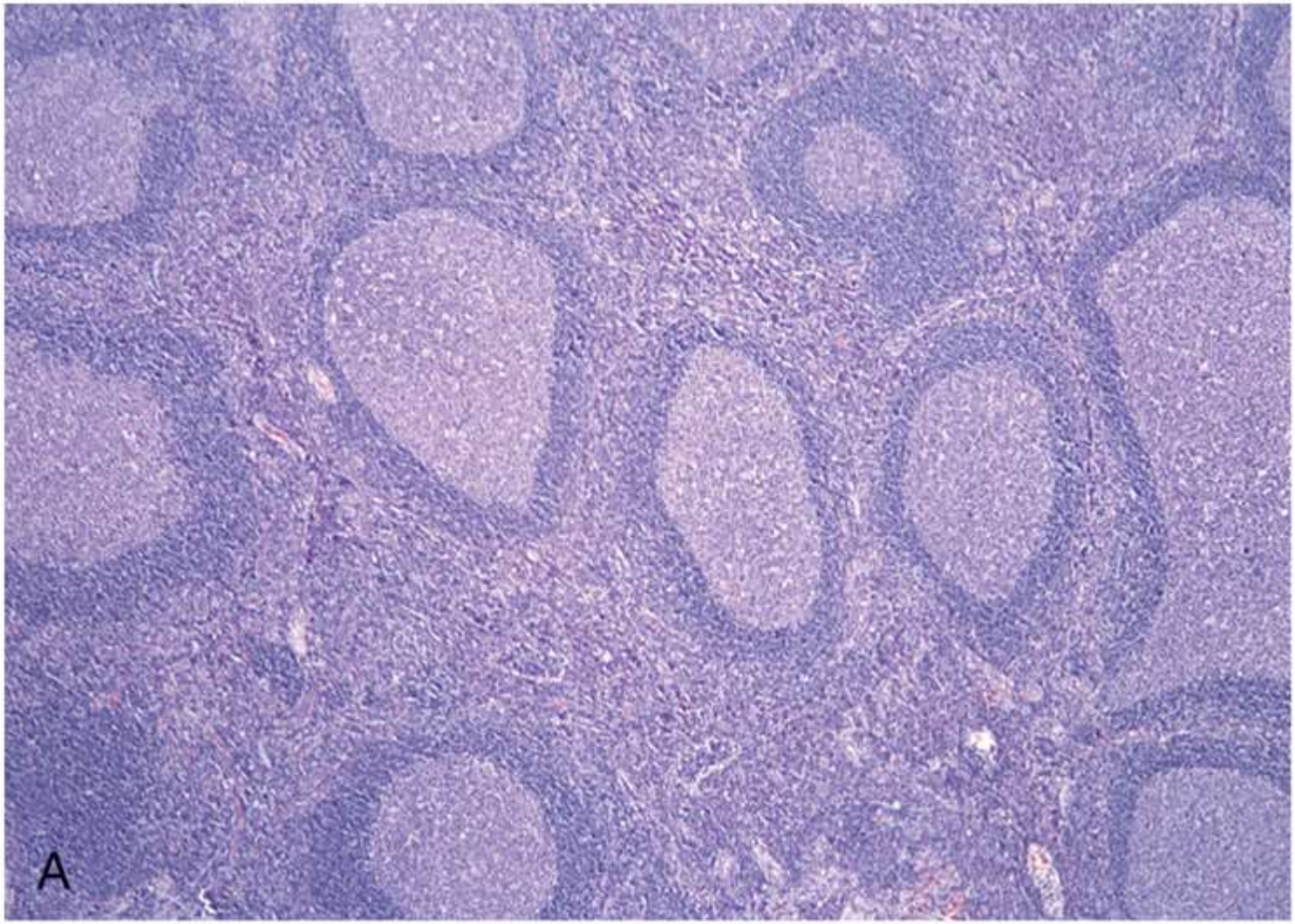
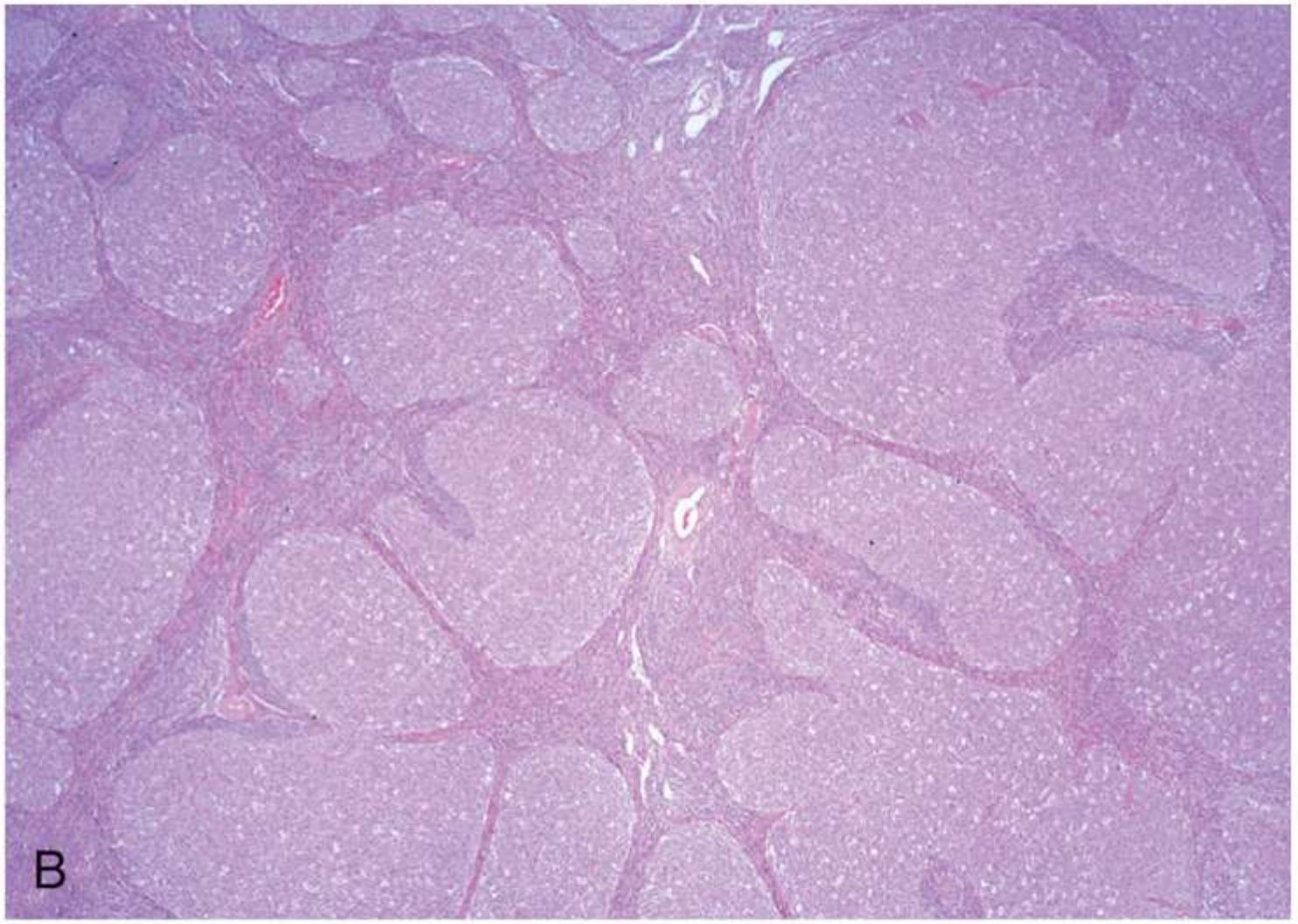
FOLLICULARITY

