Updates in Lymph Node Cytology

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Outline

Part 1

- WHO structured reporting system for lymph node cytology

Part 2

- Patient Evaluation Tips

Part 3

- Pattern-based diagnostic approach with case presentations

Part 1. WHO Lymph Node Cytology Structured Reporting System

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Fine Needle Aspiration

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A Proposal for the Performance, Classification, and Reporting of Lymph Node Fine-Needle Aspiration Cytopathology: The Sydney System

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International Agency for Research on Cancer

World Health Organization

WHO Reporting System for Lymph Node, Spleen, and Thymus Cytopathology

WHO Lymph Node Cytology reporting system

- Goal: Improve patient care and outcomes through use of cytopathology

- Key diagnostic Cyto features for specific diagnostic entities
- International expert consensus for first time

WHO Lymph node Reporting System

5 Categories

- Non-diagnostic
- Benign
- Atypical
- Suspicious for malignancy
- Malignant

-Categories are used to assist communication with clinicians
-Each category with:
Risk of Malignancy (ROM)
Recommendation for steps to refine DDX or achieve specific WHO diagnosis (goal)

5.0: Histiocytic/Dendritic cell neoplasms
5.1.1: Introduction
3.1: Plasmacytoid dendritic cell neoplasms
3.1.1: Plasmacytoid dendritic cell neoplasms
3.1.2: Blastic plasmacytoid dendritic cell proliferation associated with myeloid neoplasm
3.1.3: Blastic plasmacytoid dendritic cell neoplasm
3.2: Langerhans cell and other dendritic cell neoplasms
3.2.1: Langerhans cell neoplasms
3.2.1.1: Langerhans cell histiocytosis
3.2.1.2: Langerhans cell sarcoma
3.4.1: Other dendritic cell neoplasms
3.4.1.2: Interdigitating dendritic cell sarcoma
3.3: Histiocytosis/macrophage neoplasms
3.3.1: Histiocytic neoplasms
3.3.1.2: Juvenile xanthogranuloma
3.3.1.3: Erdheim-Chester disease
3.3.1.4: Rosai-Dorfman Disease
3.3.1.5: ALK-positive histiocytosis
3.3.1.6: Histiocytic sarcoma
4.0: B-cell lymphoid proliferations and lymphomas
4.0.0.1: Introduction to B-cell lymphoproliferative disorders and neoplasms
4.1: Tumour like lesions with B-cell predominance
4.1.0.0: Introduction
4.1.0.3: Reactive B-cell rich lymphoid proliferations that can mimic lymphoma
4.1.0.4: Lymphadenitis
4.1.0.5: Castleman Castleman disease
4.1.0.6: Idiopathic multicentric Castleman disease
4.1.0.8: HIV/HHV8-associated multicentric Castleman disease
4.2: Precursor B-cell neoplasms
4.2.1: B-lymphoblastic leukaemia/lymphomas
4.2.1.1: Introduction
4.2.1.5: B-lymphoblastic leukaemia/lymphoma
4.2.1.7: B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy
4.2.1.8: B-lymphoblastic leukaemia/lymphoma with hypodiploidy
4.2.1.14: B-lymphoblastic leukaemia/lymphoma with iAMP21
4.2.1.7: B-lymphoblastic leukaemia/lymphoma with BCR::ABL1 fusion
4.2.1.8: B-lymphoblastic leukaemia/lymphoma with BCR::ABL1-like features
4.2.1.9: B-lymphoblastic leukaemia/lymphoma with KMT2A rearrangement
4.2.1.4: B-lymphoblastic leukaemia/lymphoma with ETV6::RUNX1 fusion
4.2.1.15: B-lymphoblastic leukaemia/lymphoma with ETV6::RUNX1-like features
4.2.1.16: B-lymphoblastic leukaemia/lymphoma with TCF3::PBX1 fusion
4.2.1.17: B-lymphoblastic leukaemia/lymphoma with IGH::IL3 fusion
4.2.1.18: B-lymphoblastic leukaemia/lymphoma with TCF3::HLF fusion
4.2.1.6: B-lymphoblastic leukaemia/lymphoma with other defined genetic alterations
4.2.1.13: B-lymphoblastic leukaemia/lymphoma, NOS
4.3: Mature B-cell neoplasms
4.3.0: Pre-neoplastic and neoplastic small lymphocytic proliferations
4.3.11.1: Introduction
4.3.1.2: Monoclonal B-cell lymphocytosis
4.3.1.3: Chronic lymphocytic leukaemia/small lymphocytic lymphoma
4.3.2: Splenic B-cell lymphomas and leukaemias
4.3.2.1: Introduction
4.3.2.2: Hairy cell leukaemia
4.3.2.5: Splenic marginal zone lymphoma
4.3.2.4: Splenic diffuse red pulp small B-cell lymphoma
4.3.2.3: Splenic B-cell lymphoma/leukaemia with prominent nucleoli
4.3.3: Lymphoplasmacytic lymphoma
4.3.3.1: Lymphoplasmacytic lymphoma
4.3.4: Marginal zone lymphoma
4.3.4.1: Introduction
4.3.4.3: Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue
4.3.4.4: Nodal marginal zone lymphoma
4.3.4.5: Follicular lymphoma
4.3.4.6: Paediatric-type follicular lymphoma
4.3.4.8: Duodenal-type follicular lymphoma
4.3.5: Follicular lymphoma
4.3.5.1: Introduction
4.3.5.2: Primary cutaneous follicle centre lymphoma
4.3.7: Mantle cell lymphoma
4.3.7.1: Introduction
4.3.7.2: In situ mantle cell neoplasm
4.3.7.3: Mantle cell lymphoma
4.3.7.4: Leukaemic non-nodal mantle cell lymphoma
4.3.8: Transformations of indolent B-cell lymphomas
4.3.8.1: Introduction
4.3.8.2: Transformations of indolent B-cell lymphomas
4.3.9: Large B-cell lymphomas
4.3.9.1: Introduction
4.3.9.2: Diffuse large B-cell lymphoma, NOS
4.3.9.3: T-cell/histiocyte rich large B-cell lymphoma
4.3.9.4: Diffuse large B-cell lymphoma / high grade B-cell lymphoma with MYC and BCL2 rearrangements
4.3.9.5: ALK-positive large B-cell lymphoma
4.3.9.6: Large B-cell lymphoma with IRF4 rearrangement
4.3.9.7: High grade B-cell lymphoma with 11q aberrations
4.3.9.8: EBV positive diffuse large B-cell lymphoma
4.3.9.9: EBV-positive diffuse large B-cell lymphoma
4.3.9.10: Diffuse large B-cell lymphoma associated with chronic inflammation
4.3.9.11: Fibrin-associated large B-cell lymphoma
4.3.9.12: Fluid overload-associated large B-cell lymphoma
4.3.9.13: Lymphomatoid granulomatosis
4.3.9.14: Primary large B-cell lymphoma of immune-privileged sites
4.3.9.15: Primary cutaneous diffuse large B-cell lymphoma, leg type
4.3.9.16: Intravascular large B-cell lymphoma
4.3.9.17: Primary mediastinal large B-cell lymphoma
4.3.9.18: Primary effusion lymphoma
4.3.11.2: High grade B-cell lymphoma, NOS
4.3.10: Burkitt lymphoma
4.3.10.2: Burkitt lymphoma
4.3.12: HIV/HHV8-associated B-cell lymphoid proliferations and lymphomas
4.3.12.1: Introduction
4.3.12.2: Primary effusion lymphoma
4.3.12.3: HIV/HHV8-positive diffuse large B-cell lymphoma
4.3.12.4: HIV/HHV8-positive germinotropic lymphoproliferative disorder
4.3.13: Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation
4.3.13.1: Introduction
4.3.13.2: Hyperplasias arising in immune deficiency/dysregulation
4.3.13.3: Lymphoid proliferative disorders arising in immune deficiency / dysregulation
4.3.13.5: EBV-positive mucocutaneous ulcer
4.3.13.6: Lymphomas arising in immune deficiency / dysregulation
4.3.13.2: Inborn error of immunity-associated lymphoid proliferations and lymphomas
4.4: Hodgkin lymphoma
4.4.0.1: Introduction
4.4.0.2: Classic Hodgkin lymphoma
4.4.0.3: Nodular lymphocyte predominant Hodgkin lymphoma
4.5: Plasma cell neoplasms and other diseases with paraproteins
4.5.0.1: Introduction
4.5.1: Monoclonal gammopathies
4.5.1.2: Cold agglutinin disease
4.5.1.1: IgM monoclonal gammopathy of undetermined significance
4.5.1.2: Non-IgM monoclonal gammopathy of undetermined significance
4.5.1.3: Monoclonal gammopathy of renal significance
4.5.2: Diseases with monoclonal immunoglobulin deposition
4.5.2.1: AL amyloidosis
4.5.2.2: Monoclonal immunoglobulin deposition disease
4.5.3: Heavy chain diseases
4.5.3.1: Introduction
4.5.3.2: Mu heavy chain disease
4.5.3.3: Gamma heavy chain disease
4.5.3.4: Alpha heavy chain disease
4.5.4: Plasma cell neoplasms
4.5.4.1: Introduction
4.5.4.2: Plasmacytoma
4.5.4.3: Plasma cell myeloma / multiple myeloma
4.5.4.4: Plasma cell neoplasms with associated paraneoplastic syndrome
5.0: T-cell and NK-cell lymphoid proliferations and lymphomas
5.0.0.1: Introduction
5.1: Tumour-like lesions with T-cell predominance
5.1.0.1: Kikuchi-Fujimoto disease
5.1.0.2: Autoimmune lymphoproliferative syndrome
5.1.0.3: Indolent T-lymphoblastic proliferation
5.2: Precursor T-cell neoplasms
5.2.1: T-lymphoblastic leukaemia / lymphoma
5.2.1.1: T-lymphoblastic leukaemia / lymphoma, NOS
5.2.1.2: Early T-precursor lymphoblastic leukaemia / lymphoma
5.3: Mature T-cell and NK-cell neoplasms
5.3.1: Mature T-cell and NK-cell leukaemias
5.3.1.1: Introduction
5.3.1.2: T-prolymphocytic leukaemia
5.3.1.3: T-large granular lymphocytic leukaemia
5.3.0.2: NK-large granular lymphocytic leukaemia
5.3.1.7: Chronic NK-cell lymphocytosis
5.3.1.8: Sézary syndrome
5.3.0.4: Aggressive NK-cell leukaemia
5.3.2: Primary cutaneous T-cell lymphoid proliferations and lymphomas
5.3.2.1: Introduction to primary cutaneous T-cell neoplasms
5.3.2.2: Primary cutaneous CD30-positive T-cell lymphoproliferative disorder
5.3.2.8: Primary cutaneous acral CD8-positive T-cell lymphoproliferative disorder
5.3.2.3: Mycosis fungoides
5.3.2.4: Primary cutaneous CD30-positive T-cell lymphoproliferative disorder: Lymphomatoid papulosis
5.3.2.5: Primary cutaneous CD30-positive T-cell lymphoproliferative disorder: Primary cutaneous anaplastic large cell lymphoma
5.3.2.6: Subcutaneous panniculitis-like T-cell lymphoma
5.3.2.7: Primary cutaneous gammadelta T-cell lymphoma
5.3.2.8: Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma
5.3.2.10: Primary cutaneous peripheral T-cell lymphoma, NOS
5.3.3: Nodal mature T-cell and NK-cell lymphoid proliferations and lymphomas
5.3.3.1: Introduction
5.3.3.2: Indolent T-cell lymphoma of the gastrointestinal tract
5.3.0.3: Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract
5.3.3.3: Enteropathy-associated T-cell lymphoma
5.3.3.4: Monomorphic epitheliotropic intestinal T-cell lymphoma
5.3.3.5: Hepatosplenic T-cell lymphoma, NOS
5.3.4: Hepatosplenic T-cell lymphoma
5.3.4.1: Hepatosplenic T-cell lymphoma
5.3.5: Anaplastic large cell lymphoma
5.3.5.1: Introduction
5.3.5.2: ALK-positive anaplastic large cell lymphoma
5.3.5.3: ALK-negative anaplastic large cell lymphoma
5.3.5.4: Breast implant-associated anaplastic large cell lymphoma
5.3.6: Nodal T-follicular helper (TFH) cell lymphoma
5.3.6.1: Introduction
5.3.6.2: Nodal TFH cell lymphoma, angioimmunoblastic-type
5.3.6.3: Nodal TFH cell lymphoma, follicular type
5.3.6.4: Nodal TFH cell lymphoma, NOS
5.3.7: Other peripheral T-cell lymphomas
5.3.7.2: Peripheral T-cell lymphoma, NOS
5.3.8: EBV-positive NK-cell and T-cell lymphomas
5.3.8.2: EBV-positive nodal T- and NK-cell lymphoma
5.3.8.3: Extranodal NK/T-cell lymphoma, nasal type
5.3.8: EBV-positive T-cell and NK-cell lymphoid proliferations and lymphomas of childhood
5.3.8.1: Introduction
5.3.8.2: Severe mosquito bite allergy
5.3.8.3: Hydroa vacciniforme lymphoproliferative disorder
5.3.8.4: Systemic chronic active EBV disease
5.3.8.5: Systemic EBV-positive T-cell lymphoma of childhood
7.0: Stroma-derived neoplasms of lymphoid tissues
7.1.1.1: Introduction
7.1: Mesenchymal dendritic cell neoplasms
7.1.1: Follicular dendritic cell neoplasms
7.1.1.2: Follicular dendritic cell sarcoma
7.1.1.3: Interdigitating dendritic cell/follicular dendritic cell sarcoma
7.1.1.4: Fibroblastic reticular cell tumour
7.3: Myofibroblastic tumours
7.3.1: Myofibroblastic tumour
7.3.0.1: Intranodal palisaded myofibroblastoma
7.2: Spleen specific vascular-stromal tumours
7.2.1: Splenic vascular-stromal tumours
7.2.1.1: Littoral cell angioma
7.2.0.1: Splenic hemangioma
7.2.0.2: Sclerosing angiomatoid nodular transformation (SANT) of spleen
8.0: Genetic tumour syndromes
8.0.0.1: Introduction
8.0.0.2: Fanconi anaemia
8.0.0.3: Bloom syndrome
8.0.0.4: Ataxia-telangiectasia syndrome
8.0.0.5: Ambiguities

