

FNA Cytology of the Head and Neck: Common Cases and Their Pitfalls

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Objectives

- Review some of the more common cytodiaognoses of the Head and Neck
- Establish an approach to some of the diagnostic dilemmas using a case based tactic
- Emphasized topics include lymph nodes, cystic neck masses, reactive reparative changes, and salivary gland lesions



Lymph Nodes

- In a bulk of cases FNAs of the neck are performed to investigate clinically suspicious lymphadenopathy (LAD)
- The primary differential diagnoses include:
 - Reactive/Infectious LAD
 - Metastatic Disease
 - Lymphoma



Reactive Lymphadenopathy

- De novo head and neck LAD in pediatric FNAs are frequently benign (65%)
- Pediatric patients with a history of malignancy also have a high rate of benignancy in aspirated nodes (43%)
- FNAC avoided additional surgical procedures in 61% of cases in one review
- The cytodiagnosis of reactive lymph nodes is most accurate in patients under 50 years (~5% risk of subsequent malignant diagnosis)
- A higher rate (29%) of subsequent open biopsy finding of malignancy occurs in patients over 50 following a cytodiagnosis of benign (mixed) lymph node

Vande Schoot L et al. J Pediatr Surg. 2001. 36(1):7-11

Yu GH, McGrath CM. Diagn Cytopathol. 2000. 23(4):249-52



Assessing for the Possibility of Lymphoma

- To confirm material is adequate (in node) a small drop of the aspirate is placed onto slide(s) for immediate assessment
- The remainder is rinsed in a cell preservative (eg: RPMI-1640 Roswell Park, Buffalo, NY)
- Generally 10 million cells are considered adequate for FC assessment (2-3 passes)

Caraway NP. Cancer (cytopathology)
2005;105:432-442.

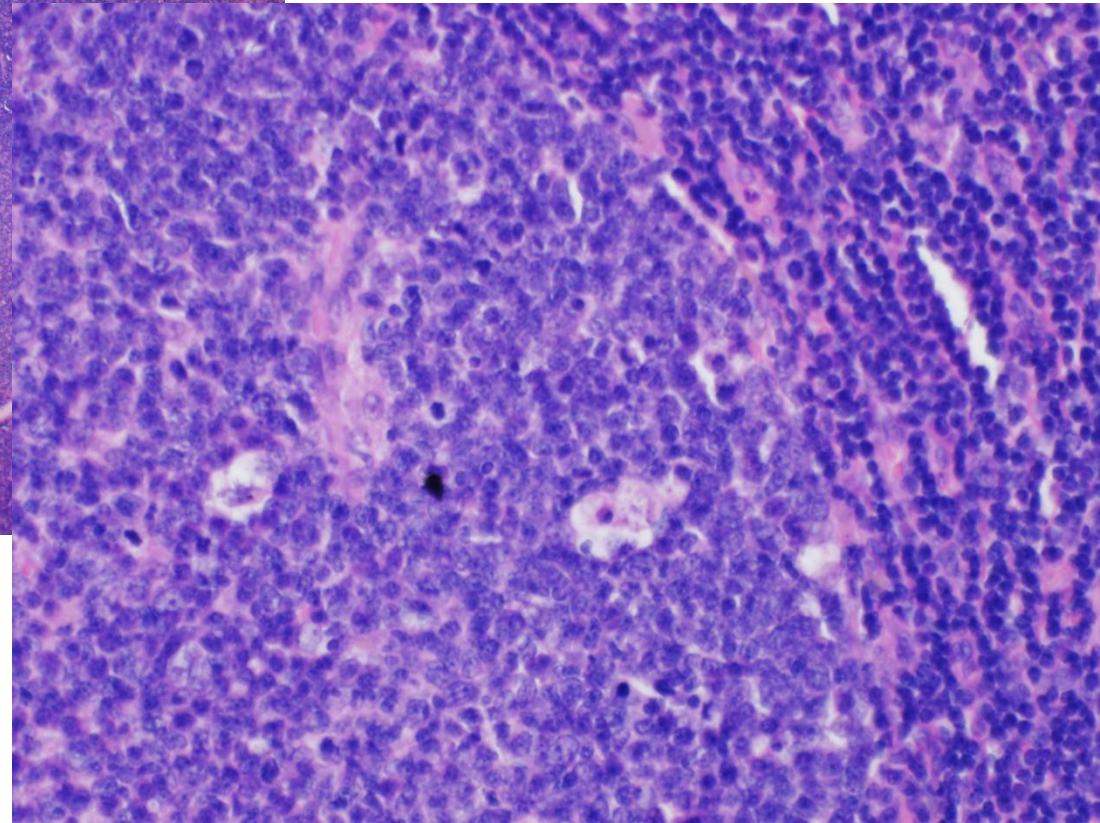
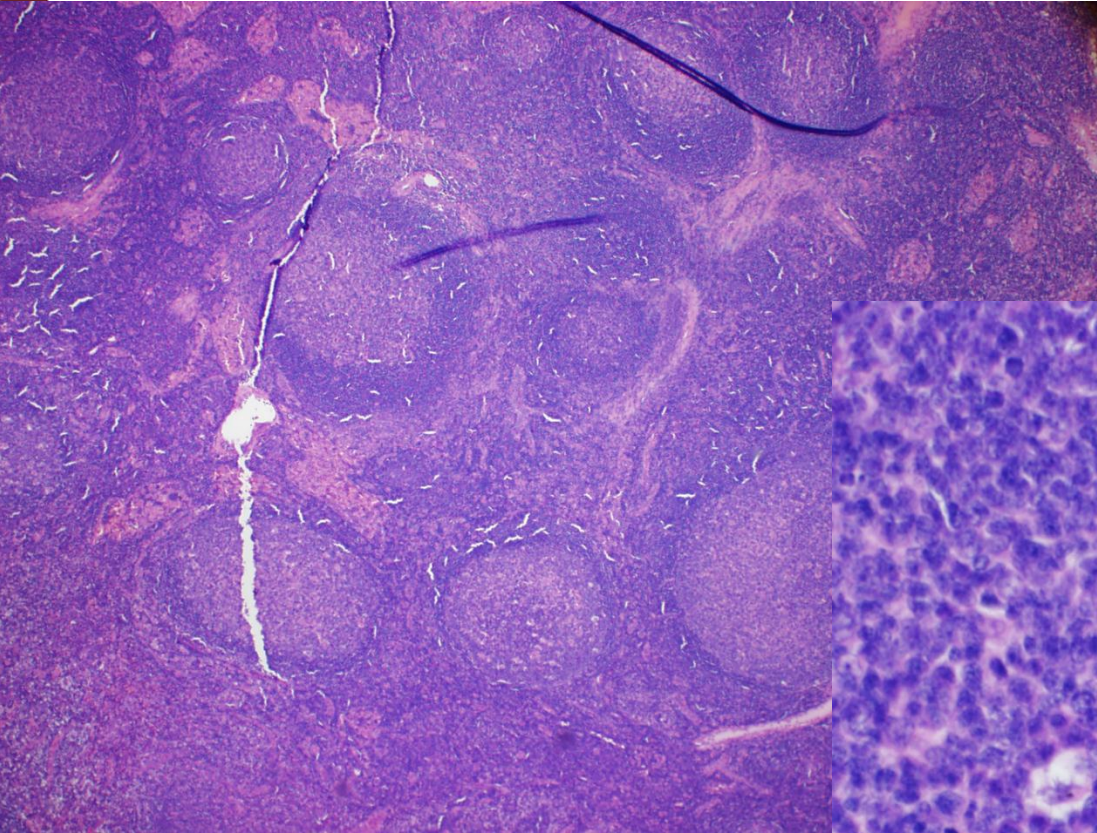


