Algorithme phénotypique dans les lymphoprolifératiions

Aide au diagnostic

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CMP 19/11/2015

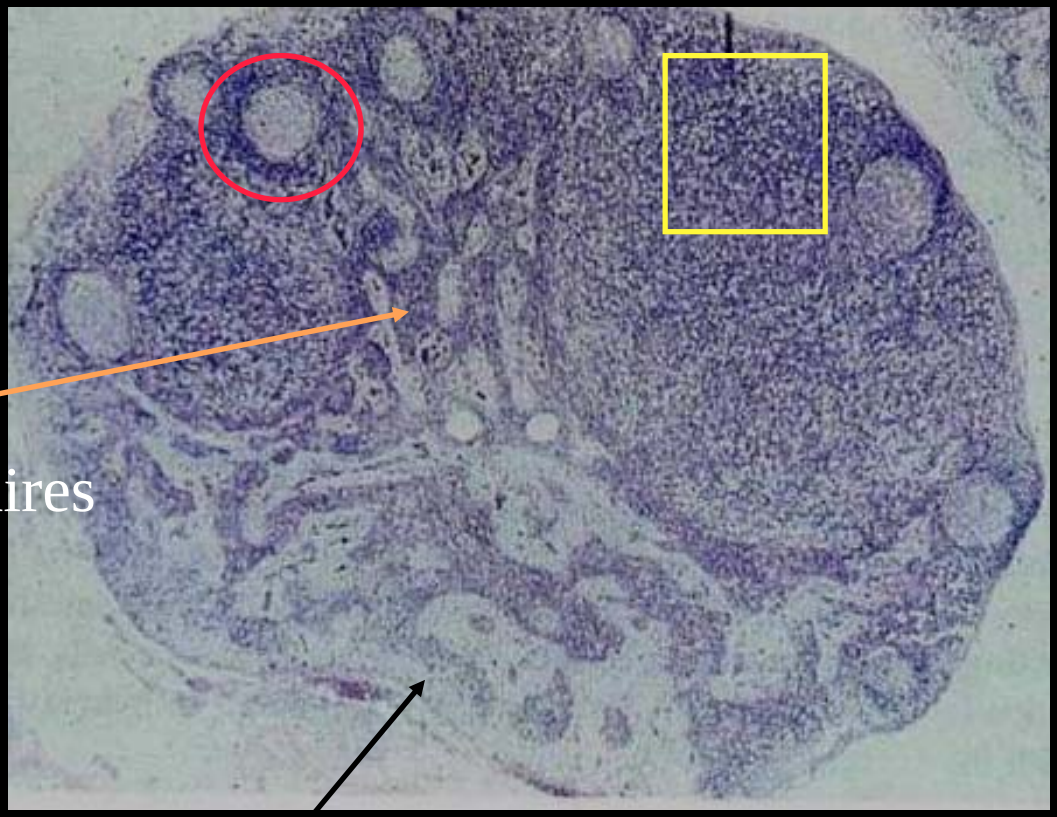
Introduction

- Pas de stress: un diagnostic est possible !
- 25% de lymphomes en dehors des ganglions
  - Tube digestif
  - Anneau de Waldeyer
  - Peau
- Un diagnostic de lymphome est souvent multidisciplinaire (cytométrie, bio mol, génétique et…clinique!)
  - Bouin à proscrire !!!!
  - Formol peut permettre
    - IHC
    - Biologie moléculaire: réarrangements, translocations, FISH

Histologie normale (ganglion)