International Agency for Research on Cancer

World Health Organization

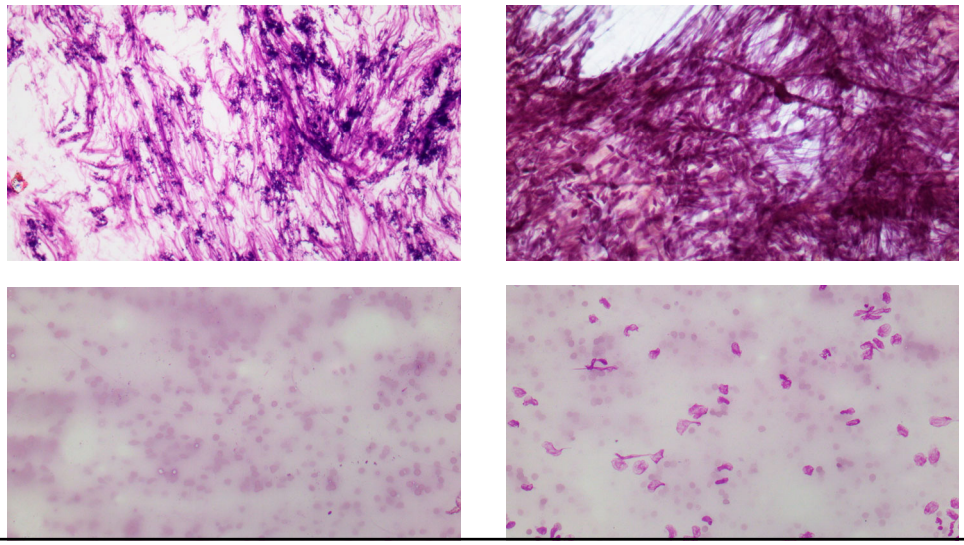
Haematolymphoid Tumours, 5th edition

Non-diagnostic Category

- Reliable interpretation not possible
- Qualitative and/or Quantitative Limitations
  - Insufficient cellularity, poor smearing technique, air-dry/fixation artifact, obscuring material
- Repeat FNAB recommended
  - with ROSE if possible
  - with core needle biopsy if available

- If ND at time of ROSE, needle rinse may enable diagnosis by flow cytometry, cell block with staining, cytogenetics, FISH etc

Non-diagnostic Category



No consensus on LN FNAB adequacy criteria

- Generally, no or very few lymphoid cells present
- Some suggested minimum 40 lymphocytes per HPF (400x) in the most cellular areas

Karunamurthy A et al. Evaluation of EBUS-FNA: correlation with adequacy and histologic follow-up. Cancer Cytopathol. 2014. PMID: 24127207.

Non-diagnostic Category

- Use one term consistently for clear communication
  - Alternatives: Insufficient, Inadequate
- Triple Test: always correlate with imaging and clinical findings
- WHO system accepts ND diagnosis in cases with good lymphoid material, but clinical findings are not explained
  - May use “Benign” category, with “sample may not be representative.”

Diagnostic categories and ROM

ROM	ND	Benign	Atypical	Suspicious	Malignant
Gupta P, Cancer Cytopathol 2021	27.5%	11.5%	66.7%	88.0%	99.6%
Vigliar E, Diagnostics 2021	50%	1.92%	58.3%	100%	100%
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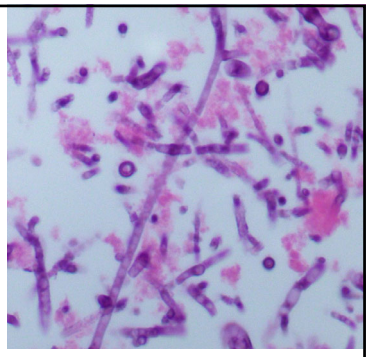
Uzun E, Diagn Cytopathol 2022	16.6%	0.7%	88.8%	100%	100%
Ahuja S, Cytopathol 2022	9.1%	1.5%	37.5%	96.9%	98.2%

Range 9.1% - 58.3%

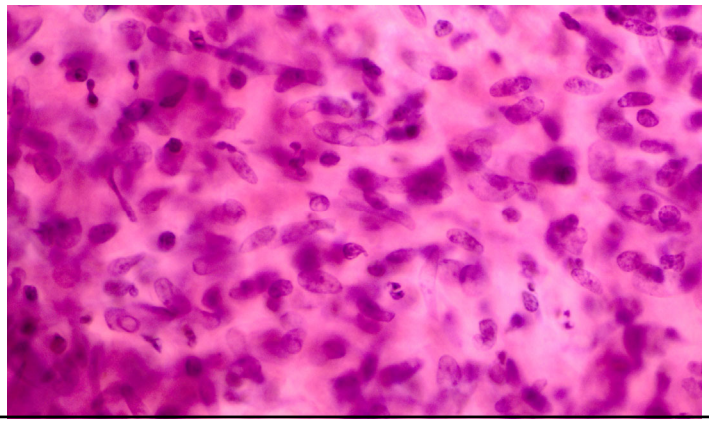
Benign Category



- Unequivocally benign; high NPV category
- More precise diagnosis not required
- Possible findings: normal lymphoid populations, necrosis, granulomas, specific infections (viral, myocobacterial, fungal)
- Support Benign diagnosis with ancillary techniques:
  - PCR, cultures
  - cell block +/- stains (e.g. GMS)
  - Flow Cytometry with reactive population

Ancillary testing: subtype Benign process, enhance FNAB diagnostic utility

"Necrotizing granulomas" at ROSE → Send for microbiology testing



Benign Category

- Potentially difficult DDX:
  - Follicular hyperplasia vs follicular lymphoma
  - EBV mononucleosis vs Hodgkin lymphoma
  - Partial involvement of lymph node by low grade lymphoma
- Cytopathologist categorization of inflammatory processes as Benign vs Atypical depends on skill and practice milieu

- **If some findings raise possibility of lymphoma, call "Atypical"

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Range 0.7% - 11.5%

Atypical Category

- Mostly supports benign process…
- Minimal features raise possibility of malignancy
- Insufficient quantity or quality of concerning features for Sus or Malignant

- ALUS: "Atypical lymphoid cells of undetermined significance" (concern for lymphoma)
- AUS: "Atypia of undetermined significance" (concern for non-lymphoid neoplasm)

- Report specific atypical features seen, and raise DDX
- Use judiciously to preserve clinical value of category

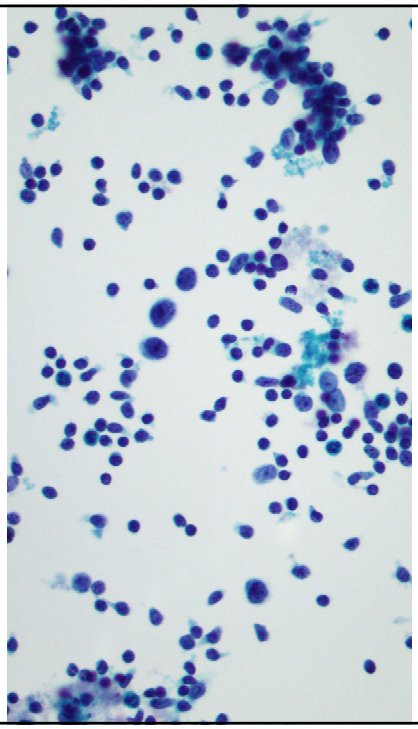
Atypical Category- Next Steps

- Repeat FNAB with material for ancillary testing by flow cytometry, or CNB for IHC evaluation
- If FC or CNB not possible, excise or closely watch 2-4 weeks
- Use clinical judgment!