Cytologic Features of Reactive Lymphadenopathy

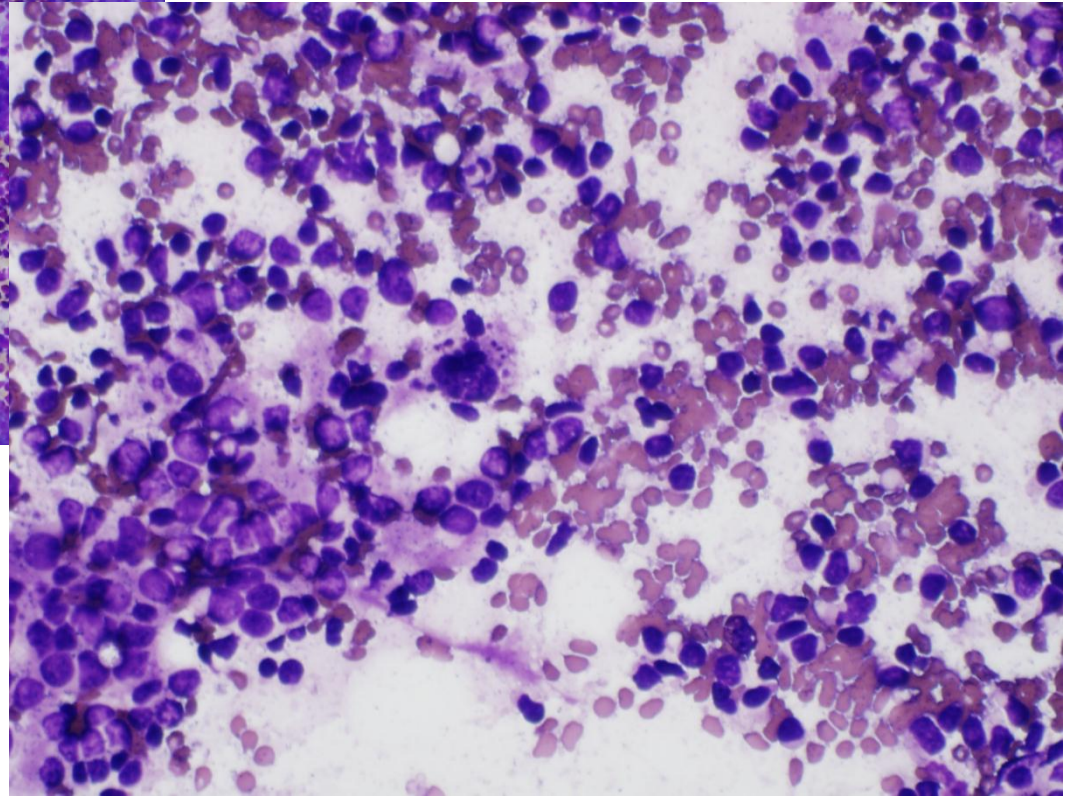
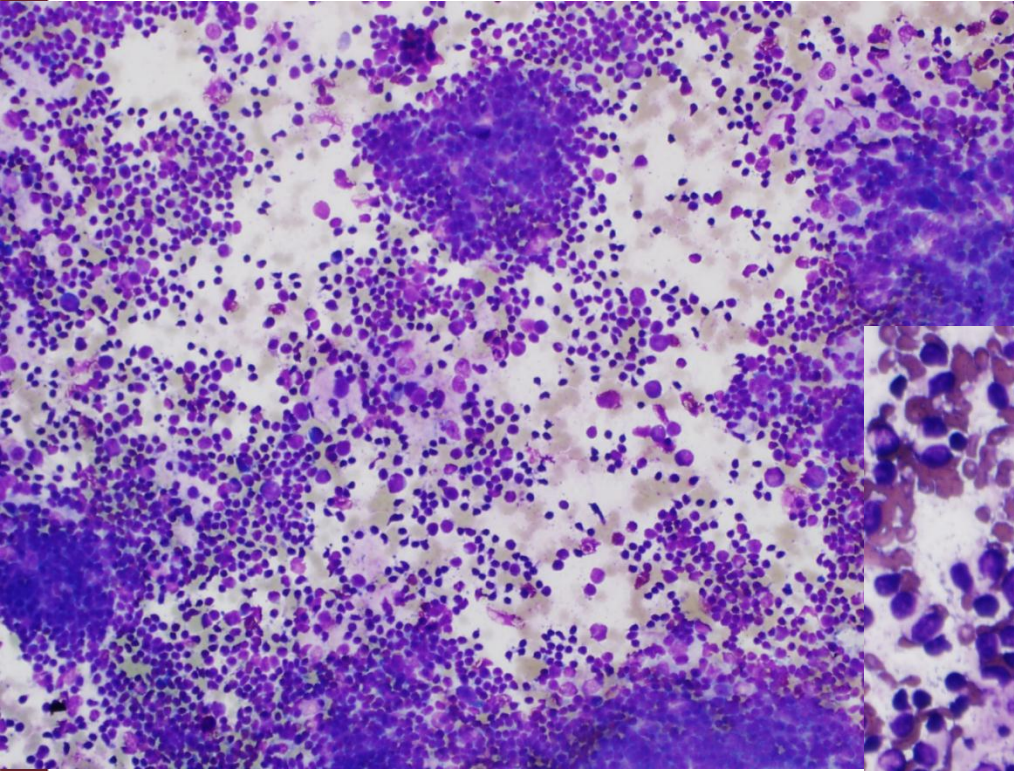
- Polymorphic lymphoid cells showing a maturational sequence
- Reactive germinal centers are prominent
- Tingible body macrophages are present
- Absence of a monomorphic lymphoid population (small, medium, or large)
- Absence of a subpopulation of large, irregular lymphoid cells (Hodgkin's Lymphoma, Anaplastic T-cell lymphoma, Large B-cell lymphoma)



Reactive Lymphadenopathy



Reactive Lymphadenopathy (37 male with history of PTC)



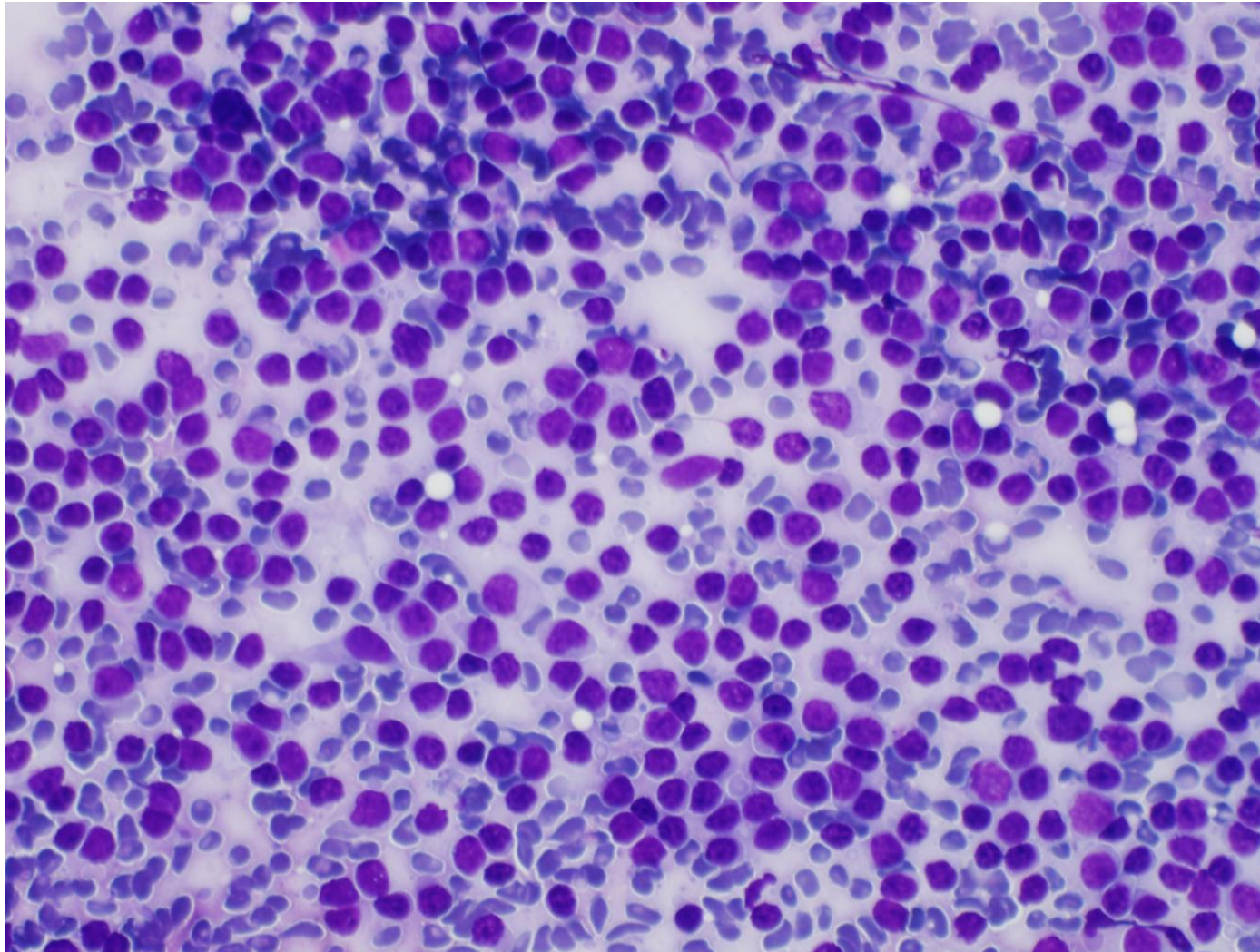
Cytologic Features of Lymphoproliferative Disorders

- Monomorphic lymphoid population
- Obvious population of small cleaved lymphocytes (Follicular lymphoma, Mantle cell lymphoma) or small lymphocytes with clumped chromatin (CLL/SLL)
- Obvious population of medium-sized cells (Lymphoblastic lymphoma, Burkitt's lymphoma, Ewing's sarcoma/PNET)
- Population of large lymphoid cells with convoluted nuclei +/- prominent nucleoli (Hodgkin lymphoma, Diffuse Large B-cell lymphoma, Anaplastic T-cell lymphoma)

Caraway NP. Cancer (cytopathology)
2005;105:432-442.