in

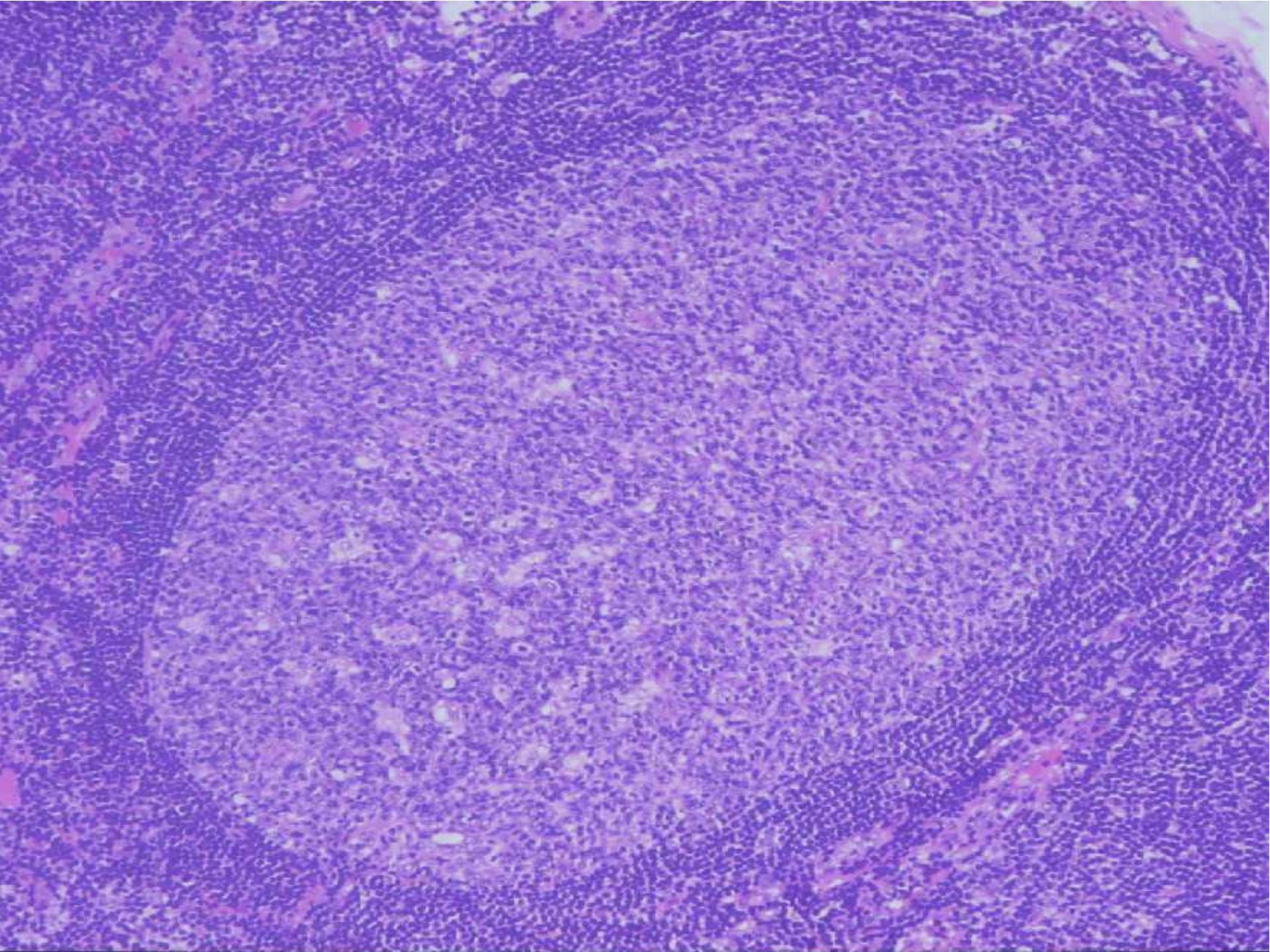
LYMPHOMA

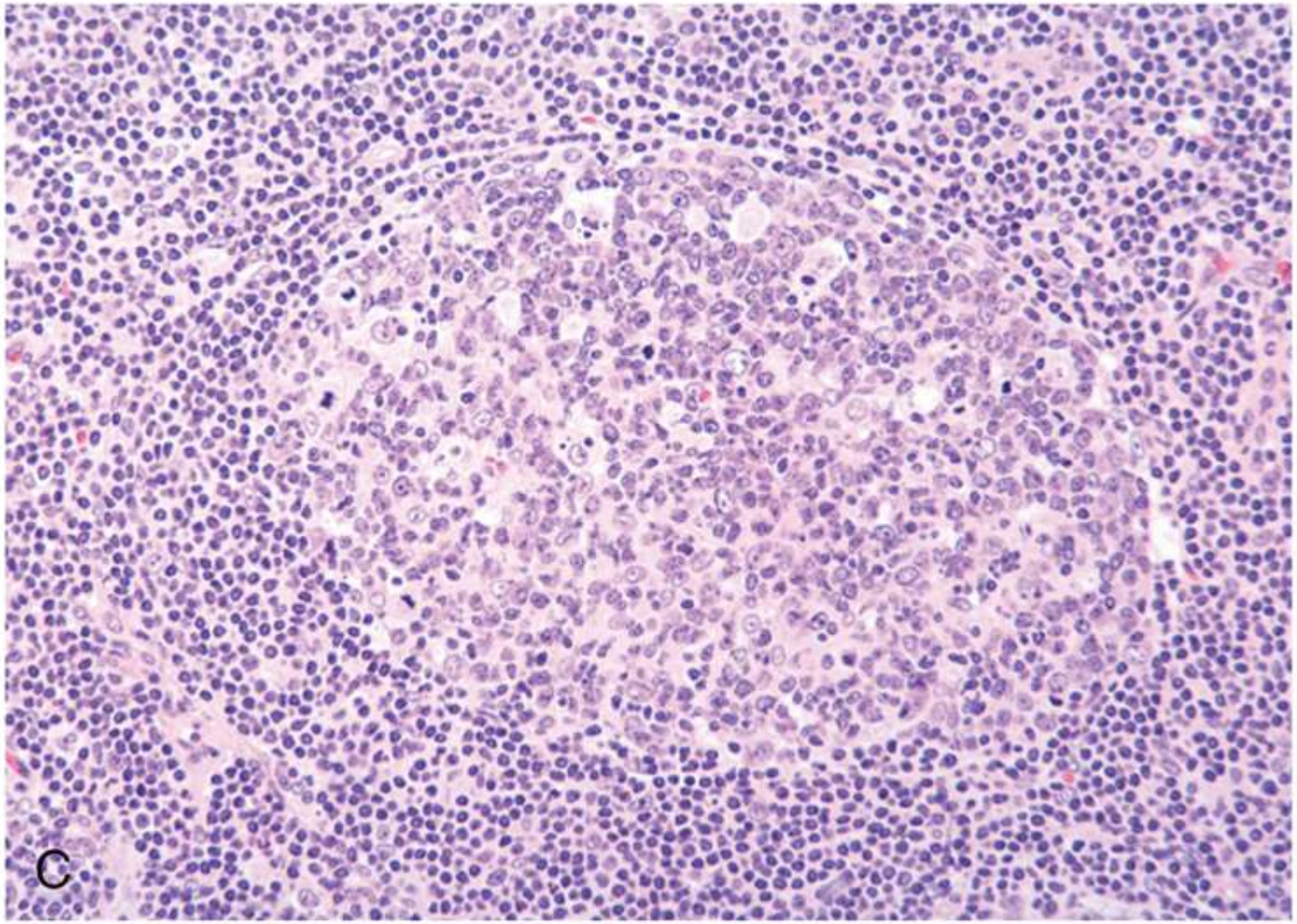


Reactive Follicular Hyperplasia

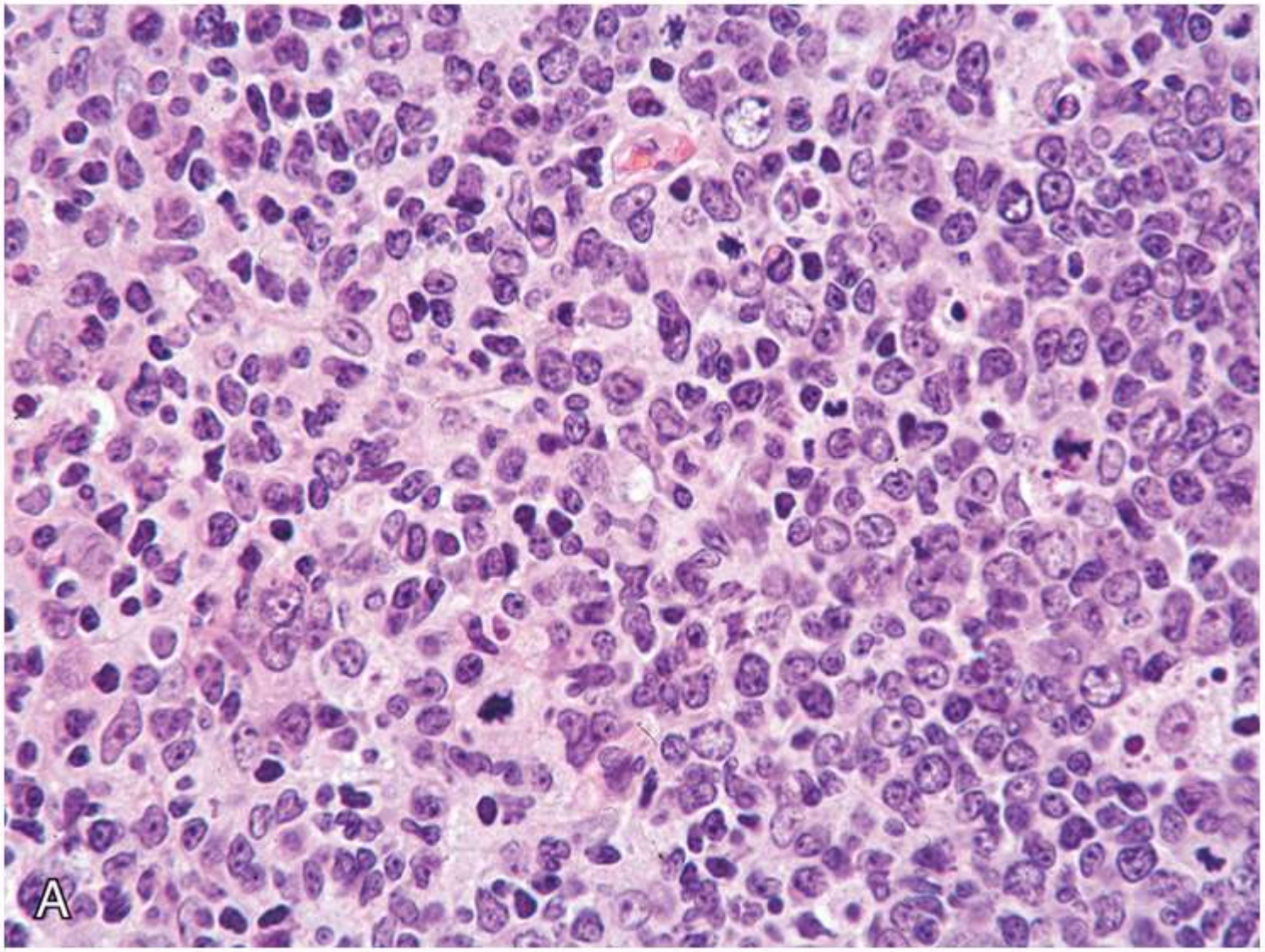


Follicular Hyperplasia – irregular follicles



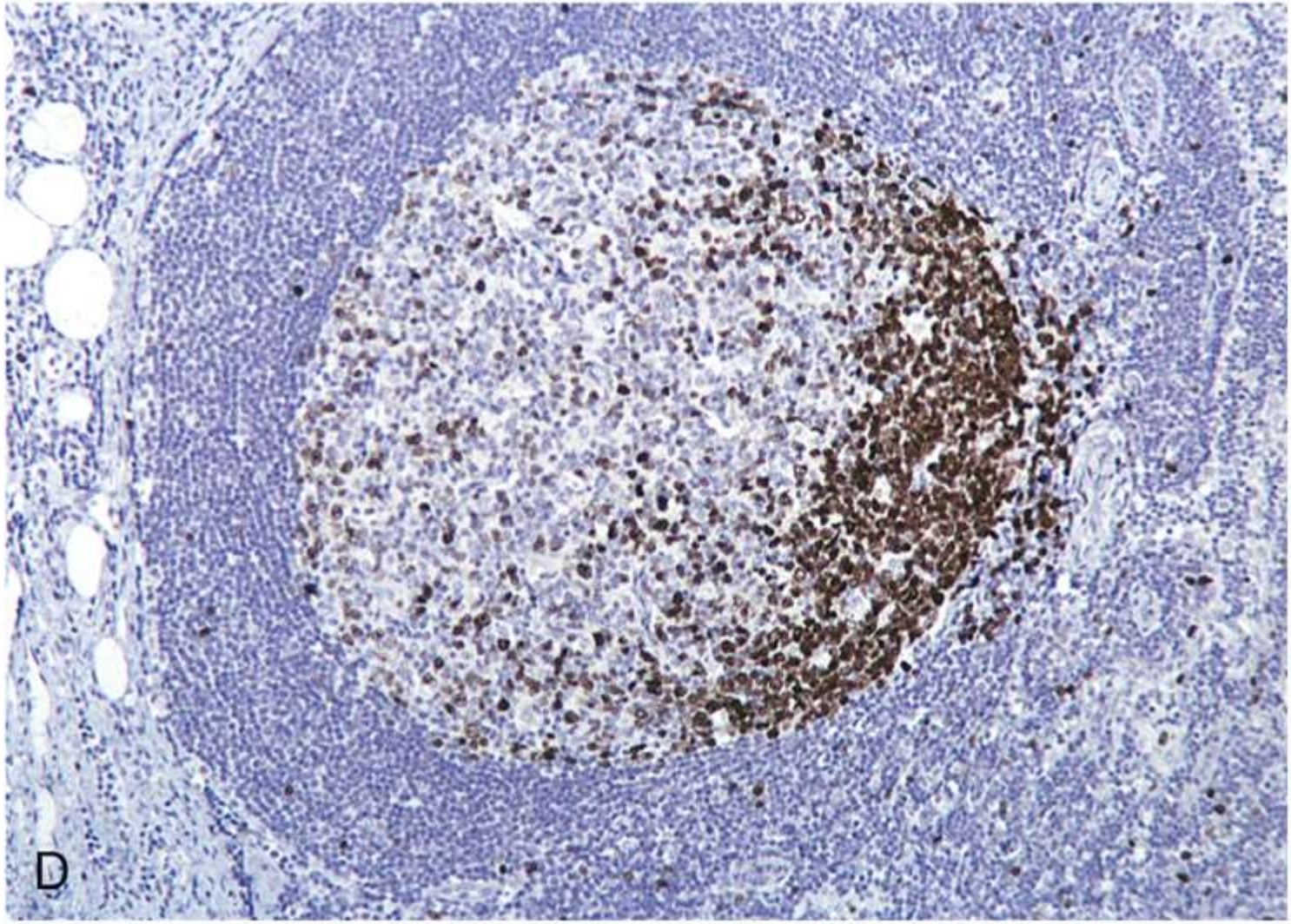


Follicular Hyperplasia – dark and light zones

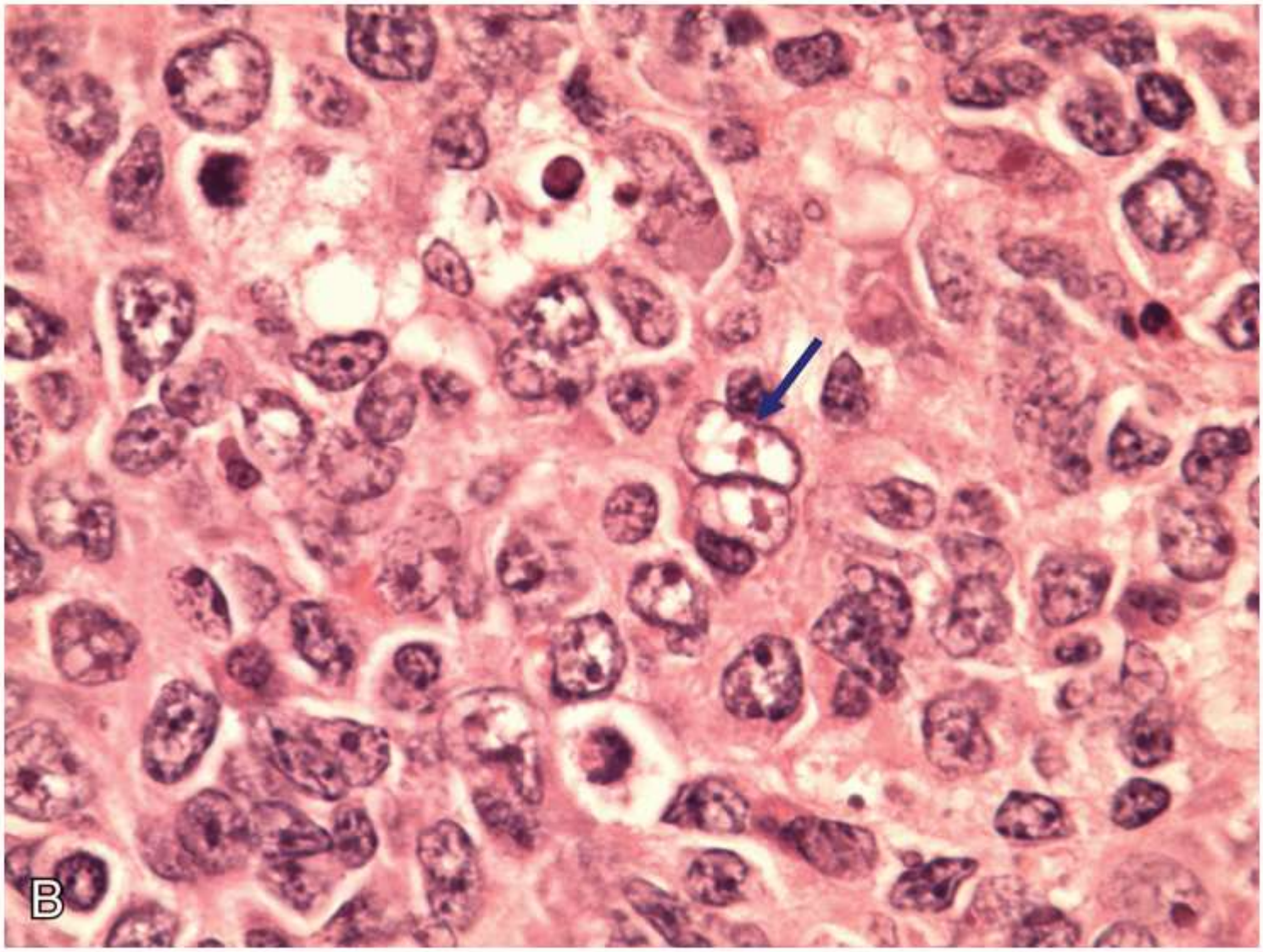


Light Zone

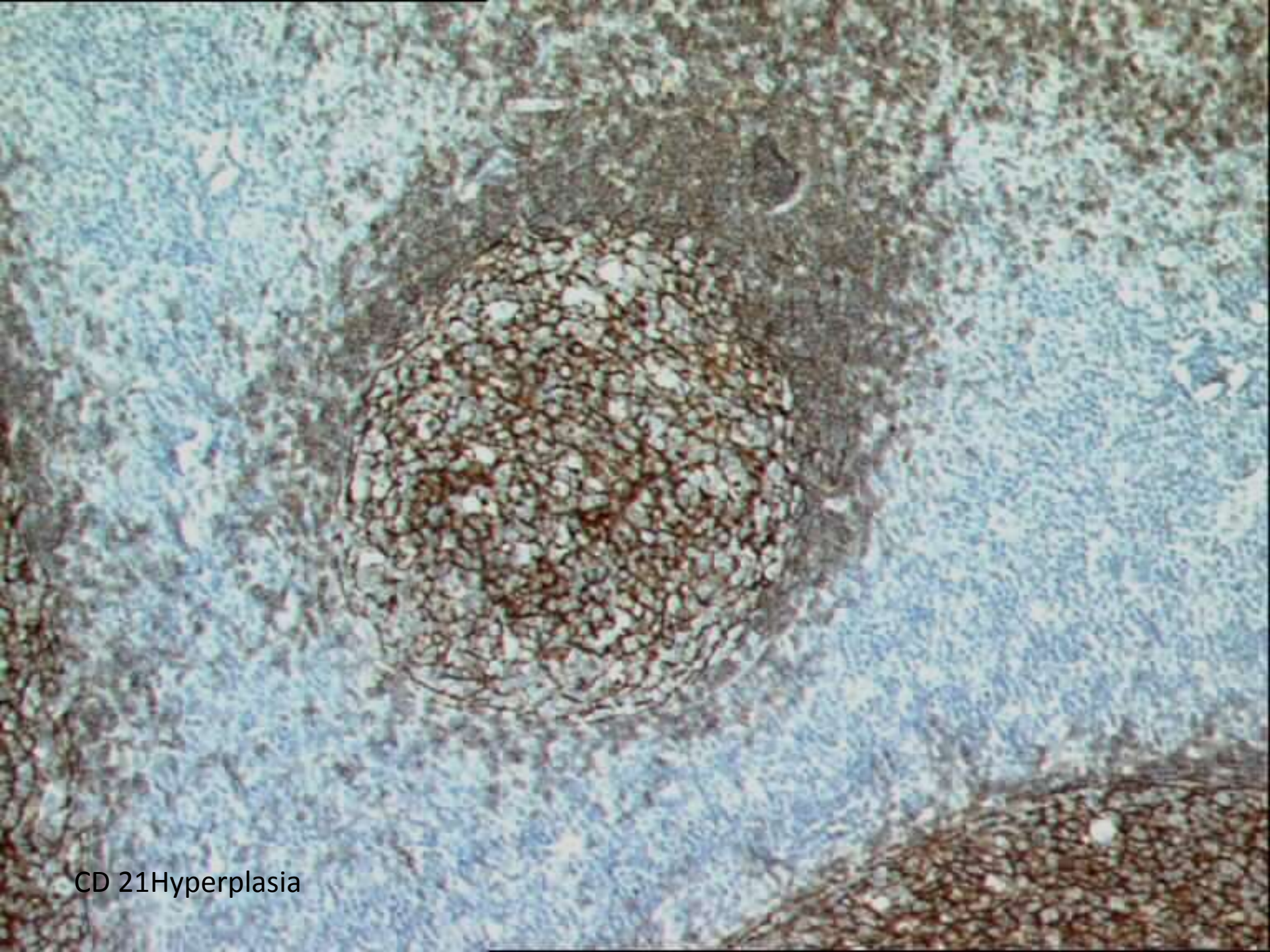
Dark Zone

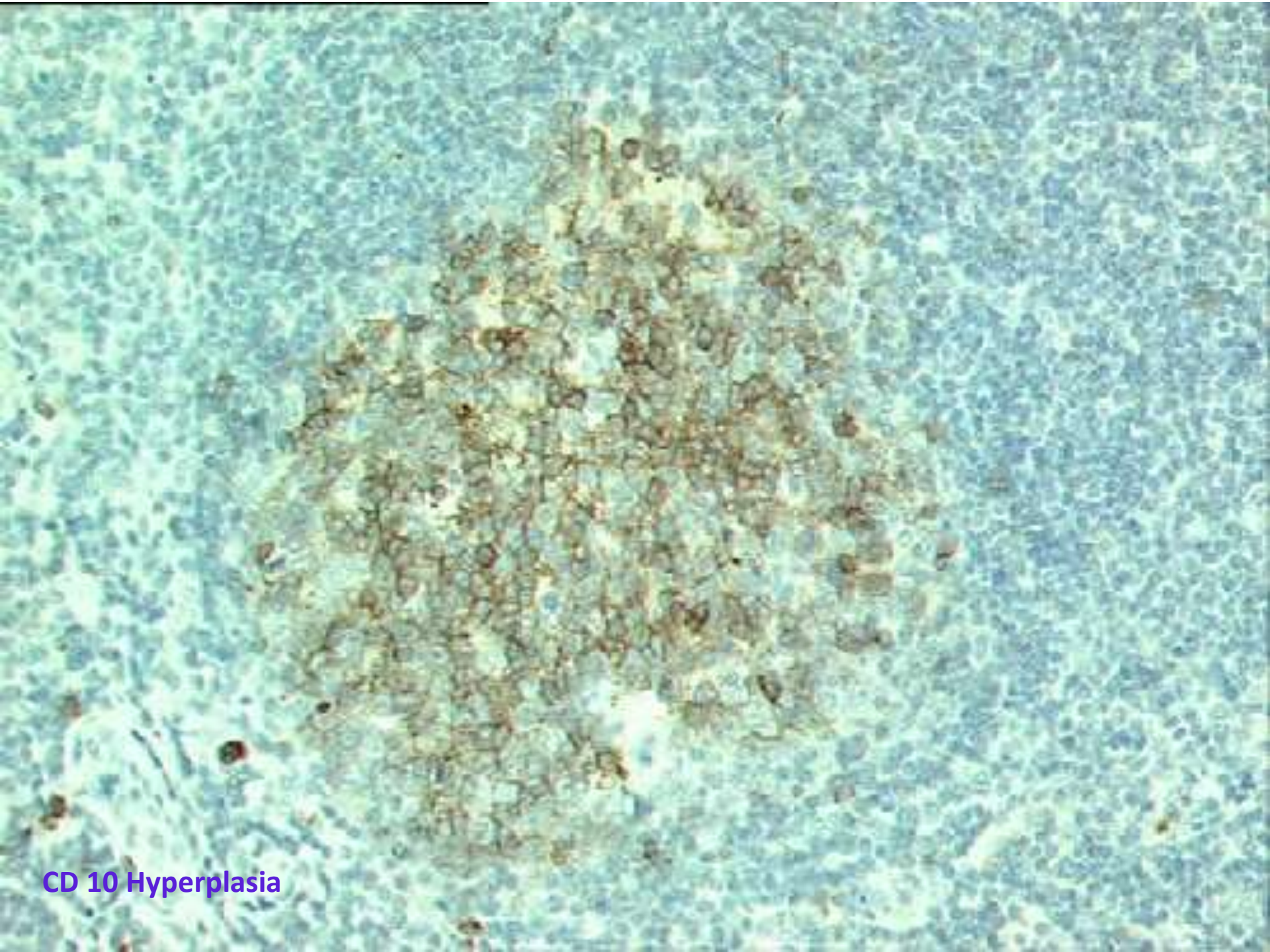


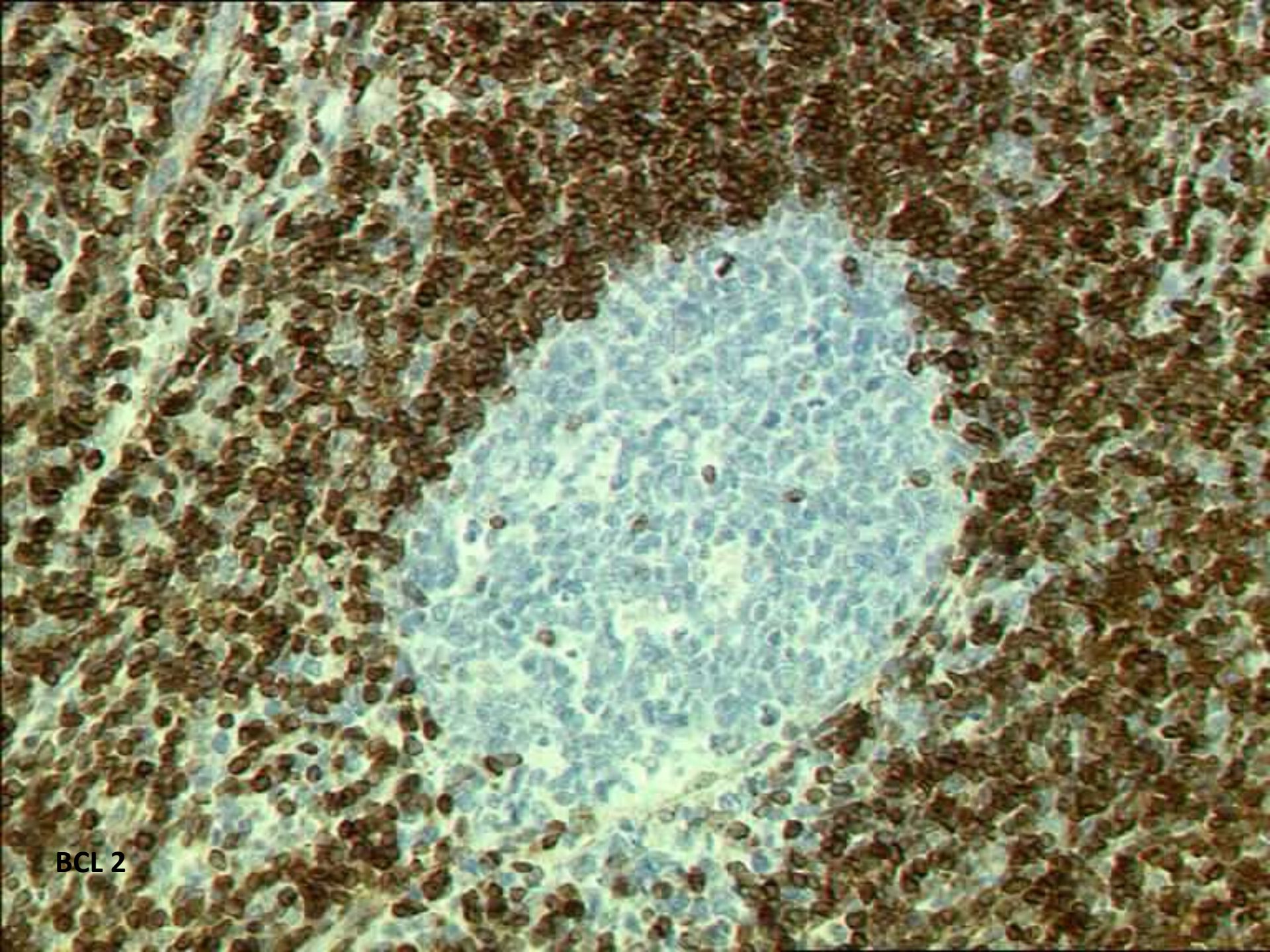
Follicular hyperplasia – MIB1

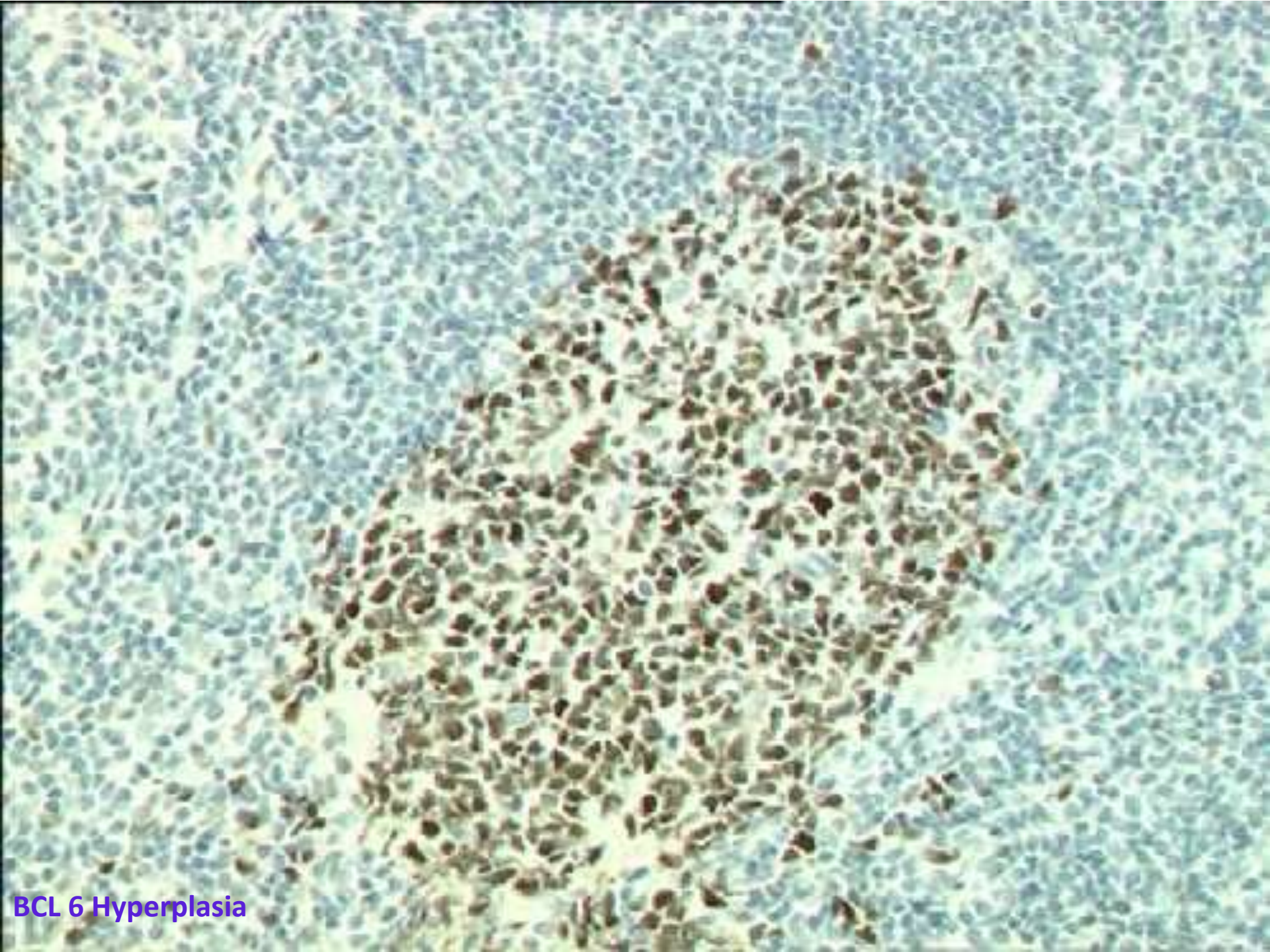


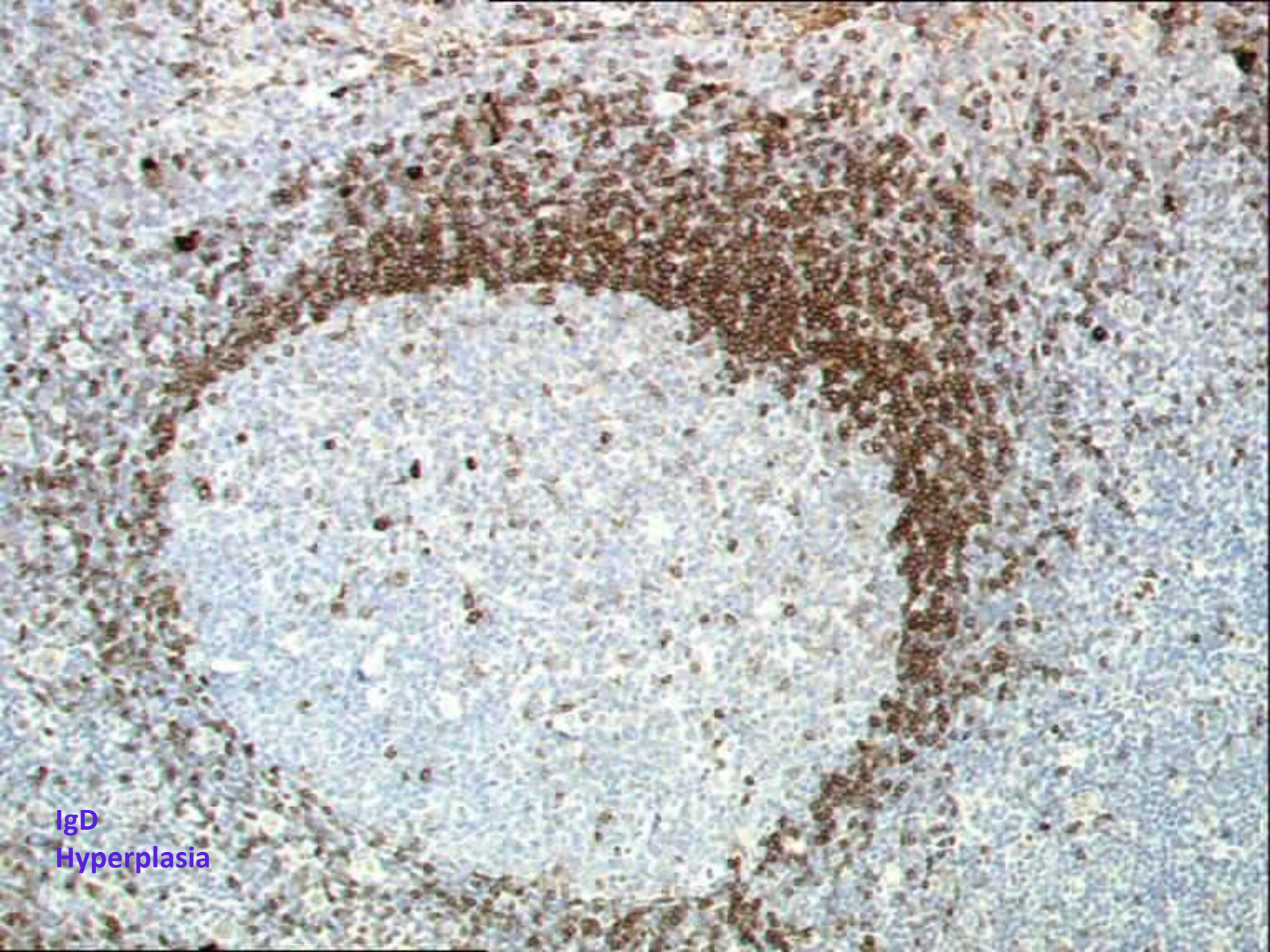
Follicular dendritic cell


CD 21Hyperplasia


CD 10 Hyperplasia


BCL 2


BCL 6 Hyperplasia


IgD
Hyperplasia

Follicular Lymphoma

Follicular Lymphoma

A lymphoma of germinal centre B cells (centrocytes and centroblasts) with typically at least a partially follicular pattern

Frequency
40% of adult lymphomas in the United States; 20% worldwide

Age Median, 55-59 years
Sex Male = female

Clinical features at presentation
Generalized lymphadenopathy, frequent splenomegaly, often asymptomatic; bone marrow positive in 40%; rare stage I, extranodal or paediatric

Morphology
1. Pattern: follicular with or without diffuse areas, or interfollicular involvement, extracapsular extension, sclerosis, vascular invasion
2. Cytology: centroblasts and centrocytes, follicular dendritic cells
3. Grade 1-2, 3A, 3B

Usual Immunophenotype

Ig+, CD19+, CD20+, CD22+, CD79a+, PAX5+, CD10+, BCL2+, BCL6+, CD43−, CD5−;
nodular meshworks of CD21+, CD23+ follicular dendritic cells

Genetic features

Immunoglobulin genes rearranged, mutated, intraclonal heterogeneity; t(14;18)(q23;q32) and IGH/*BCL2* rearranged

Postulated normal counterpart

Germinal-centre B cells

Clinical course

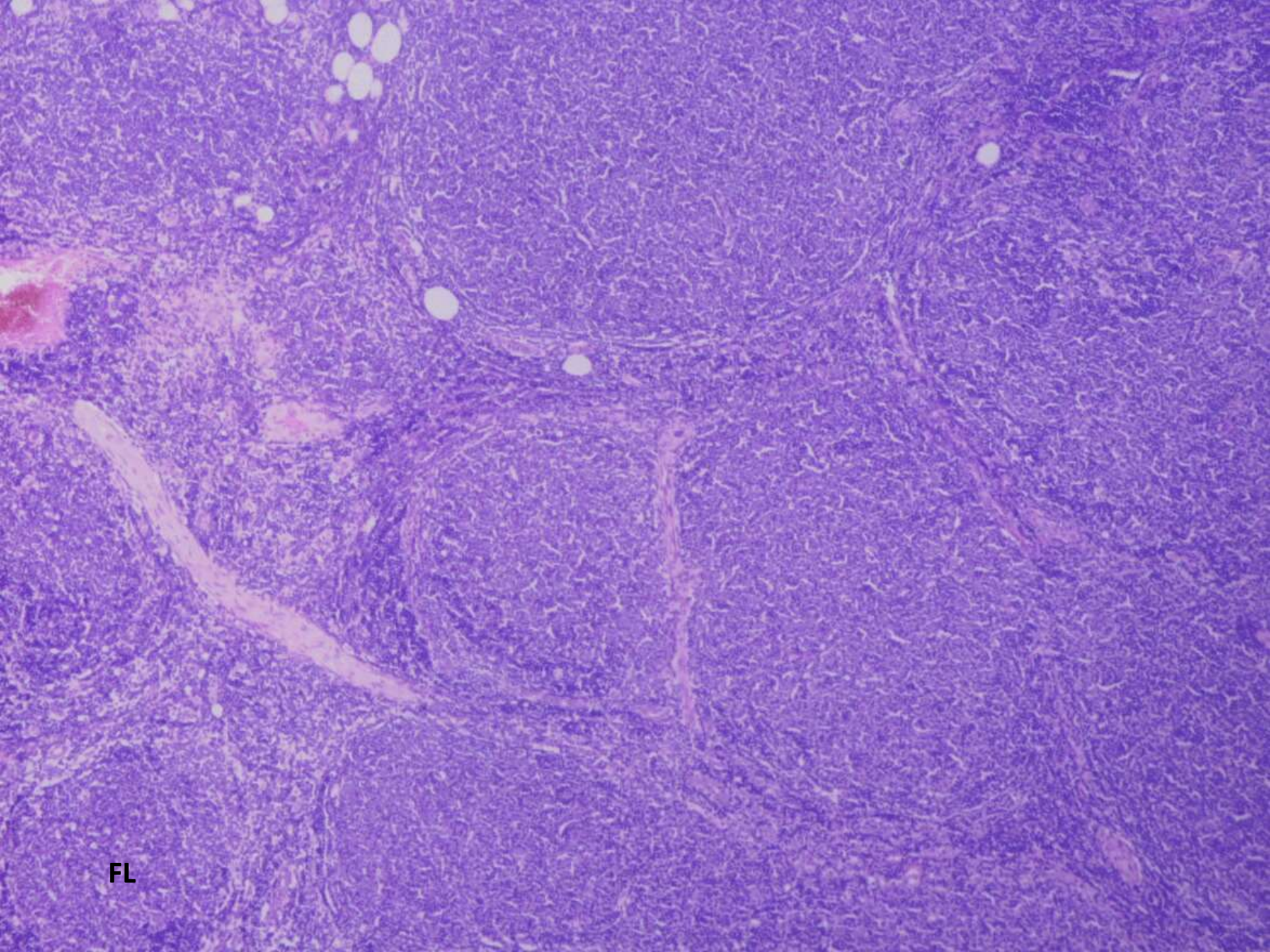
Indolent, incurable: median survival 8-10 years; prognosis based on histologic grade (grade 1 to 2 indolent, grade 3 aggressive), Follicular Lymphoma International Prognostic Index

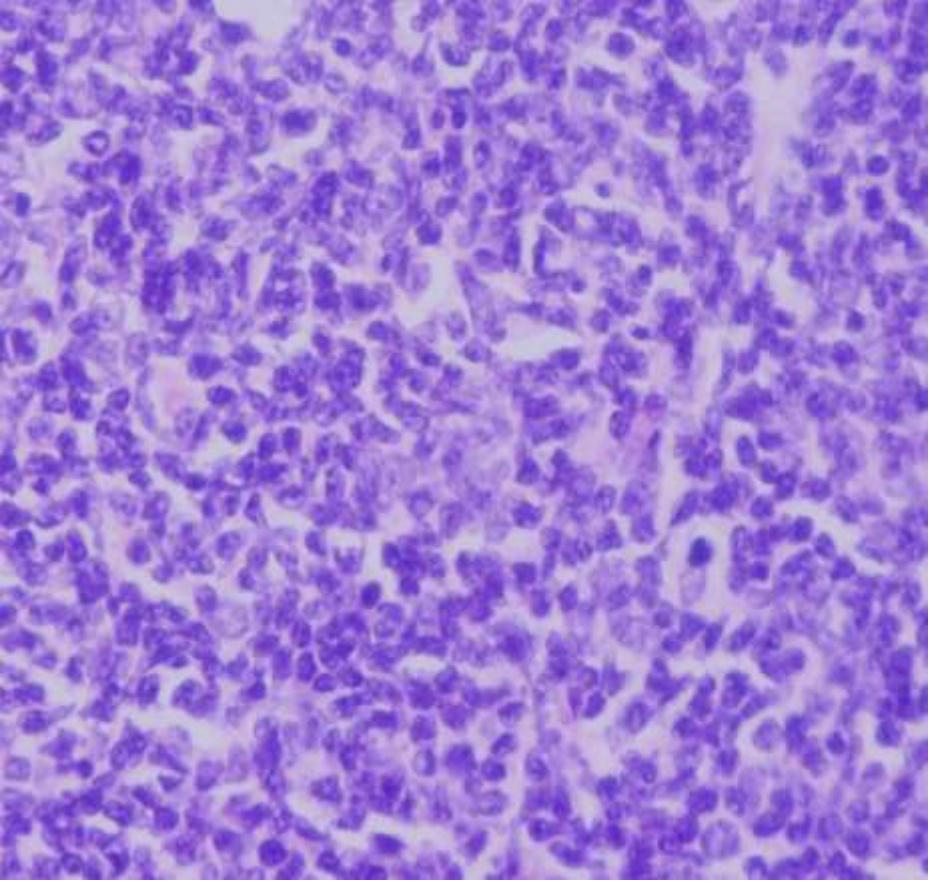
Treatment

Symptomatic for grade 1 to 2, aggressive for grade 3

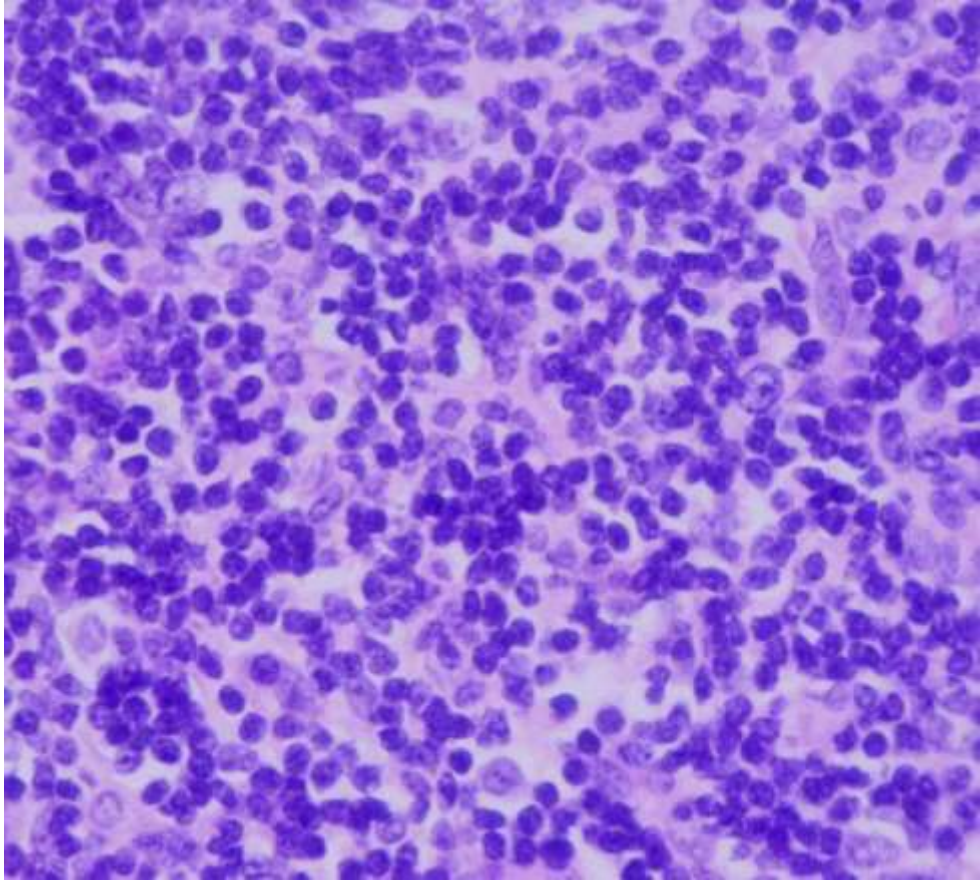
Grading of Follicular Lymphoma

Grade	Definition
Grade 1 to 2 (low grade)*	0-15 centroblasts/hpf†
Grade 1	0-5 centroblasts/hpf†
Grade 2	6-15 centroblasts/hpf†
Grade 3	>15 centroblasts/hpf†
Grade 3A	Centrocytes present
Grade 3B	Solid sheets of centroblasts
Reporting of Pattern	Proportion Follicular (%)
Follicular	>75
Follicular and diffuse	25-75‡
Focally follicular	<25‡
Diffuse	0§
Diffuse areas containing >15 centroblasts/hpf are reported as diffuse large B-cell lymphoma‡ with follicular lymphoma (grade 1 to 2, 3A, or 3B)	