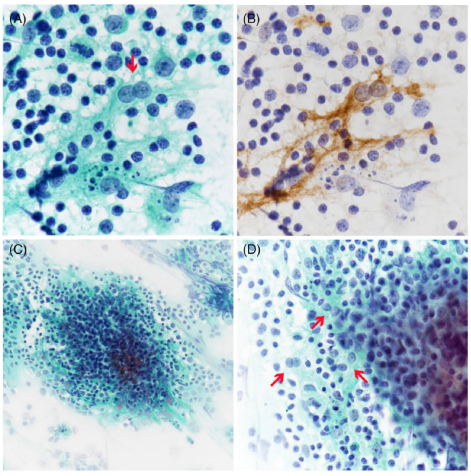
- e.g. DDX mononucleosis vs Hodgkin lymphoma– may observe, adenopathy may resolve
- e.g. DDX low grade B lymphoma vs reactive– re-sample, send material for FC or CNB/excision

Atypical Category

- Smears show enlarged lymphocytes in a polymorphous background
- If adenopathy is chronic and no FC available, may diagnose Atypical and suggest repeat FNA with FC analysis



Follicular tissue fragments more often associated with follicular processes



FTFs (>100 microns) found in

Reactive follicular hyperplasia	82.4%
Follicular lymphoma	100%
DLBCL	16.7%

› Diagn Cytopathol. 2021 Jul;49(7):842-849. doi: 10.1002/dc.24753. Epub 2021 Apr 20.

Follicular tissue fragments in fine-needle aspiration cytology of lymph nodes: A useful clue in differential diagnosis of follicular lymphoma and reactive follicular hyperplasia

Yosuke Sasaki [1], Koji Kishimoto [2], Mayumi Homma [1], Eisuke Shiozawa [1], Masafumi Takimoto [1], Toshiko Yamochi-Onizuka [1]

Affiliations + expand

PMID: 33876862 DOI: 10.1002/dc.24753

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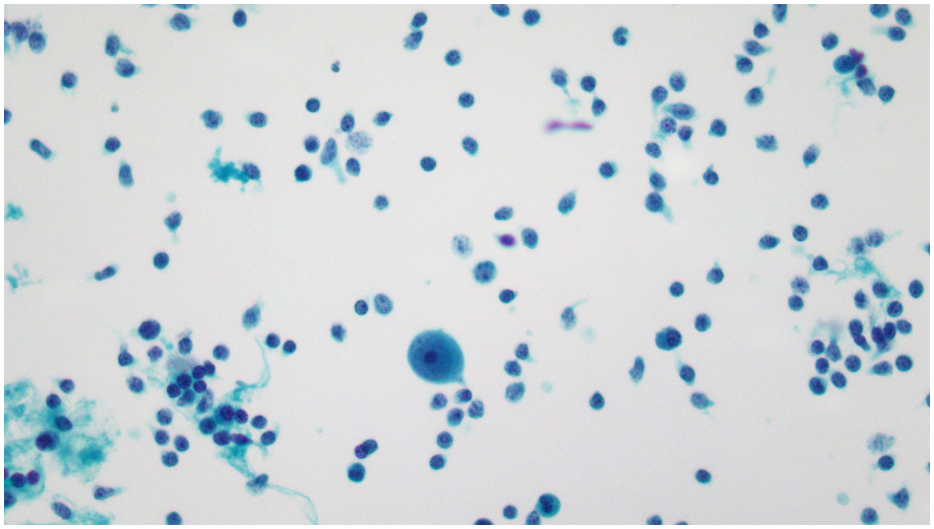
Range 28.6% - 88.8%

Suspicious for Malignancy Category

- Morphologic features concerning for malignancy
- Limited quantity/quality of findings precludes Malignant dx
- High PPV for Malignancy
- Includes lymphoid and non-lymphoid neoplasms

Suspicious for Malignancy



Discerning ATYPICAL vs SUSPICIOUS

- This is an active area of research
- The following factors have not been found to be significant:
  - Smear cellularity
  - Cell block cellularity
  - Presence of large lymphoid cells
  - Homogeneity of specimen
  - Proportion of slides with atypical findings

Trabzonlu and Ly. Investigation of various factors for discriminating between cytologic diagnosis of "atypical" vs "suspicious" in fine needle aspiration biopsy of head and neck lymph nodes. IAP 2024 (oral).

Suspicious for Malignancy Category

- Report describes the suspicious features, and provides DDX
- Utilize ancillary testing (FC, cell block with ICC) to try to move diagnosis to Malignant category
- Additional management required.
  - Repeat FNAB or CNB +ancill.
  - Excise if ancillary testing limited/not available.

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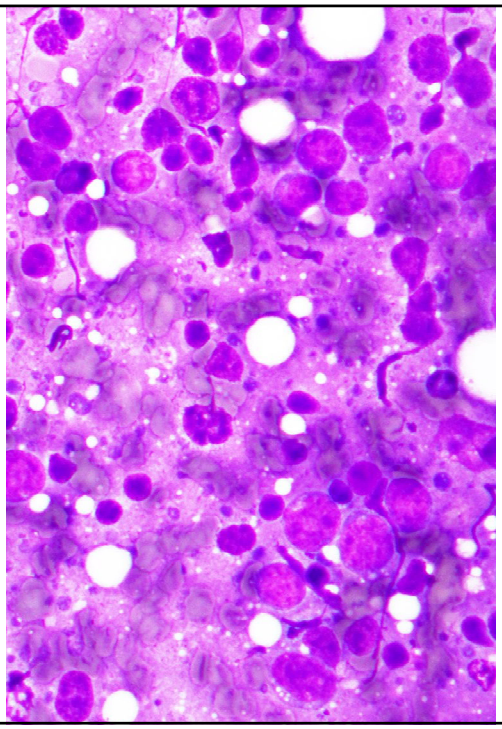
Range 88% - 100%

Malignant Category

- Unequivocal features of malignancy (any type)
- Malignant diagnosis is possible without ancillary testing
- Should have low False Positive rate



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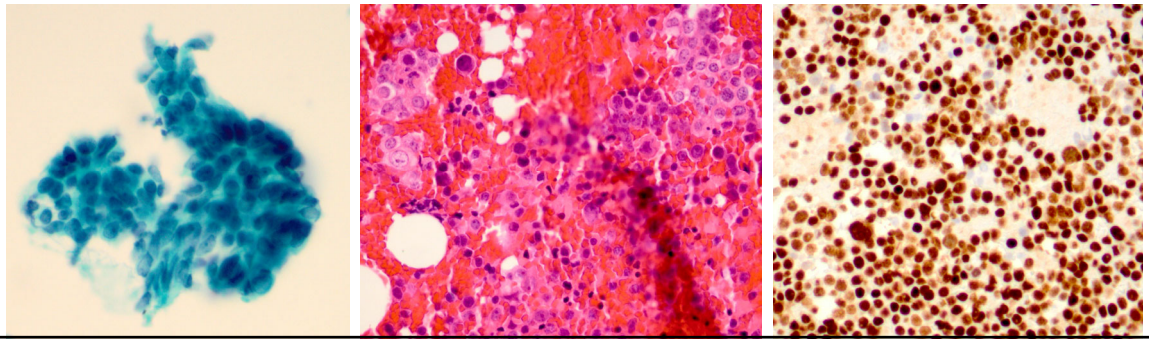
Range 98.2% - 100%

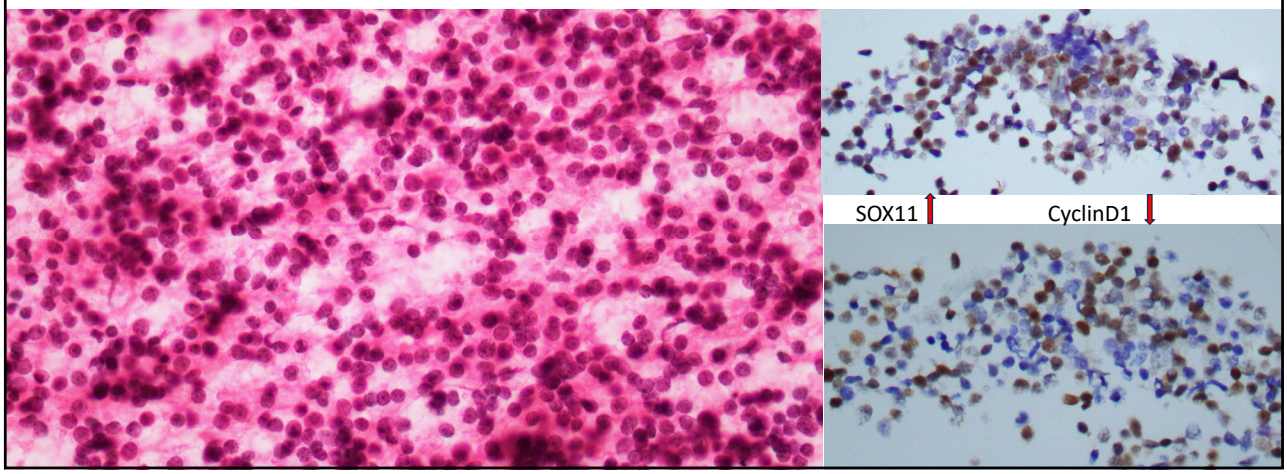
Ancillary testing: subtype Malignancy, enhance FNAB diagnostic utility

"Carcinoma" at ROSE →
Squamous cell carcinoma with p40+ on cell block



Ancillary testing: subtype Malignancy, enhance FNAB diagnostic utility

"Lymphocytes" at ROSE → Mantle cell lymphoma +FC, cell block +stains



FNA Diagnostic Utility is enhanced by:

- High quality samples (cellular, representative)
- High quality FNAB smear preparations (learn and teach good technique!)
- ROSE
  - decreases ND rate
  - supports appropriate triage for ancillaries
  - provides preliminary diagnoses
- Routine use of FC and Stains to confirm diagnoses

FNAB can triage management for the patient even if specific diagnosis cannot be made

Lymph Node FNAB Sampling and Specimen Preparation

- Split sample, create multiple direct smears
- Air-dried and alcohol-fixed smears are complementary:
  - Air-dried smears for background material and cytoplasmic quality
  - Alcohol-fixed for nuclear detail
- ROSE is possible with both fixation methods
  - Reserve air-dried smears for micro stains (GMS, Gram etc)
- Additional dedicated passes for cultures, flow cytometry, cell block, molecular (based on ROSE)

