Gastrointestinal Lymphomas

a practical approach to work-up

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Lymphoma in GI tract

- Uncommon compared to GI epithelial neoplasms
- 20% of all lymphomas occur in the GI tract
- B-cell lymphomas are far more common than T-cell lymphomas
- Most common lymphoma in GI tract is diffuse large B-cell lymphoma

GI Lymphoma Distribution

- STOMACH: 50-60%; 5-10% of all gastric malignancies
- SMALL BOWEL: 30%; 25% of all small intestinal malignancies
- COLON: 10%; 0.5% of colonic malignancies
- ESOPHAGUS, APPENDIX, LIVER, GALLBLADDER, PANCREAS: RARE

Classic Sites of GI Lymphomas

Site	Lymphoma
Stomach	MALT Lymphoma
2nd portion of duodenum	Primary intestinal follicular lymphoma
Small intestine	EATL
Terminal ileum	Burkitt lymphoma
Colonic polyps	Mantle cell lymphoma (lymphomatous polyposis)
Entire GI tract	DLBCL

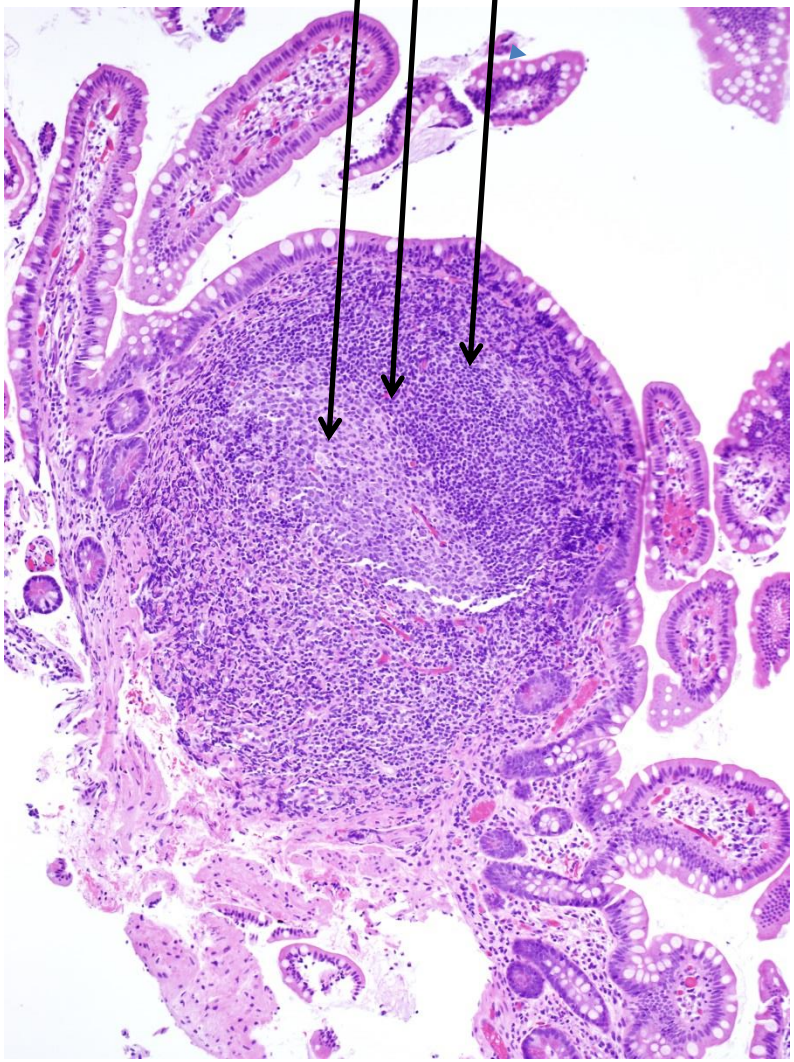
Evaluation: Clinical clues

- Patient's age and immune status
  - Young patients have more normal mucosa-associated lymphoid tissue (MALT)
  - Immune system undergoes senescence with age
  - Immunosuppression leads to decreased efficiency of immune surveillance against malignancy
  - Chronic inflammatory conditions (eg. IBD)
- Infection +/- treatment status

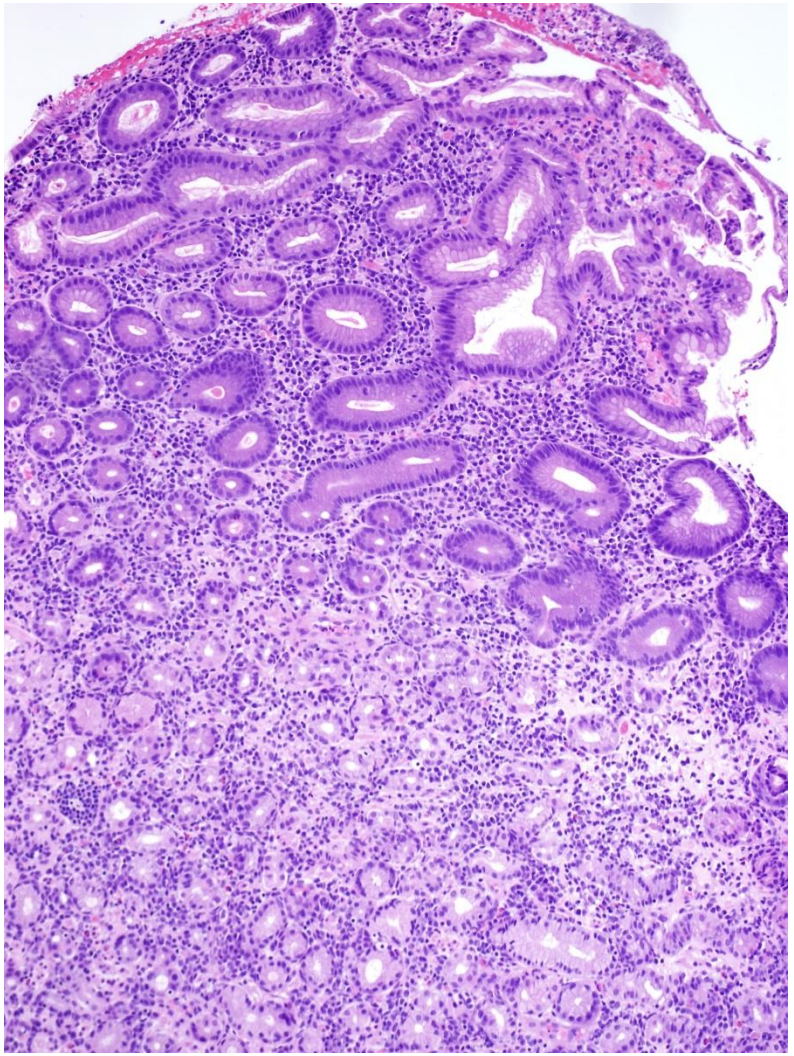
Evaluation: Endoscopic clues

- Native and acquired MALT populations
  - Terminal ileum Peyer patches may appear as visible mucosal nodularity or small polyps
  - H. pylori-associated gastritis may appear as normal mucosa or as erythema +/- ulcers
  - Rectal lymphoid hyperplasia (rectal tonsil / rectal lymphoid polyp) may be polypoid and span up to 1cm
- Lymphomas
  - Tend to form mass lesions +/- ulcers +/- perforations, but not always

Evaluation: Histologic clues



Peyer patch (native MALT)



H. pylori gastritis (acquired MALT)

Evaluation: Ancillary studies

- Immunohistochemical stains
  - Comprehensive panel vs Select stains
    - CD3, CD20 (or Pax5), CD43
  - Important prognostic markers
- Molecular/cytogenetic studies
  - Diagnostic gene rearrangements, specific translocations
  - Immunoglobulin or T-cell receptor gene rearrangements
- Flow cytometry

Evaluation: Additional Complexities

- Does a “label” of lymphoma lead to appropriate management?
- Toughest when the process is small and/or early
  - Is it really lymphoma?
    - Or inflammatory process?
    - Or normal MALT?
  - Endoscopic impression?
  - How can it be followed?
  - Should it be treated and how?

Some Practical Examples

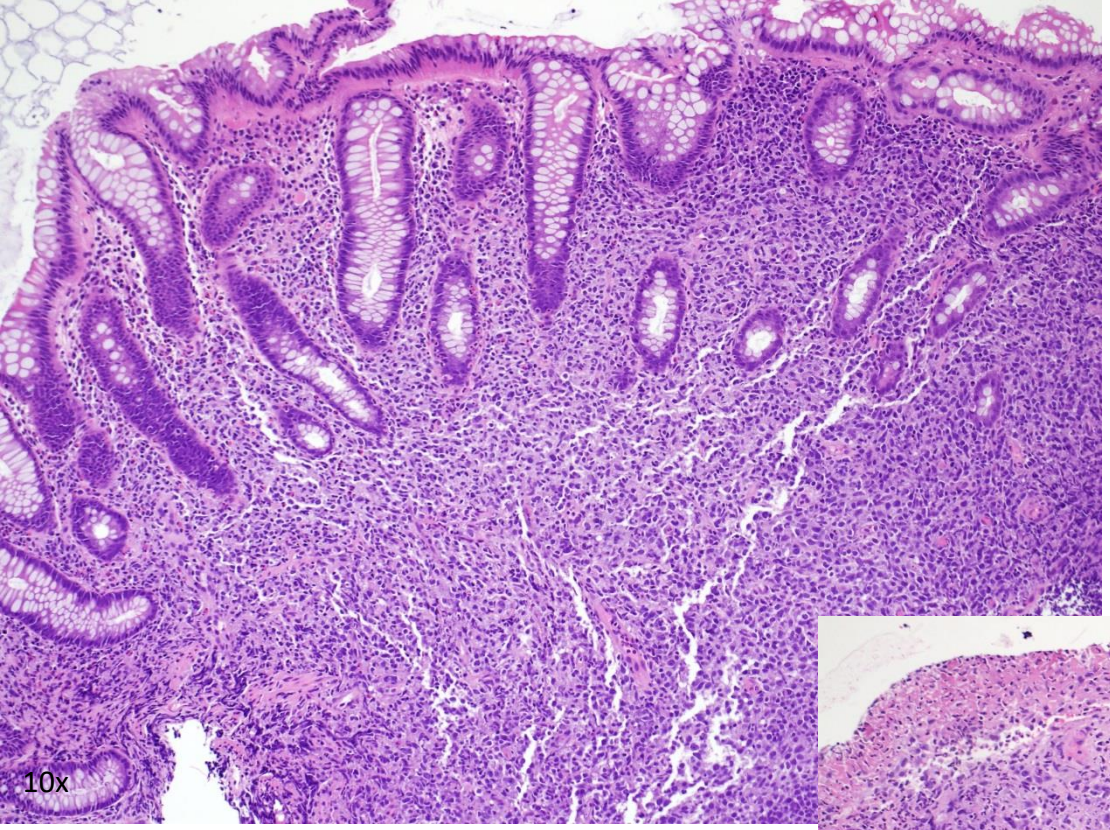
- Diffuse Large B-cell Lymphoma
- Extranodal Marginal Zone Lymphoma of Mucosa-associated Lymphoid Tissue
- Follicular Lymphoma
- Mantle Cell Lymphoma
- Burkitt Lymphoma
- Enteropathy-Associated T-cell Lymphoma
- Monomorphic Epitheliotropic Intestinal T-cell Lymphoma
- NK/T Lymphoma, nasal type
- Hepatosplenic T-cell lymphoma

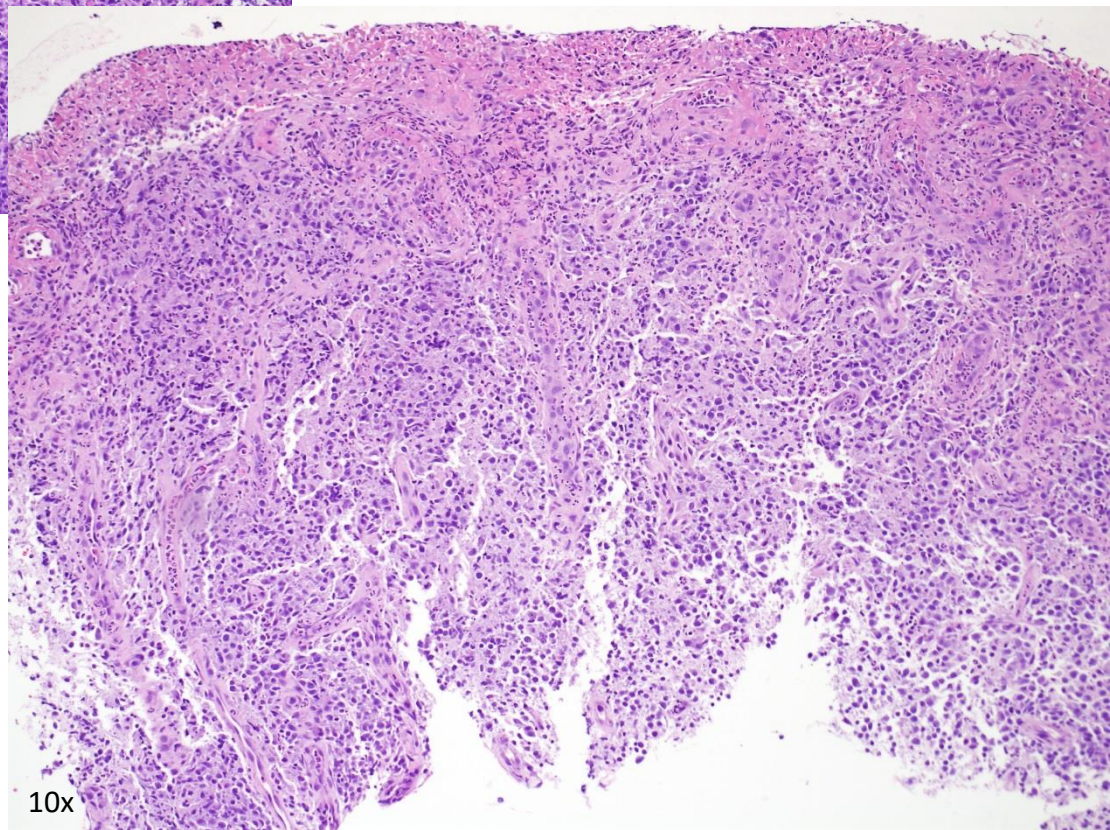
Diffuse Large B-cell Lymphoma (DLBCL)

