Selected Pitfalls in Lymphoma Diagnosis

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Things that I consider clinically significant pitfalls

- Benign versus malignant
  - Hyperplasias
  - Benign disorders that mimic lymphoid neoplasms
  - Precursor/in situ lymphoid lesions
- Misclassification of a lymphoid neoplasm: Changes in therapy and/or prognosis
- Misclassification of a lymphoid neoplasm: Hematopoietic versus non-hematopoietic neoplasm

pitfalls

Benign vs. Malignant

Benign processes possibly mistaken for neoplastic processes

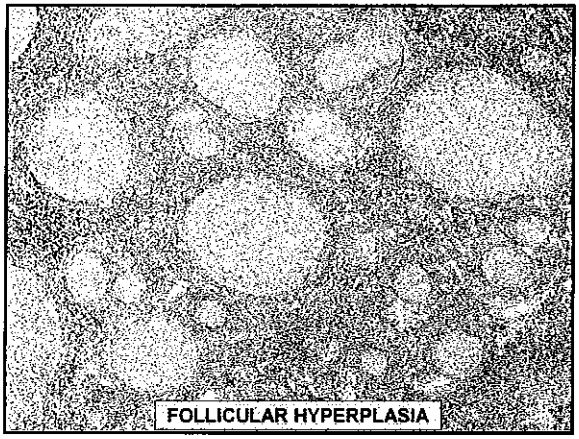
- Benign versus lymphoma
  - Mimics of lymphomas
    - Follicular hyperplasia versus follicular lymphoma
    - Marginal zone hyperplasia versus marginal zone lymphoma
    - Kimura disease
    - Acute EBV/infectious mononucleosis
    - IgG4 lymphadenopathy
    - Kikuchi-Fujimoto disease
    - PTGC versus NLPHL

pitfalls

Hyperplasias

Benign Lymph Nodes
Hyperplasia of normal components

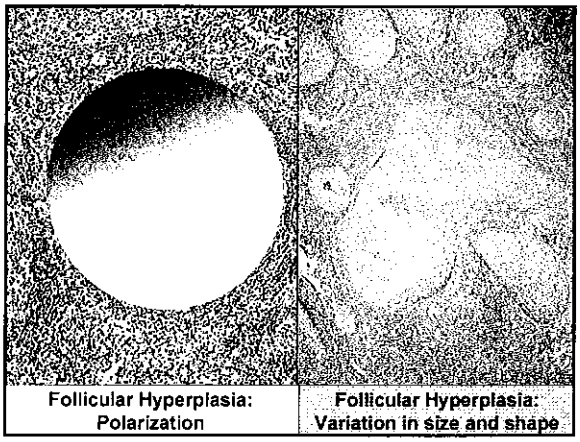
- Follicular
- Mantle zone/primary follicle
- Marginal zone
- T cell (nodular paracortical)
- Interfollicular/Immunoblastic
- Progressive transformation of germinal centers
- Plasmacytoid dendritic cells
- Other cell types



FOLLICULAR HYPERPLASIA

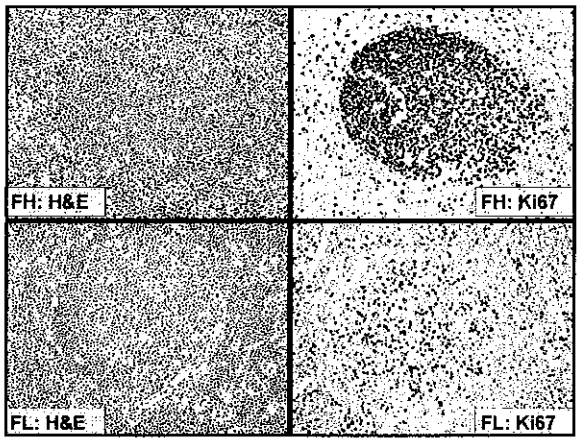
Distinction of FH from FL

Morphology	Follicular Hyperplasia	Follicular Lymphoma
Architecture	Preserved	Effaced
Follicle size and shape	Both vary	Little variation
Follicle density	Normal – increased	Increased
Follicle polarization	Often seen	Not seen
Mitotic rate	High	Low
Mantle zone	Well-formed	Poorly-formed
Cell cytology	Variety of cell types	More uniform, abnormal cells
Tingible-body macrophages	Present	Absent



Follicular Hyperplasia: Polarization

Follicular Hyperplasia: Variation in size and shape



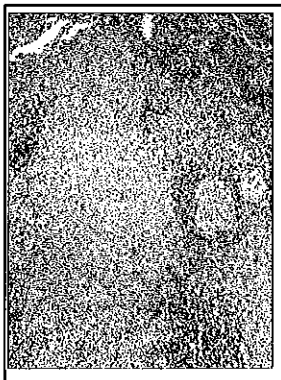
Marginal zone hyperplasia

Normal marginal zone

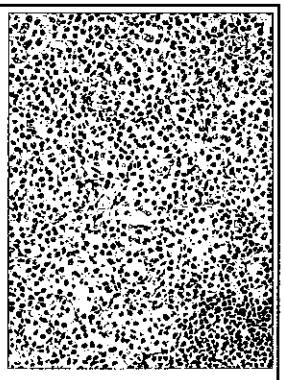
- Present in spleen, perisplenic lymph nodes, mesenteric lymph nodes
- Small lymphocytes with mature chromatin and some clear cytoplasm
- Monocytoid B-cells
- Almost always are accompanied by neutrophils (benign or malignant)

- Toxoplasmosis
- CMV lymphadenitis
- HIV/AIDS lymphadenitis
- Other viral adenopathies

- Differential Diagnosis: Marginal zone lymphoma, other lymphomas with "clear cell" differentiation



Marginal Zone Hyperplasia: Perifollicular location



Marginal Zone Hyperplasia: Clear cell cytology

Marginal zone hyperplasia

Normal marginal zone

- Present in spleen, perisplenic lymph nodes, mesenteric lymph nodes
- Small lymphocytes with mature chromatin and some clear cytoplasm
- Monocytoid B-cells
- Almost always are accompanied by neutrophils (benign or malignant)