Part 2. Patient Evaluation

Patient Evaluation: Clinical History

Duration of lymphadenopathy
Fluctuations in size
History of any malignancies
Recent travel
Exposure to infectious agents

Patient Evaluation: Clinical History

Review of systems

- Recent viral illness, cold flu, sinusitis …*think back*
- Dental procedures/problems
- B symptoms: Fever, night sweats, chills, weight loss, headache
- Skin changes: rash, itching
- Cough, pain
- Smoking history

Patient Evaluation: Physical Exam

Size

Characteristics:

- Soft, firm, mobile, fixed, matted, adjacent lymph nodes
- Location
- Amenable to biopsy?
  - By palpation
  - Under image guidance (US, CT)

Establish clinical index of suspicion

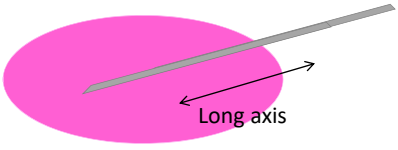
Mentally Rank DDXs:

- Clinically benign/reactive
- Possibly infectious
- Possibly metastatic
- Lymphoma
- Other

Patient Evaluation: Physical Exam

Patient Evaluation: Physical Exam

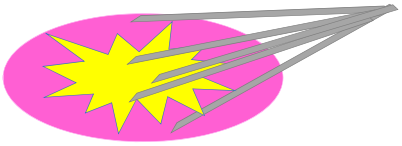
Lymph node FNAB



1st pass
Reactive lymph node
Acute or chronic lymphadenitis
Infectious process

2nd pass and additional passes
Reactive lymph node
Acute or chronic lymphadenitis
Infectious process
and
Lymphoma, non-Hodgkin

Lymph node FNAB



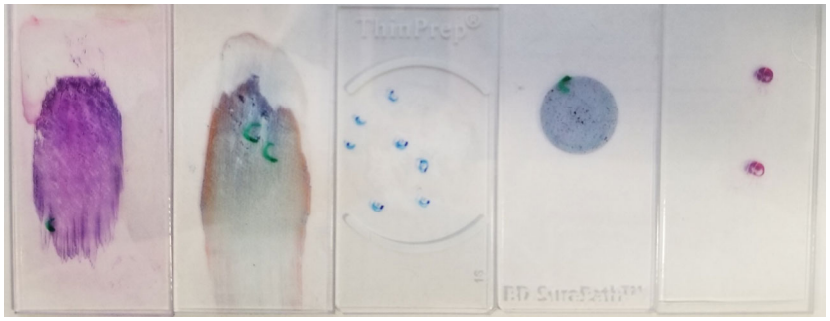
2nd and additional passes
Sclerotic lesions
Nodular sclerosing Hodgkin Lymphoma
Sclerosing large cell lymphoma
Metastatic lesions

Lymph node FNAB: Maximize Diagnostic Yield

Allocate sample:

- Smears – save unstained for testing
- Flow cytometry
- Cell block, IHC, special stains,
- Molecular testing
  - FISH
  - PCR
  - Sequencing

Part 3. Diagnostic Approach



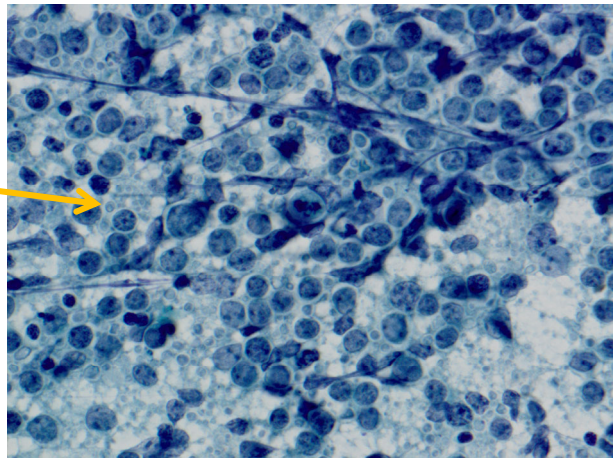
Low-power Morphologic Impression

- 1. Are there cells to evaluate?
- 2. Are the cells lymphoid or non-lymphoid? Both?
- 3. If lymphoid, identify the pattern:
  - Polymorphous
  - Monotonous, small
  - Monotonous, medium
  - Monotonous, large
  - Pleomorphic

Is a lymphoid population present?

Consistent findings in aspirated lymphoid tissue:

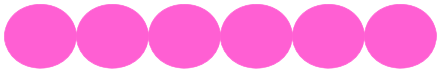
- Dispersed cell pattern
- Lymphoglandular bodies



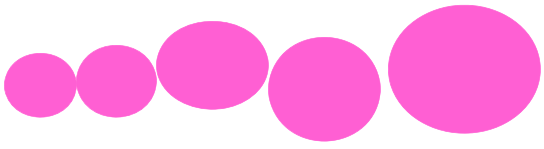
Discerning Monomorphous vs Polymorphous

Lymph node FNA Cytomorphology

"String of pearls" Visual Assessment



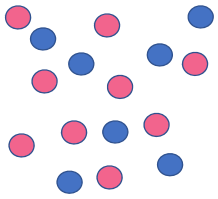
monomorphous



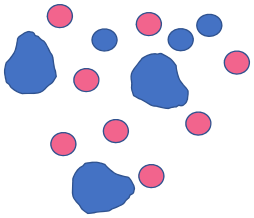
polymorphous

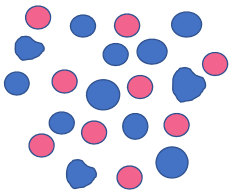
Judging Cell Size

Small lymphocyte pattern
6 to 10-12 micron
2x RBC
Smaller than histiocyte nucleus

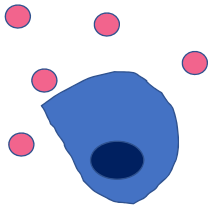


Large lymphocyte pattern
>20 micron
>3x RBC
At least 1.5x histiocyte nucleus





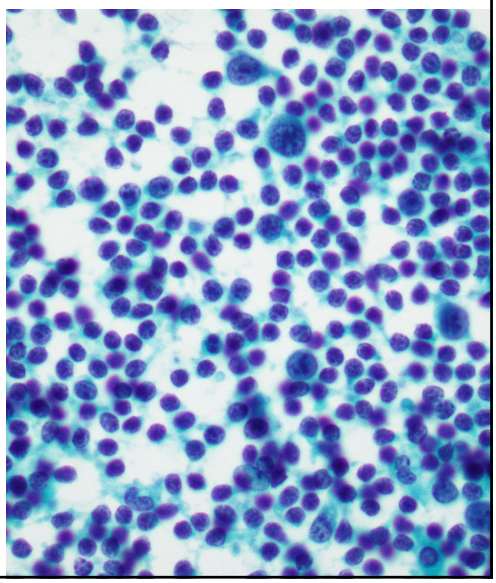
Polymorphous pattern



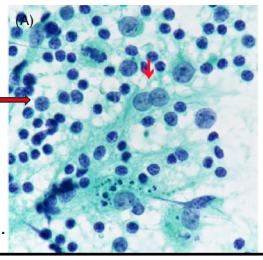
Pleomorphic pattern

Reactive lymph node populations

- Resting small lymphocytes
- Centrocytes
- Centroblasts
- Tingible body macrophages
- Follicular dendritic cells



"Kissing nuclei" of FDC



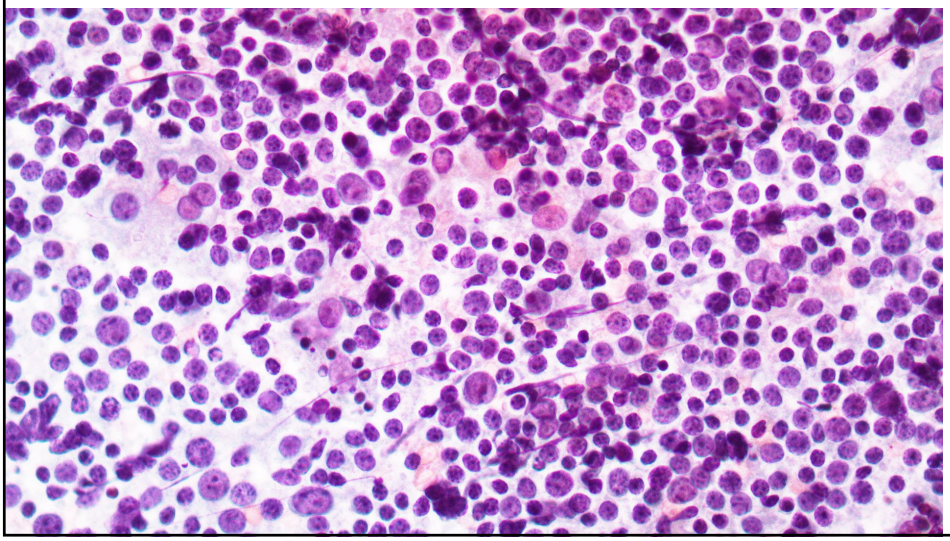
Sasaki et al. Diag Cytopathol. 2021.

Medium-High power evaluation

- Nuclear size(s)
- Nuclear shapes (membrane irregularities)
- Amount of cytoplasm (N:C ratio) – is it lymphoid?
- Chromatin quality (condensed, coarse, vesicular)

- *Relative nuclear size varies based on stain and drying artifact
- *Crush artifact and thick smears are limitations

Case 1. Axillary node, 45yo man, HIV+



What pattern?