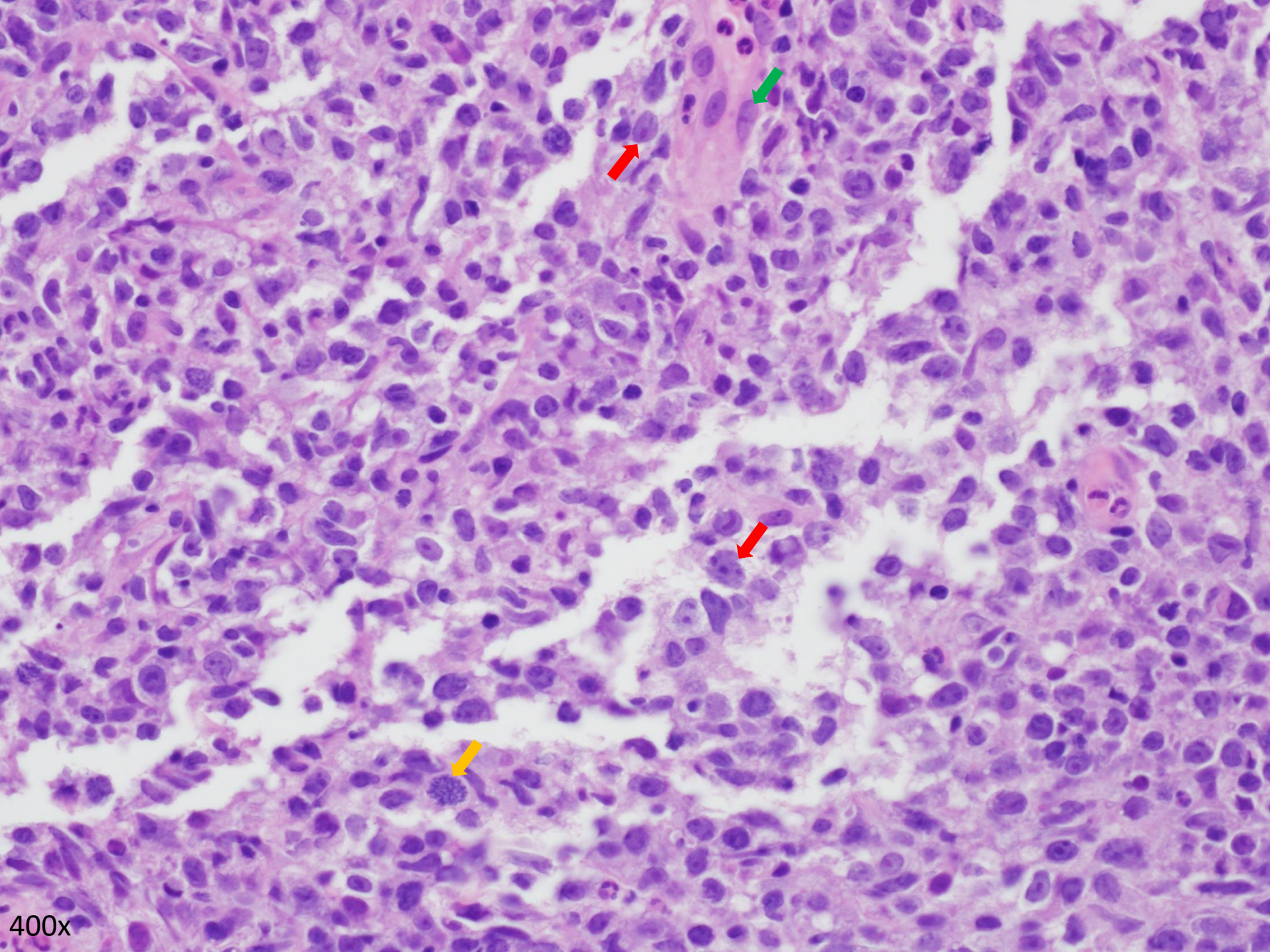
DLBCL

- Most common type of lymphoma in GI tract
- Mature large B-cell lymphoma that can occur anywhere in GI tract
- May arise de novo or evolve from underlying low-grade B-cell lymphoma
- Subtypes related to Epstein-Barr virus infection
  - Predilection for elderly and immunosuppressed
  - If arises in iatrogenically immunocompromised following transplant, then classified as monomorphic post-transplant lymphoproliferative disorder (PTLD)
- Clinically aggressive
  - Potentially curable with chemotherapy and immunotherapy
  - low-grade B-cell component may be refractory and persist

DLBCL: Morphology



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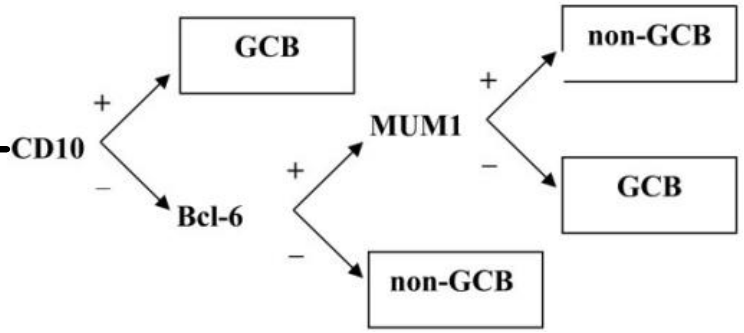
DLBCL: Immunophenotype

- Pan-B cell marker expression
  - CD20, CD79a, Pax-5
- Aberrant Bcl-2 expression (most)
- Germinal center B-cell phenotype
  - CD10, Bcl-6 expression
- Activated B-cell type
  - MUM1/IRF4 expression
- No expression of T-cell markers
  - except CD5 (~10%)

Hans Algorithm

Hans CP, et al. Blood. 2004;103(1):275-82



Expression by at least 30% cells is required for “positivity”

DLBCL: Other Immunophenotypic and Molecular/Cytogenetic Features

- MYC alterations and expression
  - *MYC* rearranged in 5-15% of DLBCL, NOS
    - Frequently associated with *BCL2* or *BCL6* translocation = “double hit” or “triple hit” lymphomas
    - new formal category in WHO2017: High-grade B-cell lymphoma (HGBL) with rearrangements of MYC and BCL2 and/or BCL6
  - MYC protein expression in 30-50% of DLBCL, associated with concomitant BCL2 expression in 20-35%
    - BUT do not carry MYC/BCL2 chromosomal alteration, thus named “double expressor lymphoma”
    - Positive expression: at least 40% for c-myc and 50% for Bcl-2 by IHC
    - Prognostic indicator: double-expressor lymphomas have worse outcome than other DLBCL, NOS but are not as aggressive as HGBL with rearrangements of MYC and BCL2 and/or BCL6

DLBCL: Other Immunophenotypic and Molecular/Cytogenetic Features

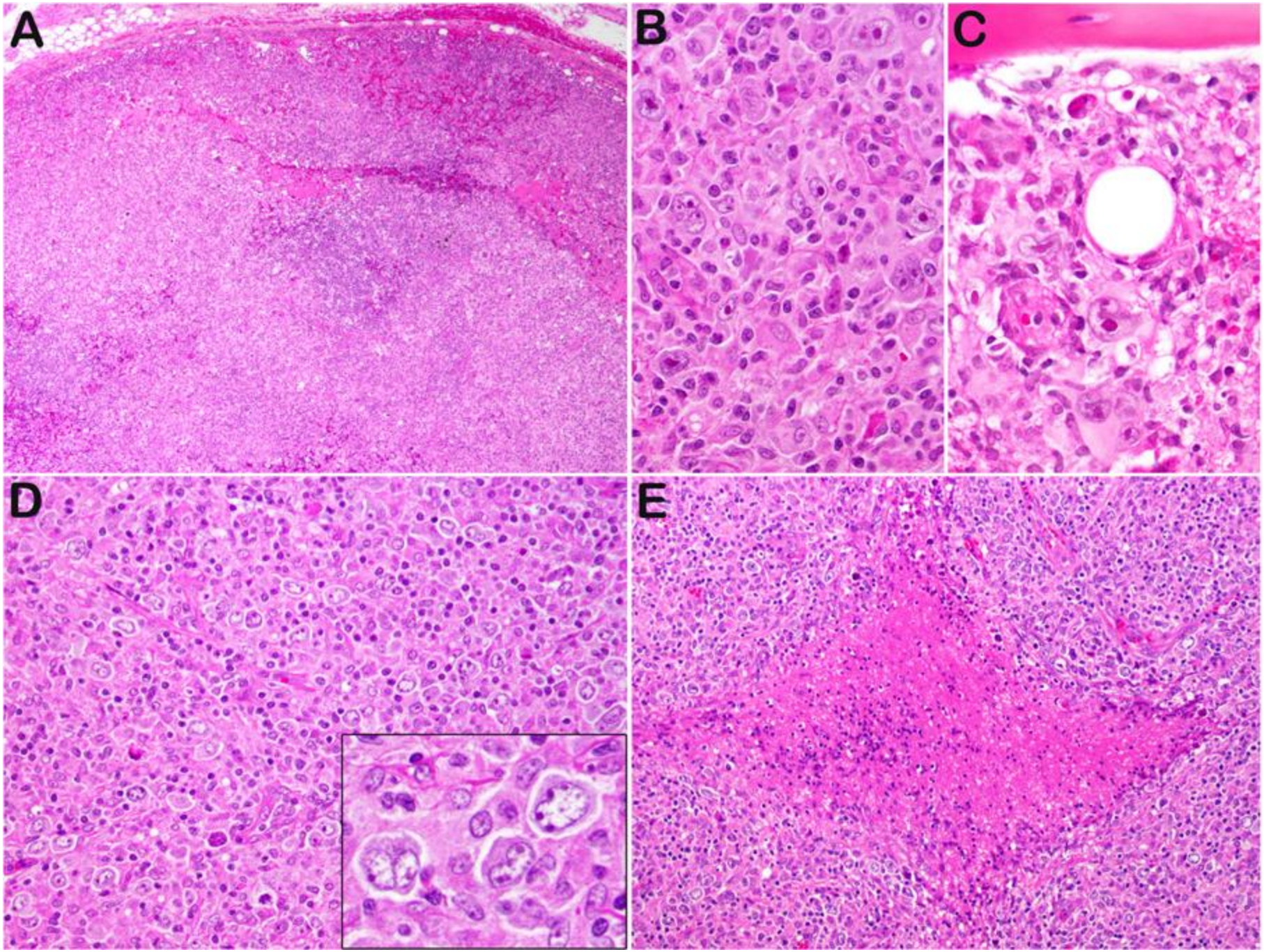
- CD30 expression
  - Target for brentuximab vedotin immunotherapy
- NGS studies
  - GCB-DLBCL: frequent alteration of histone methyl transferase EZH2, BCL2 translocations, and cell motility regulator GNA13 mutations
  - ABC-DLBCL: mutations in genes activating BCR/TLR and NFkB pathways (MYD88, CD79a, CARD11, TNFAIP3)
  - Both: inactivating mutation of TP52, immunosurveillance-related genes, alterations in epigenetic regulators, and oncogenic activation of BCL6

Subtype: EBV+ DLBCL, NOS

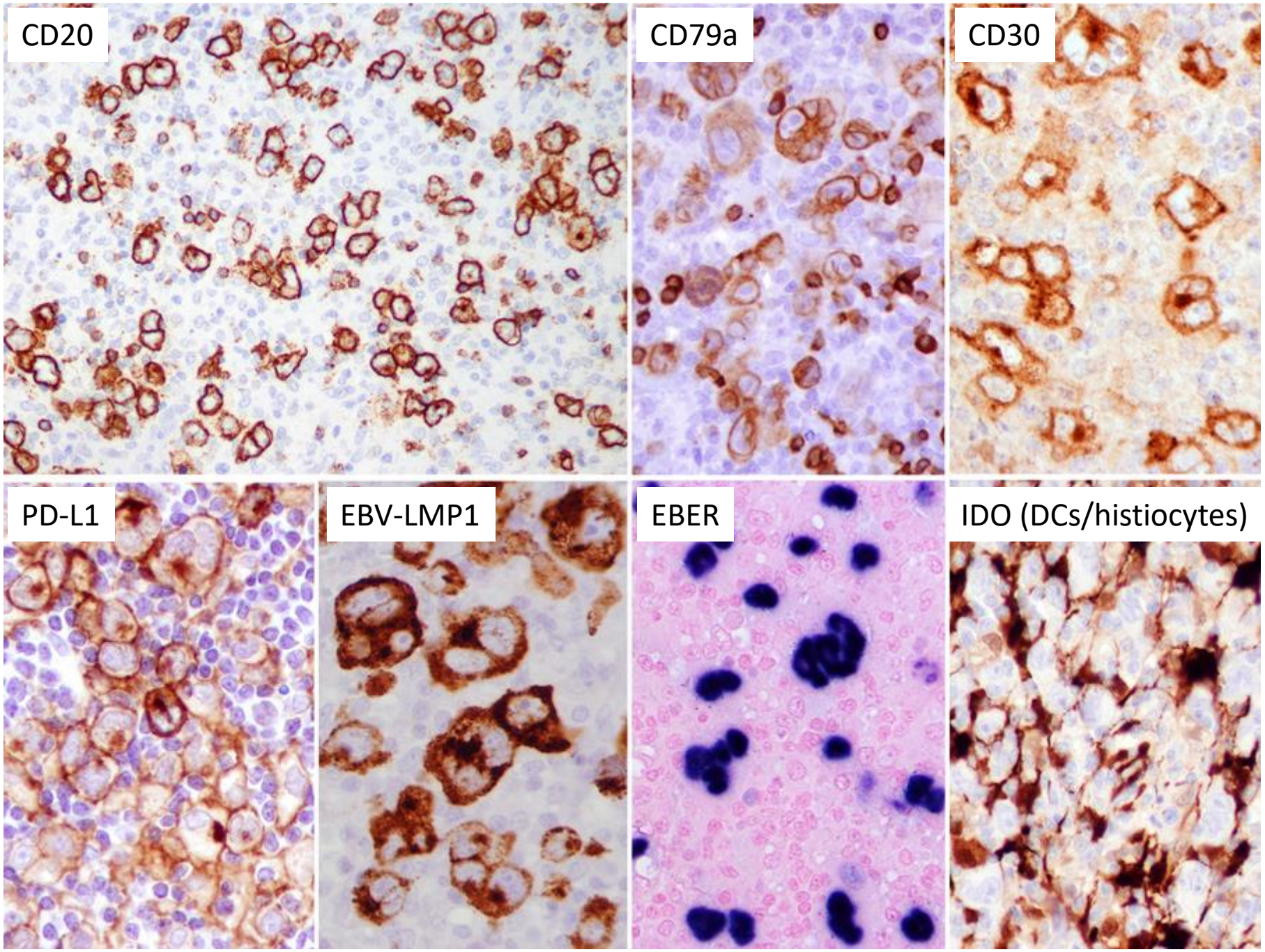
- Previously known as EBV+ DLBCL of the elderly
- In the “elderly” (>50 y): presumed immune senescence leads to development of lymphoma
  - 70% present with extranodal disease (skin, lung, tonsil, stomach)
  - Aggressive (median survival 2 y)
- Nicolae et al described a series of EBV+ DLBCL in young patients (median age 23 y) without known immunodeficiency
  - Predominantly nodal disease, 3 of 46 with liver involvement
  - Good outcome with treatment

Subtype: EBV+ DLBCL, NOS

- Morphology:
  - some resemble T-cell/Histiocyte-rich large B-cell lymphoma with scattered large B cells mimicking HRS cells and variants
  - some more conventional DLBCL-like
  - geographic necrosis common
- Usually non-GCB phenotype (CD10-, MUM1+), EBV+



Nicolae A, et al. Blood. 2015;126(7):863-72.



Nicolae A, et al. Blood. 2015;126(7):863-72.

Subtype: EBV+ DLBCL, NOS

- NOS designation excludes specific EBV-associated lymphoma subtypes (Burkitt lymphoma, classical Hodgkin lymphoma, lymphomatoid granulomatosis, primary effusion lymphoma, plasmablastic lymphoma)
- No longer “of the elderly” - Implied suggestion to screen cases with above morphologies for EBV without regard for age

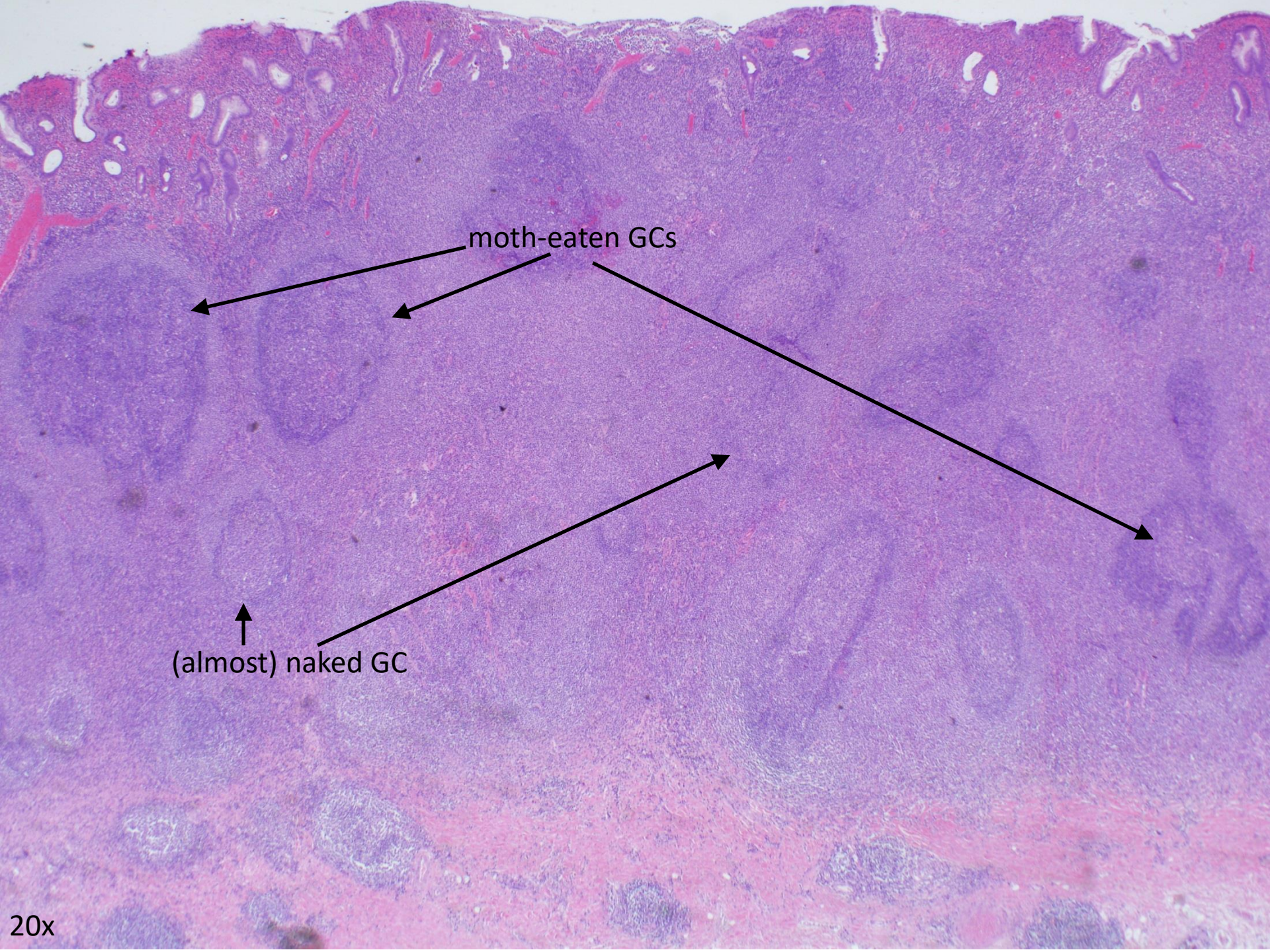
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)