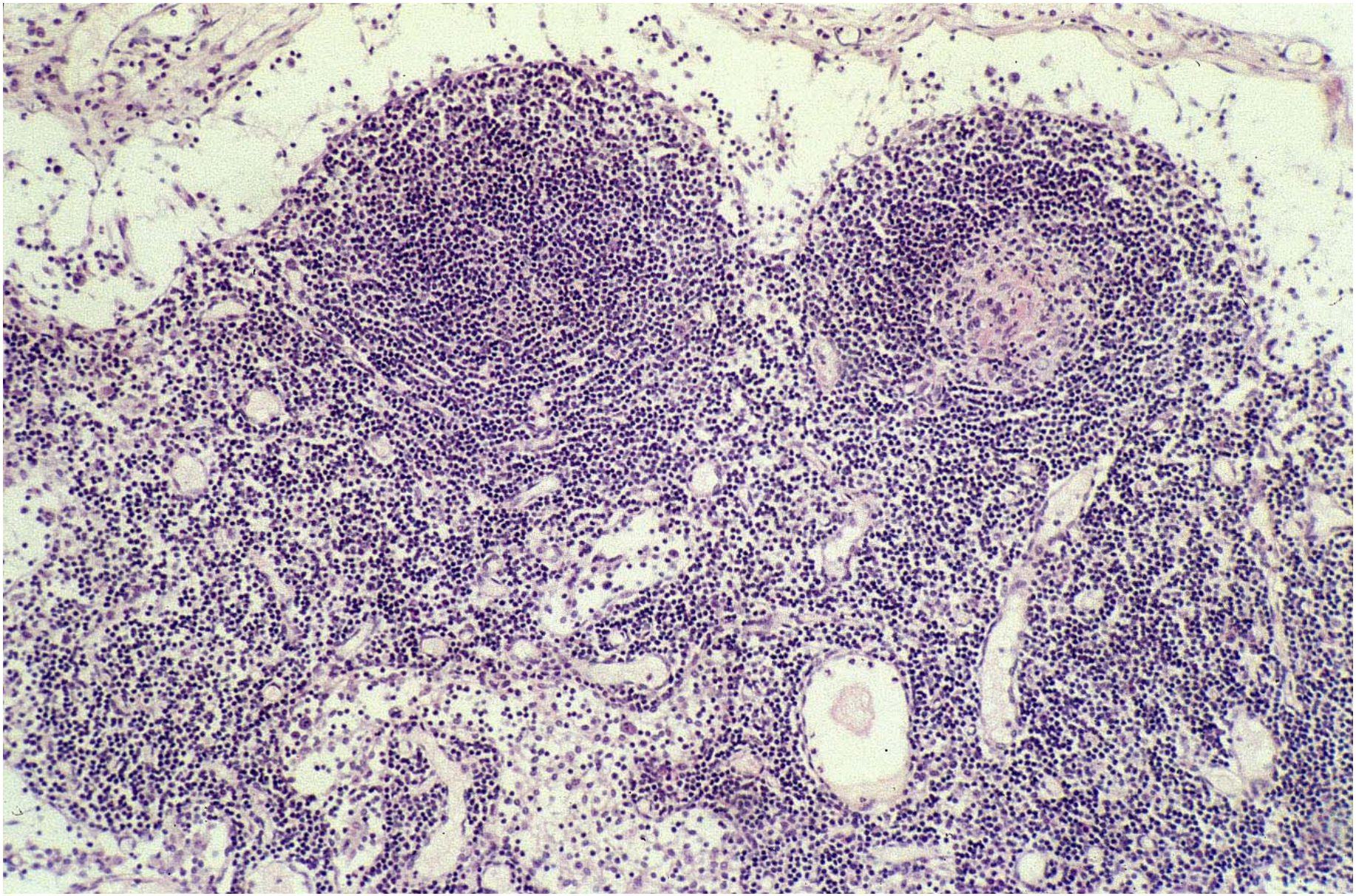
Cortex: follicule

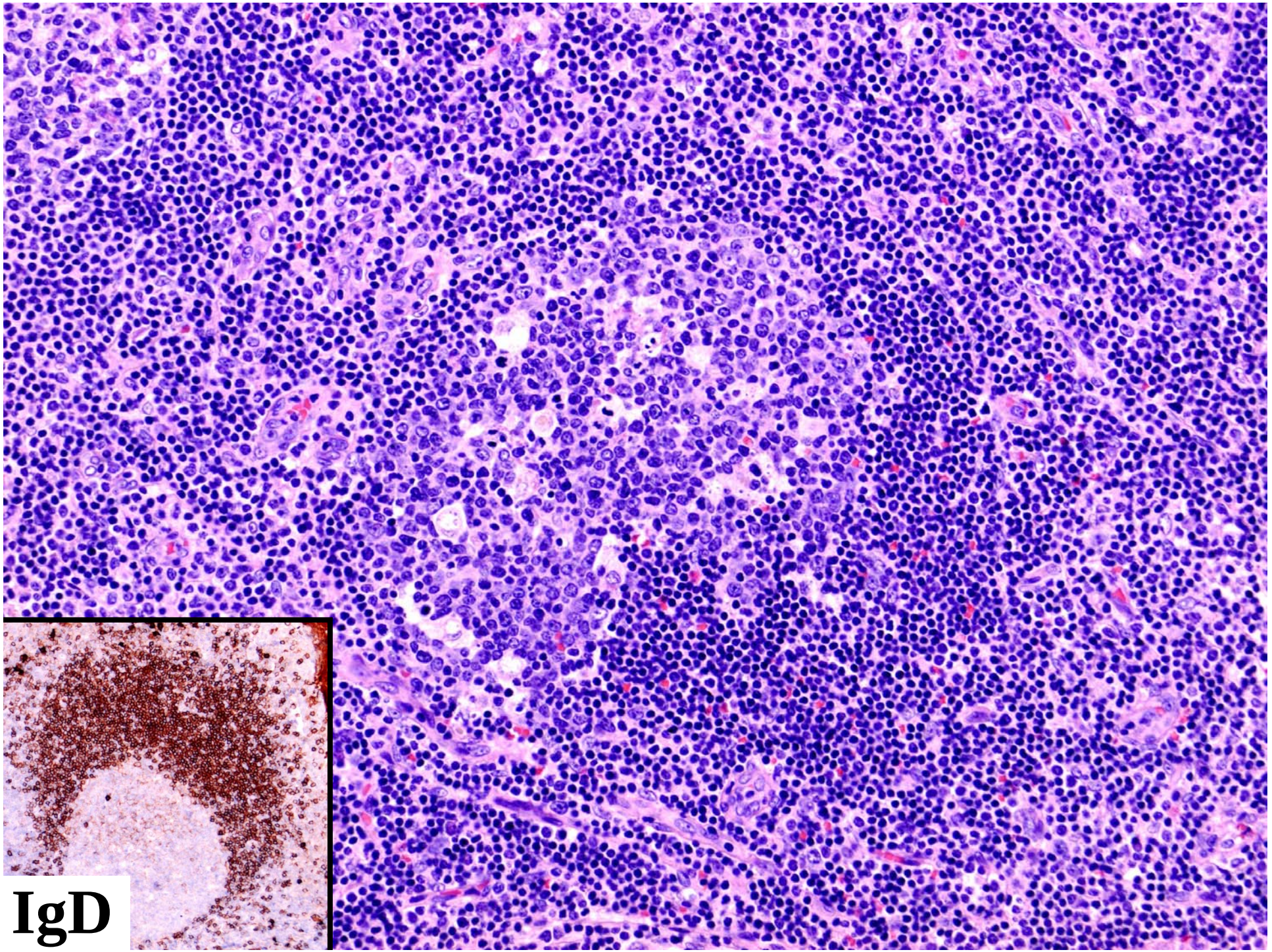
Paracortex: zone T

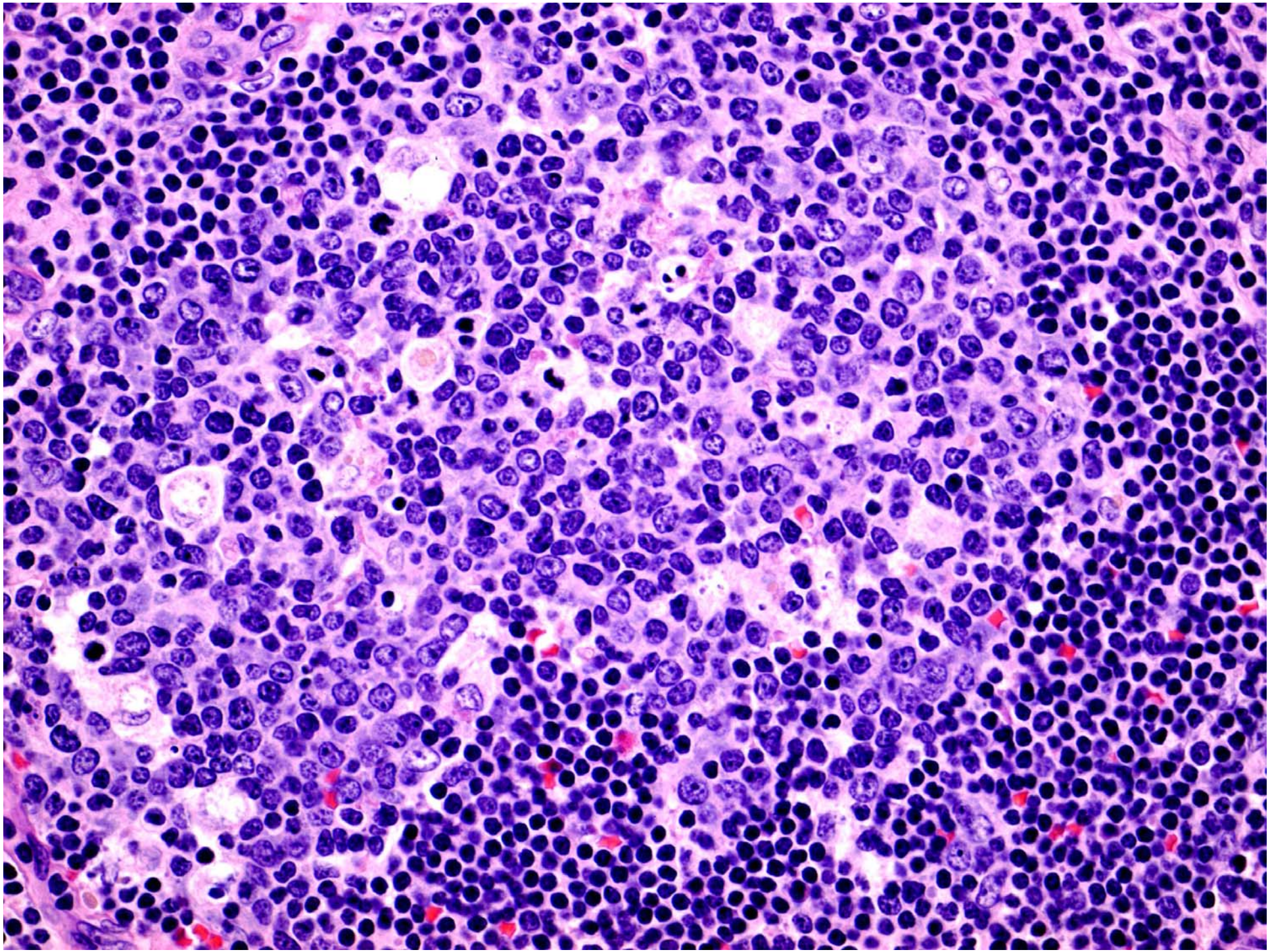


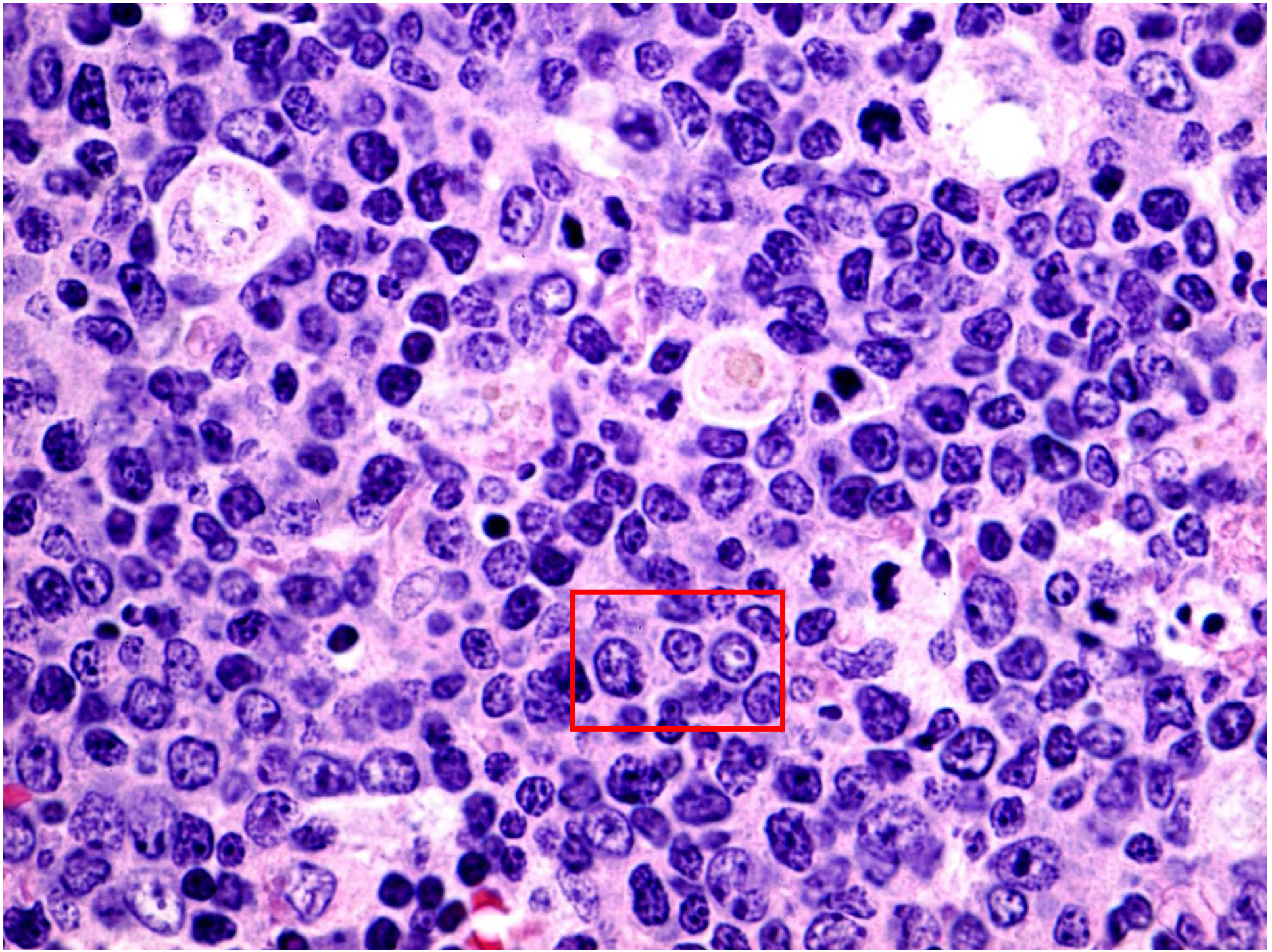
Cordons médullaires

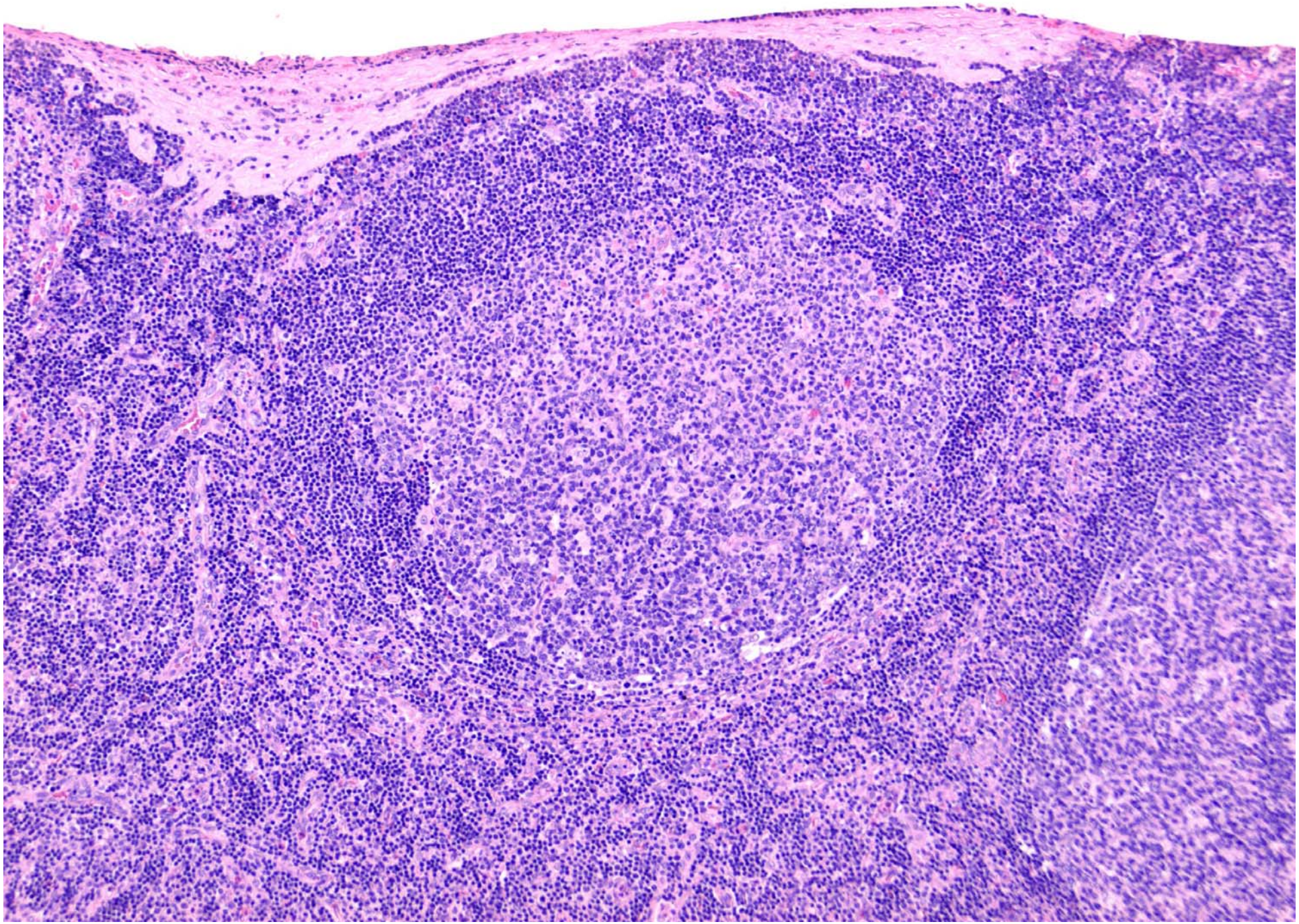
sinus

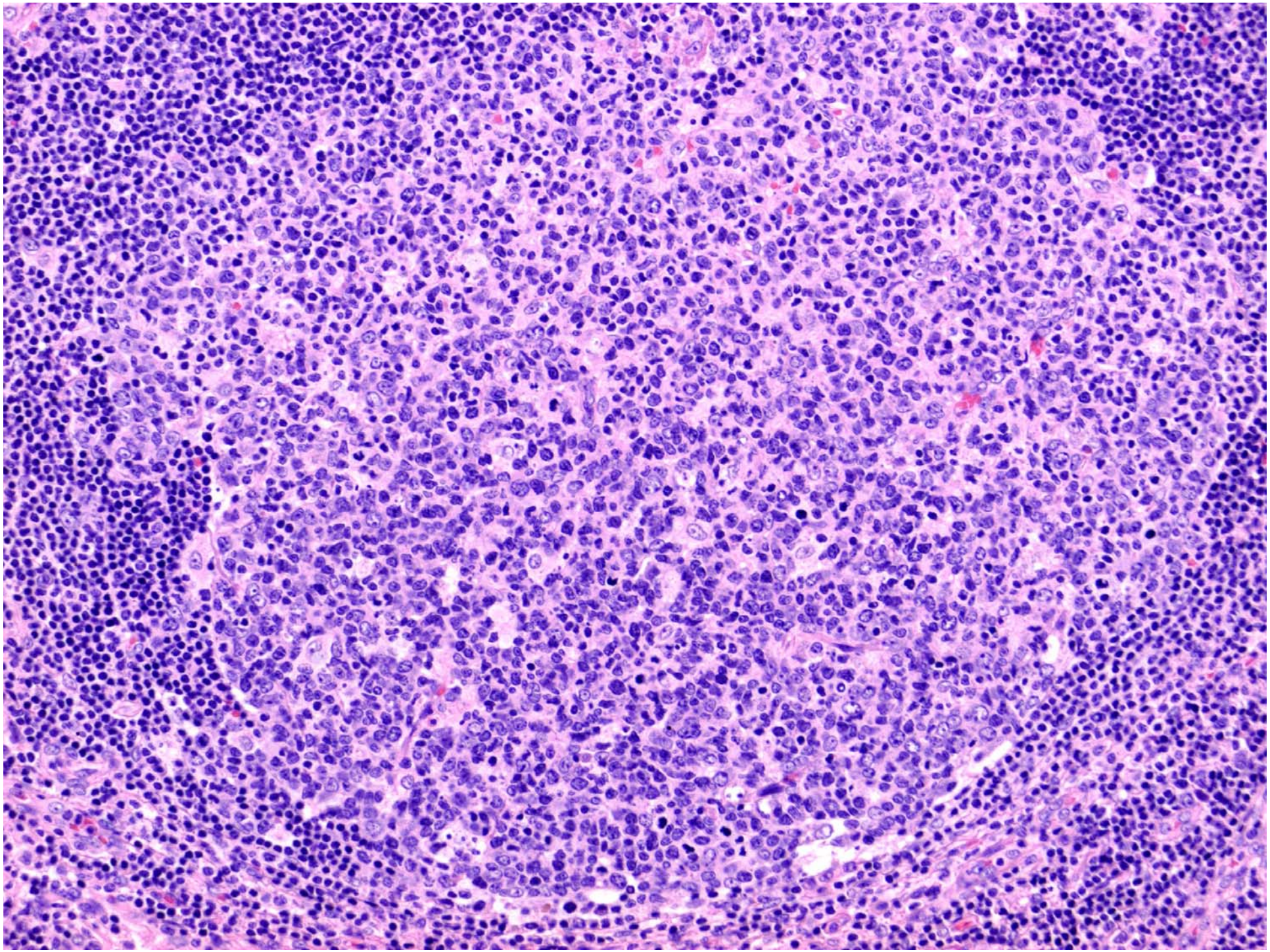


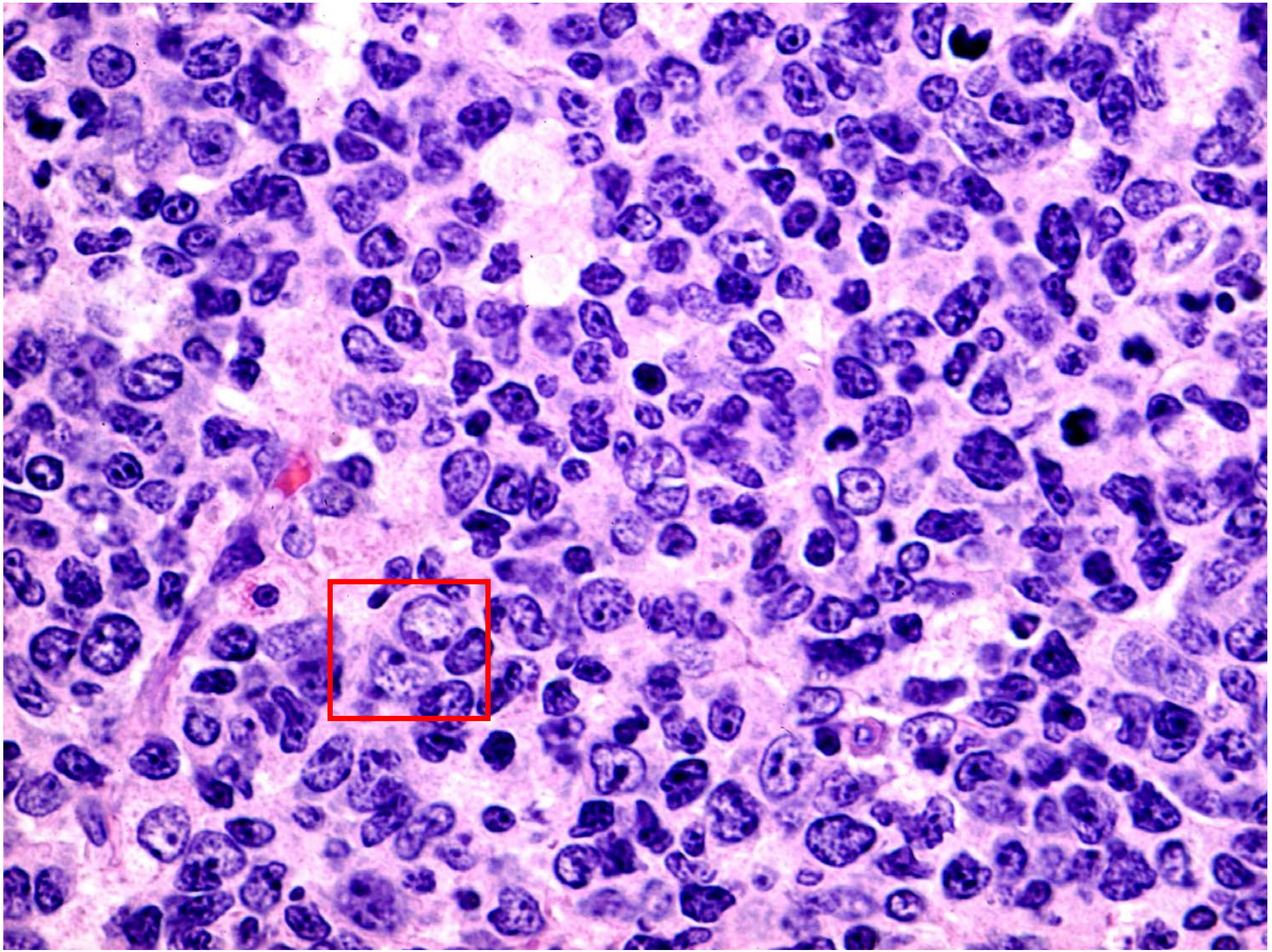

IgD

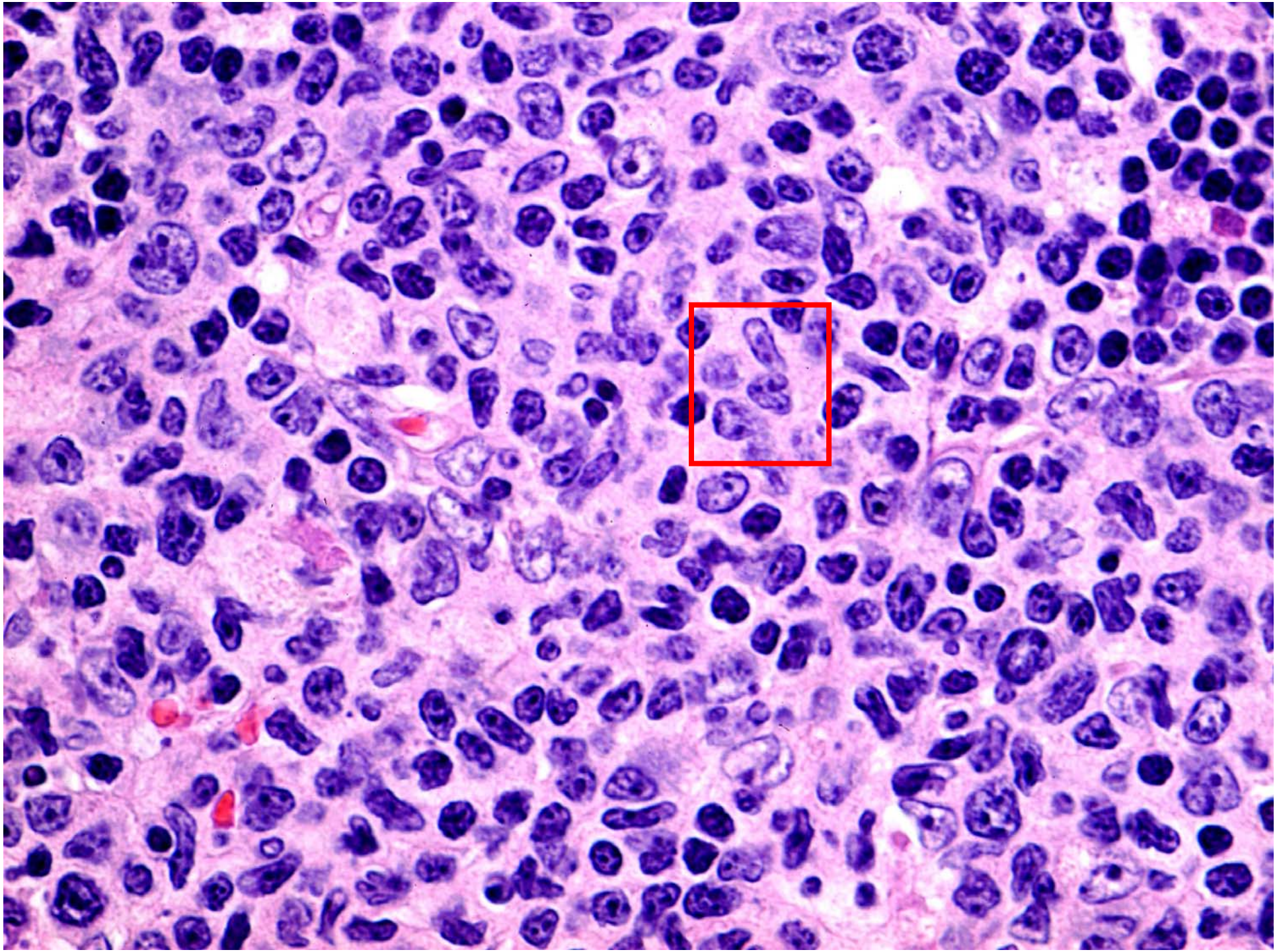


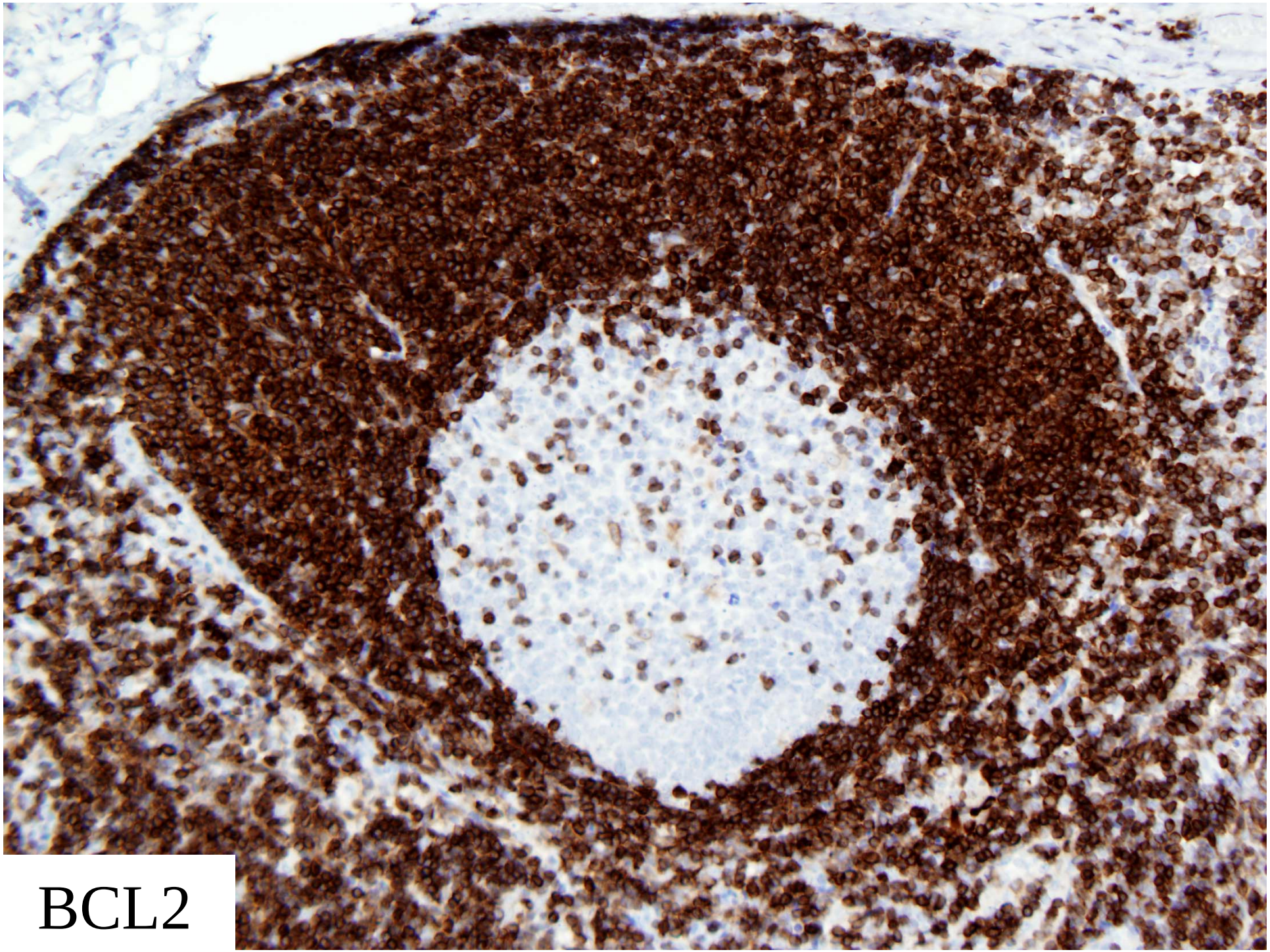




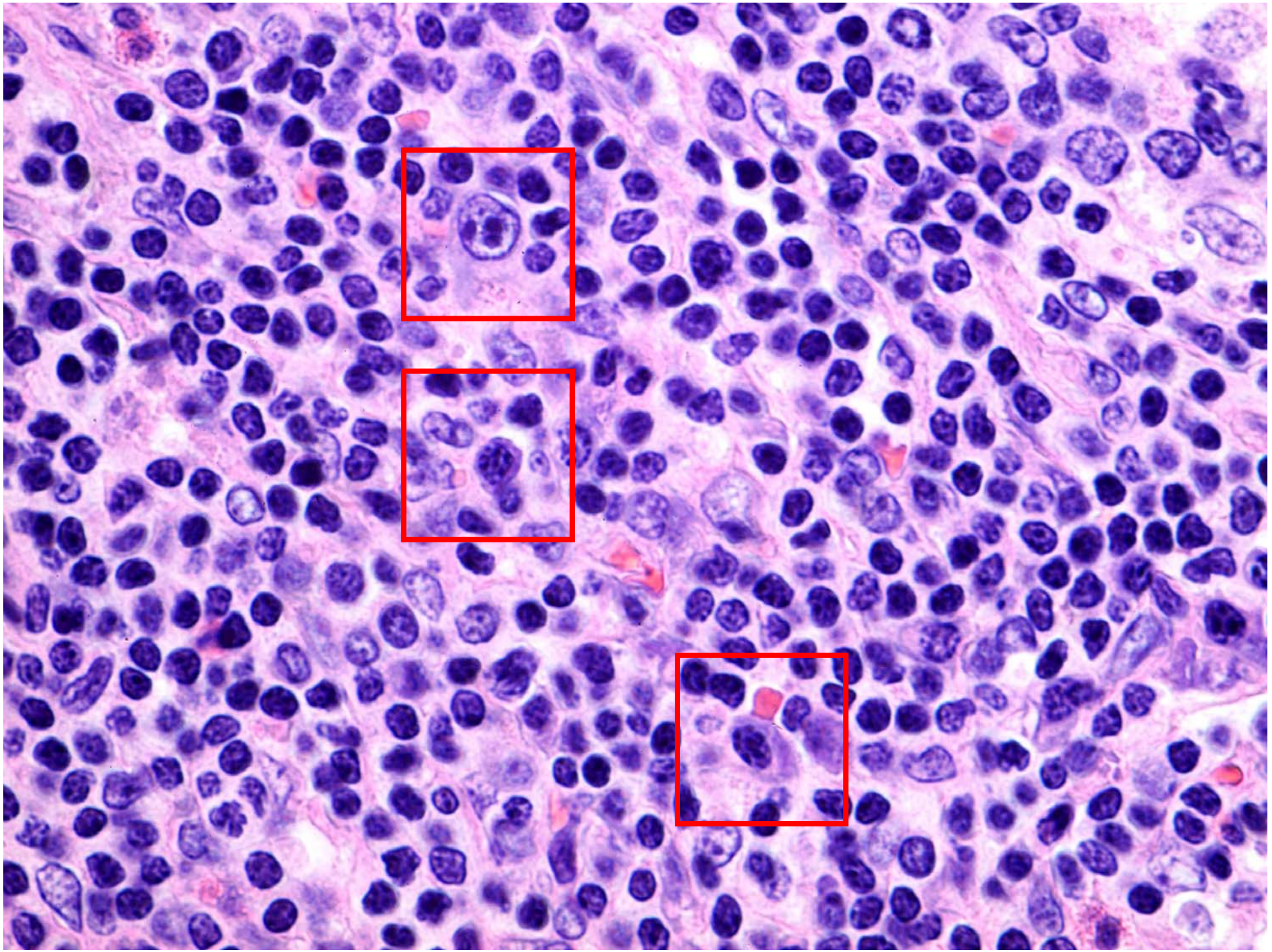


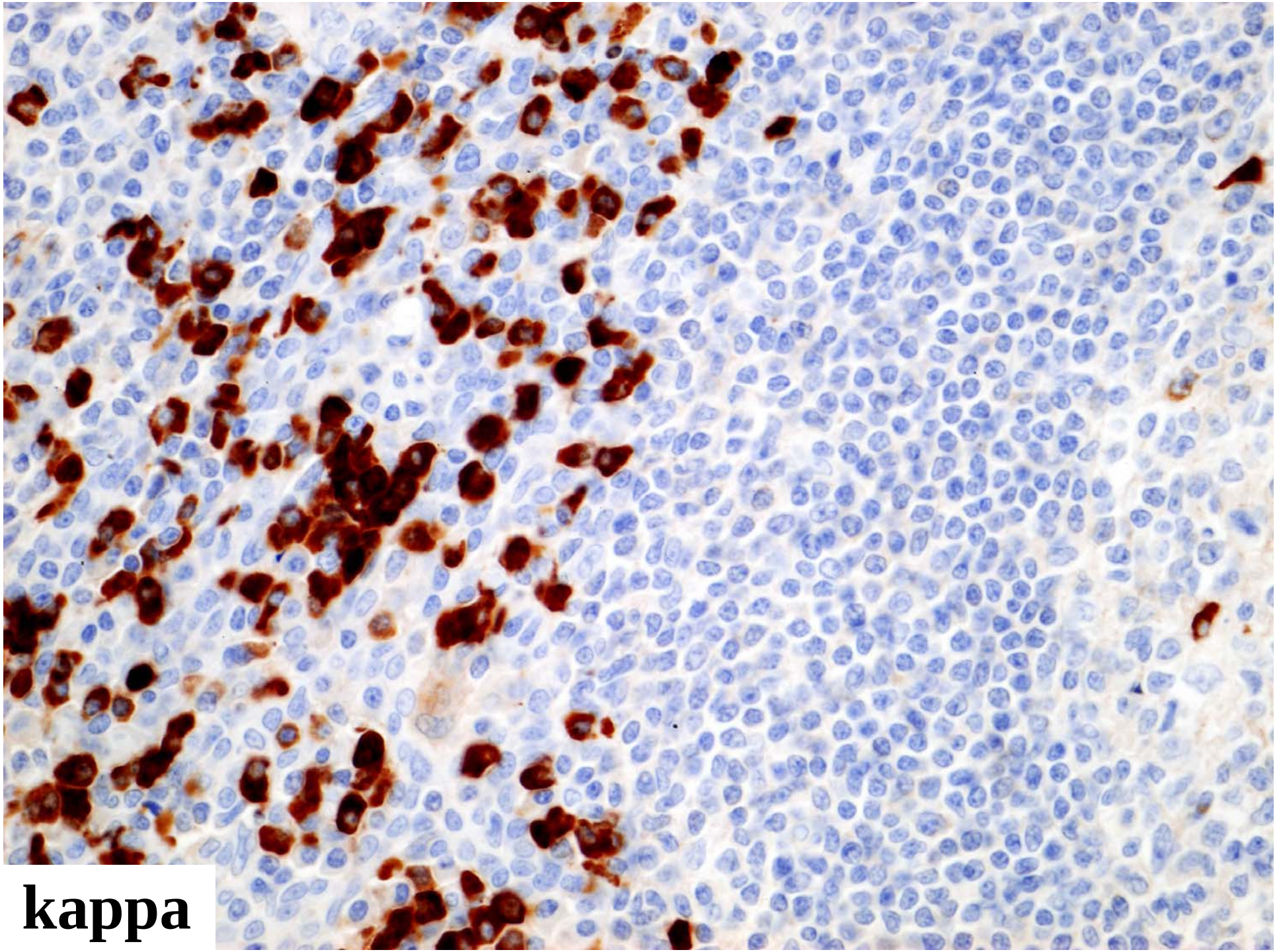


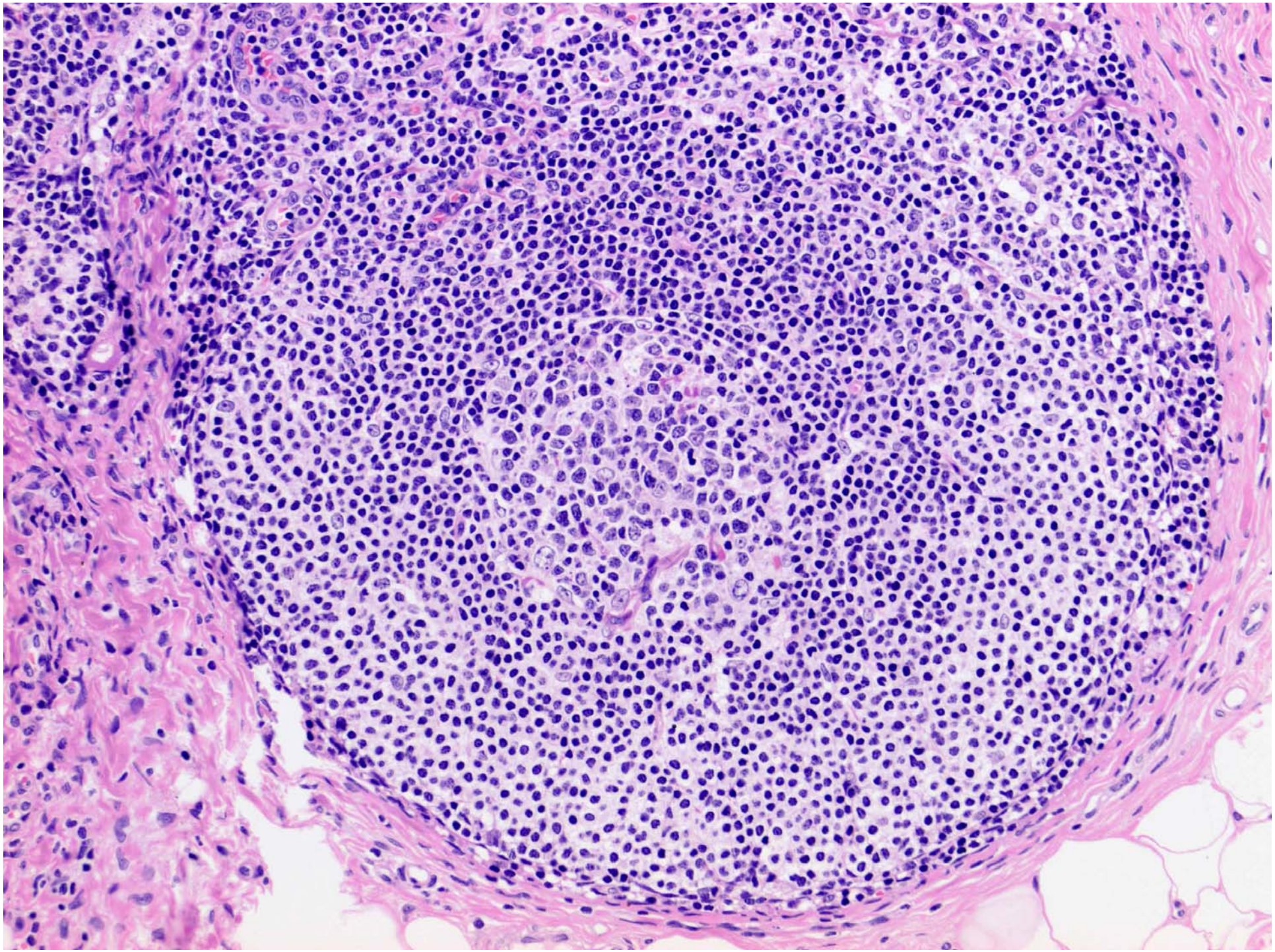


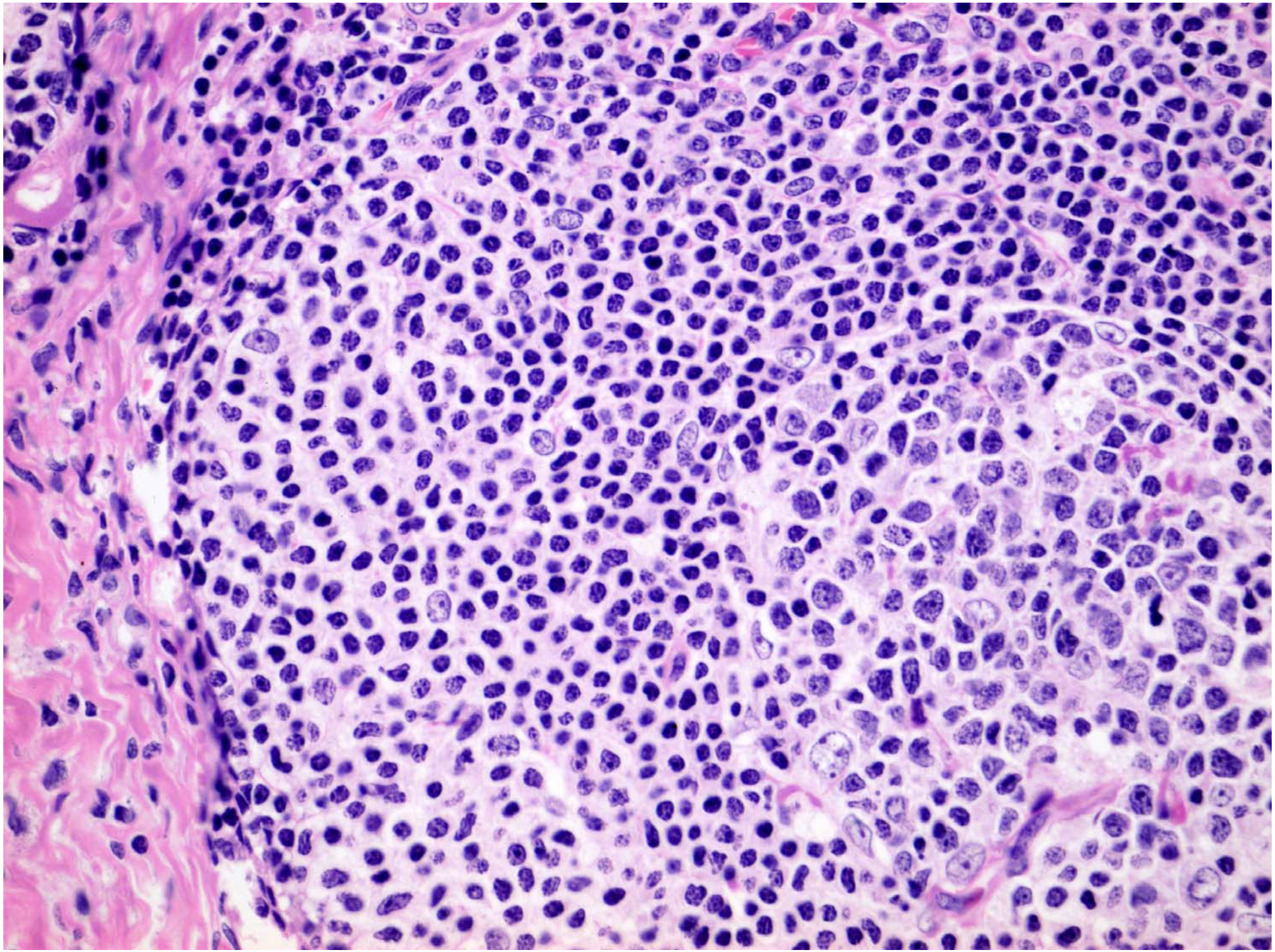


BCL2



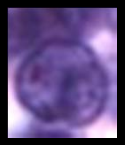

kappa





Maturation normale (cellules B)

pré-antigénique



Sang, MO

Follicule Iaire

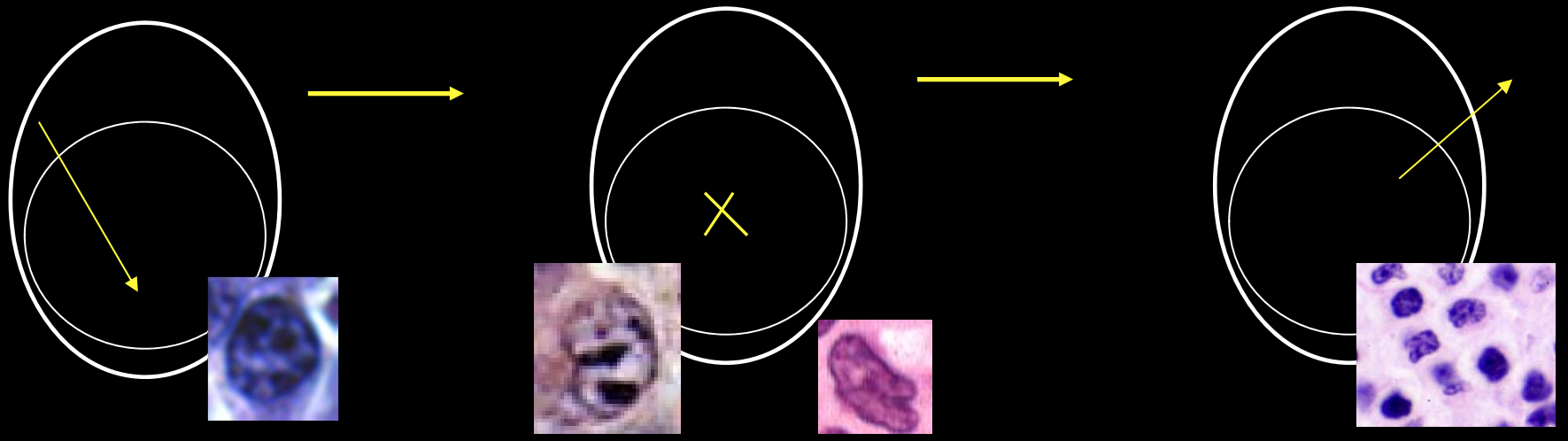
Lymphoblastes
CD19, CD79a
CD34, TdT
VDJ gene rearr

Lymphome/leucémie lymphoblastique

B matures naïves
CD19, CD20, CD79a
sIg (IgM, IgD)
CD5+
CD23-

Lymphome à cellules du manteau

Maturation normale (cellules B)
Centre germinatif et post-antigénique



Blastes folliculaires

sIgM
CD5-
CD10+
CD19,20,79a+

Burkitt

Centroblastes et centrocytes

sIg
CD5-
CD10+
CD19,20,79a

Lymphome folliculaire

Cell de la ZM

sIg
CD5,10-
CD19,20,79a+

Lymphome de la ZM

Principaux marqueurs (lymphomes B)

	CD20	CD5	CD10	CD23	Bcl-2	Bcl-1
L.lymphoblastique	-	-	+	-	+	-
LLC	+	+	-	+	+	-
L.manteau	+	+	-	-	+	+
Burkitt	+	-	+	-	-	-
Folliculaire	+	-	+	-	++	-
L.ZM	+	-	-	-	+	-

Conduite à tenir (pour tout organe)

- Architecture
  - Organe reconnaissable?
  - Destruction ?
  - Pattern « infiltratif »
- Densité de l'infiltrat
- Composition de l'infiltrat
  - Polymorphisme
    - Type cellulaire: lymphocytes, plasmocytes, histiocytes, PMN
  - Follicules lymphoïdes
  - Monotonie cellulaire

Composition de l'infiltrat

- **Polymorphisme**
  - Mélange de cellules immunitaires
  - Grands et petits lymphocytes
  - IHC:
    - CD20 et CD3 mélangés
    - Kappa, lambda
  - PCR: pas de clonalité
  - Génétique: caryotype normal

Composition de l'infiltrat

- **Follicules lymphoïdes**
  - Centres germinatifs sans zone marginale
  - Zone marginale ++
  - IHC:
    - CD20, CD10, bcl-6
    - Bcl-2
    - Kappa, lambda
  - PCR: clonalité ?
  - Génétique: FISH (inclure t(14;18)

Composition de l'infiltrat

- **Monotonie cellulaire**
  - Petites cellules
    - IHC: CD20, CD3
  - Grandes cellules
    - IHC: CD20, CD3, cytoker, CD30
  - Destruction architecturale avec mélange de grandes et petites cellules
    - IHC: CD20, CD3
      - Même phénotype: confirmation moléculaire ou génétique
      - Phénotype différent: regarder si grandes cellules B. Bio mol et génétique peu utiles.
      - CONTEXTE CLINIQUE !!! (immunodépression, EBV,…)

Diagnostic par organe: ganglion

- Tout est possible !
- Algorithme reste valable
- Architecture:
  - Nodulaire
  - Diffuse
  - Mixte

Diagnostic différentiel: architecture nodulaire, petites cellules

- Lymphomes B+++
  - FL
  - MZL
  - MCL
  - SLL
- Lymphomes T
  - Follicular variant (TFH)

CD20, CD3, CD5,
CD23, cyclinD1
CD10, bcl-6, bcl-2,
Ki67

SOX-11, LEF-1
HGAL, stathmin-1
IRTA-1, MNDA
CXCL13, PD-1

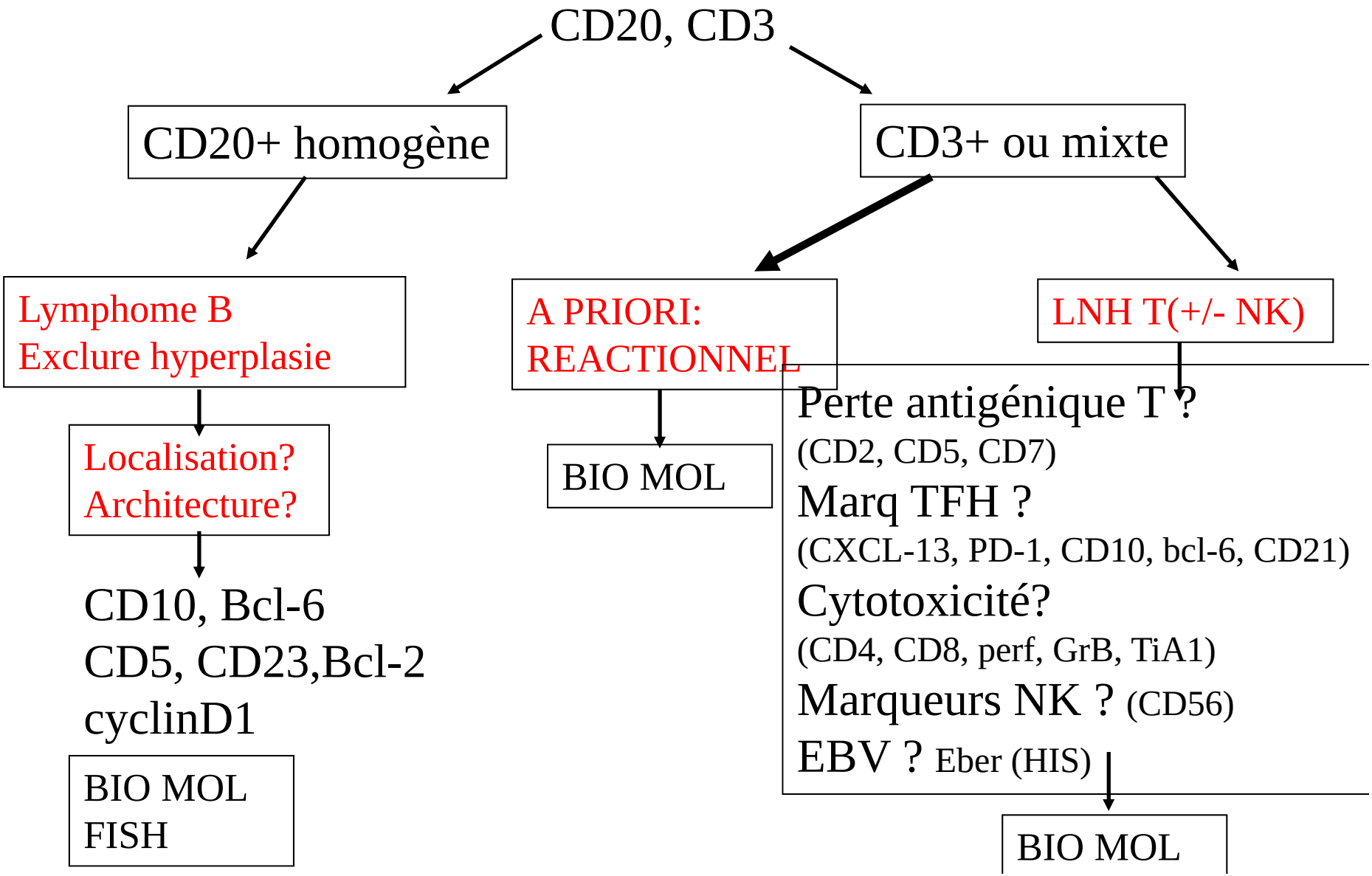
Diagnostic différentiel: architecture diffuse, petites cellules

- Lymphomes T+++
- Lymphomes B
  - FL diffus
  - MCL
  - LPL
  - MZL
  - (SLL)

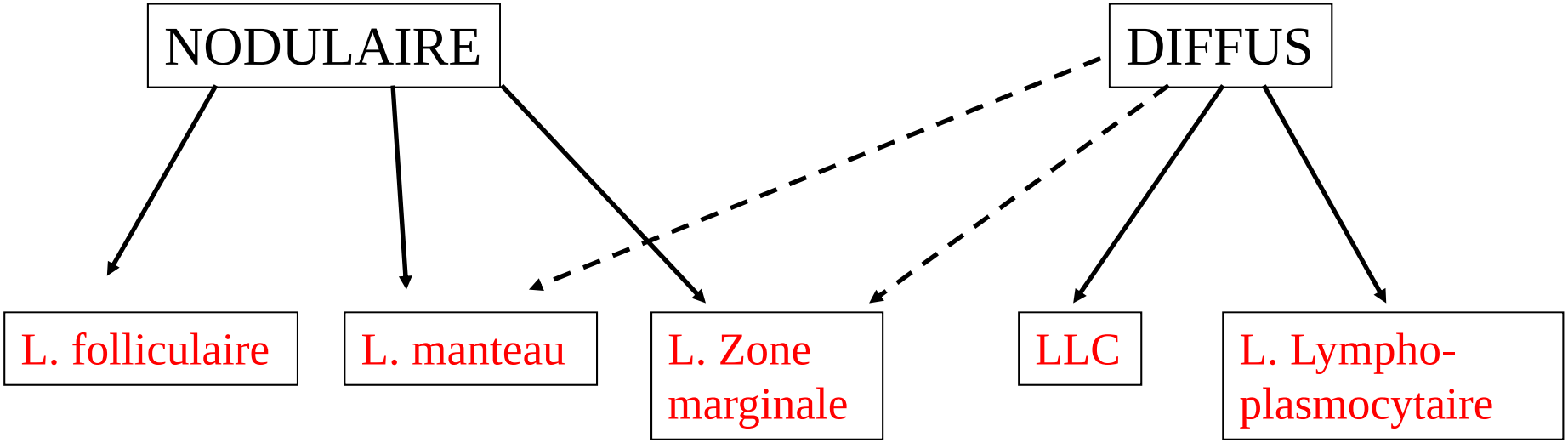
CD20, CD2, CD3,
CD5, CD56, CD23,
cyclinD1
CD10, bcl-6, bcl-2,
kappa, lambda, Ki67

SOX-11, LEF-1
HGAL, stathmin-1
IRTA-1, MNDA
CXCL13, PD-1

Prolifération à « petites cellules »

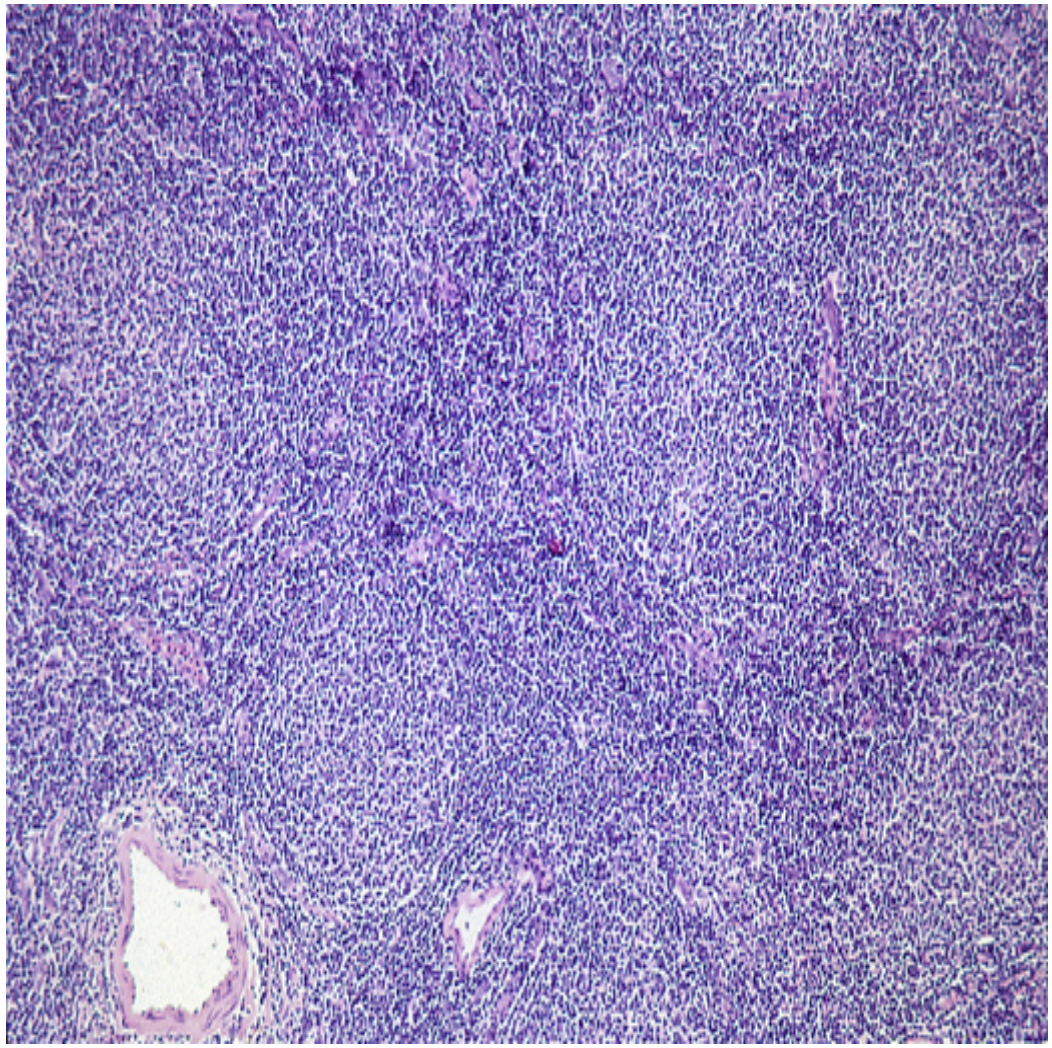


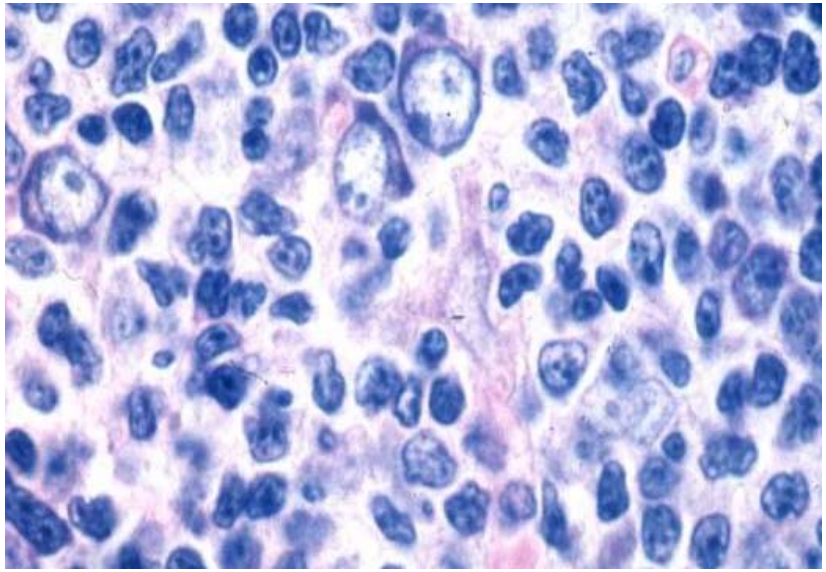
Lymphome B à « petites cellules/mixtes »

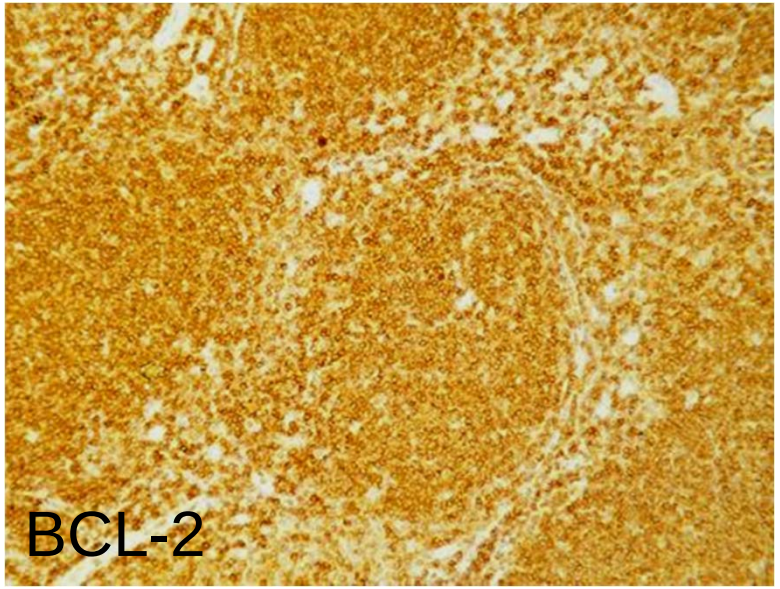


L. folliculaire	L. manteau	L. Zone marginale	LLC	L. Lympho-plasmocytaire
CD5 - CD23 - CD10 + Bcl-6 + Bcl-2 + cyclinD1 – HGAL:+ Stathmin +	CD5 + CD23 - CD10 - Bcl-6 + Bcl-2 + cyclinD1 + Sox-11 +	CD5 - CD23 - CD10 - Bcl-6 - Bcl-2 + cyclinD1 -	CD5 + CD23 + CD10 - Bcl-6 - Bcl-2 + cyclinD1 – Stathmin (centres de prolif)	CD5 - CD23 - CD10 - Bcl-6 - Bcl-2 - cyclinD1 – Kappa,lambda