Polymorphous

Monotonous, small
Monotonous, medium
Monotonous, large

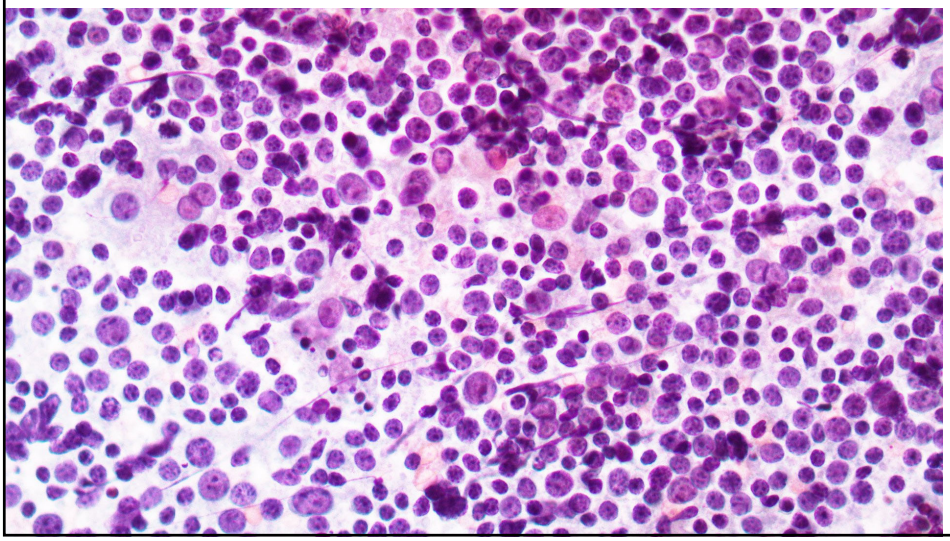
Pleomorphic

Case 1. Polymorphous pattern

DDX:

- Reactive lymphoid hyperplasia (non-specific)
- Partial involvement by small B cell lymphoma (e.g. CLL, follicular)
- Hodgkin lymphoma
- T-cell lymphoma

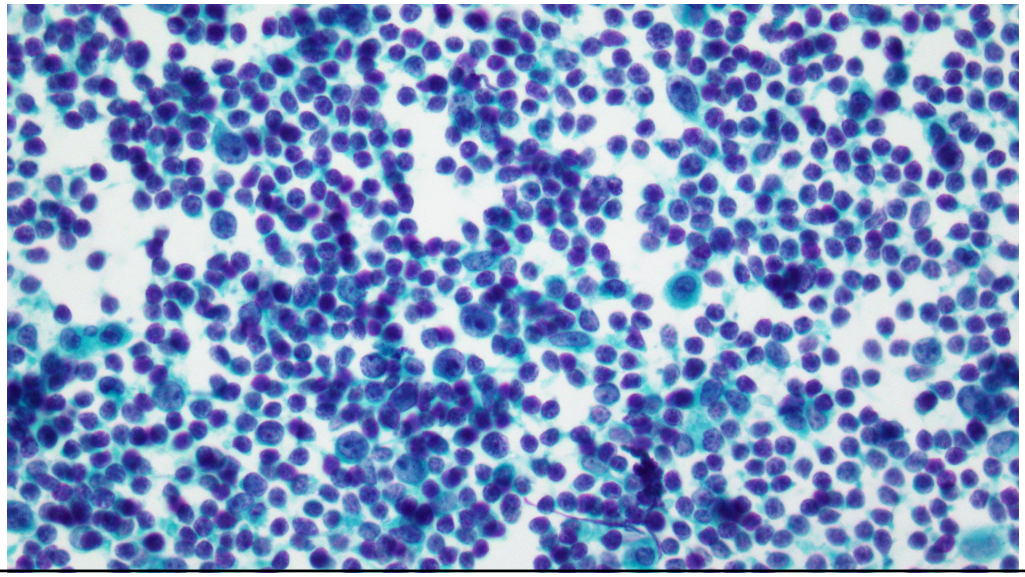
Case 1. Axillary node, 45yo man, HIV+



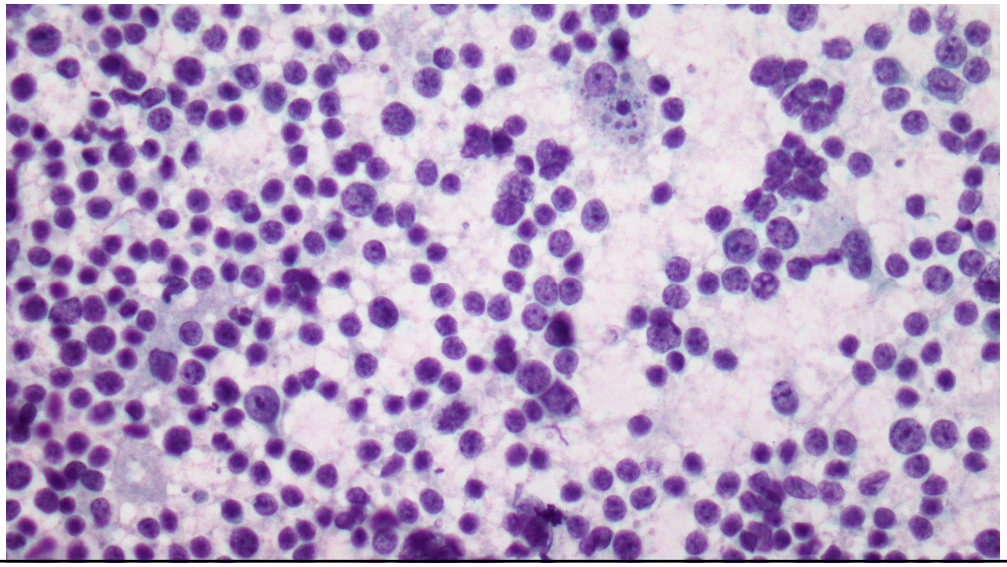
Diagnosis: Reactive hyperplasia

Flow cytometry negative

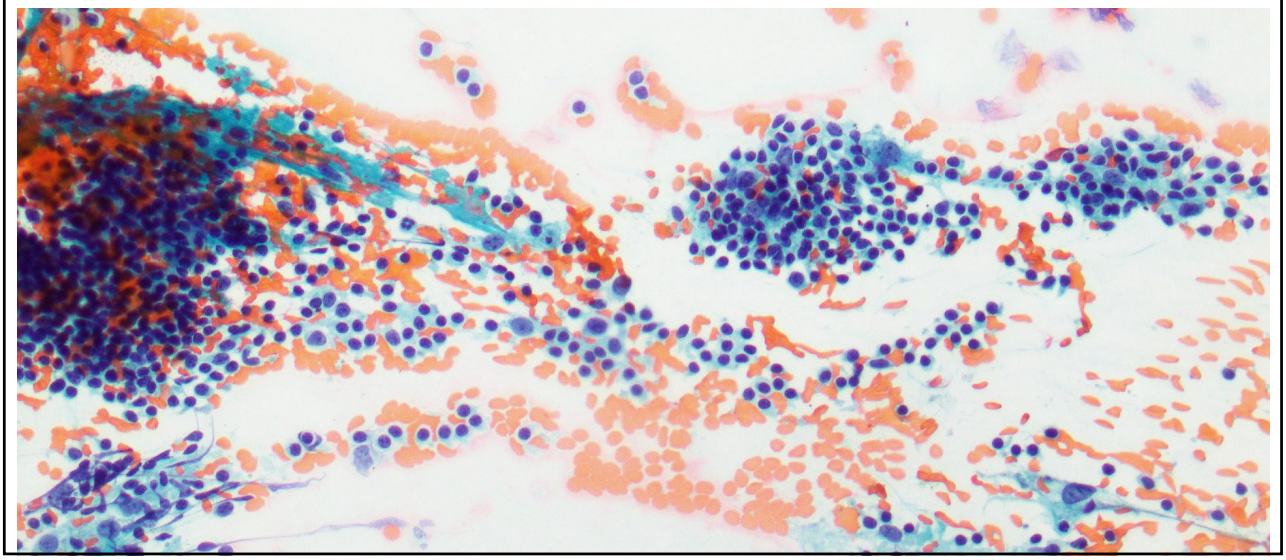
Additional examples of reactive node



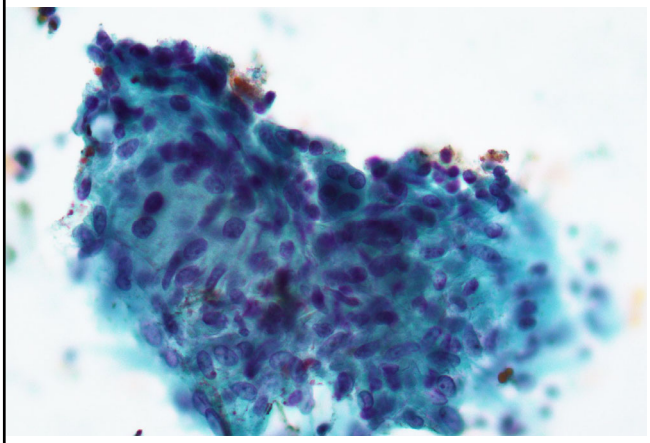
Additional examples of reactive node

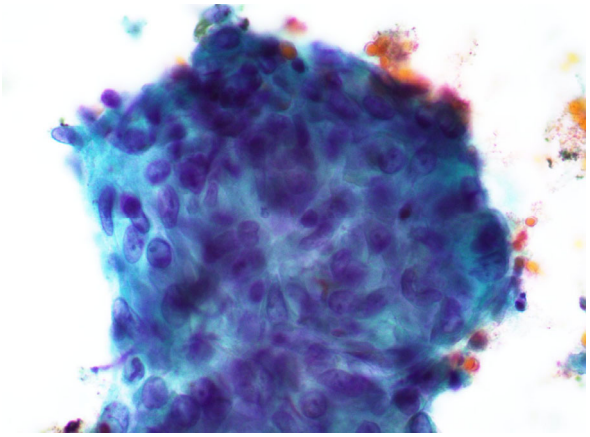


Additional examples of reactive node

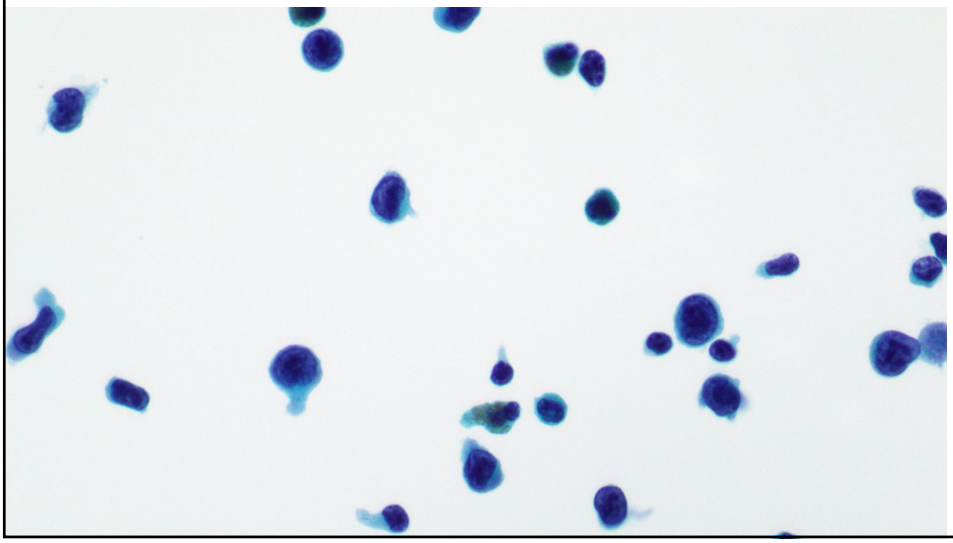


Additional examples of reactive node





Case 2. Axillary node, 80 yo woman



What pattern?