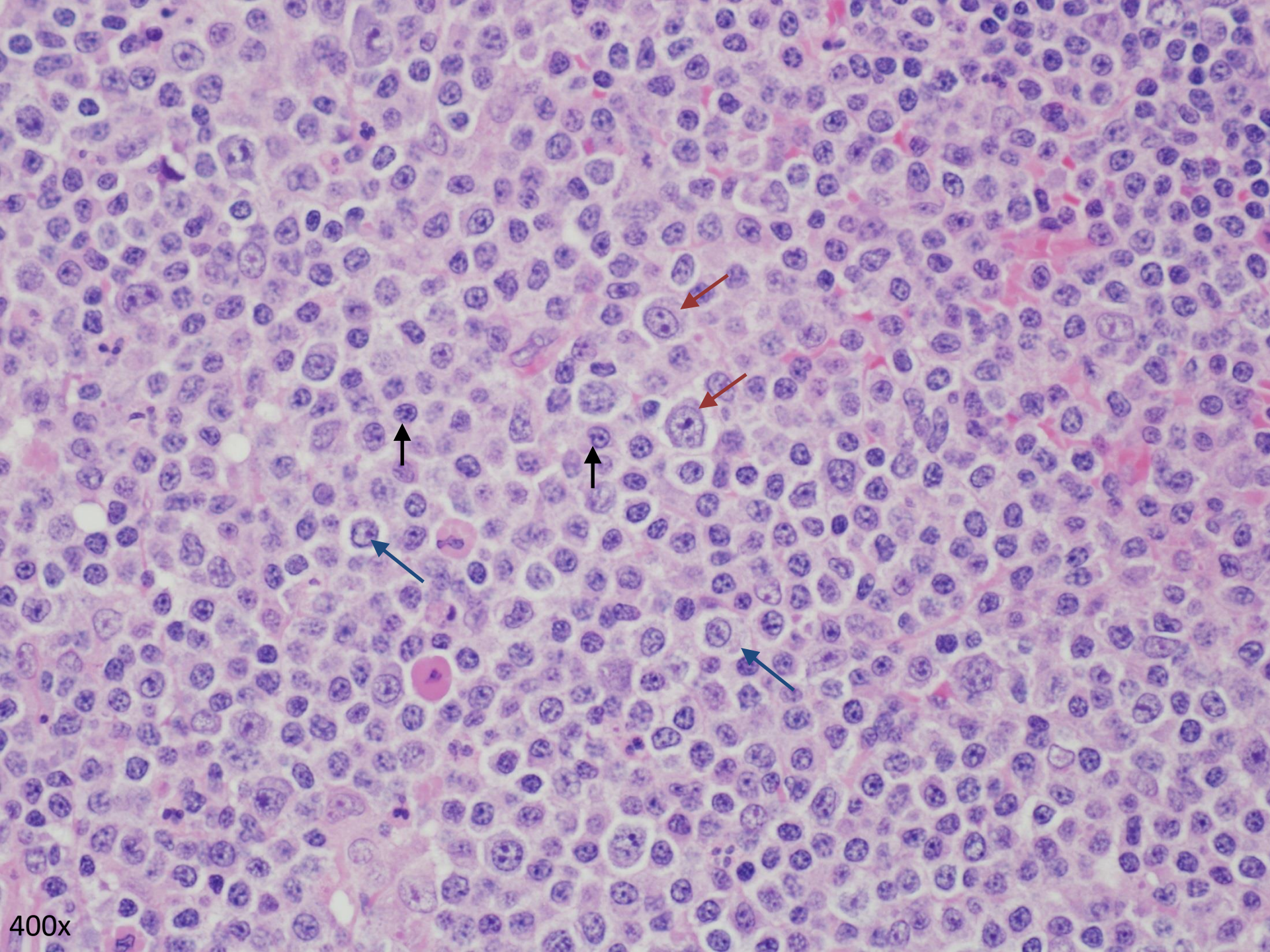
MALT lymphoma

- Mature B-cell lymphoma that can occur anywhere in GI tract
  - 85% in stomach, often in association with *H pylori*-associated gastritis
- Lymphoma of small mature B lymphocytes that has a destructive growth pattern (ulcer or thickened mucosal folds)
- Majority present with low-stage disease
- Bone marrow often uninvolved in GI cases
- M-proteins are rare, despite relatively frequent plasmacytic differentiation
  - In immunoproliferative small intestinal disease (IPSID), a subtype of MALTL associated with *Campylobacter jejuni*, a paraprotein is <u>usually</u> found (alpha heavy chain)

MALT Lymphoma: Morphology

- Reactive germinal centers commonly accompany lymphoma
  - May be invaded or disrupted, leading to “naked” or “moth-eaten” appearance
- Heterogeneous, predominantly small B-lymphocytes
  - centrocyte-like cells (indistinguishable from small cells of normal germinal center
  - monocytoid cells (slightly larger cells with more ample cytoplasm and slightly indented nuclei)
  - few scattered large cells (immunoblast- and/or centroblast-like, recapitulate centroblasts of germinal center)


moth-eaten GCs
(almost) naked GC
20x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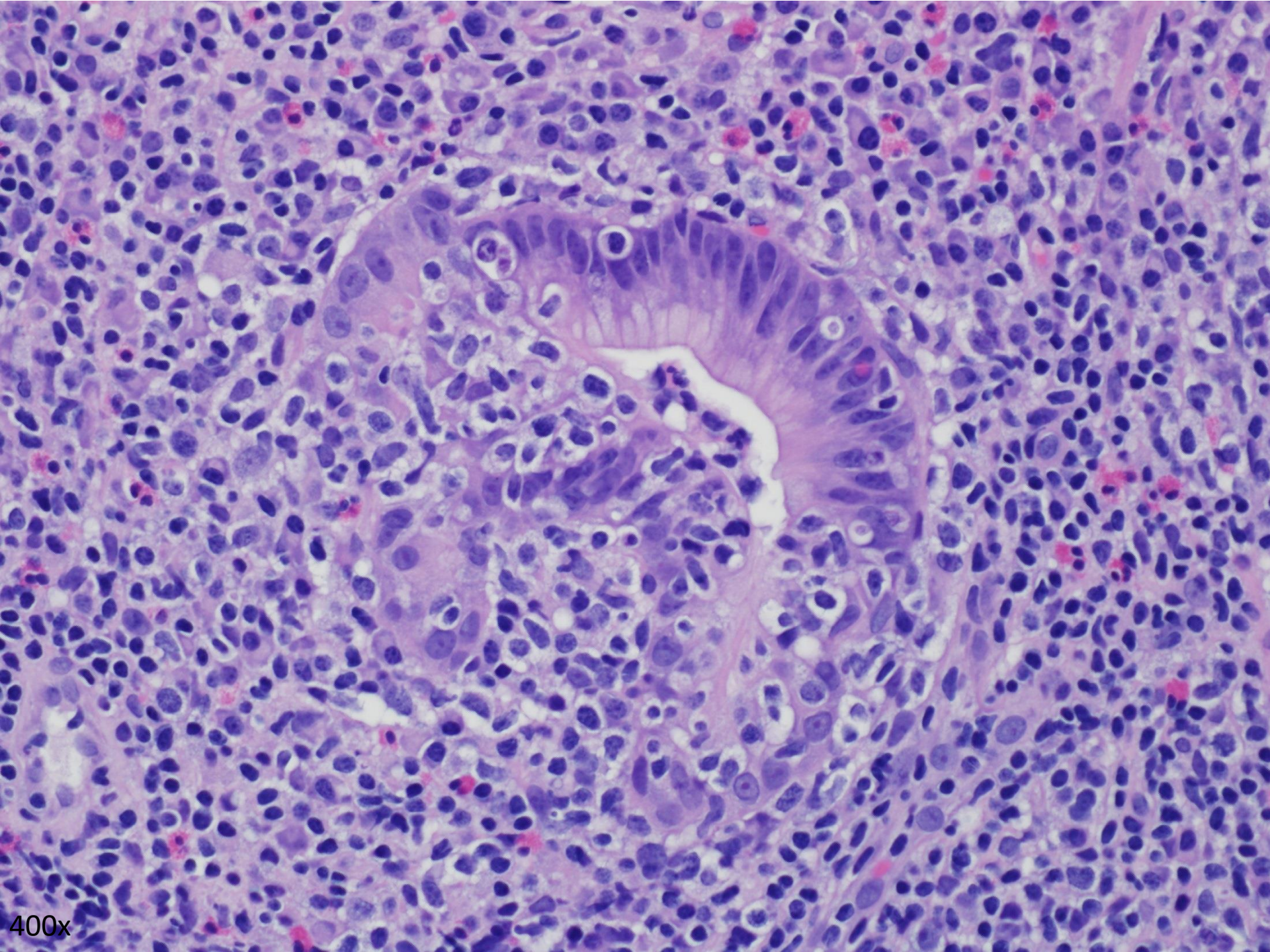
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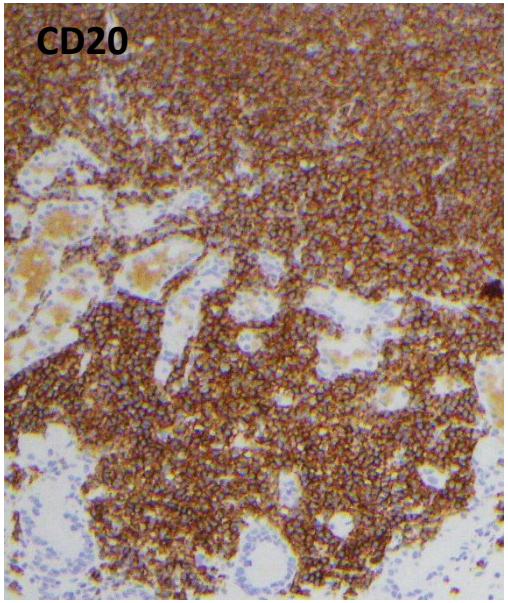
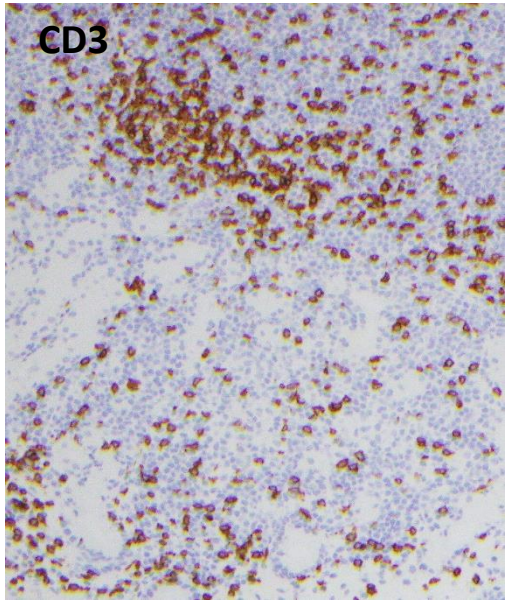
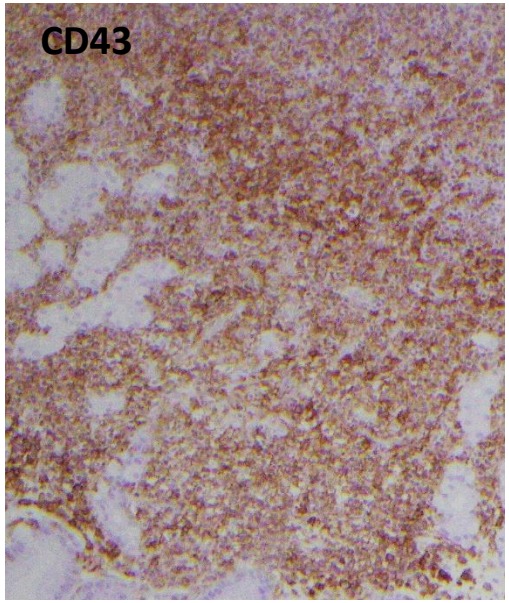
MALT Lymphoma: Morphology + IHC

- Some cases have plasma cell differentiation
  - Kappa & lambda light chain IHC may be helpful in establishing clonality
- No distinctive immunophenotype
  - Aberrant CD43 expression in only 40-50% of cases







- Lymphoepithelial lesion (LEL) is histologic hallmark
  - Destructive epithelial infiltration by lymphoma cells
  - Characteristic but not absolutely specific

MALT Lymphoma vs *H pylori* gastritis

MALT lymphoma	*H pylori* gastritis
Mucosal destruction present	Intact architecture with inflammatory infiltrate among pits/ glands
Lymphoepithelial lesions (with B cells)	Epithelial structures intact
B cells predominate	Mixture of B and T cells
Deep follicles with colonization	Intact follicles in deep mucosa
Light chain restriction (if plasmacytic differentiation)	Polytypic plasma cells (kappa/lambda ~2:1)

Owens SR. Surg Pathol Clin. 2017;10(4):1021-1037

MALT Lymphoma: Clinical Aspects

- 80% are responsive to conservative therapy aimed at eradication of inciting entity
  - Evidence suggests that antibiotic therapy can be effective in *H. pylori*-negative cases of MALTL, *and in some cases outside the stomach*
  - Gastric MALT lymphomas with t(11;18)(q21;q21) translocation resulting in API2-MALT1 fusion occur independent of *H pylori* stimulus and are resistant to conservative therapy
- Resolution of atypical lymphoid infiltrate can take months (typically 4-10 months) to more than a year
  - Reporting of residual (regressing) disease on serial biopsies should include comparison statement
  - Progression is worrisome and requires another treatment modality

MALT Lymphoma: Gray zone cases

- What to do with borderline or minimal cases??
  - “Intense H. pylori gastritis with atypical lymphoid infiltrate”
  - In the comment address the possibility of early MALTL and offer a statement about typical response to conservative therapy