Lymphome folliculaire

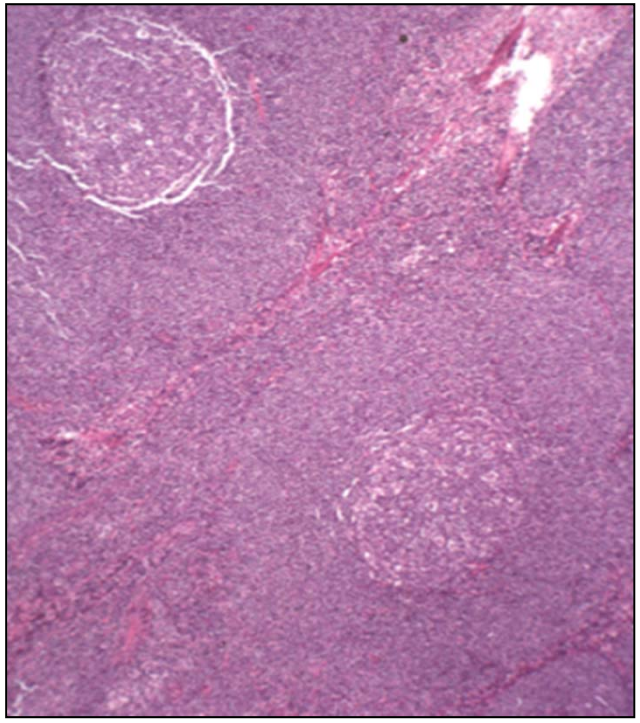


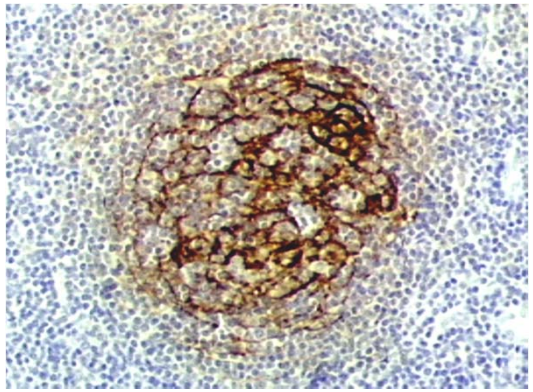




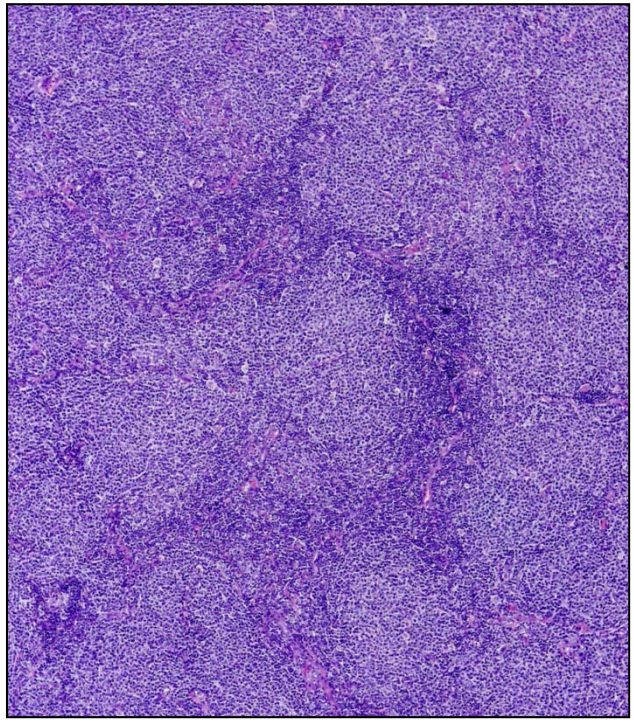
Lymphome à cellules du manteau

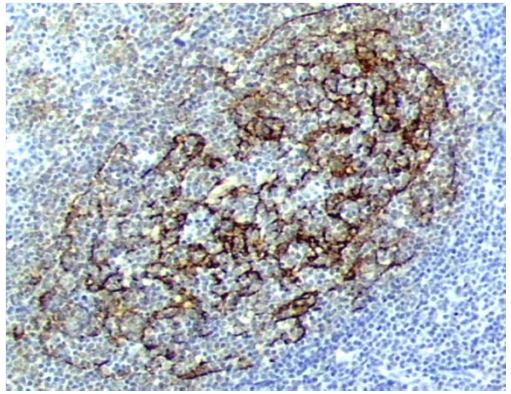
Zone du manteau



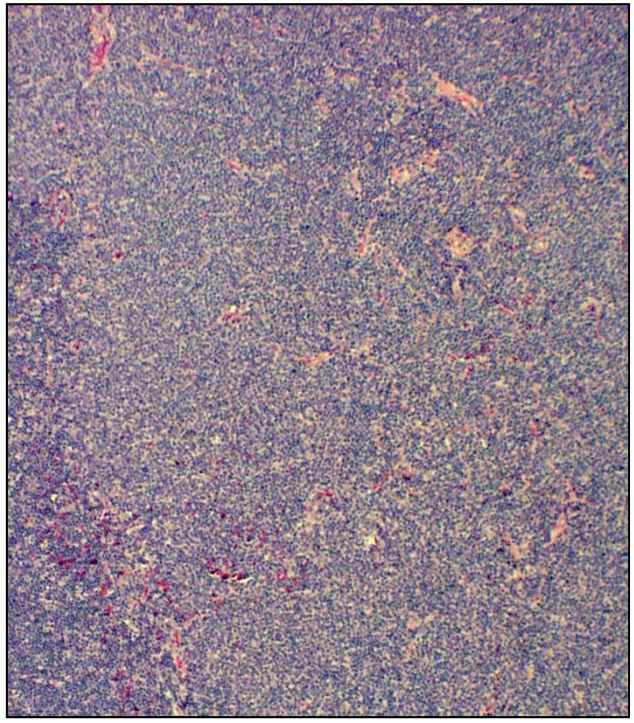


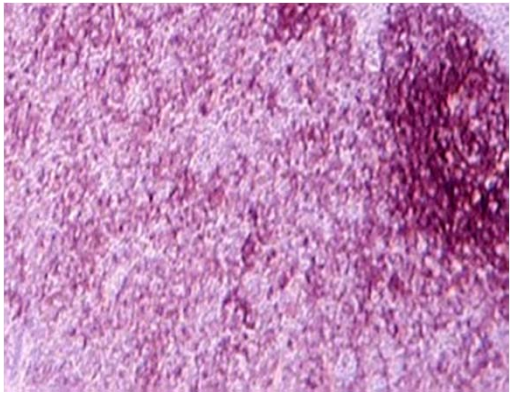
Nodulaire





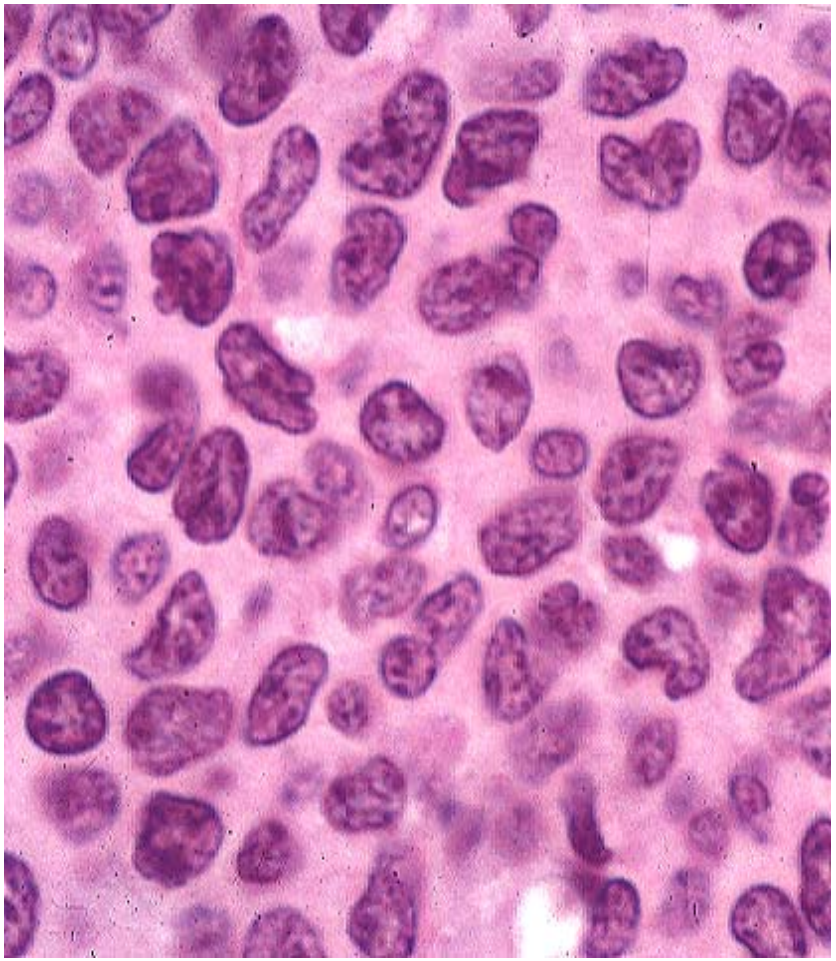
Diffuse



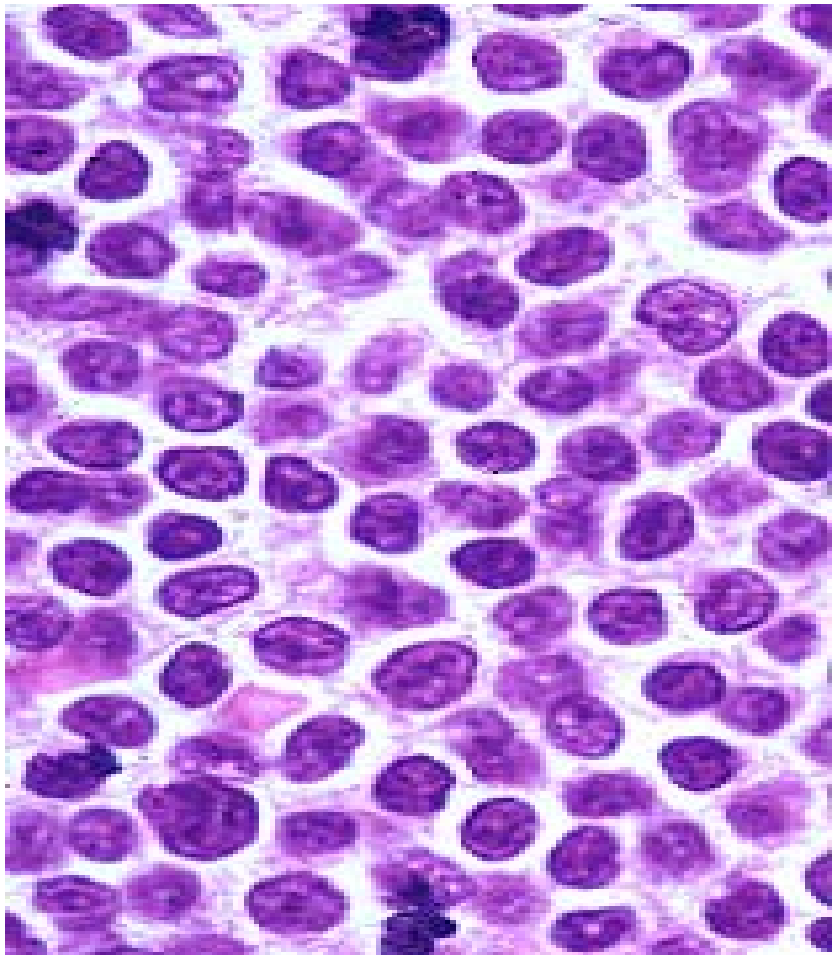


Lymphome à cellules du manteau: variants cytologiques à petites cellules

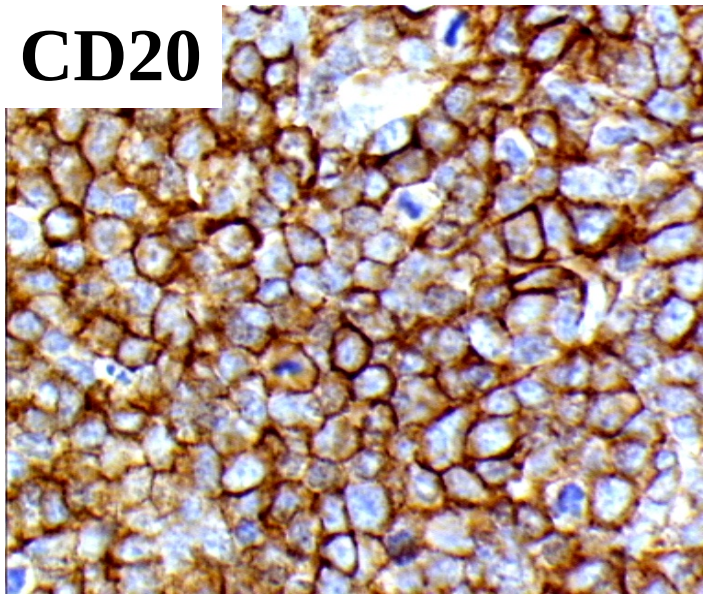
Typique

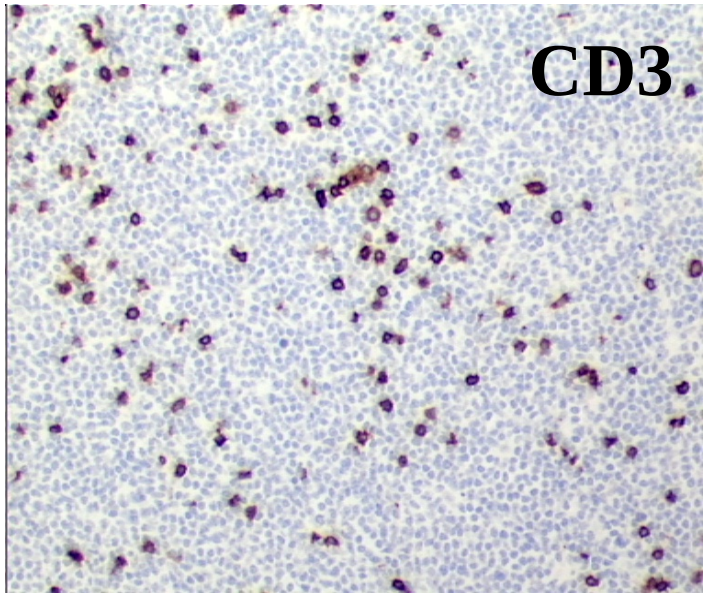


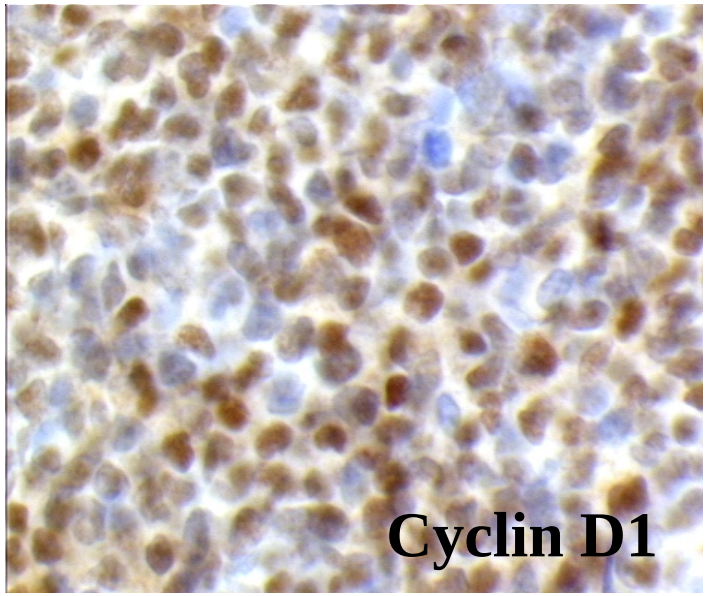
Petites cellules

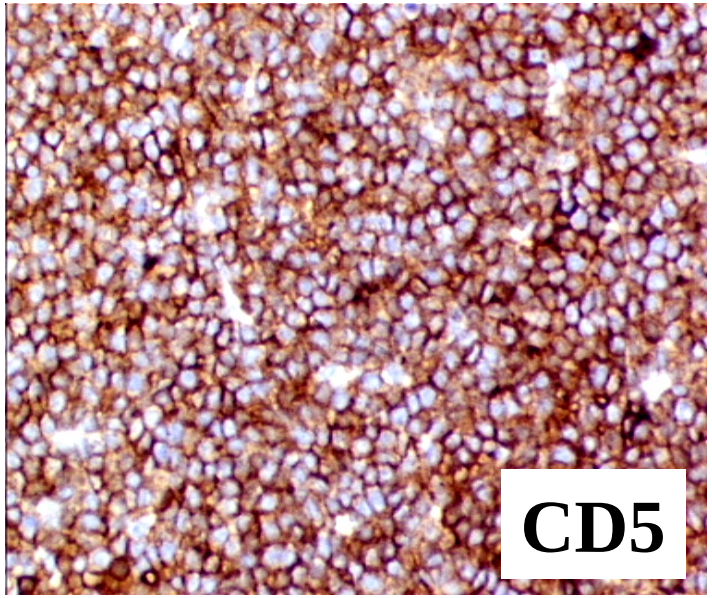


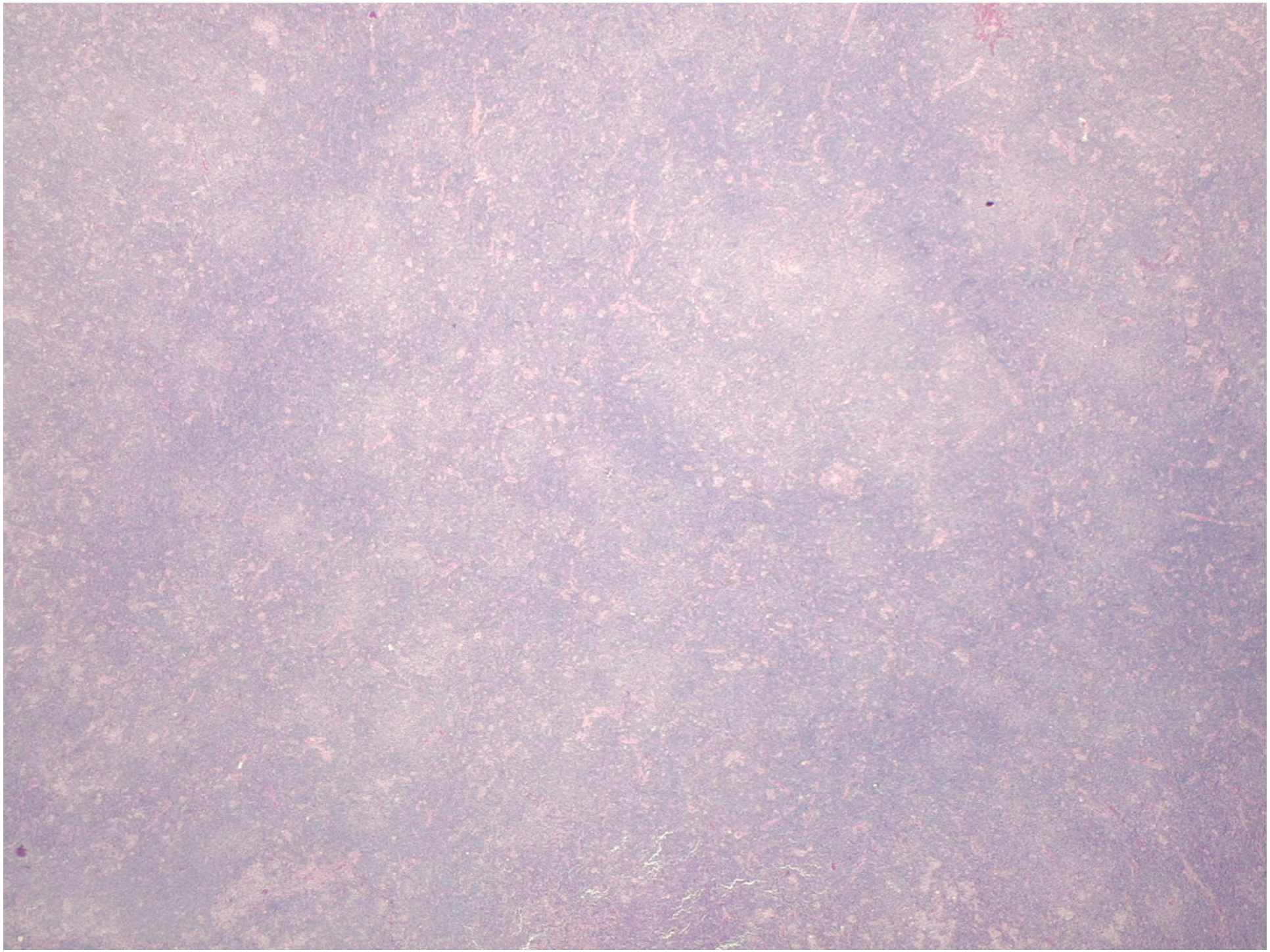
MCL Phenotype

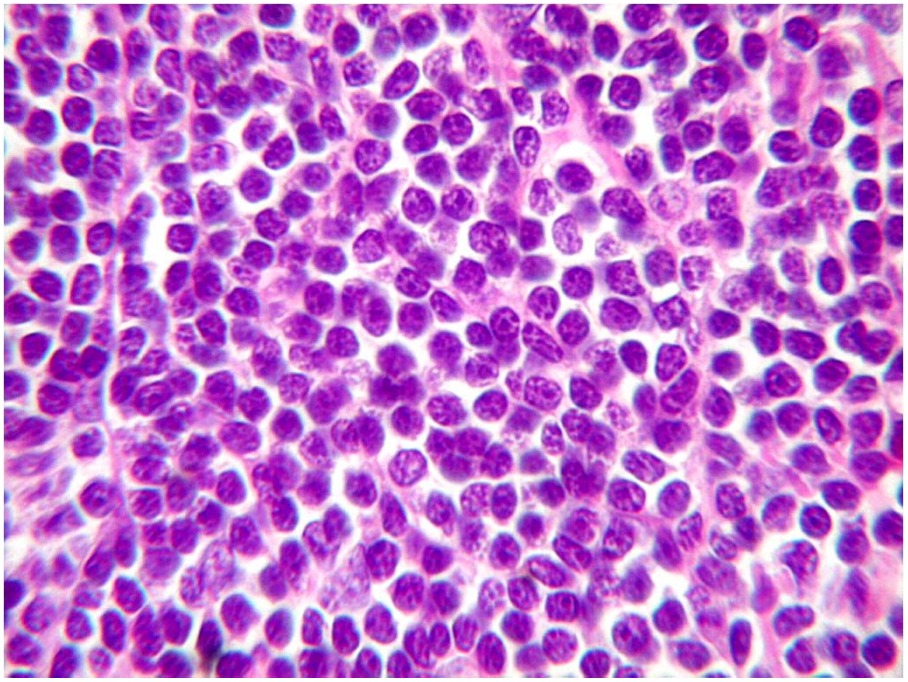


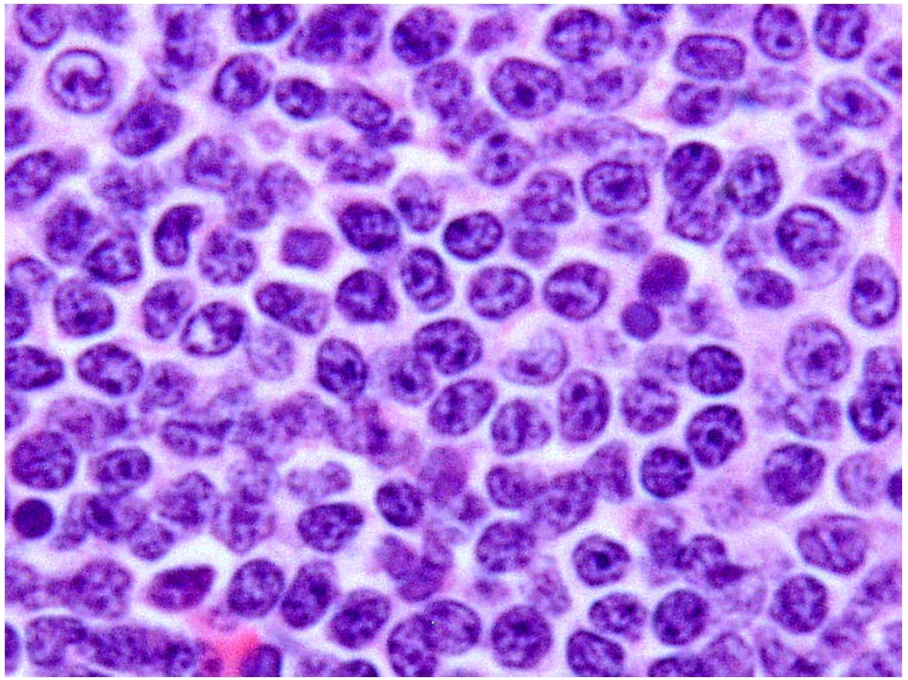


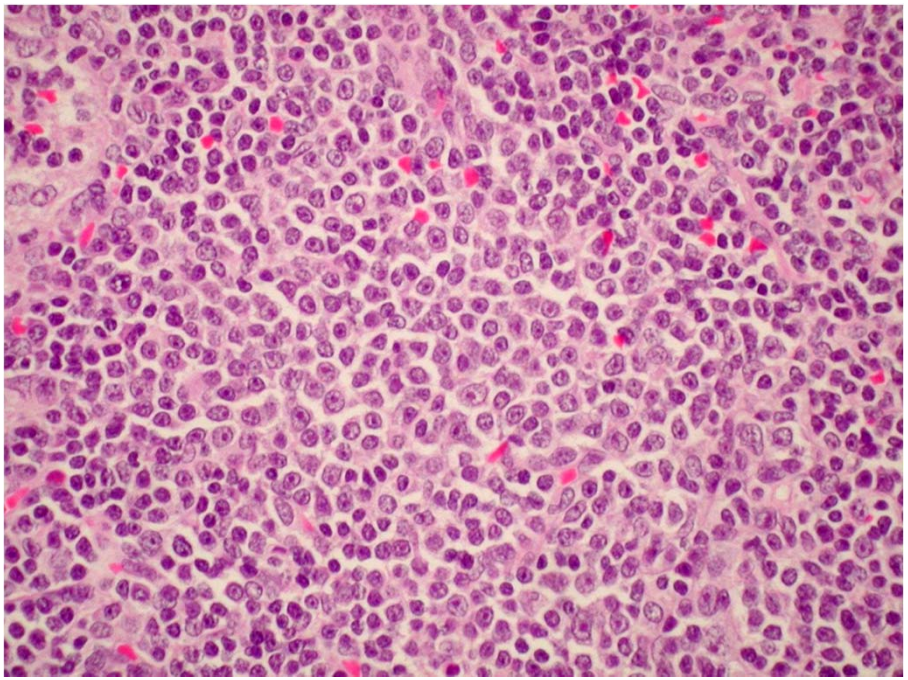


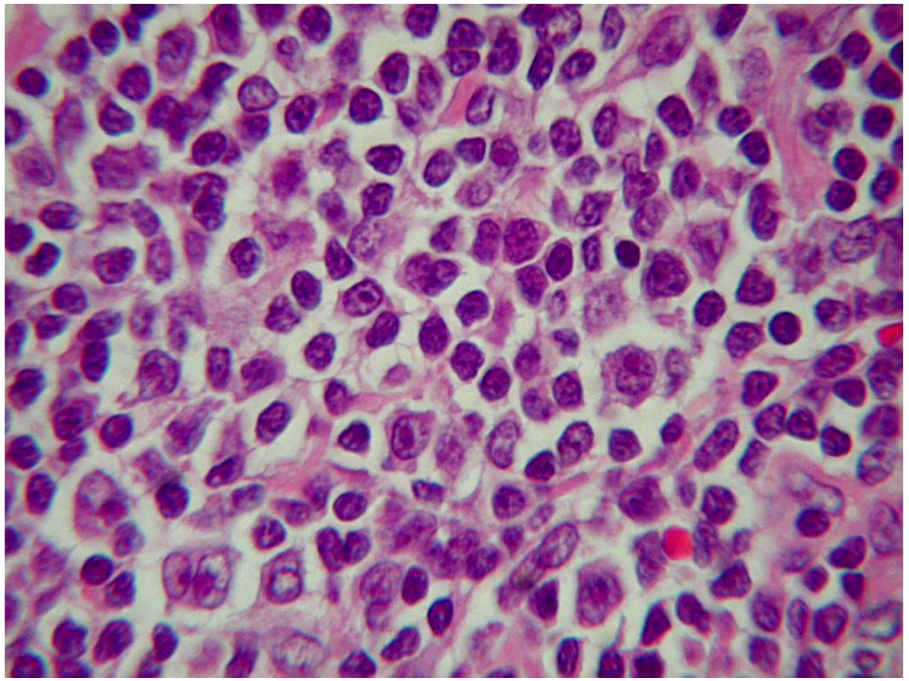


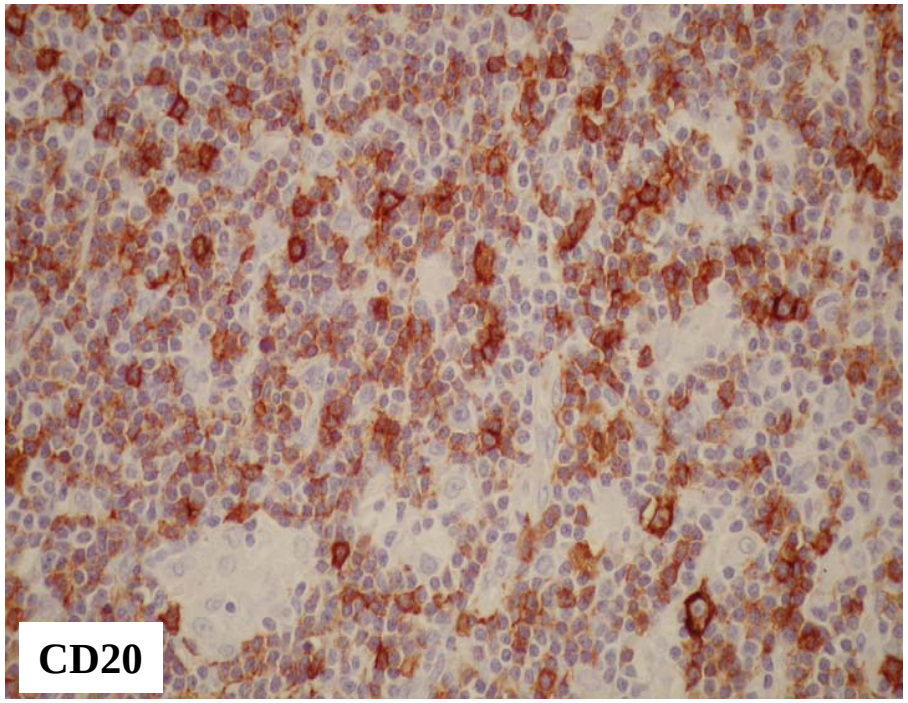


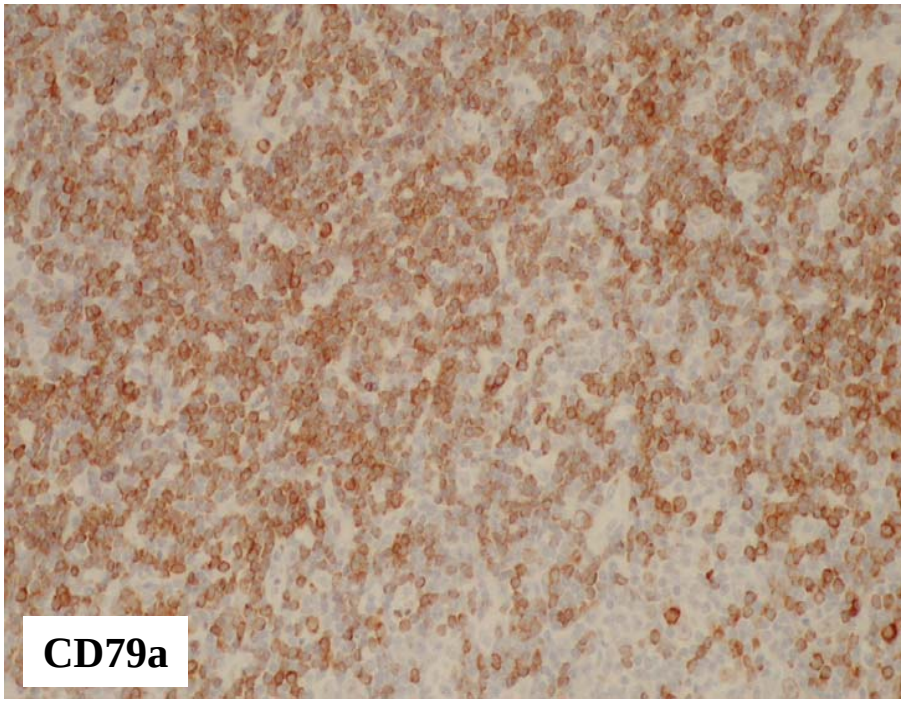


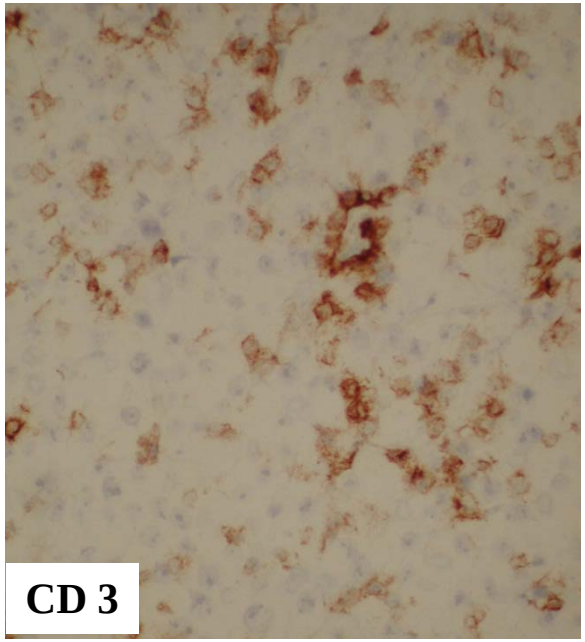







CD20


CD79a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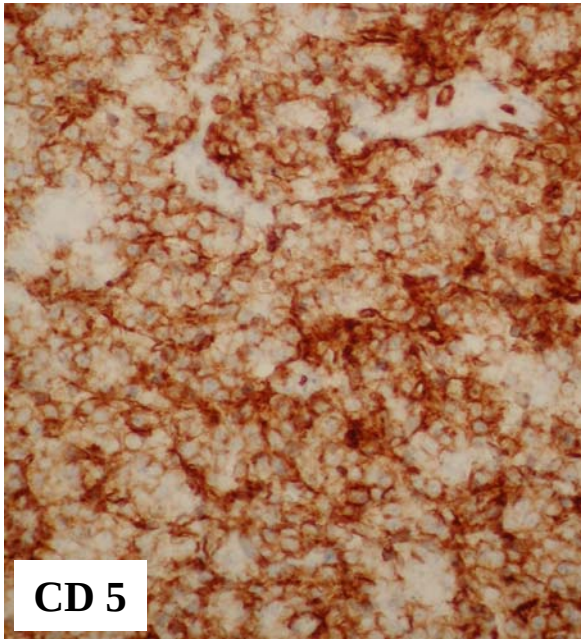
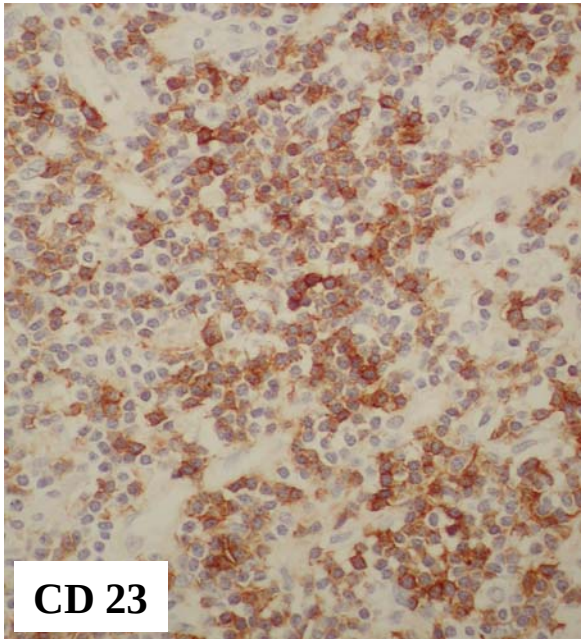
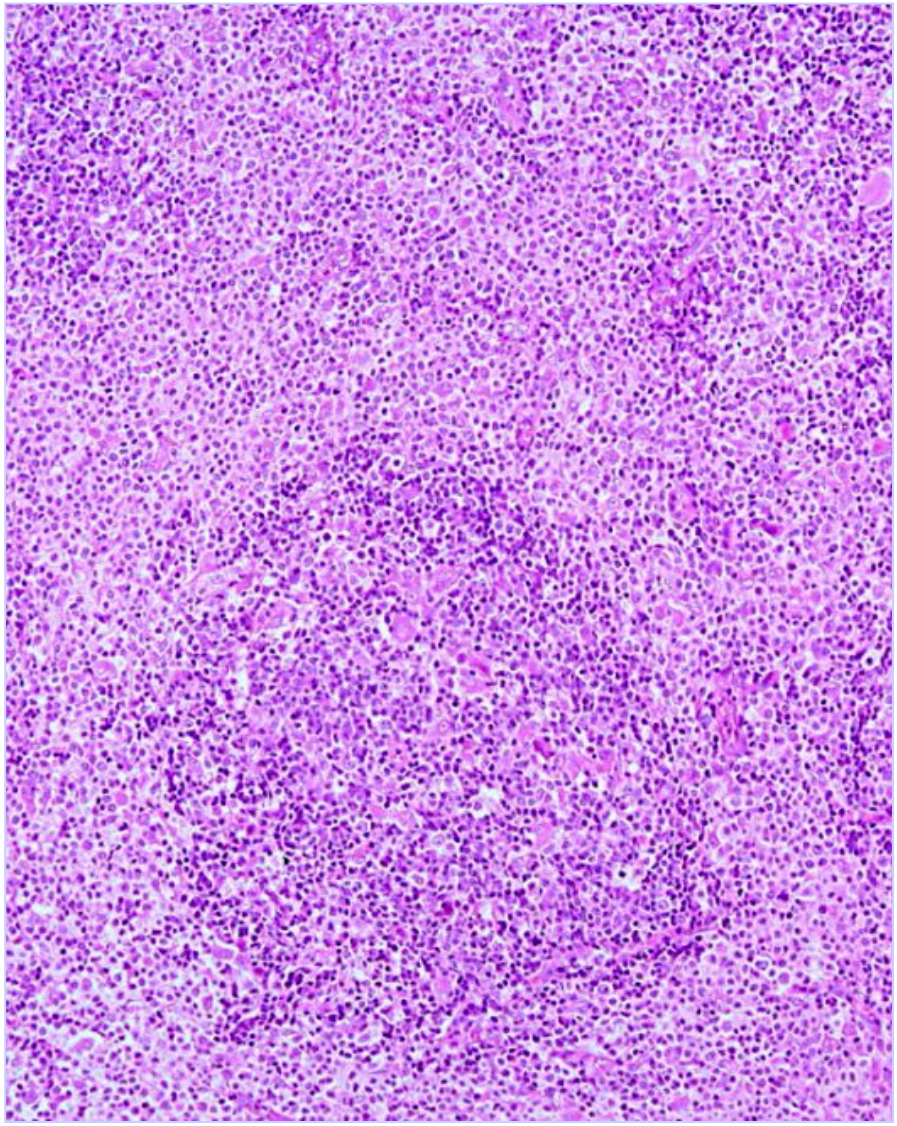
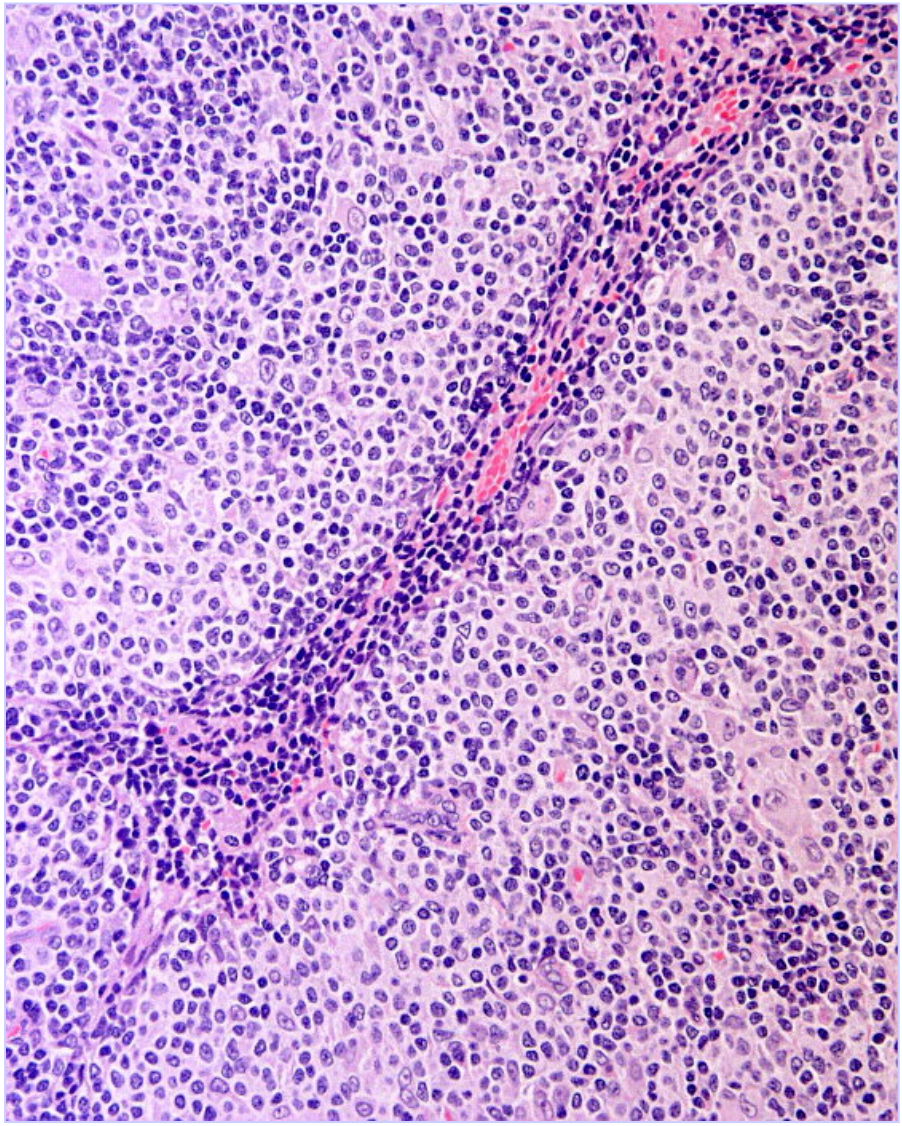