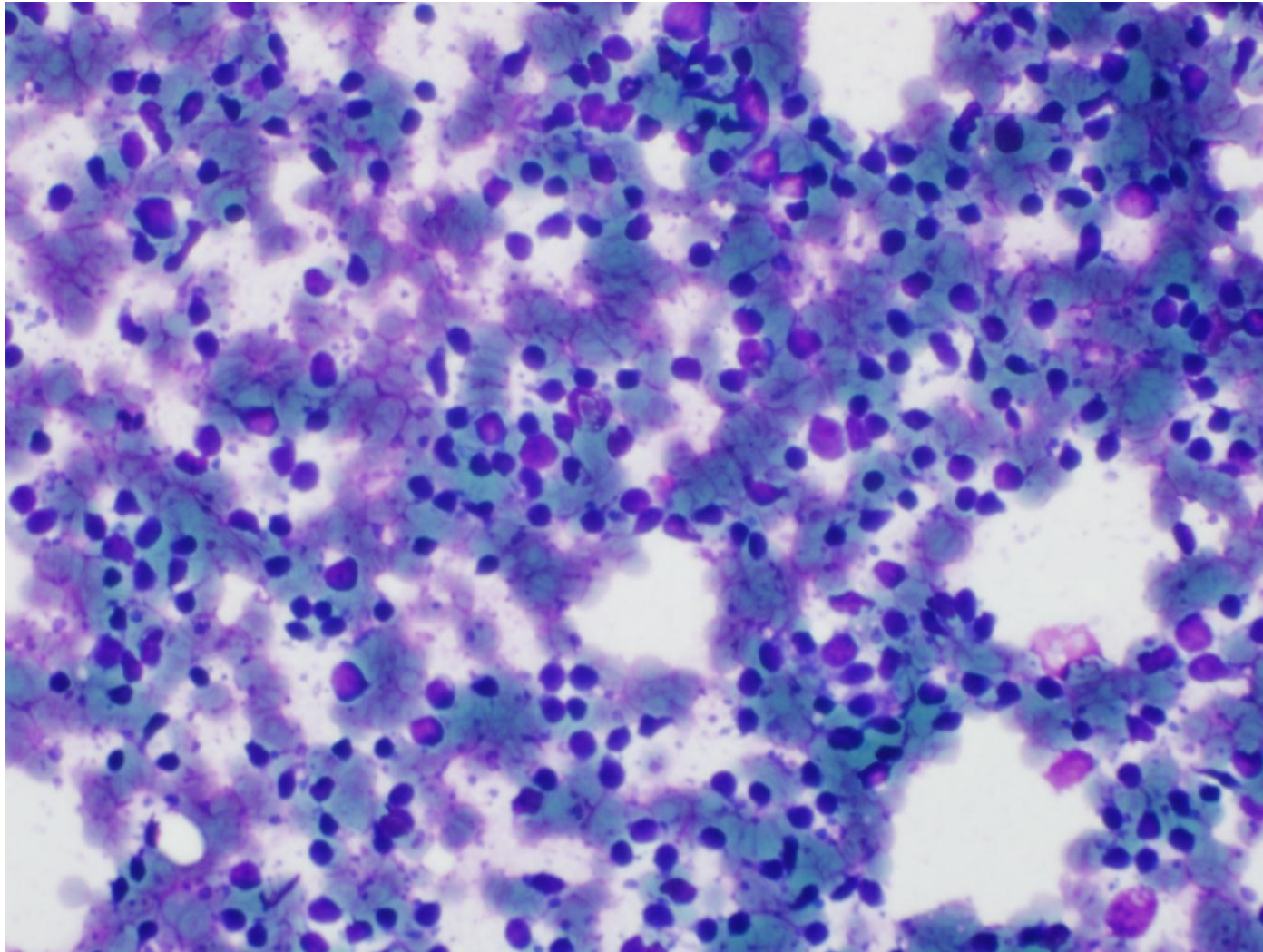


91 year old male with left cheek nodule



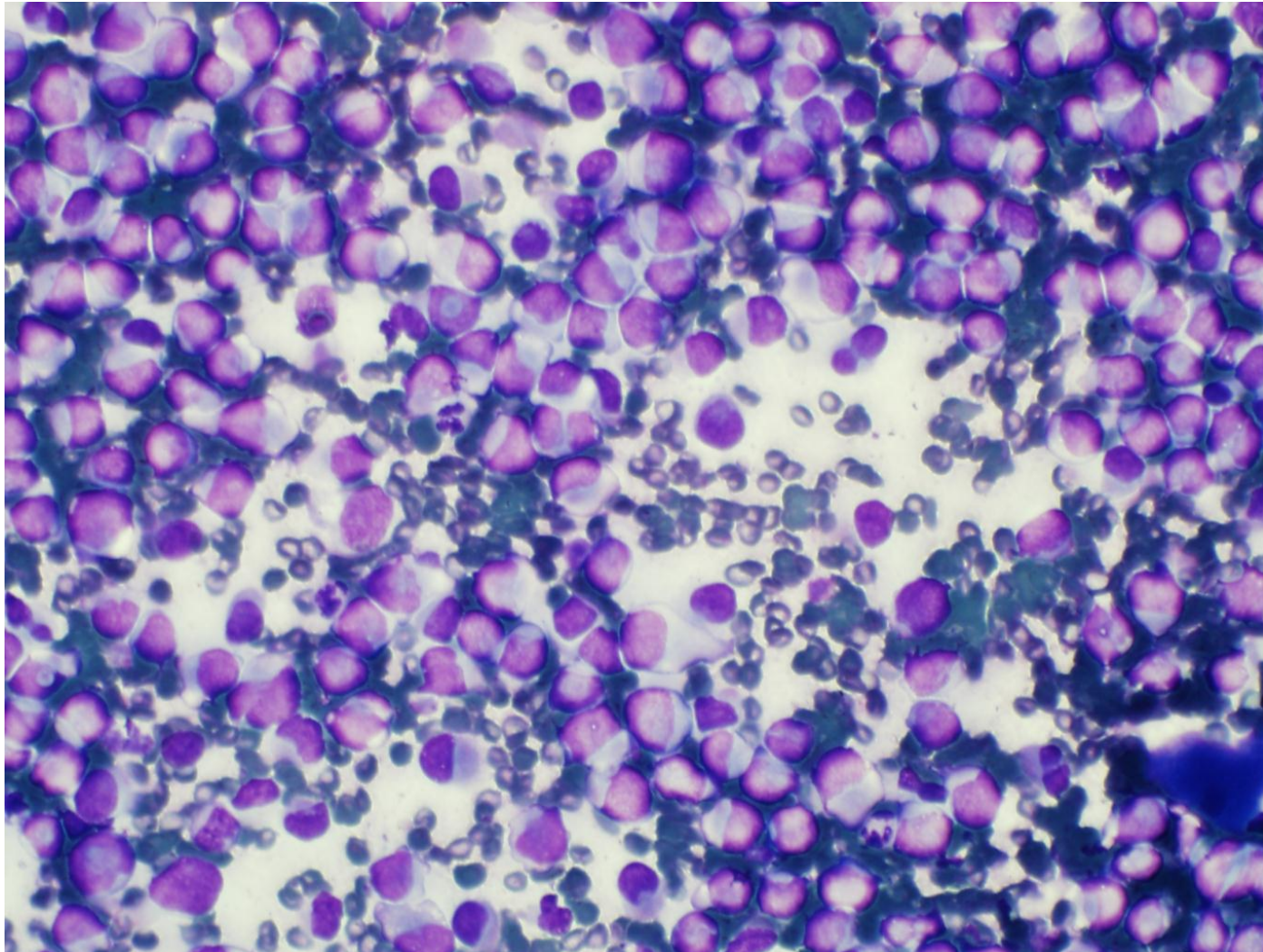
CLL

71 year old female with history of MALT now with cervical LAD

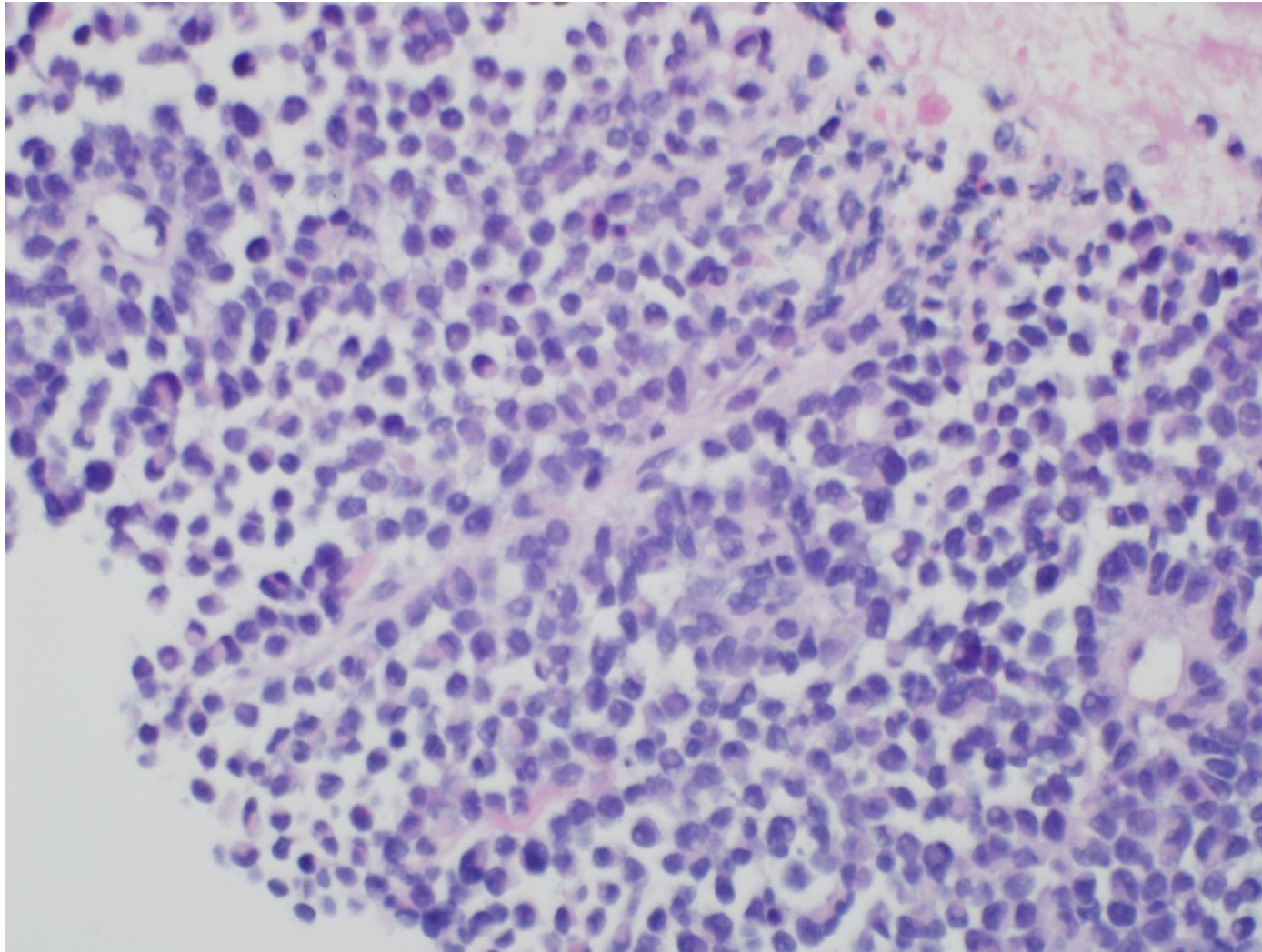


MALT

23 year old male with a posterior neck soft tissue mass

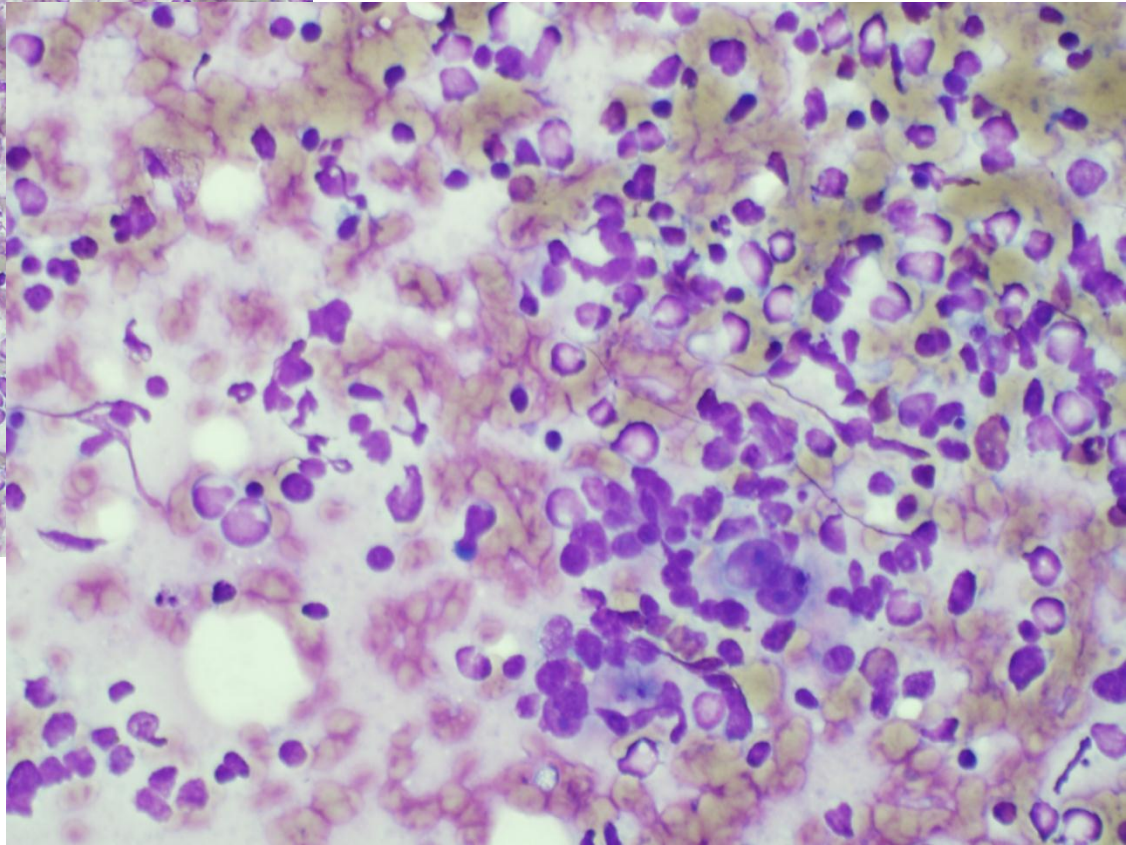
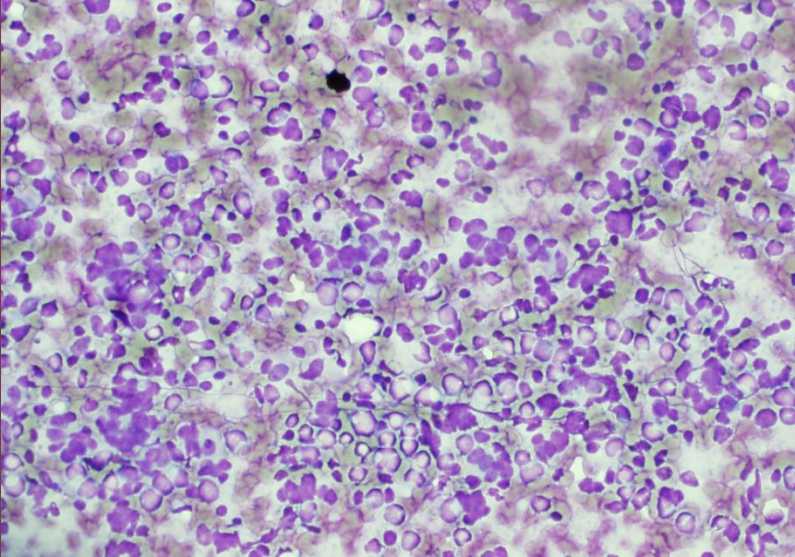
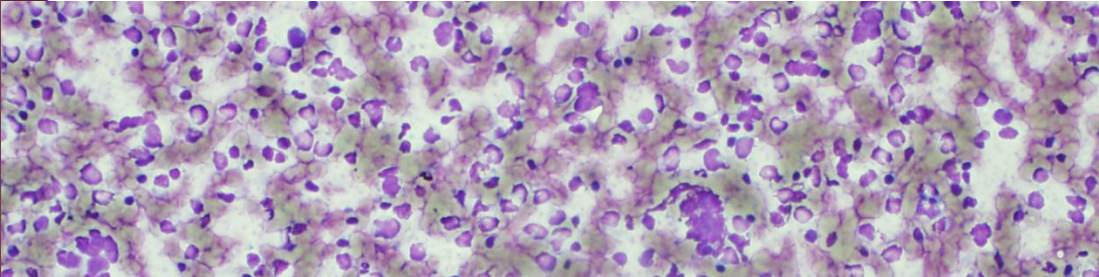


23 year old male with a posterior neck soft tissue mass (cell block)