Polymorphous

Monotonous, small
Monotonous, medium
Monotonous, large

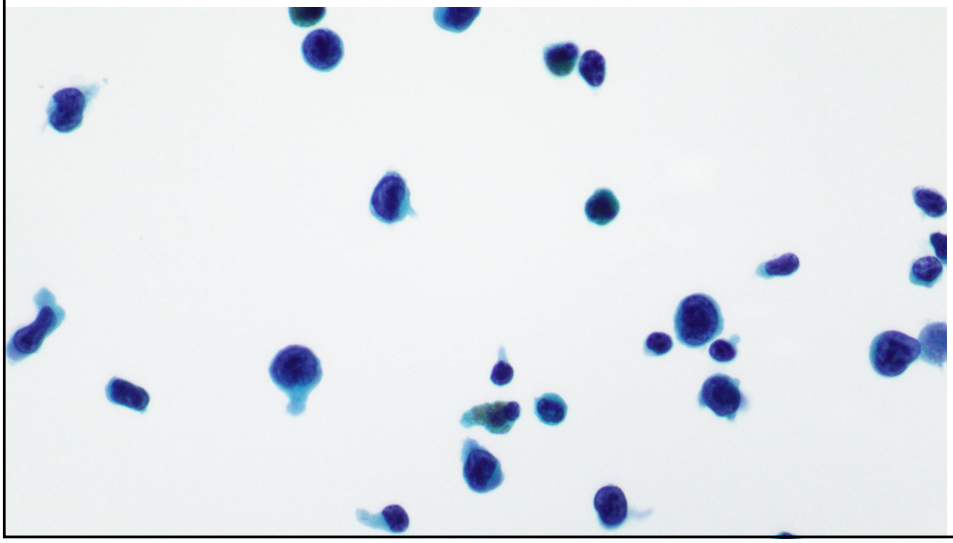
Pleomorphic

Case 2. Monotonous, Large cell pattern

DDX:

- DLBCL
- Grade 3 follicular lymphoma
- Transformation of low grade B lymphomas
- T cell lymphomas
- Blastoid mantle cell lymphoma
- Non-lymphoid metastases

Case 2. Axillary node, 80 yo woman



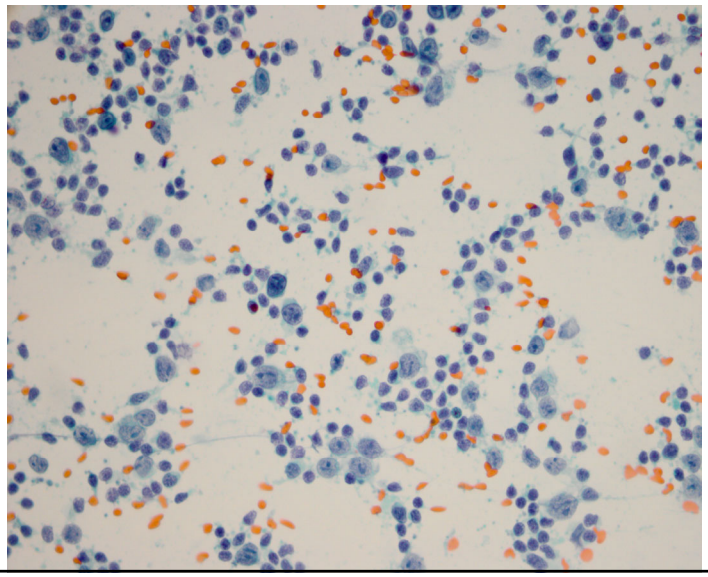
Diagnosis: Peripheral T cell lymphoma

Aberrant T cell population (15%) on flow cytometry:
CD2+/CD3+/CD4+/CD5+
CD7-/CD8-/CD56-

IHC on subsequent excision:
CD4+ (weak)
CD25+
CD30+
MUM1+
PAX5-/ALK-/CD15-/EMA-/perforin-

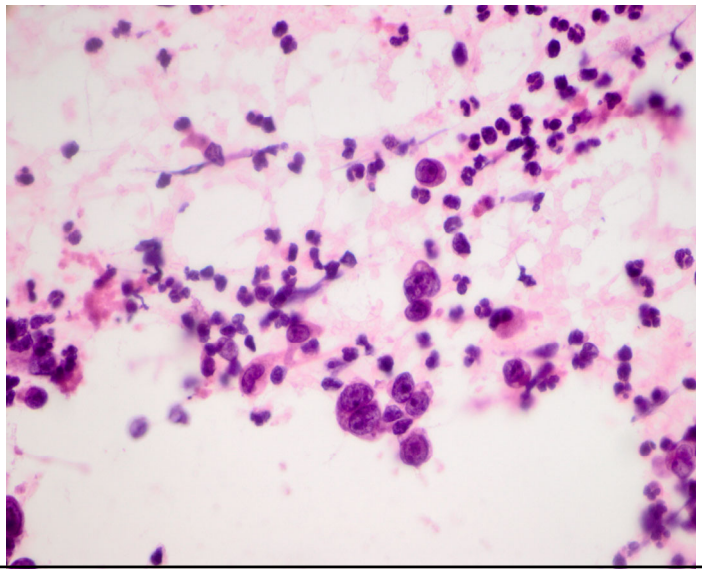
Additional examples of large cell pattern

DLBCL



Additional examples of large cell pattern

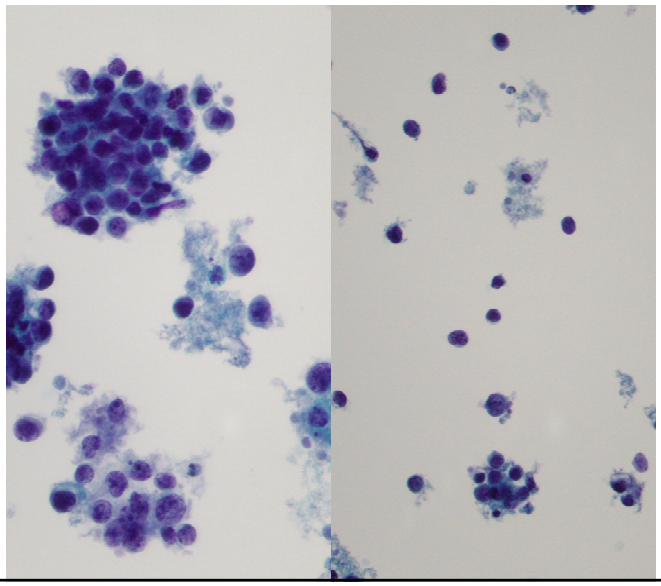
Hodgkin
Lymphoma



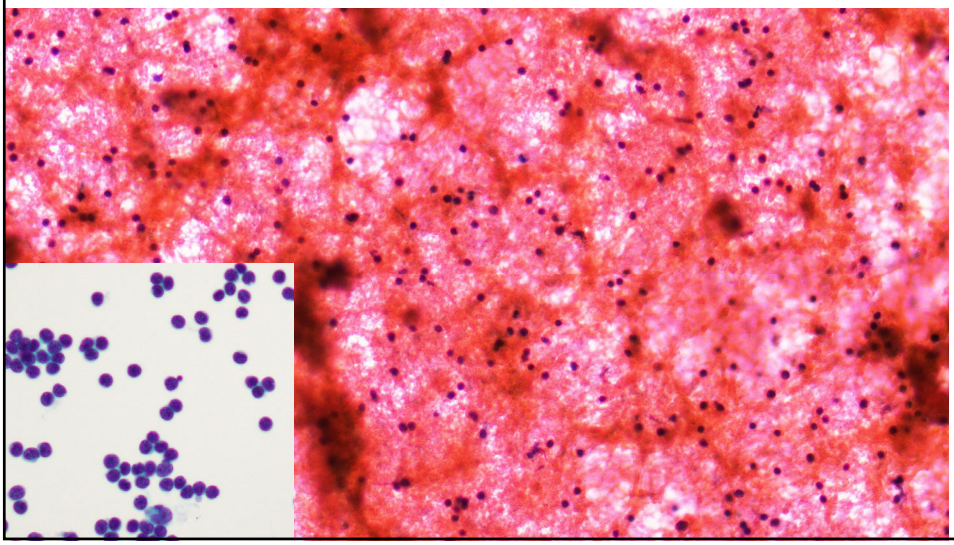
Additional examples of large cell pattern

High grade B cell lymphoma, NOS

(FISH studies failed, no other specimens, began chemo)



Case 3. Retroperitoneum, 62 yo man



What pattern?

Polymorphous

Monotonous, small
Monotonous, medium
Monotonous, large

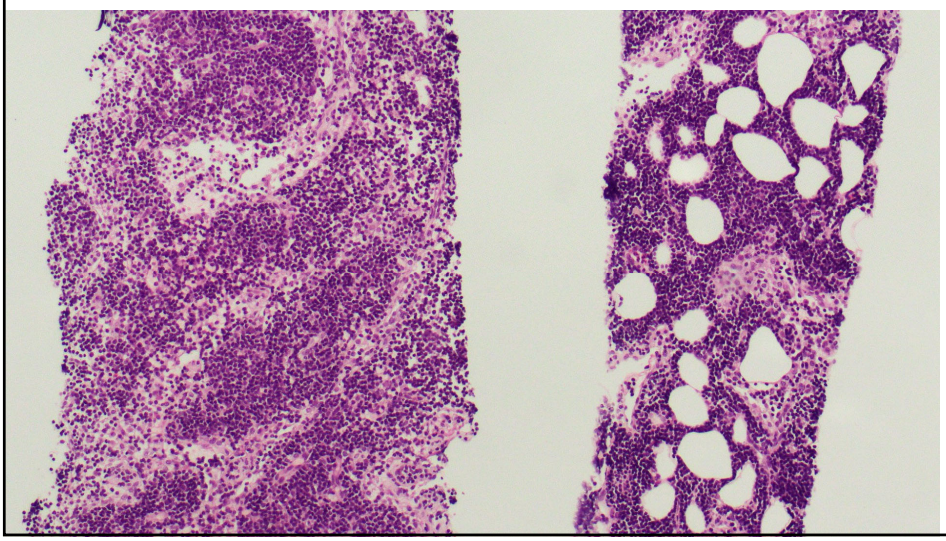
Pleomorphic

Case 3. Monotonous, small cell pattern

DDX:

- Reactive lymphoid hyperplasia
- Small B cell lymphomas (e.g. SLL/CLL, follicular, mantle cell, marginal zone)
- Small cell carcinoma metastases