CD 5

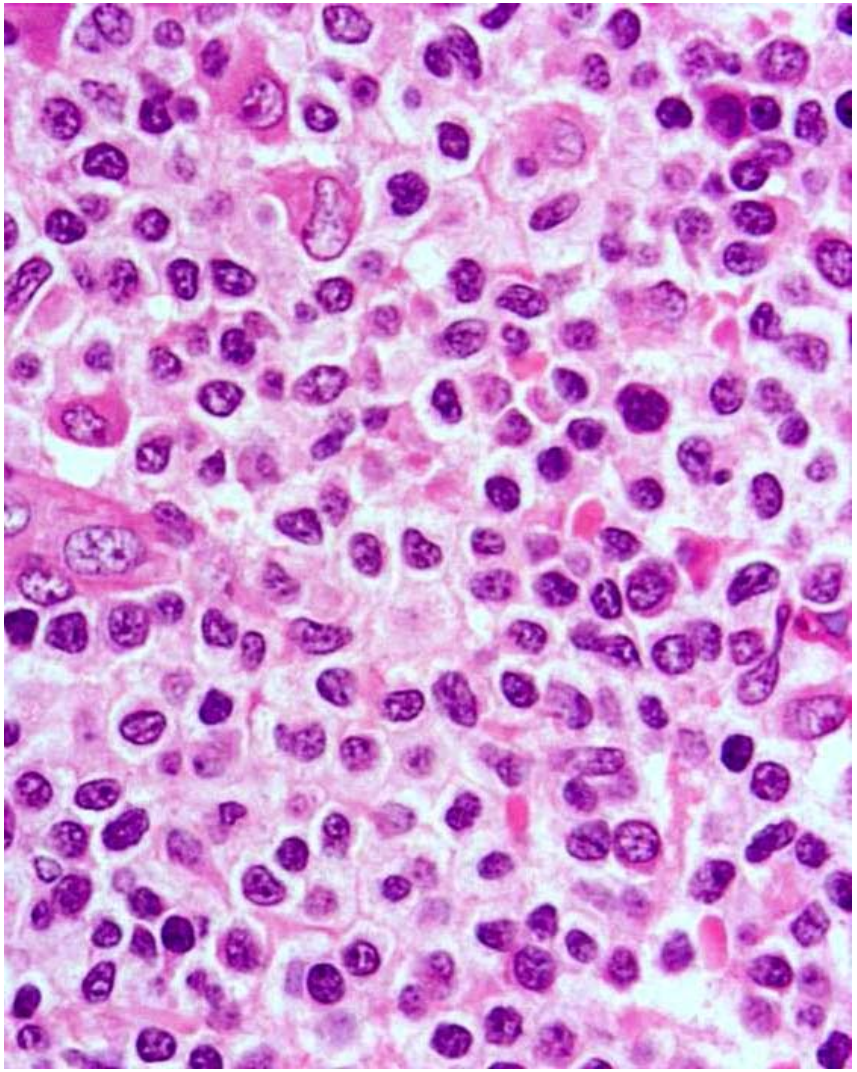

CD 23

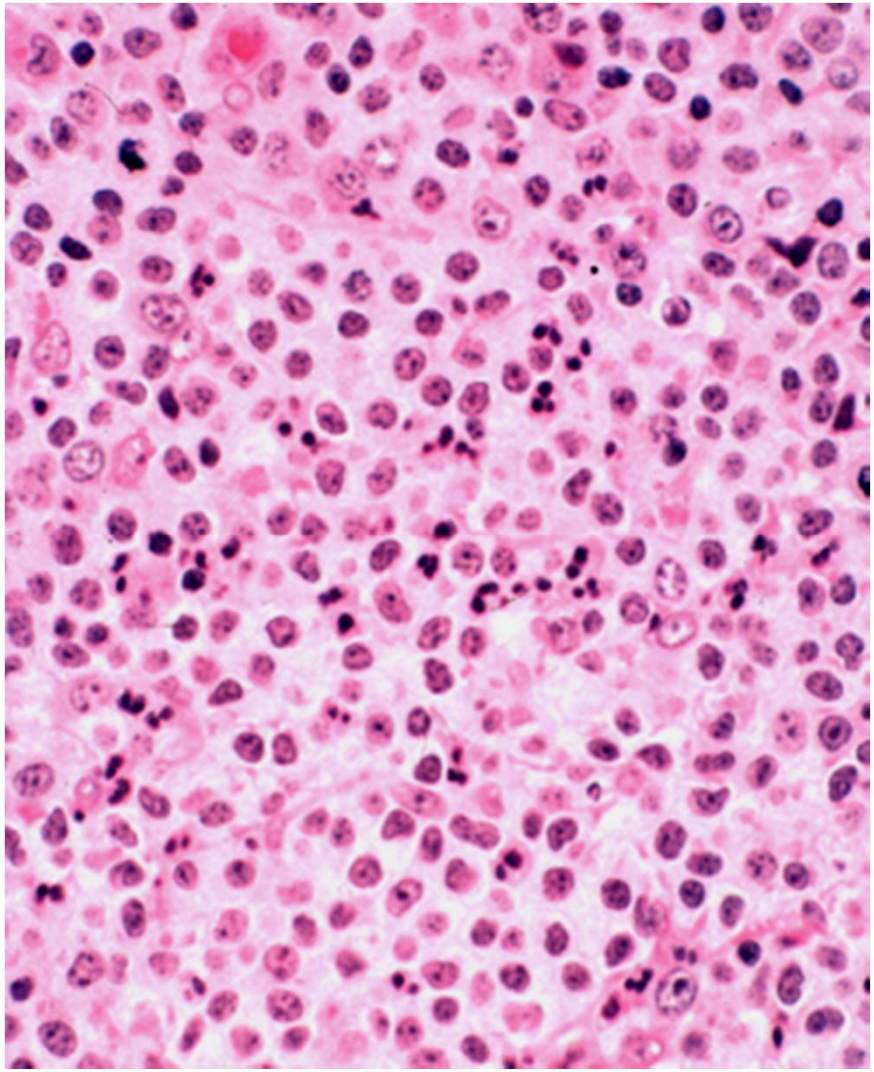
Nodal Marginal Zone Lymphoma



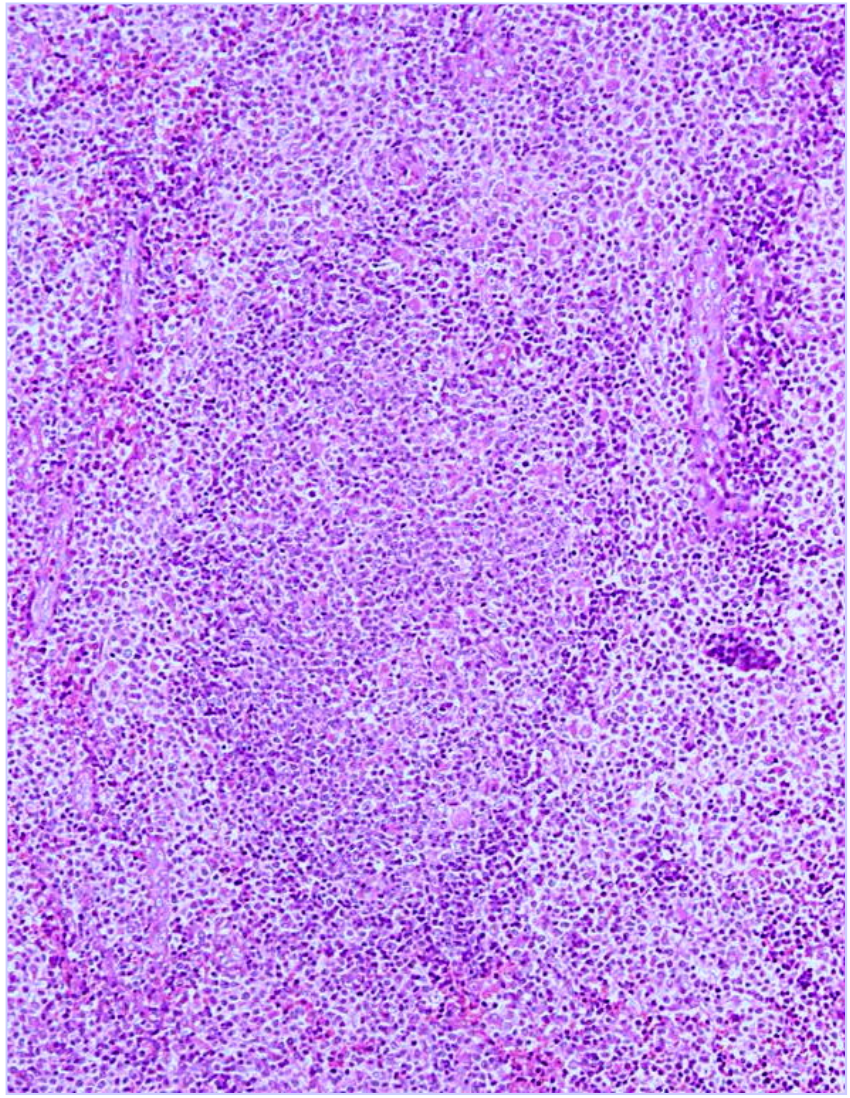


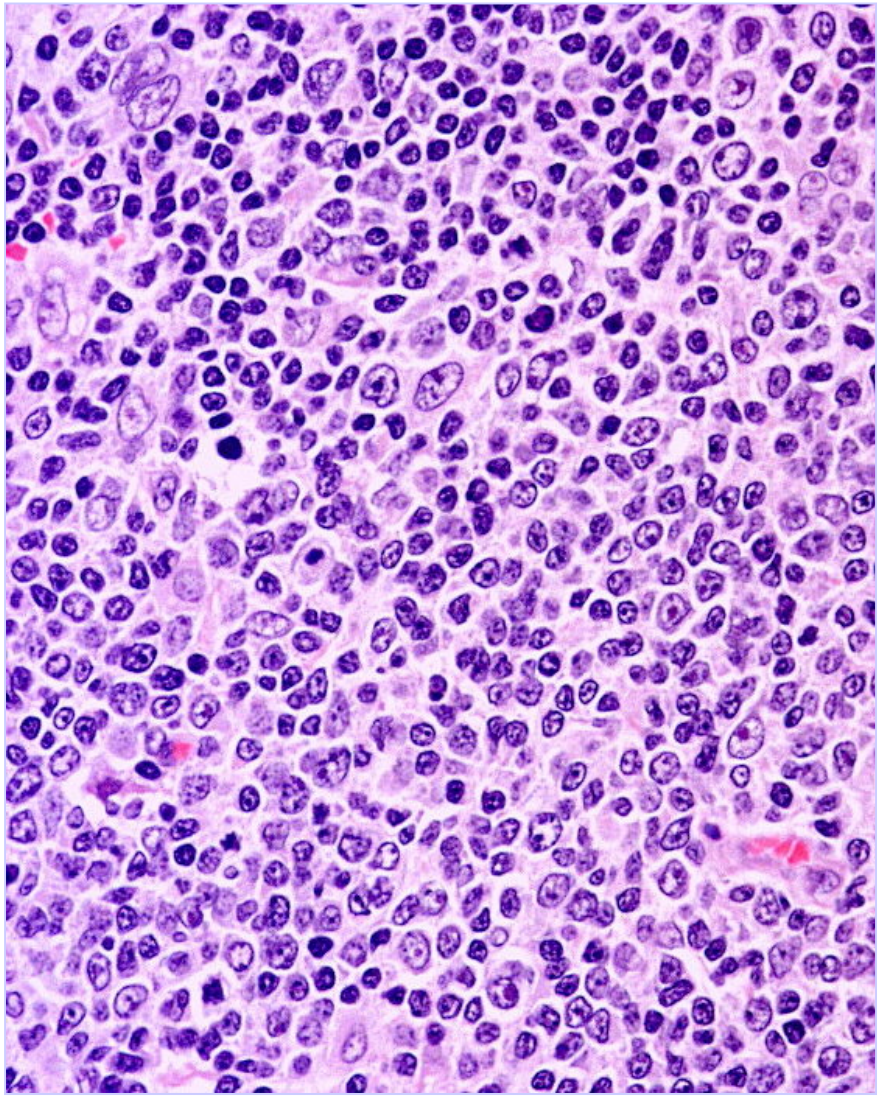
Nodal Marginal Zone Lymphoma

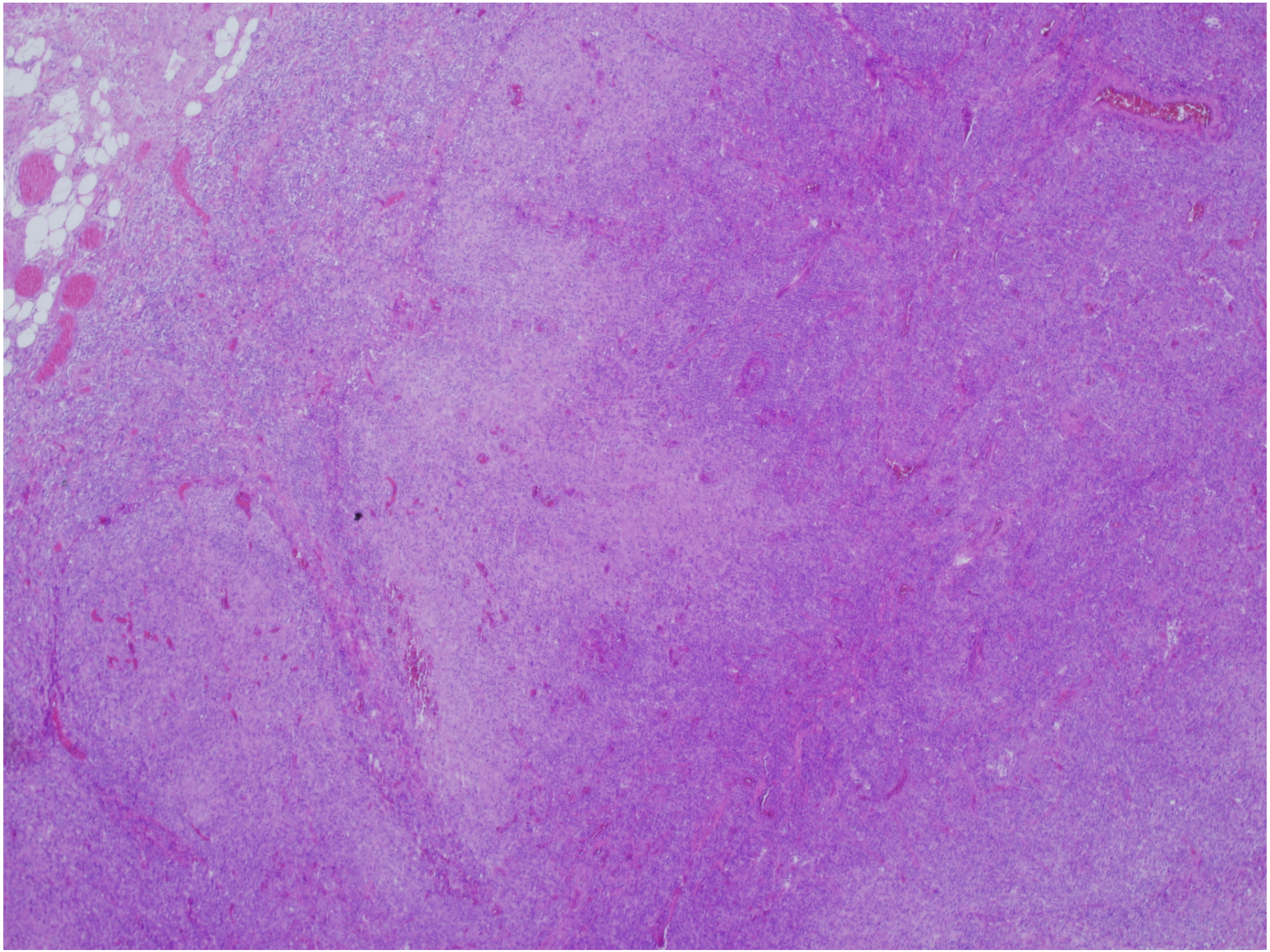


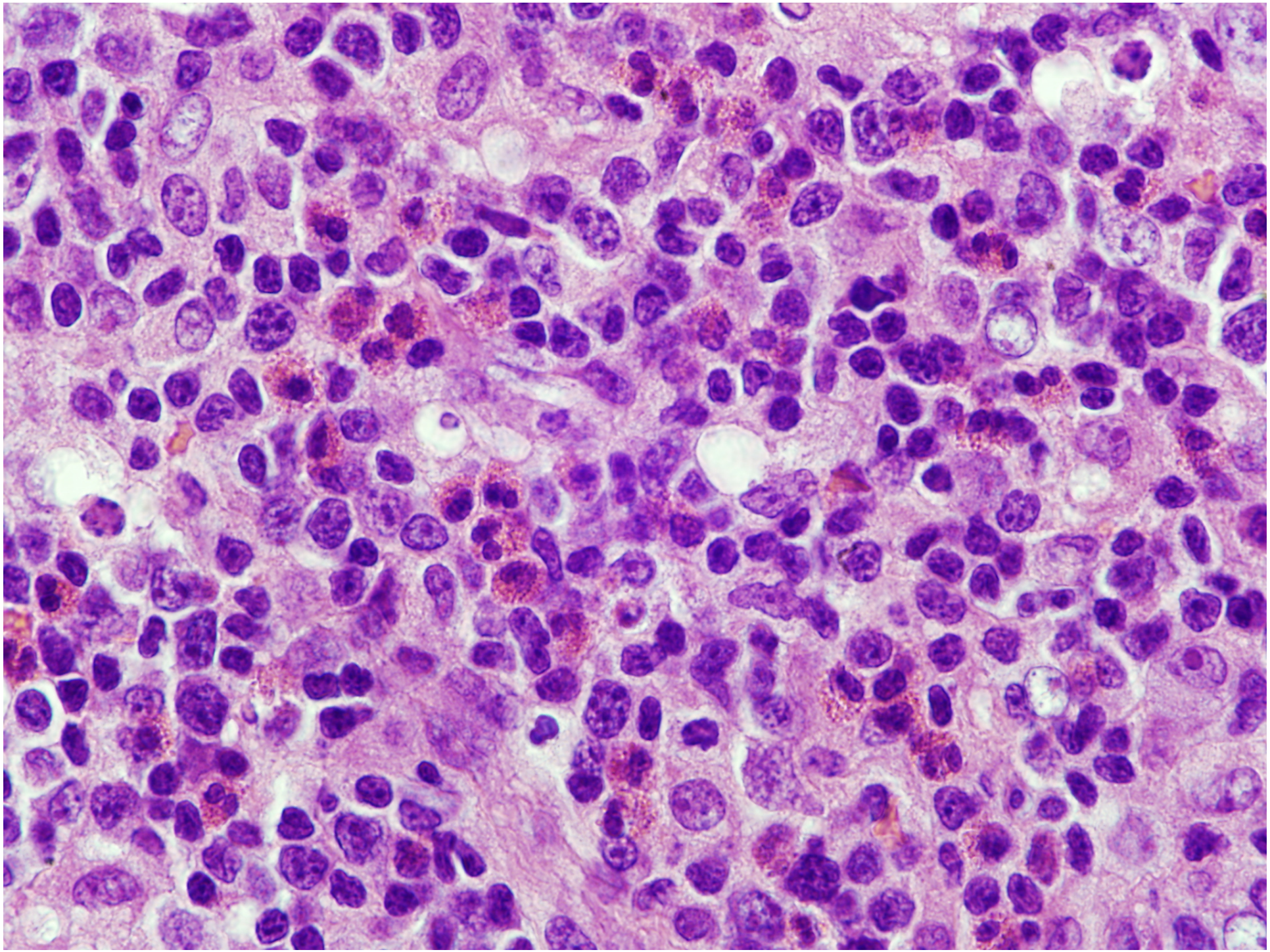


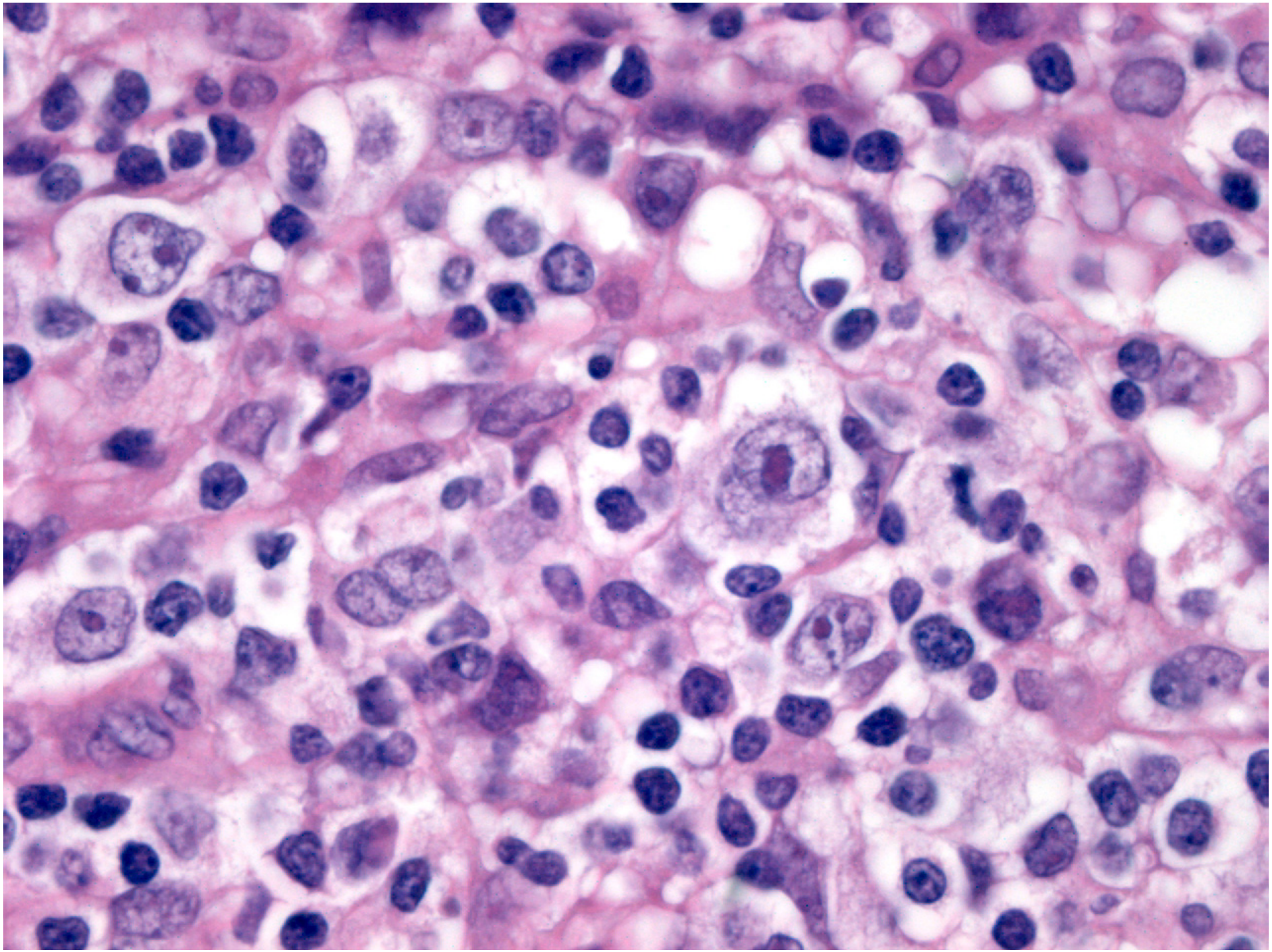
Nodal Marginal Zone Lymphoma

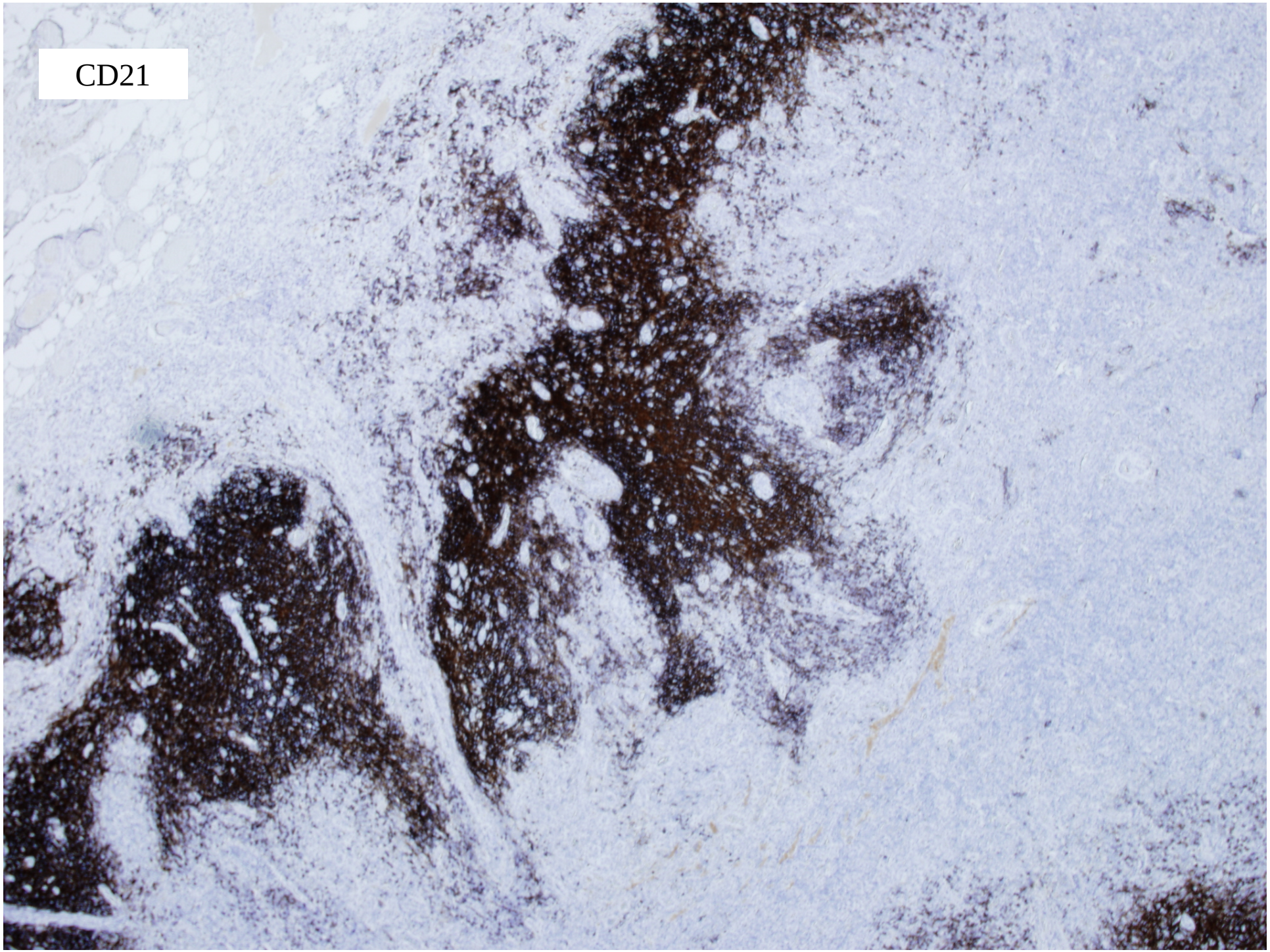


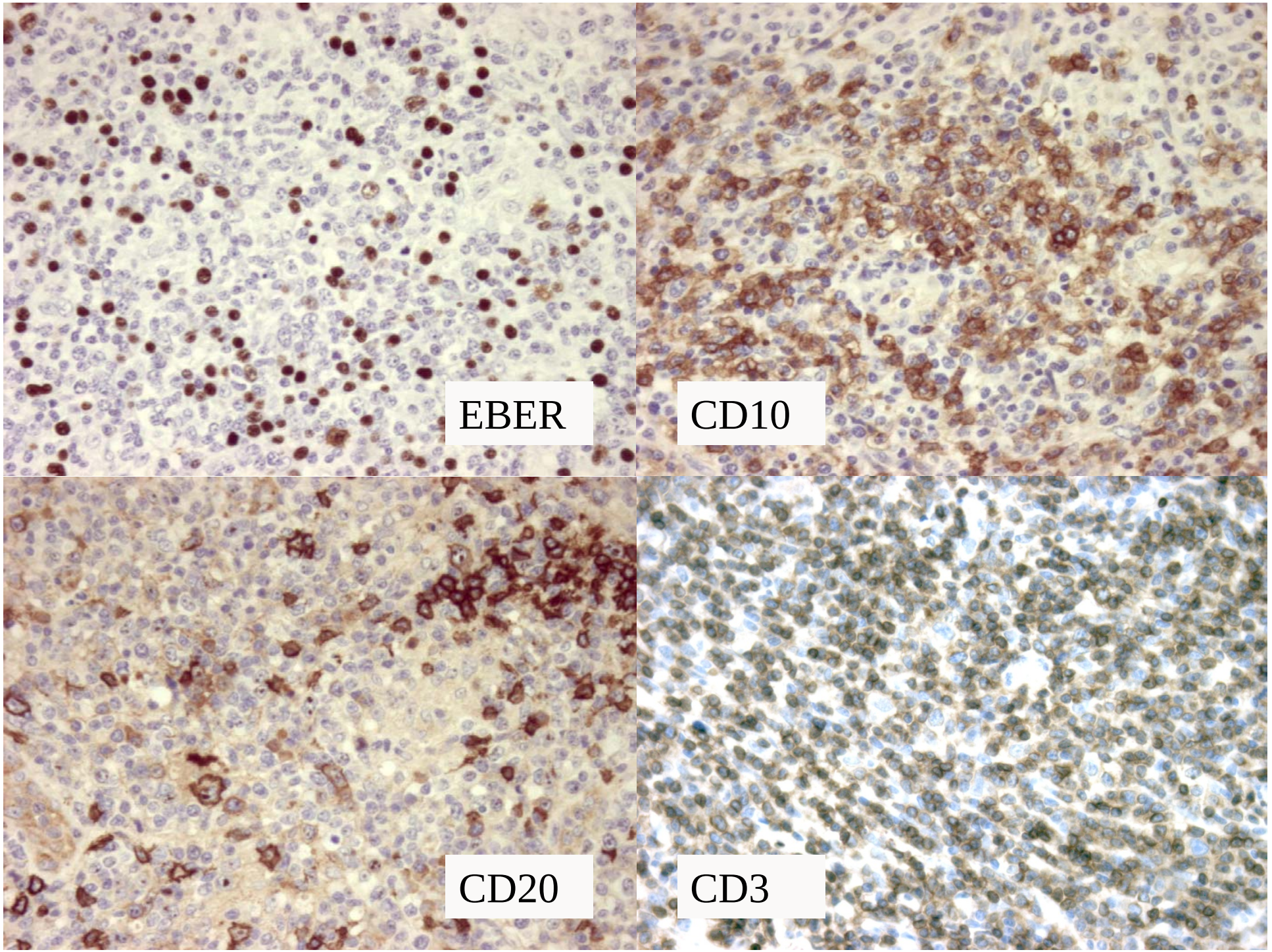









CD21

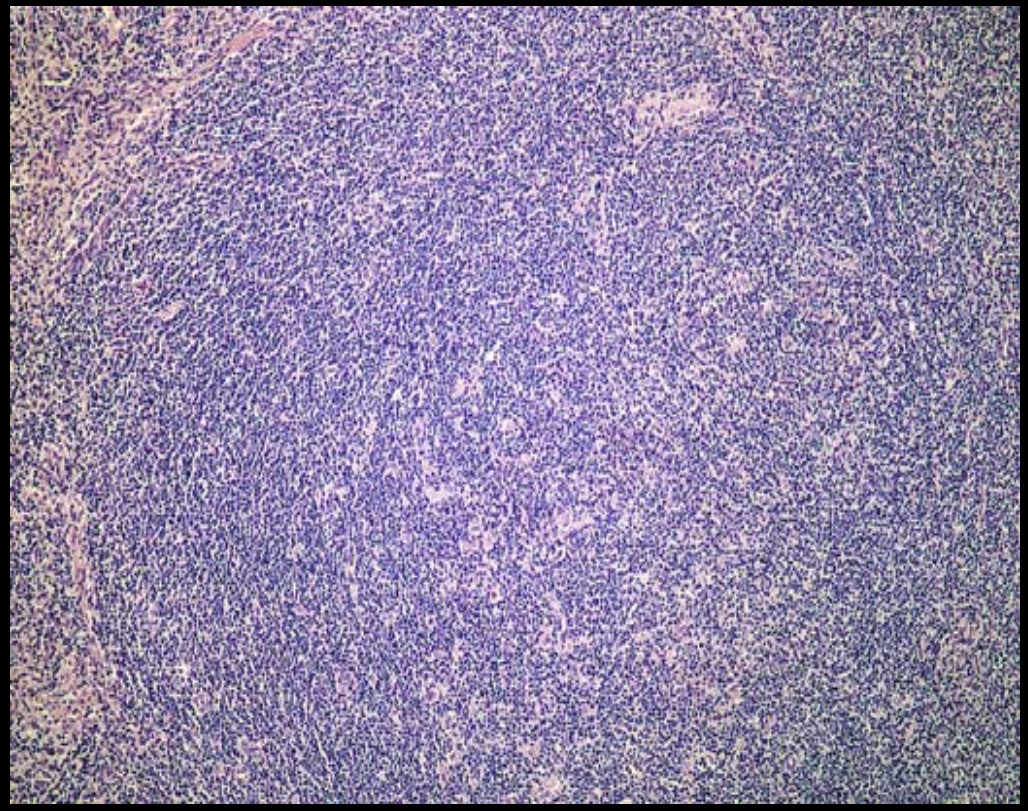

EBER
CD10
CD20
CD3

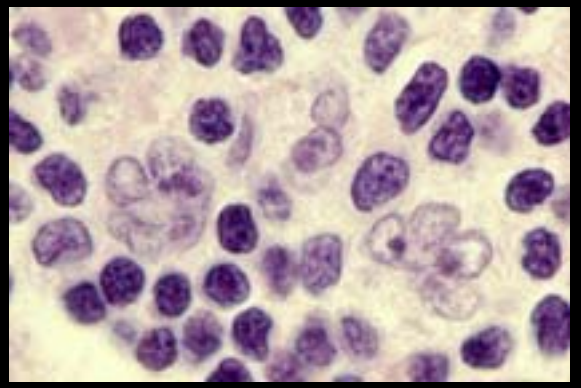
Diagnostic différentiel: architecture nodulaire, grandes cellules

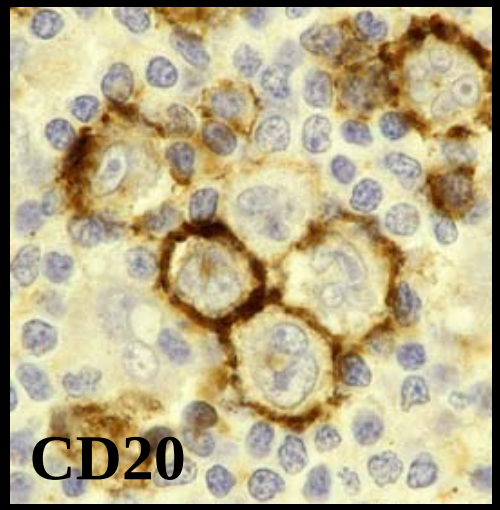
- Lymphomes B:
  - DLBCL
  - cHL: NS, NLPHL
- Lymphomes T: ALCL mimant cHL NS

CD20, Pax-5, CD30,
CD5, CD15, ALK-1
CD21, Eber

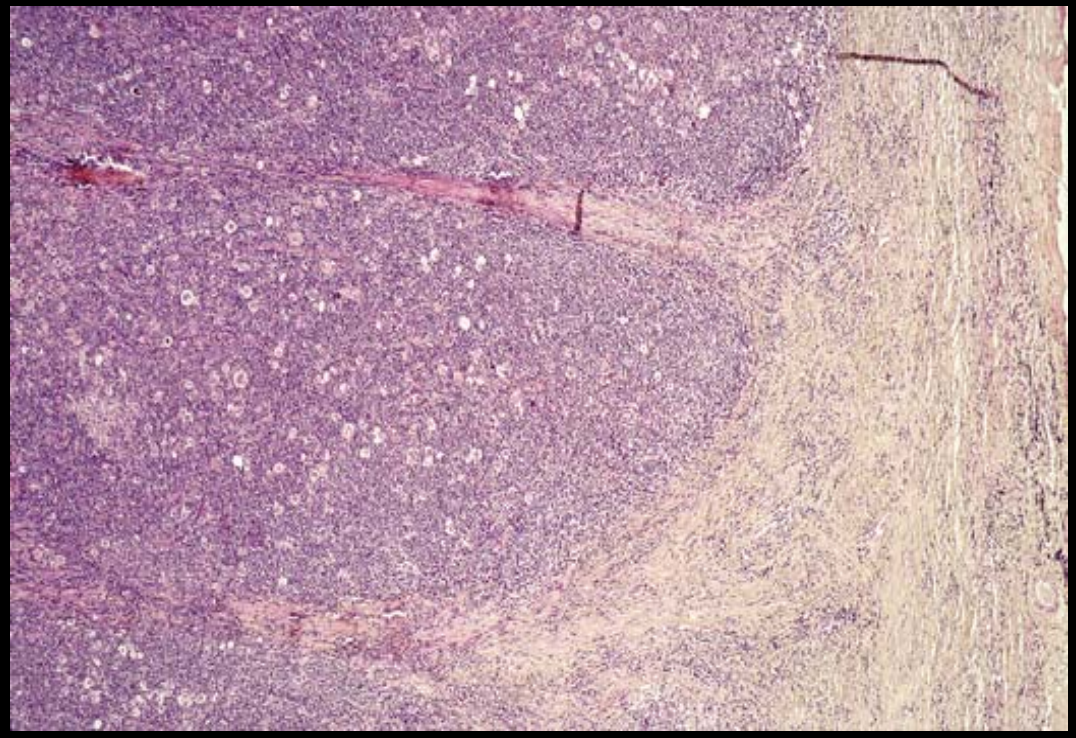
Lymphome de Hodgkin à prédominance lymphocytaire

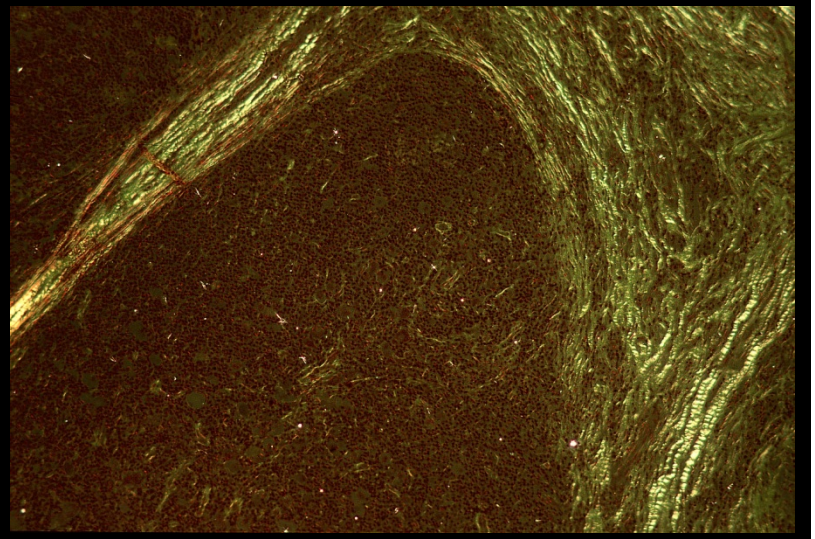


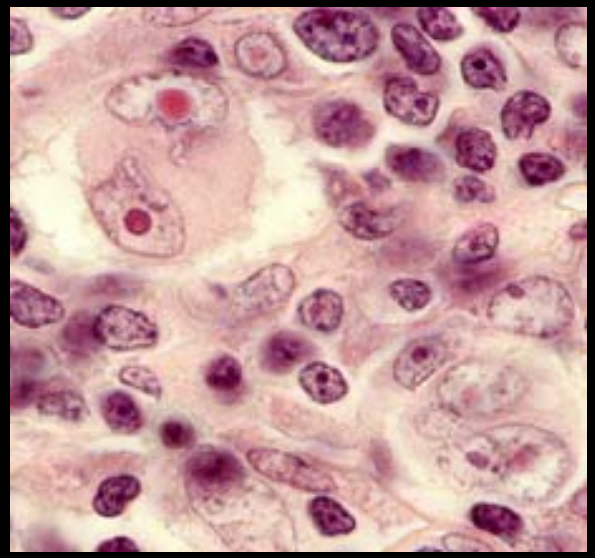


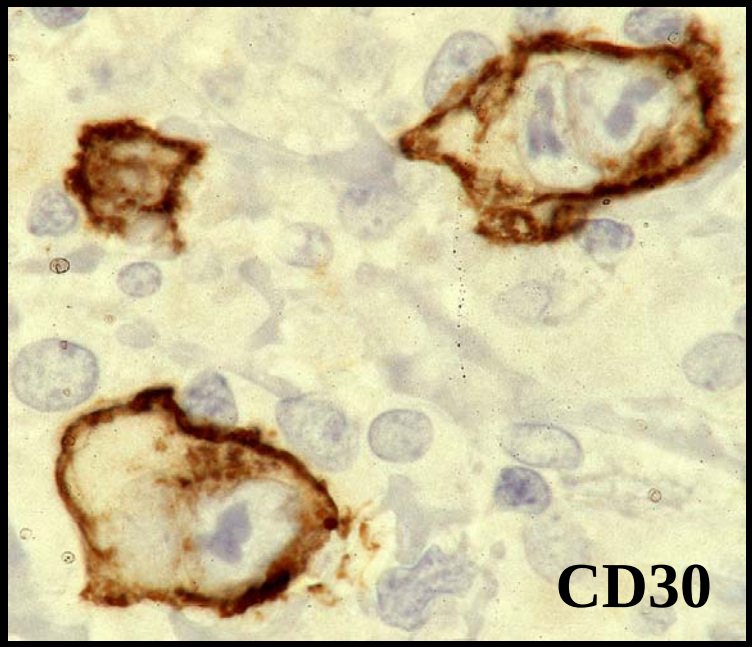


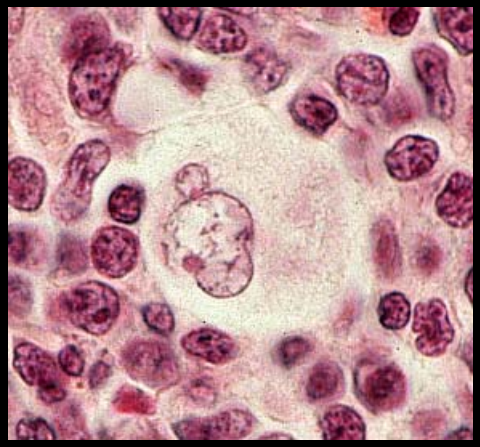
Lymphome de Hodgkin variante sclérosante nodulaire

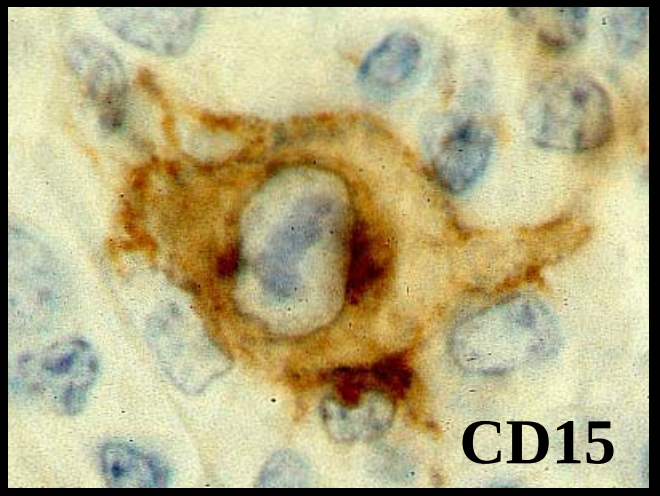







CD30




CD15

Diagnostic différentiel: architecture diffuse, grandes cellules

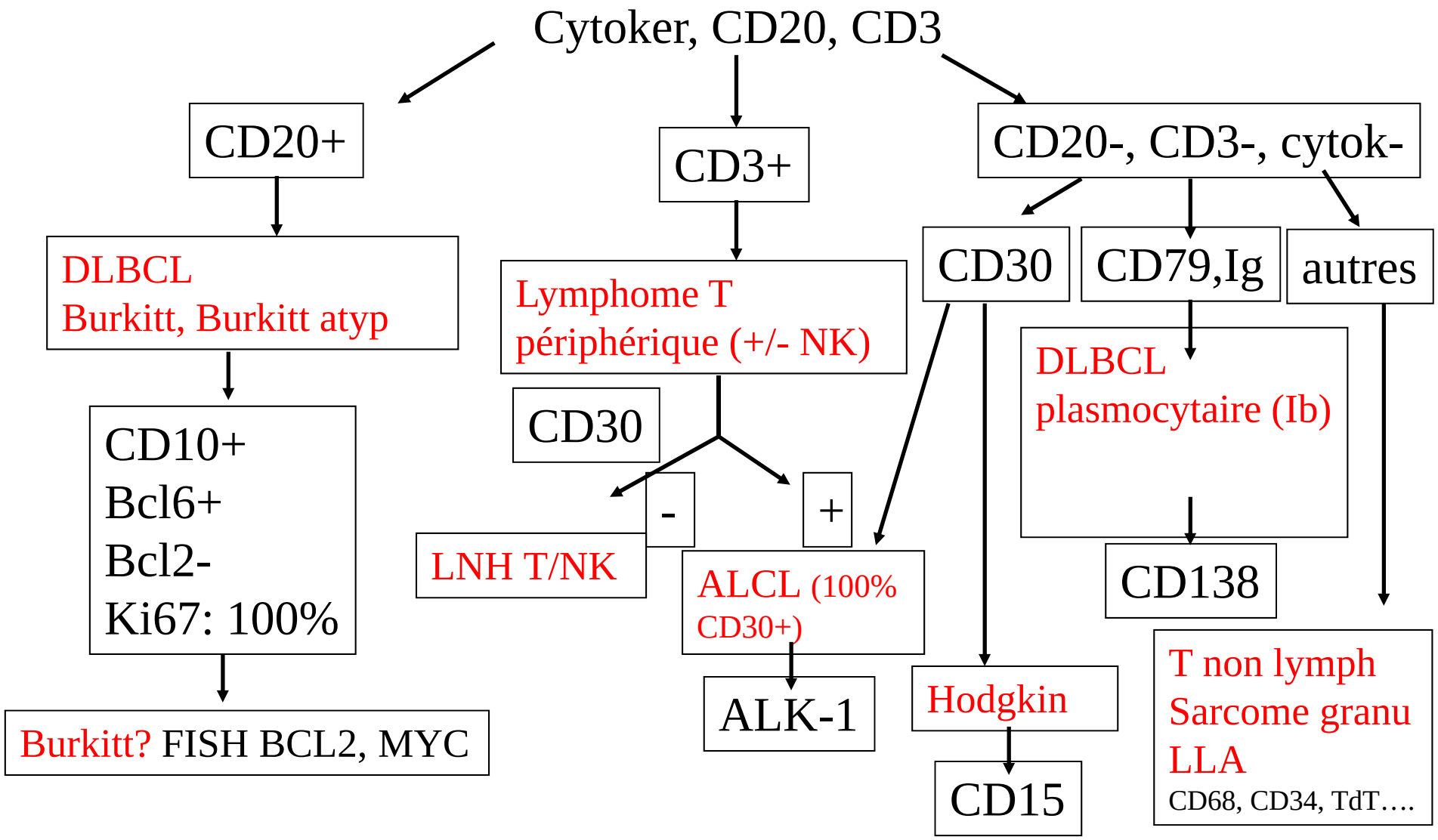
- Lymphomes B+++
  - DLBCL
  - MCL pléo
  - Ly plasmablastique
- cHL (NS et LD)
- Lymphomes T
  - ALCL