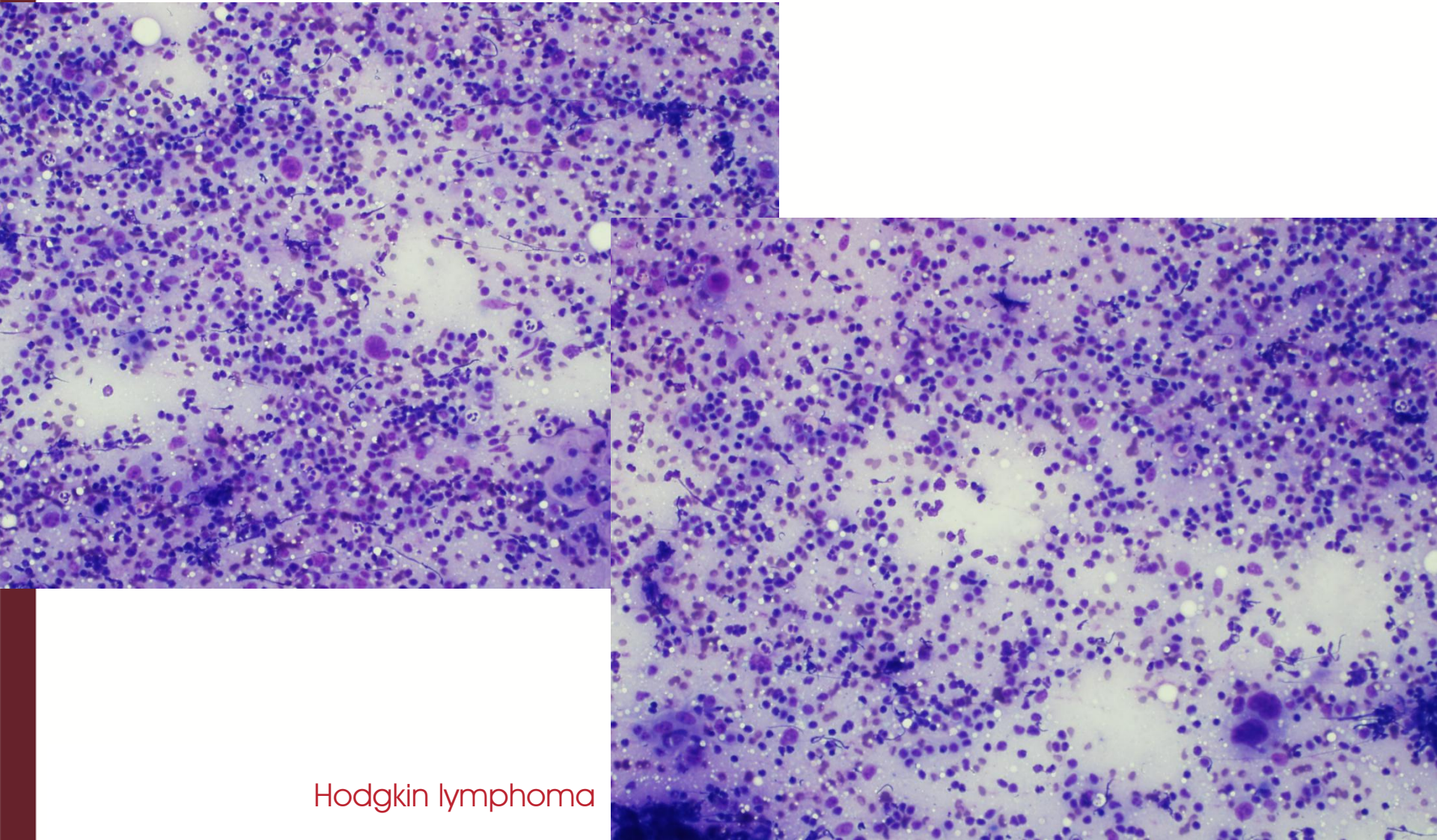
Ewing's
sarcoma

65 year old female with multifocal LAD



DLBCL

31 year old female with cervical LAD



Hodgkin lymphoma

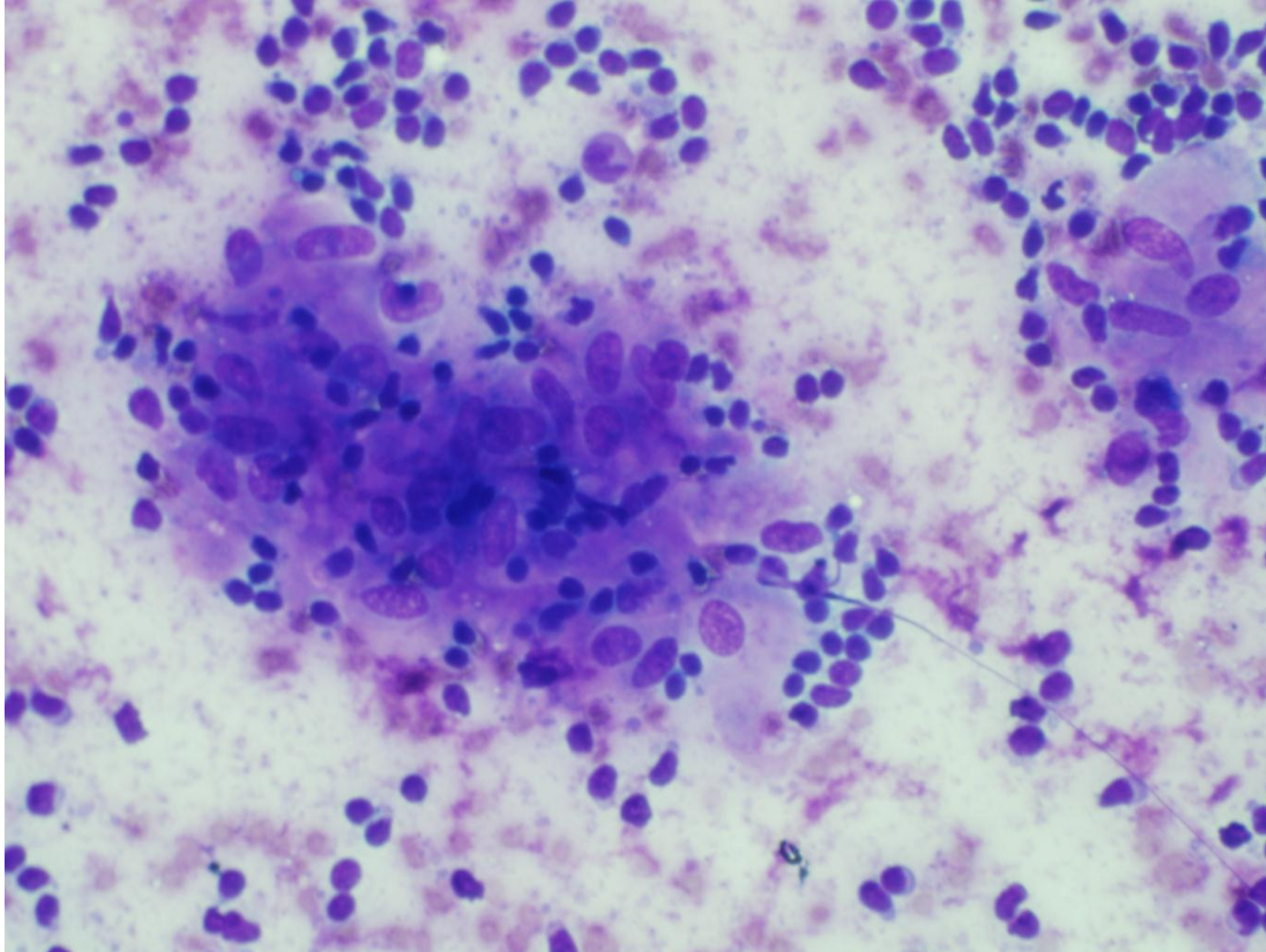
Lymph Nodes: Lymphadenitis

- Necrotizing granulomata are the hallmark of tuberculosis infection; also seen in fungal infection and other AFB infections (eg: scrofula in children)
- Suppurative granulomata suggests nontuberculous AFB if in cervical node of a child; cat scratch disease is also primary a consideration
- Granulomas without necrosis can be suggestive of sarcoidosis, toxoplasma, or foreign body reaction in the right setting
- Series of passes for microbiologic cultures and/or PCR testing is recommended
 - Bartonella PCR (cat scratch disease), mycobacteria
- Serologic tests may be useful in a subset of cases (arthralgias, fever, leukopenia)
 - Differentiate Systemic Lupus Erythematosus Lymphadenitis from Kikuchi- Fujimoto's disease (histiocytic necrotizing lymphadenitis)
- **A florid granulomatous reaction can be present obscuring metastatic carcinoma, NHL, and HL**

Orell & Sterrett's. Fine Needle
Aspiration Cytology 5th Edition. 2012.

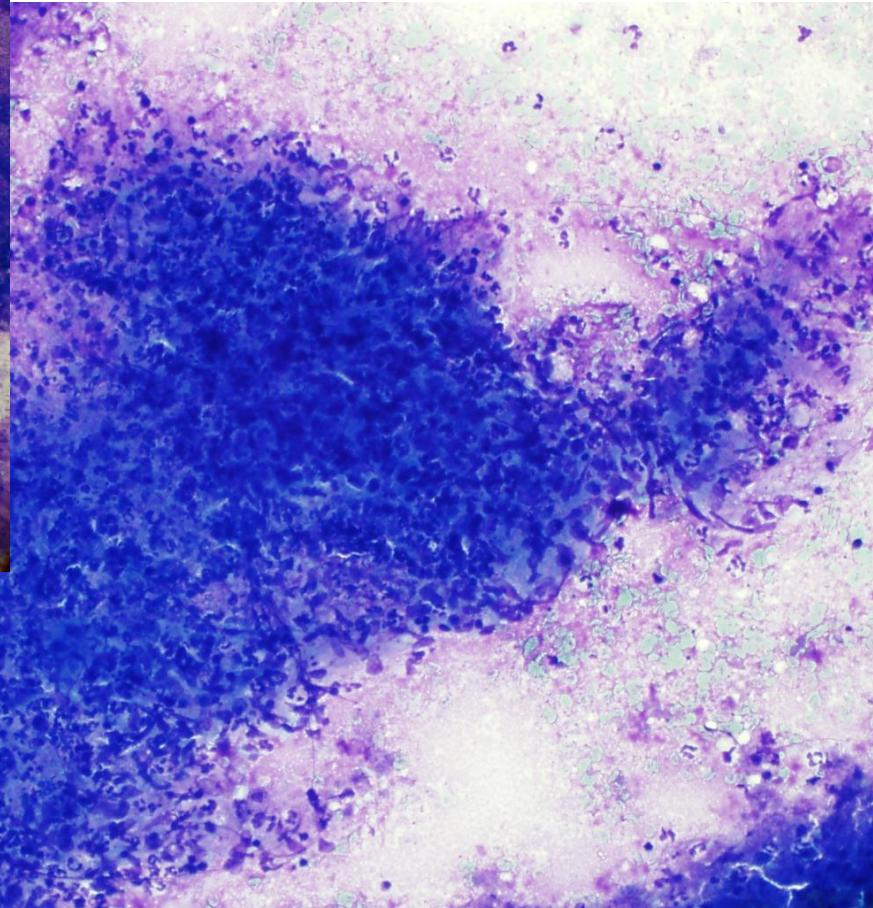
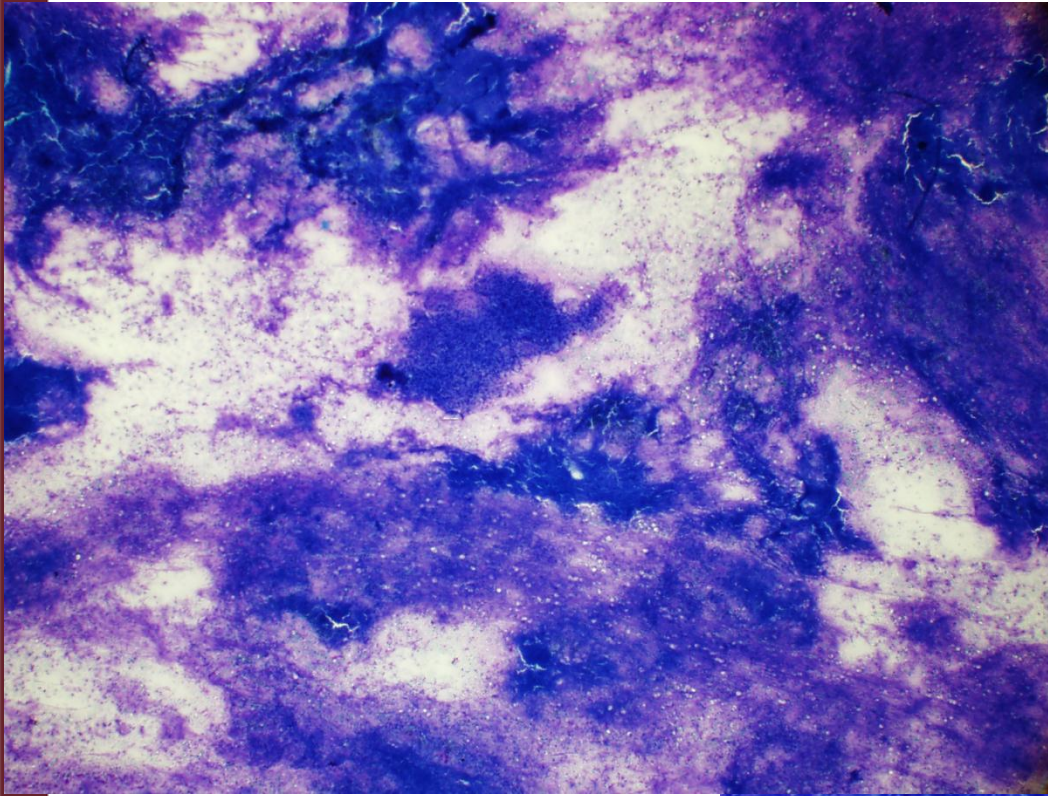


Non-necrotizing Granulomatous Inflammation



Sarcoidosis

Suppurative Necrotizing Granulomatous Inflammation



Kikuchi-Fujimoto's disease

Lymph Nodes: Metastatic Disease

- Diagnostic accuracy of FNA for metastatic disease ranges from 83-97%
- Cervical LAD is the most common presenting sign of malignant disease elsewhere in the head and neck
 - Squamous cell carcinoma (90% after age 40)
 - Nasopharyngeal carcinoma, salivary gland tumor metastases, thyroid carcinoma, melanoma, carcinomas from visceral organs
- 75% of branchial cysts occur in patient age 20-40.