MZ Hyperplasia

- Toxoplasmosis
- CMV lymphadenitis
- HIV/AIDS lymphadenitis
- Other viral adenopathies

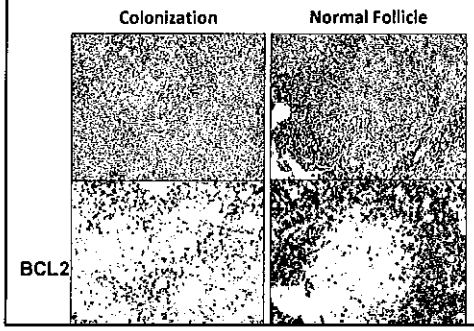
- Differential Diagnosis: Marginal zone lymphoma, other lymphoma with "clear cell" differentiation

	MZH	Early MZL	MZL
Limited extent	+	+	-
Follicular colonization	-	-/+	+
MZ distribution	+	+	+/- (diffuse)
Dendritic cell networks	NL	Abnormal (focal)	Abnormal
Low Ki67 in follicles	-	-/+ (focal)	+
CD43 coexpression	No	-/+	-/+

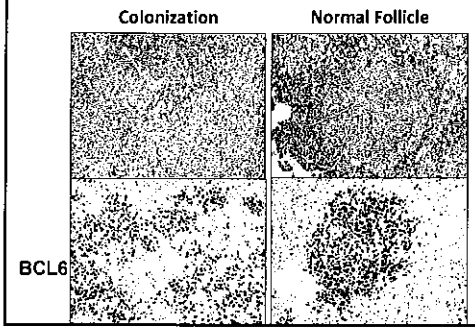
Marginal Zone Lymphoma and *follicular colonization*

- Follicular colonization can make follicles appear abnormal
- Other times, the abnormalities can only be seen by immunohistochemistry
- Marginal zone lymphoma cells have a propensity to invade or *colonize* non-neoplastic follicles
- These then are composed of an admixture of benign and neoplastic elements

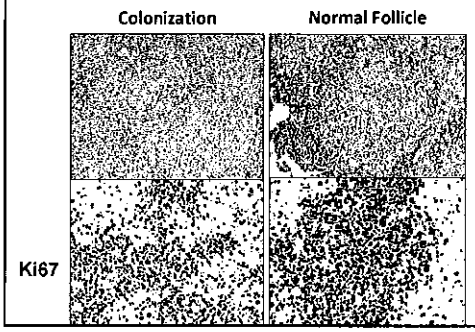
Marginal Zone Lymphoma Follicular Colonization



Marginal Zone Lymphoma Follicular Colonization

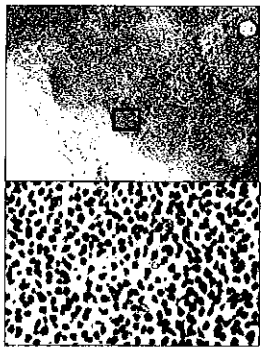


Marginal Zone Lymphoma Follicular Colonization

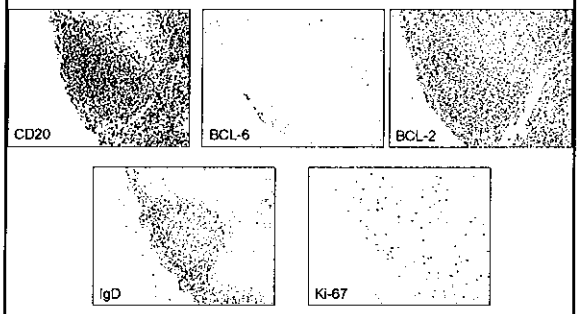


Primary Follicles

- Unreacted follicles
- Germinal center reaction has not occurred
- Composed of mantle zone-type lymphocytes
- Small, mature chromatin, scant cytoplasm
- DDX: May mimic low grade B cell lymphomas



Primary Follicles



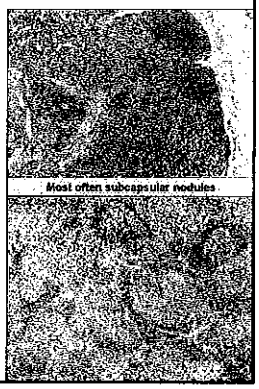
Benign Lymph Nodes

Paracortical Hyperplasia

- Reaction of T-cell zones of lymph node
- Mottled appearance – macrophages and Immunoblasts (activated T-cells)
- Will have S100/CD1a positive Langerhans cells present

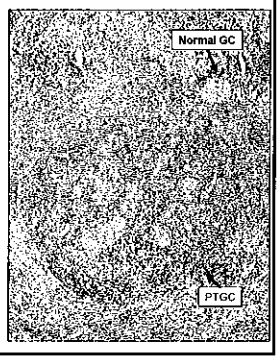
Causes

- Non-specific/unknown
- Dermatopathic changes – draining region of skin problem
- Viral
- Post-vaccinial



Progressive Transformation of Germinal Centers (PTGC)

- Clinical
  - Most often young, male
  - Single asymptomatic enlarged node
- Partial nodal involvement
- Typically background of follicular hyperplasia
- Large nodule composed of numerous mantle cells with irregular central core of germinal center cells
- No Hodgkin cells
- Eosinophilia common
- Differential Diagnosis: NLPHL, interfollicular CHL