CK, CD20, Pax-5, CD30, CD5, Ki67

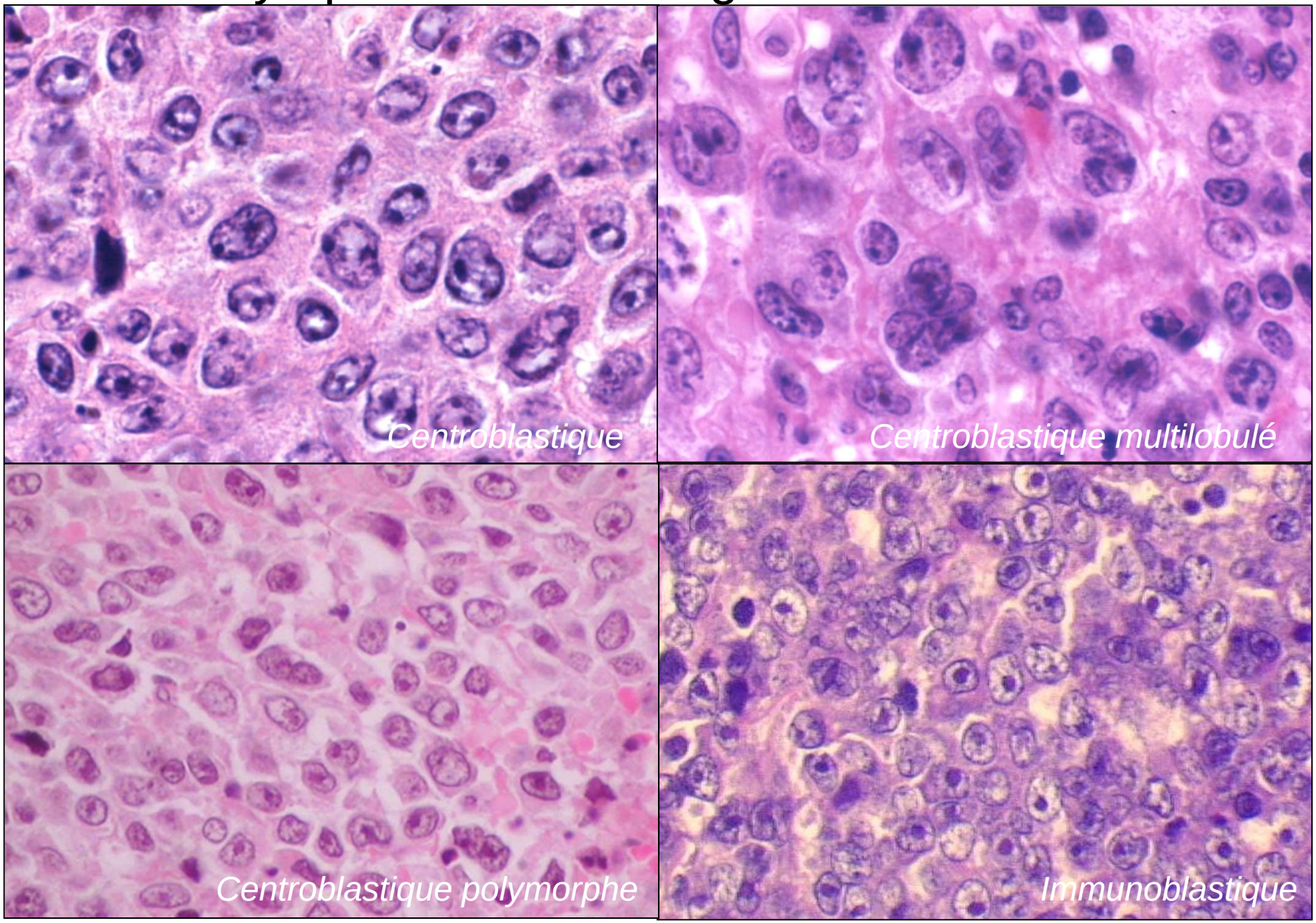
CD138, CD15, cyclinD1, Eber

Si DLBCL: CD10, bcl-6, MUM-1, bcl-2, c-myc
Si CD30: ALK-1

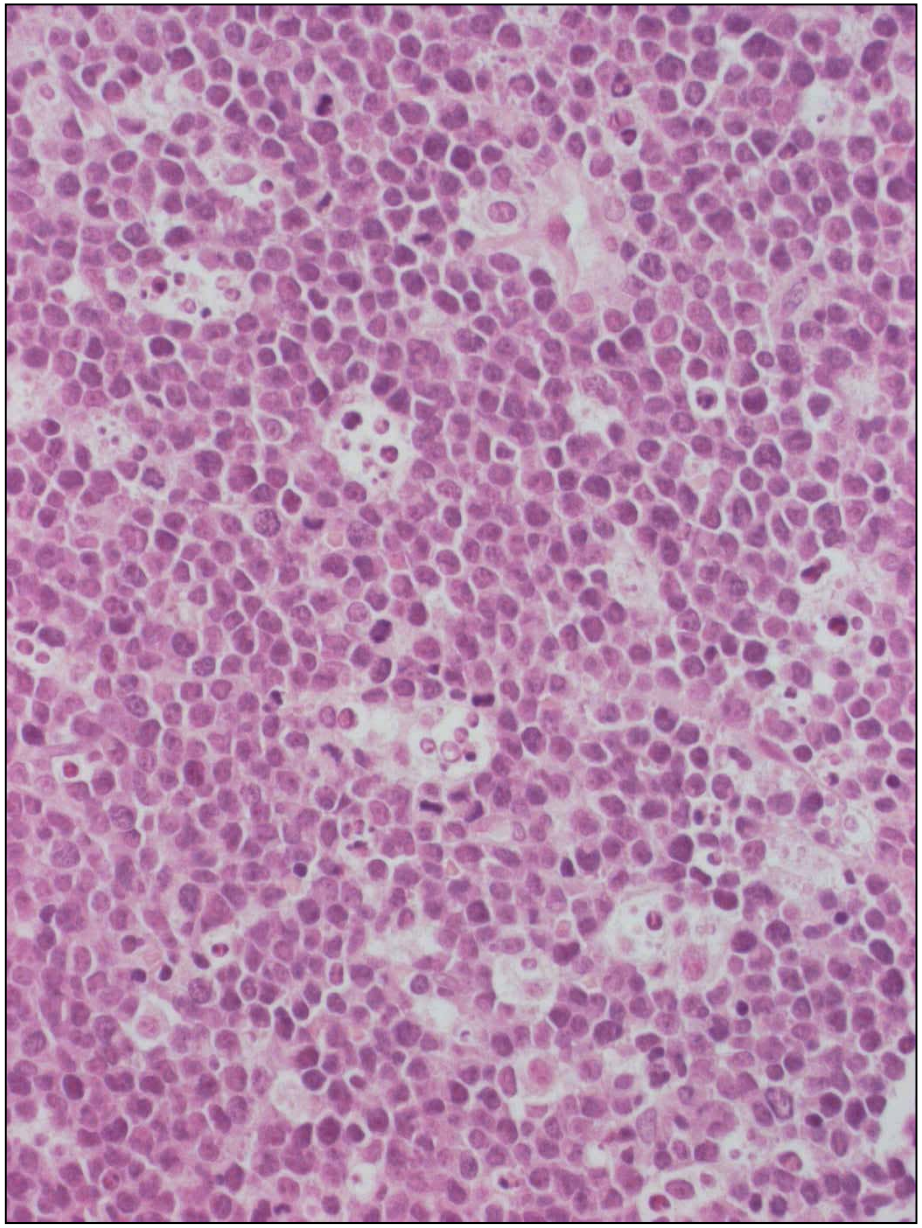
Prolifération à grandes cellules (2x taille d'un noyau de lymphocyte) si doute: Ki67

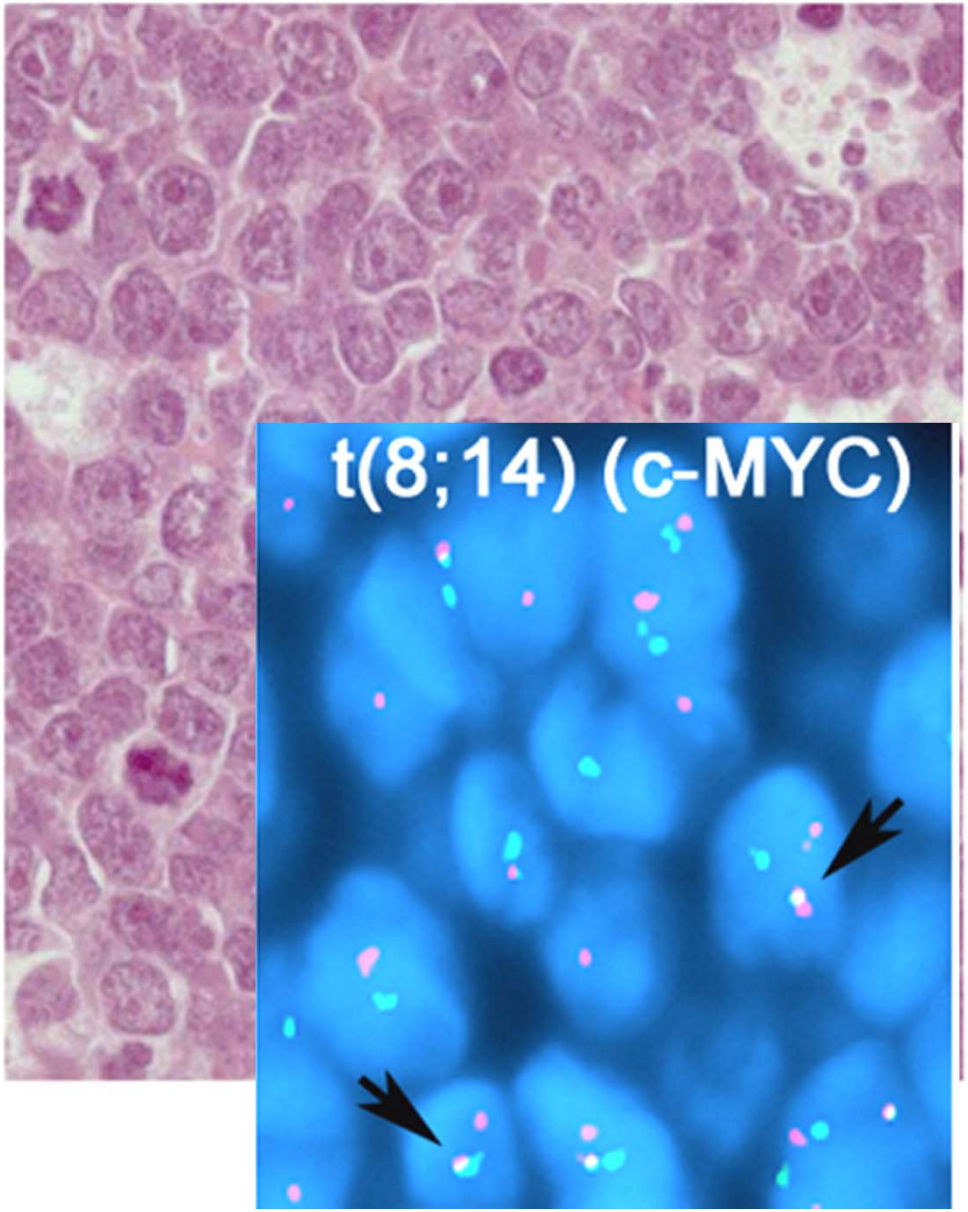


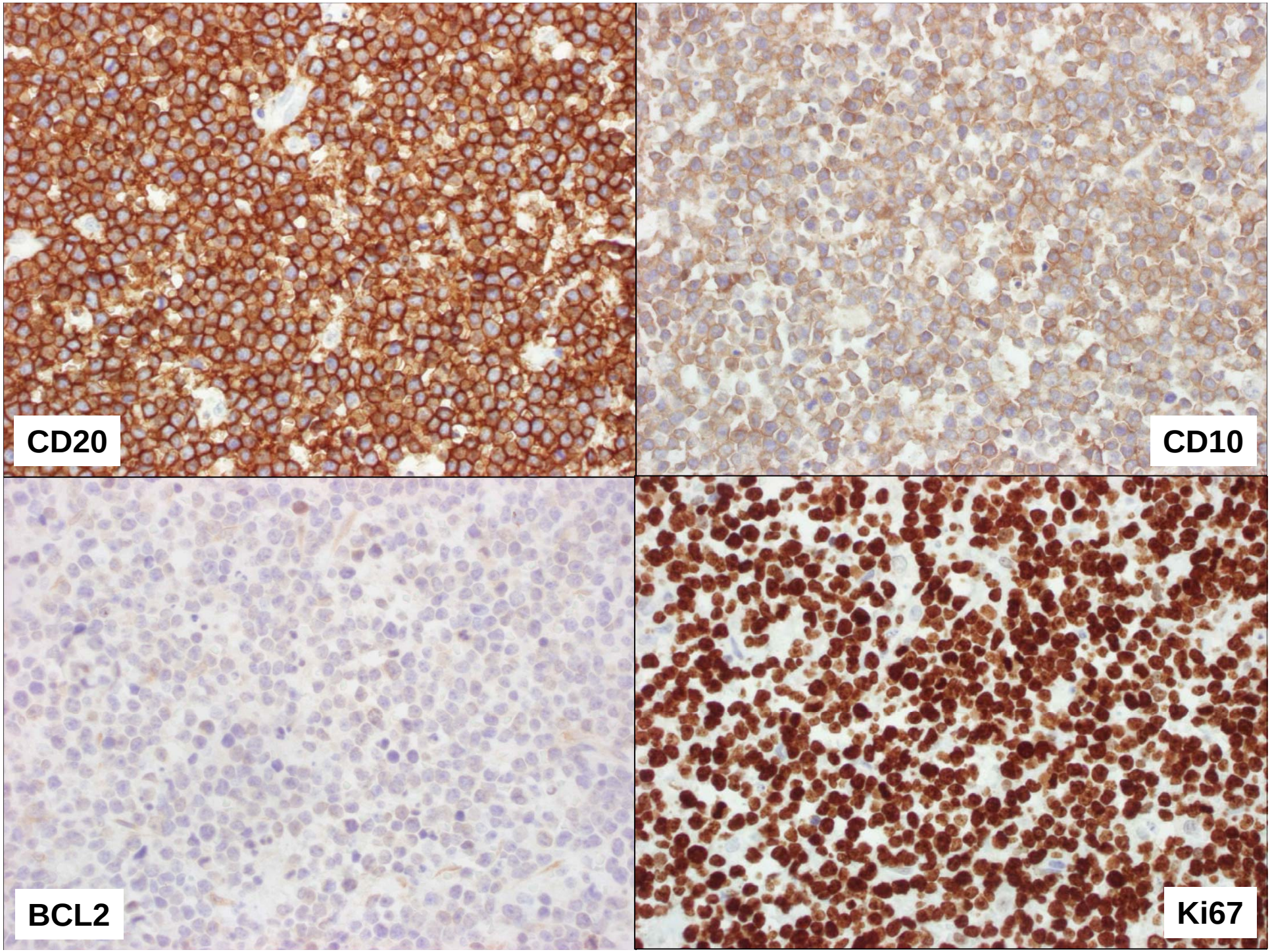
Lymphomes diffus à grandes cellules



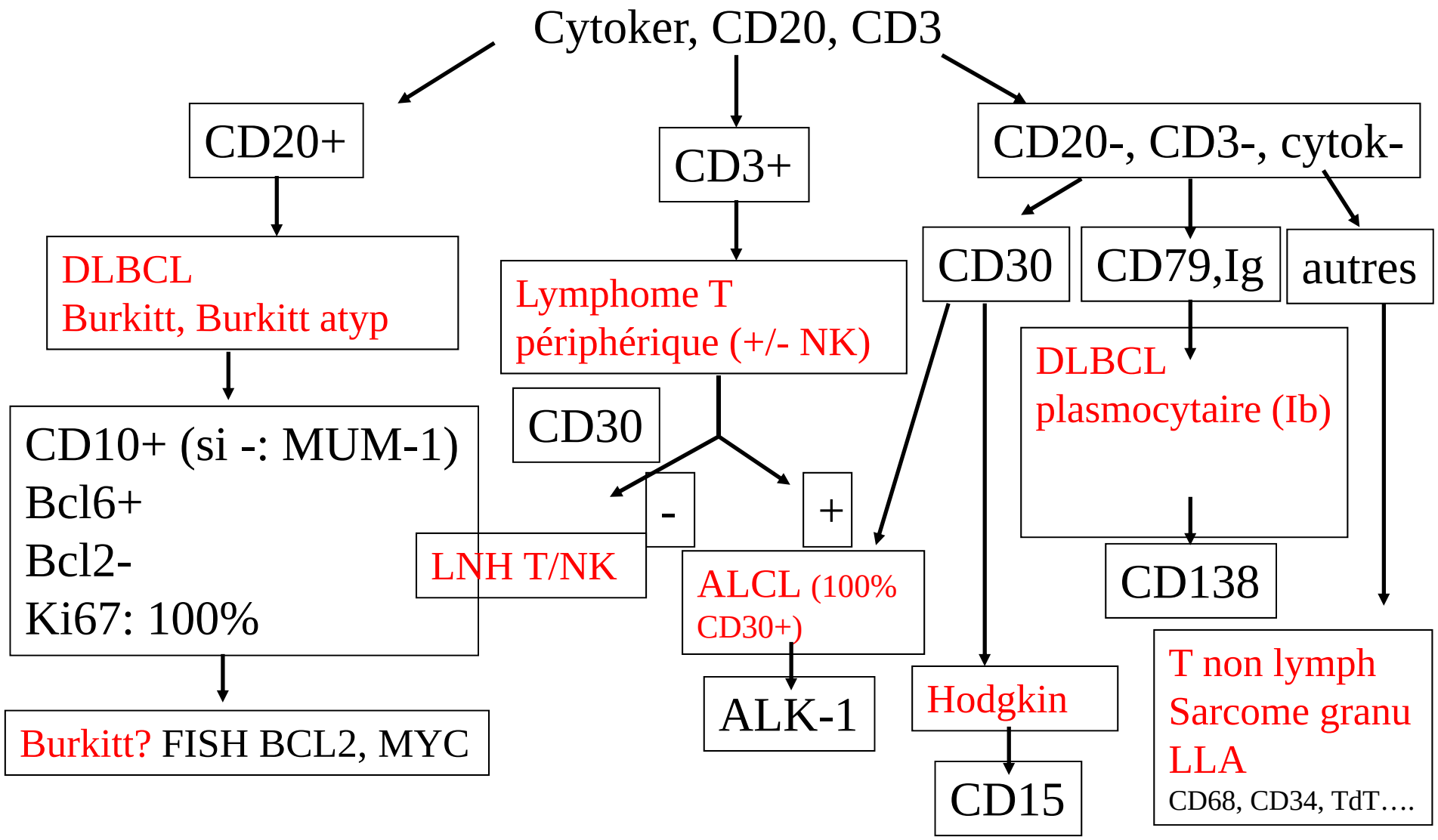
Burkitt

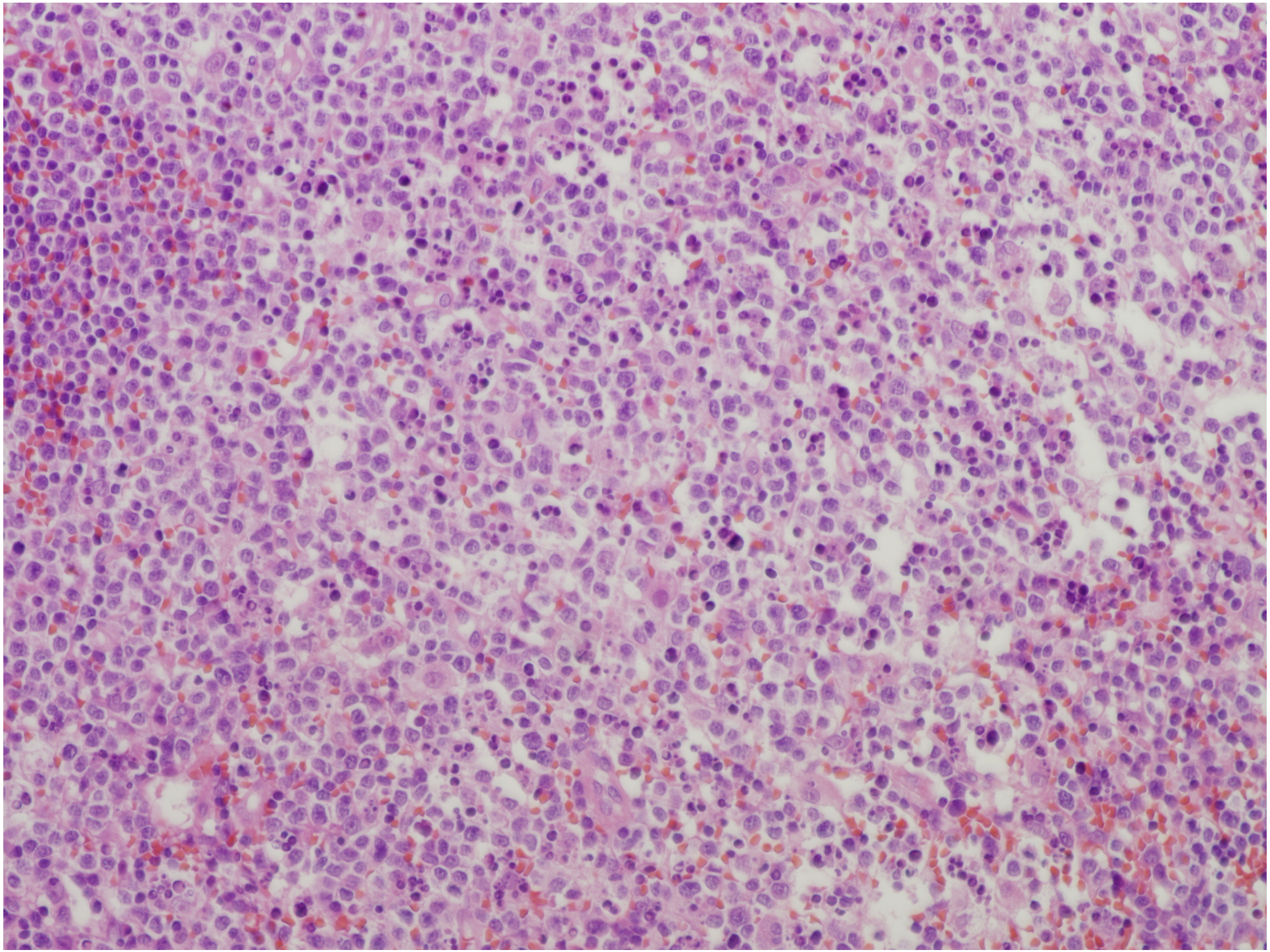


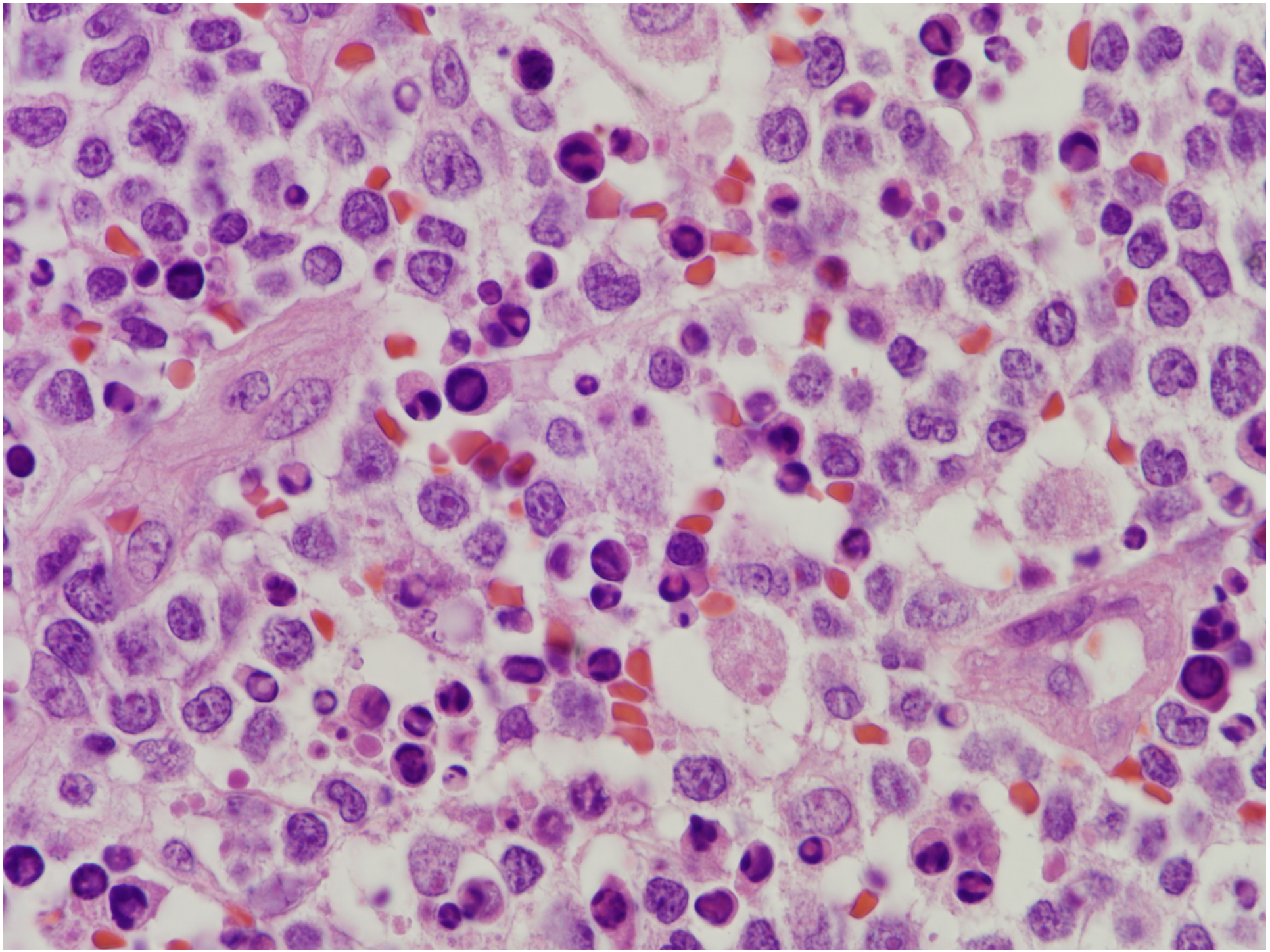


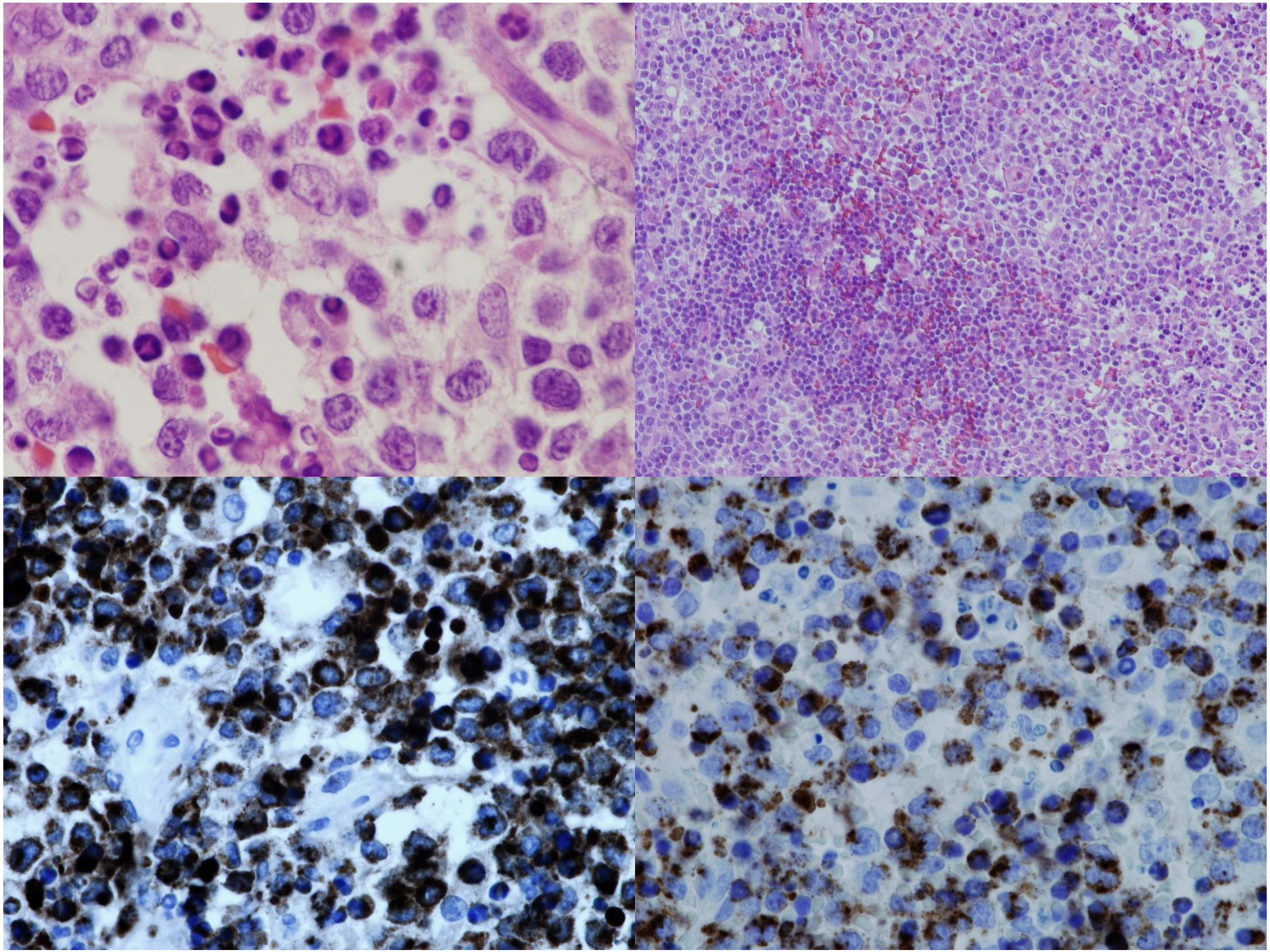

CD20
CD10
BCL2
Ki67

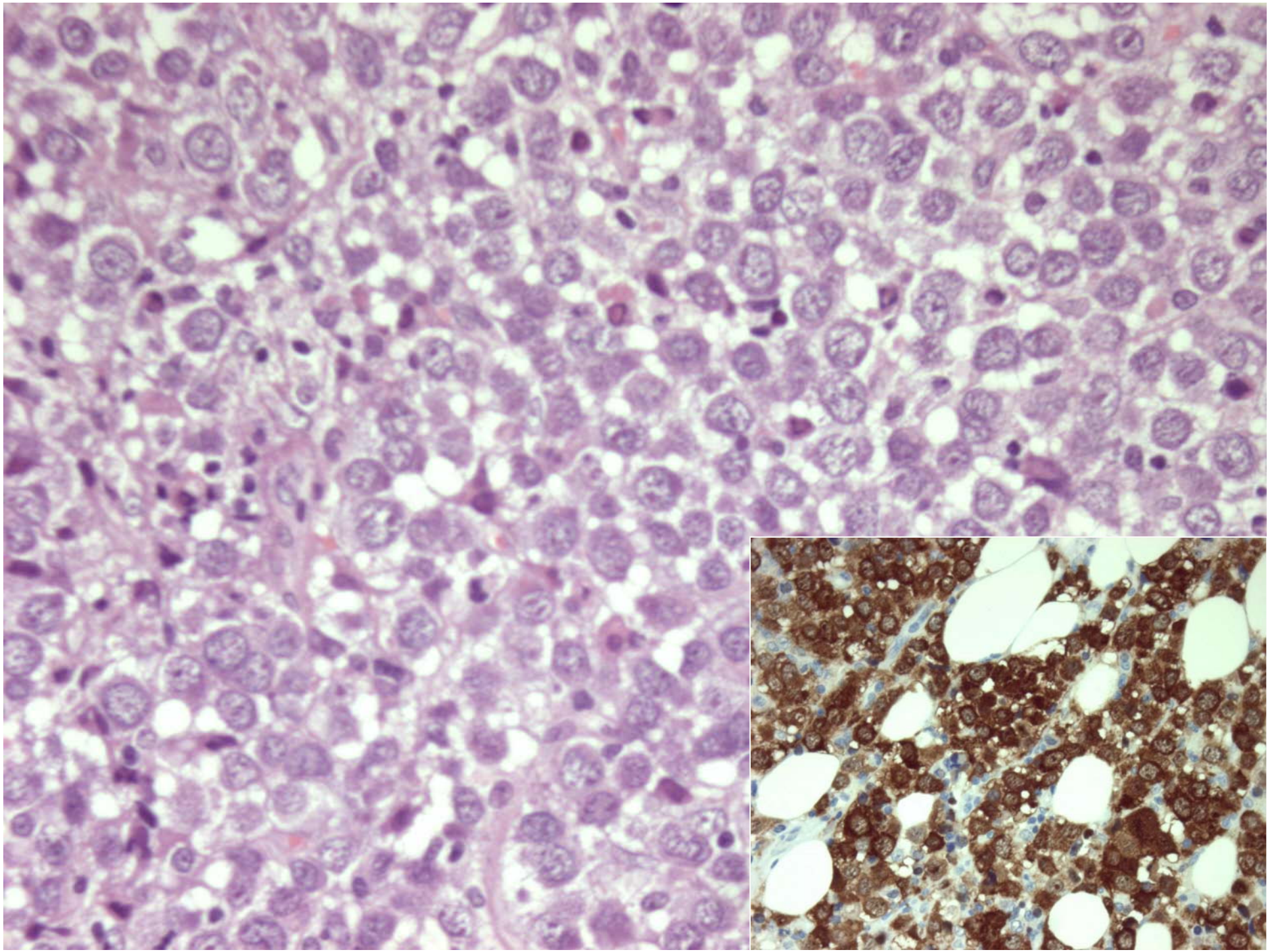
Prolifération à grandes cellules (2x taille d'un noyau de lymphocyte) si doute: Ki67