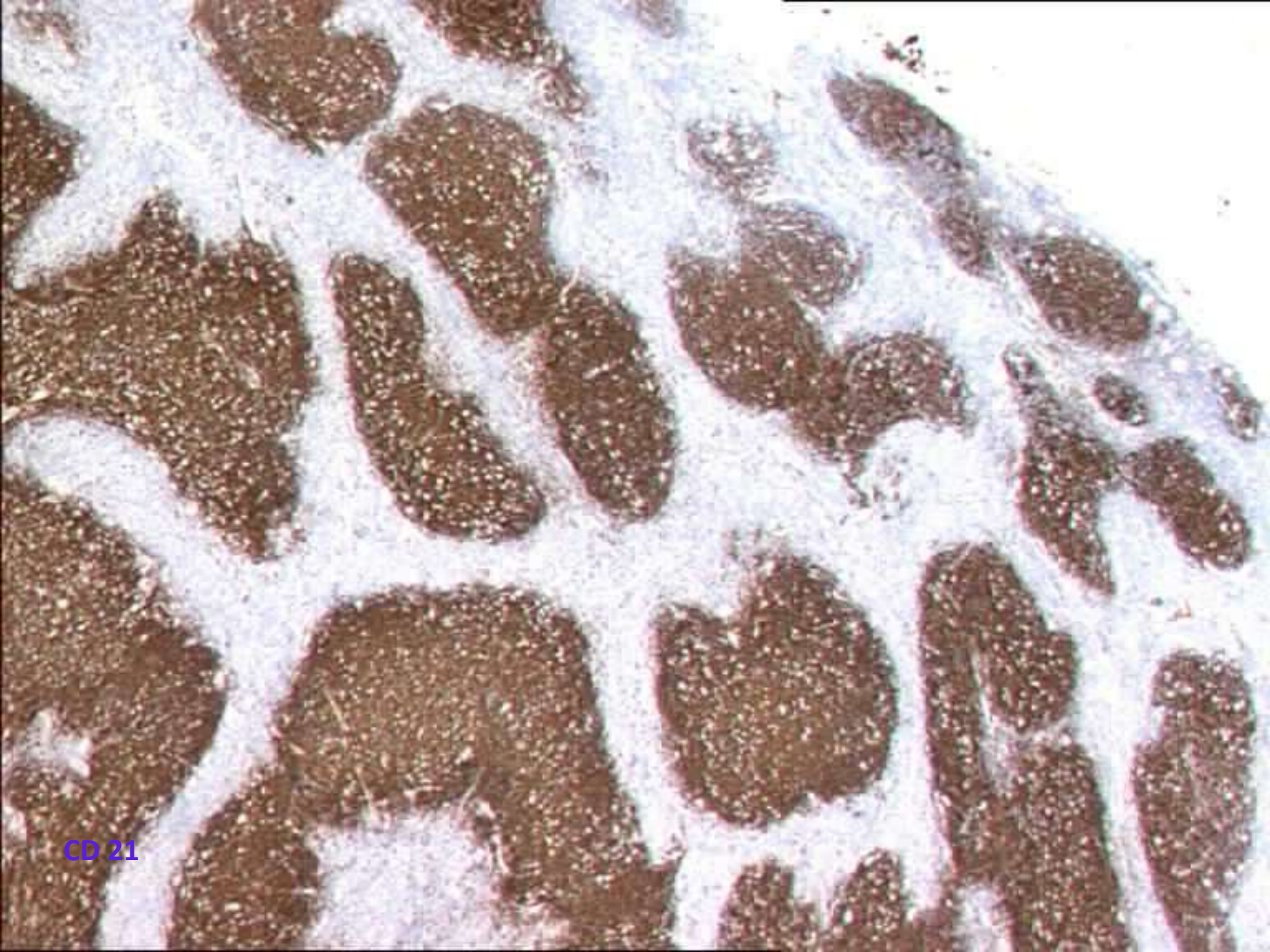

FL

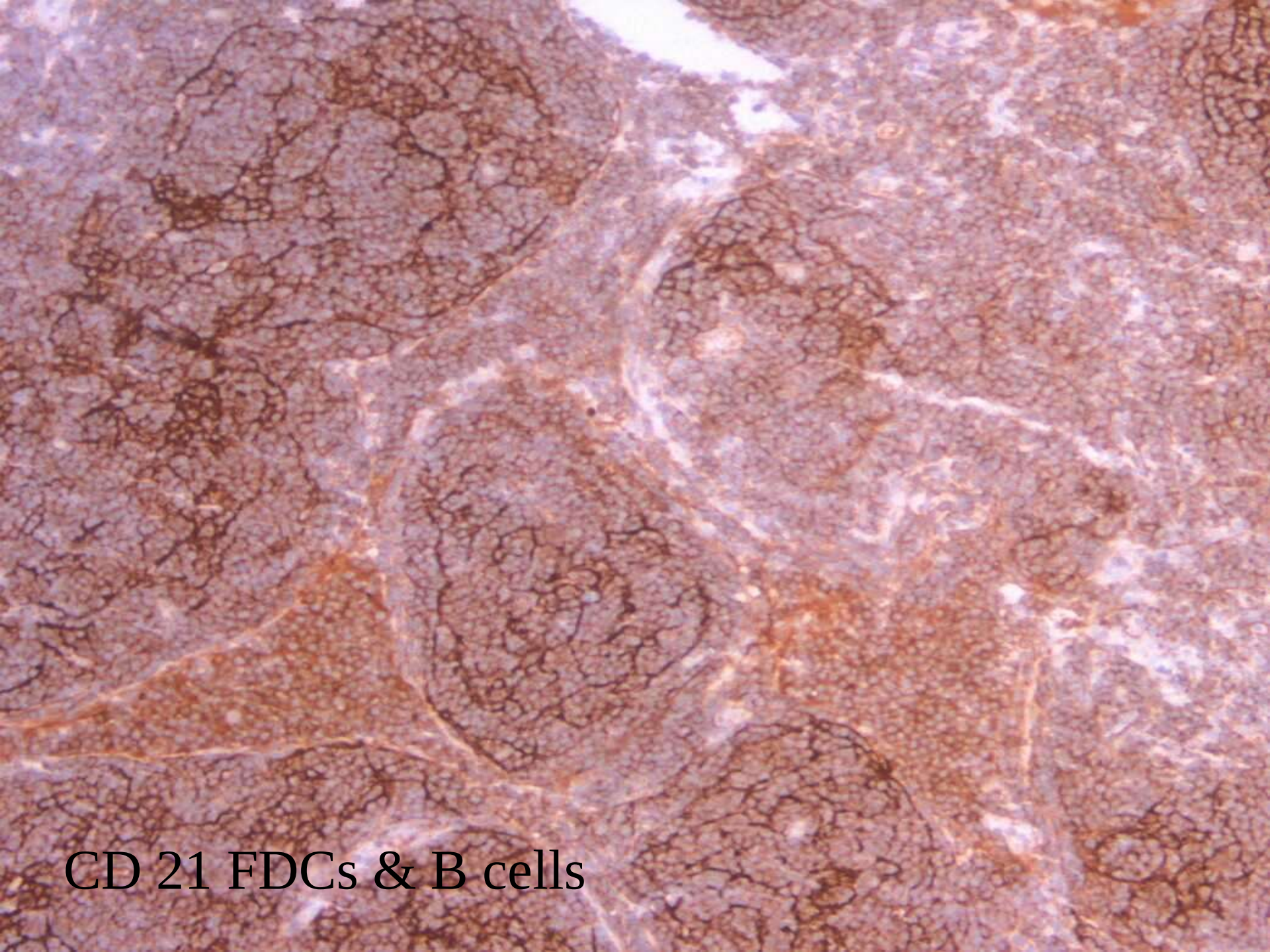


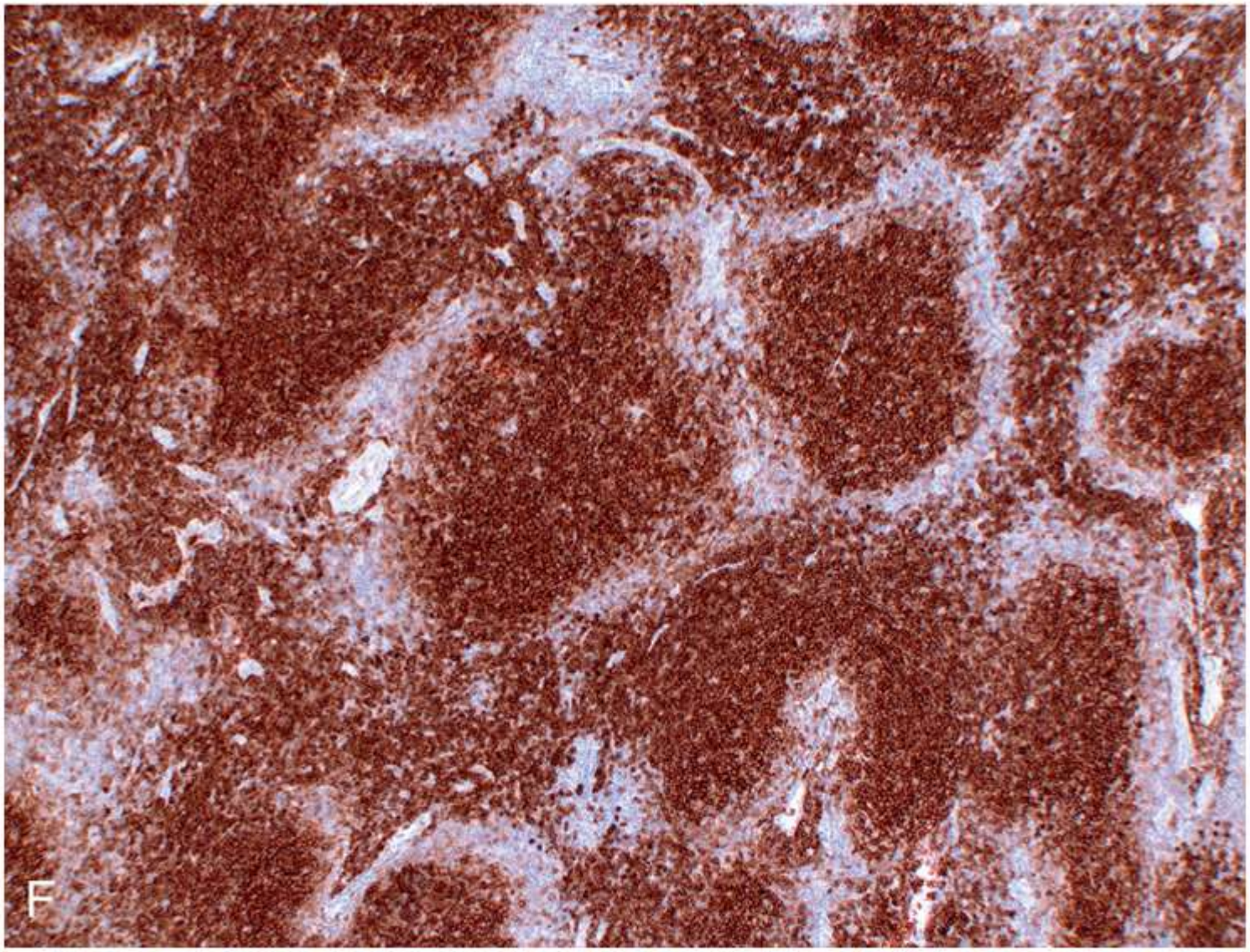
Follicle Centre Cells



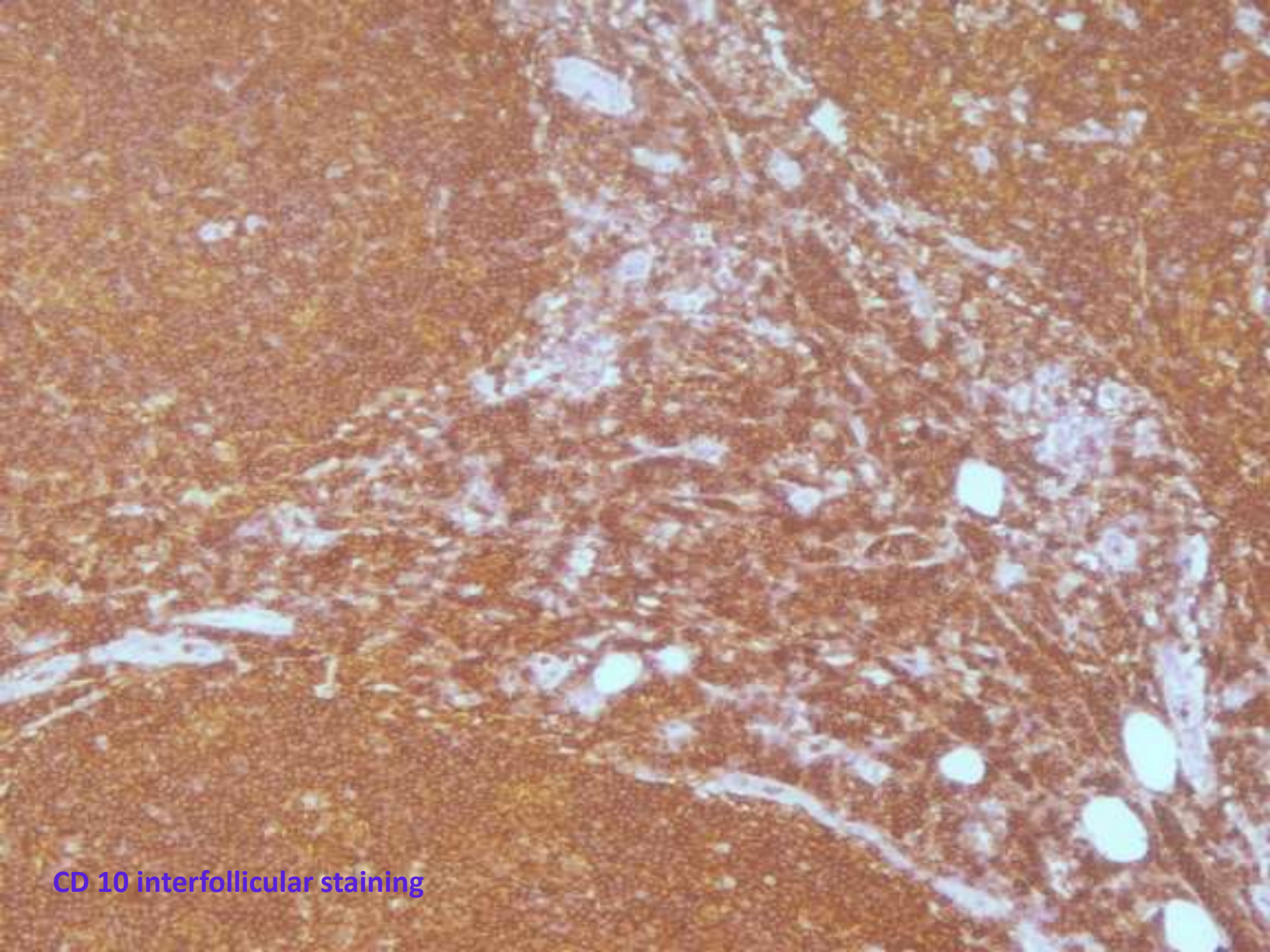
Interfollicular Cells

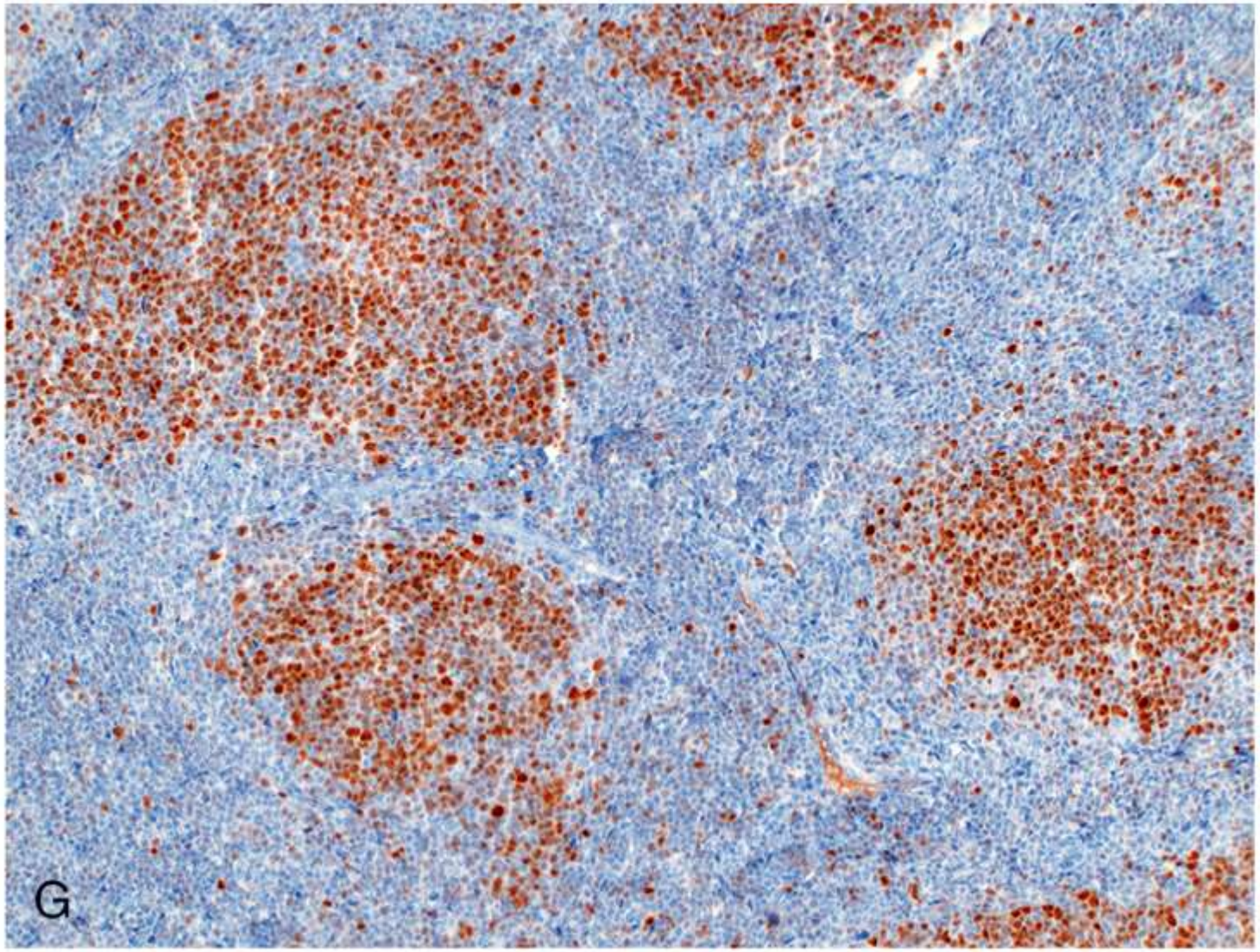

CD 21


CD 21 FDCs & B cells

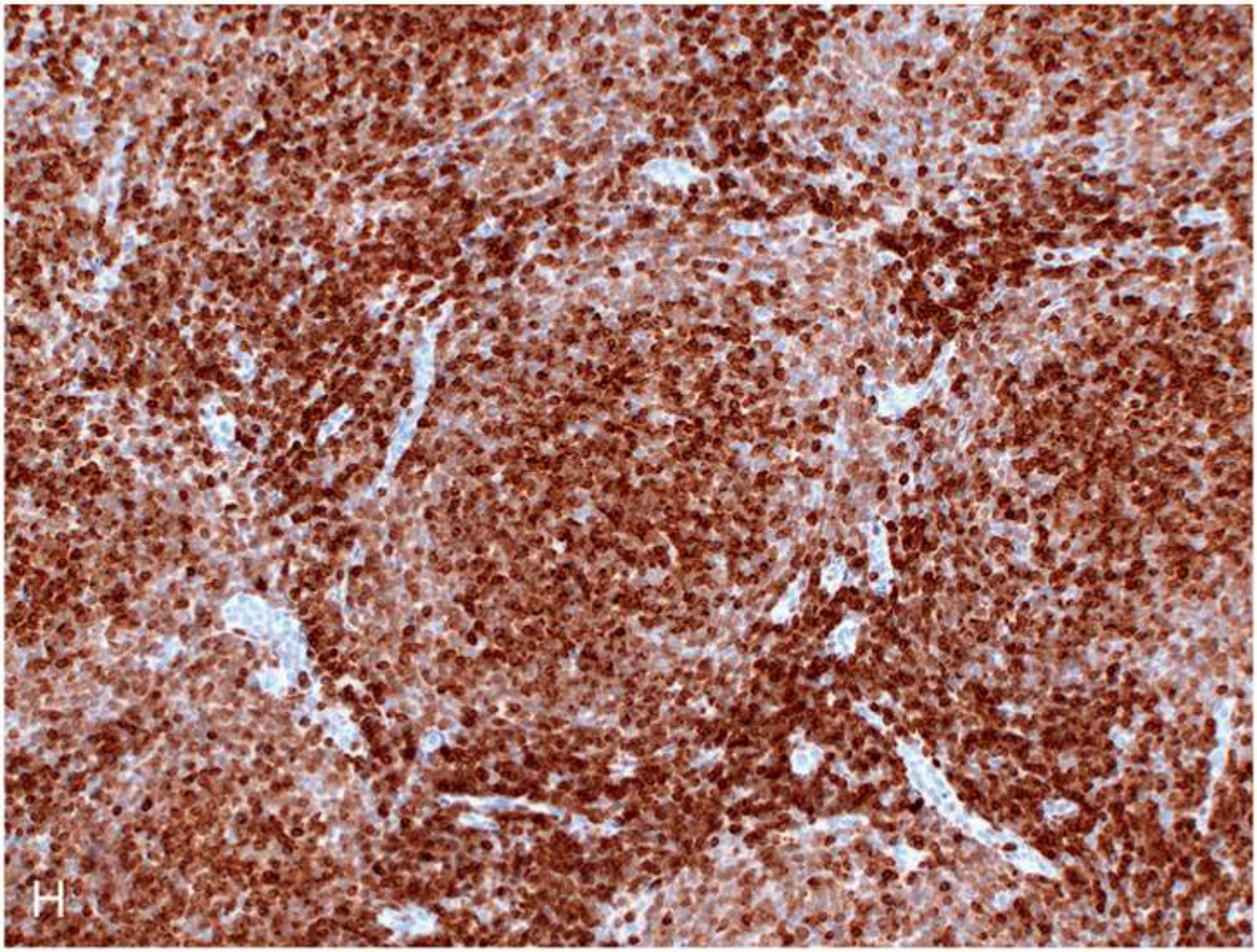


CD10

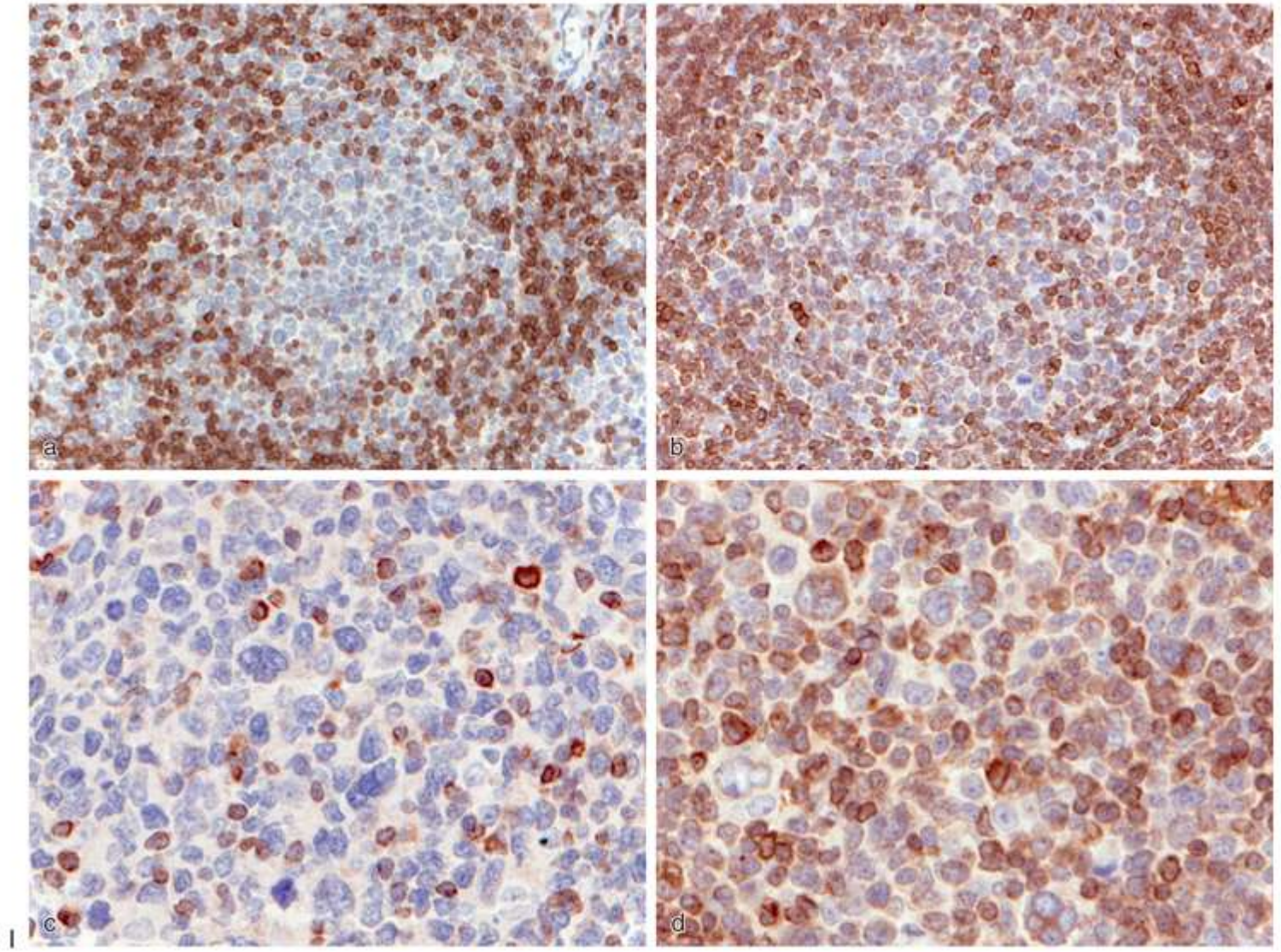

CD 10 interfollicular staining



BCL6



BCL2



a & c Dako BCL2

b & d Epitomics BCL2

Light chains are only sometimes helpful in FL

IgD can be a great help

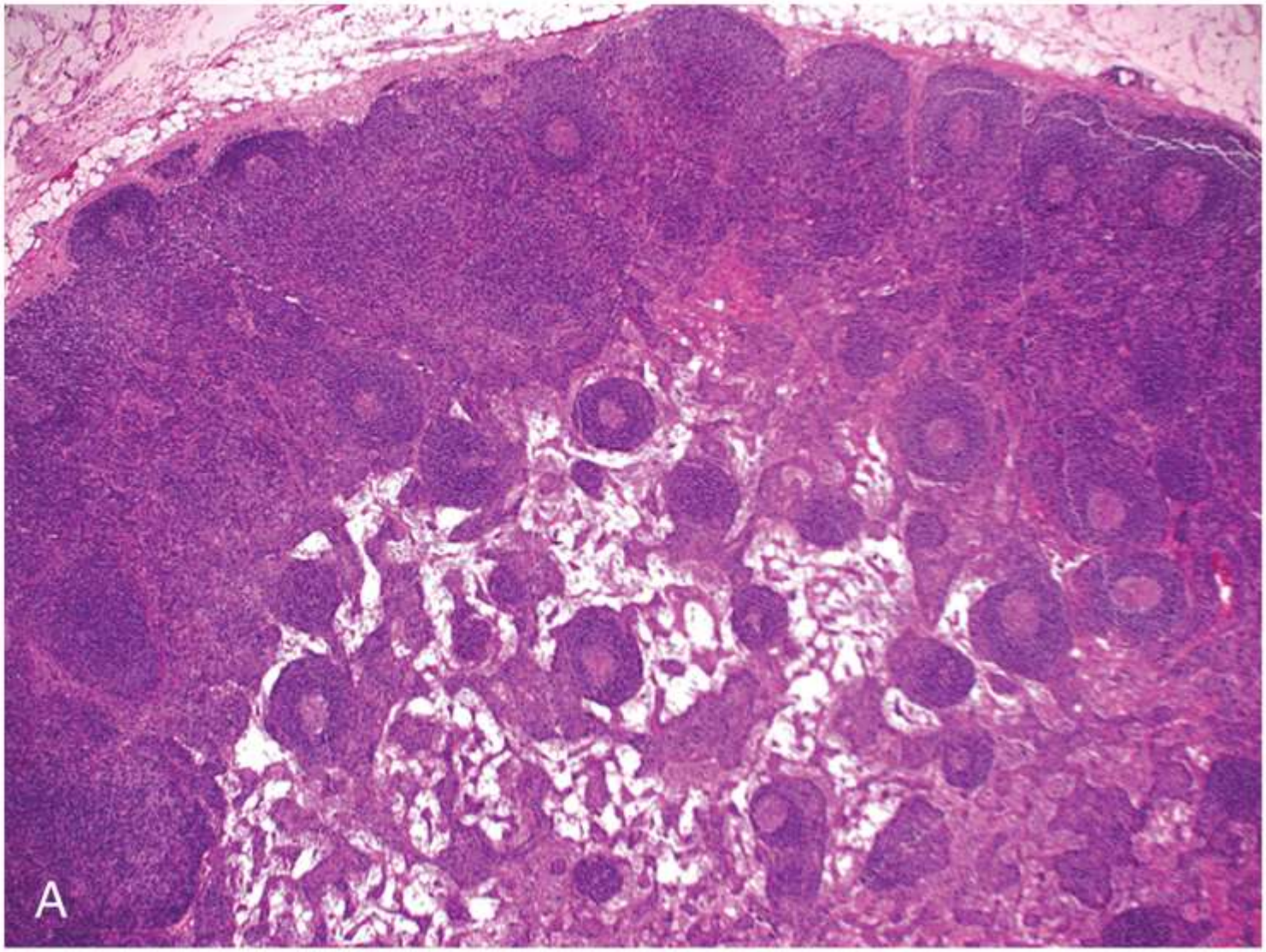
In situ Follicular Neoplasia

Definition
Clonal BCL2+ follicles on an architecturally normal backgound

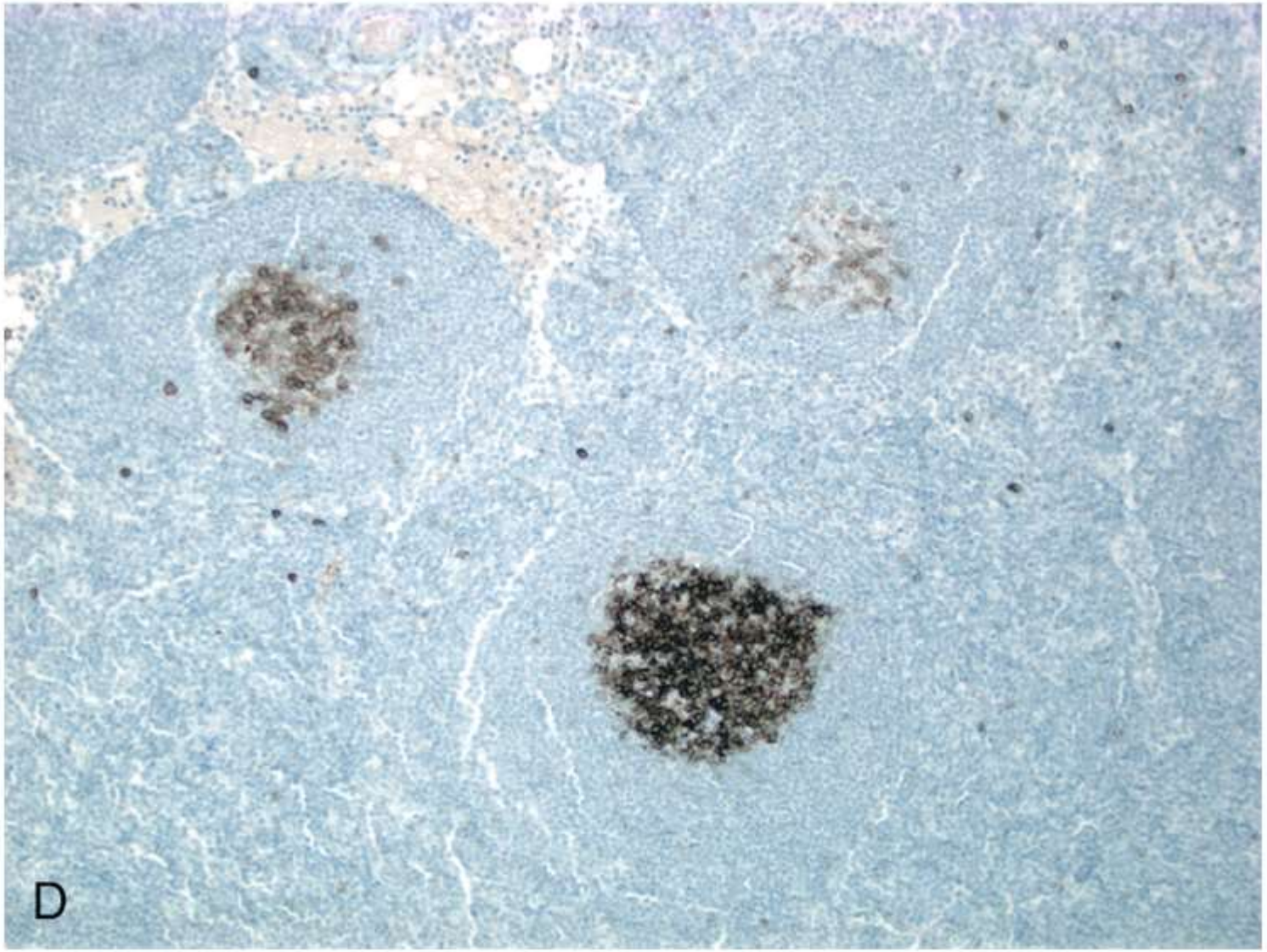
Possibilities
Nothing
History of follicular lymphoma
Concurrent follicular lymphoma
Heralds Follicular lymphoma

Do NOT make diagnosis of FL on the basis of this finding

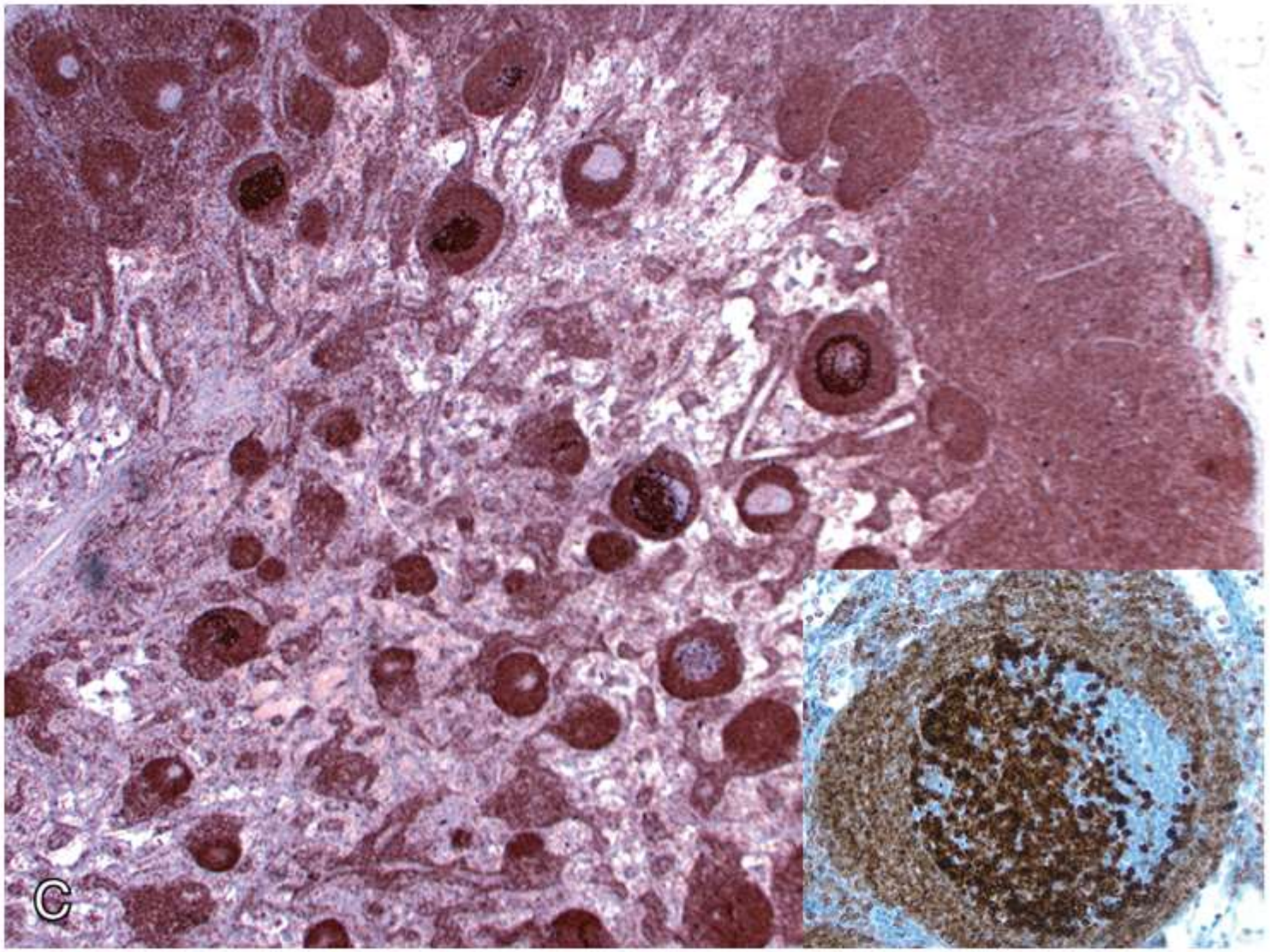
Clinical assessment required



In situ follicular neoplasia (ISFN): reactive looking follicles



CD10 ISFN



BCL2 ISFN

Extranodal Marginal Zone Lymphoma: MALT Lymphoma

MALT lymphoma is an extranodal lymphoma comprising morphologically heterogeneous small B cells, including marginal-zone (centrocyte-like) cells, cells resembling monocytoid cells, small lymphocytes, and scattered immunoblast and centroblast-like cells.

There is plasma cell differentiation in a proportion of cases. The infiltrate is in the marginal zone of reactive B-cell follicles and extends into the interfollicular region.

In epithelial tissues, the neoplastic cells typically infiltrate the epithelium, forming lymphoepithelial lesions.

MALT lymphomas account for 7% to 8% of all B-cell lymphomas and at least 50% of primary gastric lymphomas

MALT Lymphoma sites

- Gastrointestinal tract
  - Stomach
  - Intestine (including immunoproliferative small intestinal disease)
- Salivary glands
- Respiratory tract
  - Lung, pharynx, trachea
- Ocular adnexa
  - Conjunctiva, lacrimal gland, orbit*
- Skin
- Thyroid gland
- Liver
- Genitourinary tract
  - Bladder, prostate gland, kidney
- Breast
- Thymus

MALT lymphomas only rarely arise from native MALT

Usually arise from MALT that has been acquired as a result of a chronic inflammatory disorder at sites normally devoid of MALT such as the stomach, salivary gland, lung, thyroid gland, and ocular adnexa.