PTGC versus NLPHL

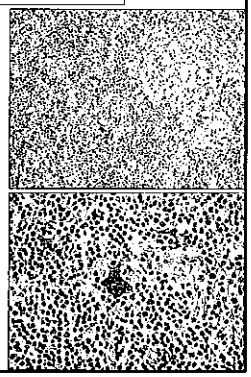
Partial nodal involvement	Complete nodal involvement
Presence of reactive germinal centers	Normal germinal centers not typically present
Some transformed cells (centroblasts)	LP cells
Immunohistochemistry	
T cells scattered	T cell rosettes (CD3, CD57)
Large cells variable	Large cells strong positive for CD20

pitfalls

Benign Disorders that mimic Lymphoproliferative Disorders

Kimura disease

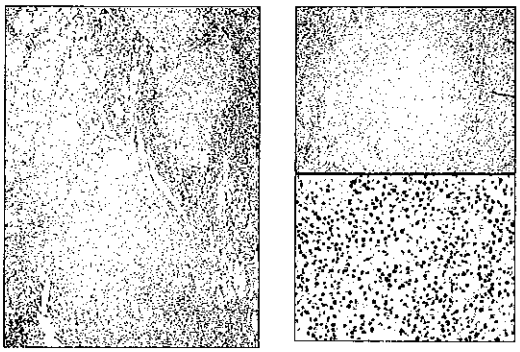
- Clinical: Young to middle aged male.
- Sites: salivary gland, head/neck
- Histology: Follicular hyperplasia, eosinophils, polykaryotic cells.
- Associated with nephrotic syndrome
- Possible etiologies: virus, ?
- Therapy: resection, steroids, radiation, immunosuppressive therapies
- Prognosis: Good, but recurrence possible



Kimura Disease Histology

- ✓Follicular hyperplasia
- ✓Eosinophilia
  - Eosinophilic microabscesses
  - Eosinophils within germinal centers
- ✓Polykaryotic cells
- Vascular proliferation
  - Increased HEV or activated vascular elements
- Fibrosis

Kimura Disease



Kimura Disease Differential diagnosis

- Angiolymphoid hyperplasia with eosinophilia:
  - Not! This is an *epithelioid hemangioma with prominent eosinophilia*
  - Also female, superficial site
  - No elevated IgE
  - Older literature confused ALHE with Kimura disease
- Eosinophilia with lymphadenopathy
  - Medications or parasites
- Langerhans cell histiocytosis
- T cell lymphoma
- Hodgkin lymphoma
- Hypereosinophilic syndrome

Acute EBV Infection Infectious mononucleosis

<u>Clinical</u>

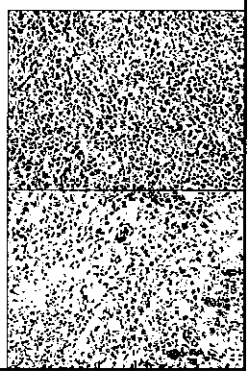
- Patients typically children or young adults young or immunosuppressed
- Flu-like illness, splenomegaly, lymphocytosis, lymphadenopathy

<u>Morphology</u>

- Distortion of normal architecture
- Follicular hyperplasia
- Paracortical T cell hyperplasia
- +/- Focal necrosis
- Vasculitis
- Capsular inflammation or infiltration
- Large, atypical cells present (may be Hodgkin-like)

<u>Differential Diagnosis:</u>

- Large cell lymphoma, Hodgkin lymphoma



IgG4-related lymphadenopathy

Associations: IgG4-related diseases

- Pachymeningitis
- Hypophysitis
- Lacrimal gland lesion (Mikulicz's disease)
- Sclerosing sialadenitis
- Thyroid gland
- Mastitis
- Pulmonary disorders
- Autoimmune pancreatitis
- Hepatitis
- Sclerosing cholangitis
- Retroperitoneal fibrosis
- Prostatitis
- Inflammatory aortic aneurysm
- Tubulointerstitial nephritis
- Lymphadenopathy (80% of cases)
- Skin lesions

After: Sato et al. Pathology International. 2010.

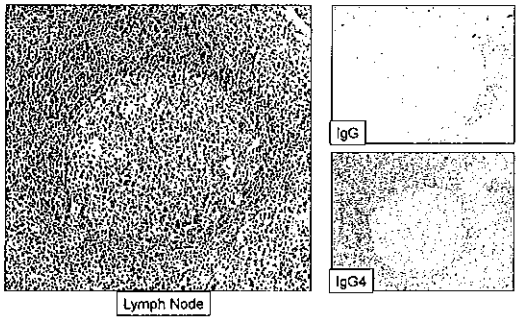
Histology: Lymph Node

- Diverse findings
  - Reactive follicular hyperplasia
  - Multicentric/PC Castleman-like
  - Interfollicular plasmacytosis and immunoblasts
  - PTGC-like
  - Inflammatory pseudotumor-like
    - fibrosis

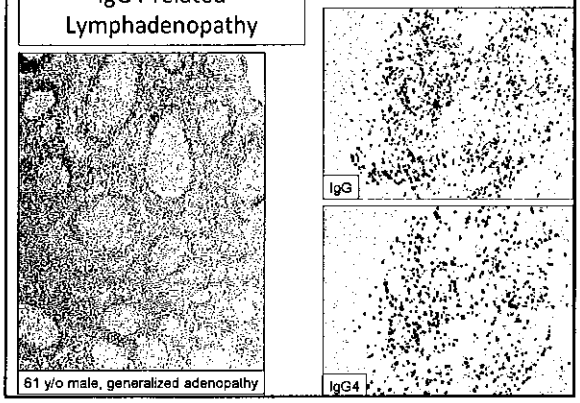
Sato et al. 2010. Cheuk & Chan. 2010.

Useful Note: IgG4 stains can only be interpreted easily with a concurrent IgG stain

Normal IgG4 staining



IgG4-related Lymphadenopathy



IgG4-related lymphadenopathy Differential Diagnosis

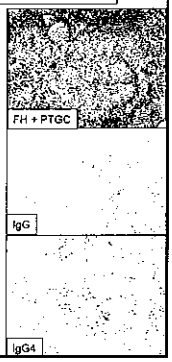
- Autoimmune lymphadenitis
  - SLE, rheumatoid arthritis
- Multicentric Castleman disease
- PTGC
- "True" inflammatory pseudotumor and other related entities
- Marginal zone lymphoma
- Lymphoplasmacytic lymphoma

When do I perform IgG4 staining*

- Follicular or immunoblastic hyperplasias in older adults (50+)
- PTGC in older adults (50+)
- Fibrotic lesions with lymphoplasmacytic infiltrates (inflammatory pseudotumor)
- Anything that looks like Plasma Cell Castleman disease