Layfield LJ. Diagnostic
Cytopathology. 2007;
35(12):798-805



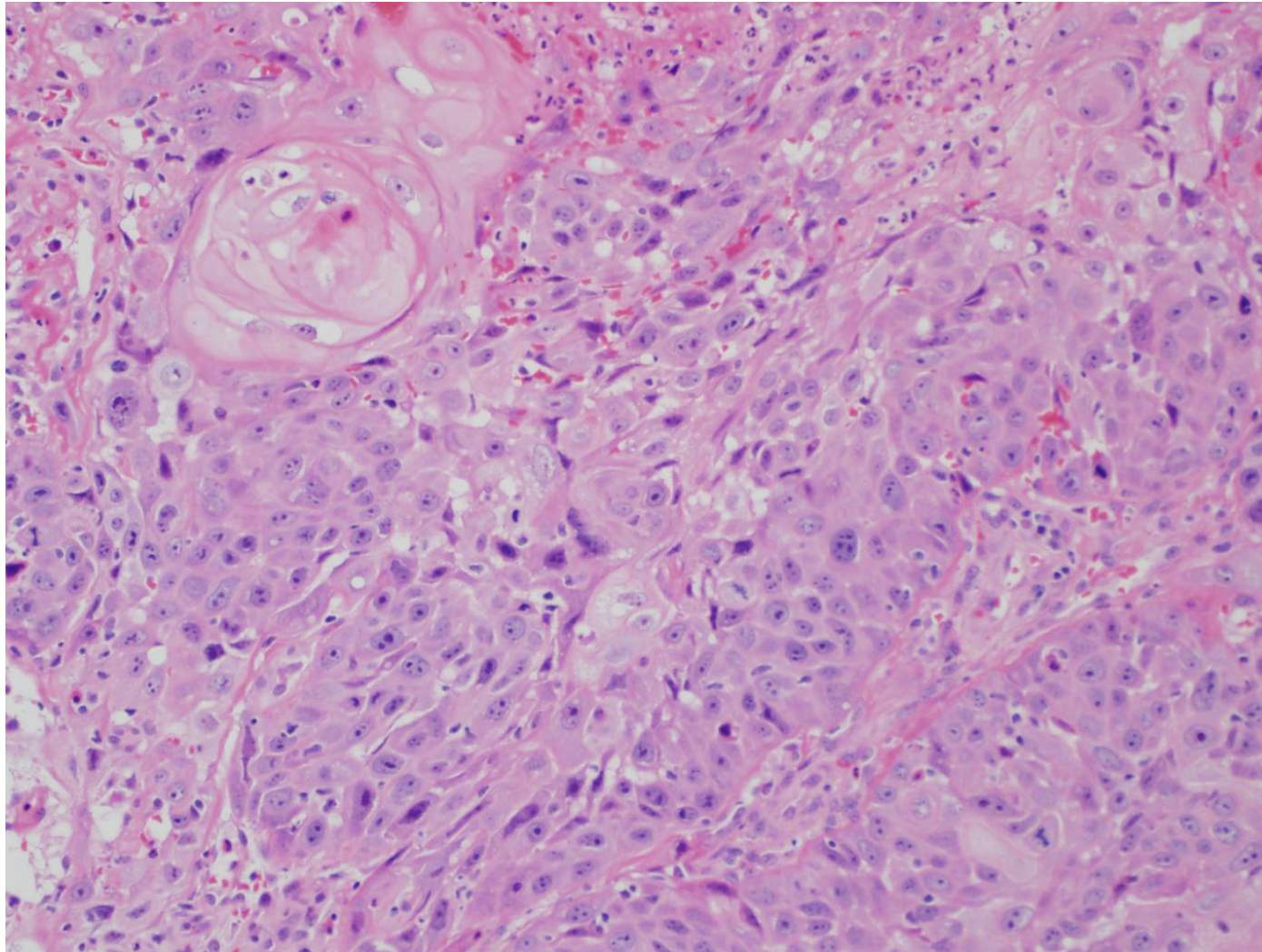
Classic FNA Cytomorphology: Benign Squamous Cysts versus SCCA

Benign Squamous-Lined Cysts	Squamous Cell Carcinoma
Abundant inflammation (PMNs)	Large number of squamous elements
Few squamous epithelial cells	Occasional nuclear hyperchromasia
Bland nuclear features in squamous cells	Occasional nuclear membrane irregularity
Crystals	High N/C ratio

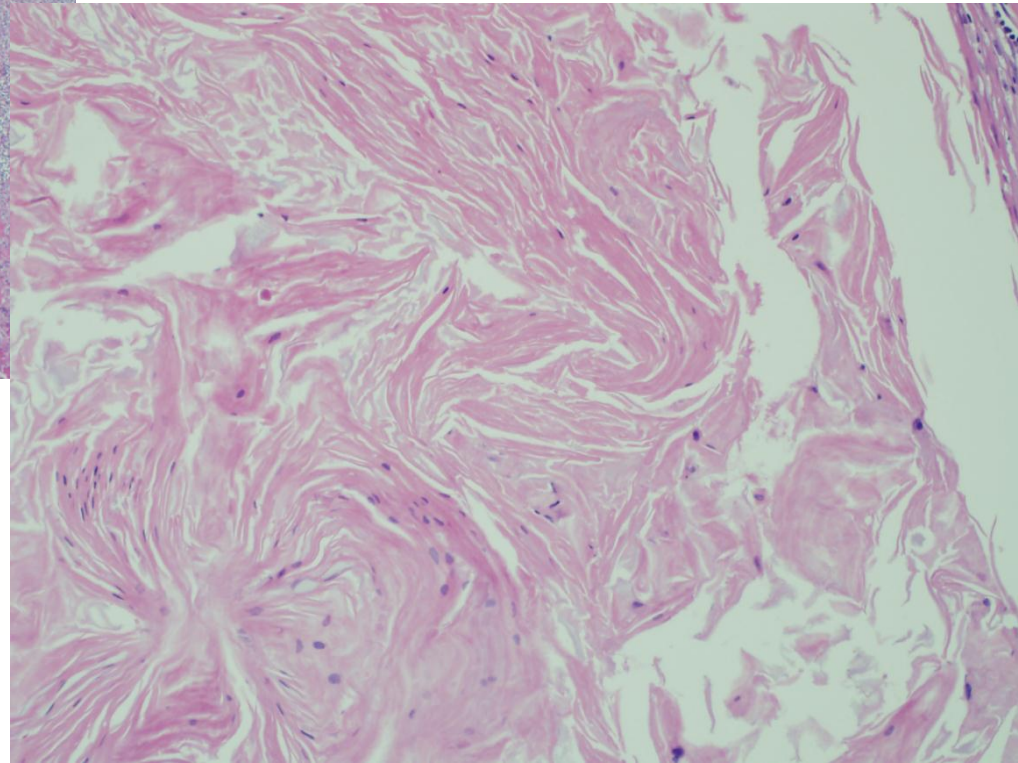
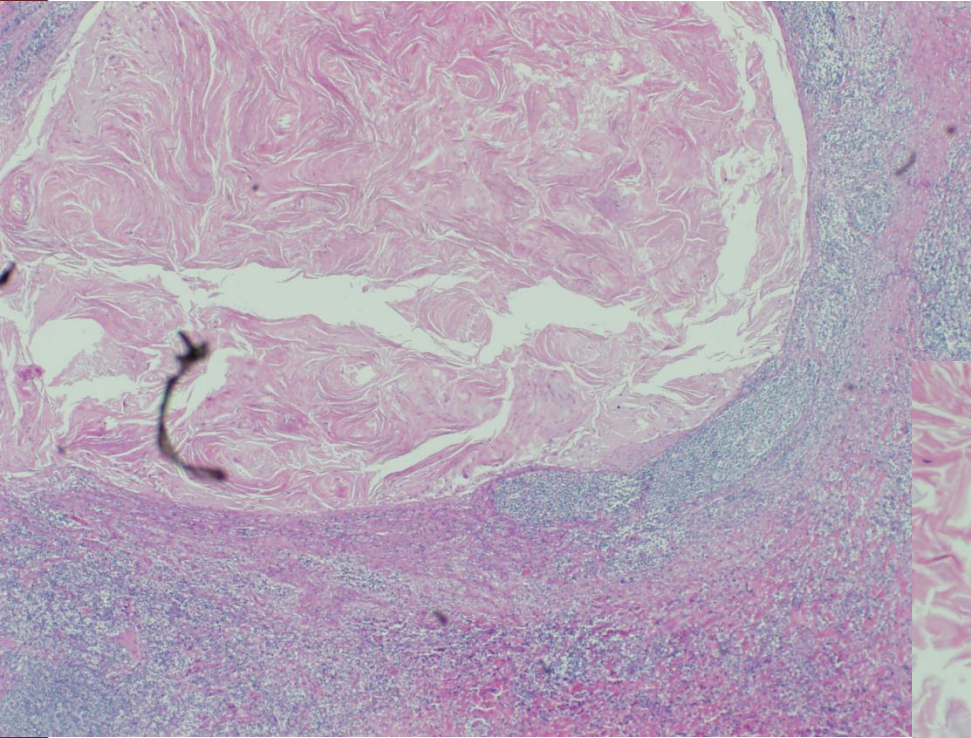
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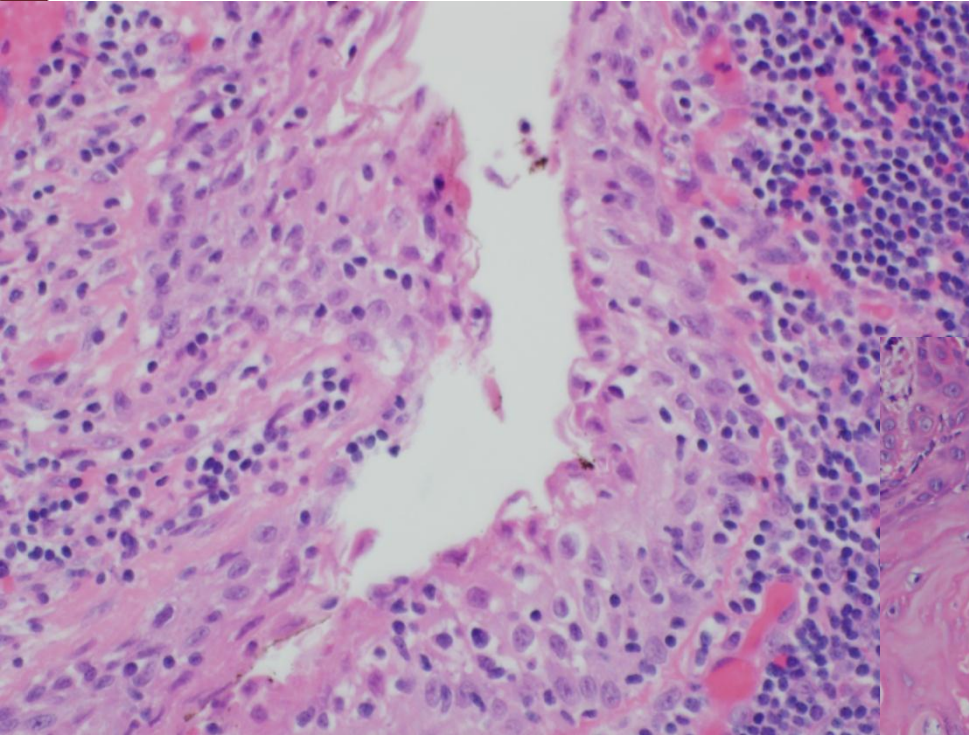
Lymph Nodes: Differentiating SCCA from Benign Epithelial Cysts