MALT lymphomas of the salivary gland and thyroid gland, organs normally containing no lymphoid tissue, are always preceded by an autoimmune lymphoid infiltrate - Sjögren's syndrome and Hashimoto's thyroiditis, respectively

Infectious agents

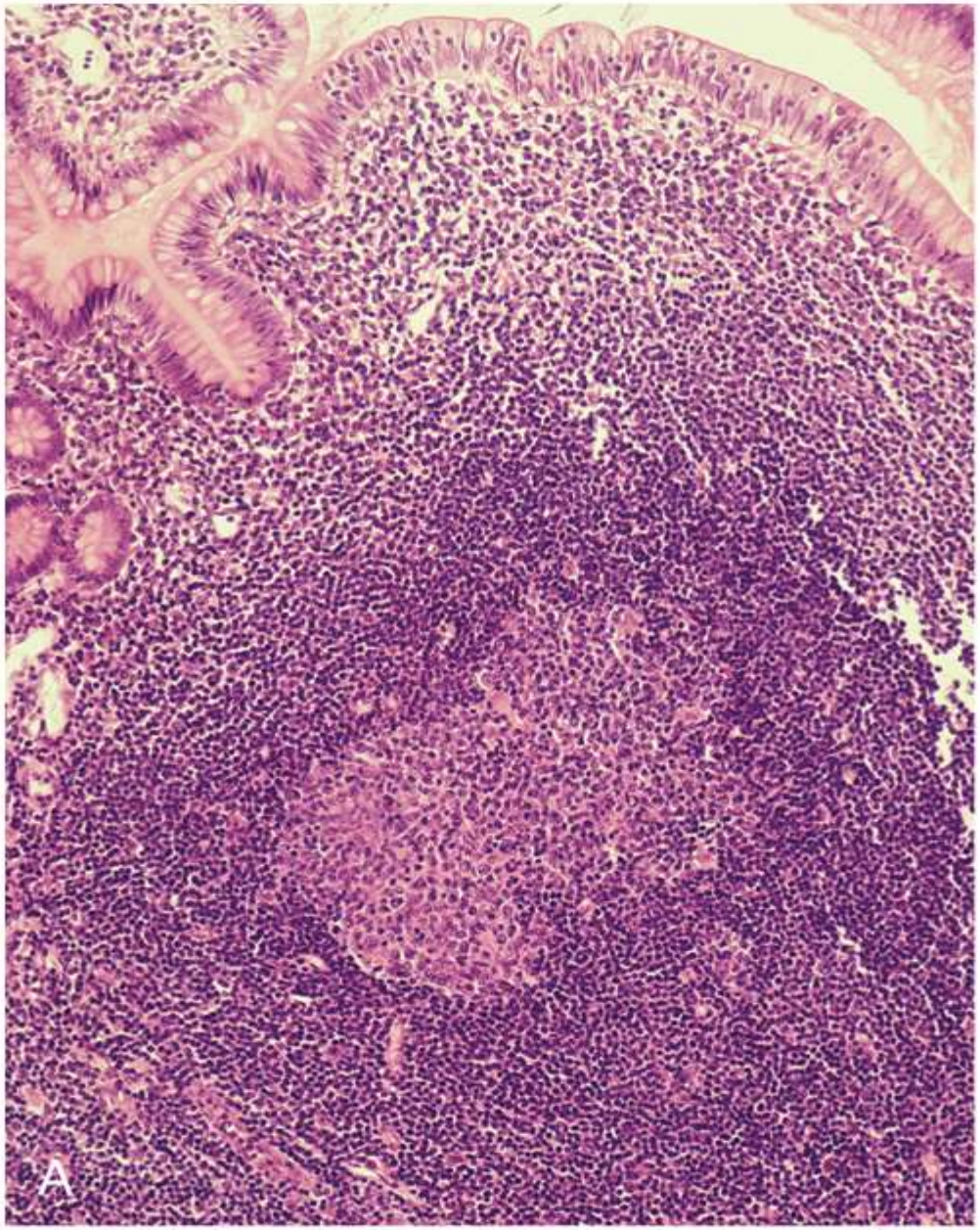
H. Pylori (gastric MALT lymphoma))

Campylobacter jejuni (immunoproliferative small intestinal disease – Middle East, India, Cape region of South Africa)

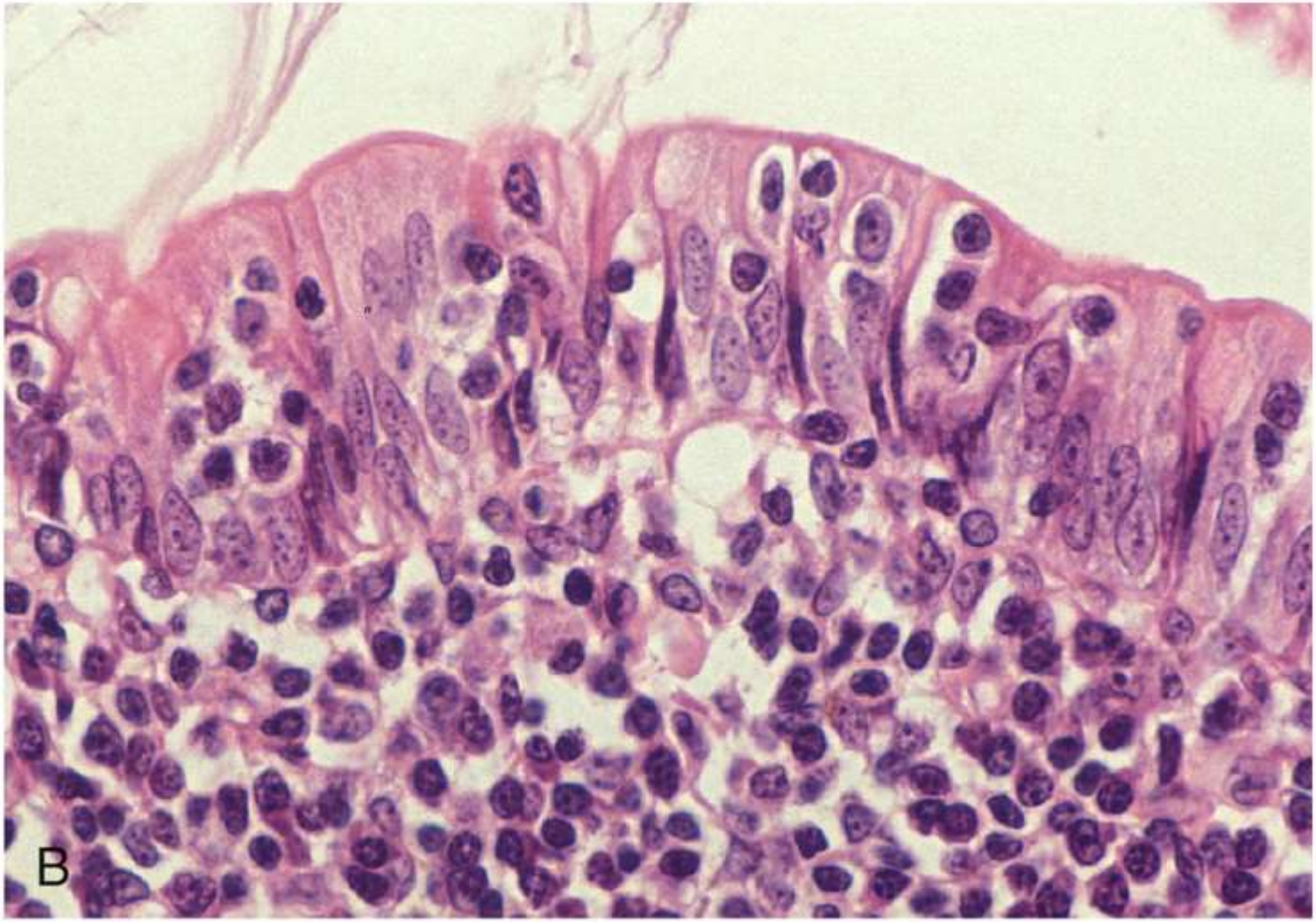
Borrelia burgdorferi (cutaneous MALT lymphoma)

Chlamydia psittaci (Ocular adnexal MALT lymphoma)

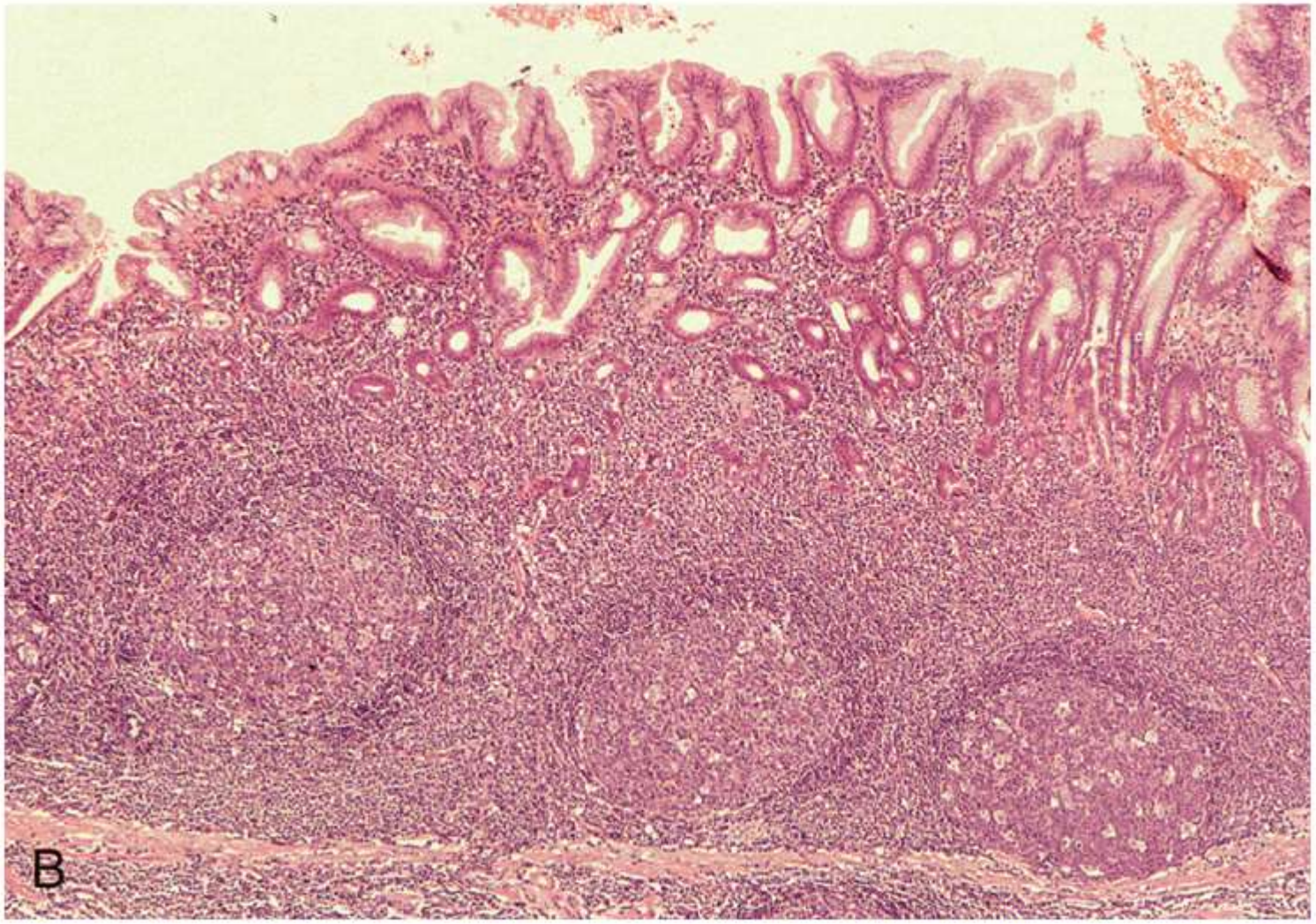
NB Association is not proof of aetiology



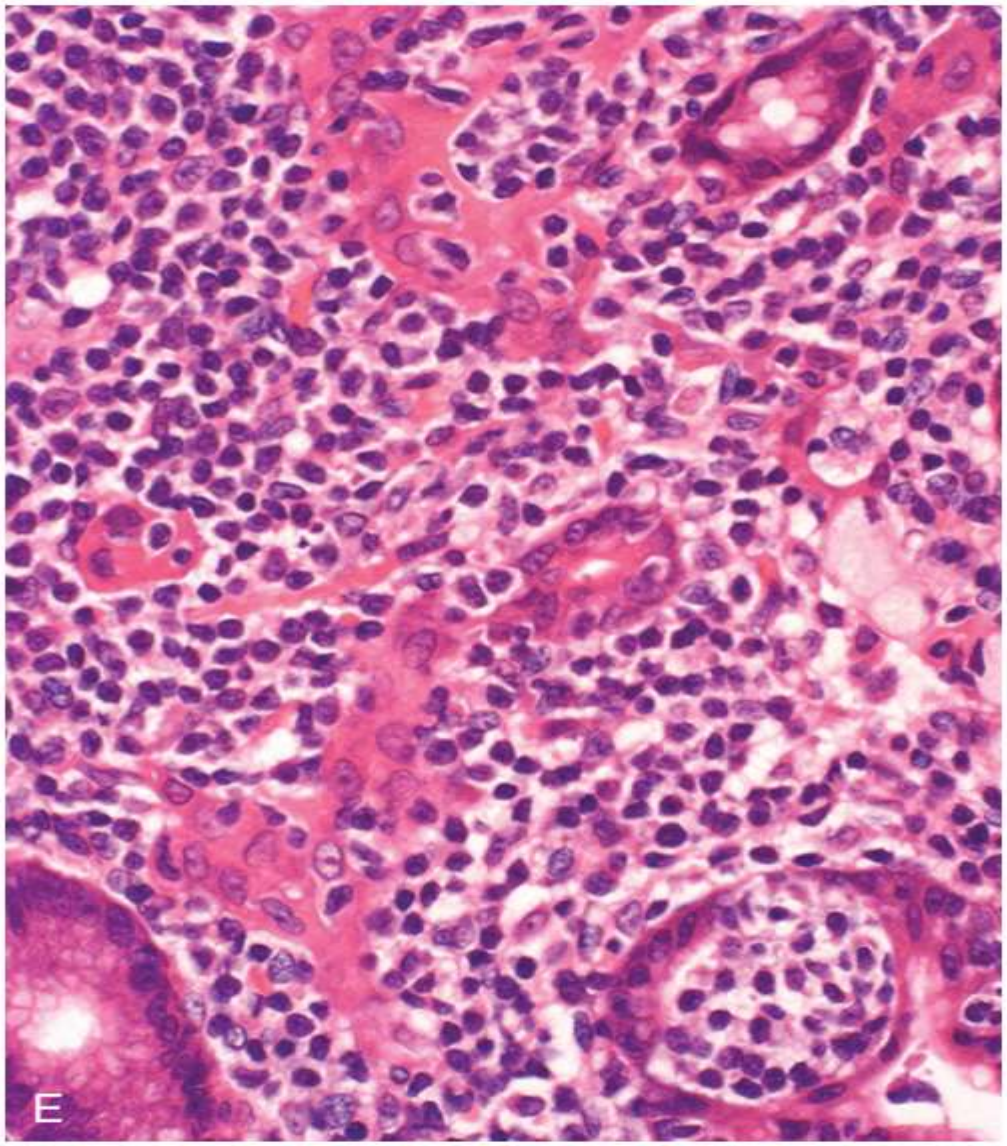
Peyer's Patch



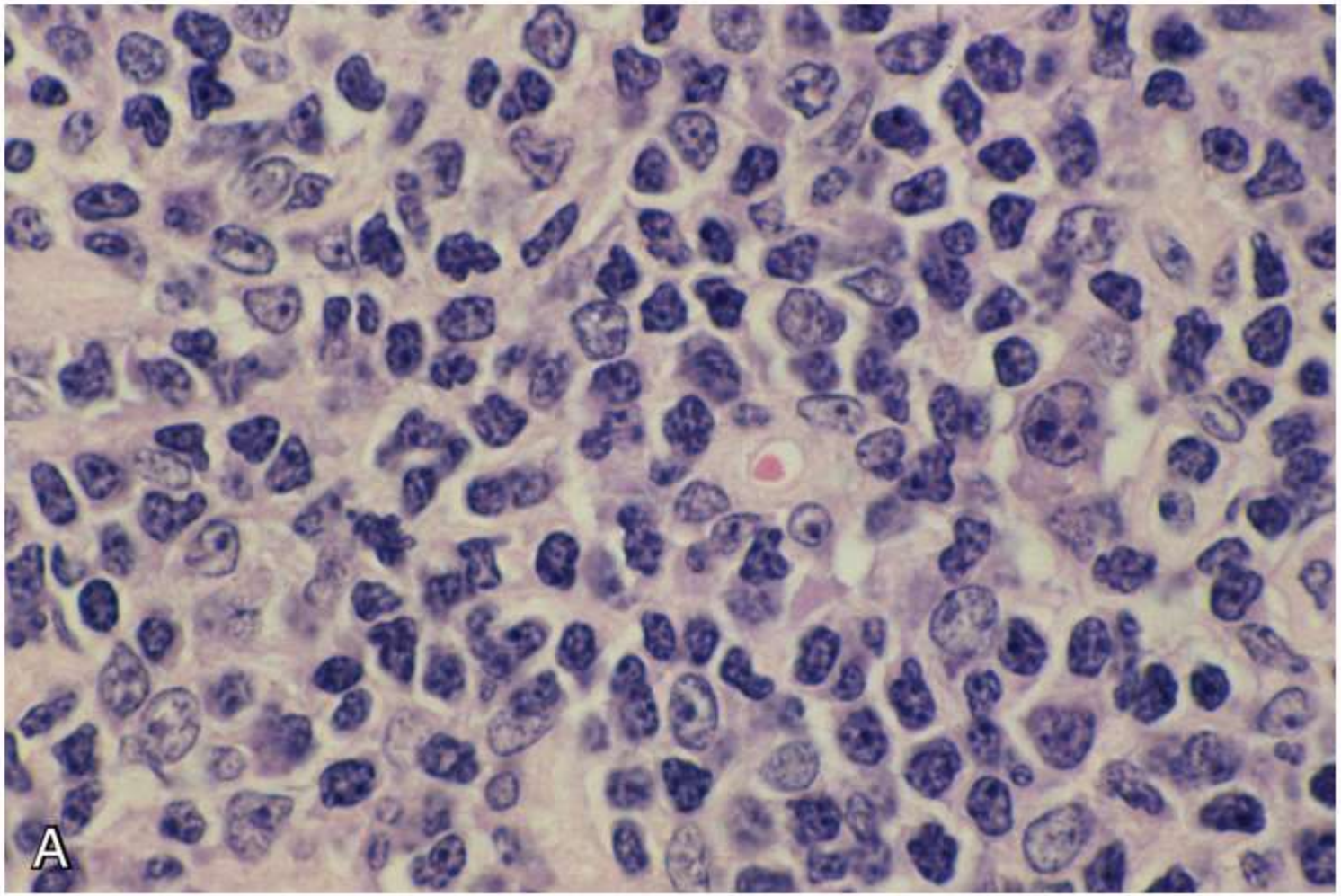
Lymphoepithelium of Peyers patch



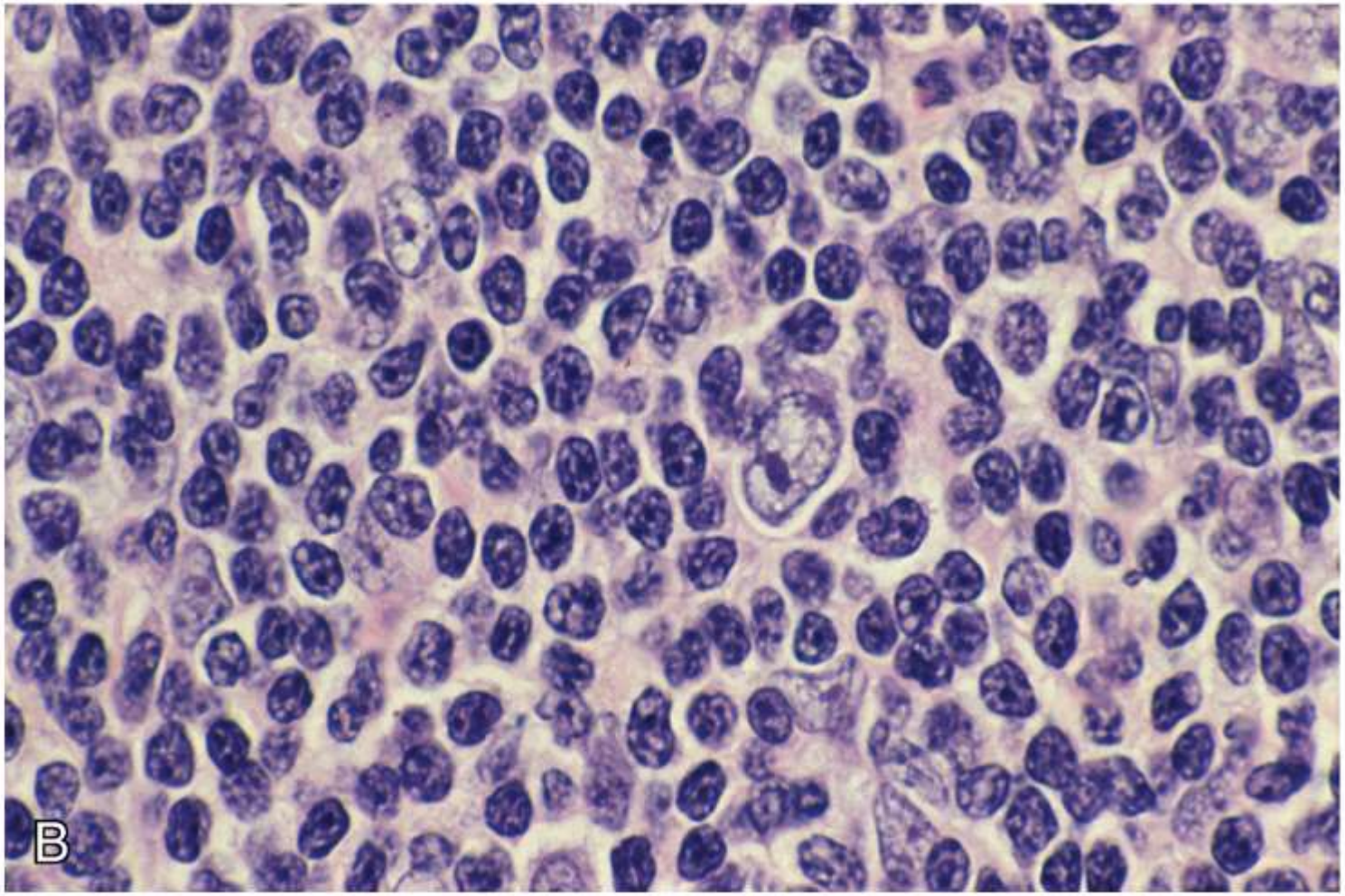
Gastric MALT Lymphoma



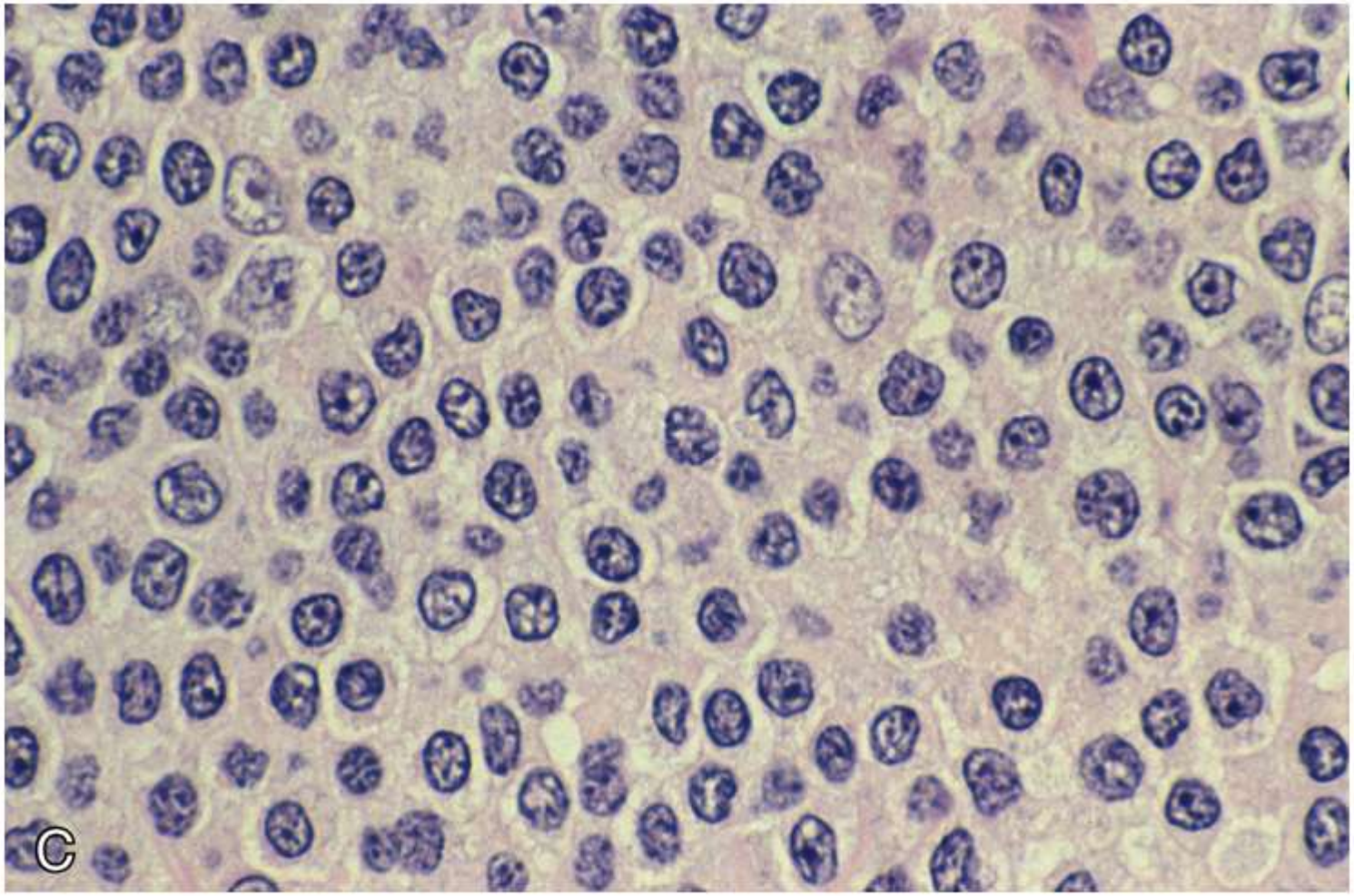
Gastric MALT Lymphoma - Lymphoepithelial lesions



Cell morphology gastric MALT lymphoma – centrocyte like

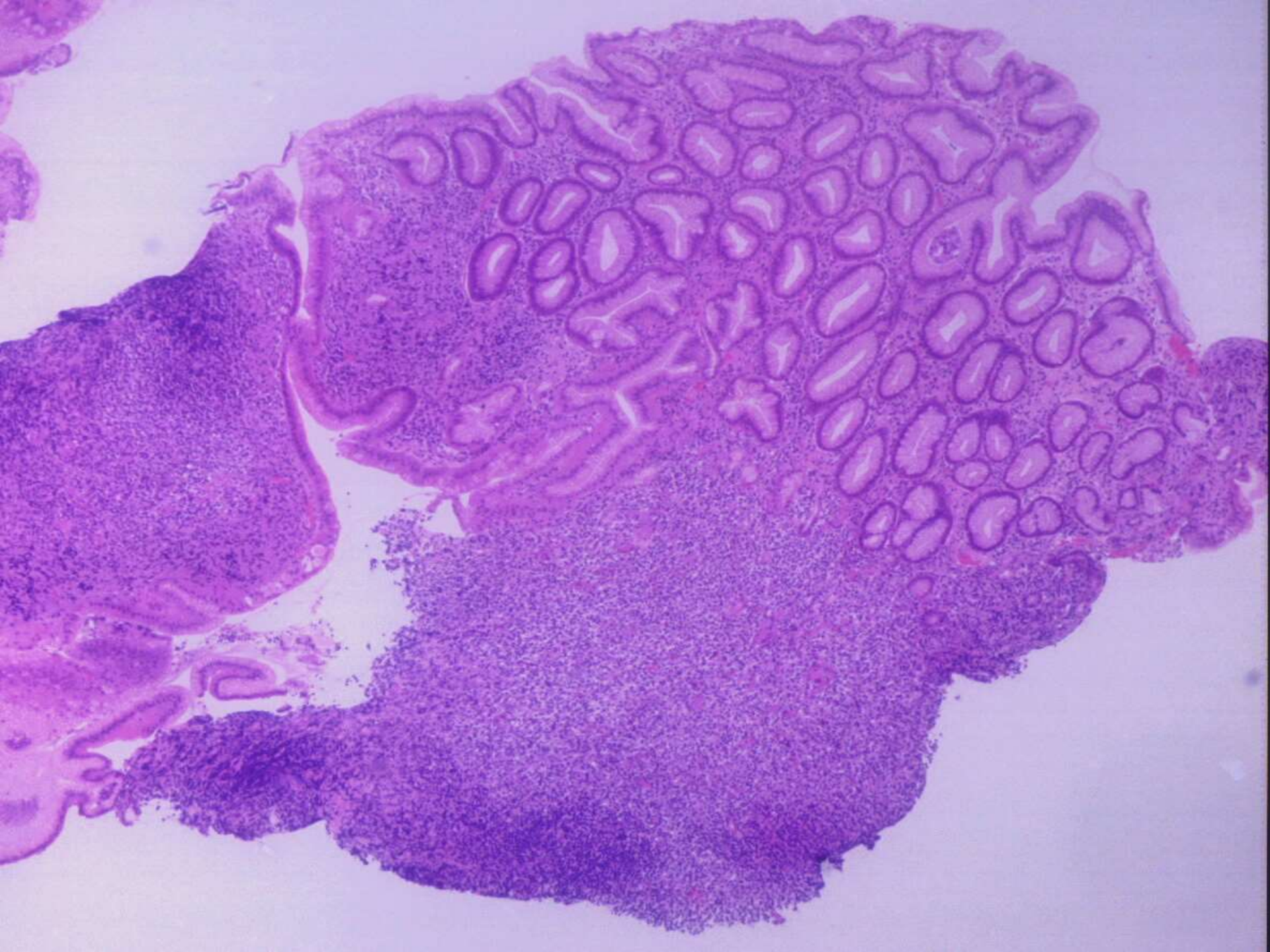


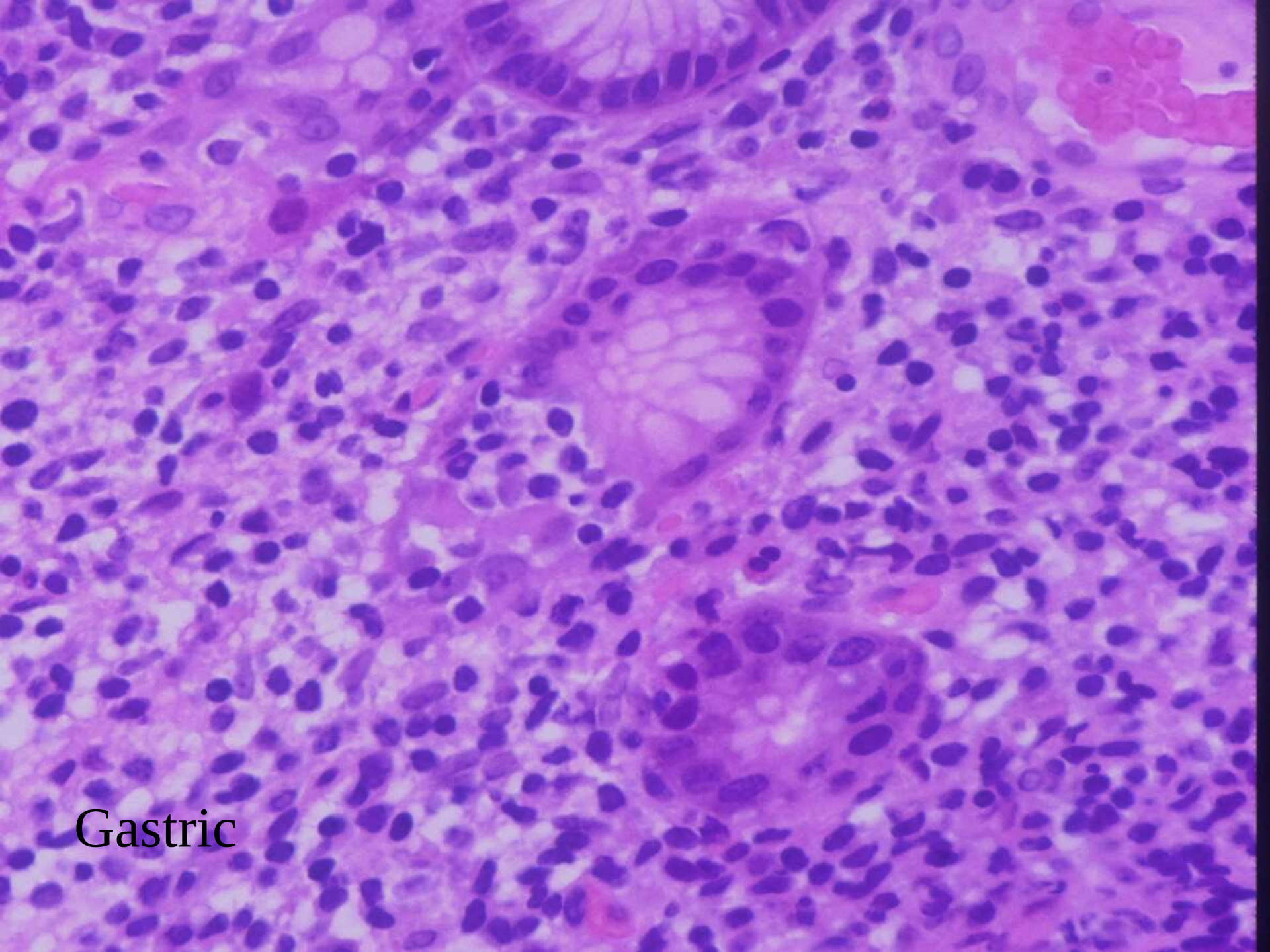
Cell morphology gastric MALT lymphoma – small lymphocytes