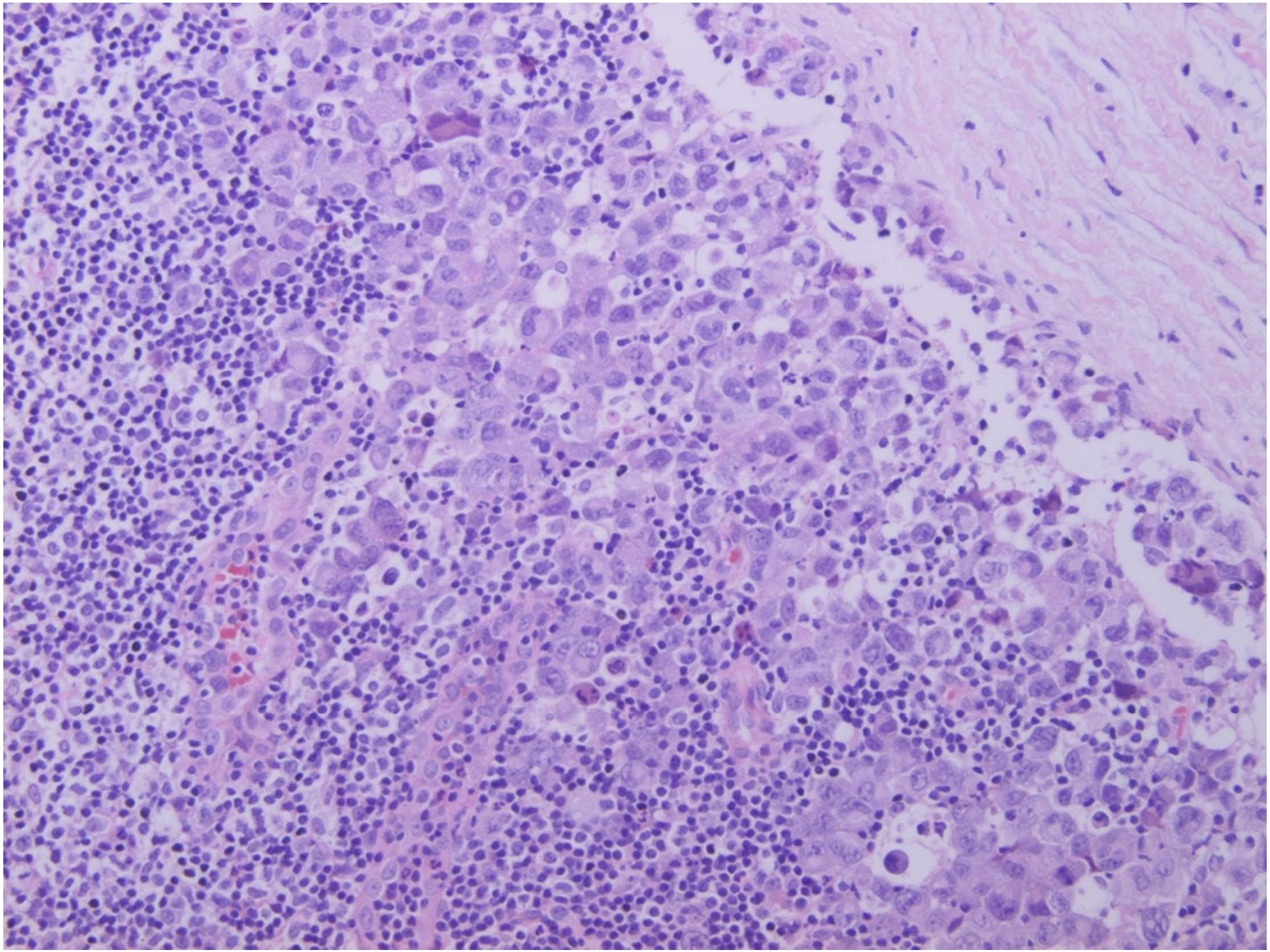




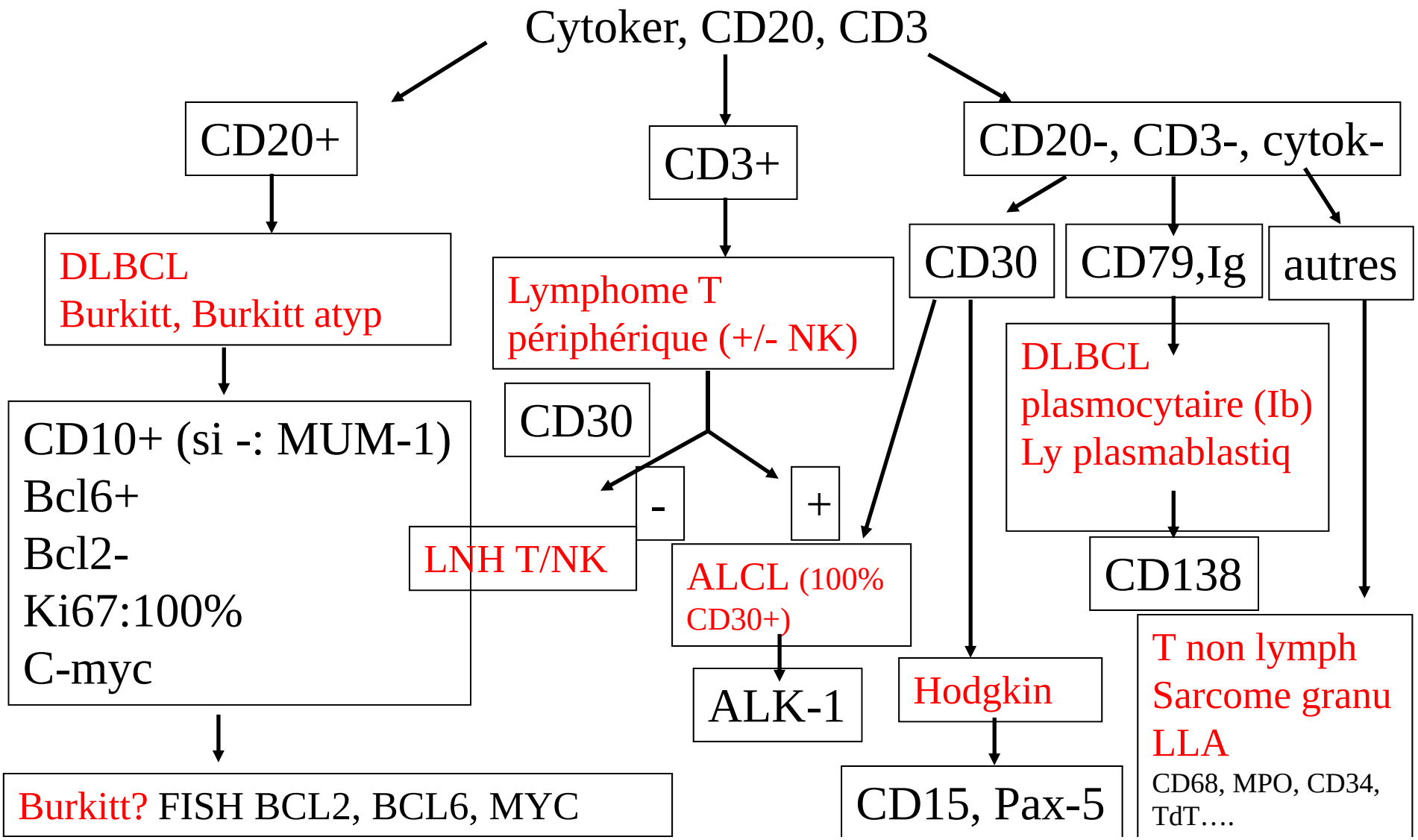




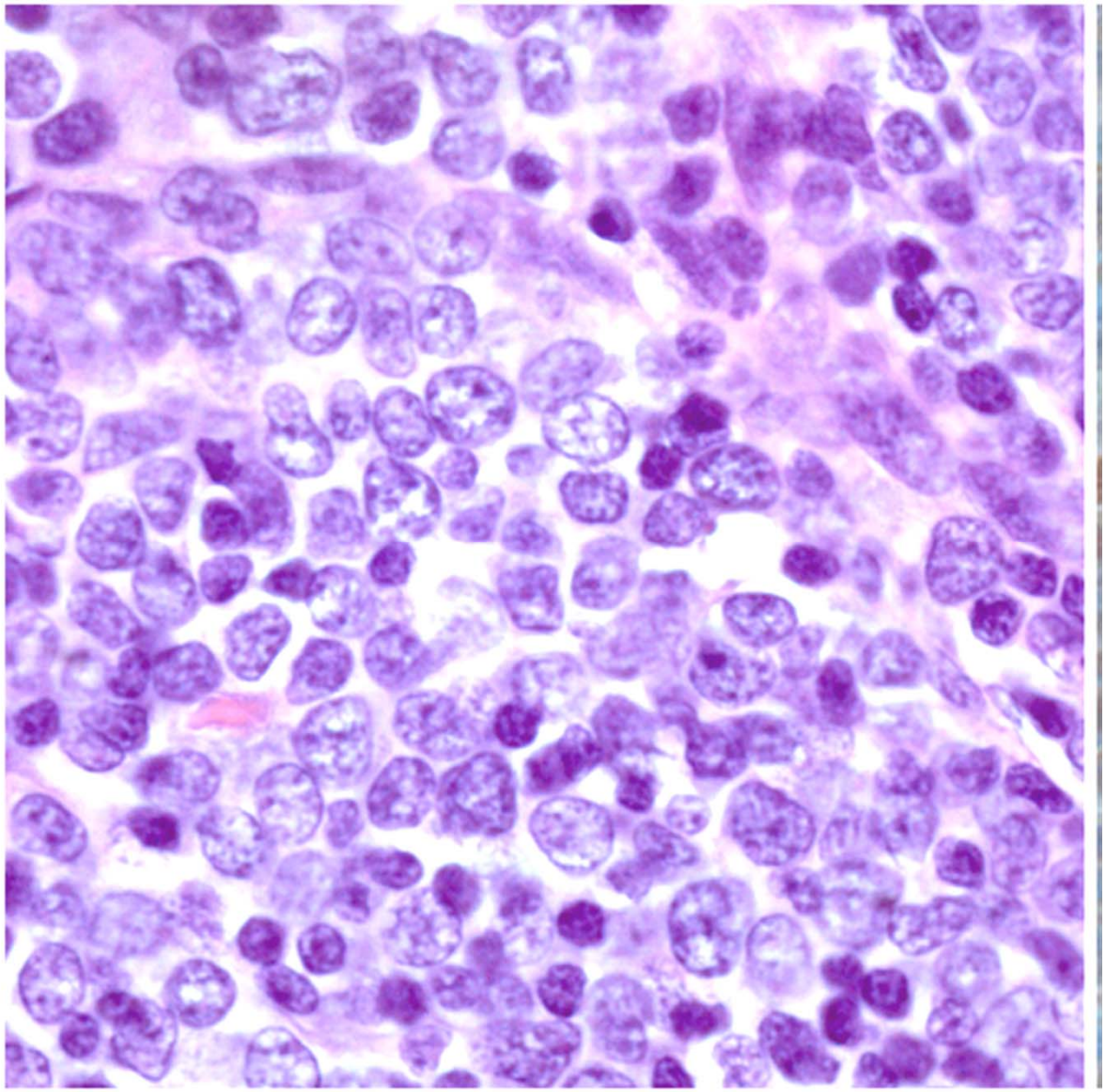


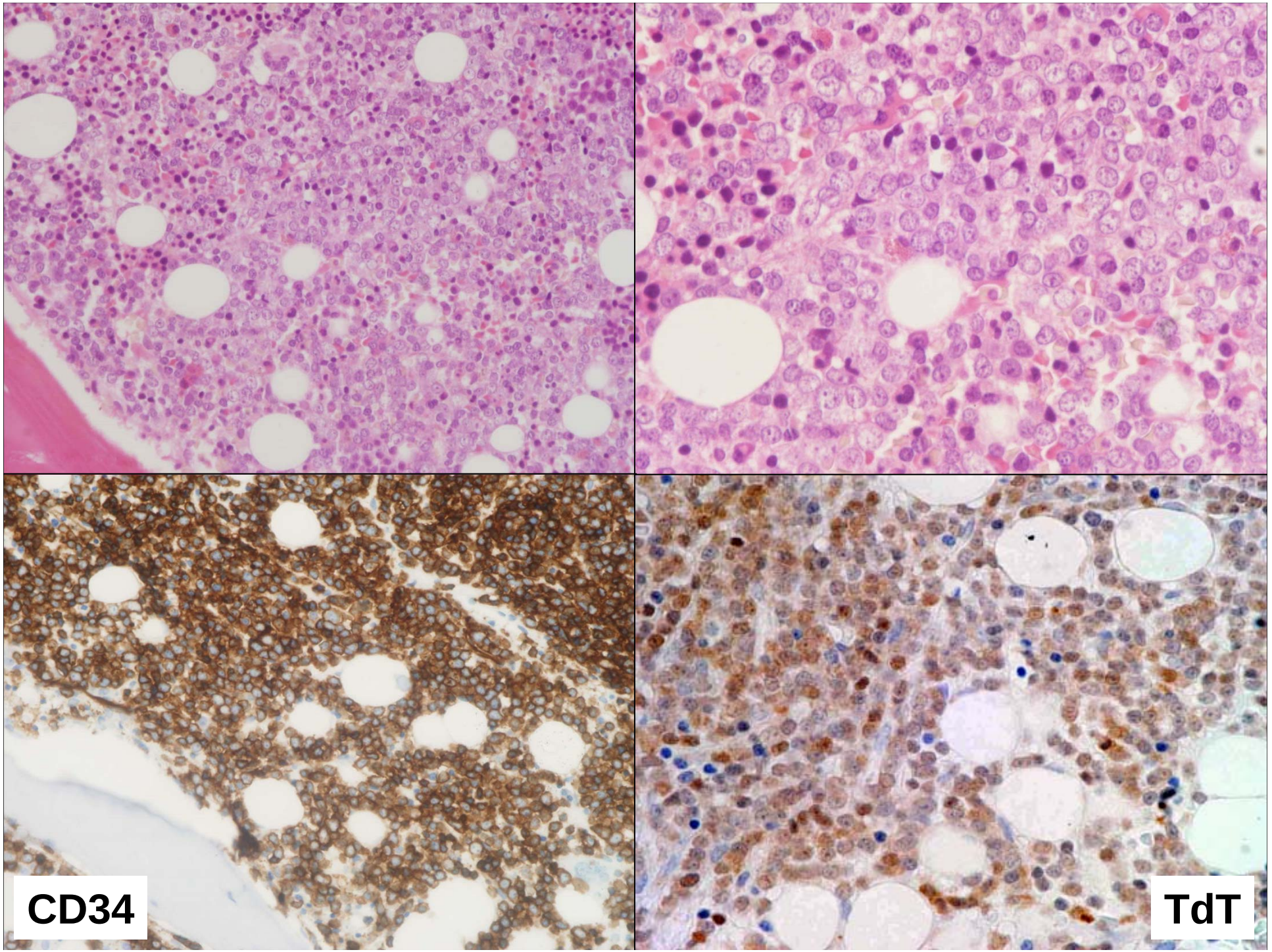


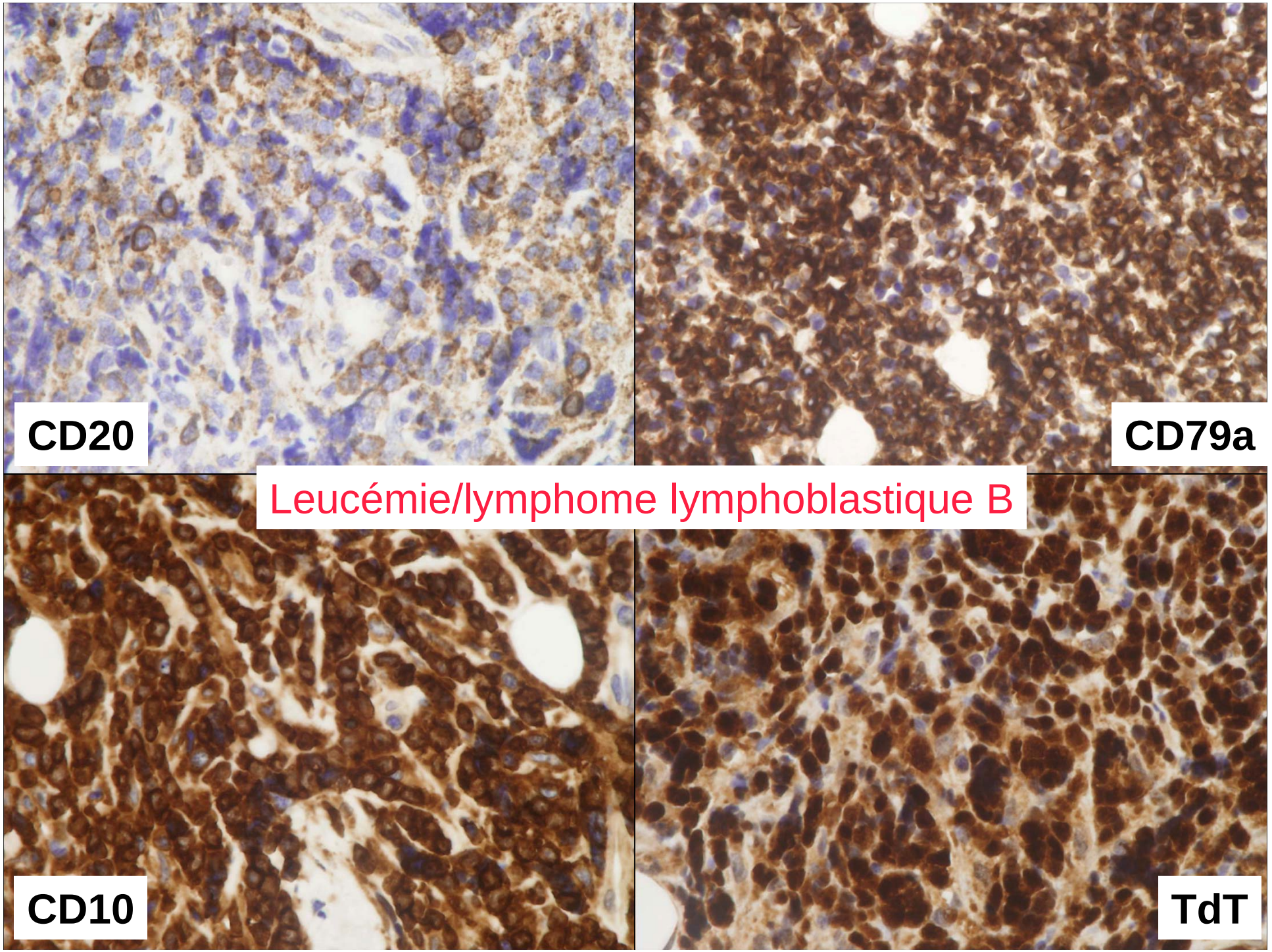
Prolifération à grandes cellules (2x taille d'un noyau de lymphocyte) si doute: Ki67

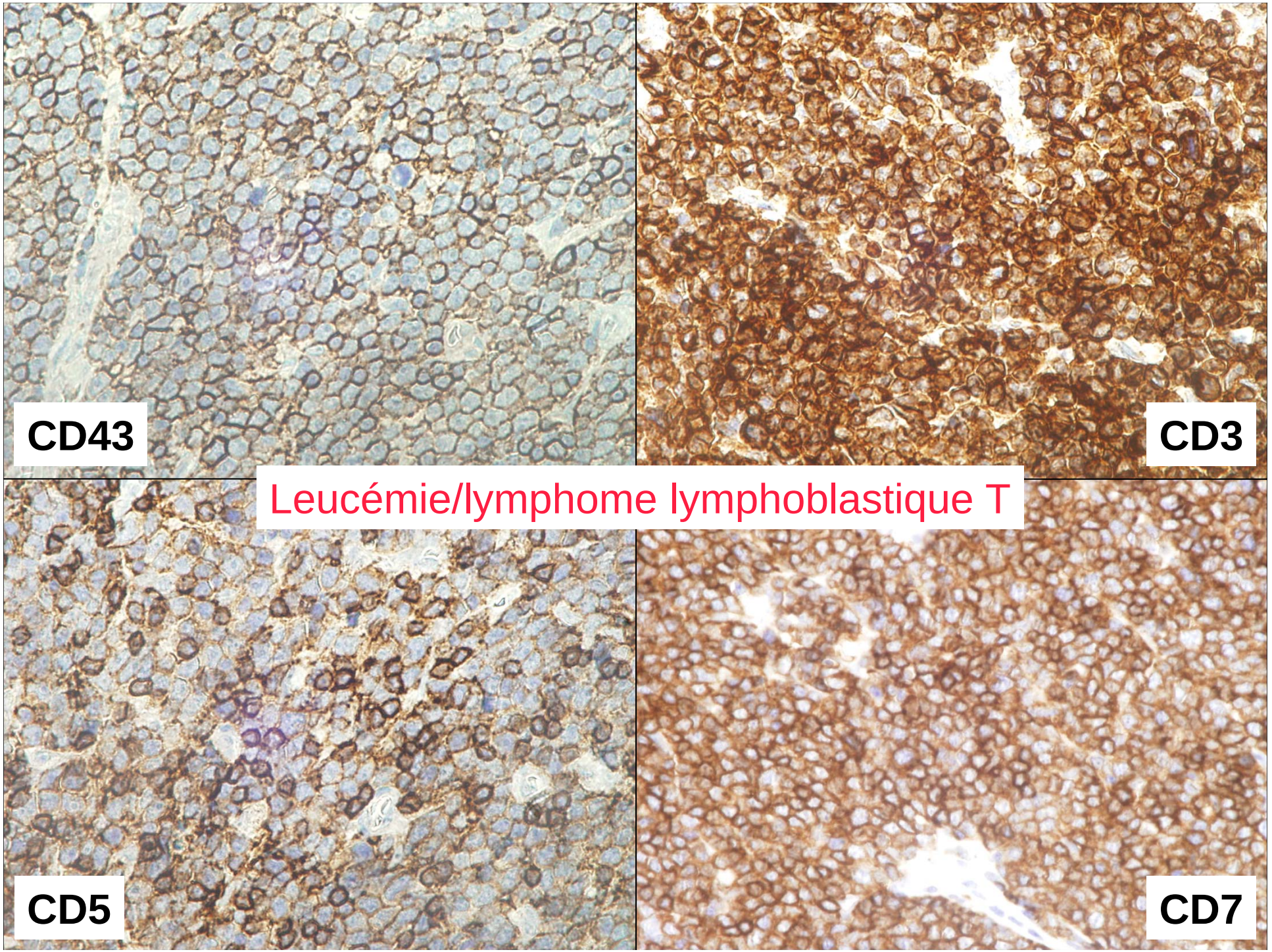


Leucémie/lymphome lymphoblastique



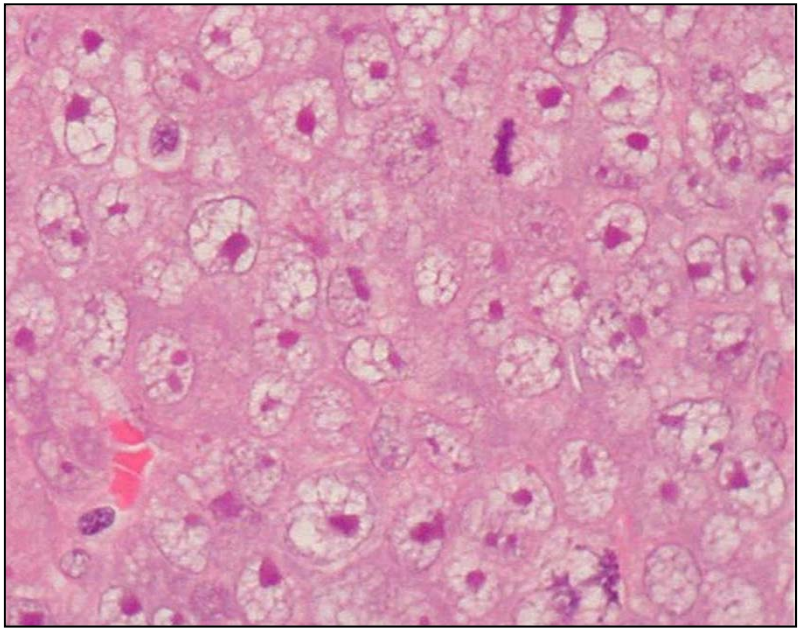

CD34
TdT

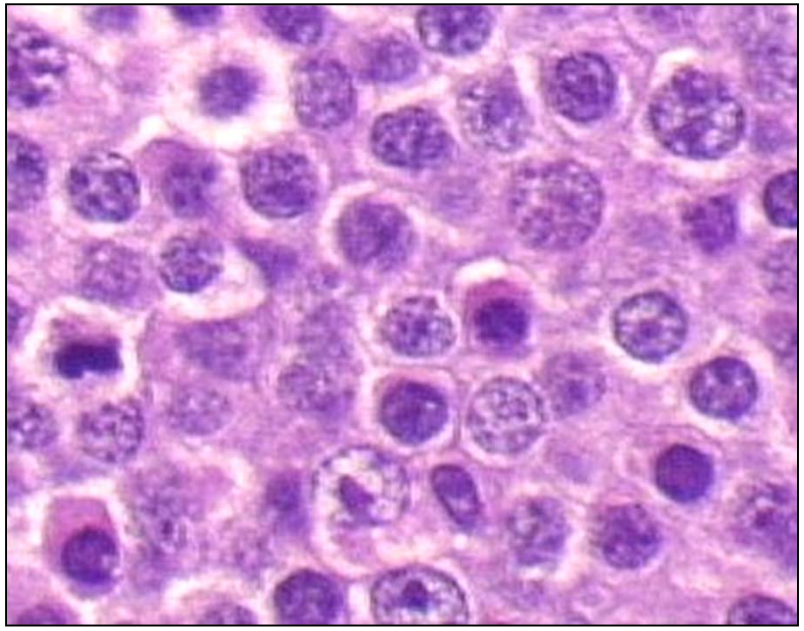

CD20
CD79a
Leucémie/lymphome lymphoblastique B
CD10
TdT

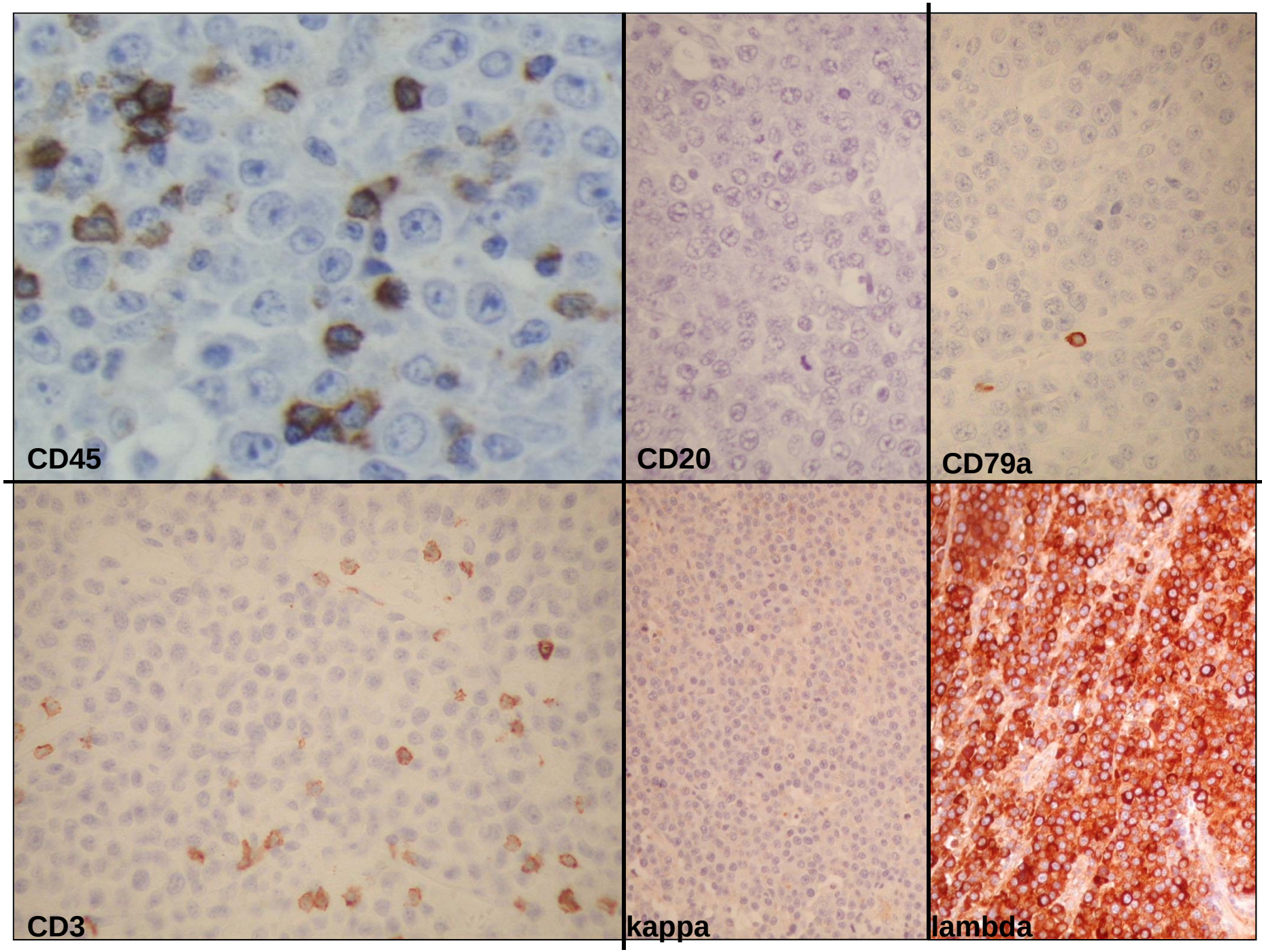

CD43
CD3
Leucémie/lymphome lymphoblastique T
CD5
CD7

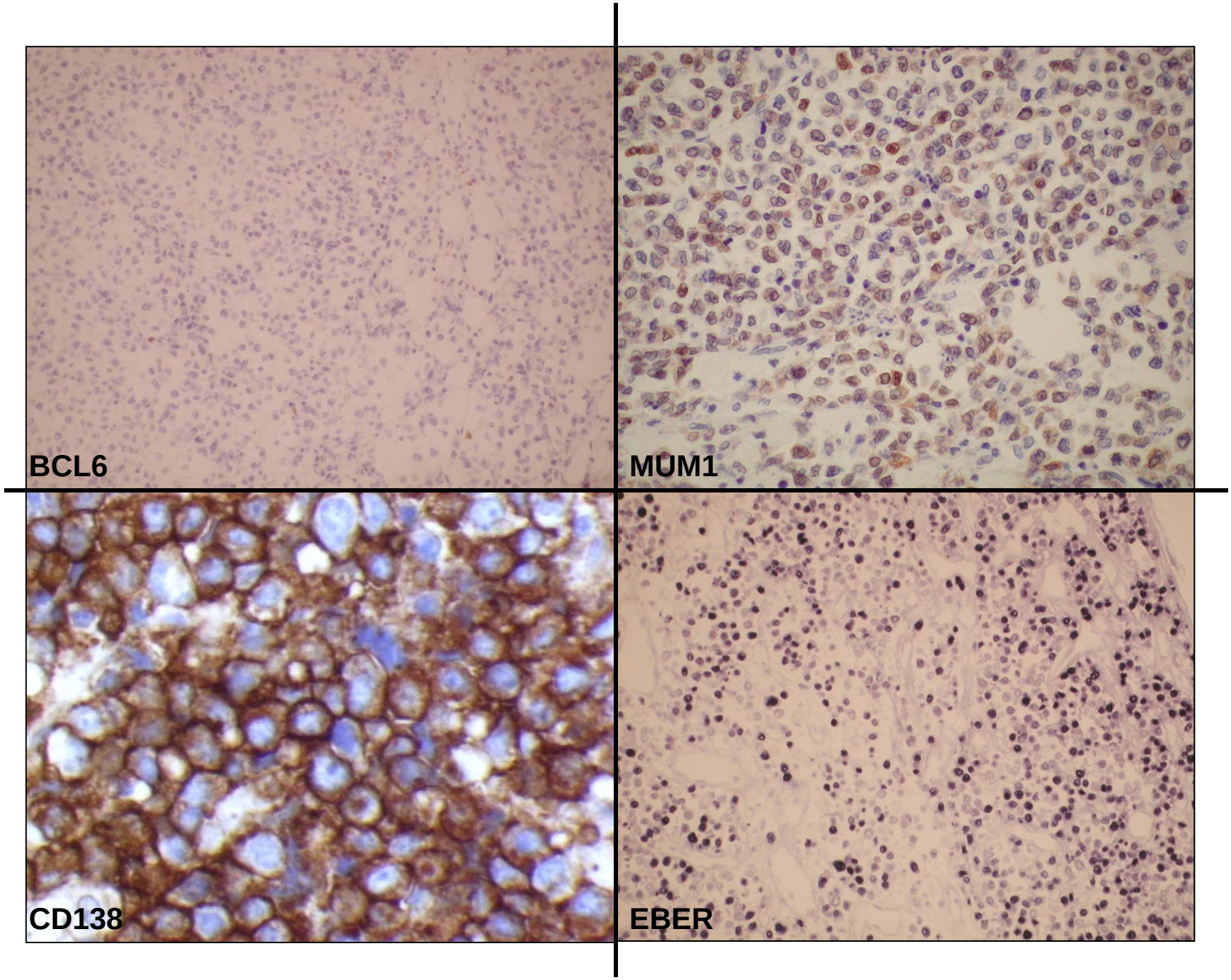
PLASMABLASTIC LYMPHOMA

Morphologic heterogeneity

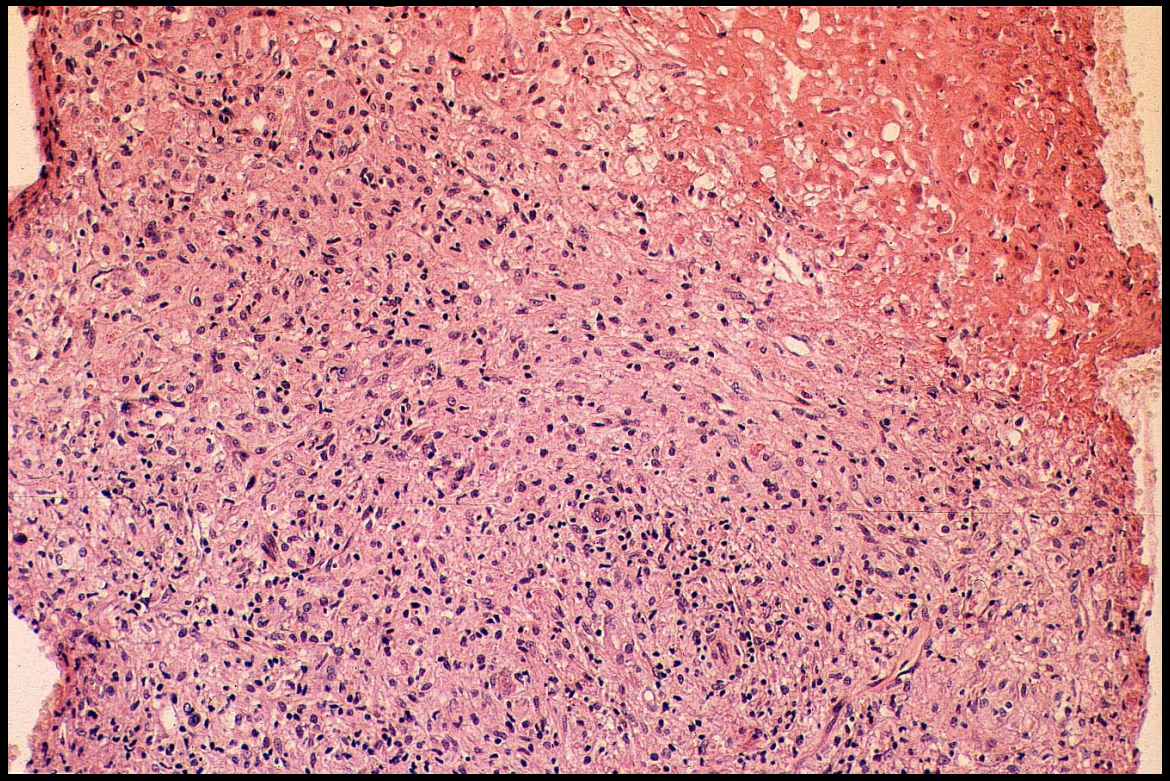


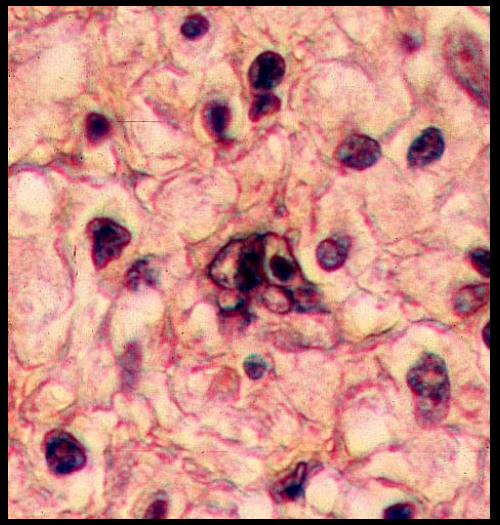


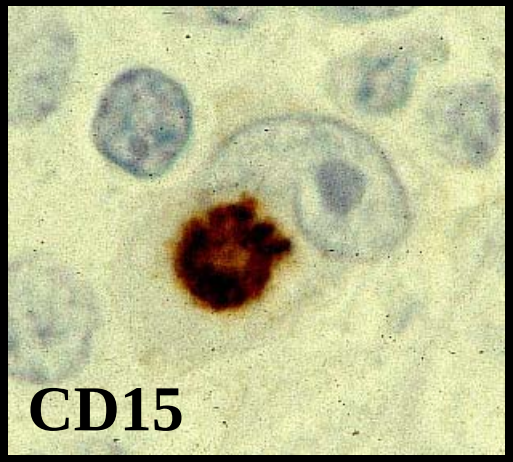

CD45
CD20
CD79a
CD3
kappa
lambda

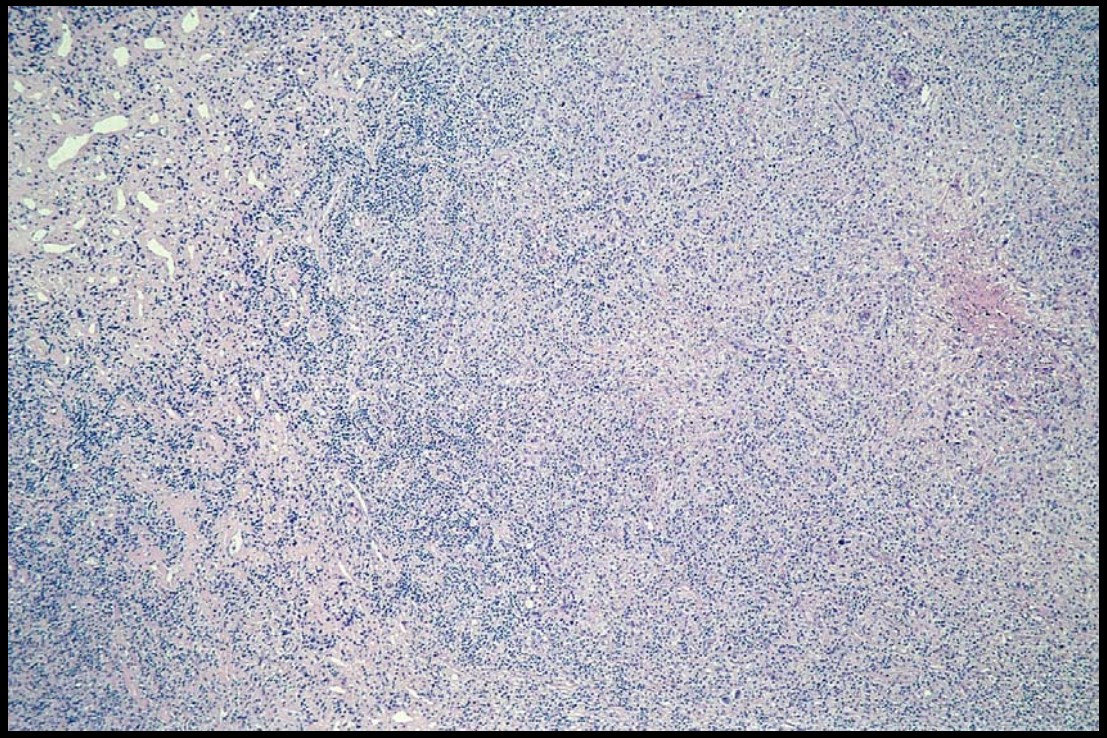

BCL6
MUM1
CD138
EBER

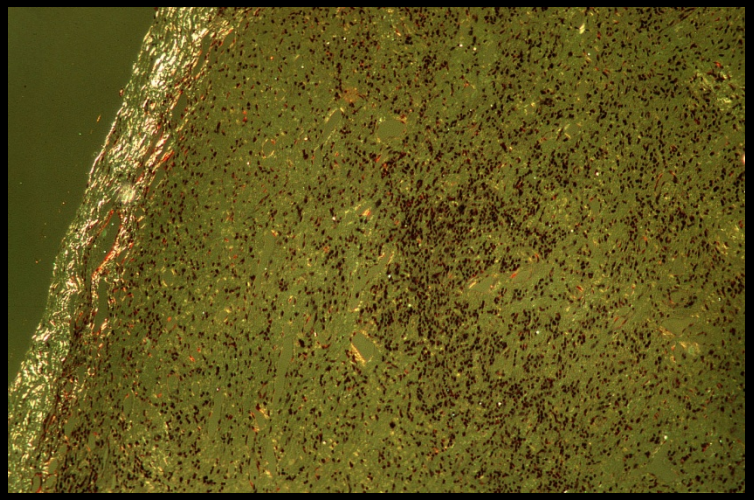
Lymphome de Hodgkin variante à déplétion lymphocytaire

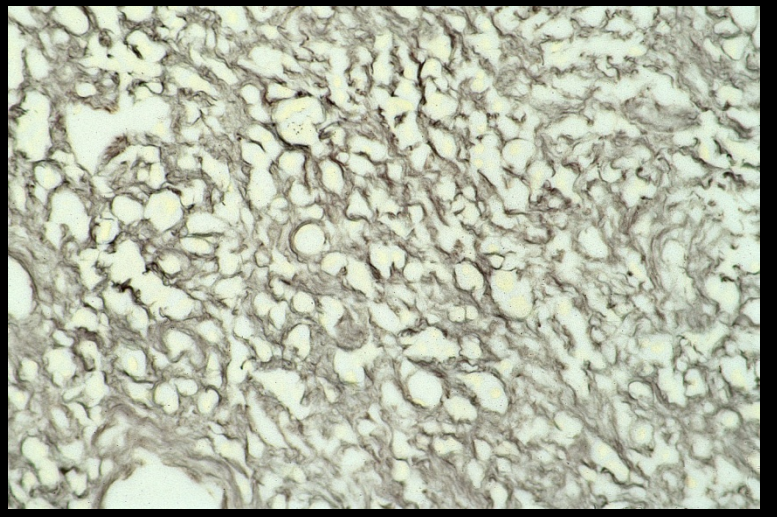




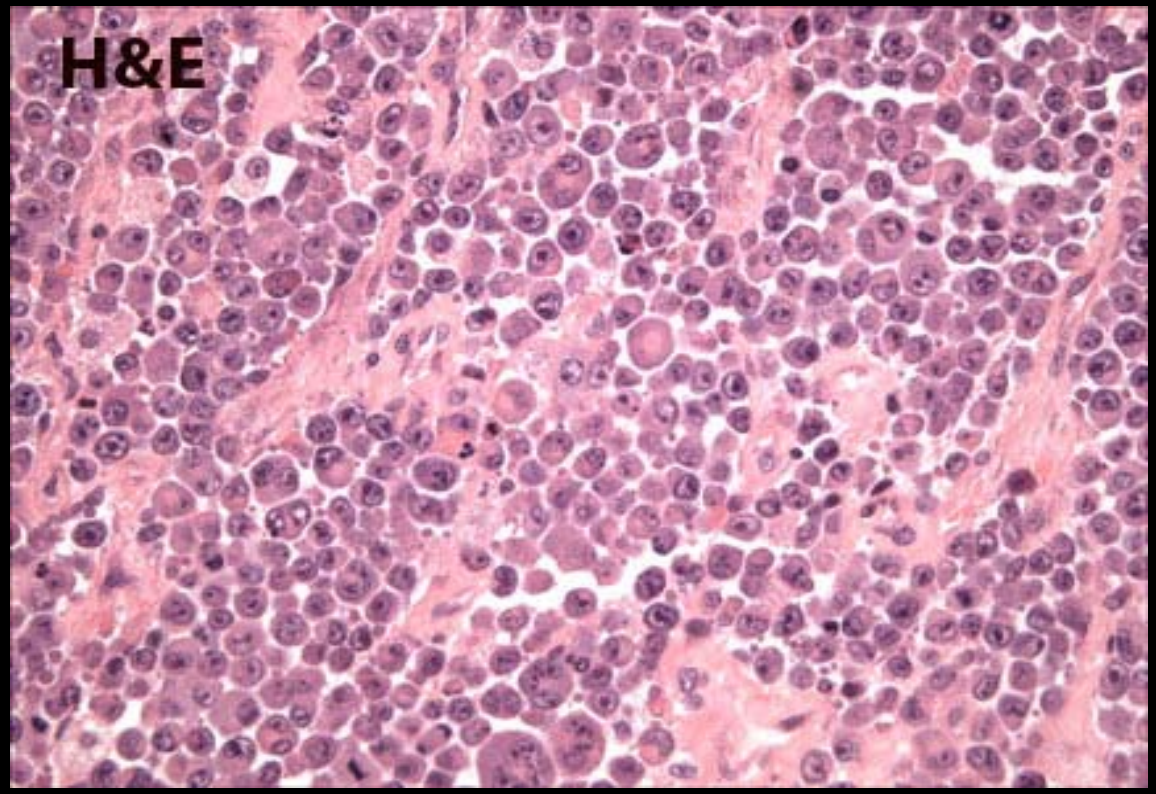


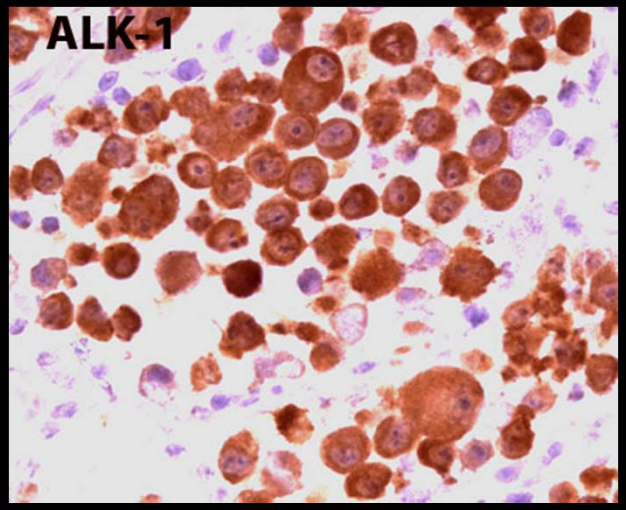






Ceci n’est pas un Hodgkin



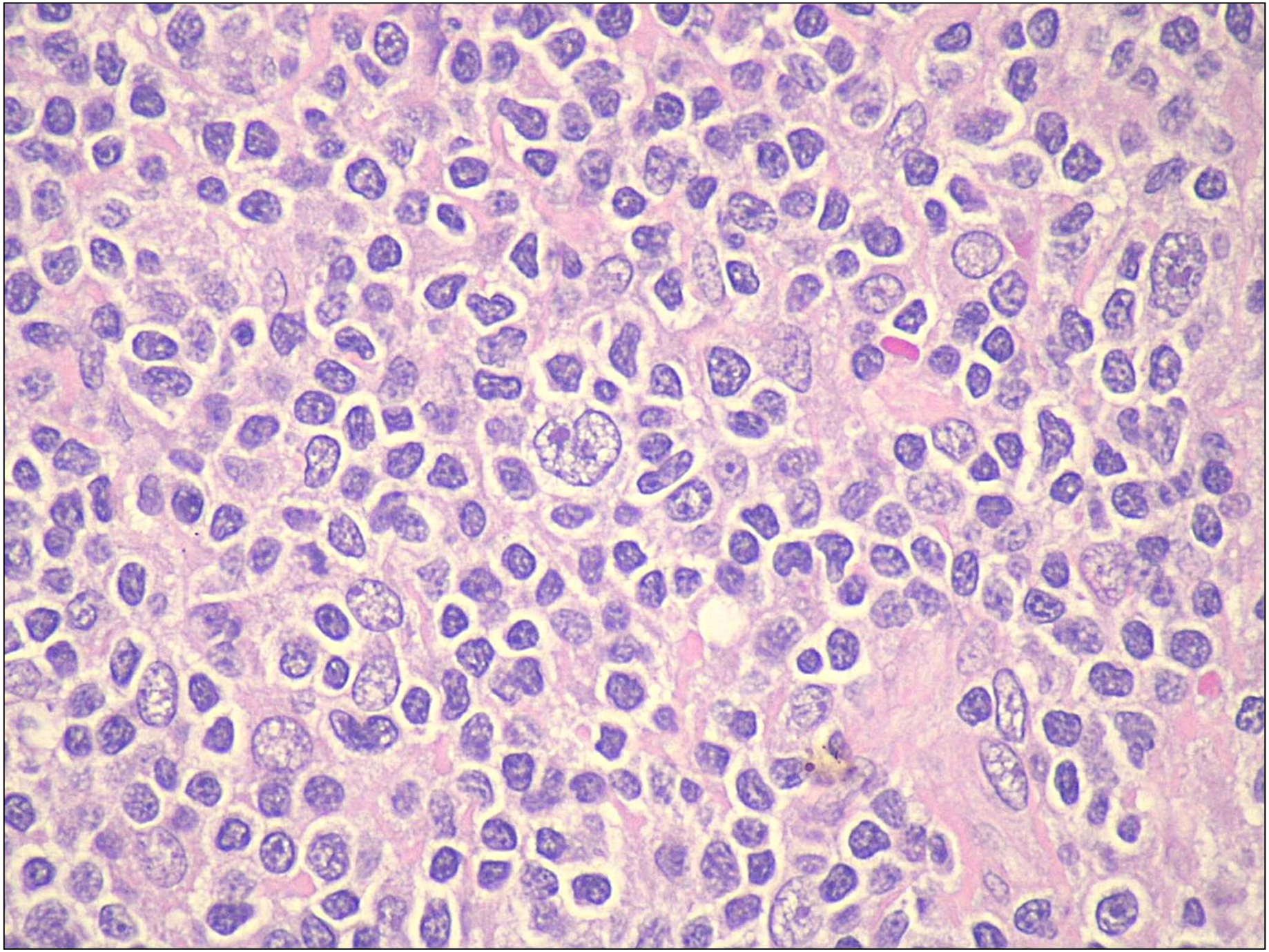


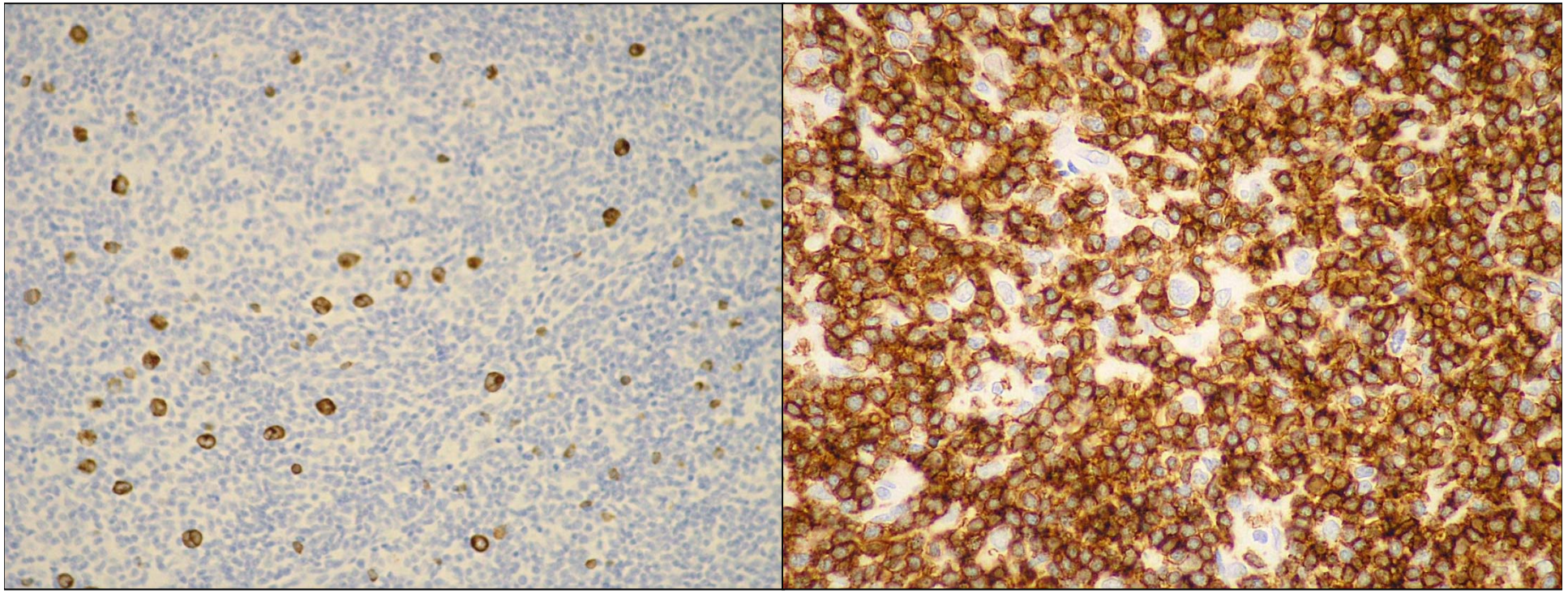
Lymphome anaplasique à grandes cellules, ALK-1