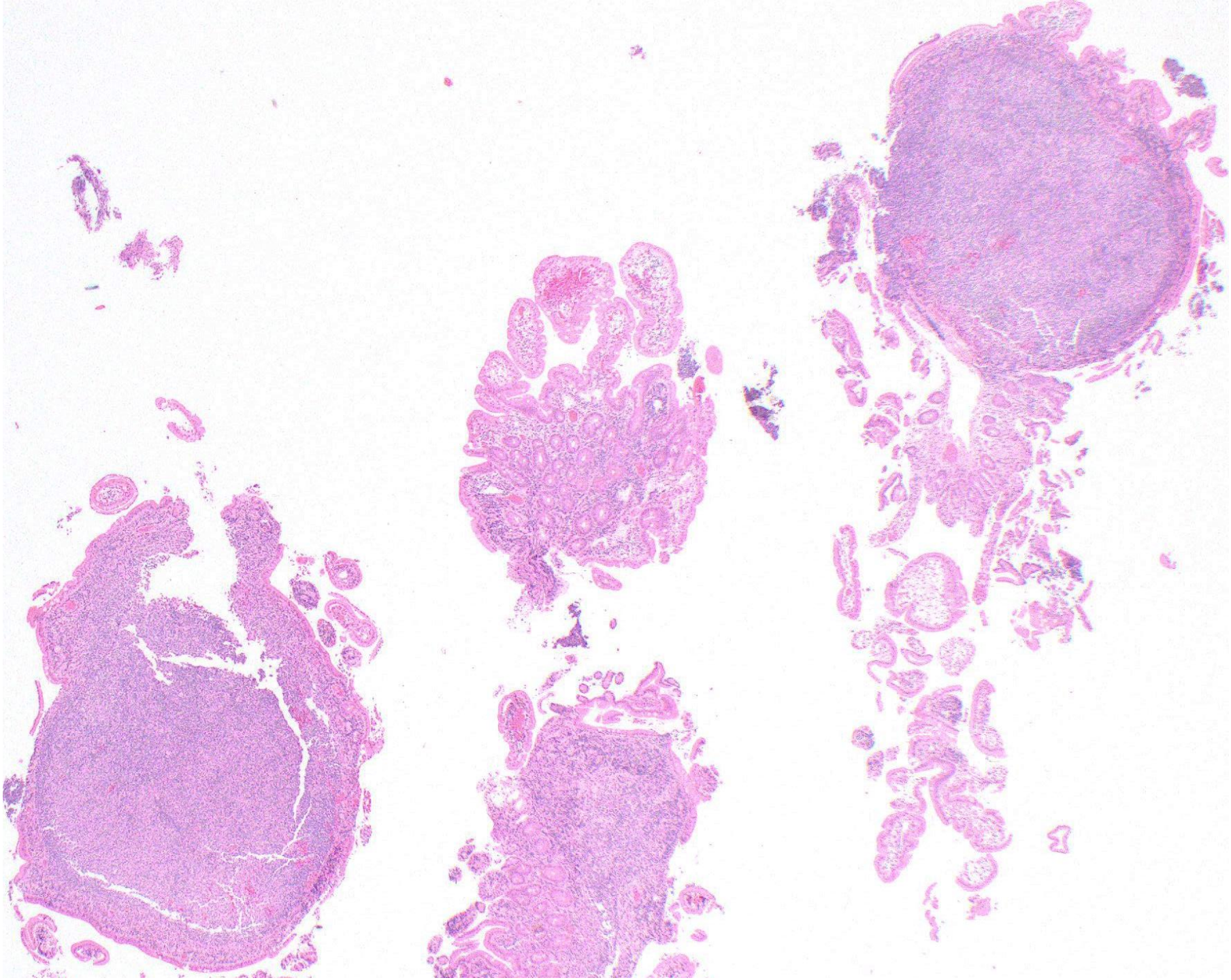
Follicular Lymphoma

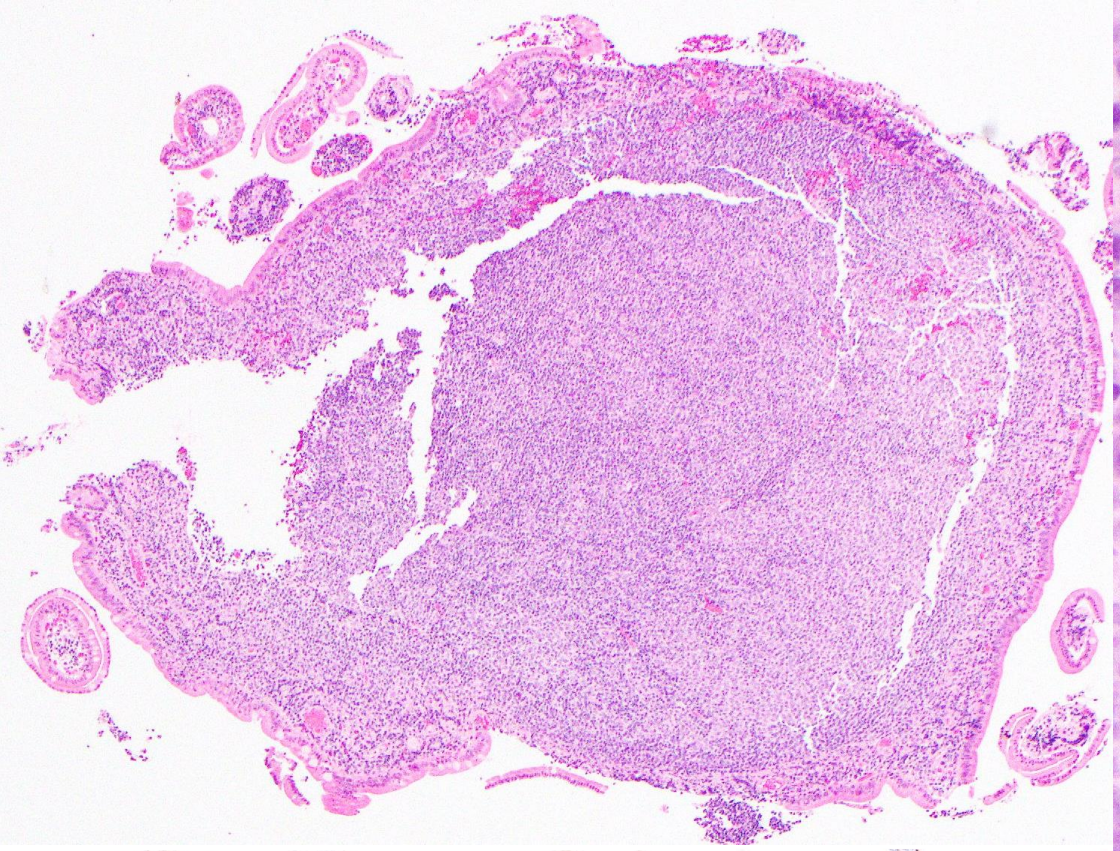
Follicular Lymphoma

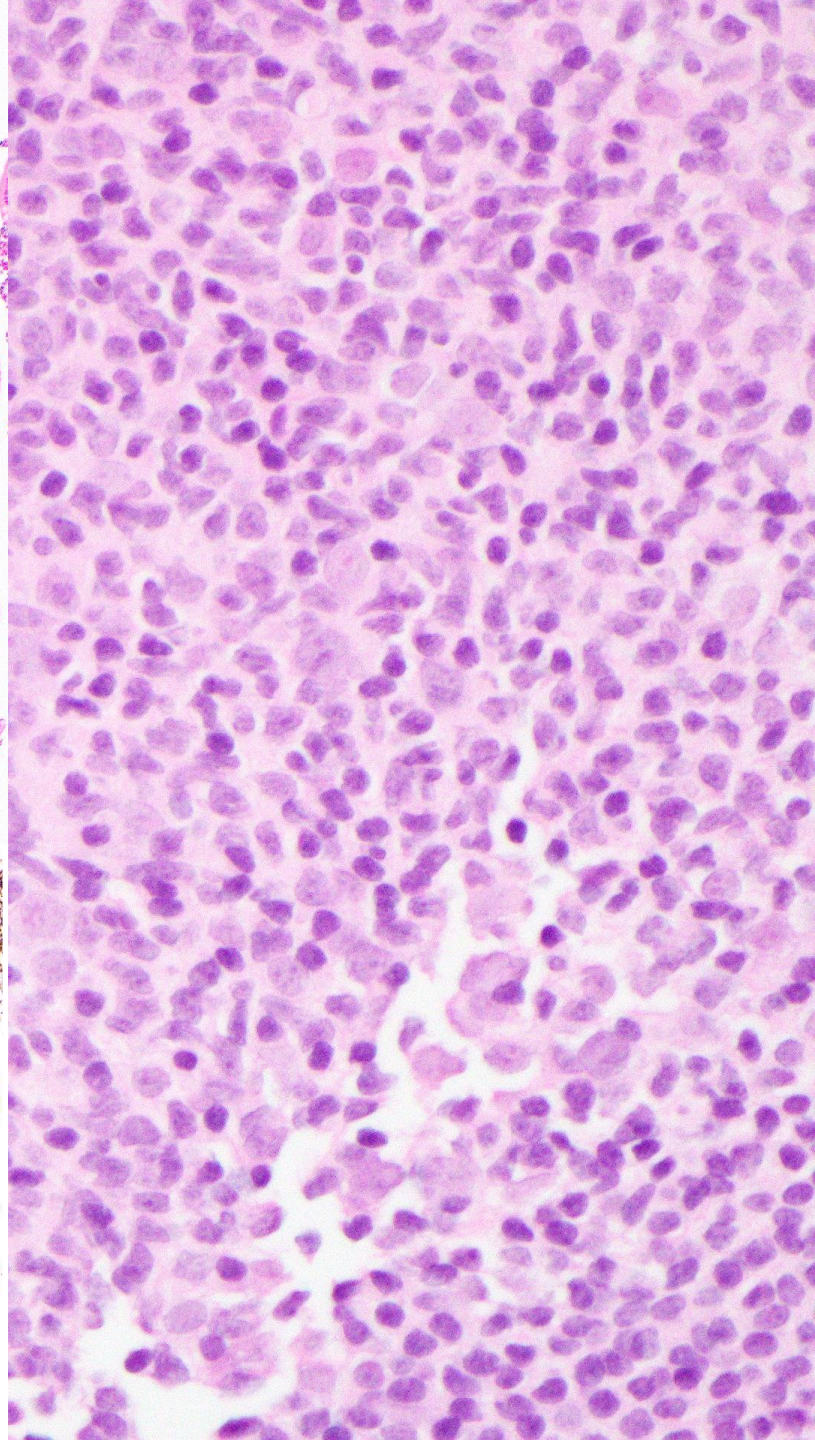
- Mature B-cell lymphoma that may involve the GI tract secondarily or occasionally primarily
  - Duodenal-type FL presents as multiple small polyps
  - Formal clinical staging work-up must be performed
    - CANNOT diagnose primary GI/duodenal-type FL on histology alone
- Nodular infiltrate of small mature lymphocytes that recapitulate follicle center B-cells (centrocytes and centroblasts)
  - Proportions of each population determine grade
- Typically indolent
  - Frequently involve bone marrow and can be difficult to cure
  - Duodenal-type FL very indolent, may not need additional therapy beyond local excision

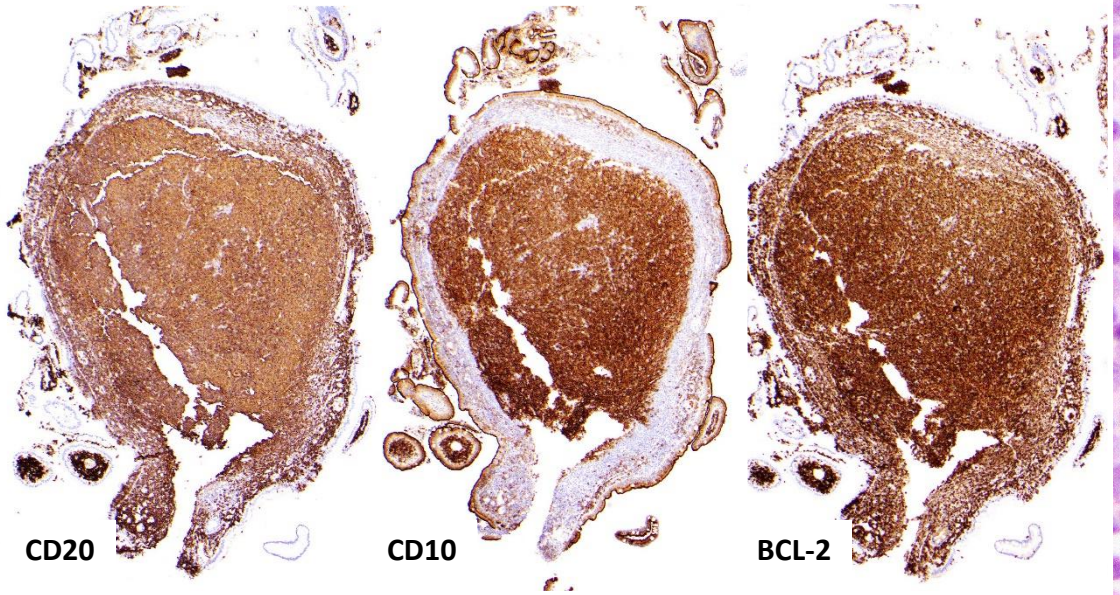
Follicular Lymphoma: Morphology

- Nodular infiltrate with closely-packed follicles with attenuated or absent mantle zones
- Neoplastic follicles have randomly distributed centrocytes and centroblasts without tingible-body macrophages
  - In contrast, reactive germinal centers of normal follicles demonstrate polarization due to centrocytes and centroblasts occupation of different zones and have tingible-body macrophages








CD20
CD10
BCL-2

Follicular Lymphoma: Immunophenotype & Cytogenetics

- Pan-B cell marker expression (CD20, Pax5)
- Follicle center cell differentiation (CD10, Bcl-6)
- Dendritic cell meshwork present in neoplastic follicles (highlighted with CD21 and CD23)
- Aberrant expression of BCL-2
  - Also positive in many other lymphomas and normal T-cells and plasma cells
  - Negative in germinal centers of reactive follicles
- All forms associated with t(14;18)(q32;q21) translocation involving *IGH* and *BCL2*

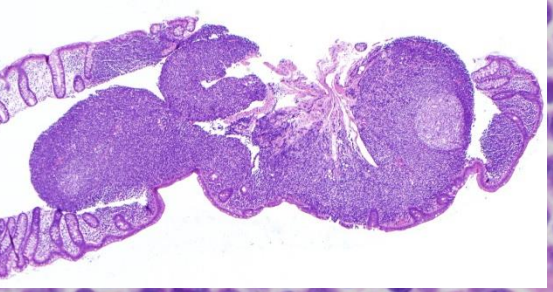
Mantle Cell Lymphoma

Mantle Cell Lymphoma

- Systemic small mature B-cell lymphoma
  - Involves GI tract in one-third of cases
  - Hepatosplenomegaly, lymphadenopathy, PB involvement common
- Classically / distinctively presents as lymphomatous polyposis
  - Multiple (sometimes hundreds) of polyps throughout GI tract
- Aggressive, with overall survival of 3-5 years

Mantle Cell Lymphoma: Morphology

- Monomorphic lymphoid proliferation
  - Pattern can be diffuse, nodular, “mantle zone”
    - Mantle zone pattern has central follicle surrounded by neoplastic cells
- small to medium-sized neoplastic lymphoid cells with dark angulated nuclei
- interspersed hyalinized small vessels (thick-walled capillaries) and epithelioid eosinophilic histiocytes (mimicking “starry sky” appearance)
- Blastoid and pleomorphic variants may mimic ALL and DLBCL
  - Important to recognize as the latter two are potentially curable, whereas MCL is not



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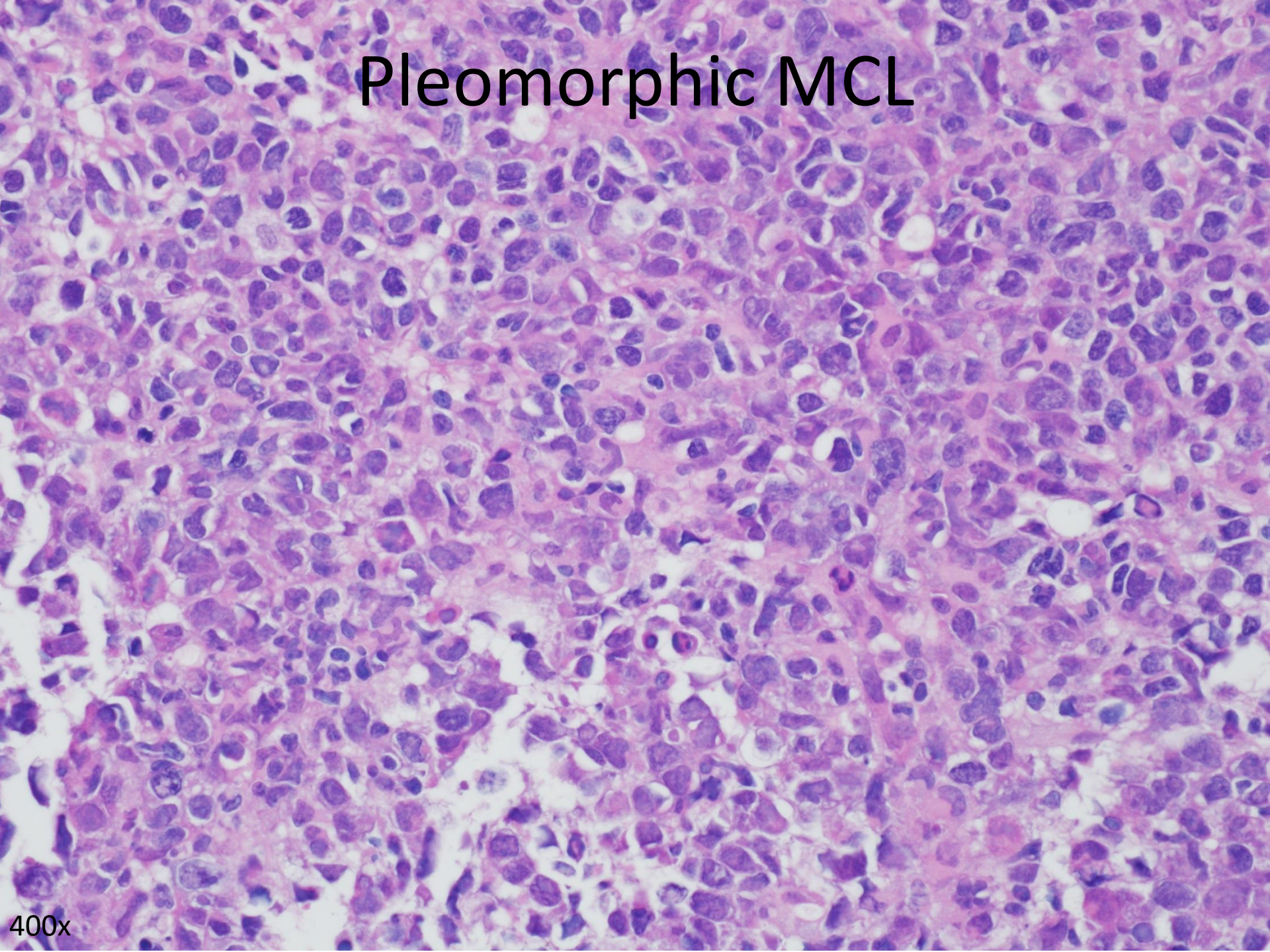