IgG4-related lymphadenopathy SUMMARY

- Clinical: Older male
- Histology: Lymph nodes showing a broad range of reactive changes
- Possible etiologies: Unknown, possible autoimmune
- Therapy: Steroid and/or rituximab therapy very effective
- Prognosis: Good, but disease may persist despite therapy

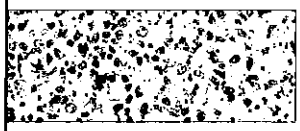


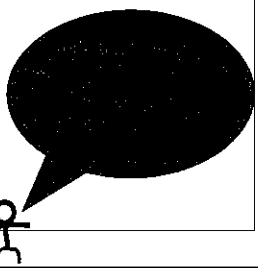
Kikuchi-Fujimoto disease

- Clinical
  - Young women
  - More frequent in Asian
  - Some systemic symptoms
  - Benign clinical course
- Preserved architecture
- Necrosis without neutrophils
- Macrophages with crescent shaped nuclei
- Plasmacytoid dendritic cells
- Activated/transformed lymphocytes, immunoblastic appearance
- Differential Diagnosis
  - Large cell lymphoma

Kikuchi-Fujimoto Disease Lymphoma Mimicry

- Large B cell lymphoma
  - Including EBV-associated (with necrosis)
- T cell lymphoma





- "Classic description"

Kikuchi-Fujimoto Disease Histology

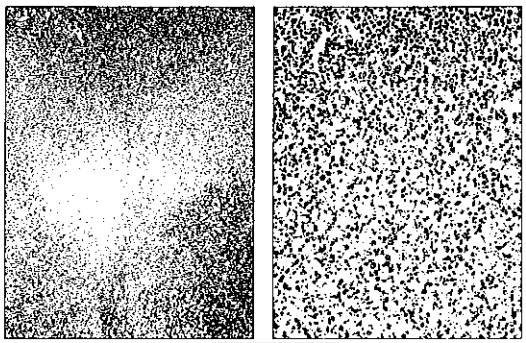
- Three phases

1) Early phase: proliferative
2) Intermediate phase: necrotizing
3) Late phase: Xanthogranulomatous

- Preserved architecture
- Necrosis without neutrophils
- Macrophages with crescent shaped nuclei
- Plasmacytoid dendritic cells
- Activated/transformed lymphocytes, immunoblastic appearance

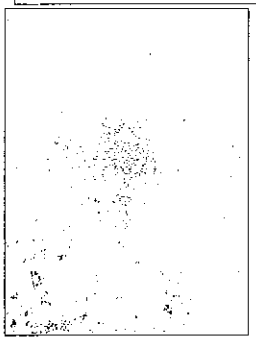
Cytologic appearance – YIKES!

Kikuchi-Fujimoto disease

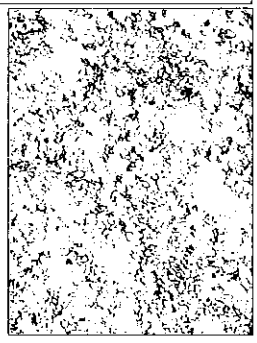


Necrotizing stage

Kikuchi-Fujimoto disease



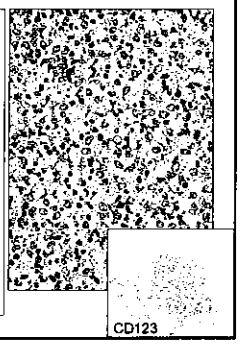
CD123 low magnification



CD123

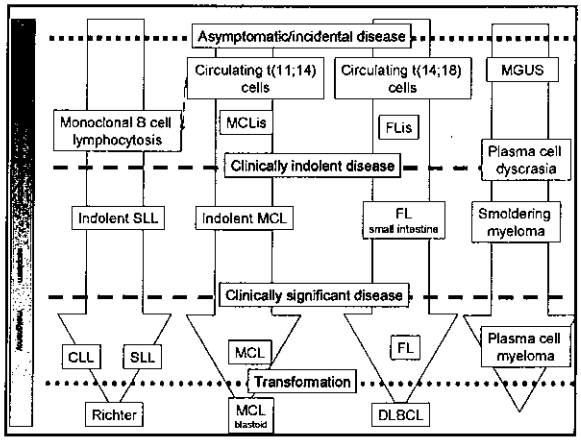
Kikuchi-Fujimoto Disease SUMMARY

- Clinical: Young female, isolated cervical nodes
- Histology: necrosis without neutrophils, proliferations of plasmacytoid dendritic cells (CD123 staining)
- Possible etiologies: virus, lupus
- Therapy: Supportive
- Prognosis: Excellent



pitfalls

Precursor/In situ Lesions



Follicular lymphoma *in situ*

- Clumsy terminology: focal FL, or partial nodal involvement by FL
- Almost always limited stage disease
- Sometimes an incidental finding
- Most cases do NOT progress
- Diagnosed by performance of bcl2 staining on suspicious nodes/follicles

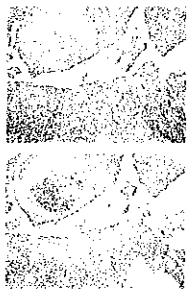
FL in situ

- Up to 70% of "normal" older individuals may have IgH/bcl2 translocations in cells in blood
- Increased incidence with
  - Exposure to pesticides
  - Hepatitis C patients
  - Increased age
- These are not naïve B cells

FL in situ

- 66% - no evidence of follicular lymphoma (28 months average f/u)
- 33% - developed B cell lymphoma

Follicular lymphoma in situ



	FL	FLIS	FH
Bcl2	+	**Focally +**	-
Ki67	Low	**Focally low**	High
CD20	Diffuse positive	Diffuse positive	Diffuse positive
Bcl6/CD10	Diffuse positive	Diffuse positive	Diffuse positive
CD21	Dendritic cell networks	Dendritic cell networks*	Dendritic cell networks*