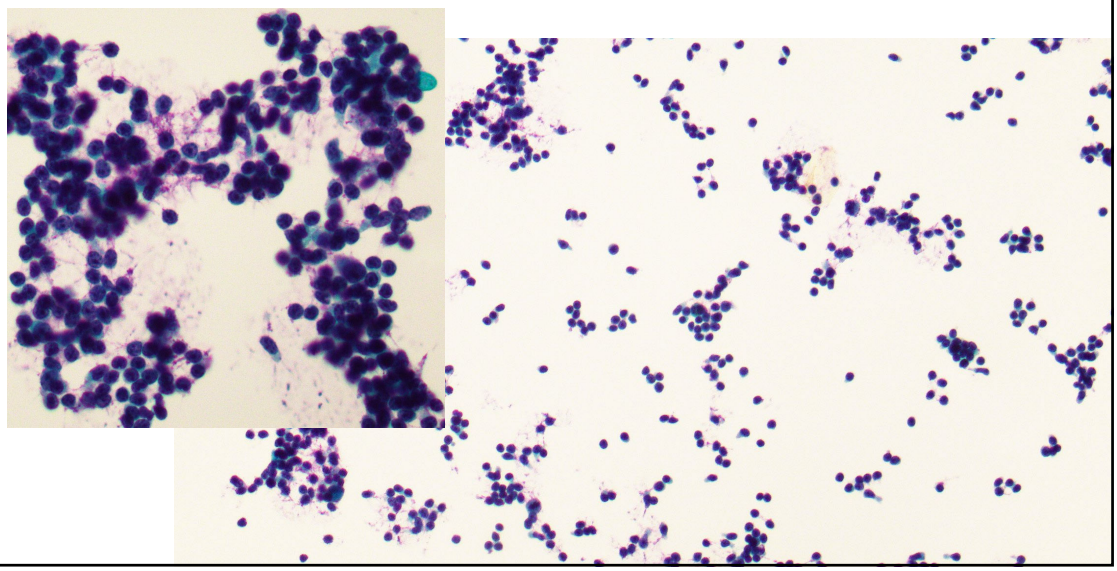
Case 3. Retroperitoneum, 62 yo man



Follicular lymphoma, grade 1

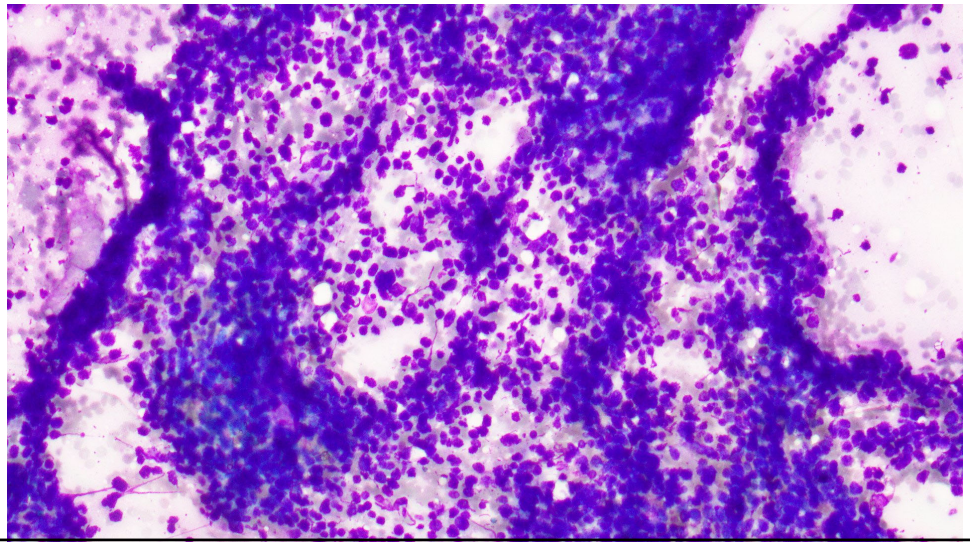
Additional examples of small cell pattern

CLL



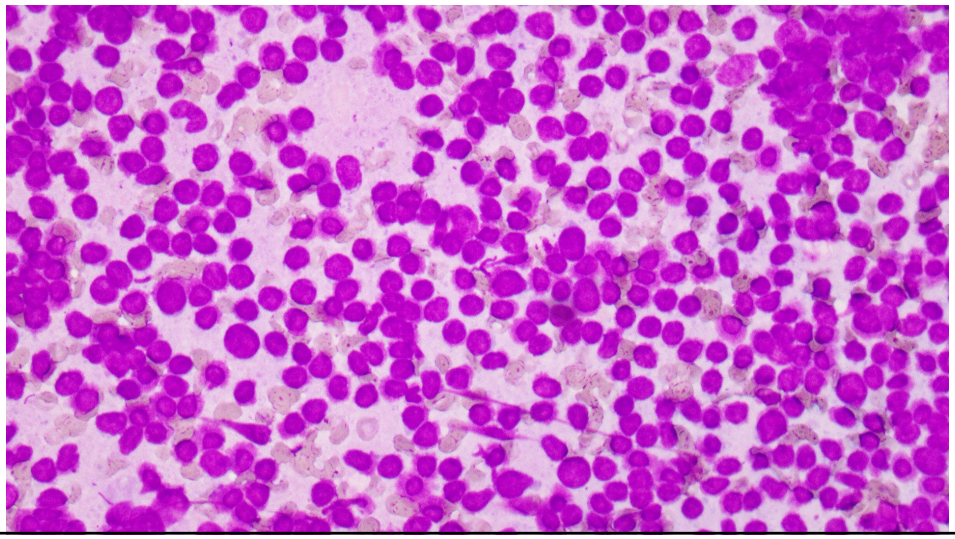
Additional examples of small cell pattern

Submandibular
Lymphoblastic
Lymphoma



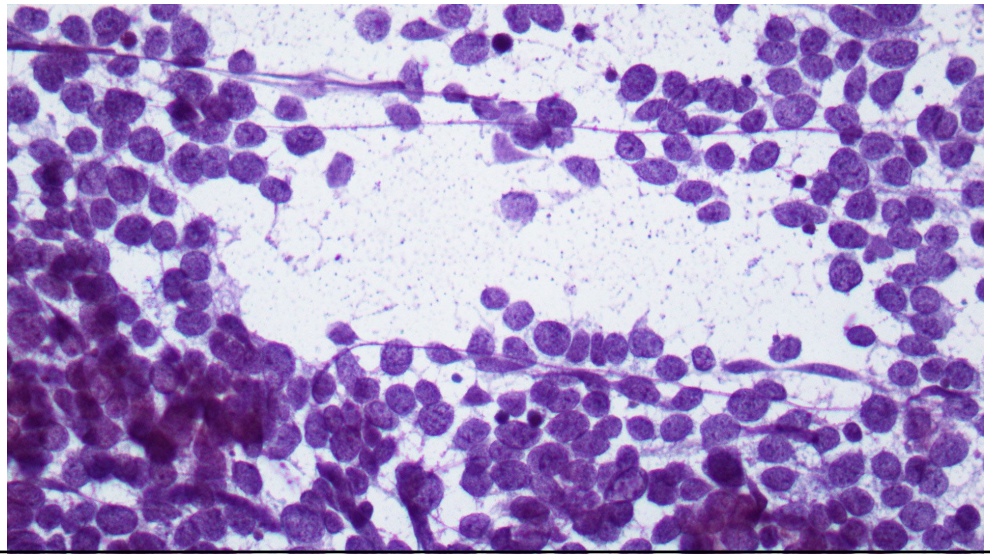
Additional examples of small cell pattern

Mantle cell lymphoma

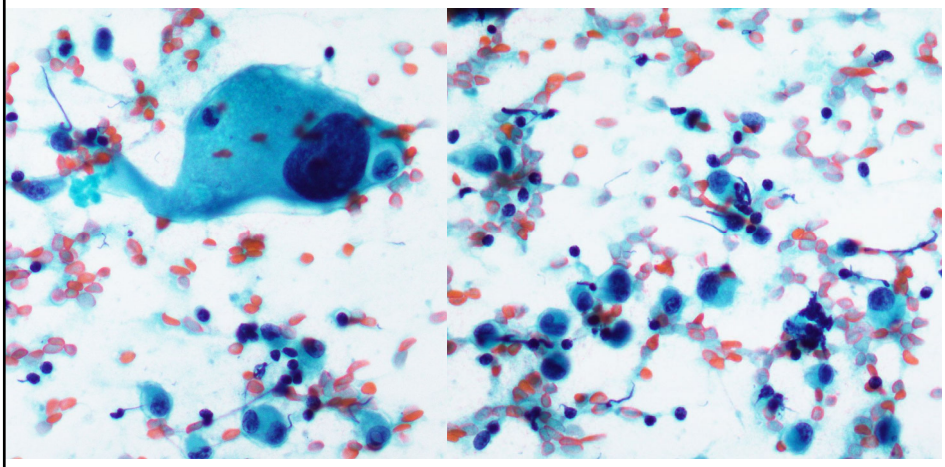


Additional examples of small cell pattern

Small cell carcinoma



Case 4. Axillary node, 45yo man



What pattern?

Polymorphous

Monotonous, small
Monotonous, medium
Monotonous, large

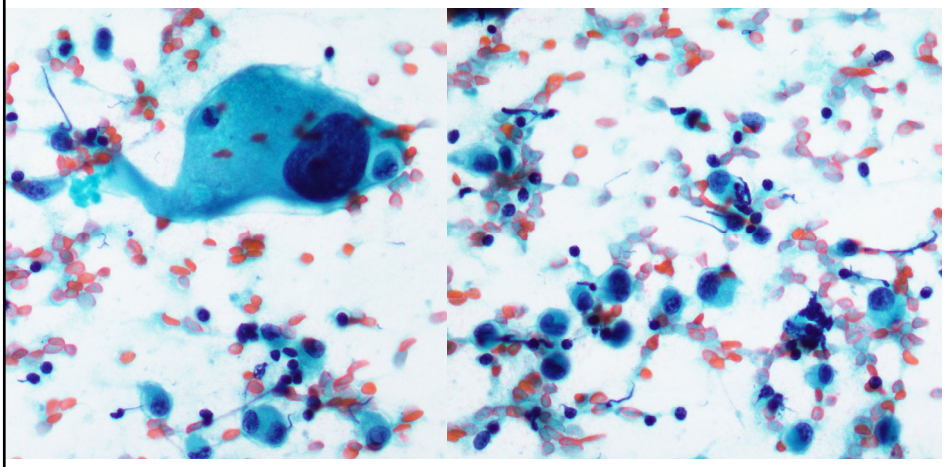
Pleomorphic

Case 4. Pleomorphic pattern

DDX:

- Hodgkin lymphoma
- Anaplastic large cell lymphoma
- DLBCL
- Transformation of low grade B lymphoma
- T cell lymphomas
- Metastatic malignancies