Pleomorphic MCL
400x

Classical Mantle Cell Lymphoma: Immunophenotype

- Pan-B cell marker expression (CD20, Pax5)
- Aberrant expression of CD5 (rarely negative), CD43 (usually), BCL-2, nuclear CyclinD-1 (very rare negative cases express cyclin D2 or cyclin D3)
- Surface IgM and/or IgD expression
- Sox11 expression
- Negative for CD10, BCL-6, CD23

Classical Mantle Cell Lymphoma: Cytogenetics

- Ig genes
  - IgH rearranged
  - IgH Variable regions unmutated or minimally mutated
- t(11;14)(q13;q32) rearrangement
  - Involves IgH and CyclinD1 genes (PRAD1, BCL1)
  - Classical cytogenetics detects 70-95%
  - FISH detects ~100%
- Other
  - p53, p16, p18 (especially in blastoid variant)
  - 13q14 deletion
  - Total or partial trisomy 12

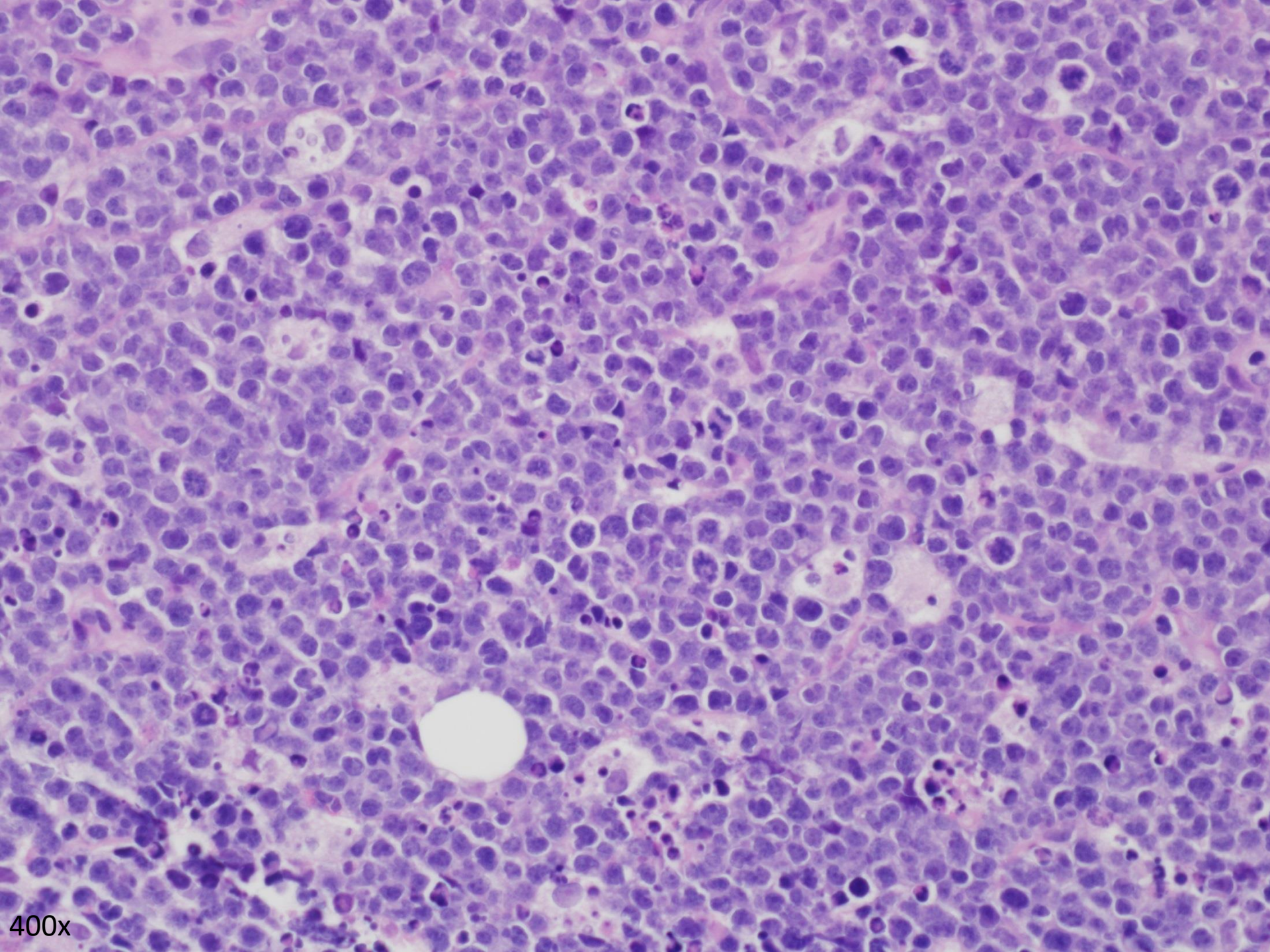
Burkitt Lymphoma

Burkitt Lymphoma

- Mature B-cell lymphoma of children and young adults
- Has very short doubling time
- Presents often in extranodal sites or as acute leukemia
  - Classic lesion is large and destructive mass in distal ileum and/or cecum
  - Can involve any portion of GI tract
- Variable global distribution
  - Endemic: equatorial Africa and Papua New Guinea
  - Sporadic: around globe
- Epstein-Bar virus association
  - Endemic: majority of neoplastic cells in all patients
  - Sporadic: 30% of cases
  - Immunodeficiency-associated (HIV): 25-40% of cases
- Good prognosis (up to 90% survival) with appropriate therapy

Burkitt Lymphoma: Morphology

- Low magnification: “starry sky”
  - Sheets of lymphoma cells are punctuated by tingible-body macrophages with cellular debris
- Lymphoma cells are monotonous, medium-sized, with round nuclei, dispersed chromatin, inconspicuous nucleoli, scant basophilic cytoplasm
- Nearly 100% proliferative fraction, numerous mitotic figures, lots of apoptotic debris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Burkitt Lymphoma: Immunoprofile & Cytogenetics

- B-cell marker expression (CD20, CD19, CD79a)
- Germinal center cell differentiation (CD10, Bcl-6)
- High Ki-67 proliferative index (nearly 100%)
- Negative for Bcl-2 (weakly positive in 20%), TdT, CD5

- MYC translocation is characteristic (but not specific)
  - t(8;14)(q24;q32): c-MYC and IgH (75%)
  - t(2;8)(p12;q24): Ig kappa and c-MYC (15%)
  - t(8;22)(q24;q11): c-MYC and Ig lambda (10%)

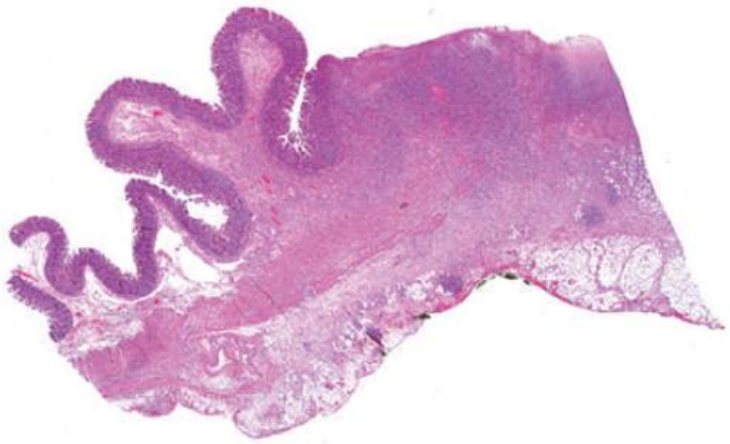
Enteropathy-Associated T-cell Lymphoma (EATL)

EATL

- Aggressive T-cell lymphoma that produces large, destructive masses, often in jejunum
- Arises in patients with celiac disease
  - In setting of refractory sprue
  - As sentinel event in patients with undiagnosed celiac disease
- Associated with HLA haplotypes DQ2 and DQ8
  - Northern European descent
- Poor prognosis due to aggressive nature and debilitated state of patients with malabsorption
  - Common presentation is ulcerated mass +/- perforation
  - Median survival of months

EATL: Morphology

- Diffuse, destructive infiltrate of intermediate-sized or large cells with angulated or pleomorphic nuclei (resembling those of DLBCL) with prominent nucleoli
- Tumor infiltration by inflammatory cells including histiocytes and eosinophils
- Neoplastic cells infiltrate individual crypts
- Areas of necrosis may be present
- Adjacent intestinal mucosa demonstrates variable degree of enteropathy (villous atrophy, crypt hyperplasia, intraepithelial lymphocytosis)



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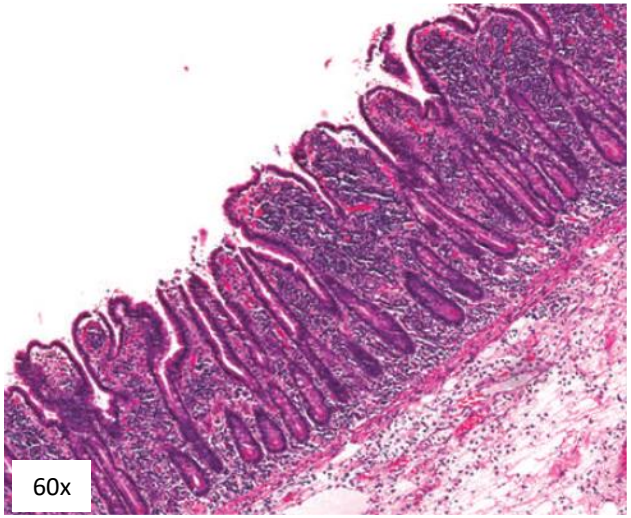

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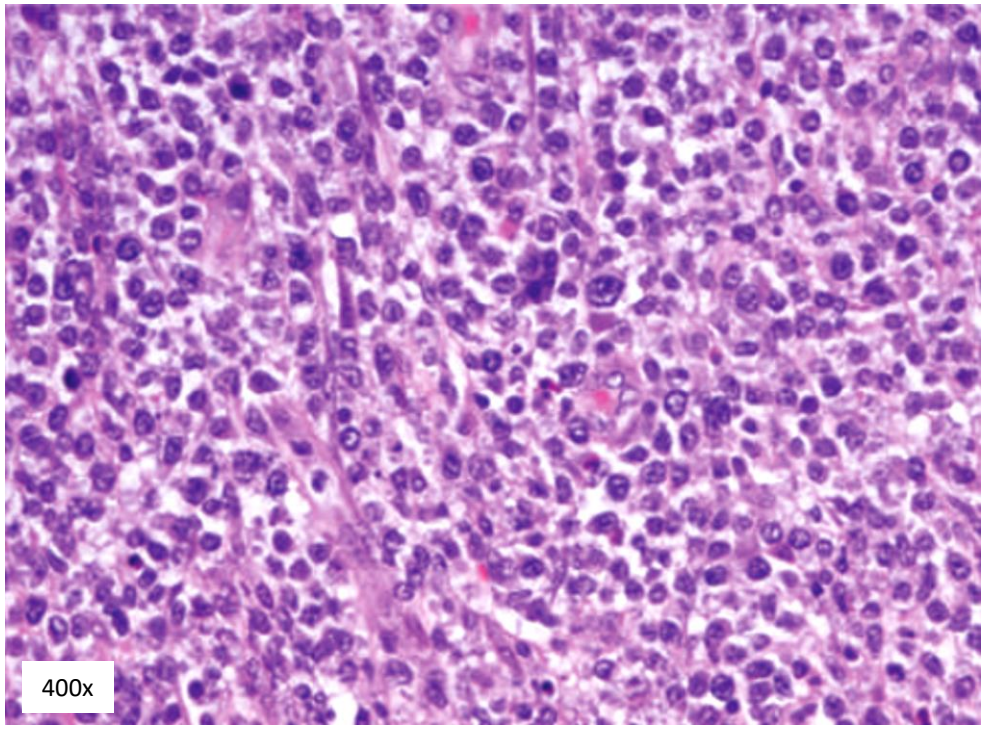

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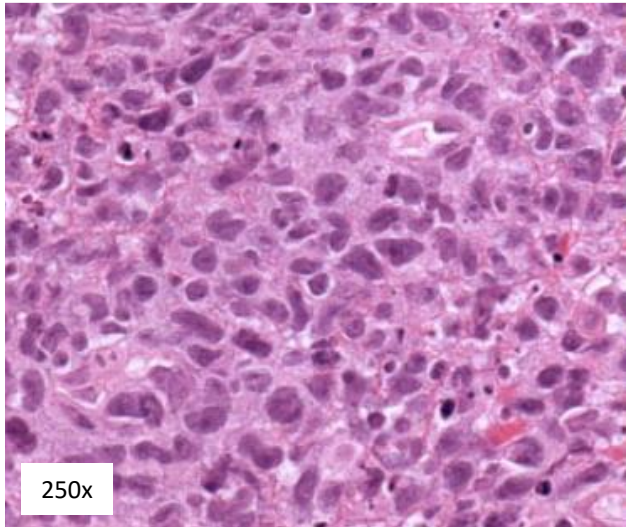

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Arps DP, Smith LB. Arch Pathol Lab Med. 2013;137(9):1227-31.
Delabie J, et al. Blood. 2011;118(1):148-55.