*May be disrupted

FL in situ	Partial involvement by FL
Normal architecture (low magnification)	At least focally altered architecture
Normal follicles size	Increased size in follicles
Sharp border of follicles	Irregular borders of follicles
Intact mantle zones	Abnormal or attenuated mantles
Scattered	Abnormal follicles are clustered together
Strong bcl2 expression Strong CD10 expression	Weak bcl2 expression Weak CD10 expression
Almost pure centrocytes	Mixed cytologic composition

FL in situ	Partial involvement by FL
Ki67 low	Ki67 low
By definition "low grade"	Can be higher grade
IgH/BCL2 present	IgH/BCL2 present

- FL in situ can recur!
- Reporting should include number of follicles and percent of node involvement
  - (# + %)

Monoclonal B cell Lymphocytosis

- Monoclonal B cell lymphocytosis
  - CLL-type (e.g. CD5+, CD23+, dim 20, dim sK/L)
  - Atypical CLL-type (CD5+, CD23-)
  - Non-CLL type (CD5-, CD10-)
- >40 years old 6.7%
- The abnormal cells persist
- Phenotype remains stable
- FISH
  - Del 13 q 47%, +12 11.8%, ATM deletion 0%
- Almost all CLL are preceded by an MBL phase (90%)

Mantle cell lymphoma in situ

- Minimal involvement of lymphoid tissue by cells with characteristic of mantle cell lymphoma
- Present in mantle zone
- Identified by staining/screening with cyclin D1 stain
- May have non-progressive disease
  BUT... need to stage/clinically evaluate these patients carefully!

Mantle Cell Lymphoma

- SOX-11 (somewhat controversial – not confirmed in larger studies)
  - – Conventional MCL +
  - – Indolent MCL –
- In normal people those that have IgH/bcl2 in blood have IgH/BCL1 as well!
  - – Frequency is about 1/10 of those with t14;18

Mantle cell lymphoma
Clinically indolent!

- Typically leukemic or spleen only disease
- Relatively low peripheral blood counts
- Low grade/small cell morphology (no blastoid or pleomorphic)
- Often CD5 negative
- No evidence of high proliferation
- Often hypermutated Ig (post-GC MCL)
- Simple karyotype
- May lack SOX-11 expression

pitfalls

Misclassification of a Lymphoid Neoplasm

Changes in therapy and/or prognosis

Neoplastic processes with differences in therapy and/or prognosis

- Mantle cell lymphoma versus other small B cell lymphomas
- Follicular lymphoma (FL) grade 2 versus FL grade 3
- DLBCL versus Burkitt lymphoma
- DLBCL prognosis/subtypes
- Hodgkin lymphoma versus DLBCL variants
- Classical Hodgkin lymphoma versus Nodular lymphocyte predominant Hodgkin lymphoma

Mantle Cell Lymphoma

Morphology	Small cells, uniform, irregular nuclei, scant cytoplasm Admixed pink histiocytes	CLL: dimorphic FL: dimorphic, cleaved MZL: polymorphic
IHC	CD5+ Cyclin D1 +	CLL: CD5 and CD23 FL: CD10, BCL6; NO CD5 MZL: No CD5
Genetic	t(11;14)	CLL: various changes FL: t(14;18) MZL: various changes

Mantle Cell Lymphoma

- Specificity of t(11;14) translocation
  - – Can be seen in some other tumors
  - – Myeloma
- Specificity of cyclin D1 staining
  - – Can be seen in other tumors
  - – Myeloma, hairy cell leukemia, epithelial tumors
  - – USE SOX11 to confirm!
- Variation in clinical behavior
- Range of morphologic appearance

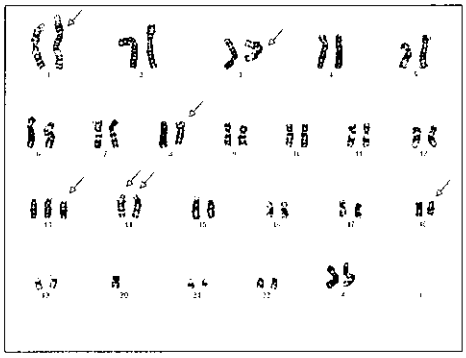
Grading of Follicular Lymphoma

Cytology	Mixture of small cleaved cells (majority) and larger transformed cells (5-15/HPF)	Mixture of large cells (>15/HPF) and small cleaved cells	Uniform population of large cells in nodular/follicular pattern
Proliferation rate (Ki-67)	10-30%	30-50%	>50%
Genetics	t(14;18)	t(14;18)	IGH/BCL6
Therapy	Low grade	Low grade	"High-grade"

	TCRBCL	CHL
Background mostly T cells	Y	Y
Histiocytes prominent	Var	Var
Individual large cells	Y	Y
IHC		
CD15	N	Y
CD45	Y	N
CD30	Rare (10-30%)	Y
EBV	N	Y (~70%)
Oct2/BOB.1	Y/Y	N/N

	Burkitt	DLBCL
t(8;14)*	Yes (always)	Some (10%)
C-myc IHC	Yes	Var
Ki67>95%	Yes	Occasional
Homogeneous cytology	Yes	Occasional
CD10/bcl6	Yes	Some
BCL-2 by IHC	No	Many

* Or equivalent translocation



t(14;18), with some other abnormalities

Morphology	Large cells, irregular	Medium sized, uniform (usual) Intermediate-large, irregular nuclei (rare)
IHC: CD20, CD10, BCL6	+	+/-
BCL2	+	-/+
Ki67	50-100%	100%
CMYC IHC	20-100%	100%
MYC FISH	5-10%	100%
IGH/BCL2 FISH	30-40%	0%
EBV	5-10%	30-40%
Cytogenetics "simple" (MYC translocation without other abnormalities)	Unusual	Usual

Then, there's the other thing...