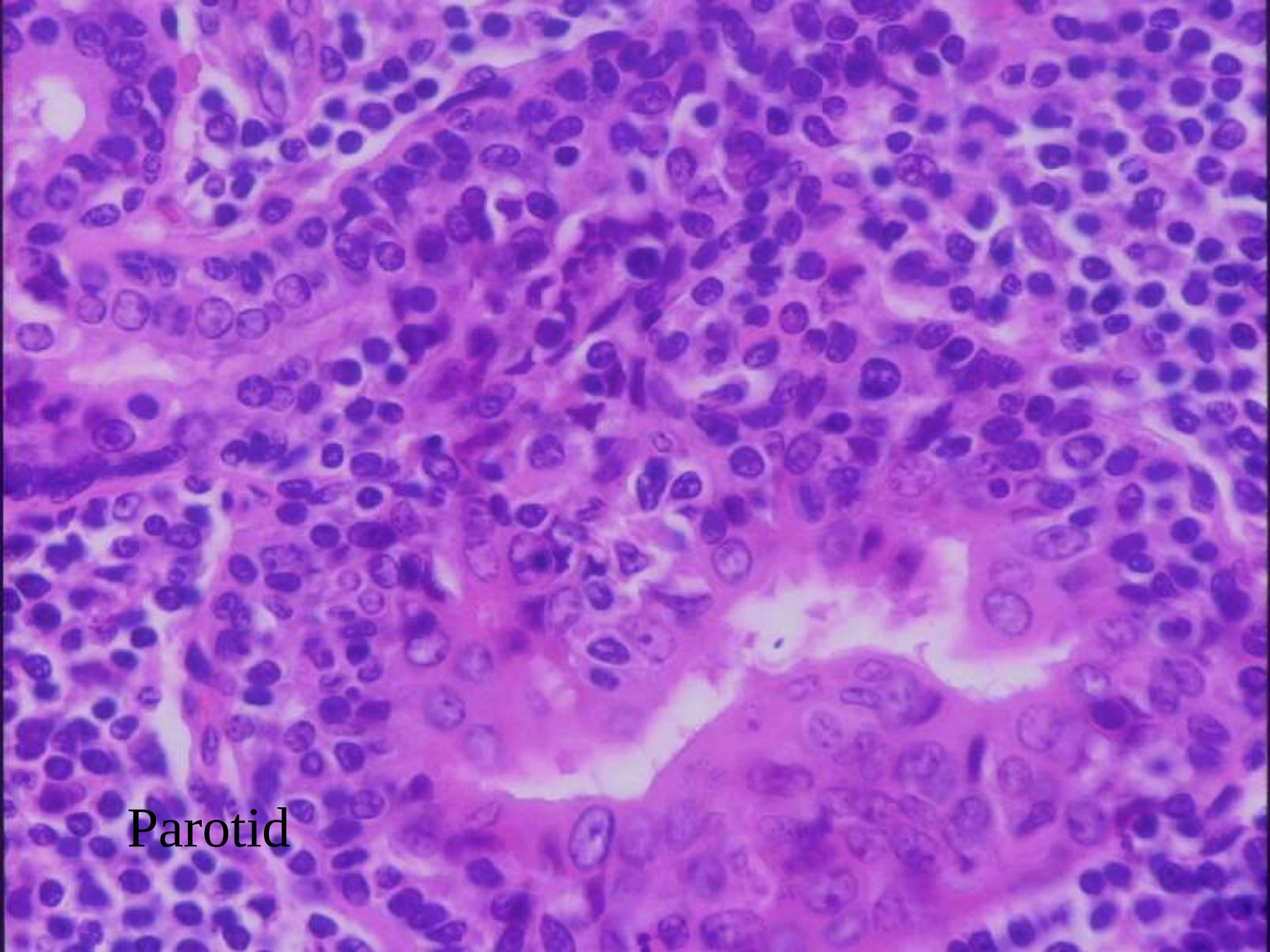


Cell morphology gastric MALT lymphoma – monocytoid cells

But be careful……

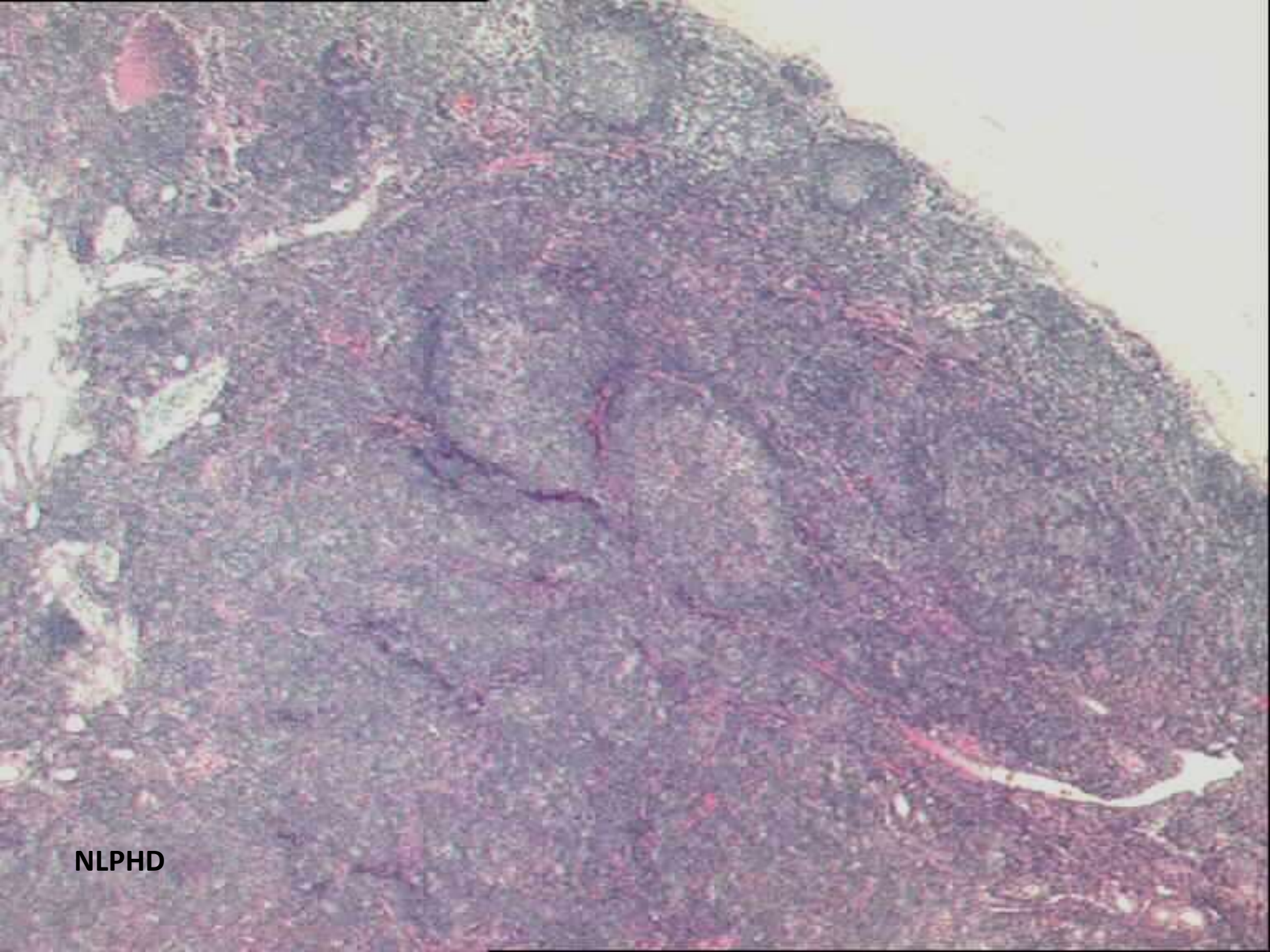


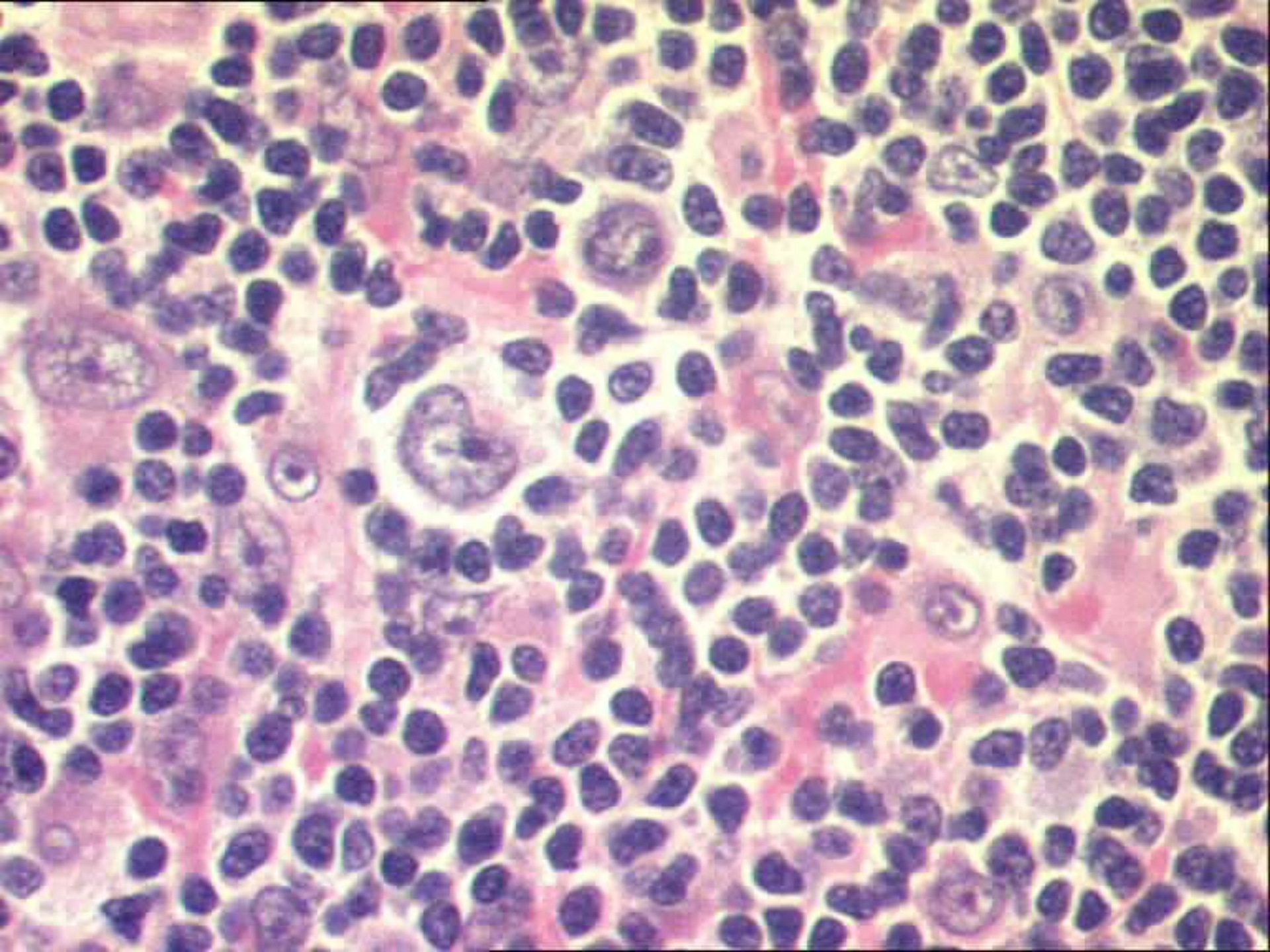

Gastric

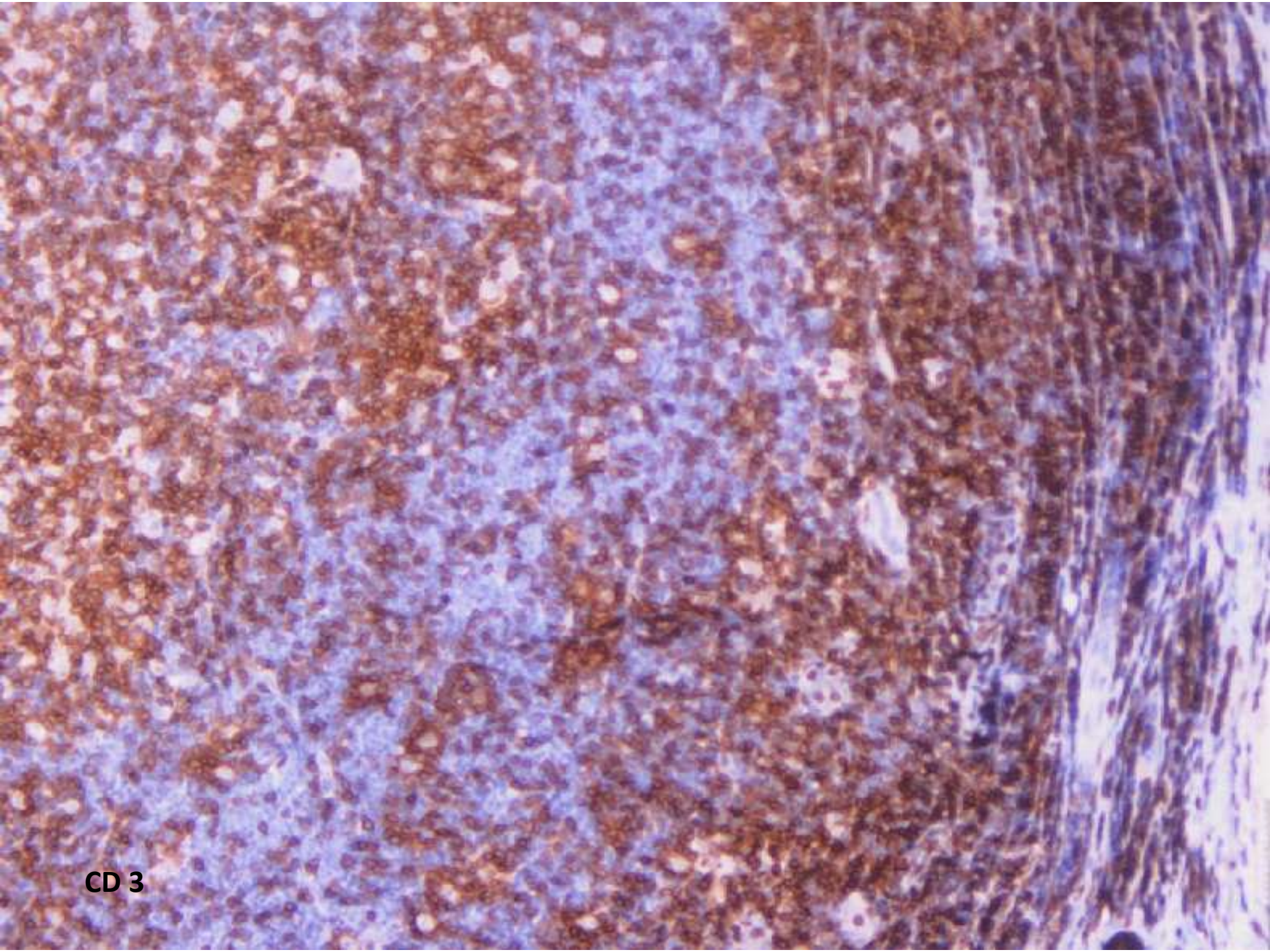

Parotid

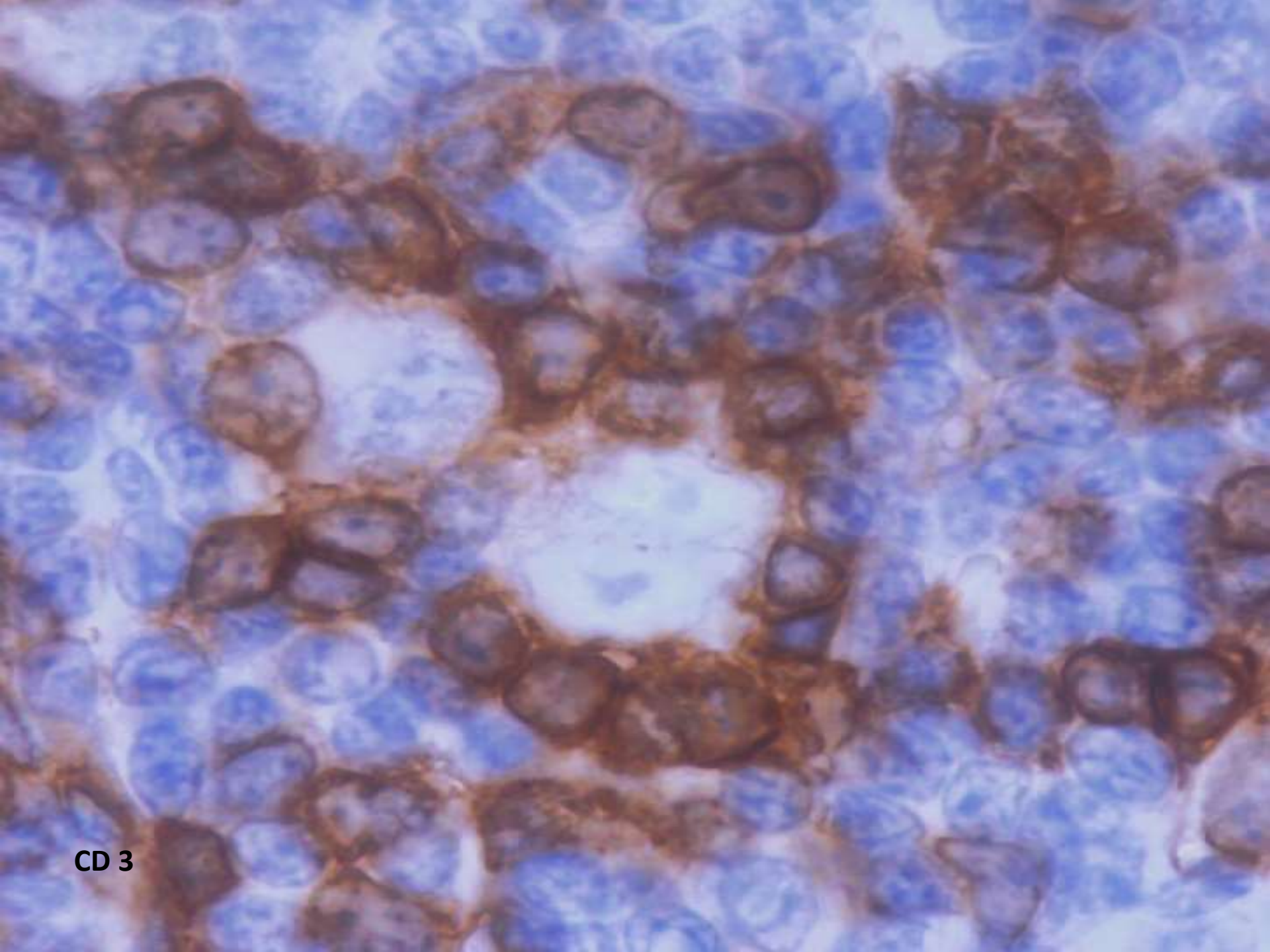
Each of these represents a follicular lymphoma!

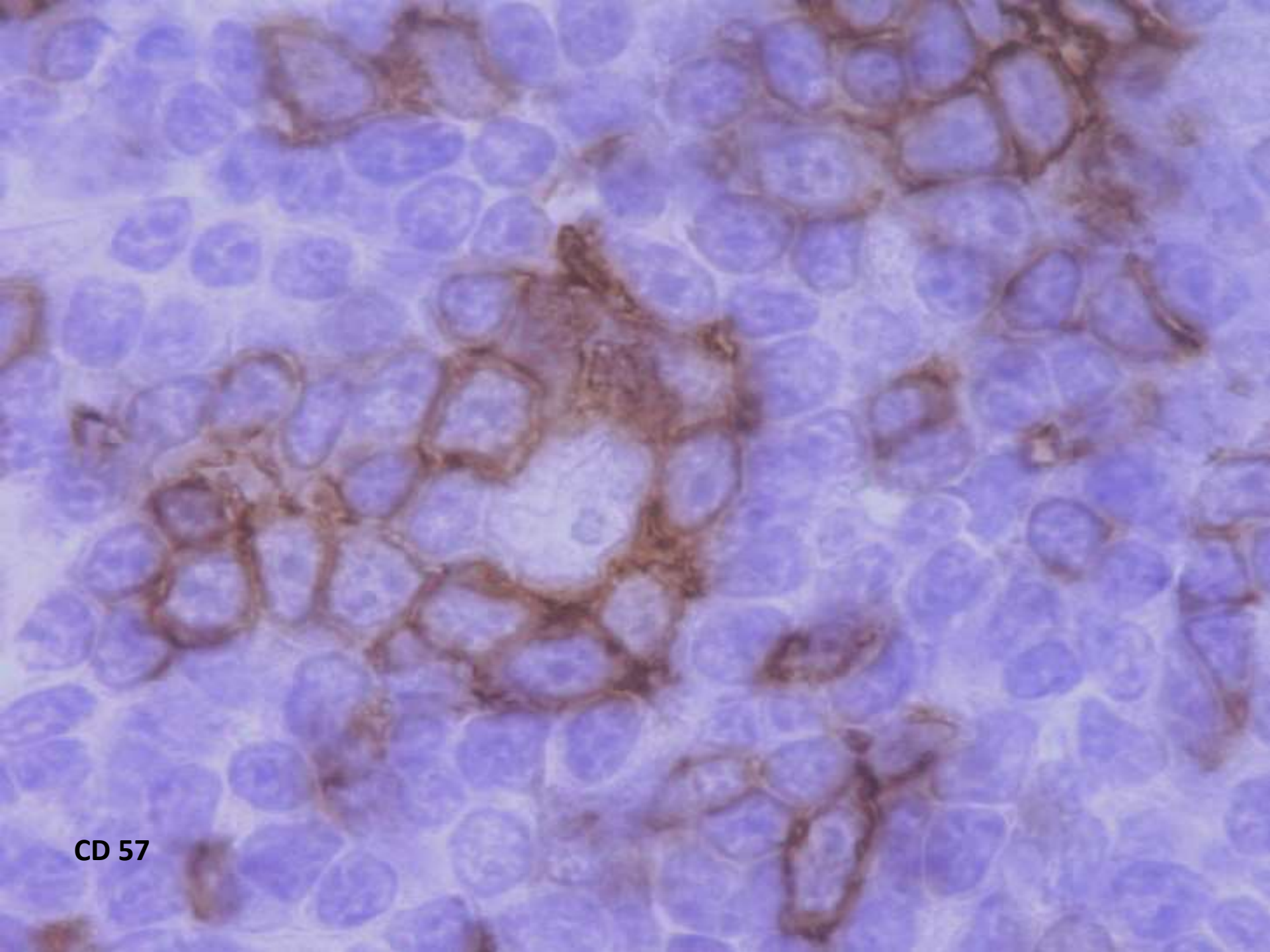
What’s this one?

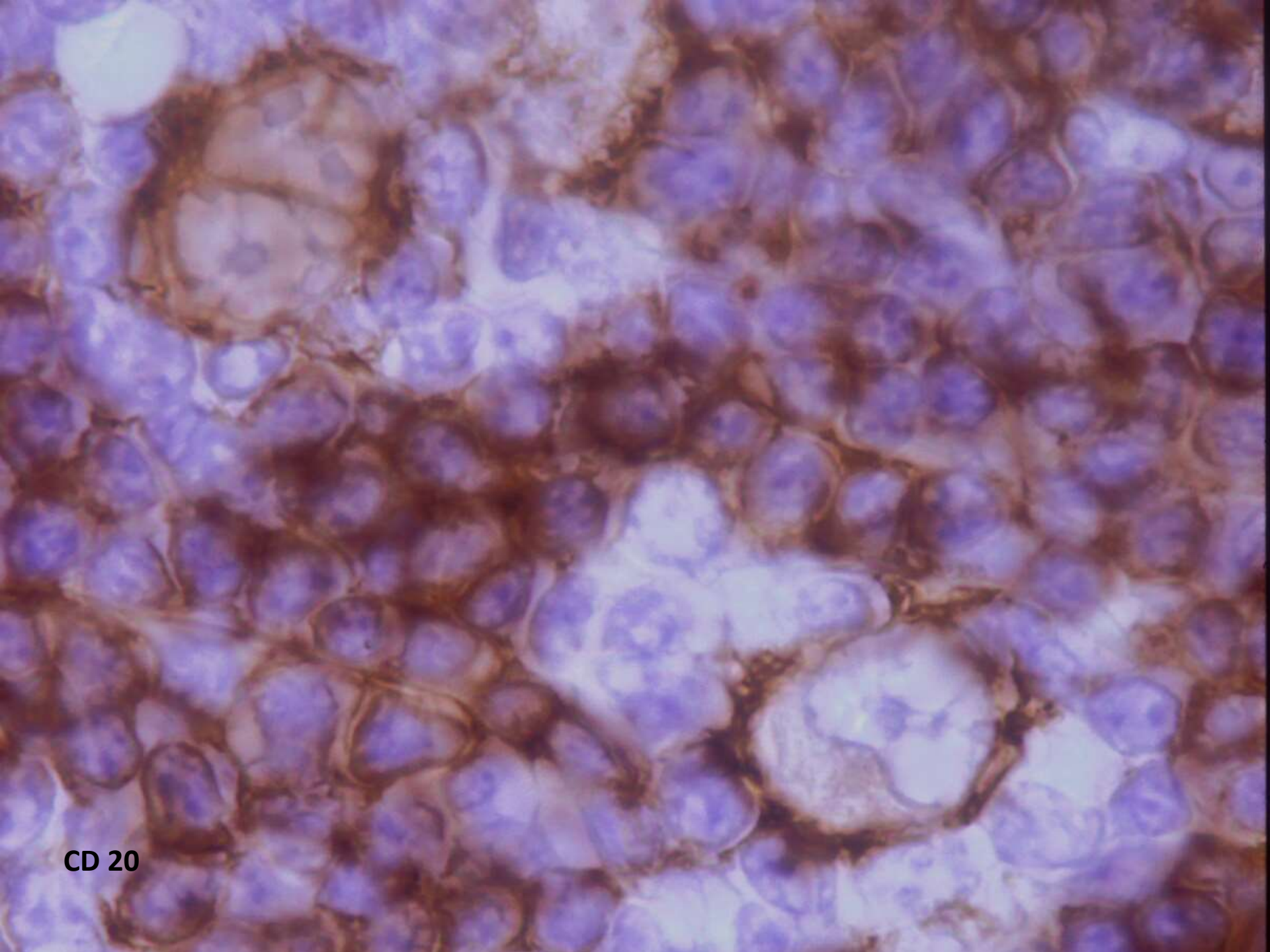

NLPHD

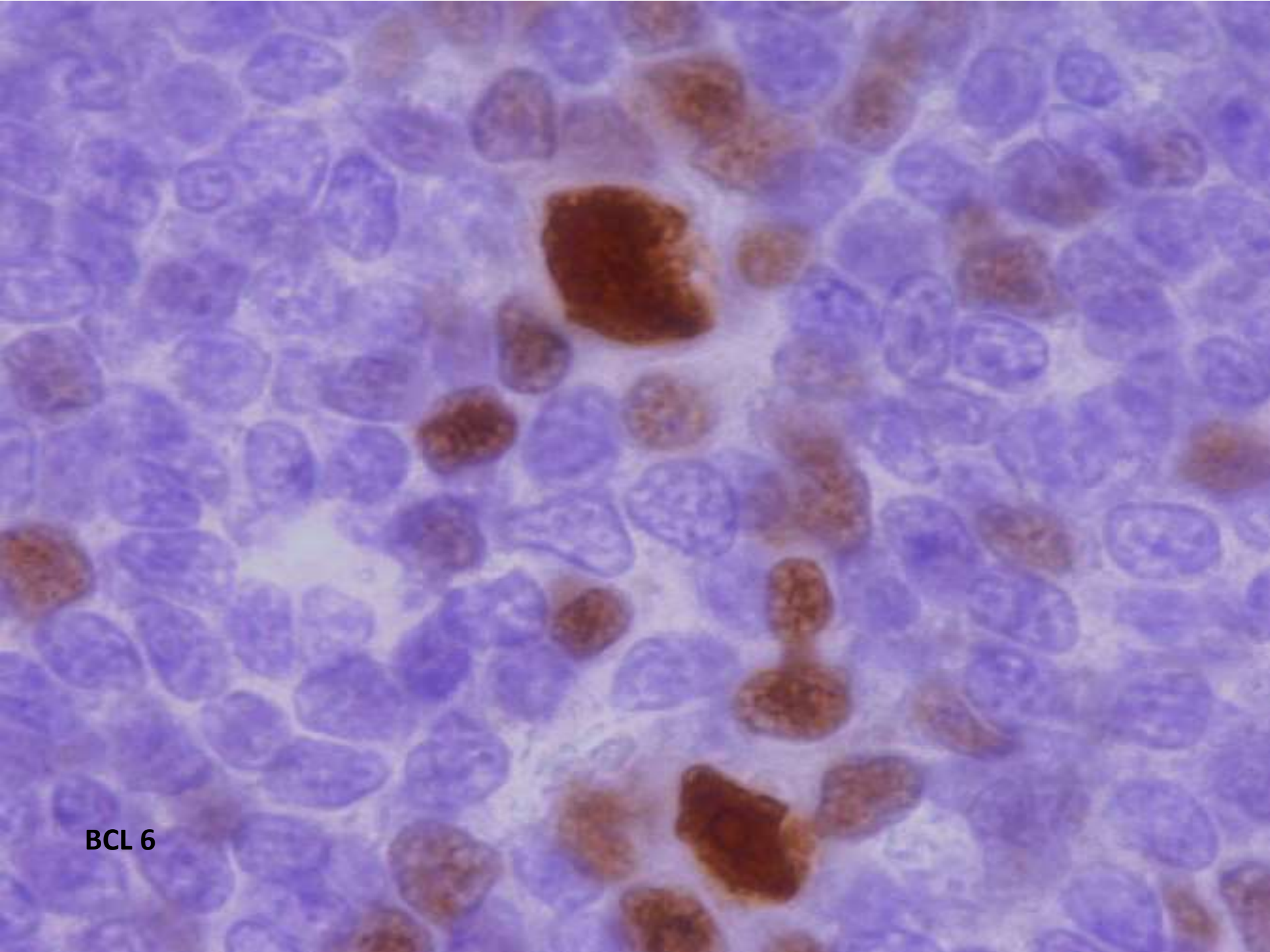


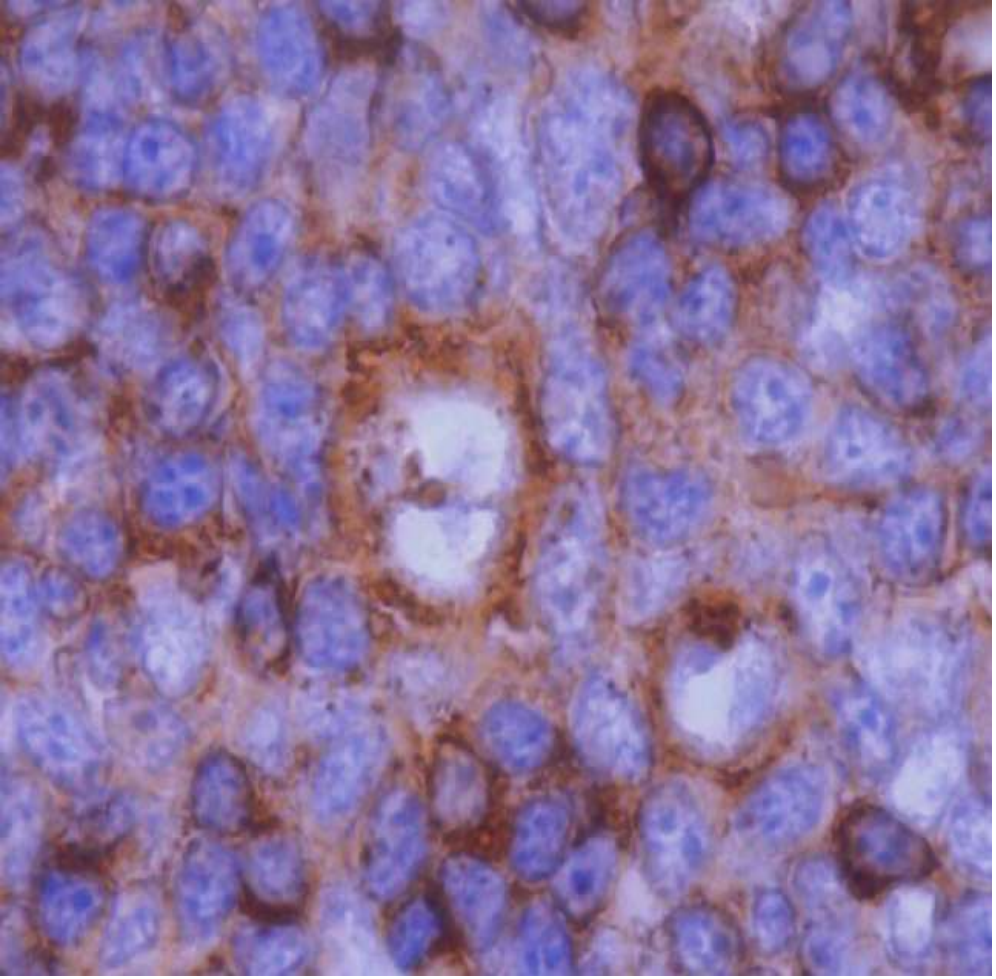

CD 3

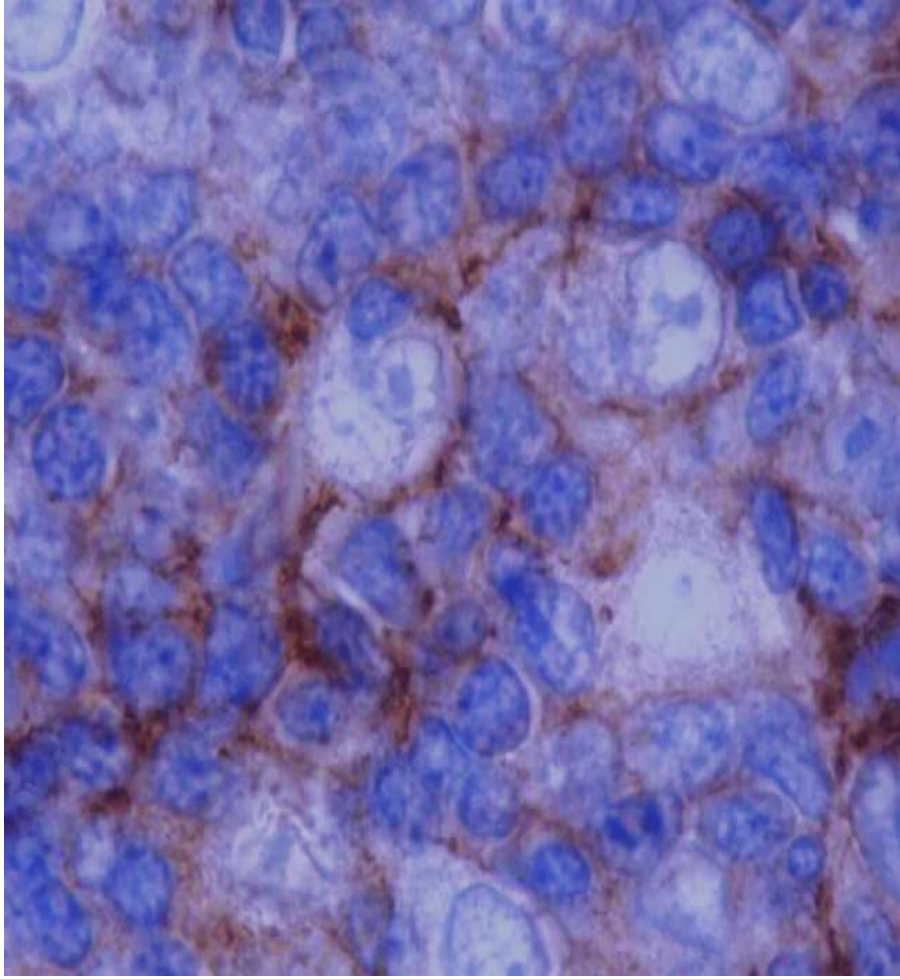

CD 3


CD 57


CD 20


BCL 6





kappa

lambda

Answer: NLPHL

Mantle cell lymphoma (MCL)

Definition

Mature B-cell neoplasm generally composed of monomorphic small to medium-sized lymphoid cells with irregular nuclei that carries 11q13 translocations, leading to overexpression of cyclin D1.

Neoplastic transformed cells (centroblasts), paraimmunoblasts, and pseudofollicles are absent.

Extranodal involvement is frequent in MCL. Gastrointestinal infiltration has been reported in 10% to 25% of patients, either at presentation or during the course of the disease. A peculiar manifestation of this involvement is lymphomatoid polyposis,

Other extranodal sites commonly involved are Waldeyer's ring, lung, and pleura (5%-20%).

Less common localizations are skin, breast, soft tissue, thyroid, salivary gland, peripheral nerve, conjunctiva, and orbit.