EATL: Immunophenotype

- Cytotoxic phenotype (granzyme B, TIA-1)
- TCR alpha/beta in most cases
- Typically positive for CD3, CD7, occasional cases CD8+, variable CD30
- Usually negative for CD4, CD8, CD5, CD56, MATK

- Intraepithelial lymphocytes in the adjacent enteropathic mucosa have a similar phenotype

Monomorphic Epitheliotropic Intestinal T-cell Lymphoma (MEITL)

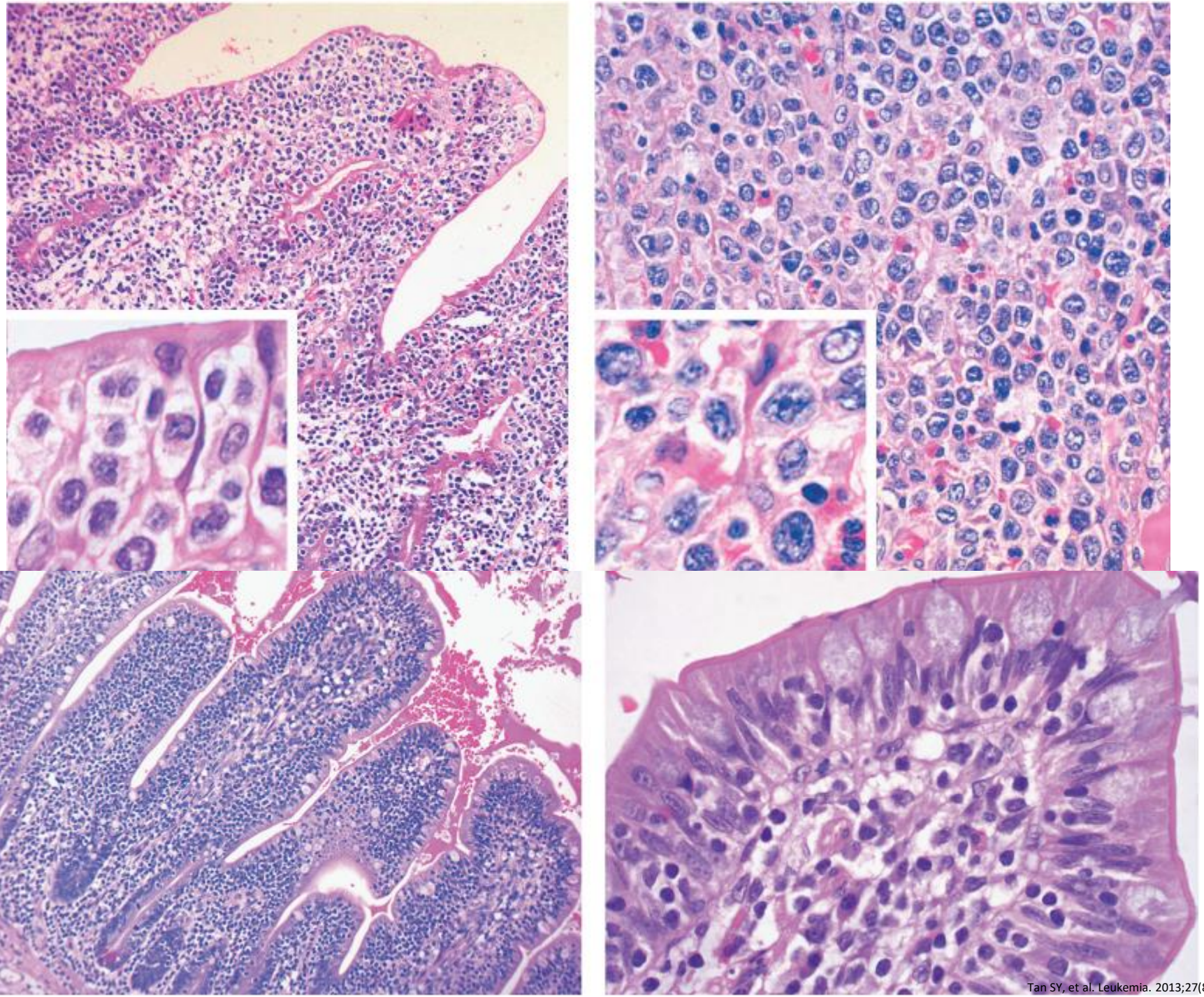
Formerly known as EATL II or EATL, monomorphic form

MEITL

- Aggressive T-cell lymphoma
- NO association with celiac disease
- Apparent increased frequency in patients of Asian and Hispanic descent
- Poor prognosis due to aggressive nature and debilitated state of patients
  - Common presentation is ulcerated mass +/- perforation
  - Median survival of months

MEITL: Morphology

- Diffuse, destructive, often ulcerated infiltrate of monotonous medium-sized lymphoid cells with dispersed chromatin, inconspicuous nucleoli, and ample clear cytoplasm (monocytoid appearance)
- Prominent epitheliotropism of tumor cells in adjacent mucosa with little involvement of submucosa/muscularis propria (lateral spread)
- Distant mucosa without enteropathy
- Paucity of reactive inflammatory cells within tumor
- Tumor perforation frequent



Tan SY, et al. Leukemia. 2013;27(8):1688-96.

MEITL: Immunophenotype

- Cytotoxic phenotype (TIA-1, granzyme B)
- Typically express CD2, CD3, CD7, CD8, CD56, nuclear MATK
- TCR gamma/delta in most cases
  - Some TCR silent
  - Some TCR alpha/beta
- Typically negative for CD5, CD4

Enteropathy-associated T-cell lymphoma (EATL)	• Diagnosis only to be used for cases formerly known as type I EATL, typically associated with celiac disease.
Monomorphic epitheliotropic intestinal T-cell lymphoma	• Formerly type II EATL; segregated from type I EATL and given a new name due to its distinctive nature and lack of association with celiac disease.

	EATL	MEITL
Frequency	80-90%	10-20%
Epidemiology	Complication of GSE	Occurs sporadically
	associated with HLA-DQ2/DQ8	
	refractory GSE patients at high risk	
	Northern Europeans descent	Asian and Hispanic descent
Morphology	Variable, pleomorphic, intermediate to large cells	Monotonous small to intermediate-sized cells
	Angulated nuclei	Round nuclei
	Prominent nucleoli	Inconspicuous nucleoli
	Areas of necrosis	Rare necrosis
	Variable to heavy background mixed inflammatory infiltrate	Minimal background inflammatory infiltrate
Immunophenotype	CD3+, CD5-, CD7+	CD3+, CD5-, CD7+
	CD8- (80%)	CD8+ (80%)
	CD56- (>90%)	CD56+ (>90%)
	nuclear MATK-	nuclear MATK+
Cytogenetics		
+9q31.3 or -16q12.1	86%	83%
+1q32.2-q41	73%	27%
+5q34-q35.2	80%	20%
+8q24 (MYC)	27%	73%

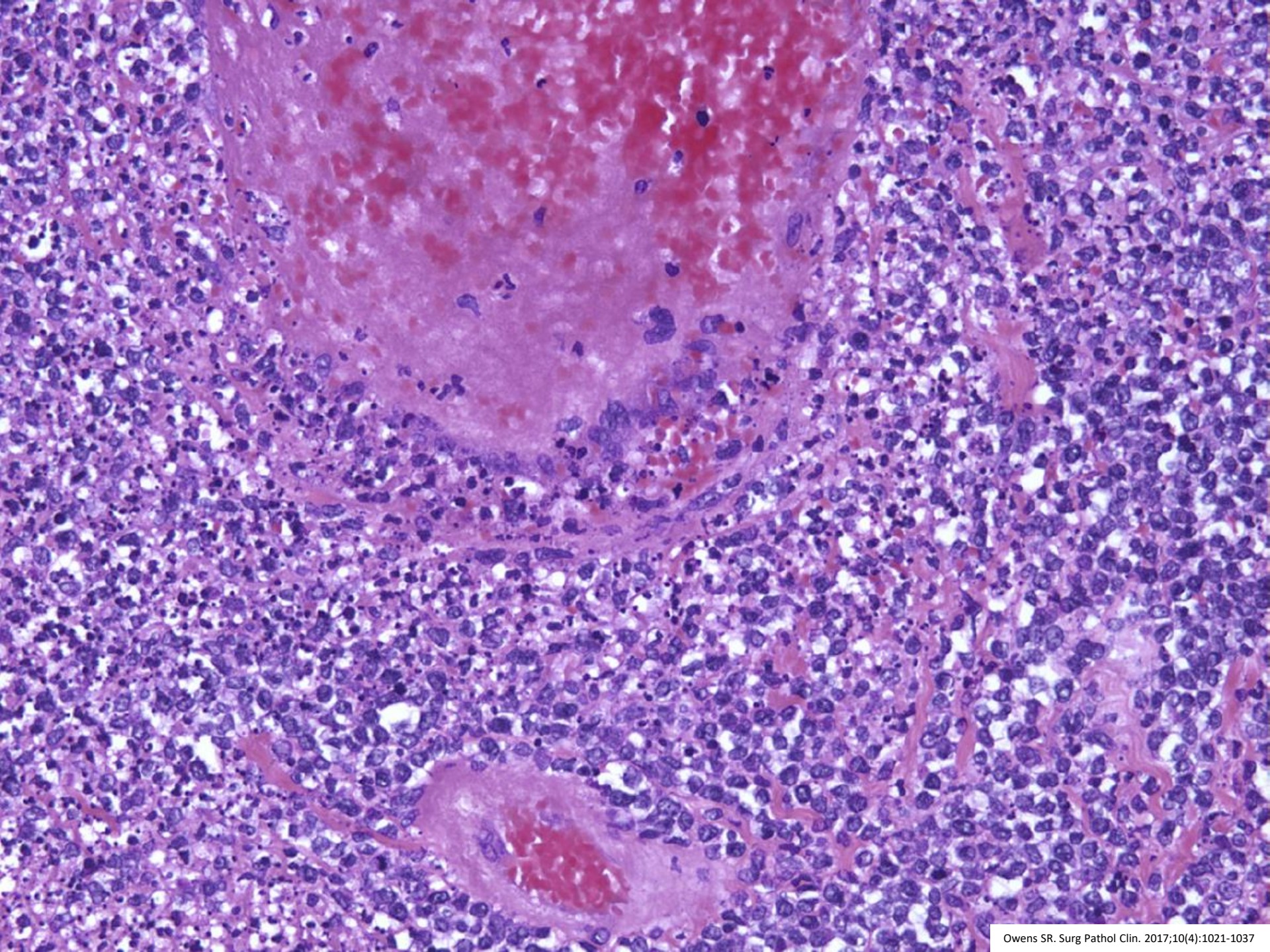
Extranodal Natural Killer/T-cell Lymphoma, Nasal Type (ENKTL)

ENKTL

- Rare, very aggressive lymphoma most commonly involving upper aerodigestive tract
  - Propensity to involve the GI tract
- Frequent tumor ulceration due to angiocentric and angiodestructive growth
- Associated with Epstein-Barr virus
- Higher prevalence in Asian and Native American populations
- Variable prognosis for nasal ENKTL, but extranasal ENKTL has short survival times and poor response to therapy

ENKTL: Morphology

- Variably-sized neoplastic cells
  - Small, medium-sized, large, or anaplastic
  - Irregularly folded nuclei with granular or vesicular chromatin
  - Inconspicuous nucleoli
  - Moderate pale cytoplasm
- Mitotic figures easily seen
- Angiocentric and angiodestructive growth with fibrinoid changes in vessels
- Coagulative necrosis and many apoptotic bodies



Owens SR. Surg Pathol Clin. 2017;10(4):1021-1037

ENKTL: Immunophenotype

- Typically express CD2, CD56, CD3epsilon (cytoplasmic), cytotoxic molecules (granzyme B, TIA1, perforin), CD43, CD25
- EBV+ (by IHC or ISH)
- Typically negative for surface CD3, CD4, CD8, CD5, CD16, CD57
- TCR in germline configuration

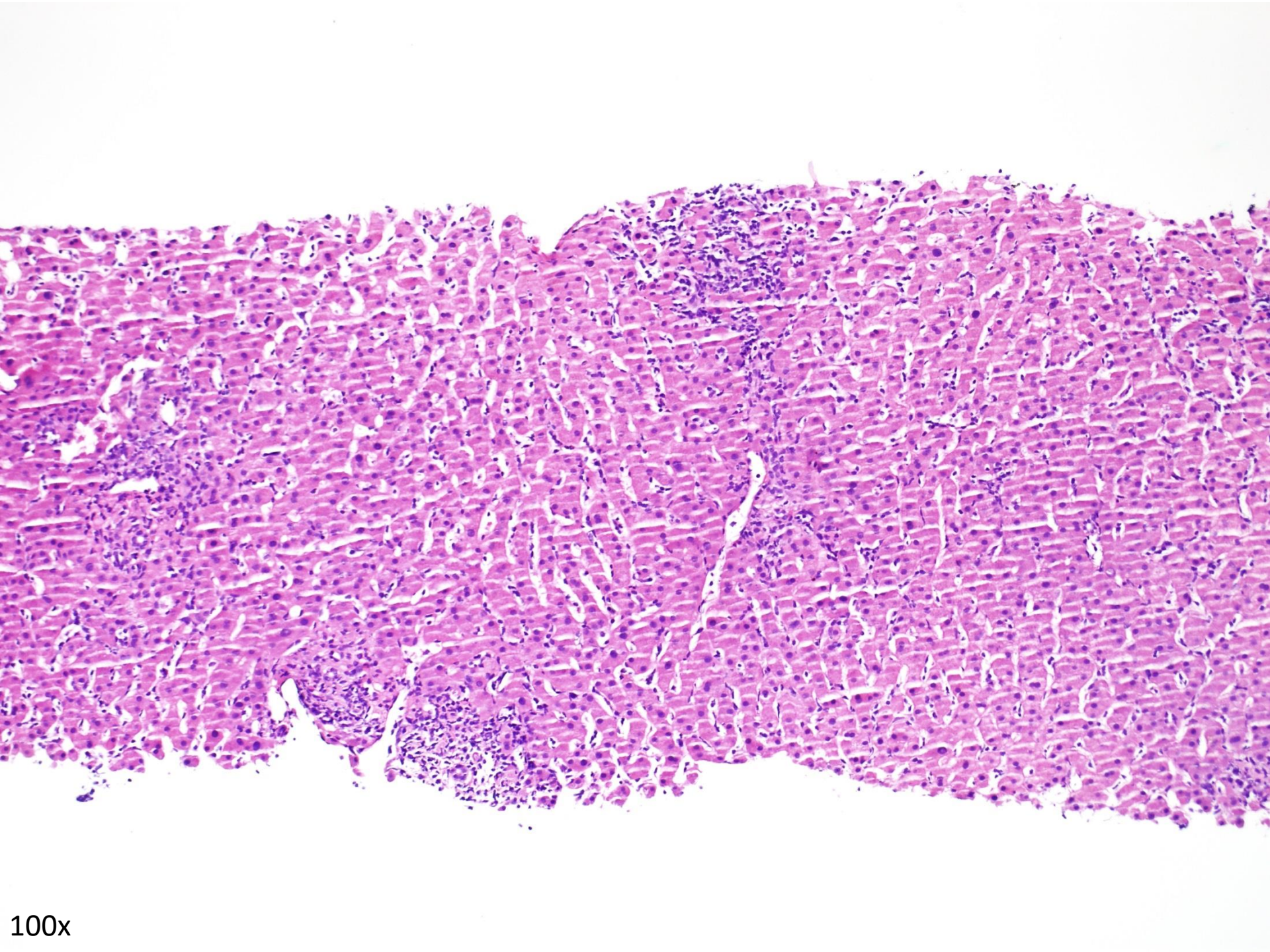
Hepatosplenic T-cell Lymphoma (HSTL)

HSTL

- Rare extranodal, systemic cytotoxic gamma/delta T-cell lymphoma of young adults
- 20% arise in setting of chronic immune suppression
  - After solid-organ transplant; considered PTLD
  - Immunosuppression for IBD
- Presents with marked splenomegaly, (usually) hepatomegaly, without lymphadenopathy, but with BM involvement
  - Marked thrombocytopenia
  - Often anemia, leukopenia
- Aggressive, with relapses after treatment is most cases
  - Median survival <2 years

HSTL: Morphology

- Spleen: diffuse involvement of cords and sinuses of red pulp, white pulp atrophy
- Liver: diffuse infiltration of sinusoids
- Neoplastic cells are monotonous medium-sized cells with pale cytoplasm