- Is there a "adult" version of Burkitt lymphoma?
  - Unequivocally yes
  - Formerly called Burkitt-like
  - Differences are biologic and possibly phenotypic
  - May be "double hit" lymphomas (both t(14;18) and t(8;14)
  - Some may be *de novo*
  - Have bcl-2 positivity, which is not "allowed" in Burkitt
  - Name "High grade B cell lymphoma, not otherwise specified" has been suggested

DLBCL morphologic subtypes

- IV DLBCL
- T/HRBCL
- Mediastinal type
- CD5+ type
  - Rule out MCL

T/HRBCL vs CHL

- Very large difference in therapy and prognosis
- Most commonly mixed cellularity Hodgkin lymphoma is the subtype
- Significant differences in IHC, and often clinical findings (esp. location) can be helpful

CHL versus TCRBCL

IHC		
CD15	+ (most)	-
CD30	+ (all_	Rare
CD45	-	+
PAX5	+ (dim)	+ (strong)
OCT2/BOB1	-/- (common) +/- or -/+ occasional	+/+
MUM1	+	+/-
EBV/EBER	-/+	-
CD20	-/+	+

Hodgkin Lymphoma

- CHL versus NLPHL
- CHL versus TCRBCL
- CHL versus benign processes
- ✓NLPHL versus PTGC

CHL versus NLPHL

- Important to recognize
- There is an entity –
  - Lymphocyte-rich classical Hodgkin lymphoma
- This entity is indistinguishable from NLPHL by morphology alone
- This variant can be easily resolved by IHC
- It is perhaps, less clinically significant, as each are very clinically indolent

LR-CHL versus NLPHL		
	LR-CHL	NLPHL
Lg blue nodules	Y	Y
Large single atypical cells	Y	Y
R-S and variants	Y	Y
Nodules of small B cells	Y	Y
CD45	N	Y
CD20	Weak, variable (30%)	Y
CD15	Y	N
CD30	Y	N (10-20%)
EBV	Some	N

pitfalls

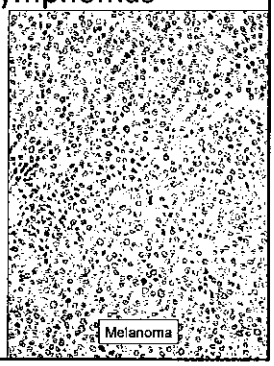
Hematopoietic versus Non-Hematopoietic Neoplasm

Mimics and more mimics

Neoplasms that Mimic Mimics of *High Grade* Lymphomas

- Myeloid sarcoma
- Carcinoma
- Melanoma
- Germ-cell tumors
- Small blue cell tumors
- Thymoma*
- Myeloma/plasmacytoma

* Thymoma is one of the only mimics that simulate a both low and grade lymphoma



Lymphoid neoplasm mistaken for non-lymphoid disorders

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- High-grade lymphoma versus small blue cell tumor
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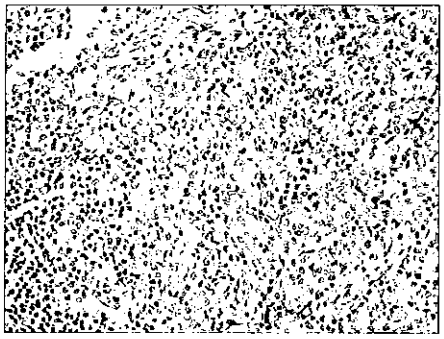
Myeloid Sarcoma



Minor clue: Eosinophils and eosinophil precursors

Metastases

- Not rare, but important as a mimic of:
  - Primary nodal disorders
  - Benign processes
  - Lymphomas
- Types... the usual suspects
  - Breast, lung, GI, neuroendocrine carcinomas
  - Some "small blue cell" sarcomas
  - Rare sarcomas and other neoplasms

Metastases

- Clear evidence
- Mimicry of benign lymphoid processes
- Mimicry of neoplastic lymphoid processes

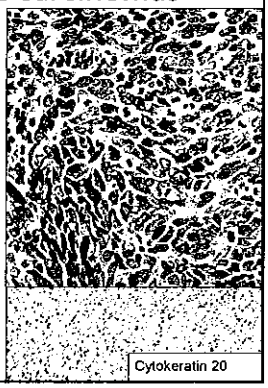
Carcinoma

- Undifferentiated Nasopharyngeal carcinoma (UNPC)
- May lose cytokeratin expression
- May be positive for CD30 (10%)

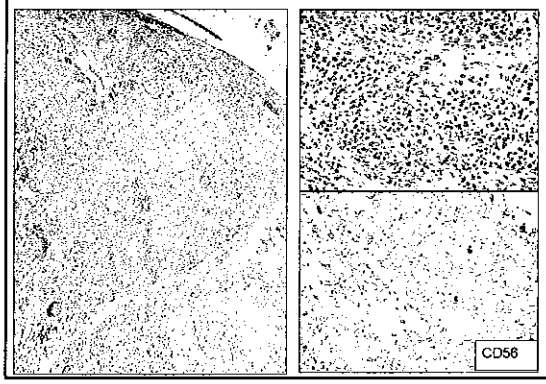
- Express p63
- Likely EBV induced

Neuroendocrine carcinomas

- Appear similar to high grade or blastic lymphomas
- Often have more coarse chromatin (salt and pepper)
- May have clustering
- Small amounts of cytoplasm
- IHC:
  - Primary:
    - Positive for keratins (some dot like positivity)
    - Negative for lymphoid markers
  - Secondary
    - Positive for synaptophysin, chromogranin
  - Immunohistochemistry PITFALLS
    - Positive for CD56
    - May be positive for PAX5 and TdT



Metastatic Neuroendocrine Carcinoma



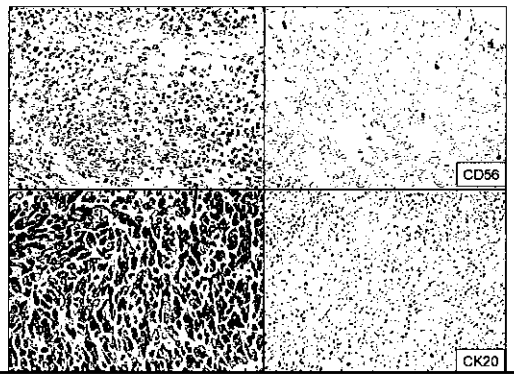
Scenario

- Imagine a case....
  - With immunohistochemical expression of:

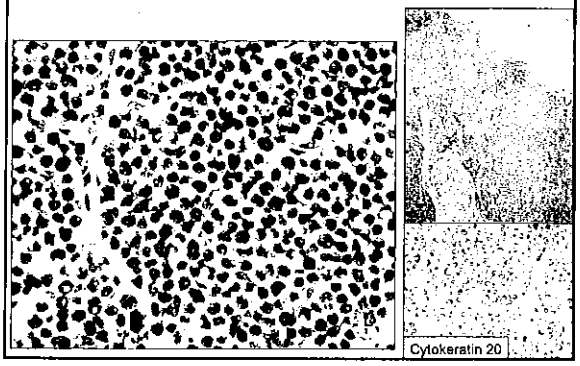
  - CD56
  - TDT
  - BCL2
  - CD8

Would this be a lymphoma?