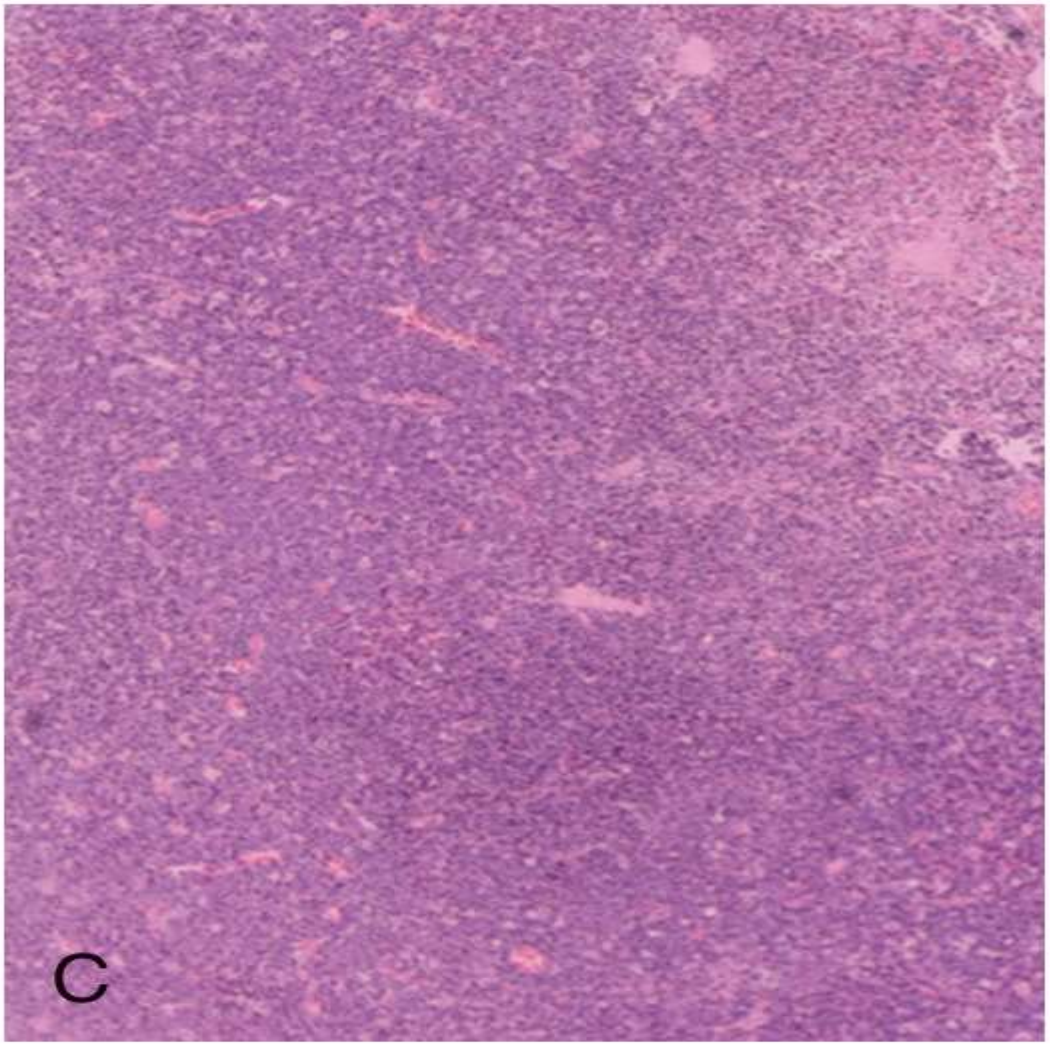
Leukaemic phase can occur

MCL Architectural Patterns

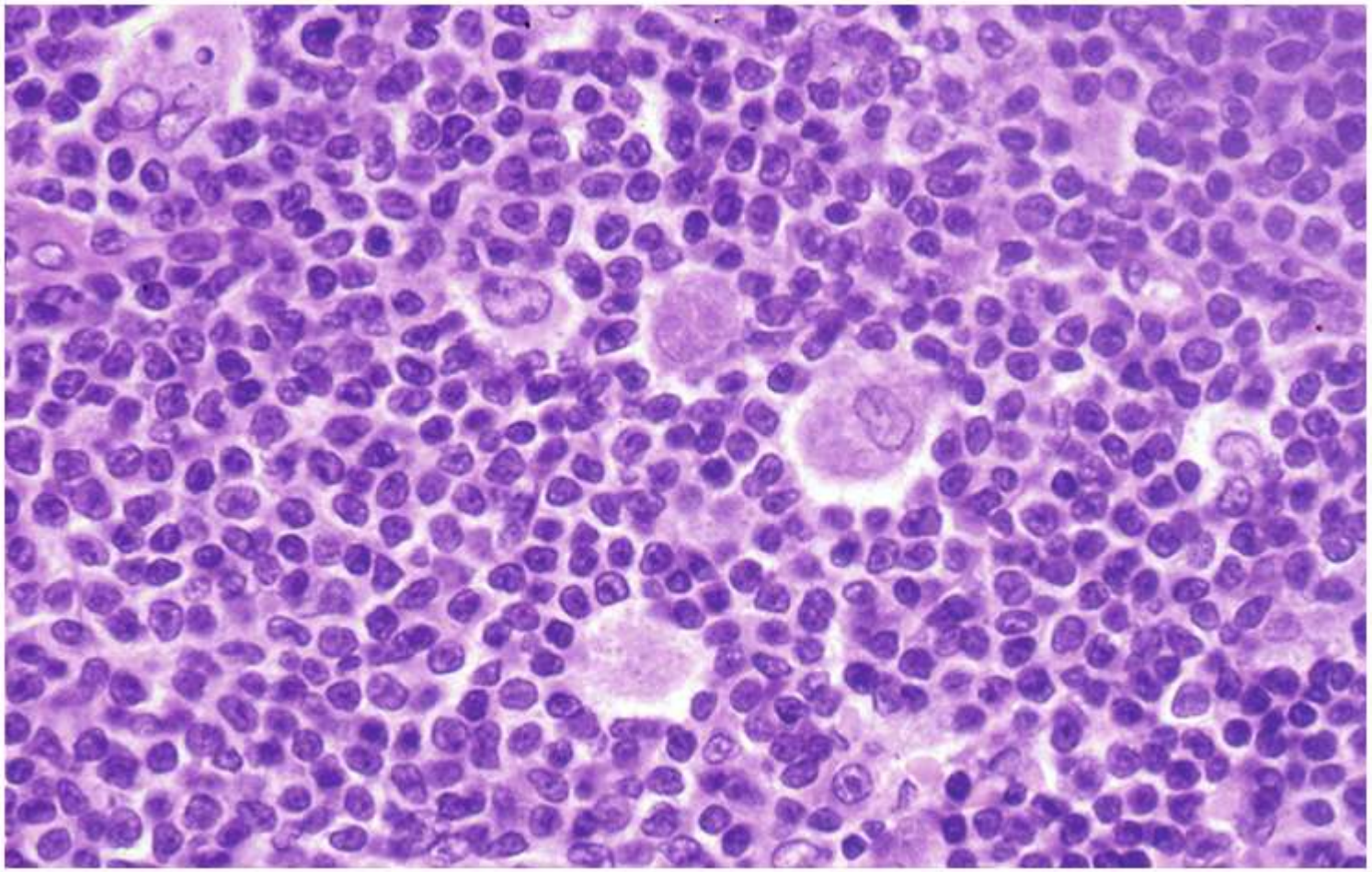
Mantle zone

Nodular

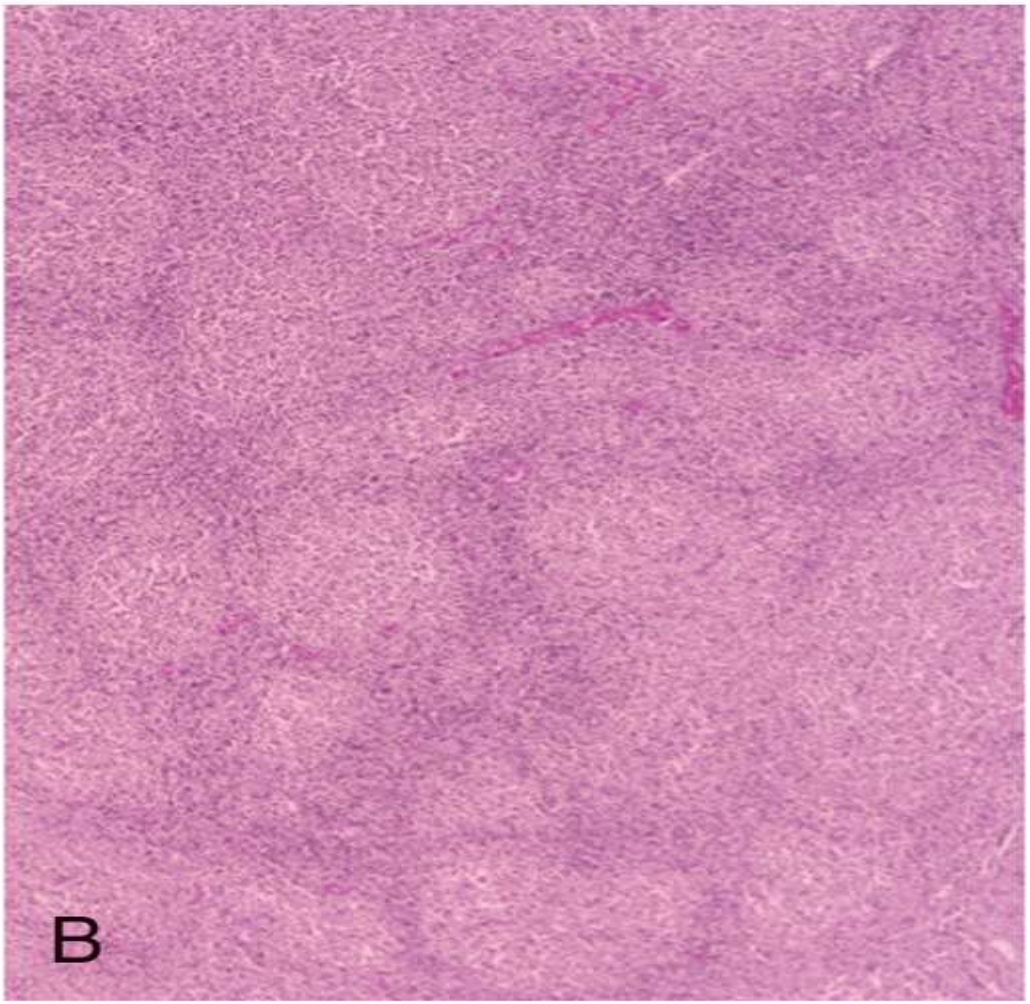
Diffuse



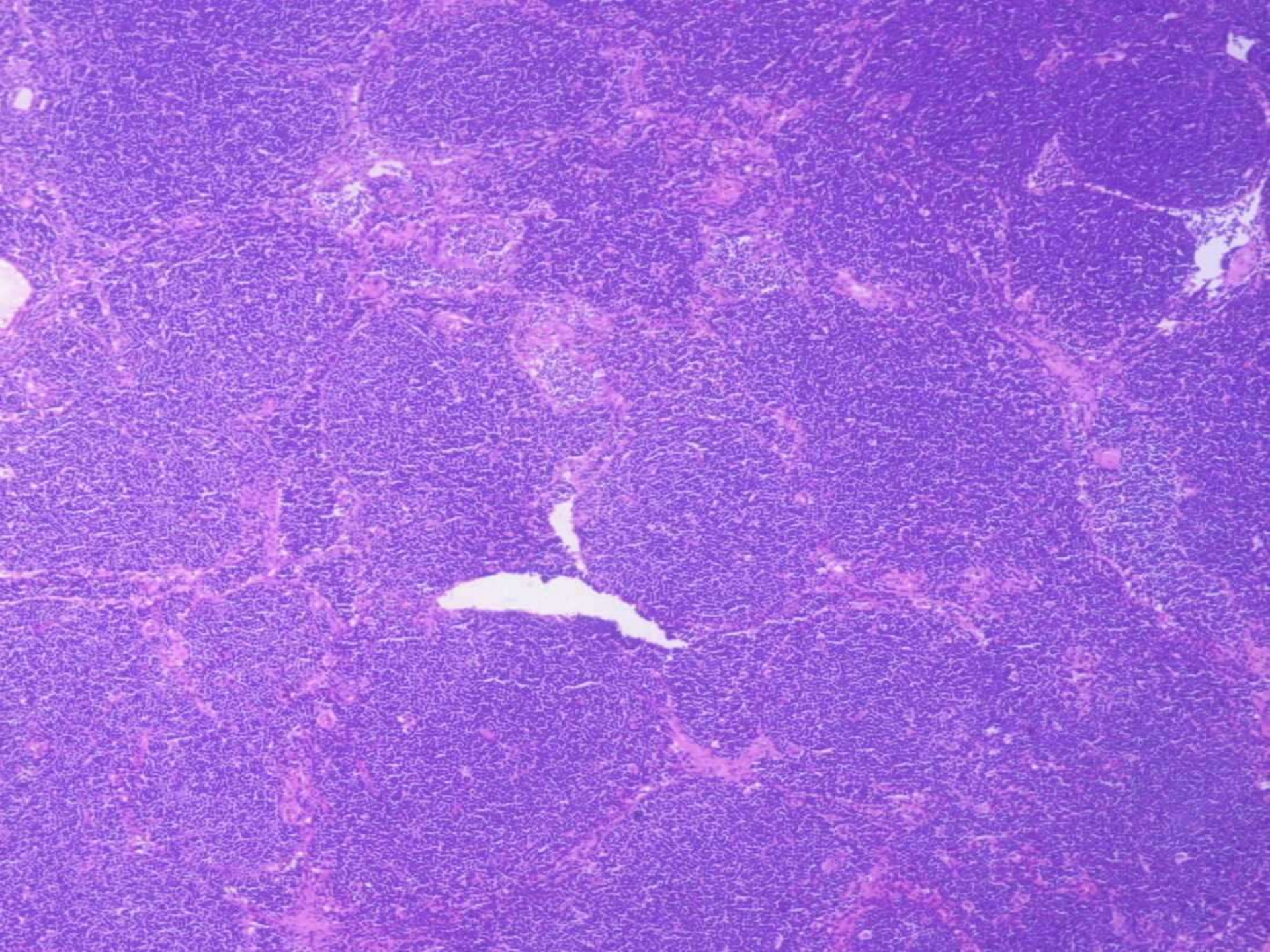
MCL – diffuse pattern

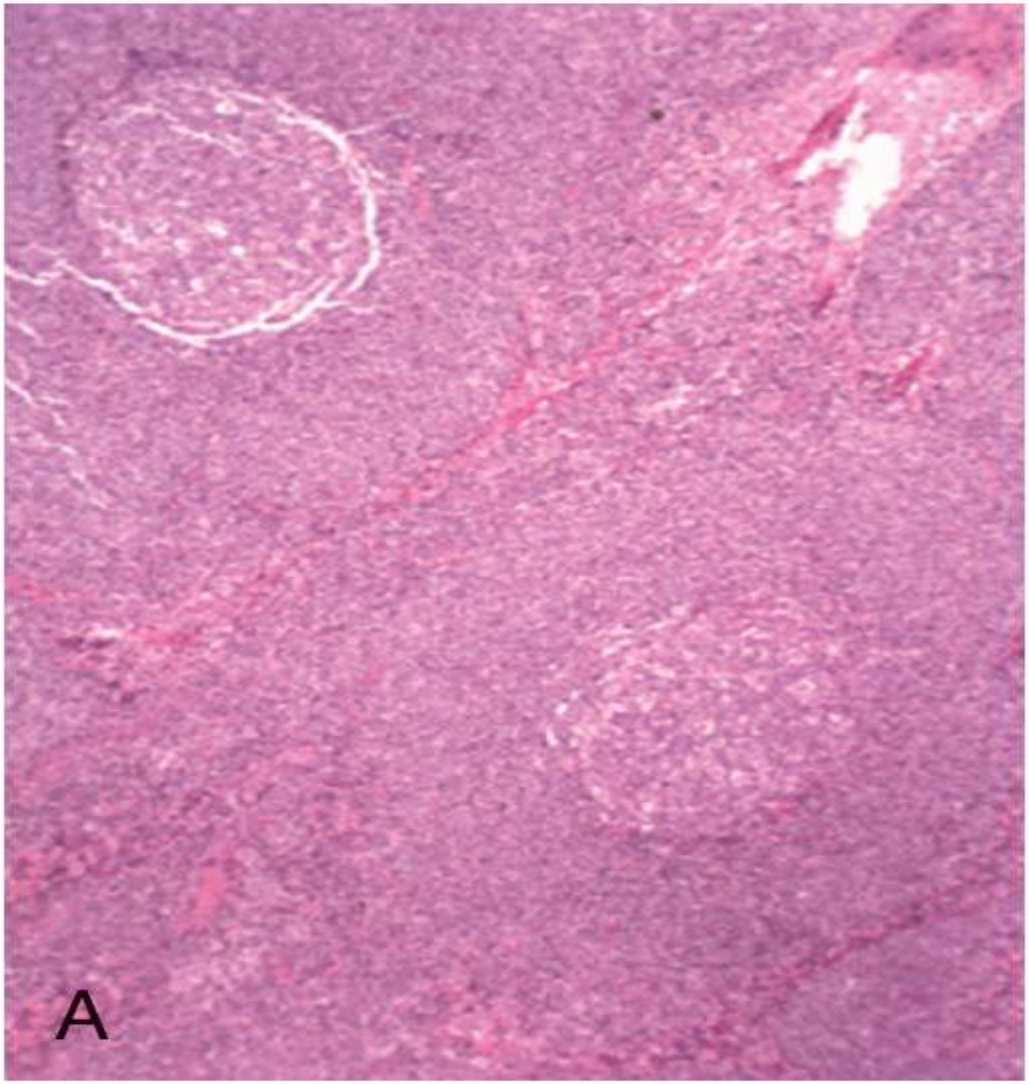


MCL - histiocytes

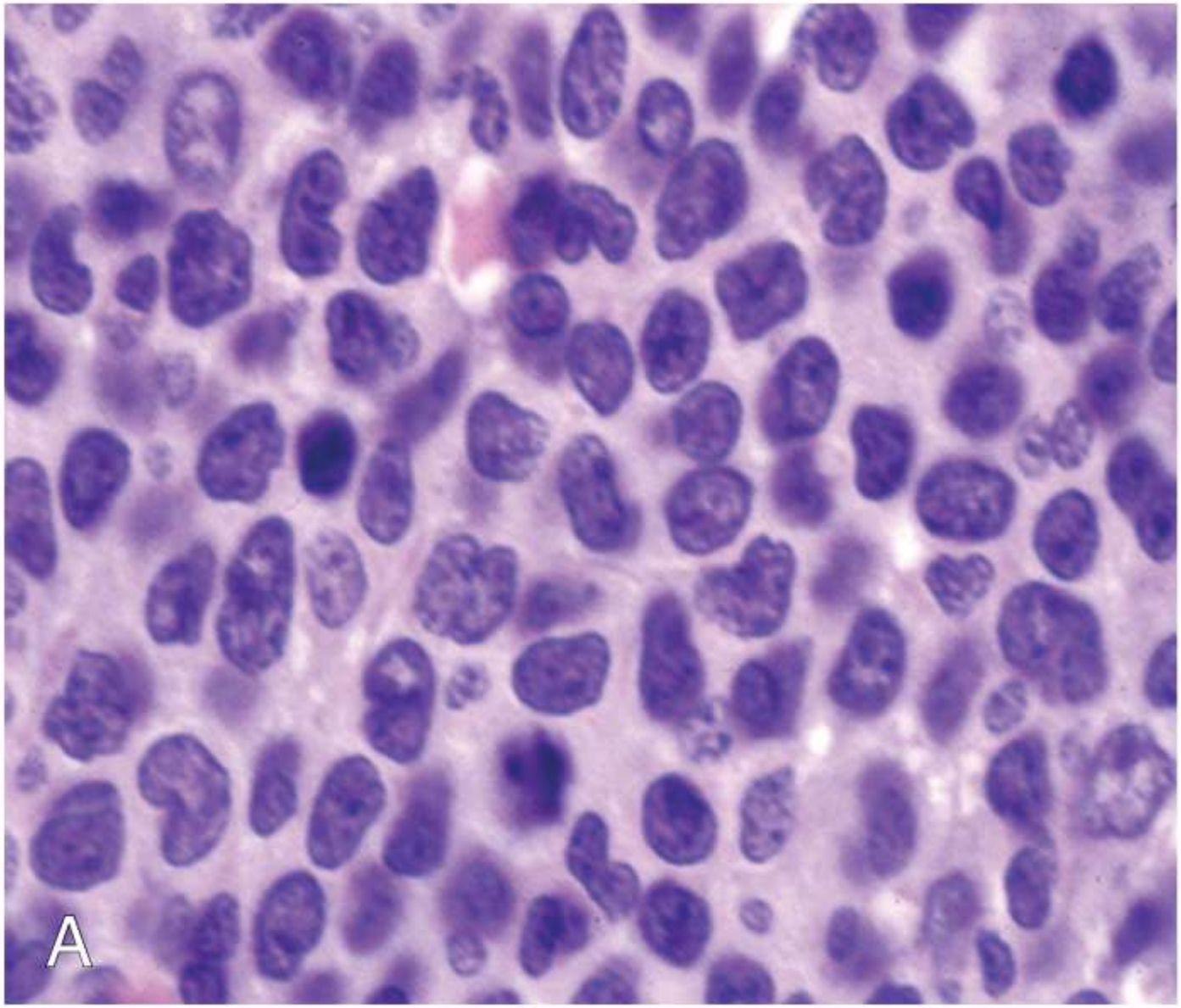


MCL – Nodular pattern

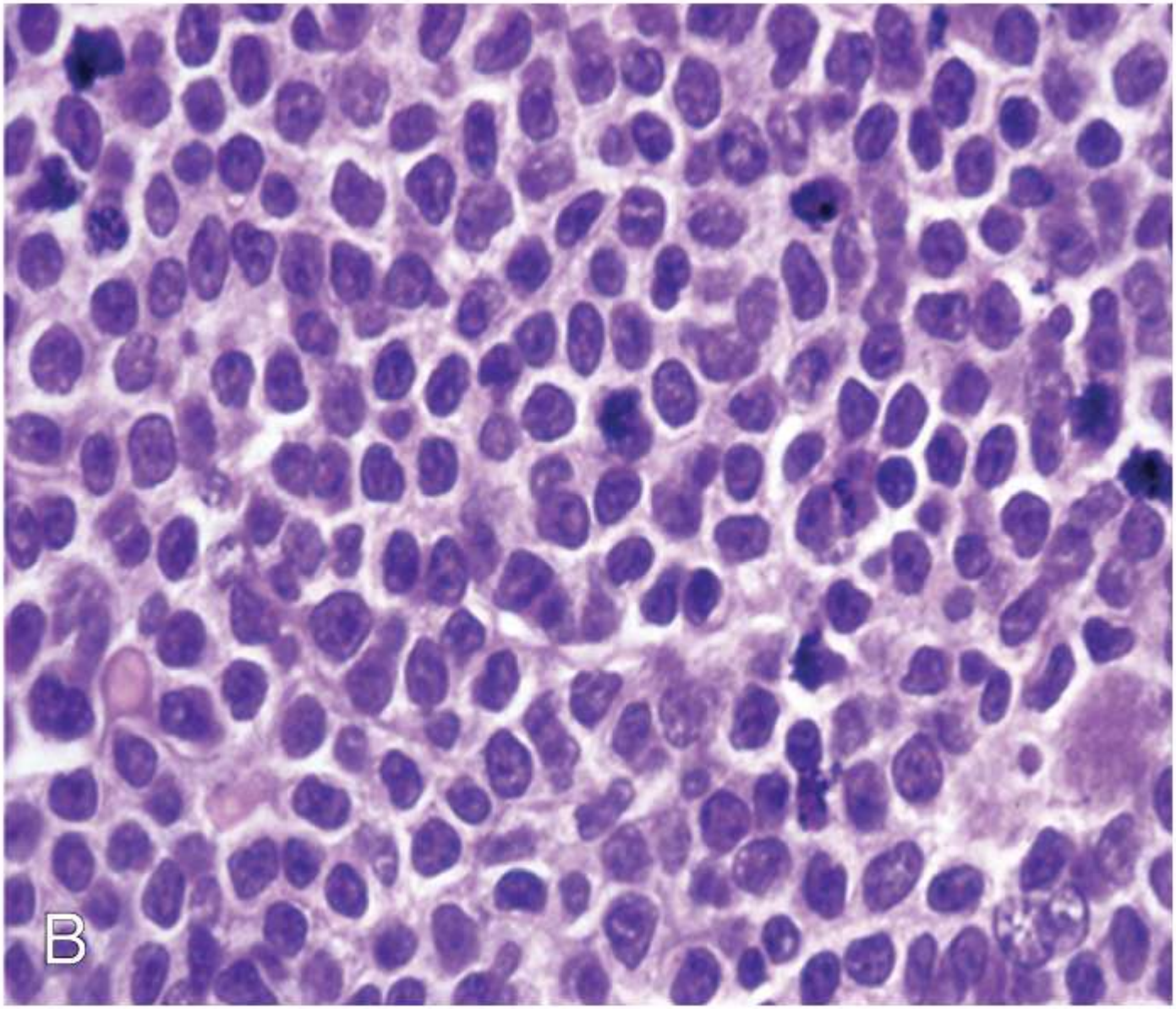




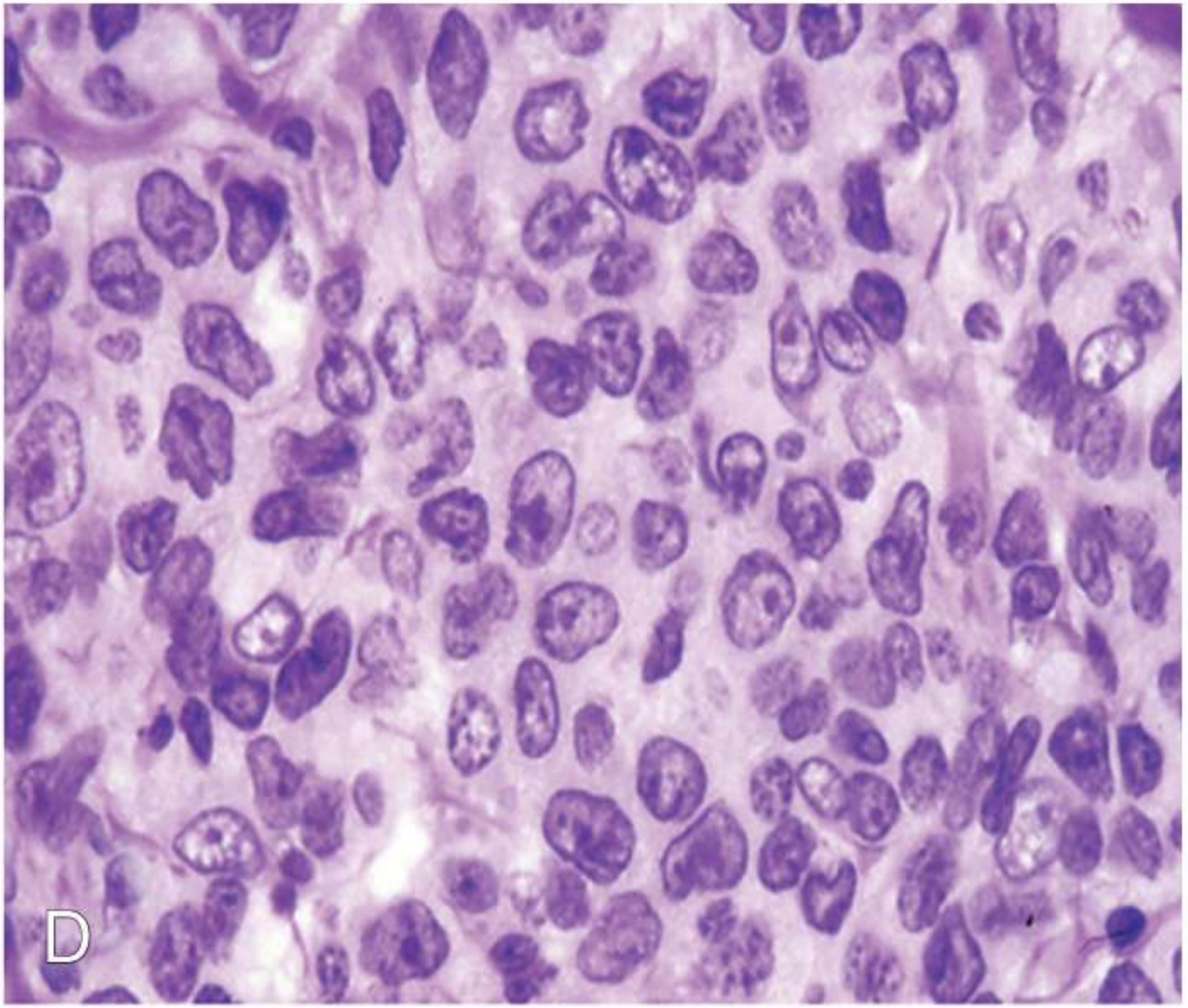
MCL - Mantle zone pattern



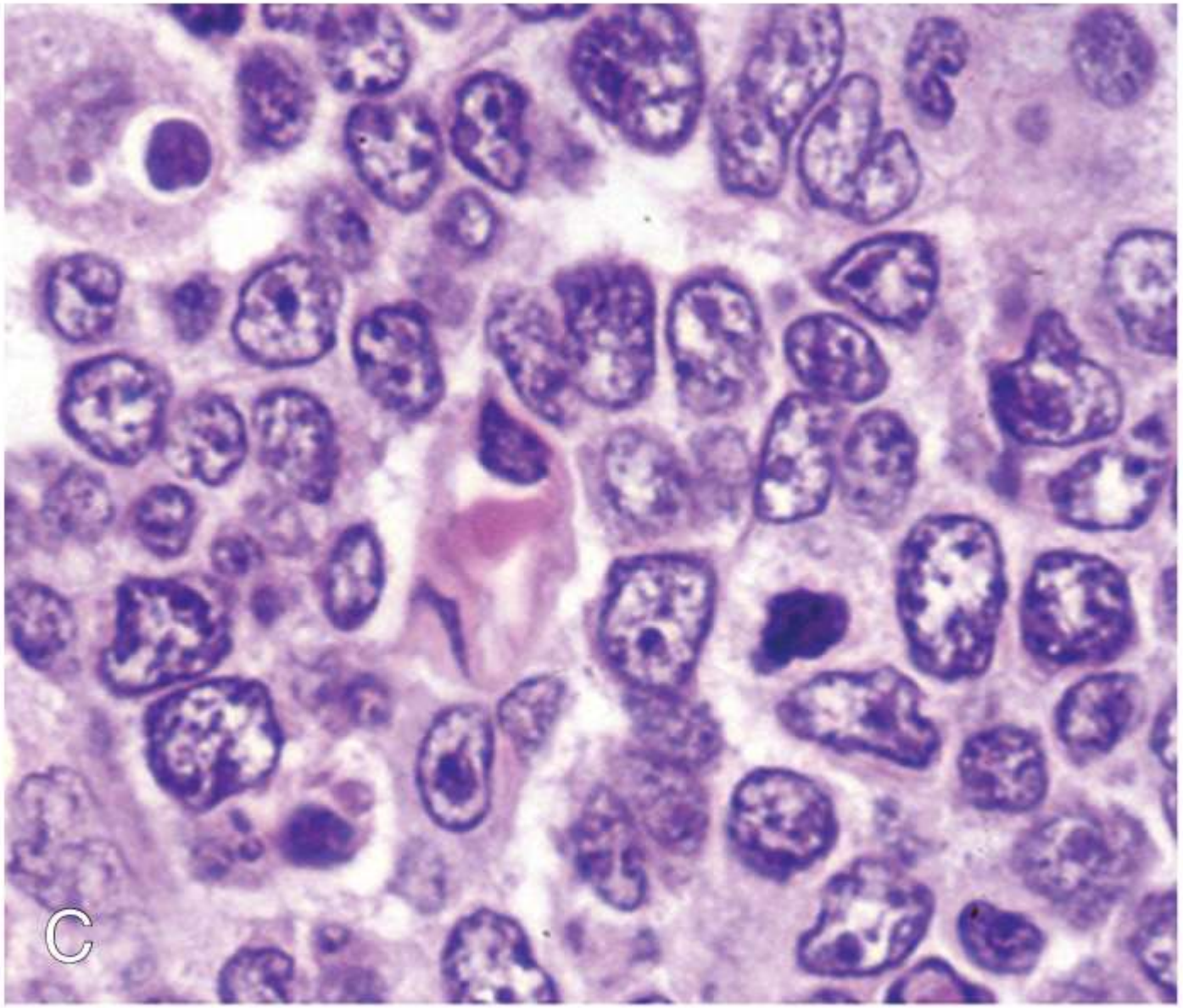
MCL – centrocyte like cells



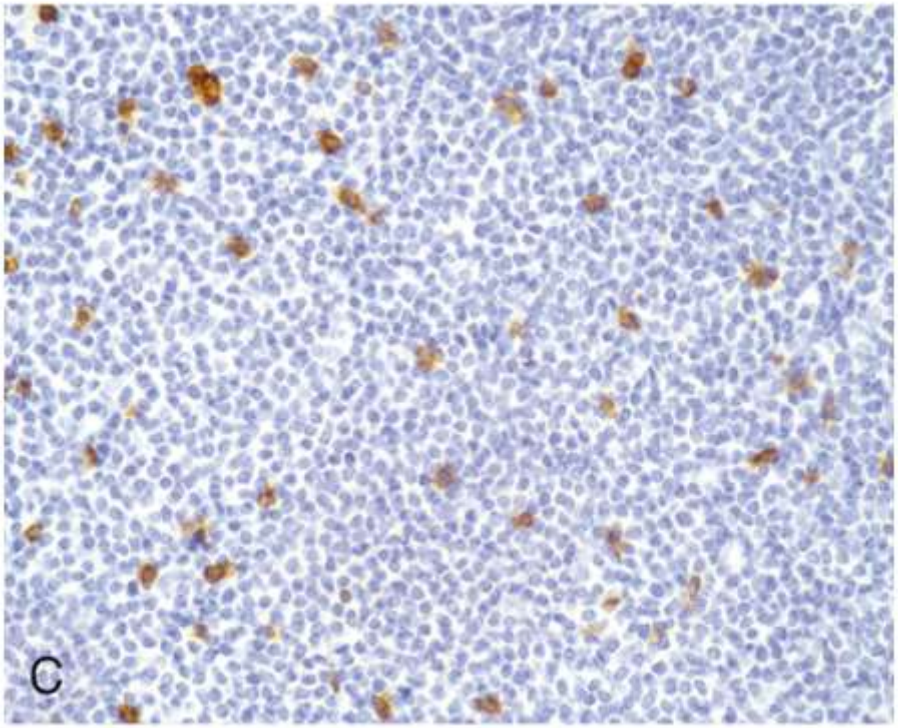
MCL – small lymphocytes