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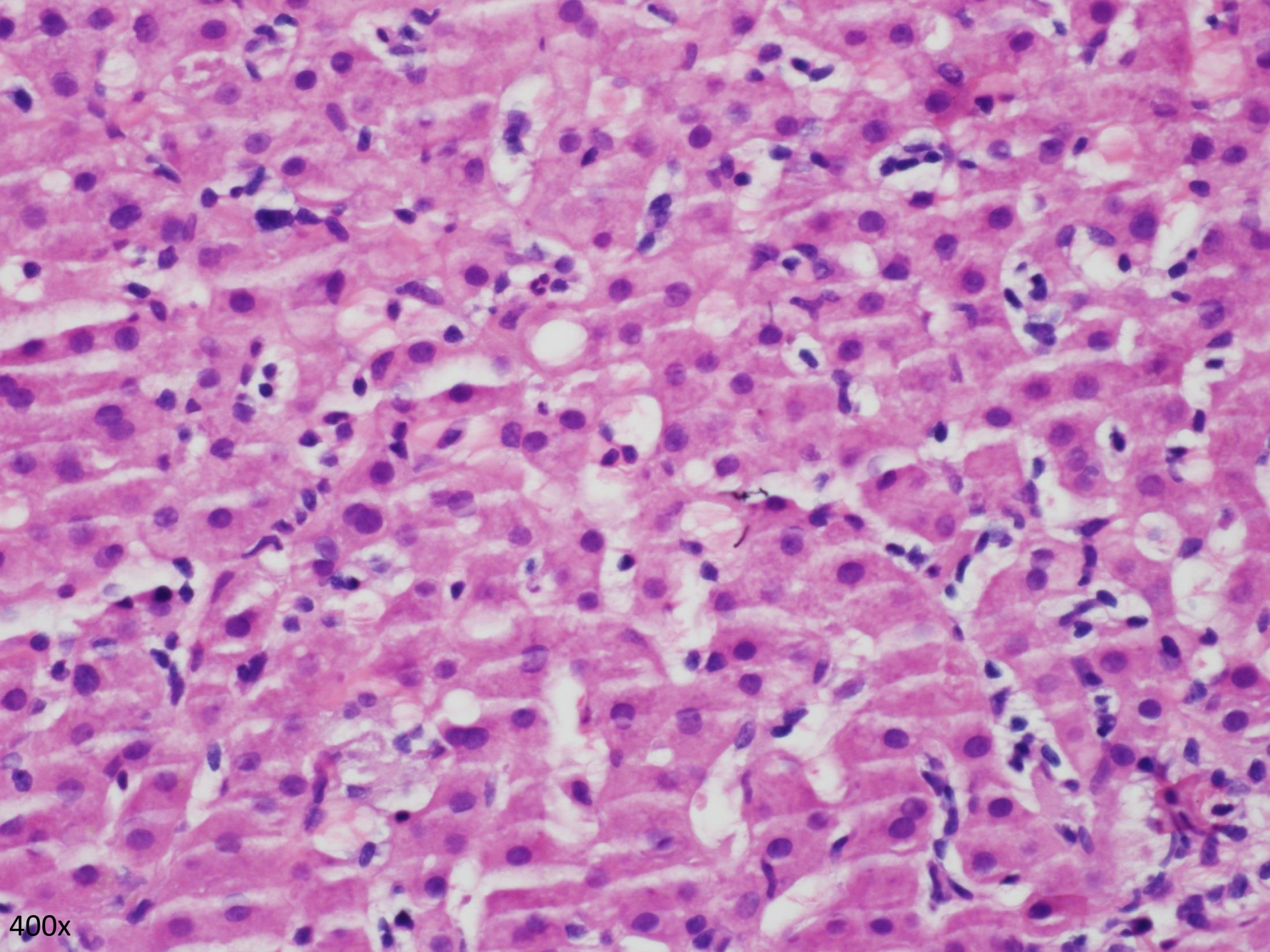
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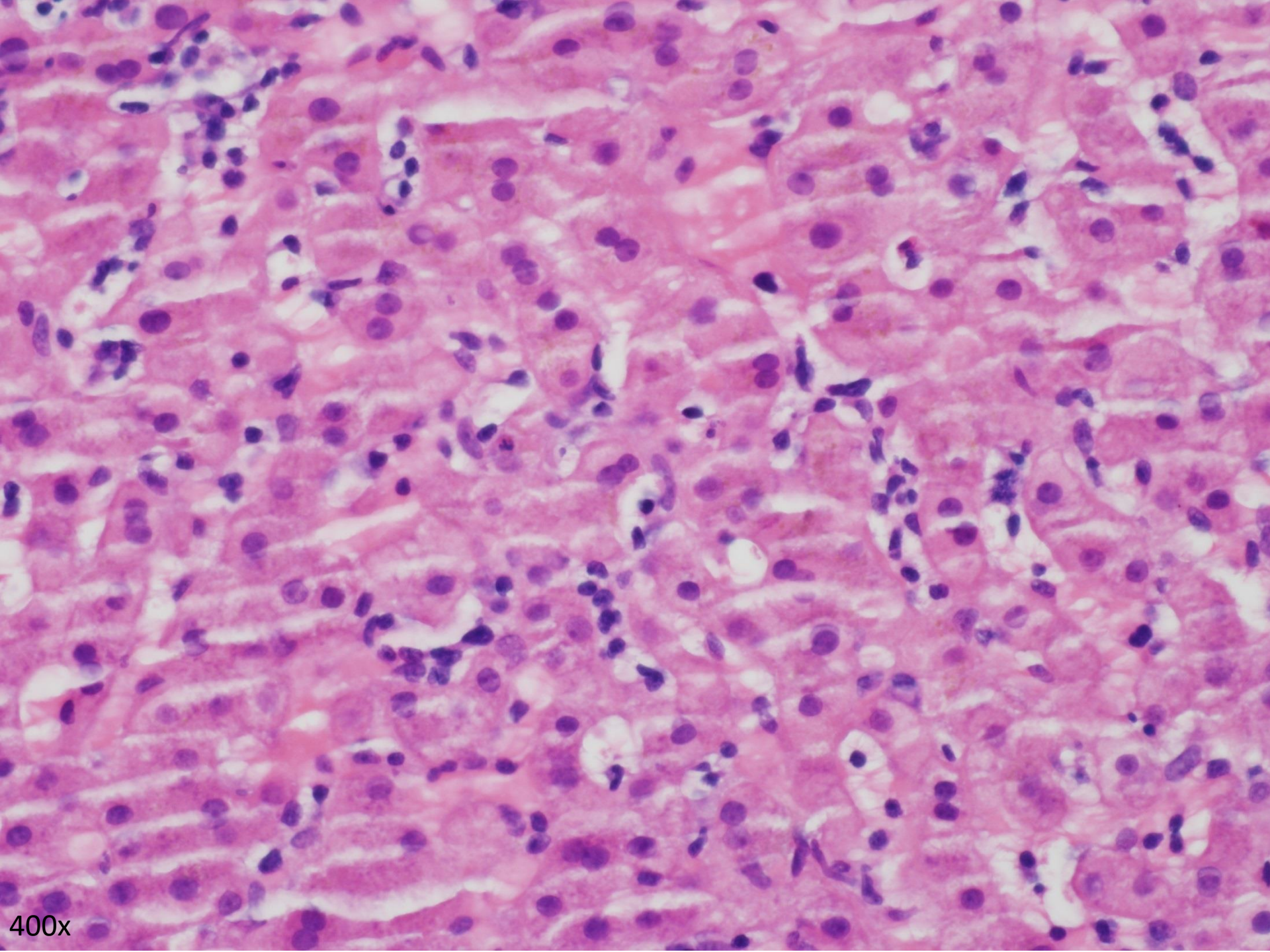
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HSTL: Immunophenotype

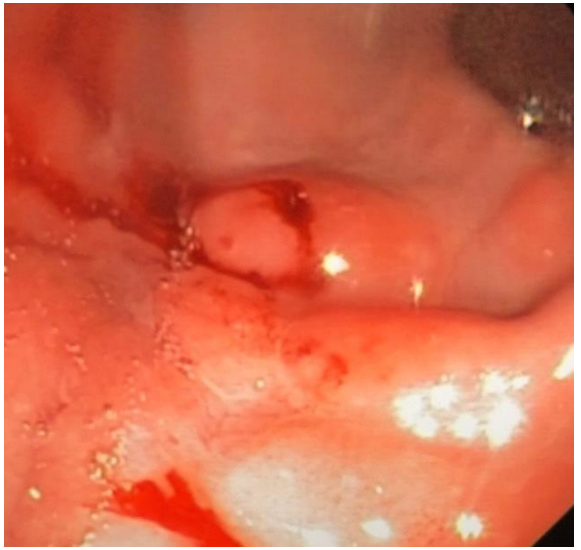
- Typically express CD3, CD2, CD56 (frequent), TCR gamma/delta (alpha/beta in a minority), and cytotoxic granule-associated proteins (TIA1 and granzyme M)
- Typically negative for CD4, CD8 (minority +), CD5 & CD7 (frequent loss), granzyme B, perforin, CD57, CD30

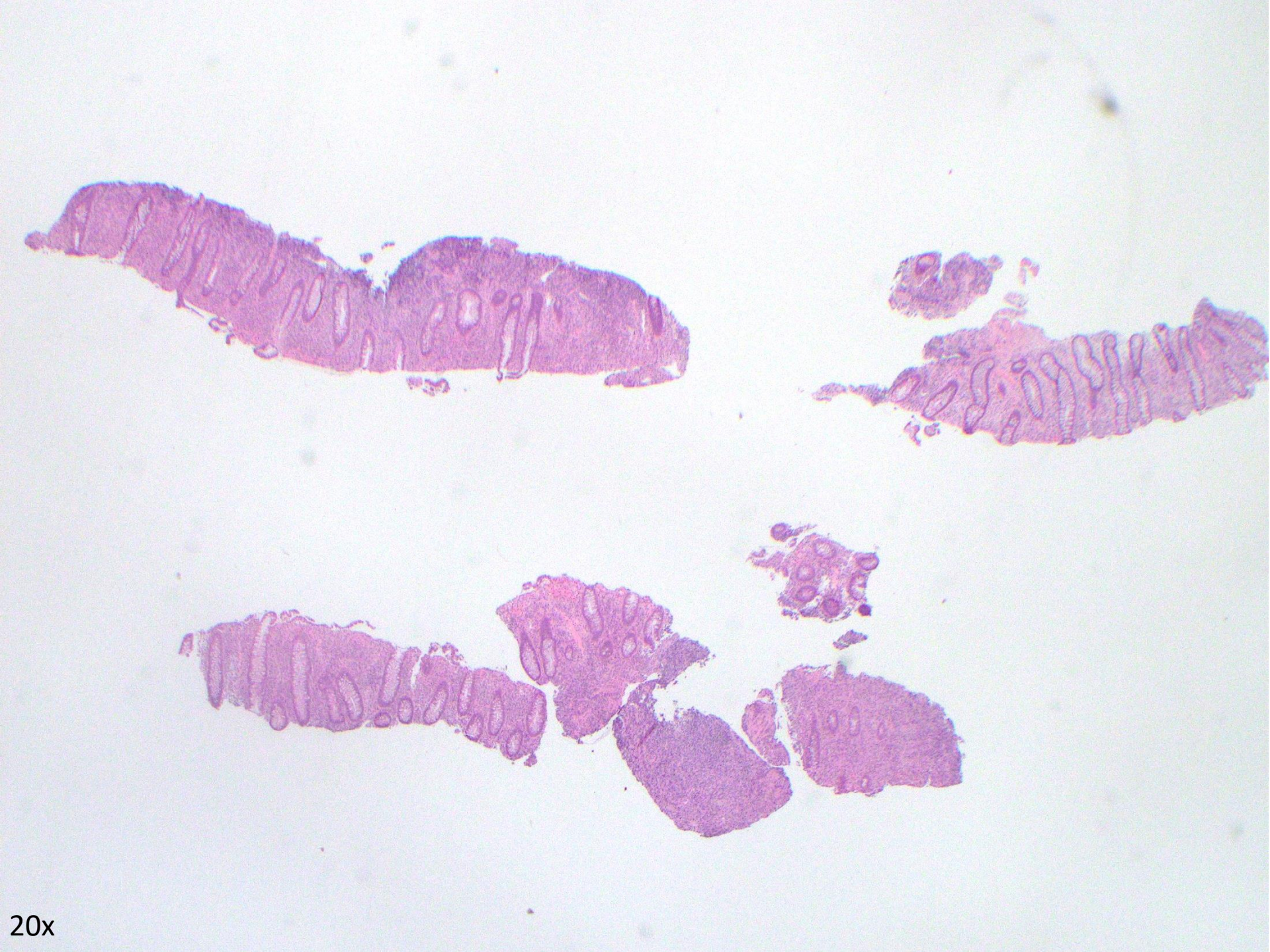
Approach Summary

- Careful morphologic evaluation within context of clinical and endoscopic data
  - Inflammatory conditions vs Lymphoma vs Another malignancy vs Normal
- Tiered immunostain panels
  - CD20, CD3, CD43
    - Reactive: T-cell predominant, but mixed
    - Aberrant CD43 expression on CD20-positive B-cells: MCL, CLL/SLL, subset of MALTL
    - CD43 expression without CD20 or CD3: possibility of myeloid neoplasm
  - Targeted additional immunos as needed to complete characterization of an entity or exclude others
  - Targeted additional immunos as needed for prognosis or treatment
- Molecular studies for specific gene alterations if needed for diagnostic refinement
- Clonality studies may not be useful
  - Benign reactive populations can have small clones that may amplify erroneously leading to lymphoma diagnosis

A parting case

- 42 year old man with HIV and painless anal masses that progressed in size over 3 months
- On sigmoidoscopy, “a field of a mix of large and small nodules”