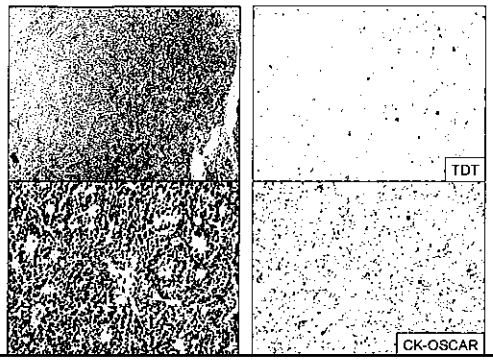
Metastatic CA



Metastatic Small Cell Carcinoma



Metastatic NE Carcinoma



Melanoma

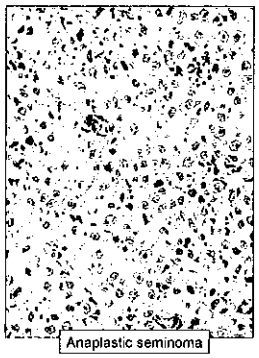
- Metastatic melanoma is more often amelanotic
- Cytologic appearance may be fairly uniform large cells and appear monotonous like a large cell lymphoma
- Clinical history and application of IHC stains will distinguish

Germ Cell tumors

- Likely to mimic large cell lymphoma

Immunohistochemistry

- Positive
  - Most are keratin positive
- Pitfalls:
  - CD30 positivity may suggest ALCL diagnosis



High Grade lymphoma versus SBCT

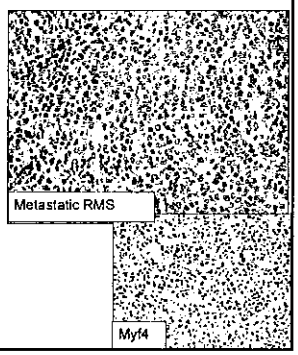
HG lymphoid	SBCT
• Lymphoblastic	• Neuroblastoma
• High grade DLBCL	• Rhabdomyosarcoma
• Burkitt	• Small cell carcinoma
• Some T cell lymphomas	• Wilms tumor

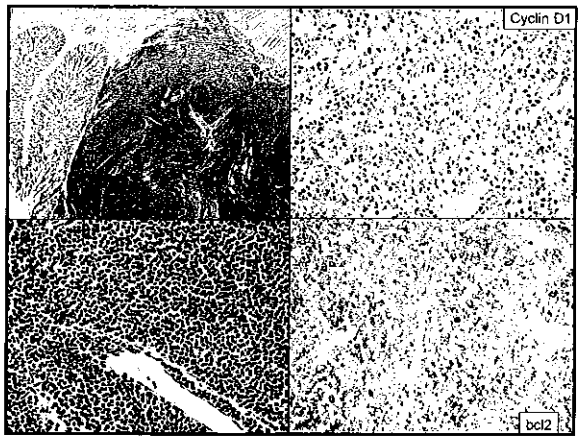
Small blue cell tumors

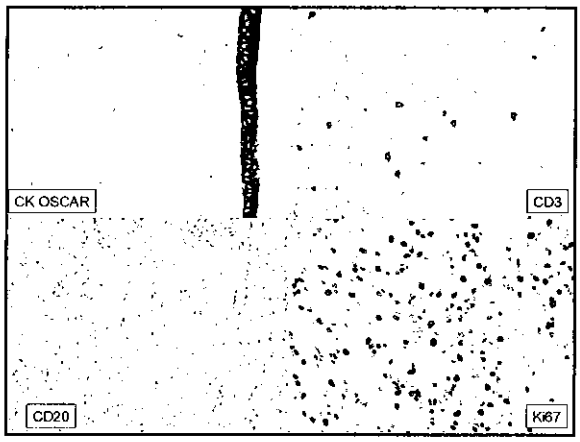
- Wilms tumor, neuroblastoma, rhabdomyosarcoma
- Mimic large cell lymphoma or ALL