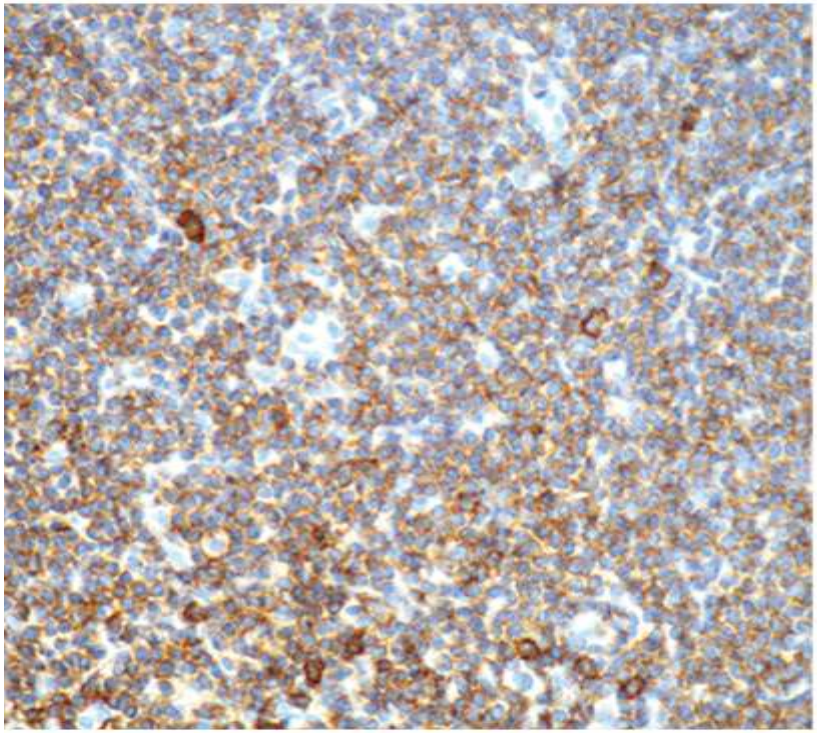
MCL – pleomorphic variant



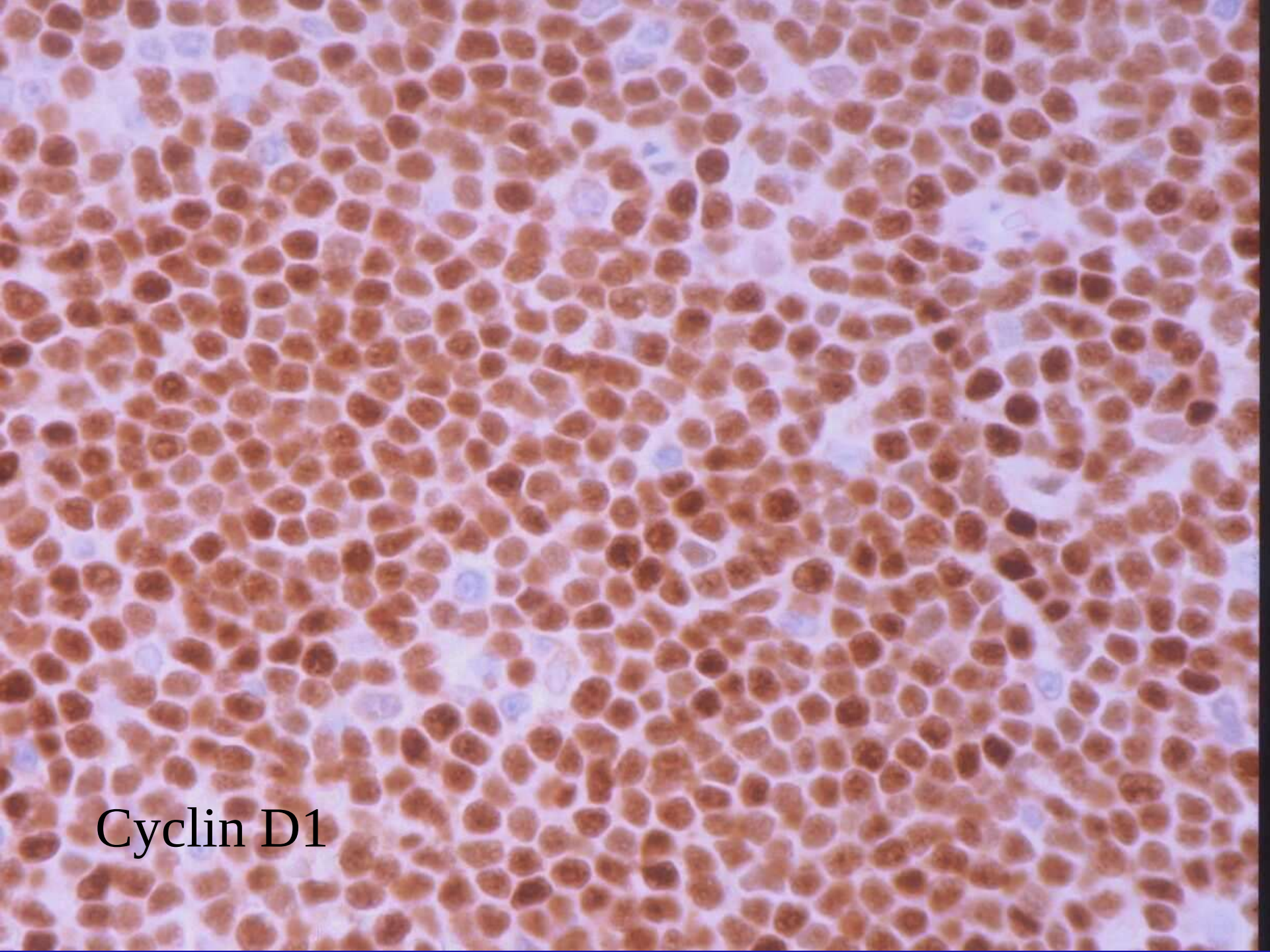
MCL – blastoid variant

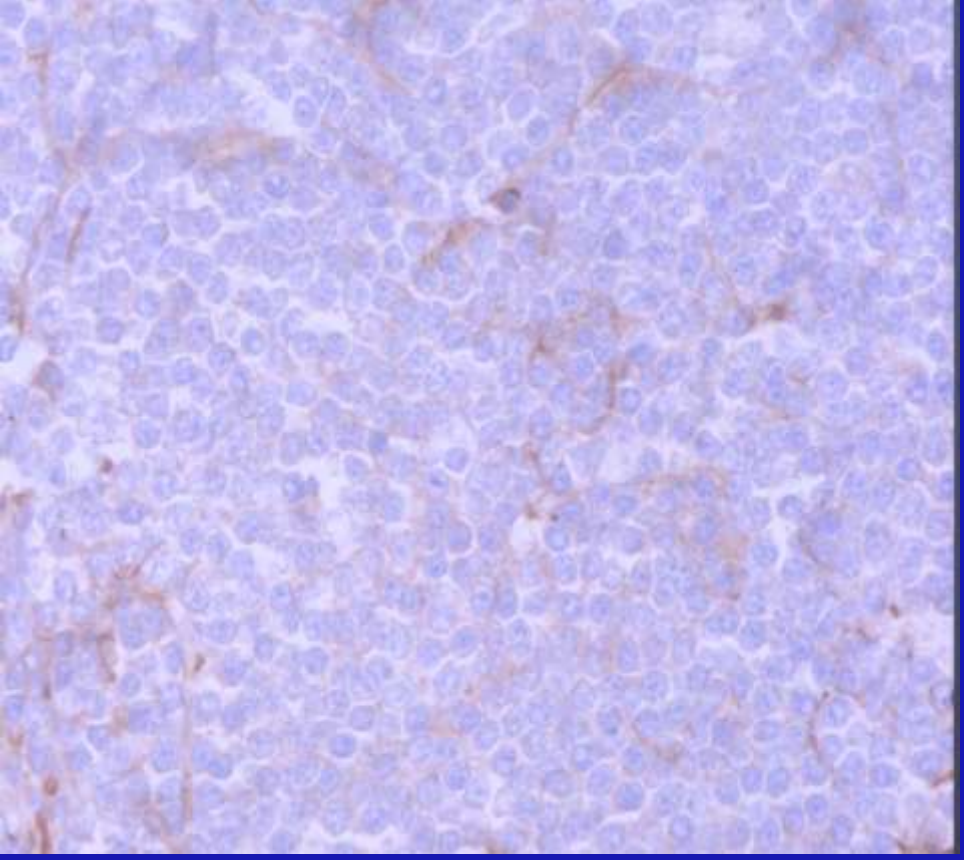


MCL – CD3

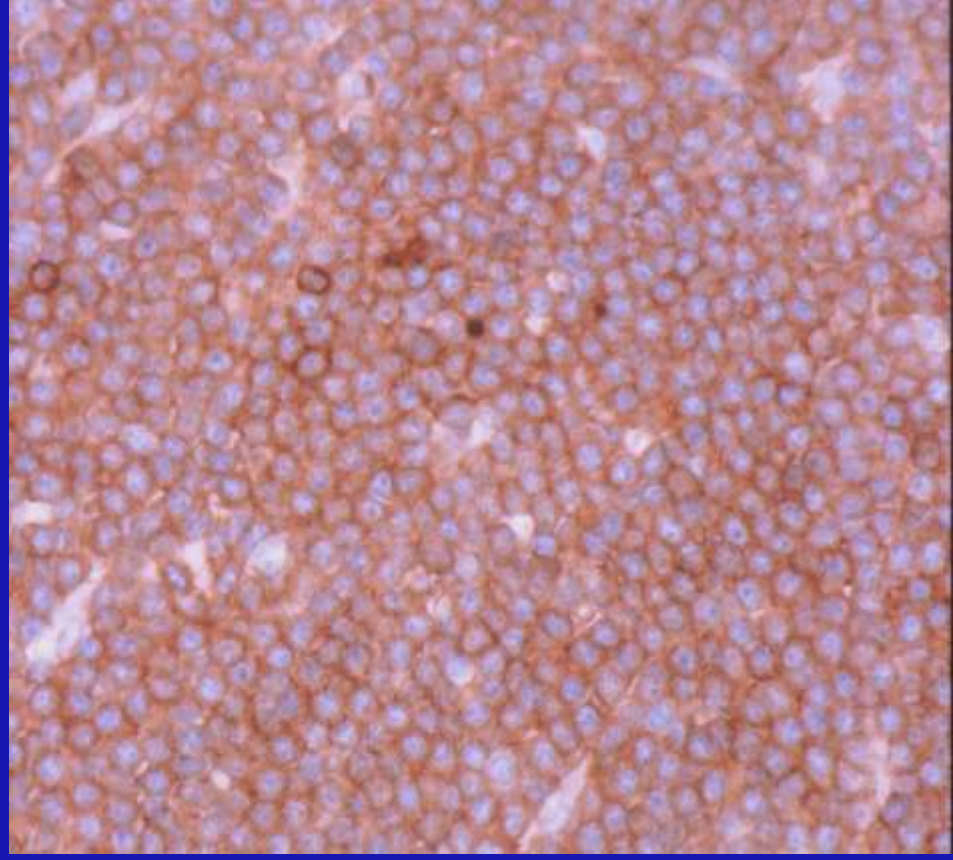


MCL – CD5


Cyclin D1

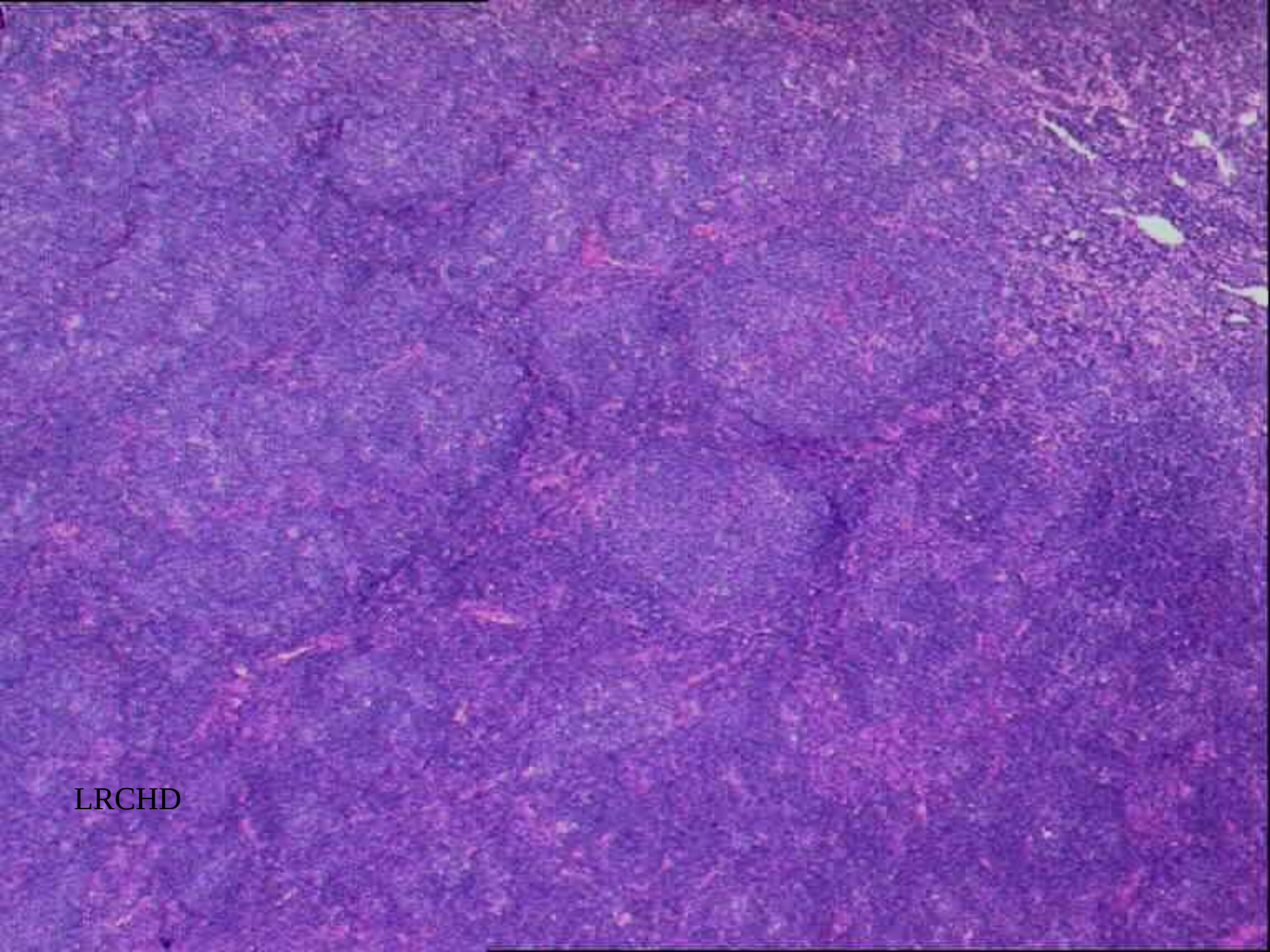


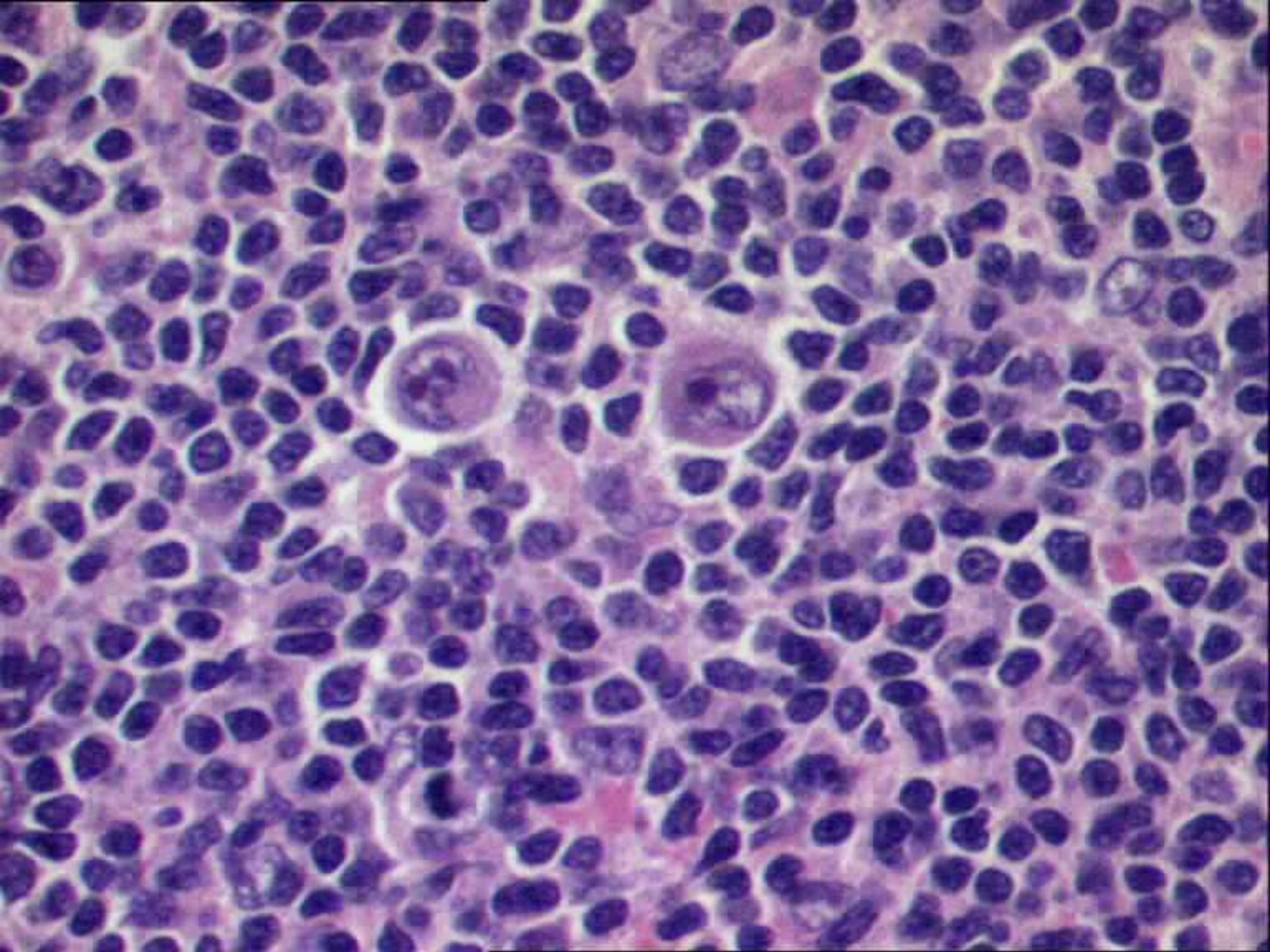
kappa

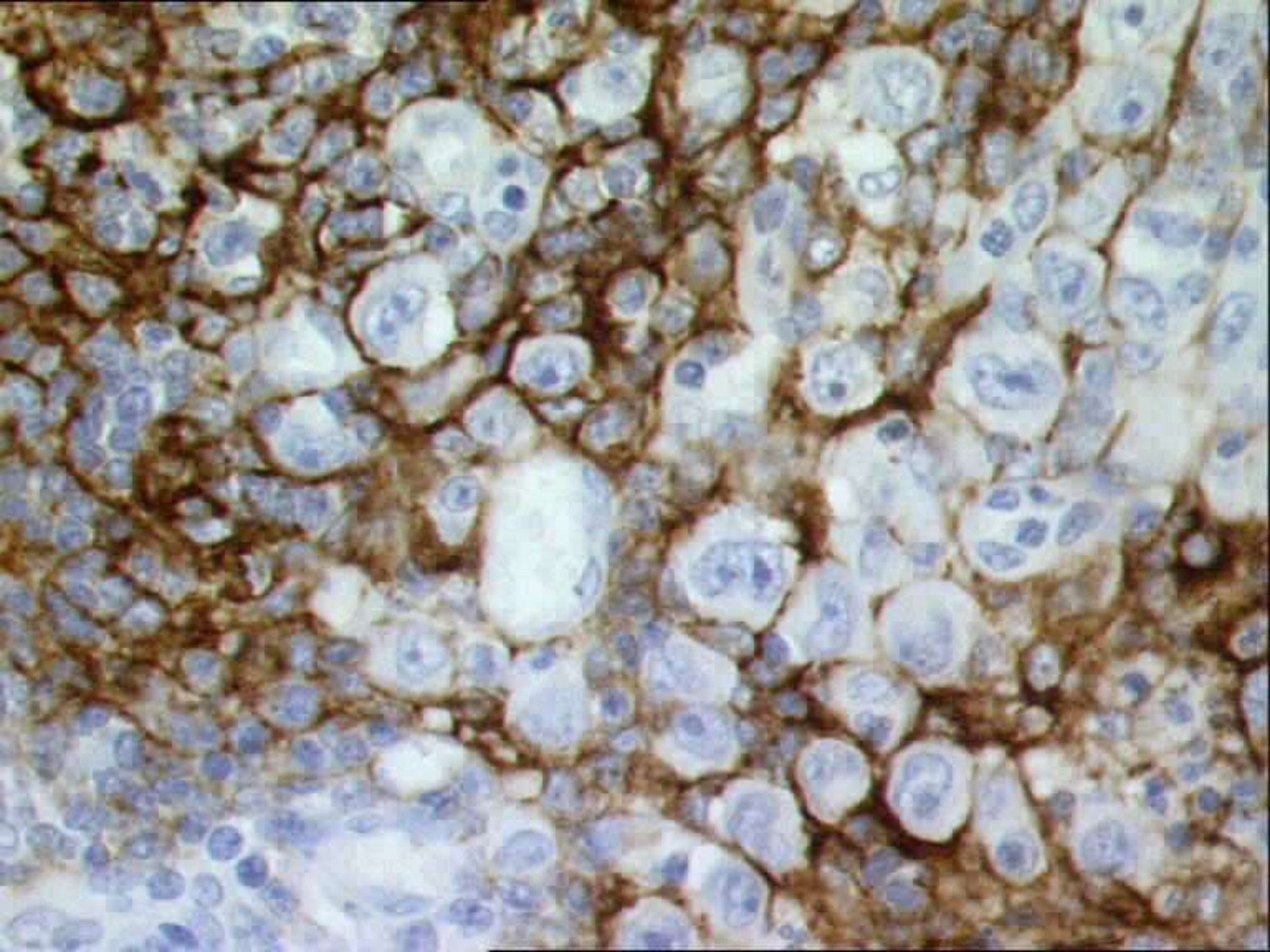


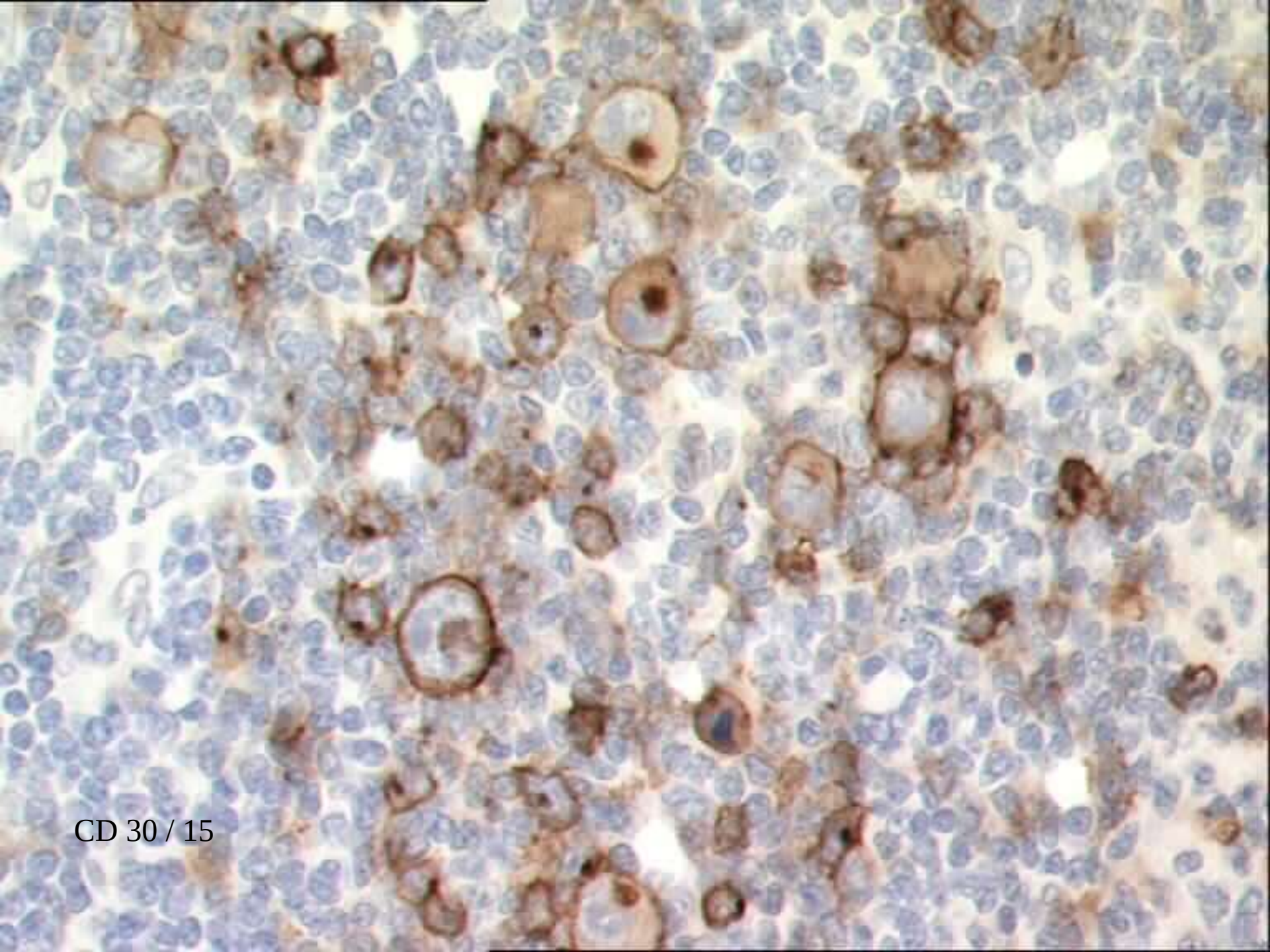
lambda

What’s this one?

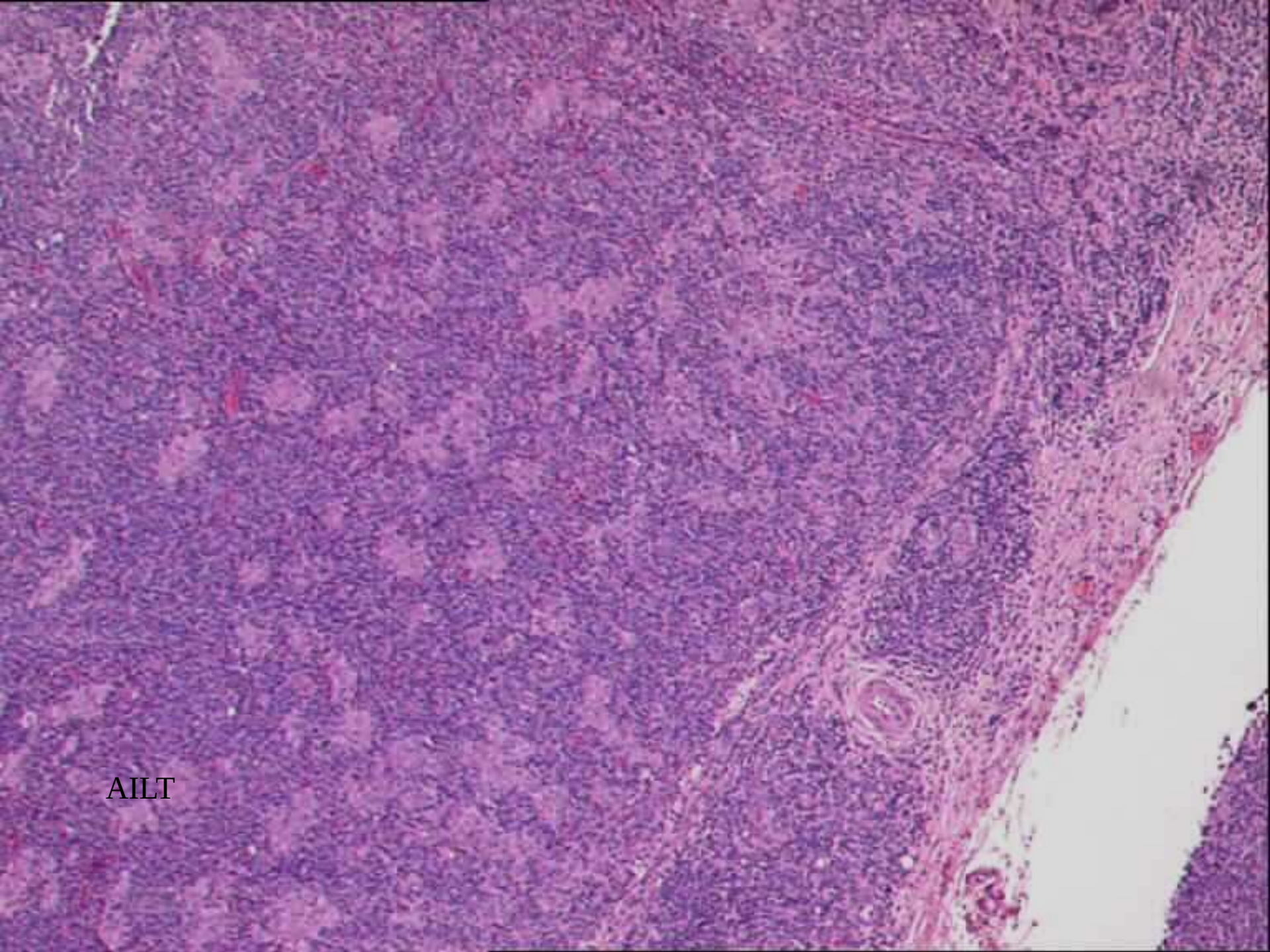

LRCHD

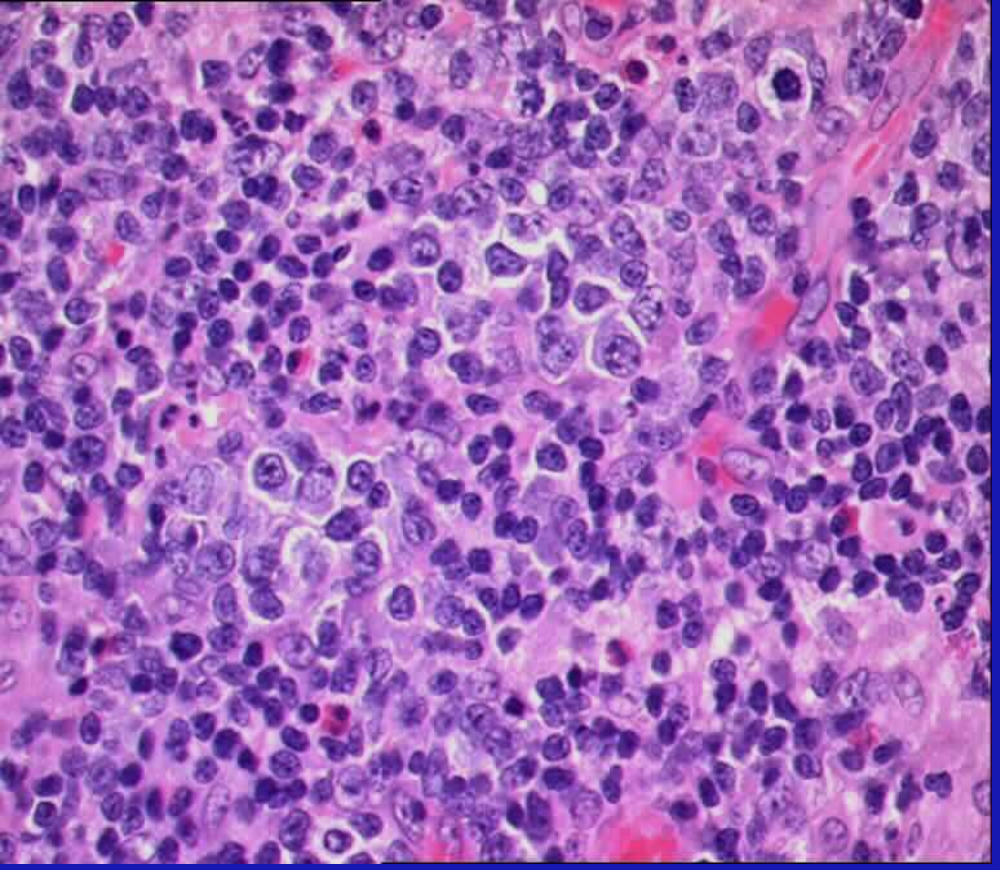




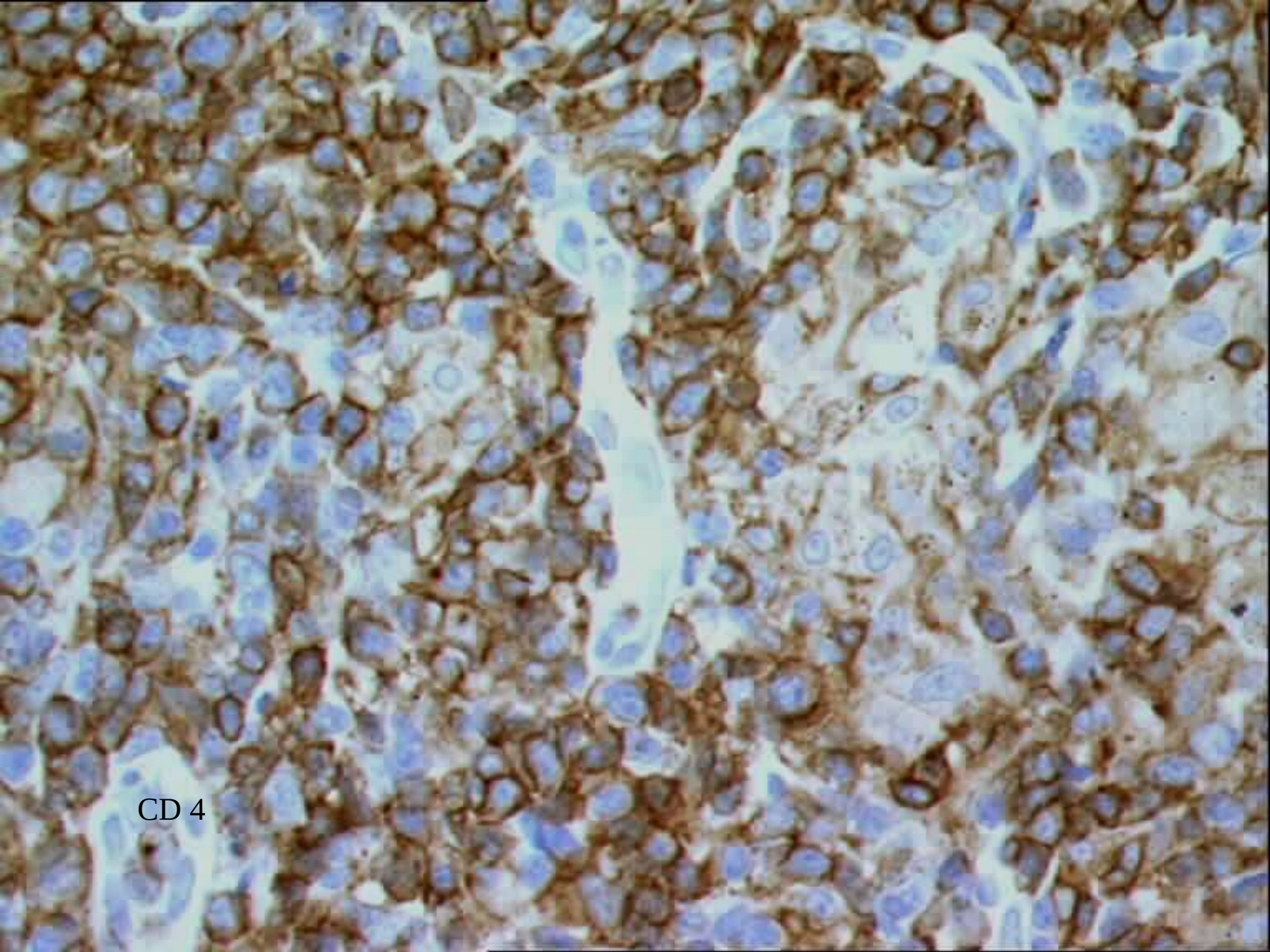

CD 30 / 15

Two more follicular tricksters…….