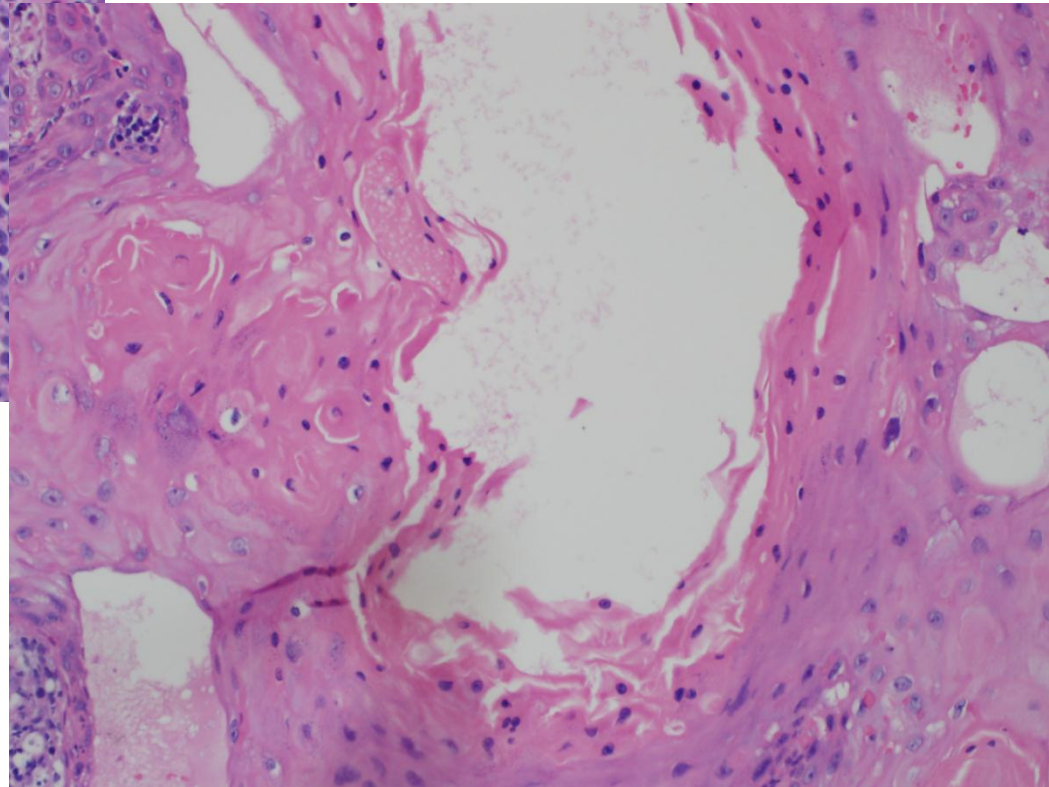
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Lymph Nodes: Differentiating SCCA from Benign Epithelial Cysts