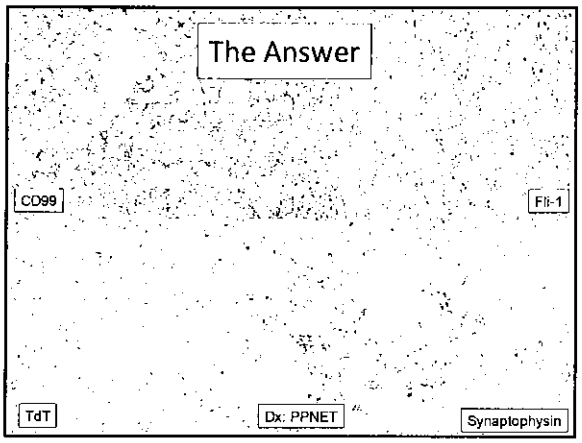
Immunohistochemistry

- Usual panel of antibodies to include or exclude lymphoma





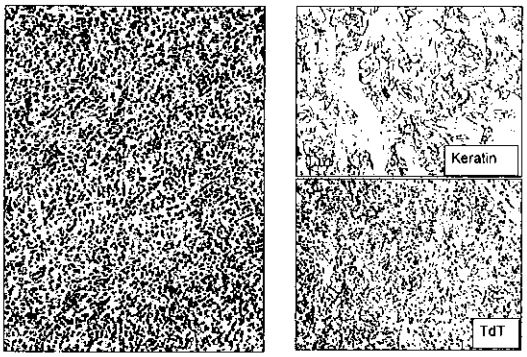




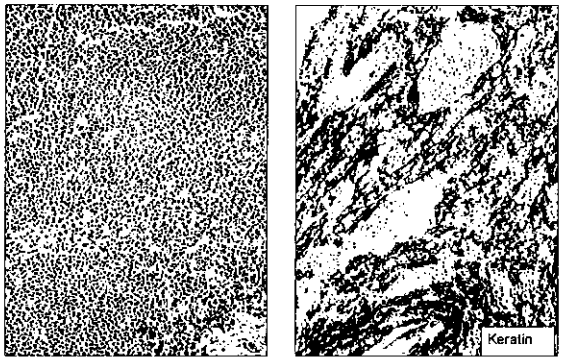
Thymoma

- Mediastinal location
  - Rarely neck or pleural
- Older (40 years or more)
- Fairly uniform population of lymphocytes
- Population of slightly larger cells (thymocytes) with open chromatin and poorly defined cytoplasmic borders
- IHC:
  - Keratin: defines thymic epithelial cells
  - Secondary:
  - TdT: defines immature thymic T cells

Thymoma

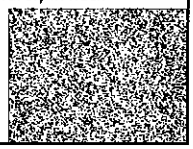


Thymoma



Thymoma vs. T-ALL

- Pitfalls:
  - In some cases, epithelial cells will be CD5 positive
  - CD117 may be positive in some cases of both
  - In both lymphocytes will be TdT and CD3 positive
  - Comparable immunophenotype in metastases
    - Thymoma may be seen in pleura or rarely in neck masses



Thymoma vs. T-ALL

- BOTH
  - Have immature thymic cells present
    - CD3 positive, TdT positive, immature "blastic" appearance
- Thymoma
  - Shows reticular framework of keratin positive epithelial cells, not present in T-ALL
  - Some cases of epithelial cells will be CD5 positive
  - CD117 may be positive in some cases of both

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Types of Lymphomas that Mimic non-hematolymphoid neoplasms

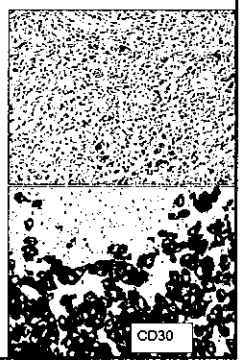
- Anaplastic large cell lymphoma
- Anaplastic plasmacytoma
- Nodular sclerosis classical Hodgkin lymphoma, syncytial variant
- Diffuse large B cell lymphoma

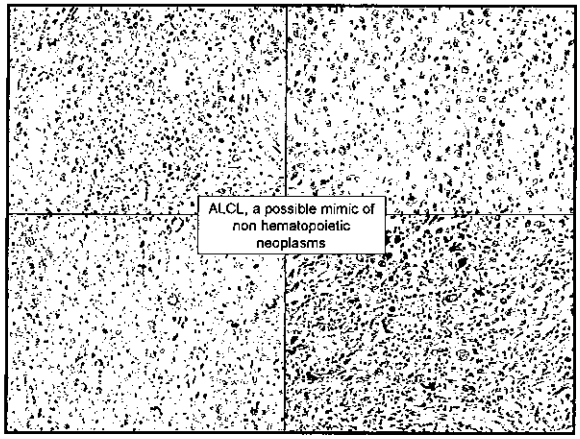
Hematologic Neoplasms that Mimic Non-Hematopoietic Tumors

- Anaplastic Large Cell Lymphoma (ALCL)
- Syncytial Variant of Classical Hodgkin Lymphoma
- Diffuse large B cell lymphoma
  - Intravascular variant
  - Signet ring form
  - Anaplastic
- Anaplastic Plasmacytoma
- Myeloid sarcoma

Anaplastic Large Cell Lymphoma

- Can mimic non-hematopoietic neoplasms
- Often sinusoidal in distribution
- Appears to be cohesive
- Highly pleomorphic
- Immunohistochemistry
  - CD30 expression





ALCL versus Non-HP

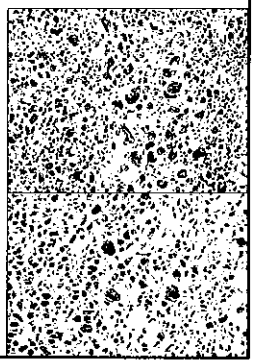
- Morphology:
  - Large, anaplastic cells, often in sinuses and forming clusters

IHC mimicry
- EMA+
- Rarely keratin+ (weak and focal)
- CD30+

Diffuse Large B cell lymphoma with anaplastic features

- Typical immunophenotype
- However, highly pleomorphic histology suggesting non-hematopoietic neoplasms

Immunohistochemistry
- CD20 expression



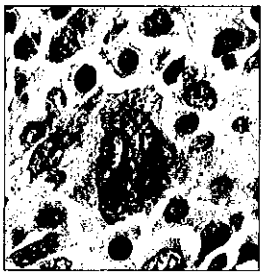
Anaplastic Plasmacytoma/Myeloma

- Plasmacytoma/myeloma can have highly anaplastic morphology, especially after therapy
- There are usually some more typical appearing plasma cells

Immunohistochemistry
- CD45 negative
- CD20 negative
- CD3 negative
- Will express kappa or lambda
- CD138 (which can be positive in adenocarcinomas)

Techniques to distinguish lymphomas from mimics

- Careful evaluation of clinical history
  - Never make an "impossible" diagnosis
- Evaluation of other laboratory findings
- Maximize histology
- Immunohistochemical staining
- Immunophenotype (flow cytometry)
- Molecular/genetic testing



Thanks for your attention!

A small request....

If you run across interesting or unusual lymph nodes or spleens I would love to see them

Also, I am in always in need of gross photos of lymph nodes and spleens

Thanks!!!!!

domalley@clarientinc.com