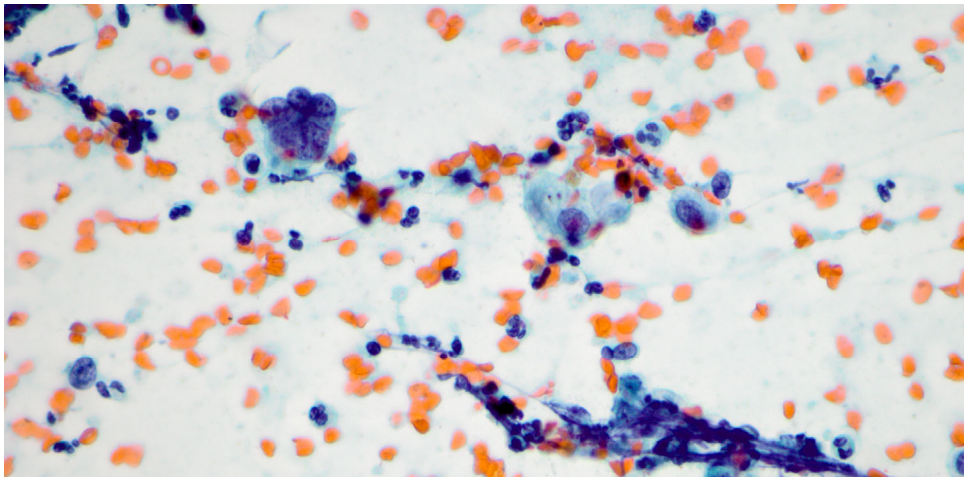
Case 4. Axillary node, 45yo man



Diagnosis:
Melanoma

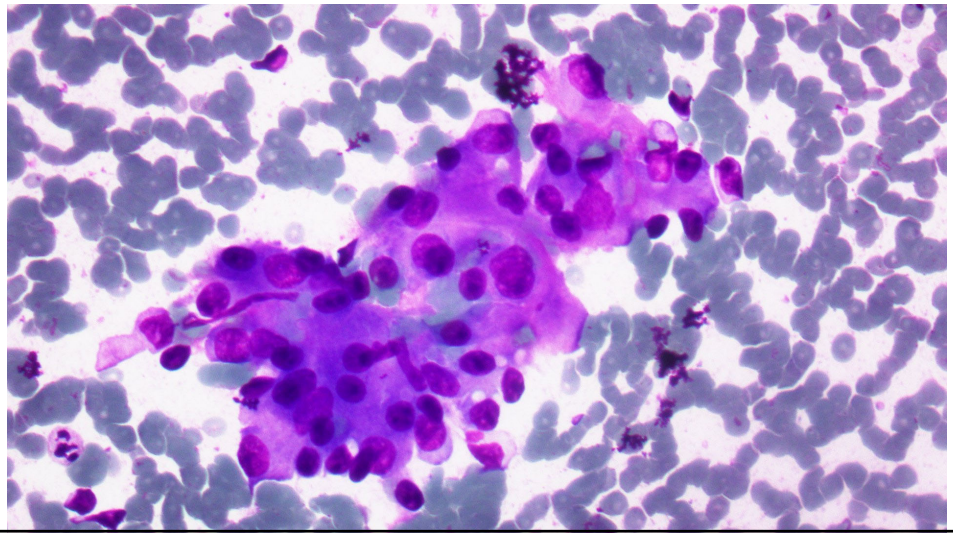
Additional examples of pleomorphic pattern

Hodgkin
Lymphoma



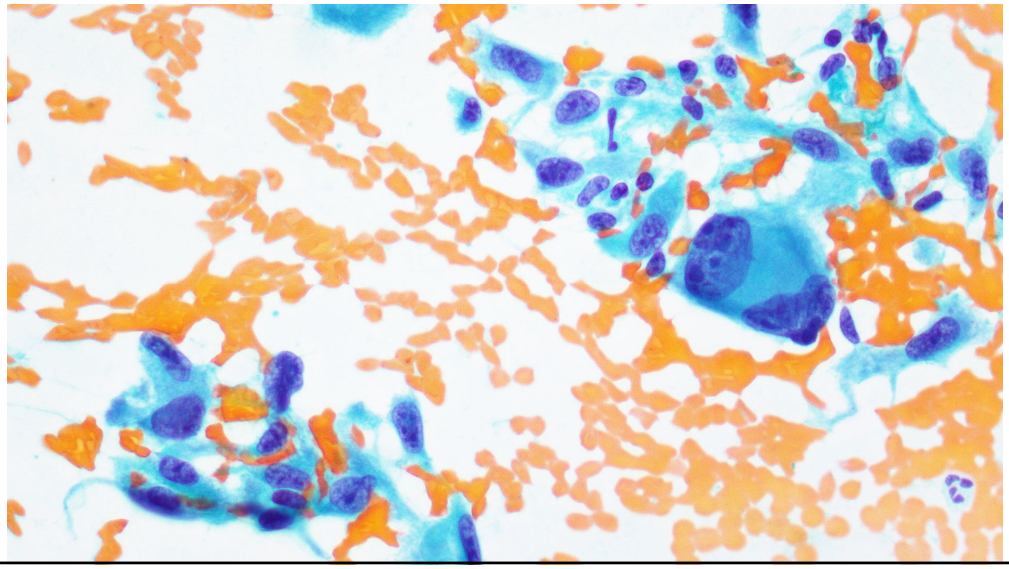
Additional examples of pleomorphic pattern

Metastatic renal cell carcinoma



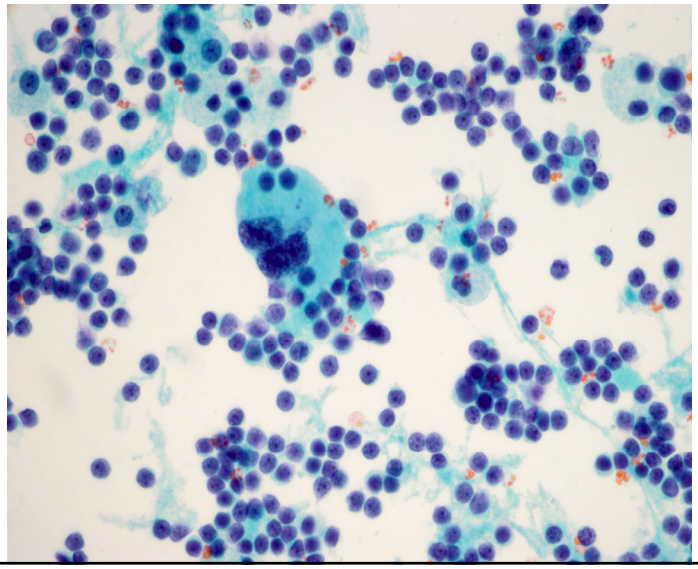
Additional examples of pleomorphic pattern

Metastatic Anaplastic Thyroid Carcinoma



Additional examples of pleomorphic pattern

Hematopoiesis in
Pleural Fluid



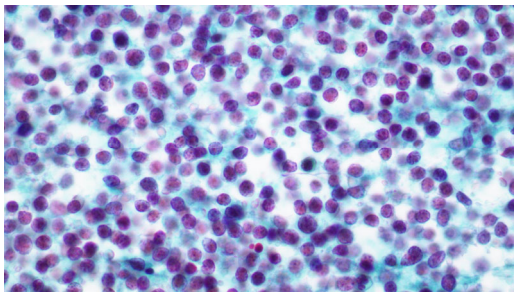
Tailor IHC panel to morphologic DDX

- Small B-cell lymphomas
- Hodgkin lymphoma
- Large cell lymphomas
- T-cell lymphomas

“Small B-cell lymphomas” suggested panel

CD3
CD20
CD5
Cyclin D1
Sox11
BCL2
BCL6
Ki67
LEF1

CLL/SLL
Follicular lymphoma
Mantle cell lymphoma
Marginal zone lymphoma
Lymphoplasmacytic lymphoma

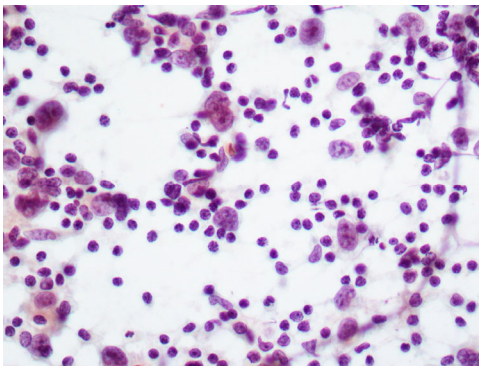


Mantle cell lymphoma

“Hodgkin” suggested panel

CD3
CD20
CD30
CD15
EBER
PAX5

Classic Hodgkin lymphoma
NLP Hodgkin Lymphoma
T cell/histiocyte-rich large B cell lymphoma
Reactive node (with many immunoblasts)



Hodgkin lymphoma

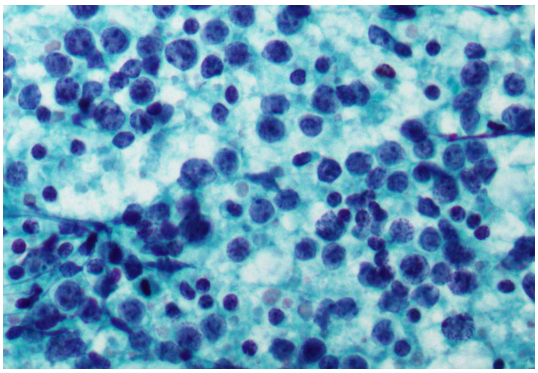
“Large cell lymphomas” suggested panel

CD3, CD5
CD10, CD20
Cyclin D1, MUM1
BCL2, BCL6
CD30, EBER
Ki67, C-MYC, p53

DLBCL

High grade B cell lymphoma

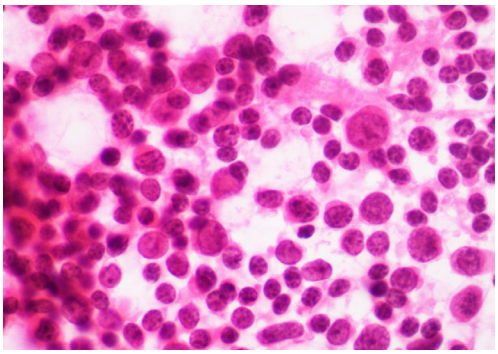
Burkitt lymphoma



DLBCL

“T cell lymphomas” suggested panel

CD2, CD3, CD4, CD5, CD7, CD8	Peripheral T cell lymphoma, NOS
CD25, CD30, CD56	ALCL (+/- ALK subtypes)
CD10, BCL2, BCL6	Reactive hyperplasia
CD21/CD23	Nodal T-follicular helper cell lymphomas (e.g. AITL)
Ki67, ALK, EBER, Ki67, PD-1	
Perforin, granzyme B	
TCRs (gamma, delta)	



Peripheral T cell lymphoma, NOS

Thank you