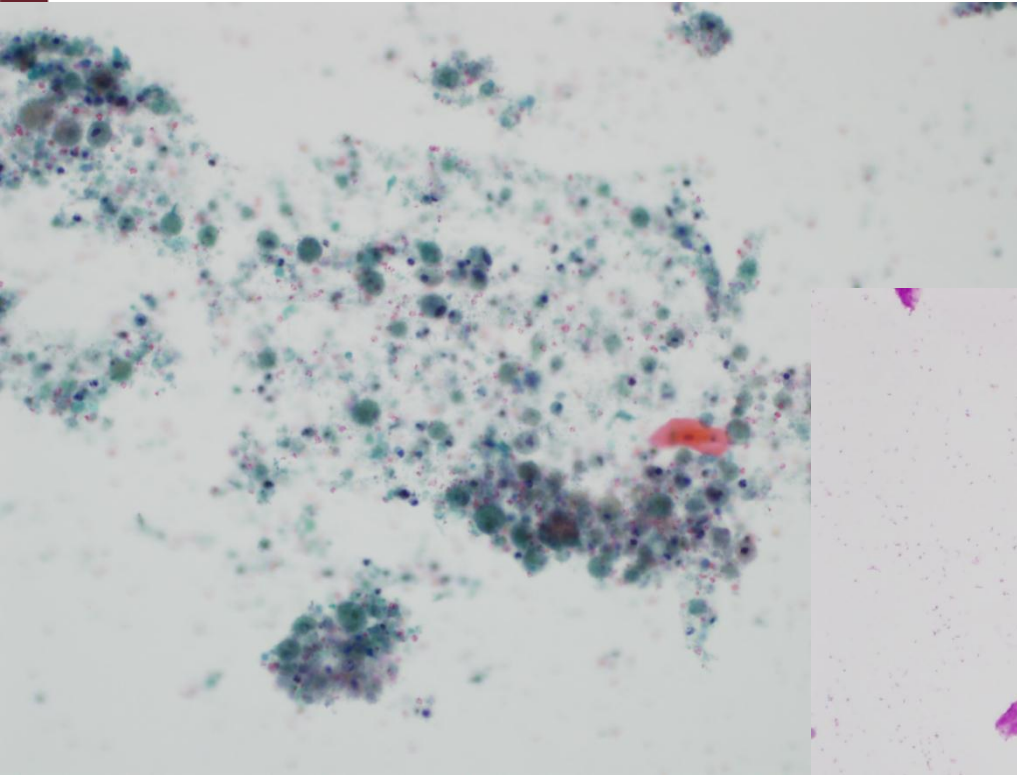


Metastatic SCCA



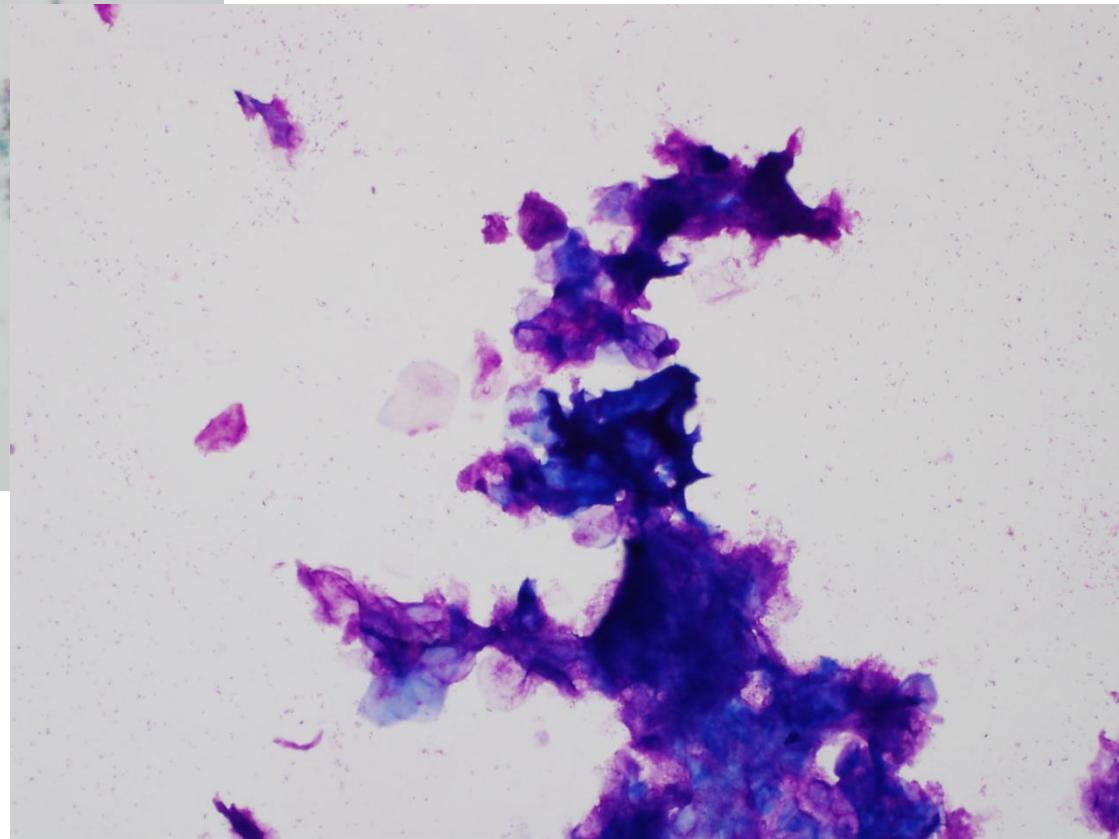
Branchial Cleft Cyst

Lymph Nodes: Differentiating SCCA from Benign Epithelial Cysts

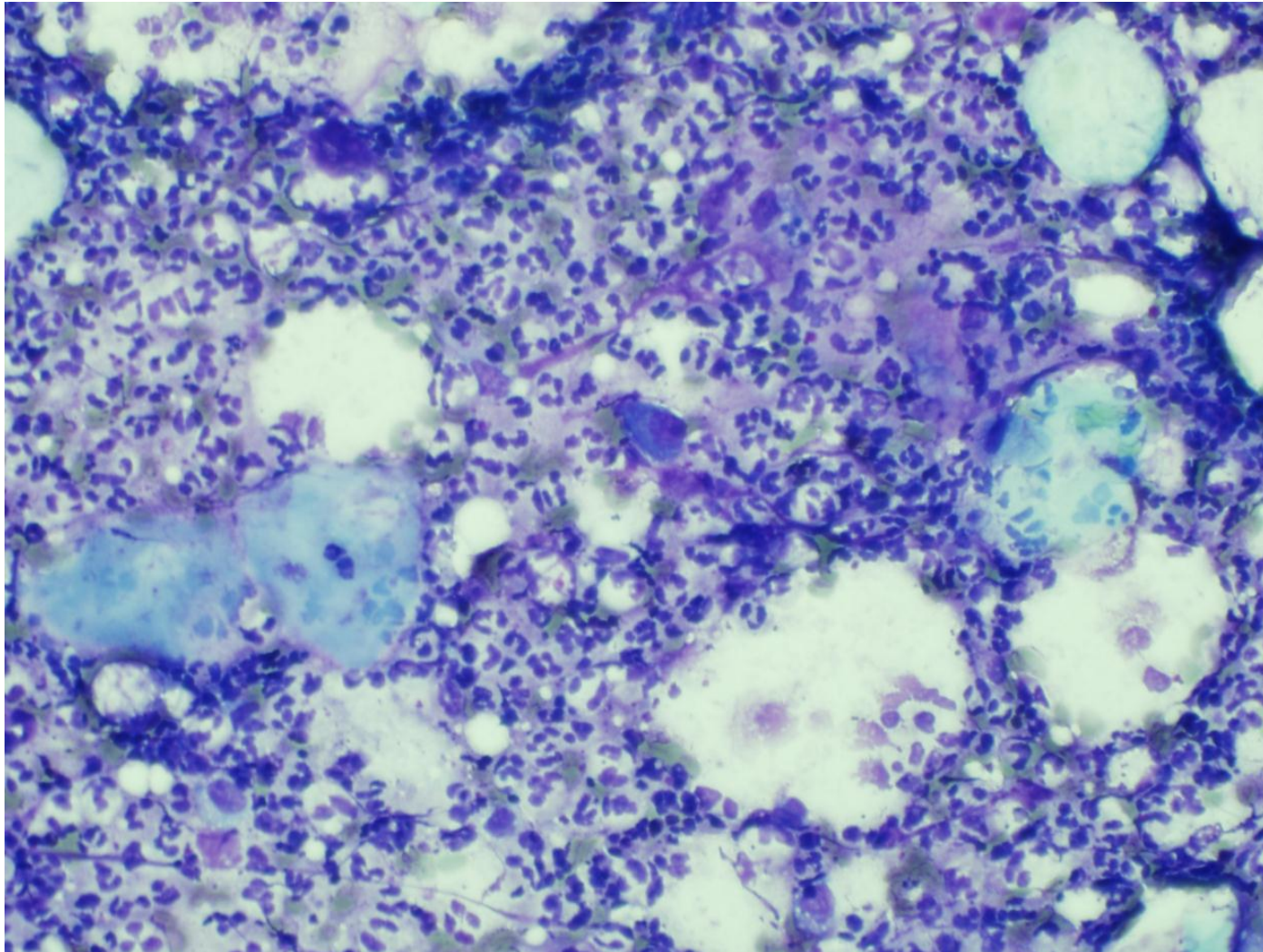