Diagnostic différentiel: architecture diffuse, grandes cellules isolées

- DLBCL (var riche en histio/ly)
- cHL (MC), NLPHL diffus
- Lymphome T NOS (Lennert), AILD
- Lymphome en transformation (Hodg-like)

CD20, Pax-5, CD30, CD3, CD5, CD15
2e step en fonction du type cellulaire

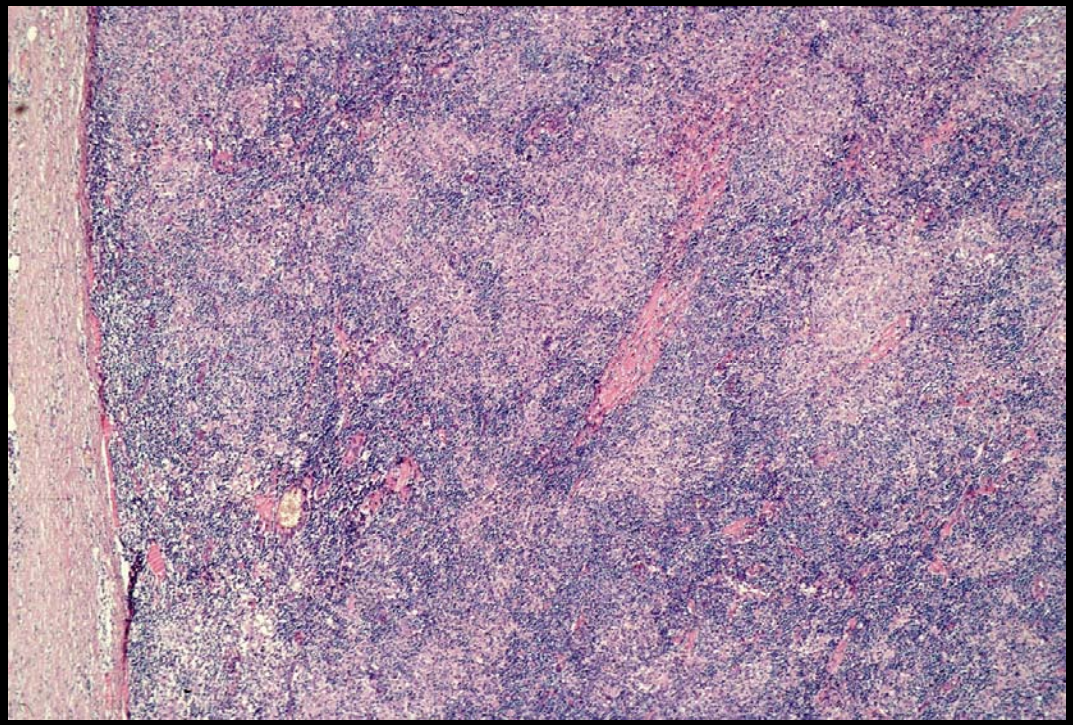


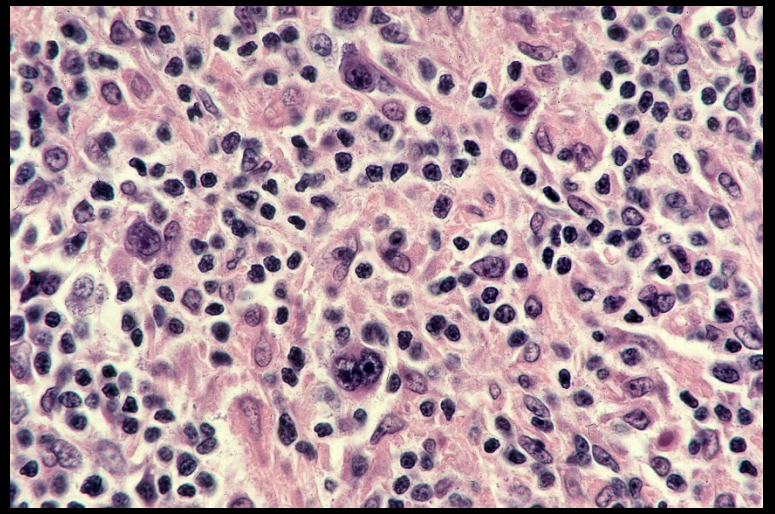


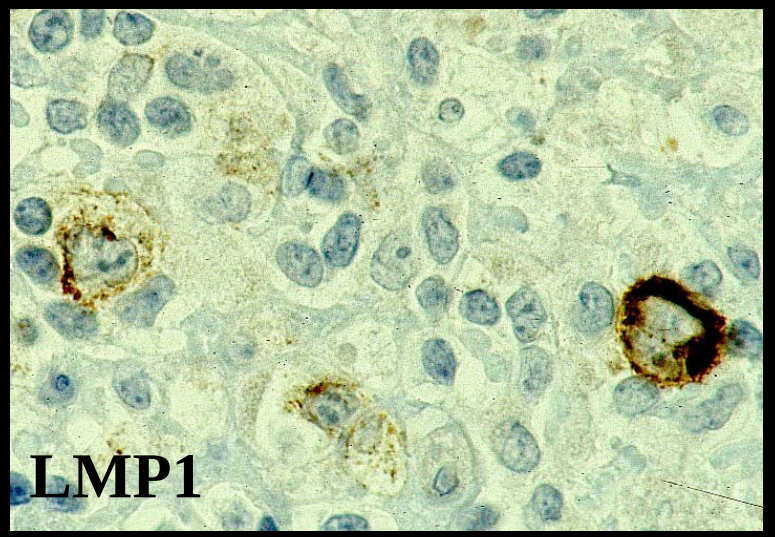
CD20

CD3

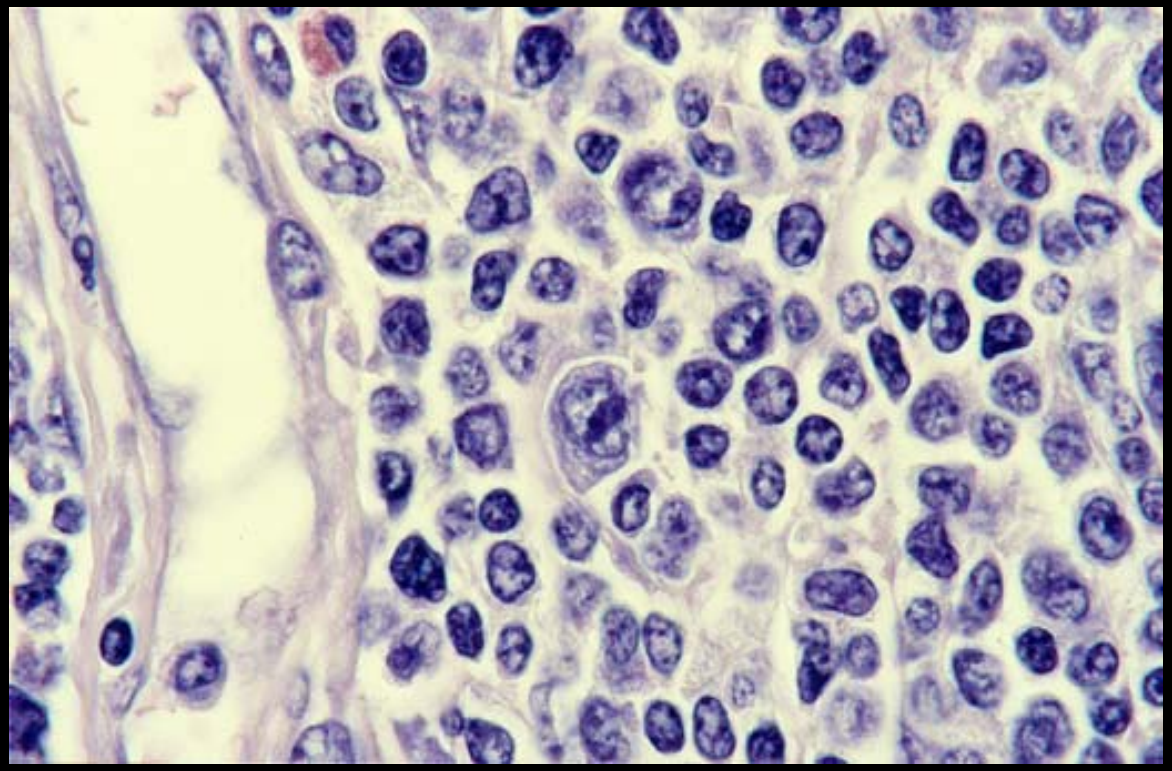
Lymphome de Hodgkin variante cellulaire mixte





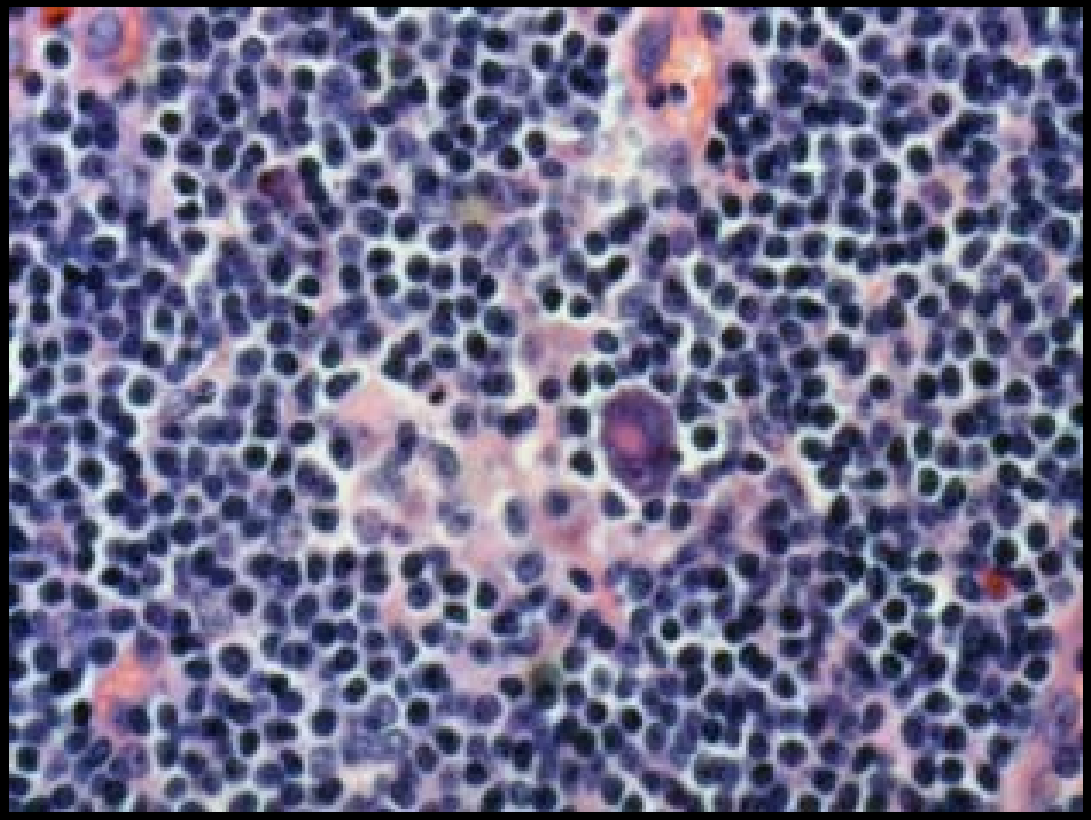


Ceci n’est pas un Hodgkin



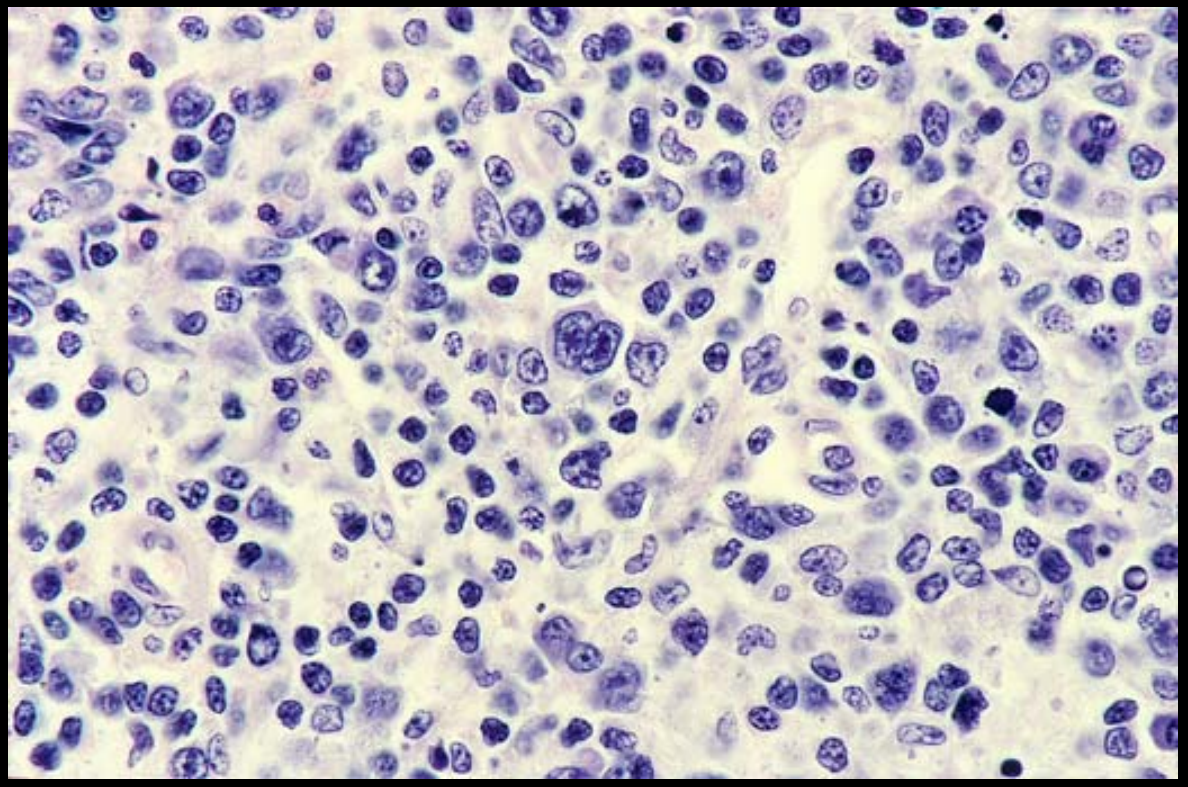
LNH-T pléomorphe

Ceci n’est pas un Hodgkin

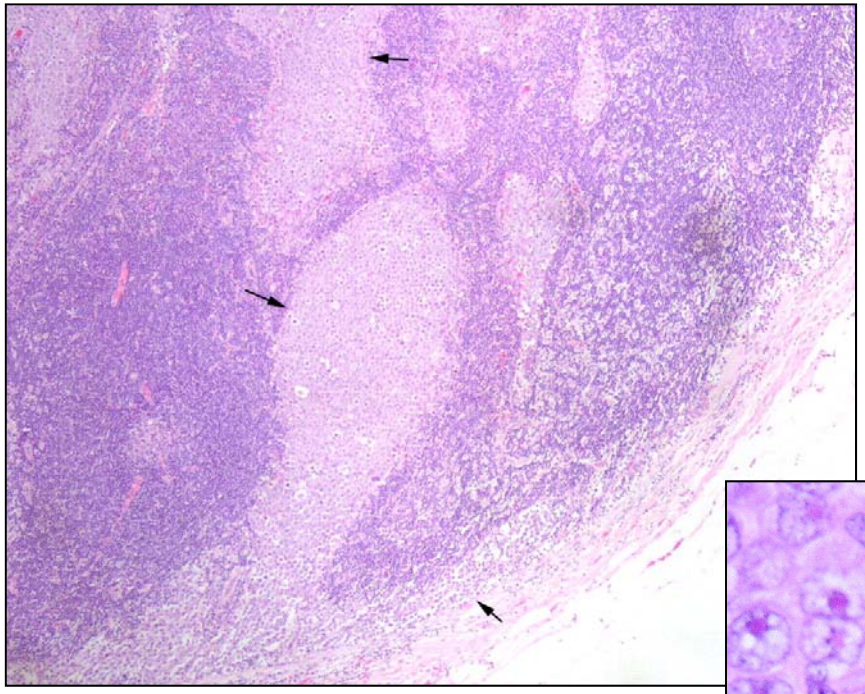


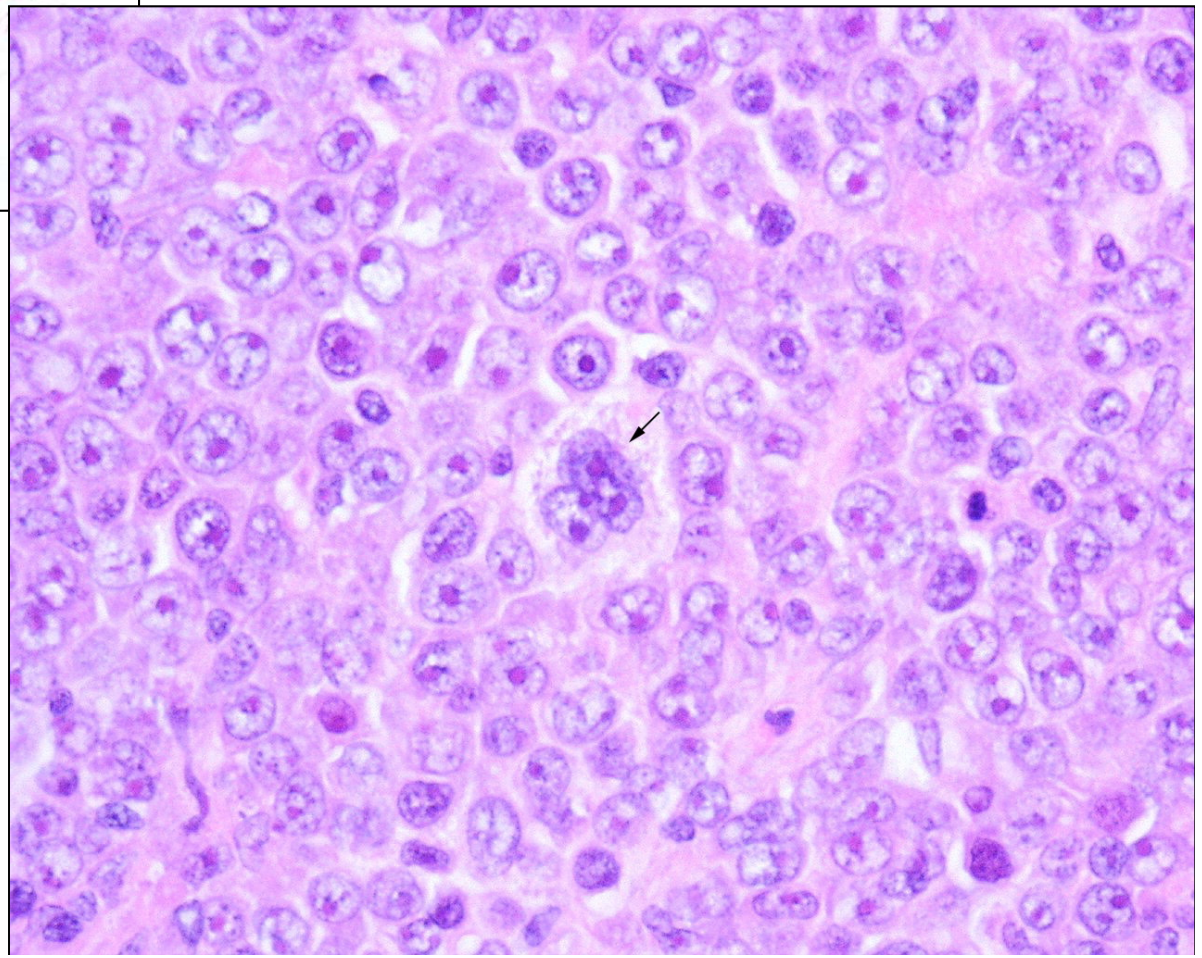
Richter

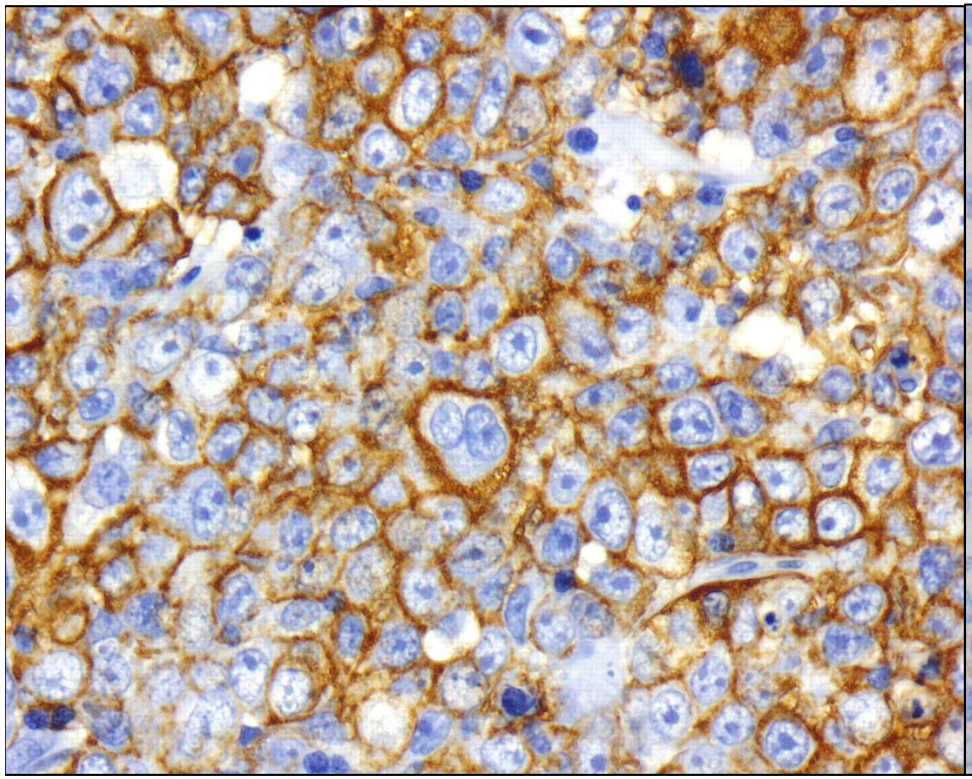
Ceci n’est pas un Hodgkin



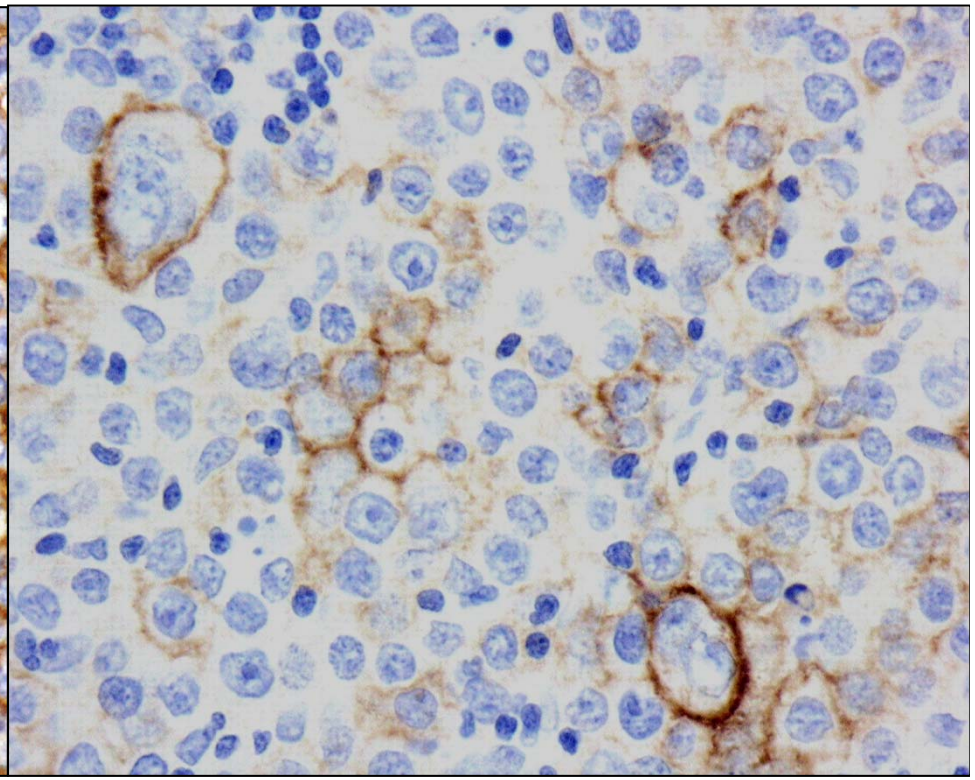
Mononucléose infectieuse







CD20

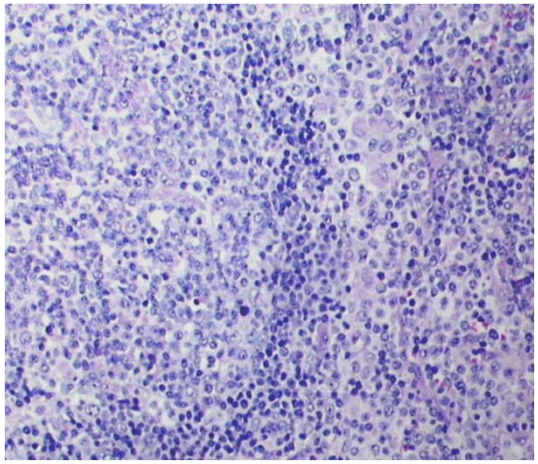
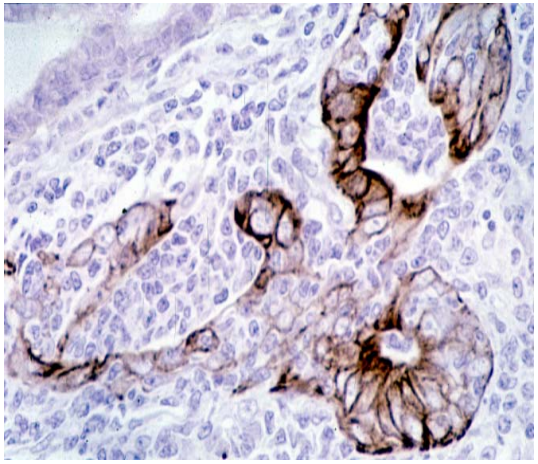
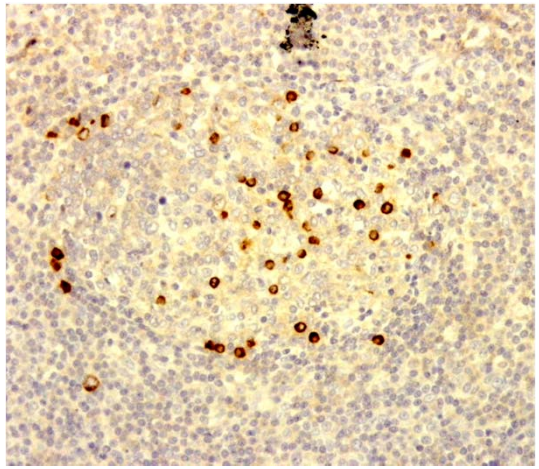
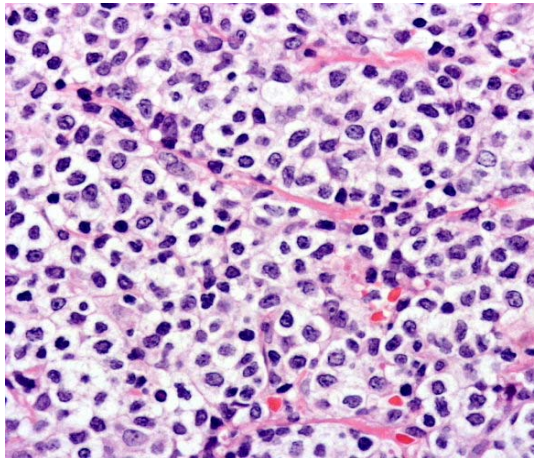
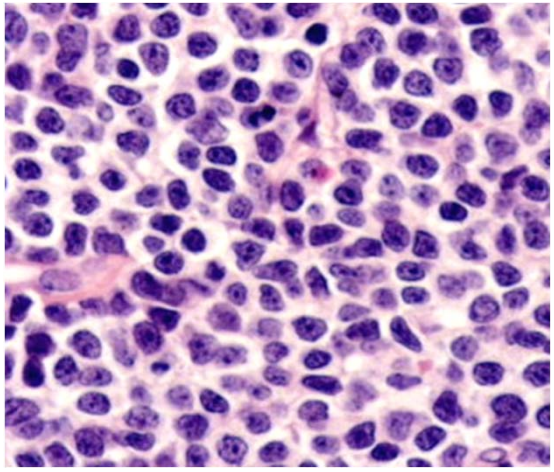
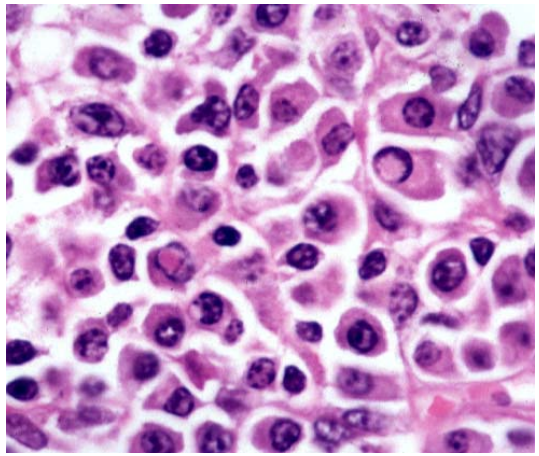


CD30

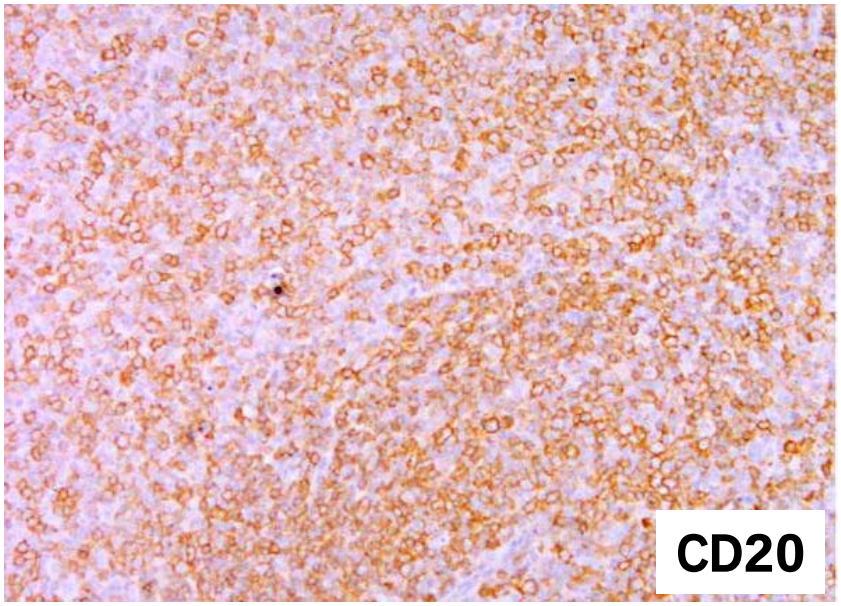
Diagnostic par organe: tube digestif

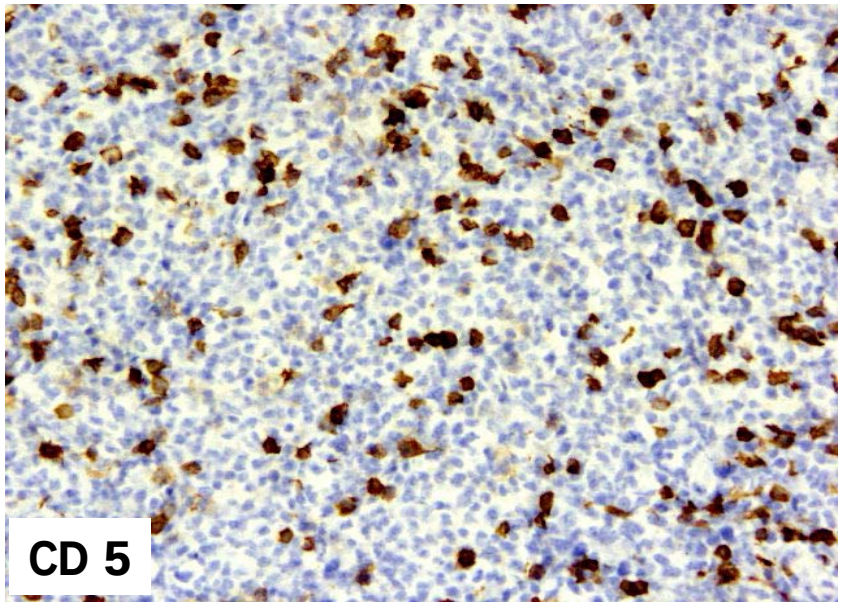
- Estomac:
  - Lymphome du MALT (zone marginale): LEL !
  - DLBCL
  - Manteau
  - Burkitt
  - Autres: plus rares ! Lymphome folliculaire, LNH-T, …

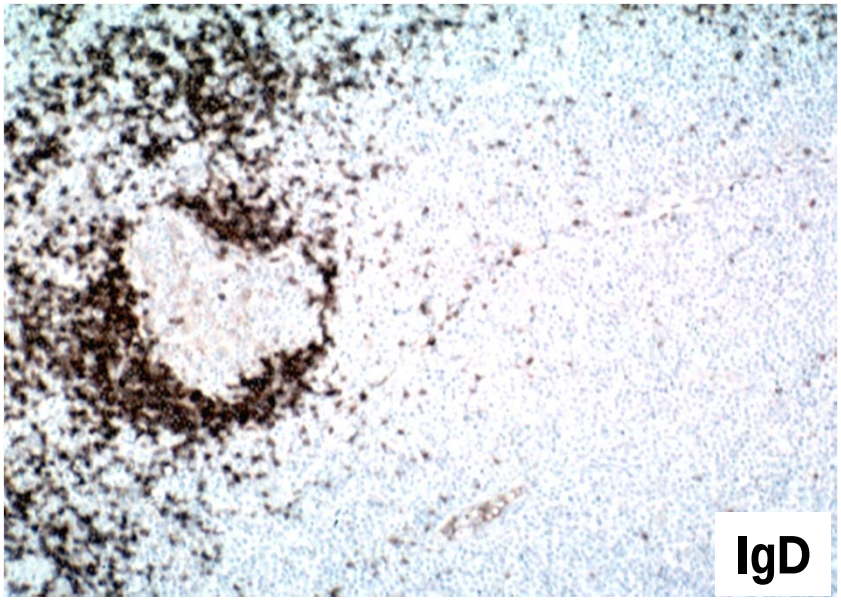
LZM extranodal: morphologie

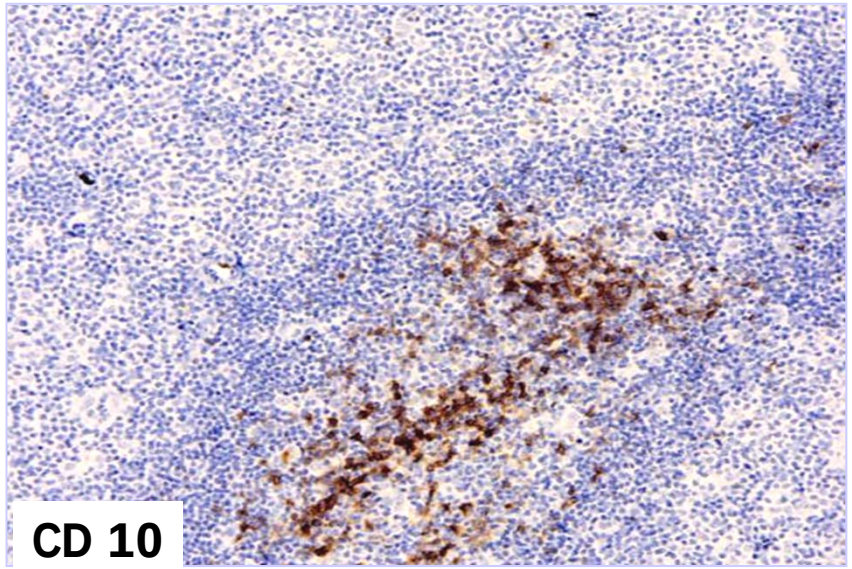







LZM: phénotype





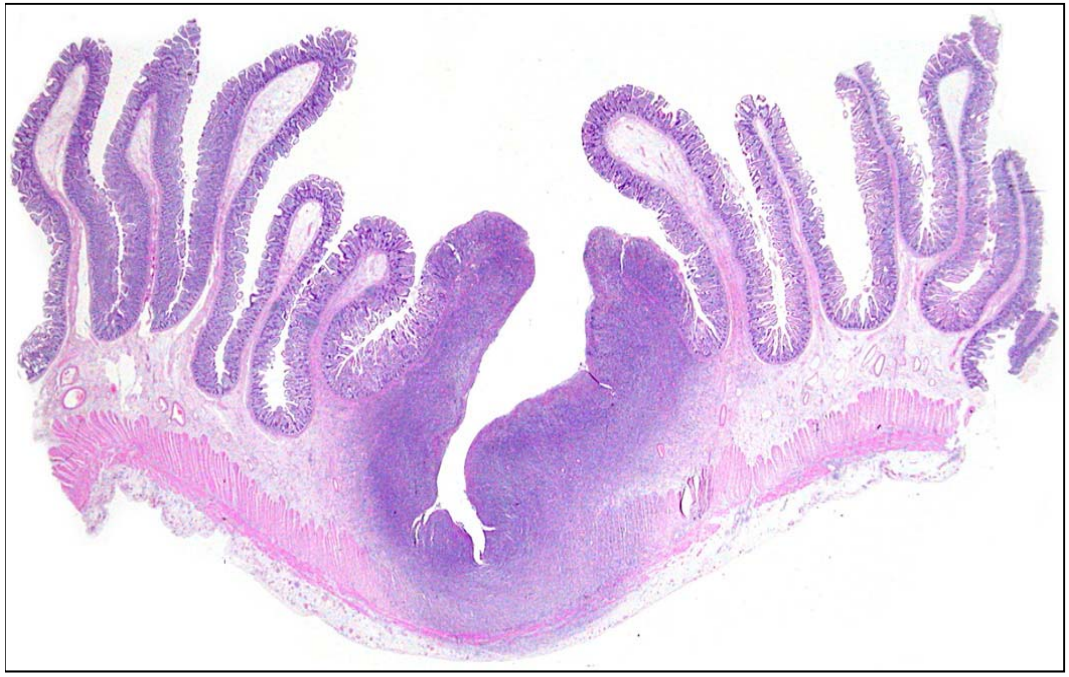


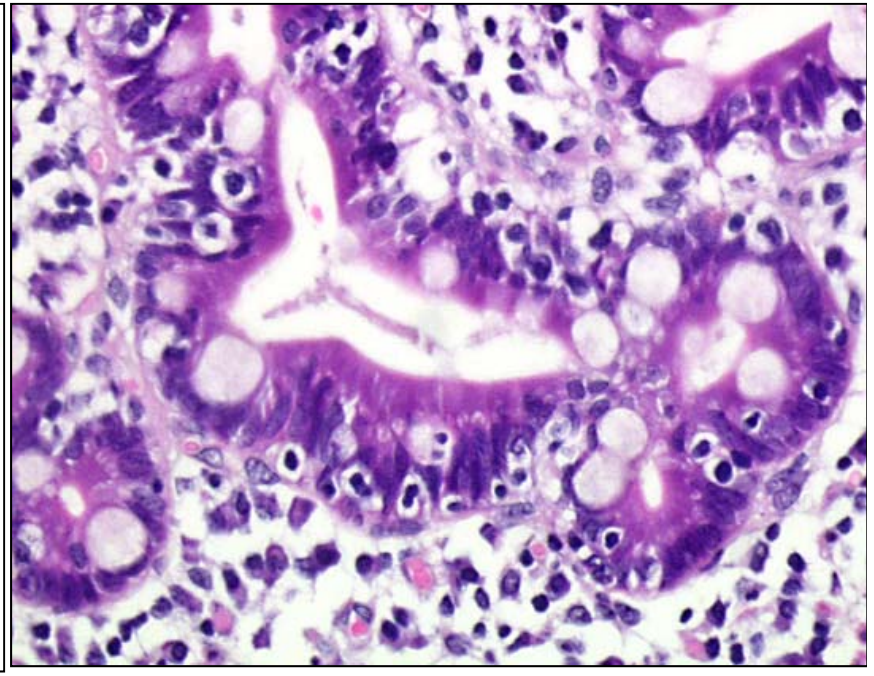


Diagnostic par organe: tube digestif

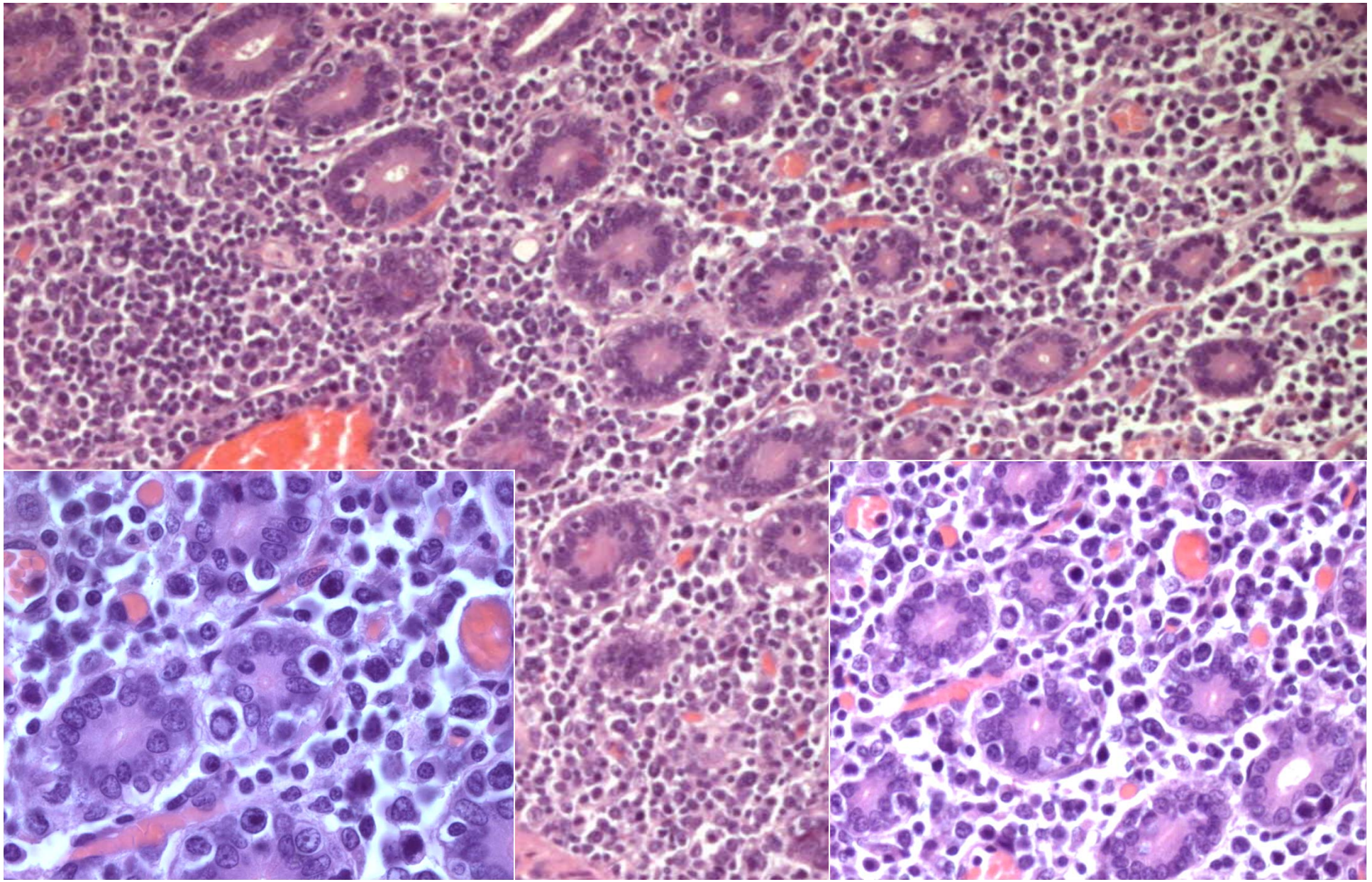
- Œsophage: exceptionnel !
- Intestin grêle:
  - DLBCL
  - Burkitt
  - Manteau (polypose lymphomatoïde)
  - Autres: plus rares ! Lymphome folliculaire,..
  - Lymphome T associé (ou non) à une entéropathie
- Côlon-rectum:
  - DLBCL
  - Lymphome folliculaire
  - Malt: très rare !