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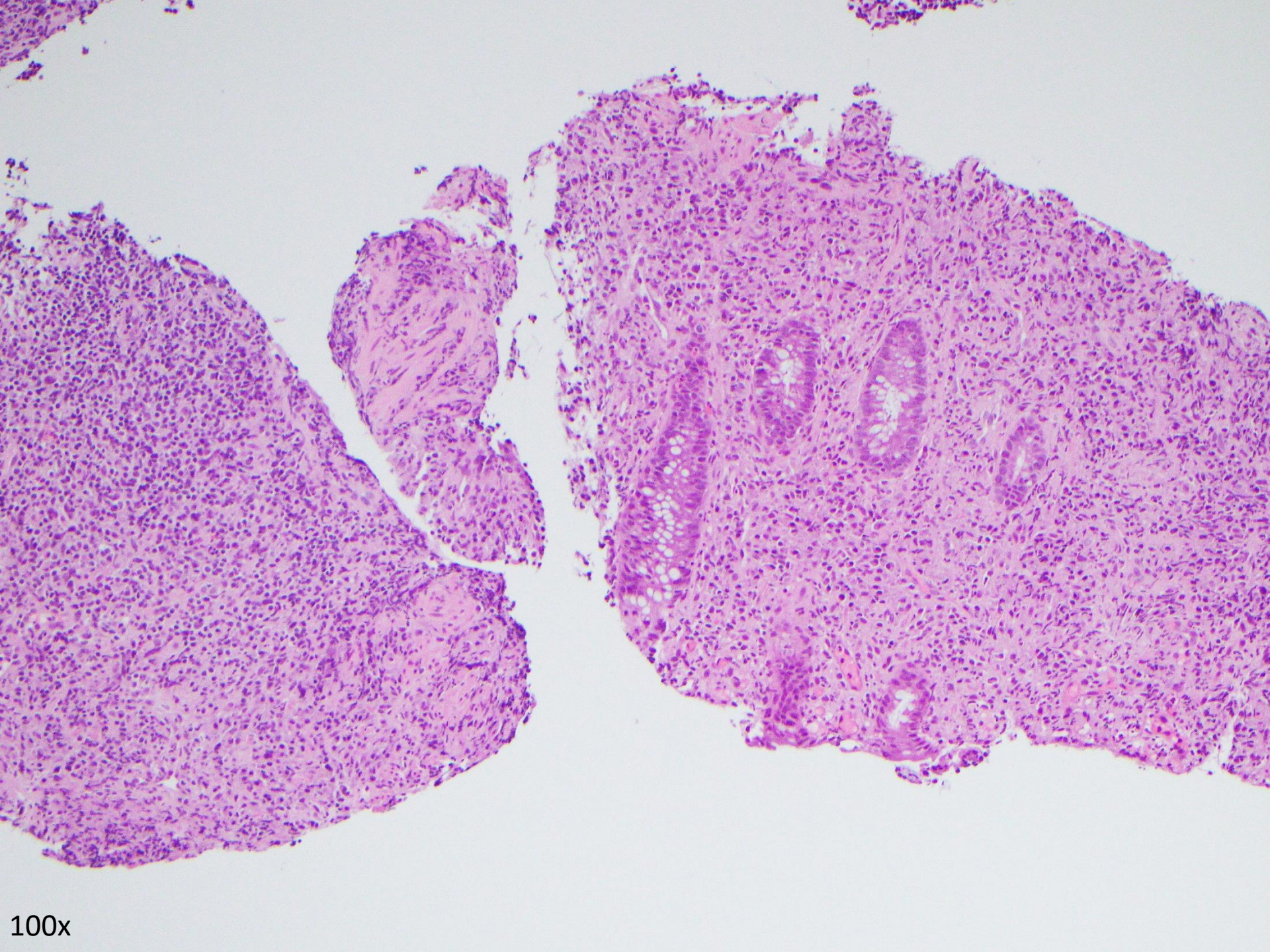
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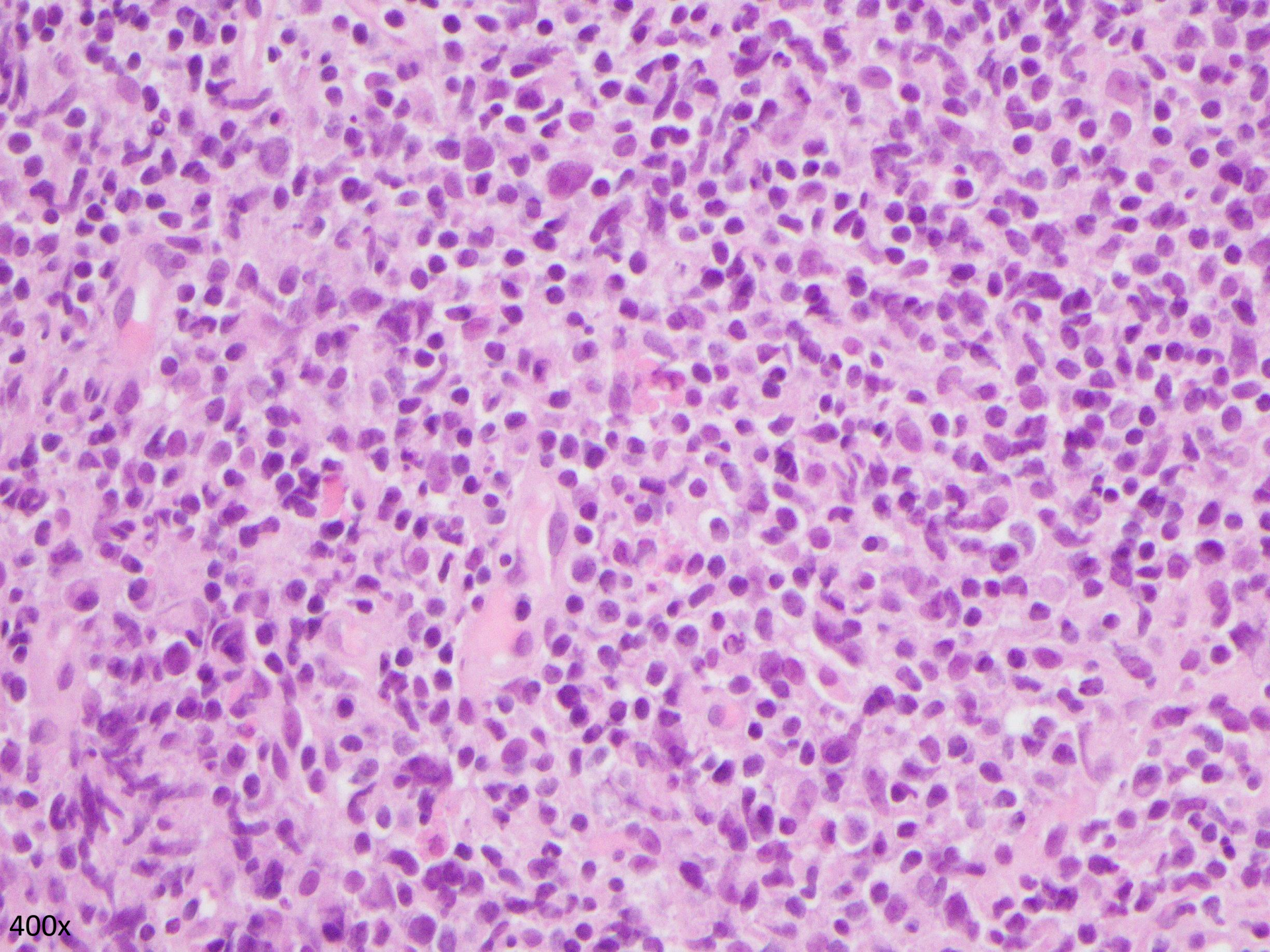
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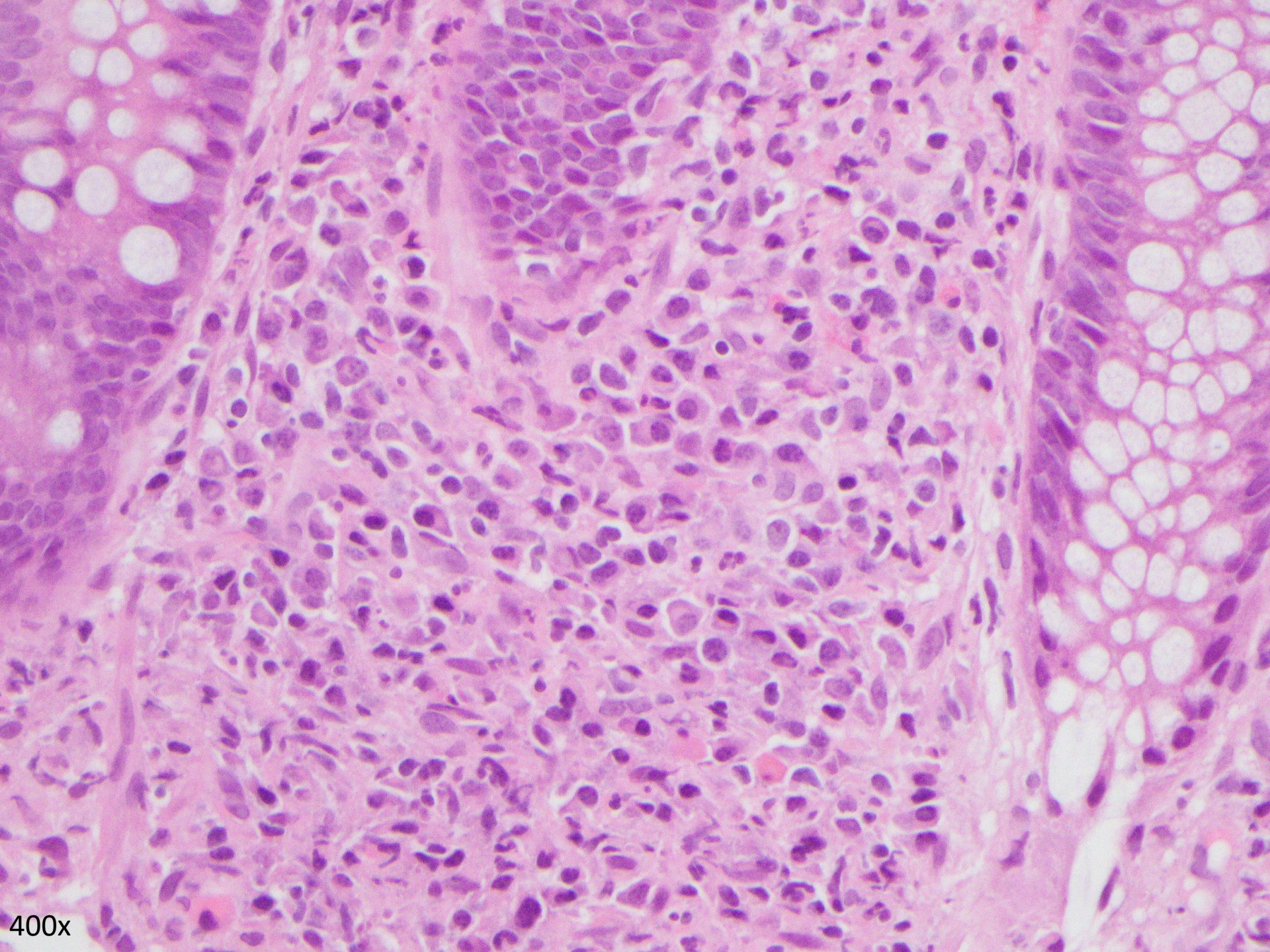
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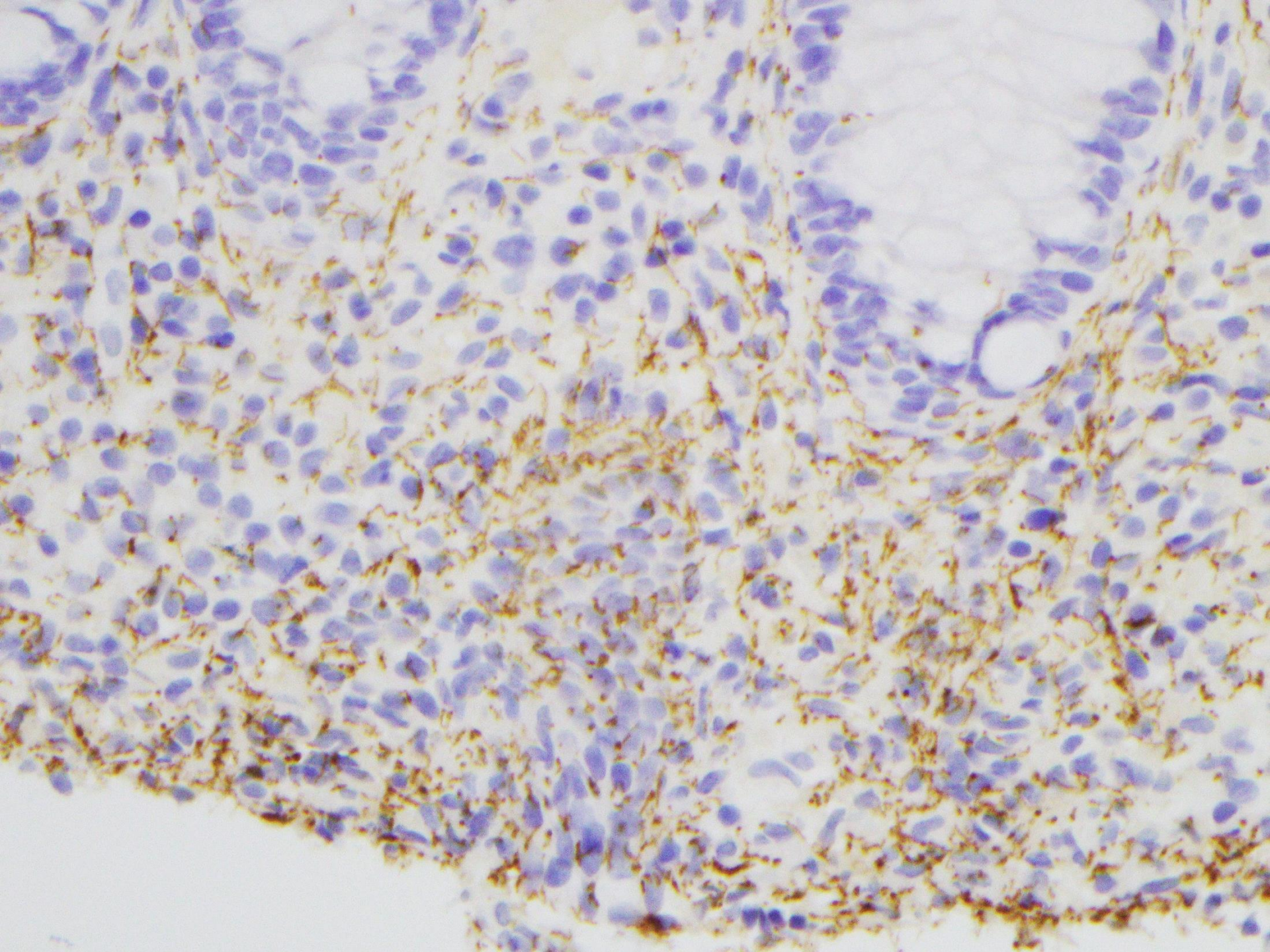

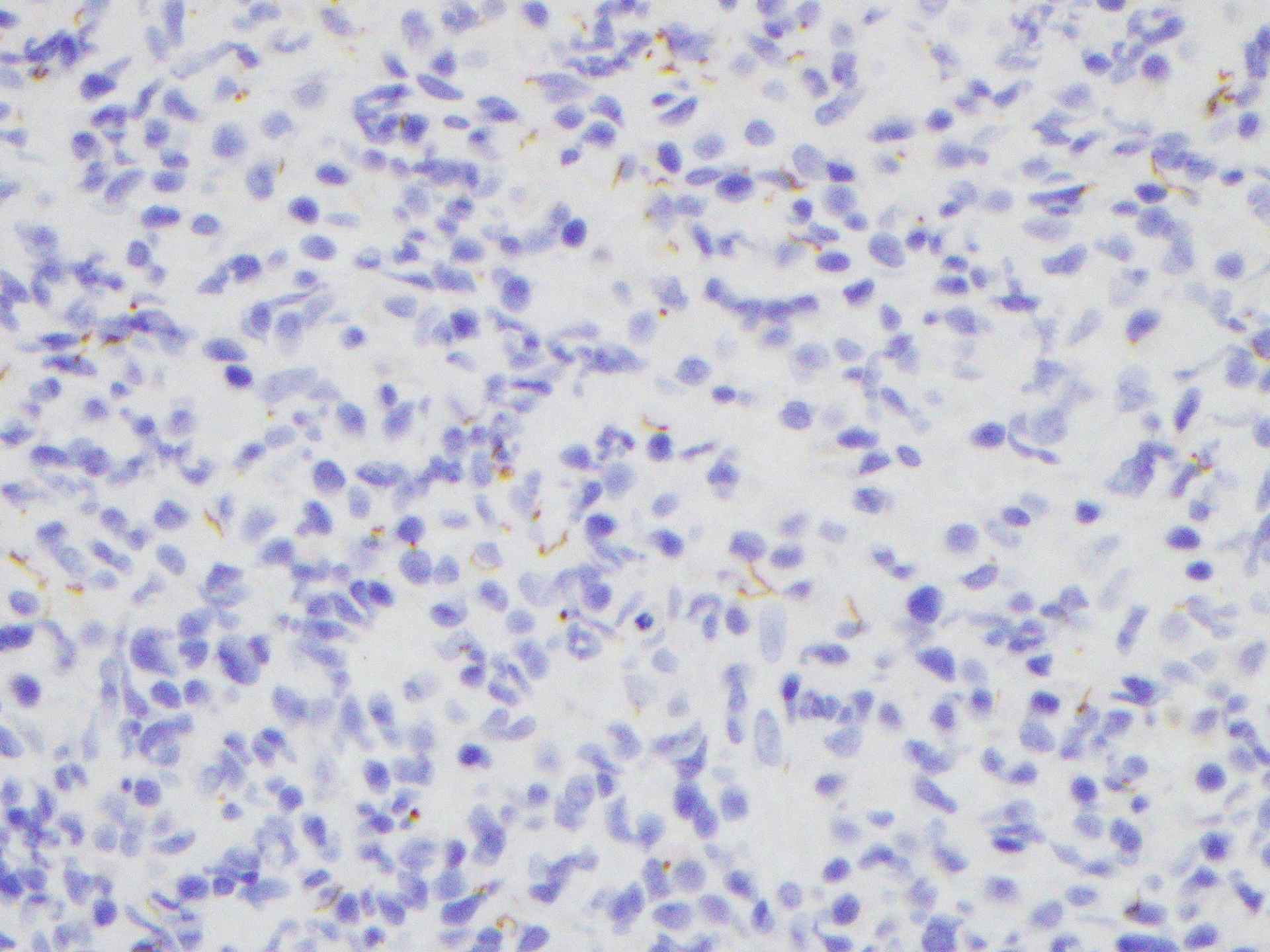

References:

- Nicolae A, et al. EBV-positive large B-cell lymphomas in young patients: a nodal lymphoma with evidence for a tolerogenic immune environment. Blood. 2015;126(7):863-72.
- Asano N, et al. Helicobacter pylori-negative gastric mucosa-associated lymphoid tissue lymphomas: A review. World J Gastroenterol. 2015;21(26):8014-20.
- Nomura E, et al. Regression of MALT lymphoma of the rectum after Helicobacter pylori eradication therapy in a patient negative for Helicobacter pylori. Nihon Shokakibyo Gakkai Zasshi. 2010;107(9):1466-73.
- Nakamura S, et al. Helicobacter pylori-negative gastric mucosa-associated lymphoid tissue lymphoma: a clinicopathologic and molecular study with reference to antibiotic treatment. Cancer. 2006;107(12):2770-8.
- Owens SR. Lymphoproliferative Diseases of the Gut: A Survival Guide for the General Pathologist. Surg Pathol Clin. 2017;10(4):1021-1037.
- Swerdlow SH, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375-90.
- Skinnider BF. Lymphoproliferative Disorders of the Gastrointestinal Tract. Arch Pathol Lab Med. 2018;142(1):44-52.
- Arps DP, Smith LB. Classic versus type II enteropathy-associated T-cell lymphoma: diagnostic considerations. Arch Pathol Lab Med. 2013;137(9):1227-31.
- Delabie J, et al. Enteropathy-associated T-cell lymphoma: clinical and histological findings from the international peripheral T-cell lymphoma project. Blood. 2011;118(1):148-55.
- Tan SY, et al. Type II EATL (epitheliotropic intestinal T-cell lymphoma): a neoplasm of intra-epithelial T-cells with predominant CD8αα phenotype. Leukemia. 2013;27(8):1688-96.
- Shi Y, Wang E. Hepatosplenic T-Cell Lymphoma: A Clinicopathologic Review With an Emphasis on Diagnostic Differentiation From Other T-Cell/Natural Killer-Cell Neoplasms. Arch Pathol Lab Med. 2015;139(9):1173-80. Review.
- Peng JC, Zhong L, Ran ZH. Primary lymphomas in the gastrointestinal tract. J Dig Dis. 2015;16(4):169-76.