplenomegaly**
- **High serum LDH level**

WHO classification uses term THRLBCL-like transformation

If treatment is R-CHOP the distinction may not matter

How is HL Treated Today?

NLPHL

Low stage disease

Recent trends are to do as little as possible

CLINICAL TRIALS AND OBSERVATIONS

Active surveillance for nodular lymphocyte-predominant Hodgkin lymphoma

Sven Borchmann,[1,2] Erel Joffe,[1,3] Craig H. Moskowitz,[1] Andrew D. Zelenetz,[1] Ariela Noy,[1] Carol S. Portlock,[1] John F. Gerecitano,[1] Connie L. Batlevi,[1] Philip C. Caron,[1] Pamela Drullinsky,[1,4] Audrey Hamilton,[1] Paul A. Hamlin Jr,[1] Steven M. Horwitz,[1] Anita Kumar,[1] Matthew J. Matasar,[1] Alison J. Moskowitz,[1] Colette N. Owens,[1,5] M. Lia Palomba,[1] Anas Younes,[1] and David J. Straus[1]

[1]Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Center for Molecular Medicine, Else-Kröner Forschungskolleg Clonal Evolution in Cancer and Department I for Medicine, University of Cologne, Cologne, Germany; [3]Institute of Hematology, Davidoff Cancer Center, Beilinson Hospital, Rabin Medical Center, Petah Tikva, Israel; and [4]Breast Medicine Service and [5]Genitourinary Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Blood 133:2121, 2019

High stage disease

R-CHOP may be better than ABVD

Encouraging activity for R-CHOP in advanced stage nodular lymphocyte–predominant Hodgkin lymphoma

Michelle A. Fanale,[1,*] Chan Yoon Cheah,[1-4,*] Amy Rich,[5] L. Jeffrey Medeiros,[5] Chao-Ming Lai,[1] Yasuhiro Oki,[1] Jorge E. Romaguera,[1] Luis E. Fayad,[1] F. B. Hagemeister,[1] Felipe Samaniego,[1] Maria A. Rodriguez,[1] Sattva S. Neelapu,[1] Hun J. Lee,[1] Loretta Nastoupil,[1] Nathan H. Fowler,[1] Francesco Turturro,[1] Jason R. Westin,[1] Michael L. Wang,[1] Peter McLaughlin,[6] Chelsea C. Pinnix,[7] Sarah A. Milgrom,[7] Bouthaina Dabaja,[7] Sandra B. Horowitz,[8] and Anas Younes[9]

[1]Department of Lymphoma and Myeloma, University of Texas MD Anderson Cancer Center, Houston, TX; [2]Department of Haematology, Sir Charles Gairdner Hospital, Nedlands, WA, Australia; [3]Department of Haematology, Pathwest Laboratory Medicine, Nedlands, WA, Australia; [4]Medical School, University of Western Australia, Crawley, WA, Australia; [5]Department of Hematopathology, [6]Physicians Network, [7]Department of Radiation Oncology, and [8]Department of Pharmacy Clinical Programs, University of Texas MD Anderson Cancer Center, Houston, TX; and [9]Lymphoma Department, Memorial Sloan Kettering Cancer Center, New York, NY

Blood 130: 472, 2017

Annals of Diagnostic Pathology 39 (2019) 105–110

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

journal homepage: www.elsevier.com/locate/anndiagpath

Original Contribution

American Registry of Pathology Expert Opinions: Immunohistochemical evaluation of classic Hodgkin lymphoma

Dennis P. O'Malley[a,*], Ahmet Dogan[b], Yuri Fedoriw[c], L. Jeffrey Medeiros[d], Chi Young Ok[d], Mohamed E. Salama[e]

Dennis O'Malley, MD

Antibodies useful to establish diagnosis of classic HL

CD3, CD15, CD20, CD30, PAX-5

Antibodies useful to distinguish NLPHL from classic HL

OCT-2, CD21 or CD23, PD-1, EBER

Take Home Points

NLPHL can occur at any age and most LN groups as well as liver, spleen, and BM

The entity has evolved and has a greater morphologic and immunophenotypic spectrum than once thought

Knowledge of the 6 patterns in NLPHL is helpful for diagnosis and may be requested by clinicians

OCT2 is a very helpful marker, particularly in needle biopsy specimens