Lymphome T associé à entéropathie





Lymphome T associé à entéropathie



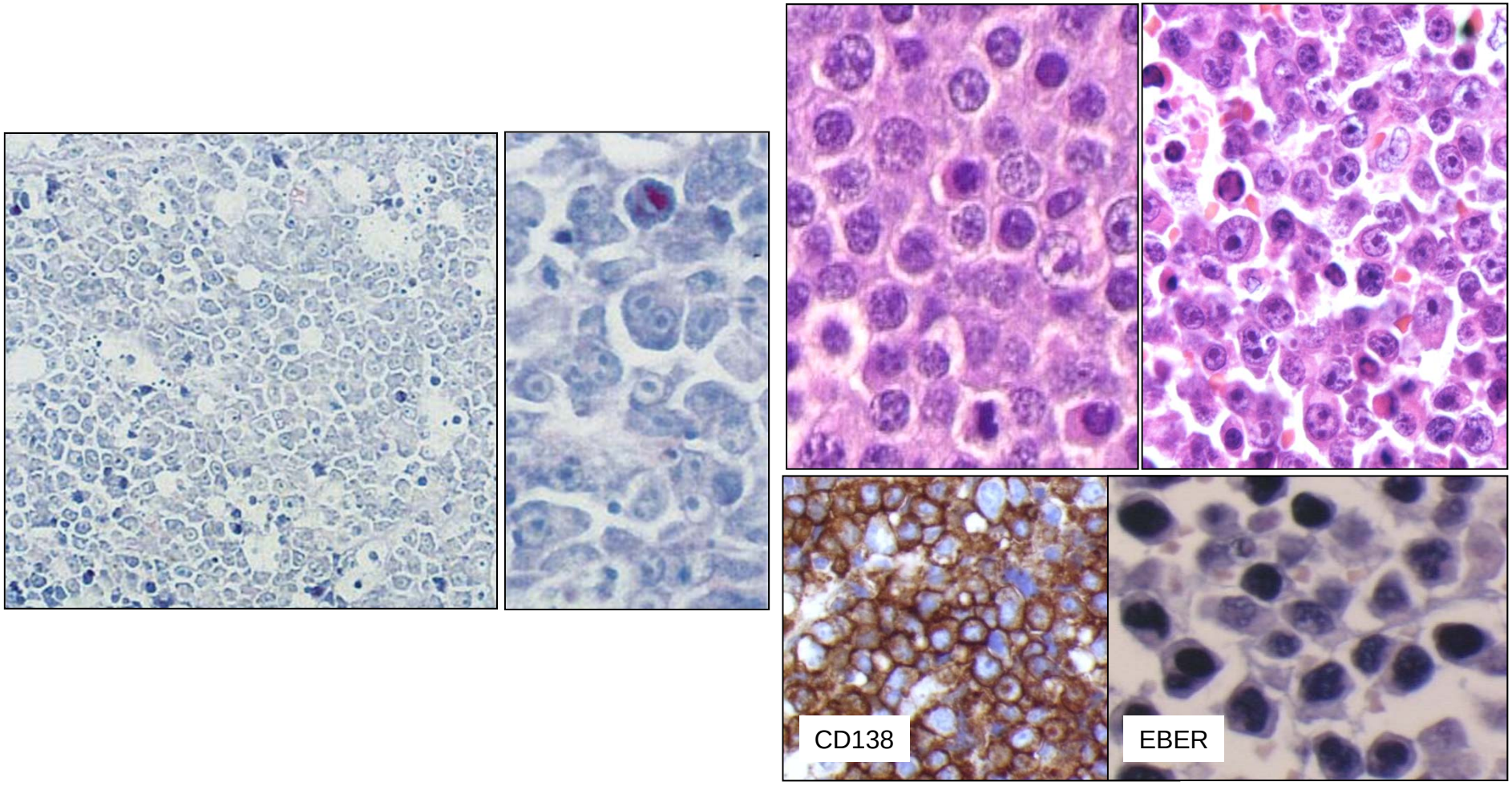
Diagnostic par organe: thyroïde, glandes salivaires

- Lymphome du MALT
  - Contexte immun: Sjögren, Hashimoto..
- DLBCL
  - 95% associés à lymphome du MALT
  - ! Carcinome à grandes cellules
- Lymphome folliculaire
  - Extension secondaire d'un lymphome ganglionnaire

Diagnostic par organe: ORL

- DLBCL
- Lymphome folliculaire
- Manteau
- Lymphome lympho-plasmocytaire
  - Enfant: MNI !
- Lymphome plasmablastique (HIV)
- Lymphome T/NK « de type nasal »

Plasmablastic Lymphoma of the Oral Cavity



Diagnostic par organe: poumons

- Lymphome du Malt
- DLBCL
  - Si immunodéprimé, penser à exclure
  - PTLD
  - Granulomatose lymphomatoïde
  - Lymphome des séreuses
- Lymphome T

Diagnostic par organe: seins

- Lymphome du Malt
- DLBCL
- Burkitt
- LLA

Diagnostic par organe: annexes de l'oeil

- Lymphome du Malt
- Manteau
- Lymphome folliculaire
- LLC

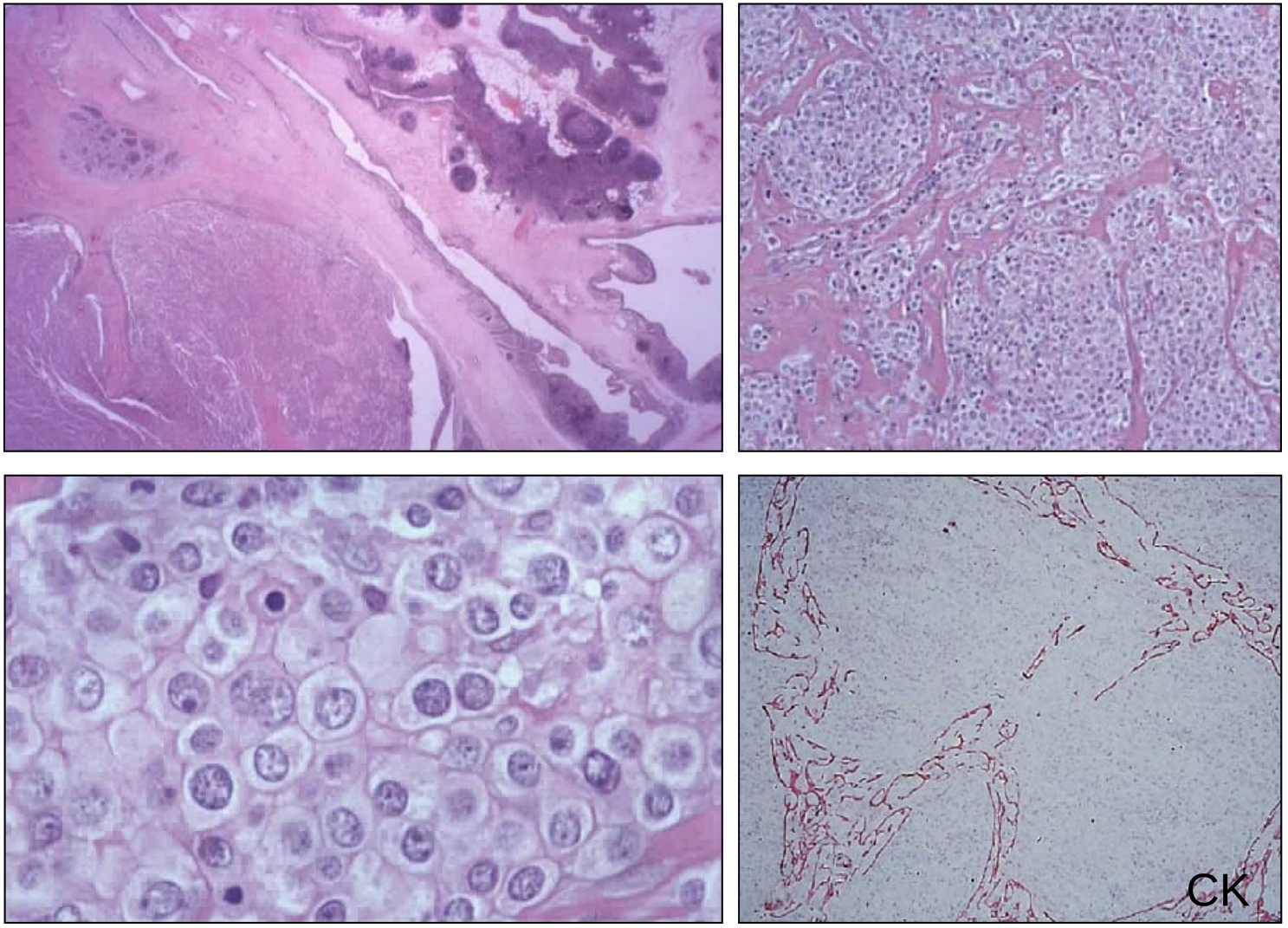
Diagnostic par organe: localisations particulières

- Os:
  - High grade
    - Plasmocytome plasmablastique
    - DLBCL
    - Hodgkin
    - ALCL

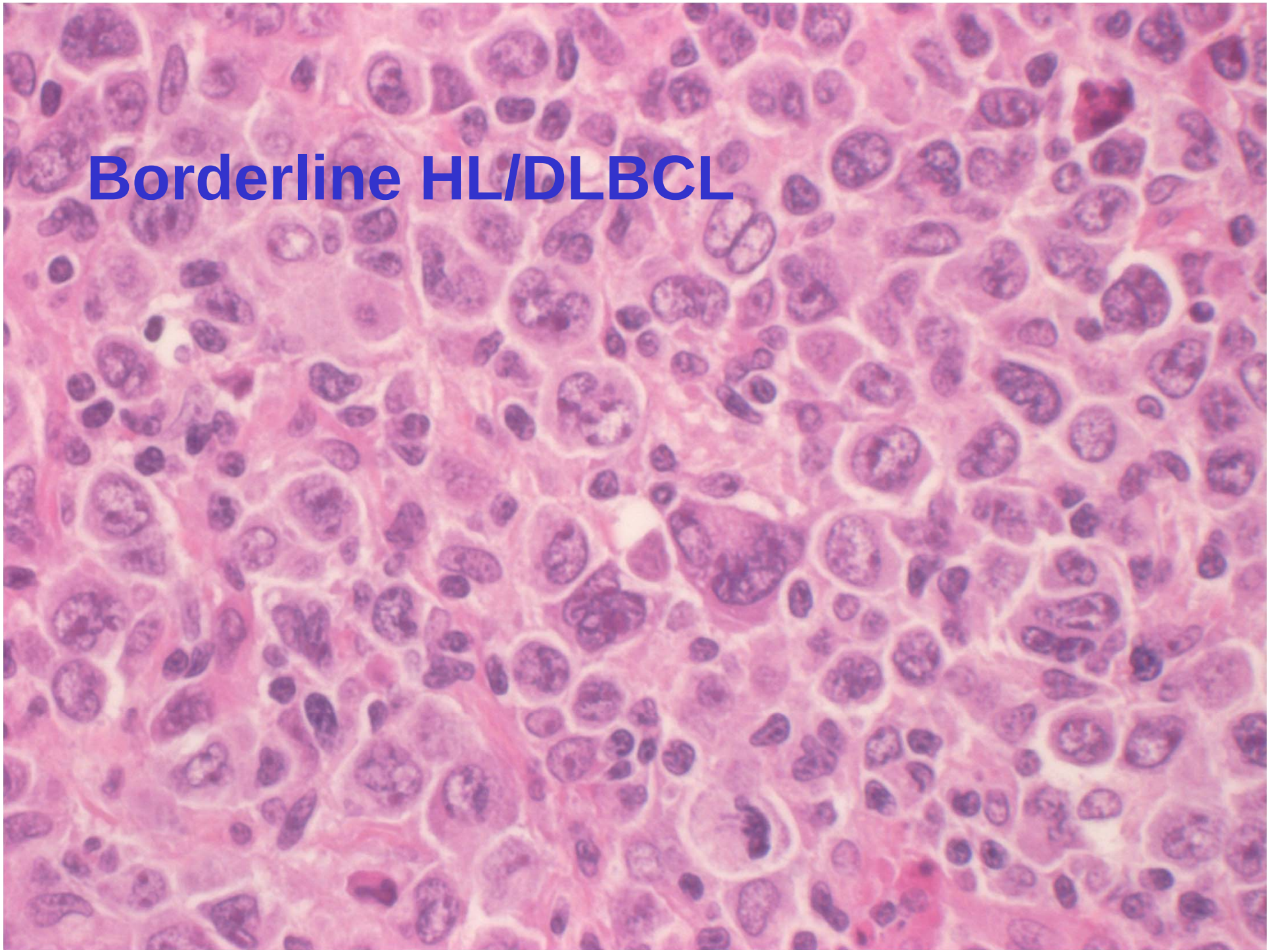
Diagnostic par organe: localisations particulières

- Médiastin
  - Hodgkin +++
  - Carcinome
  - Séminome
  - DLBCL

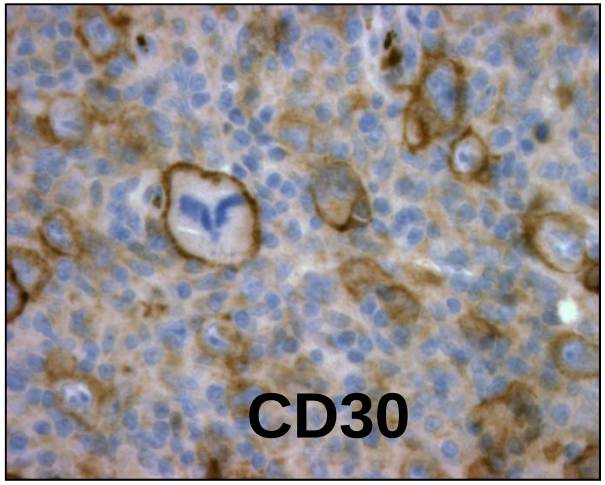
Primary Mediastinal (Thymic) Large B-cell Lymphoma

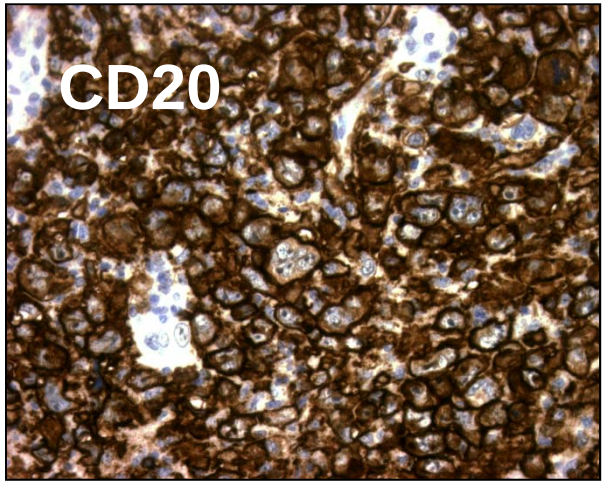


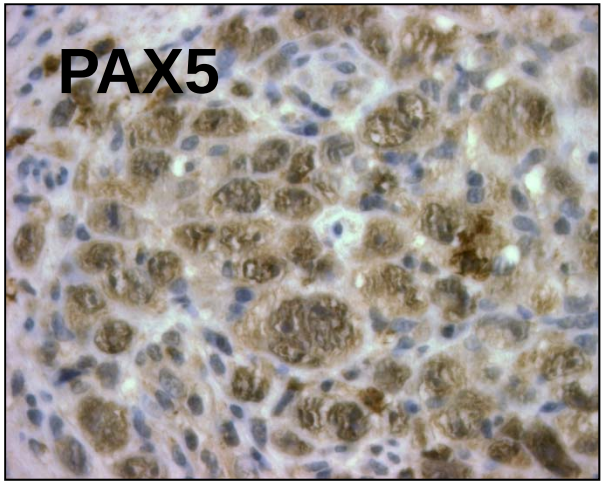
Borderline HL/DLBCL

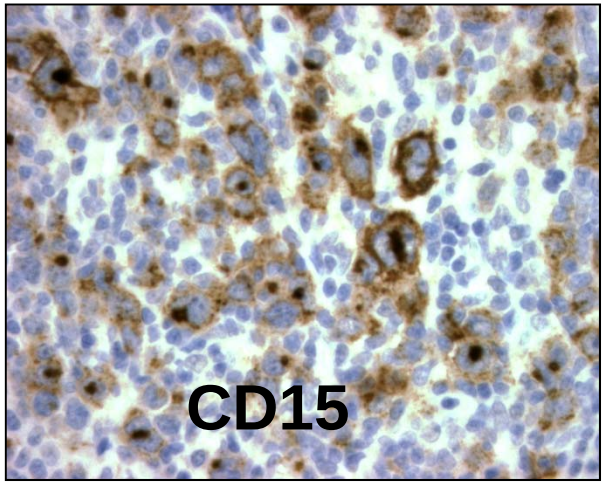


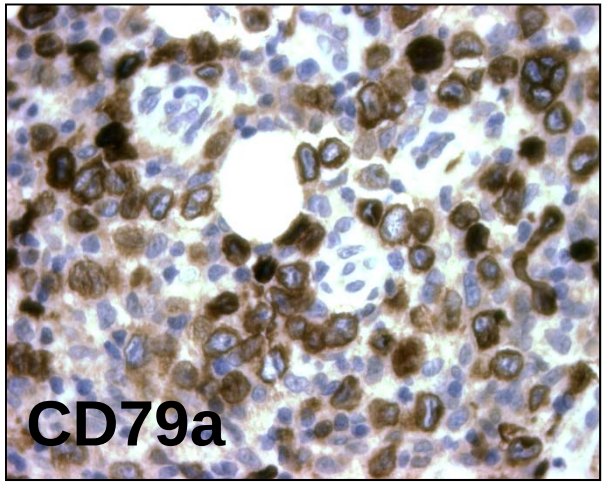
Borderline HL/DLBCL

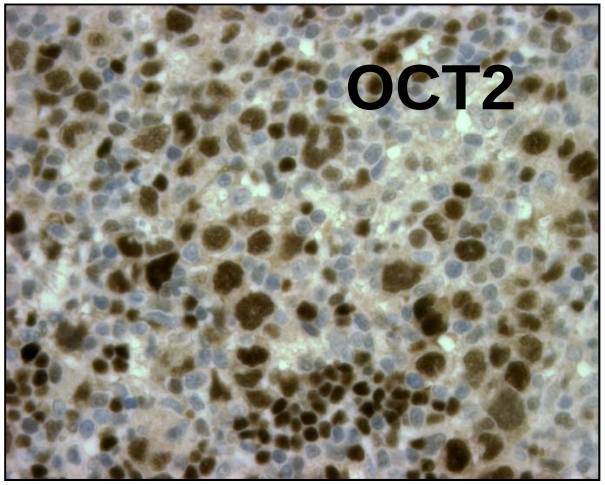








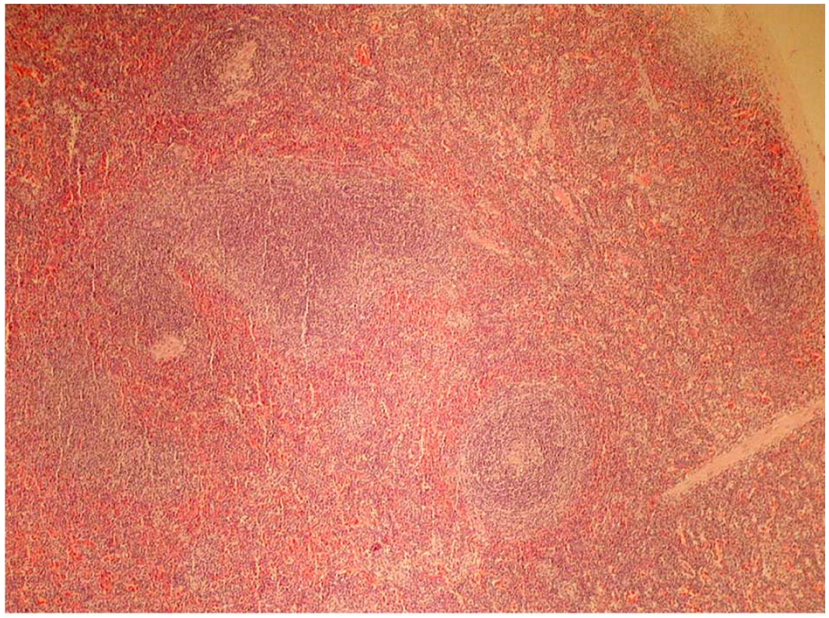


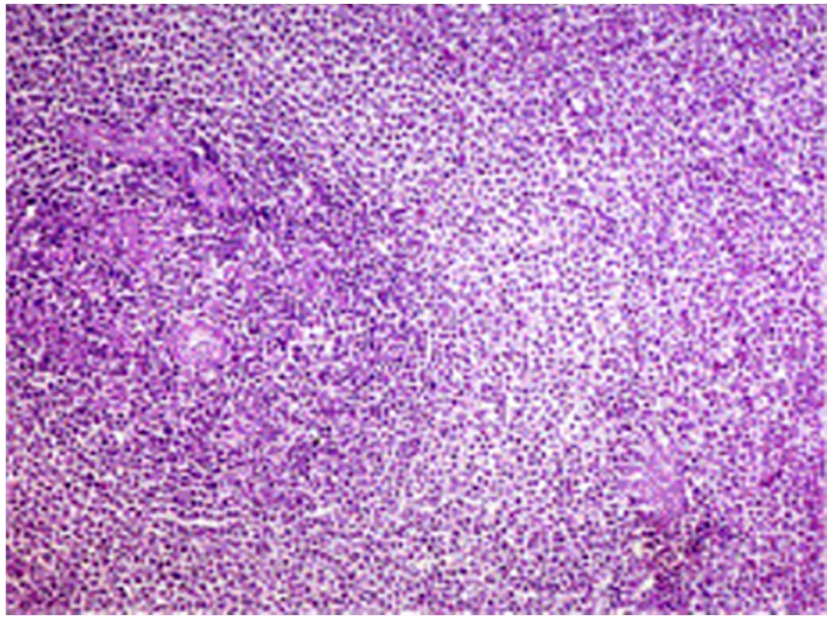


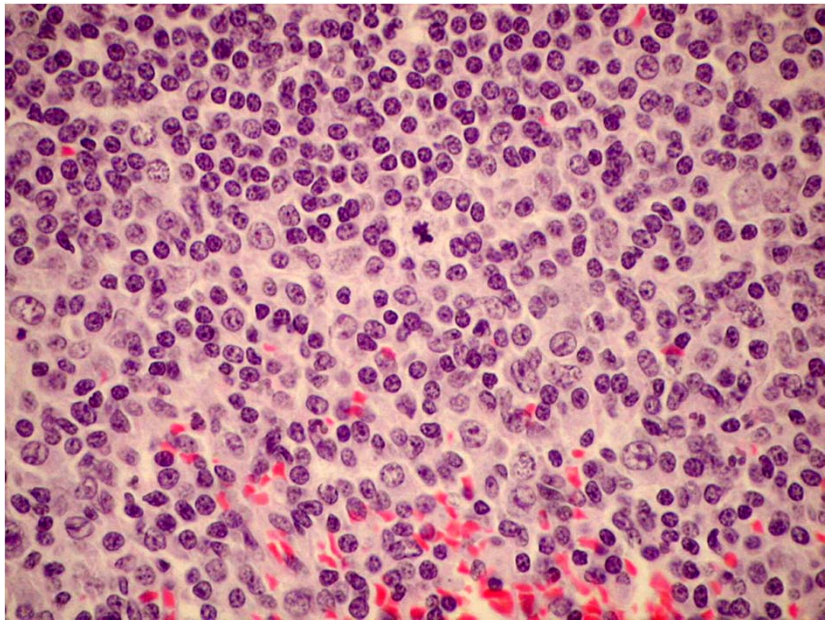
Diagnostic par organe: Rate

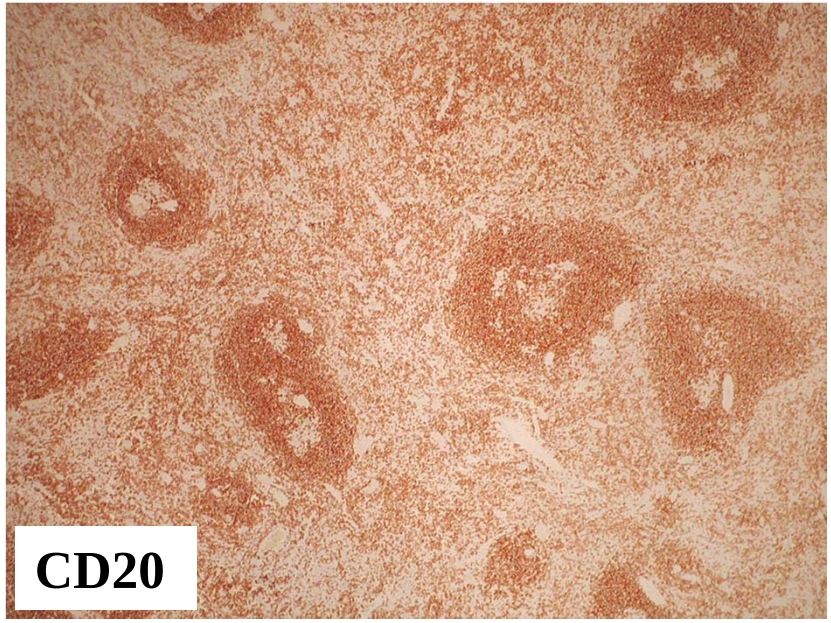
- Splenic marginal zone lymphoma
- LLC, lymphome LyPl
- Manteau
- Lymphome folliculaire
- DLBCL
- Lymphome T hépatosplénique
- Rares: splenic diffuse red pulp small B-cell lymphoma, HCLv, T-LGL,..

Lymphome splénique de la ZM

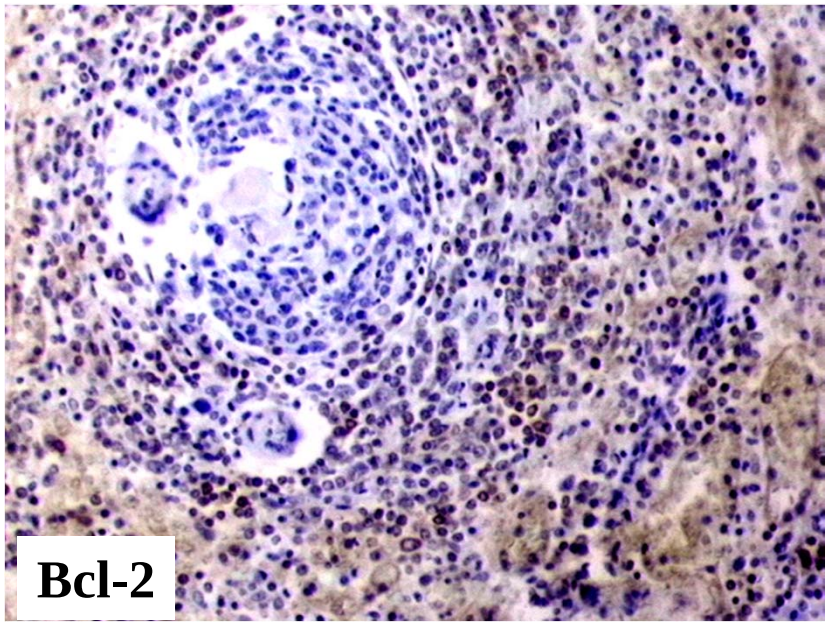


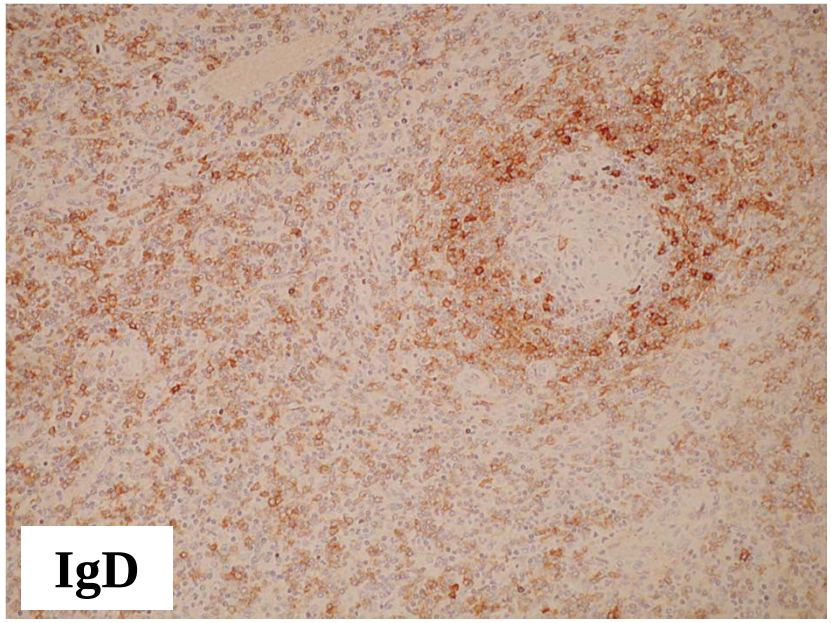


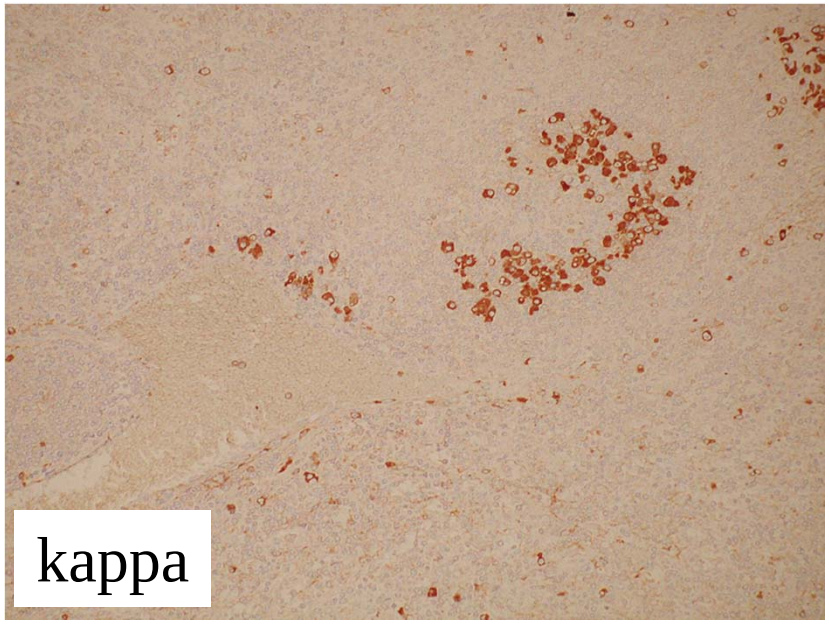


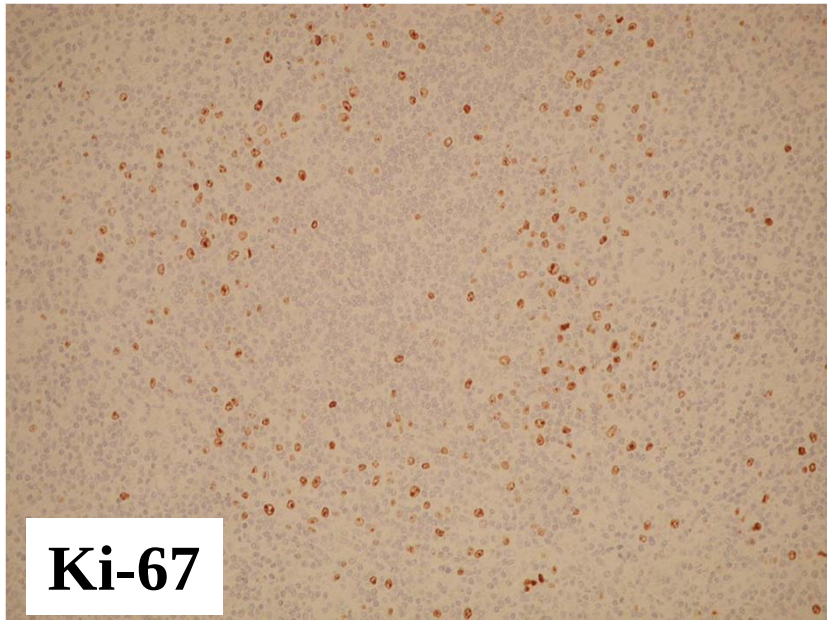


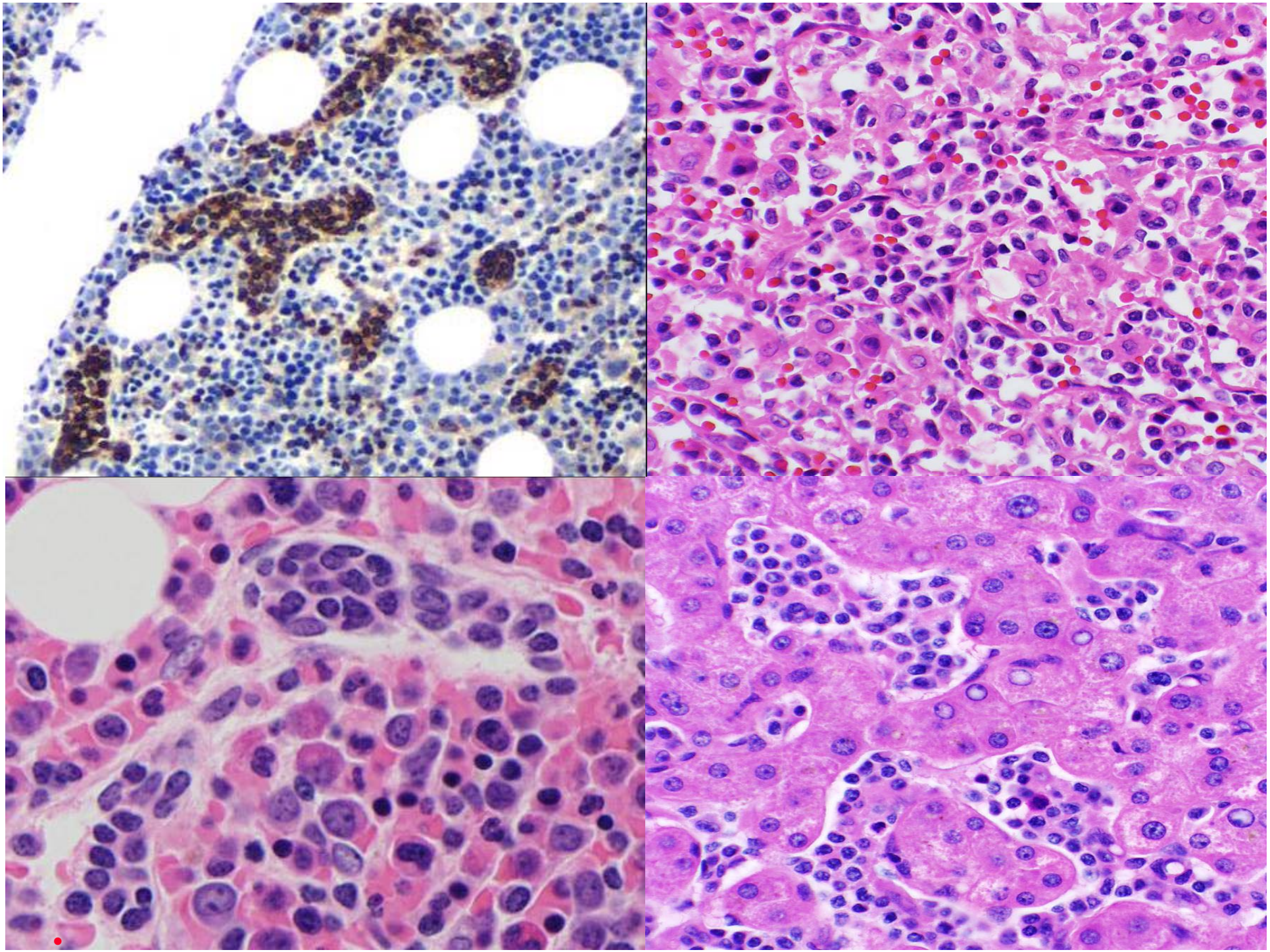
Lymphome splénique de la ZM











Conclusion

- Organe
- Soyez systématique
  - Architecture
  - Type cellulaire prédominant
  - Cellules anormales
- Panel d’anticorps
- Concertation multidisciplinaire

Proposition

- « registre » des anticorps rarement utilisés ou chers et leur localisation
  - Ex: Bob-1, Oct-2, TCL-1, BDCA-2,..