AILT



CD 21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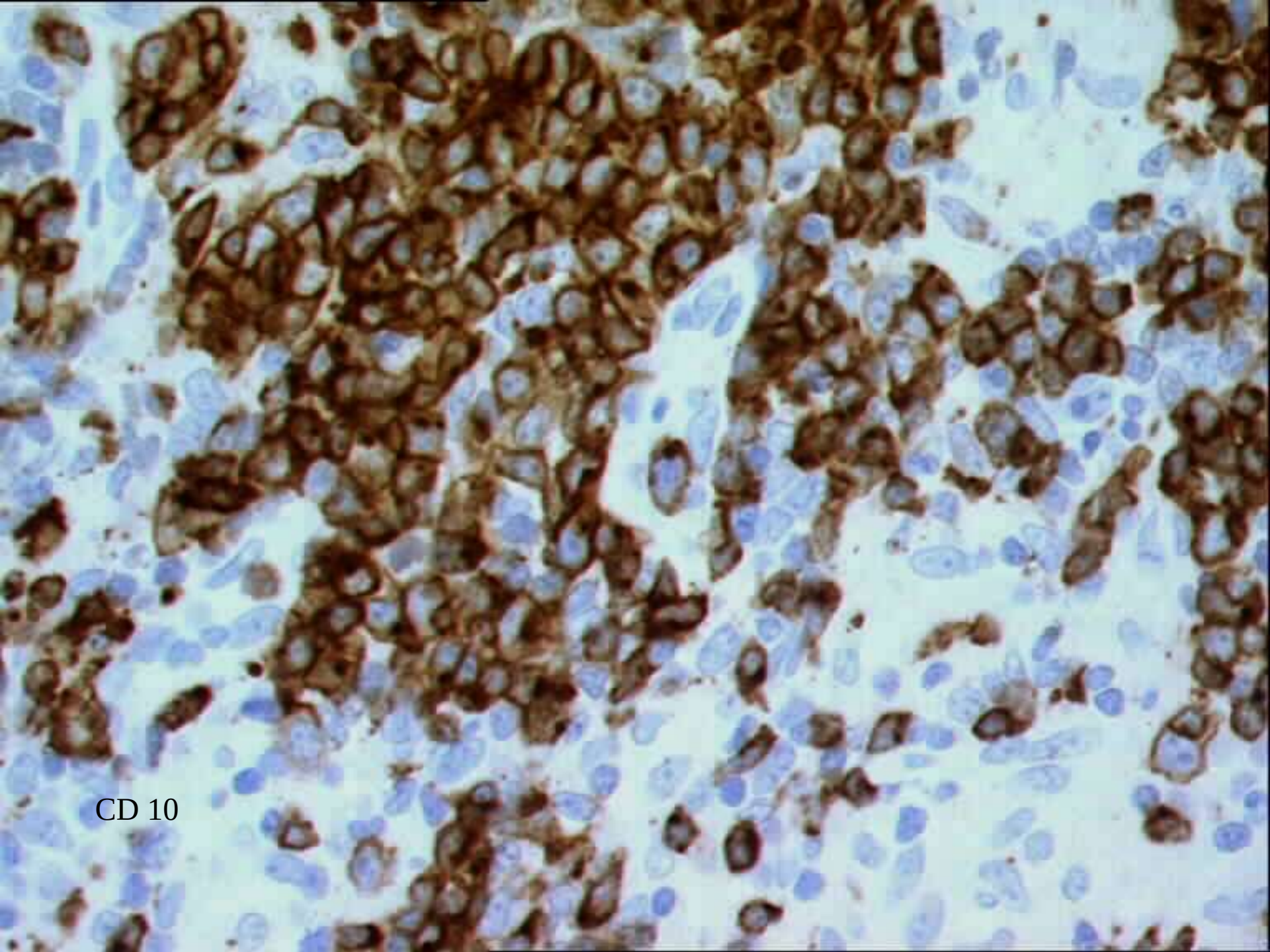
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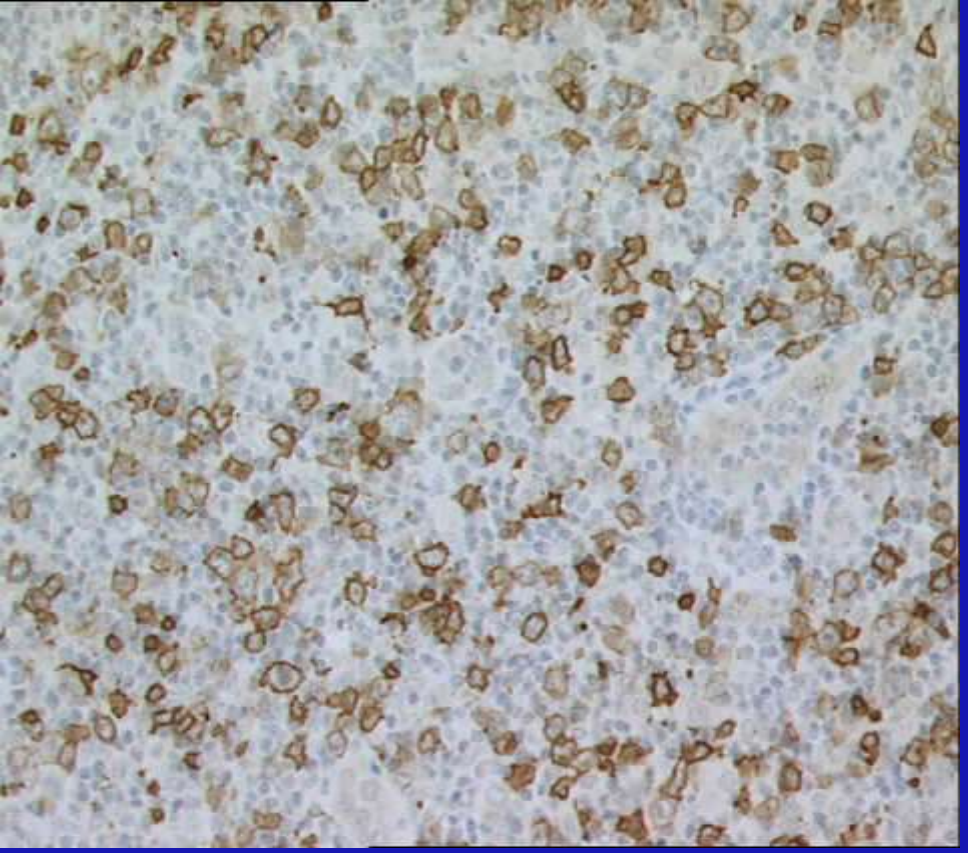

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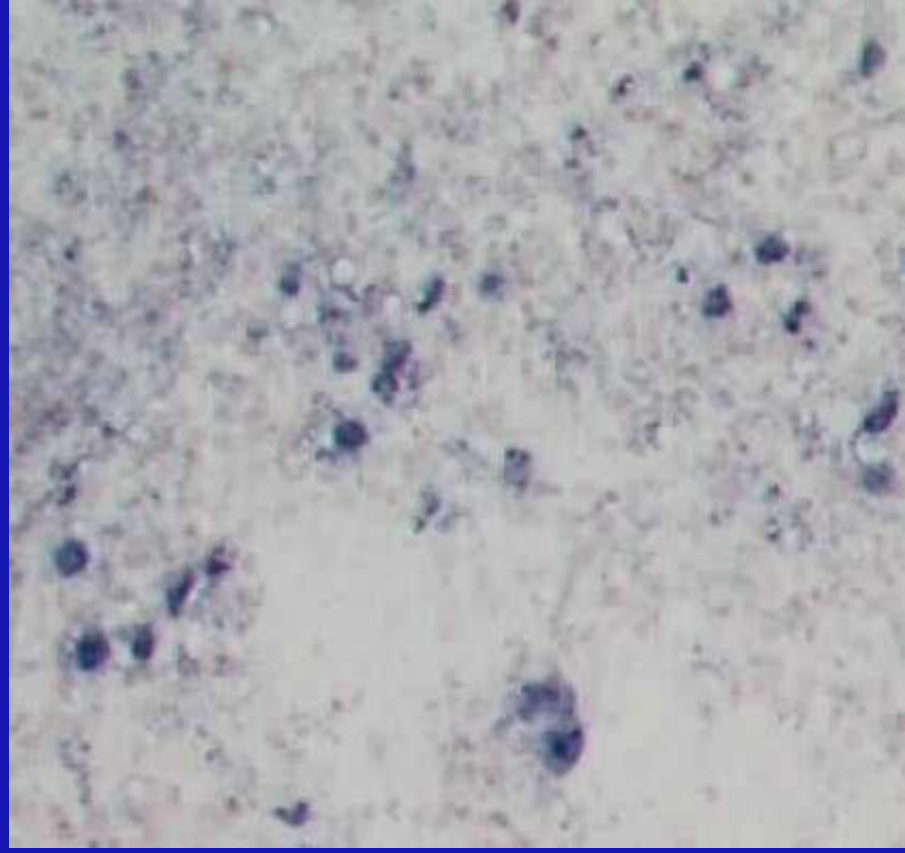
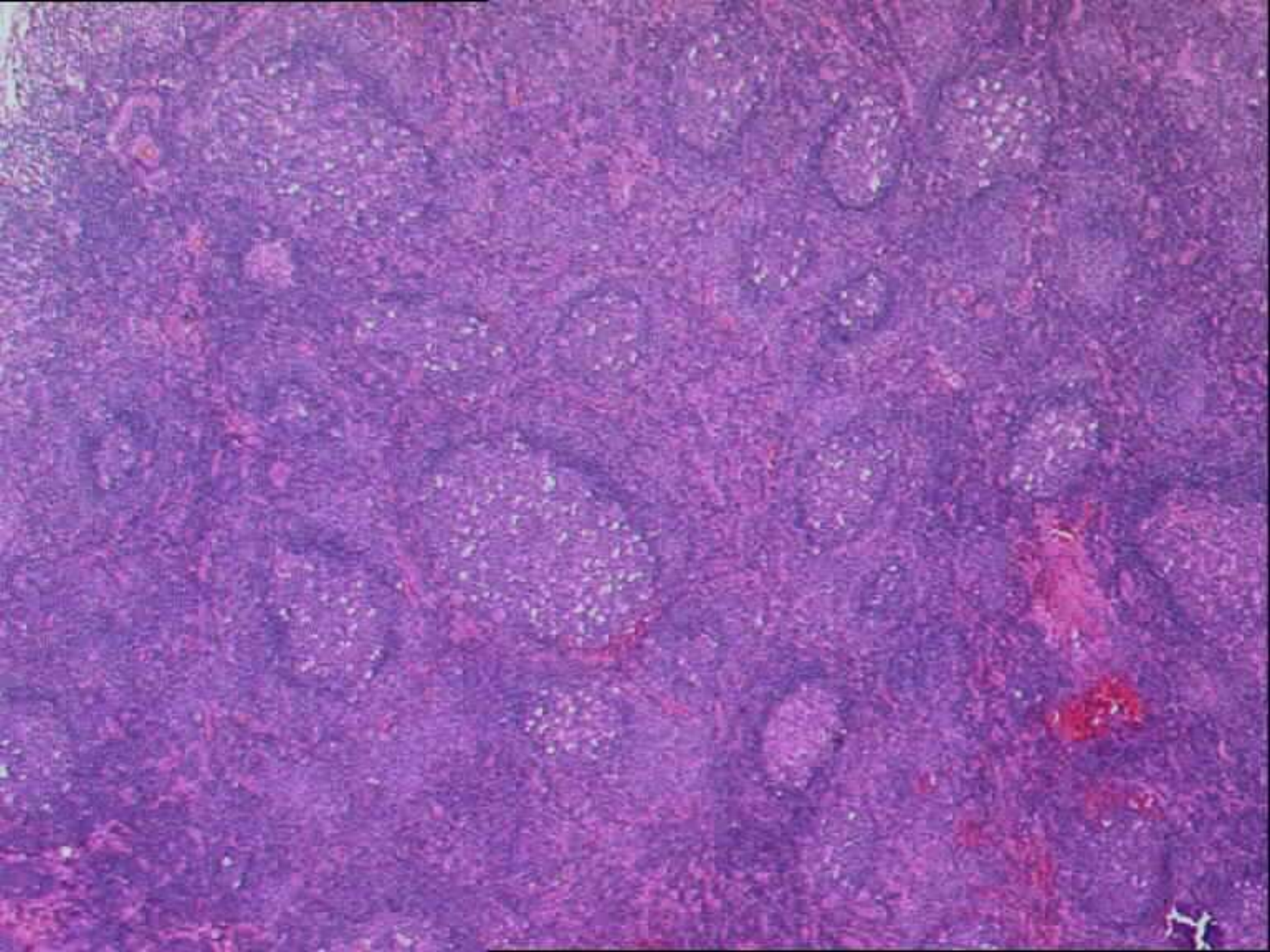
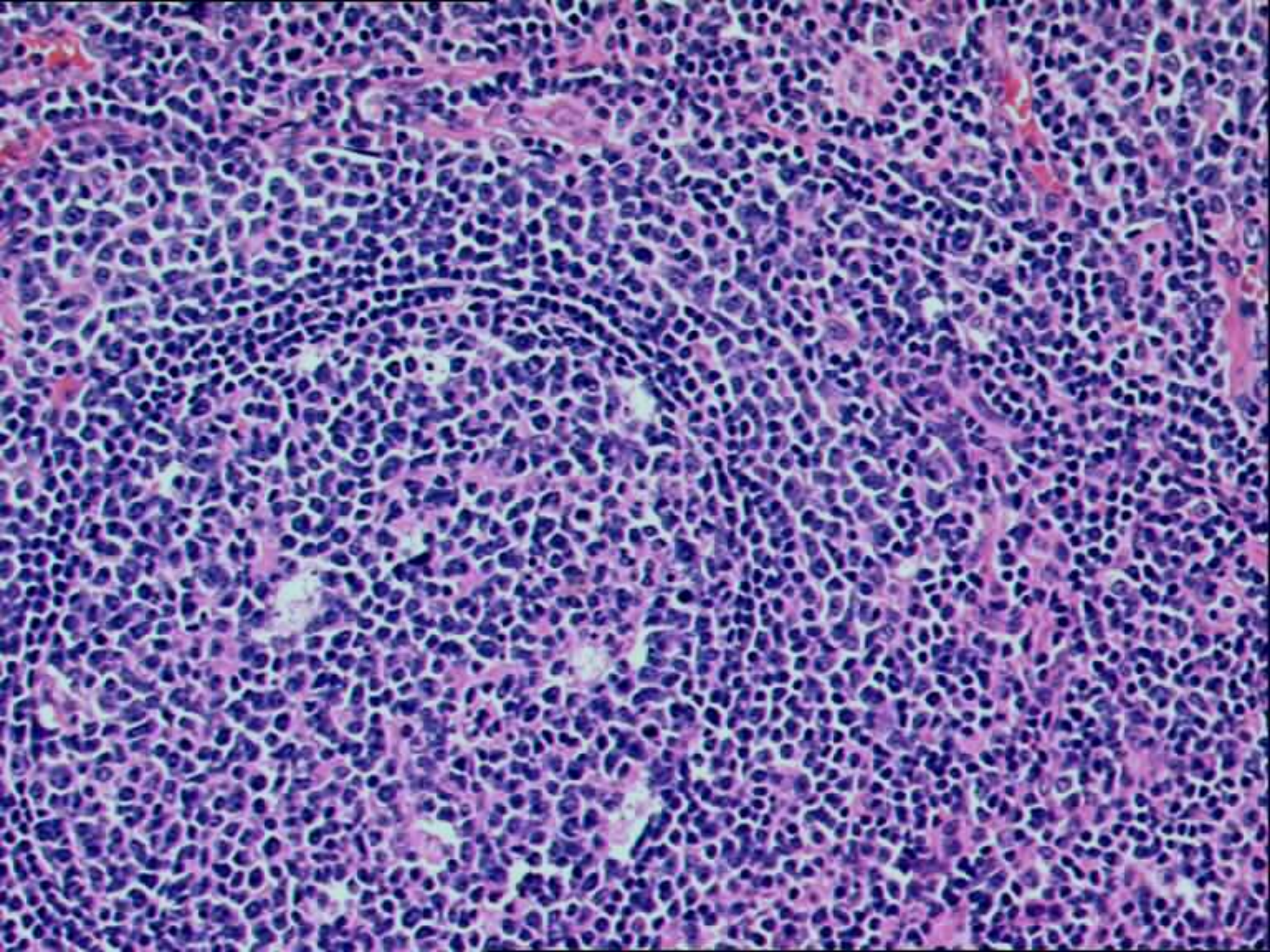


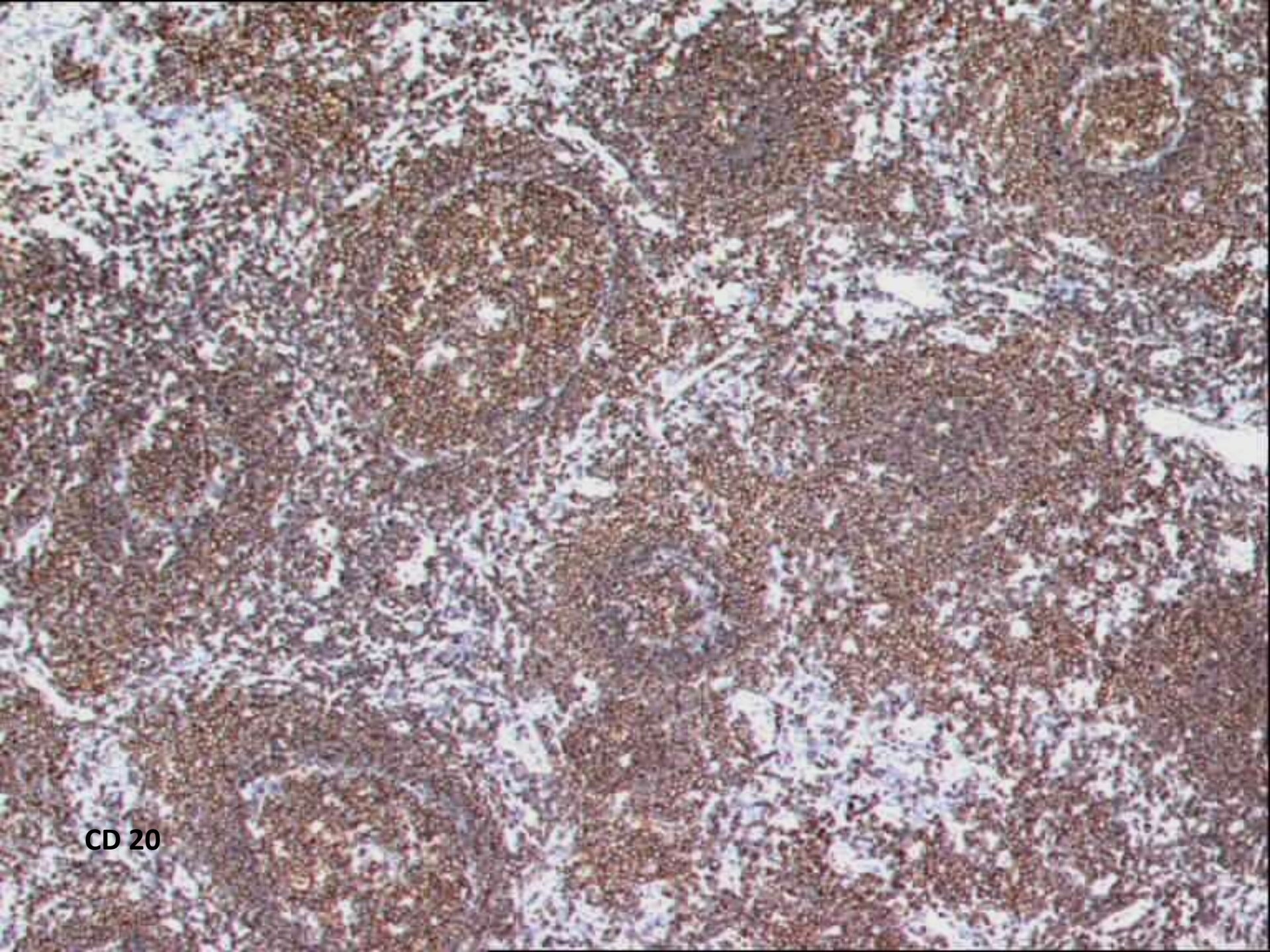
EBER

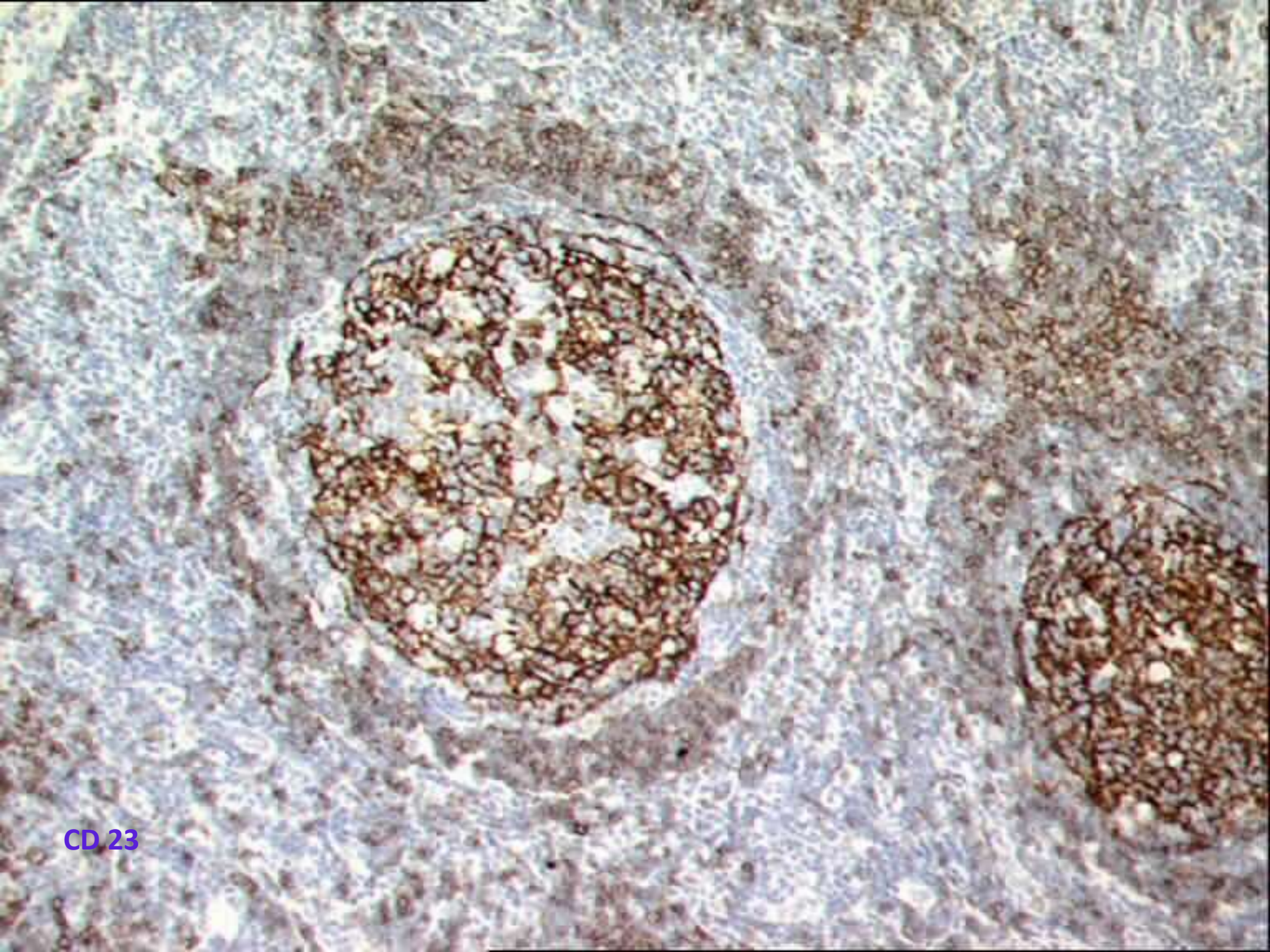
Answer: Angioimmunoblastic T cell lymphoma

What’s this one?






CD 20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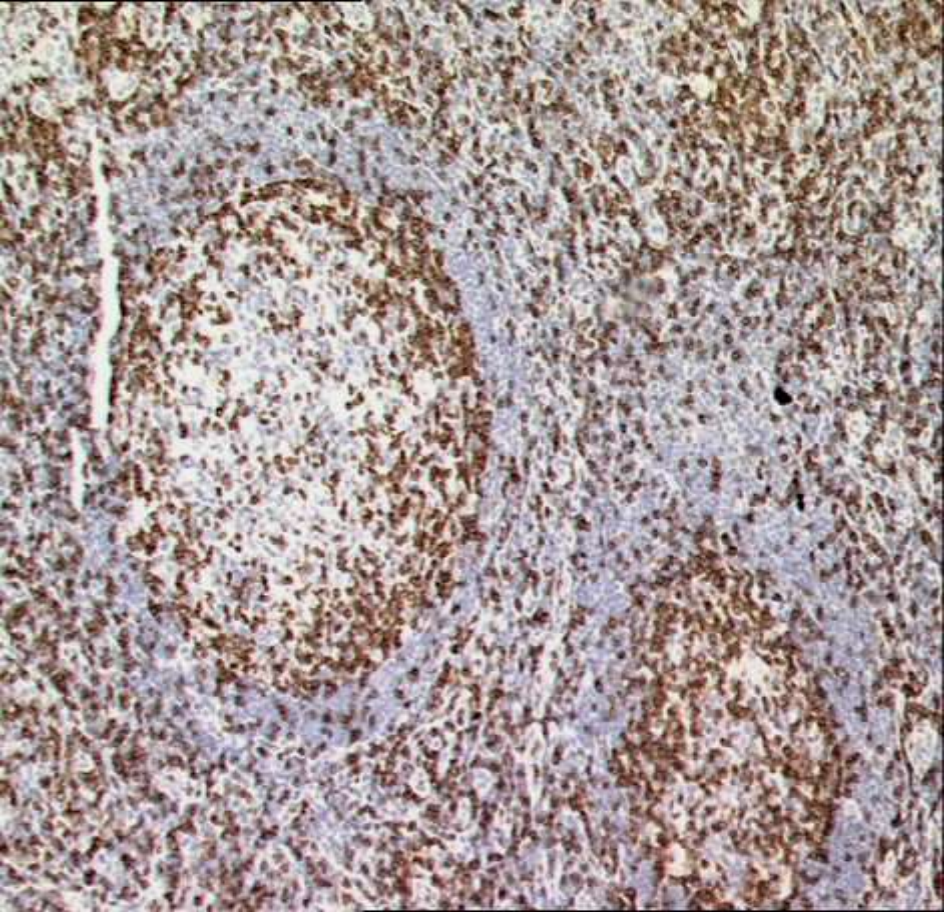
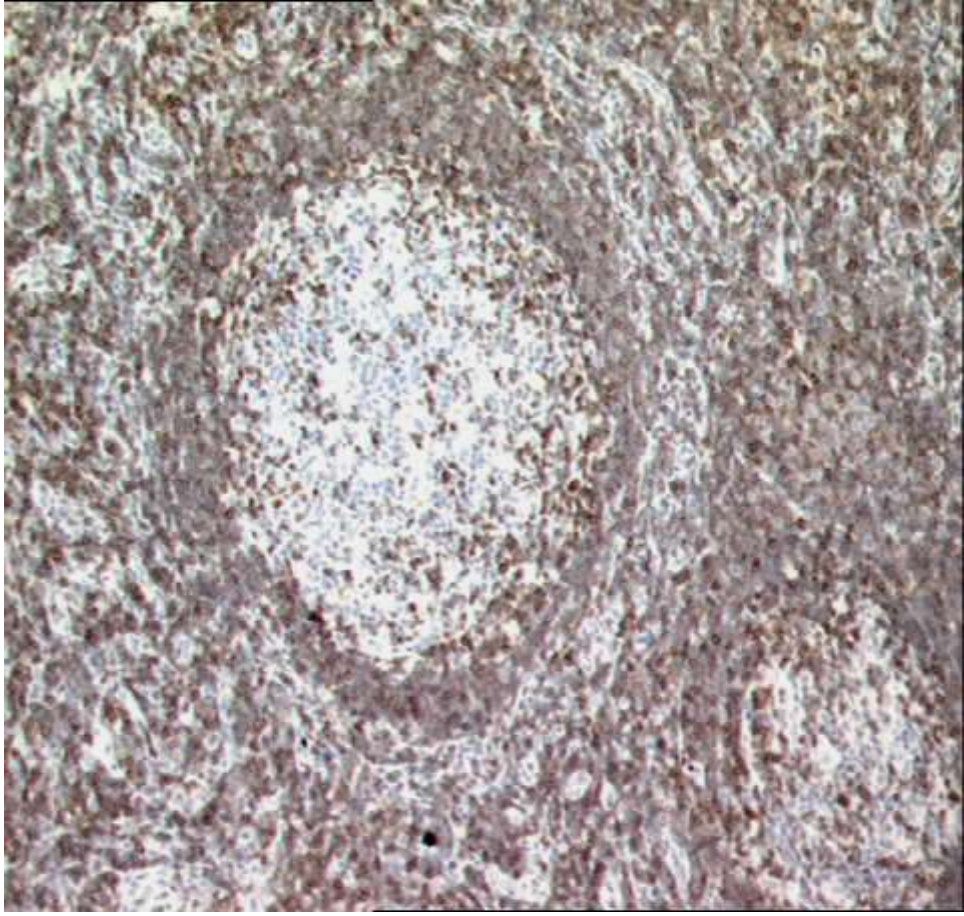


CD 3



CD 5

Answer: CLL / SLL

Other lymphomas with a marginal zone pattern

1. Follicular lymphoma
2. Mantle cell lymphoma
3. Peripheral T cell lymphoma
4. Lymphoplasmacytic lymphoma

(Benign proliferation)