Thyroglossal duct cyst

Epidermal Inclusion Cyst

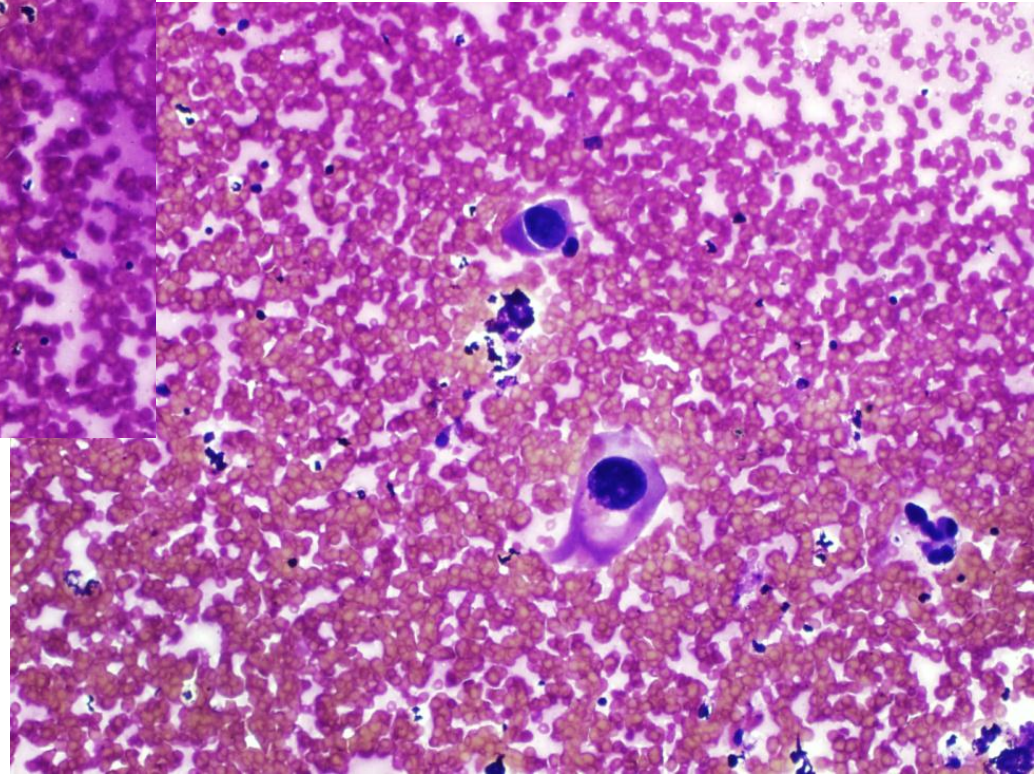
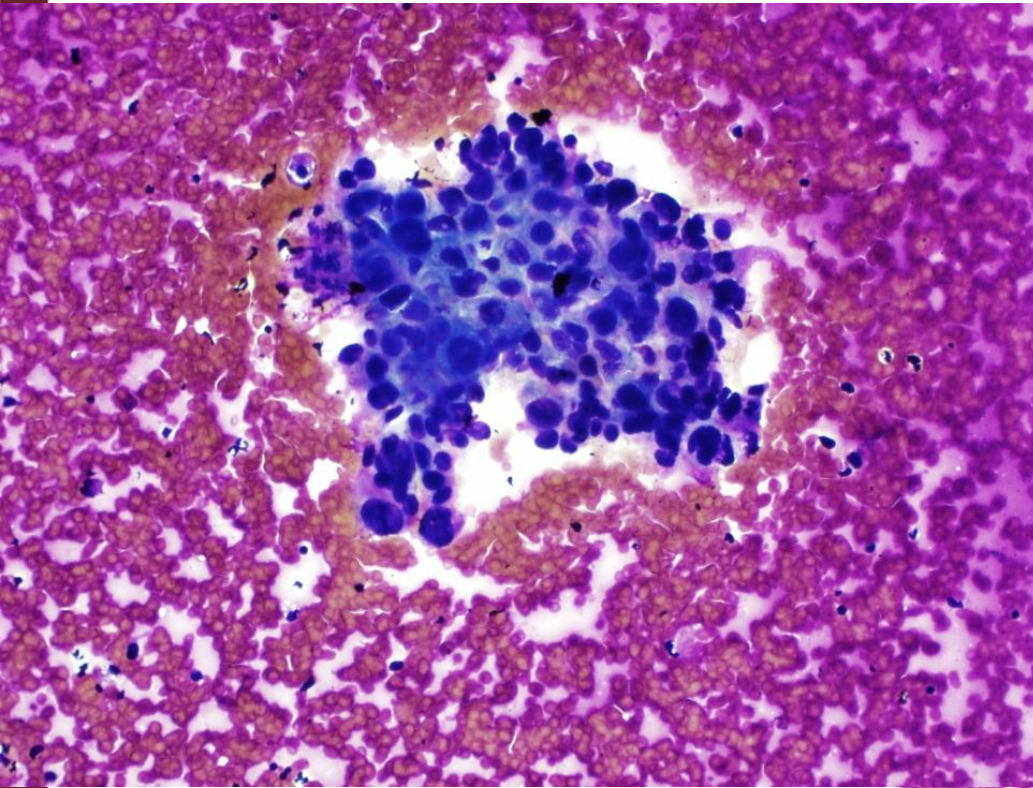


Lymph Nodes: Differentiating SCCA from Benign Epithelial Cysts

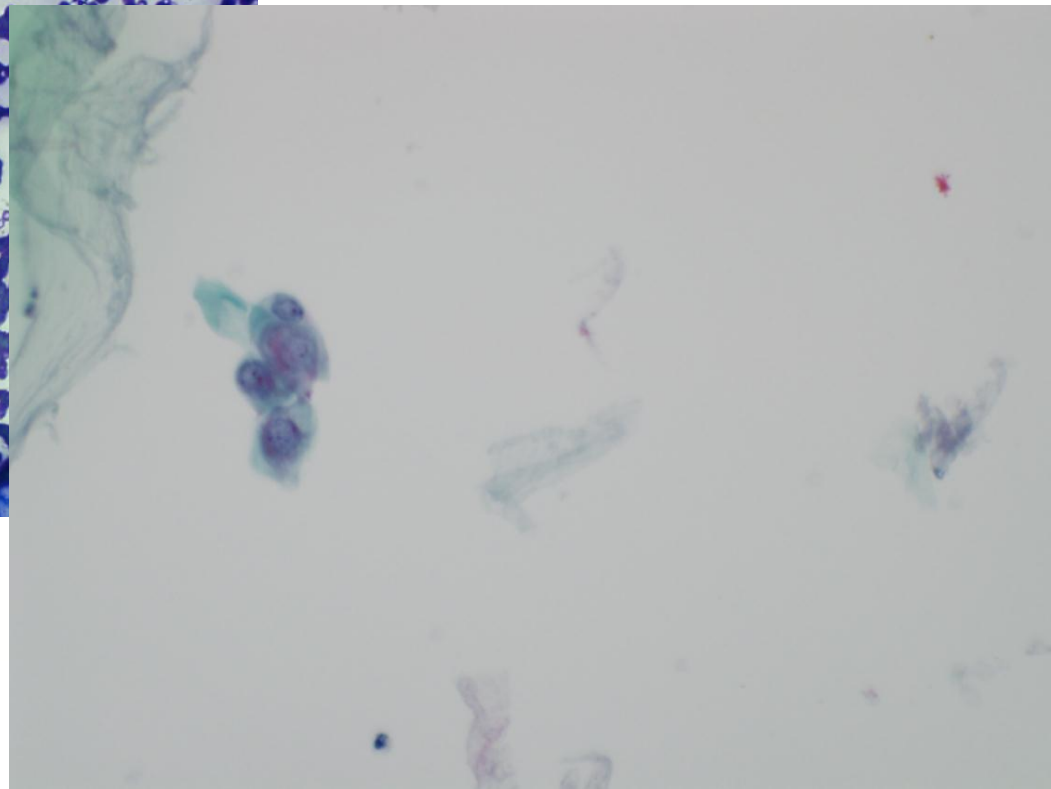
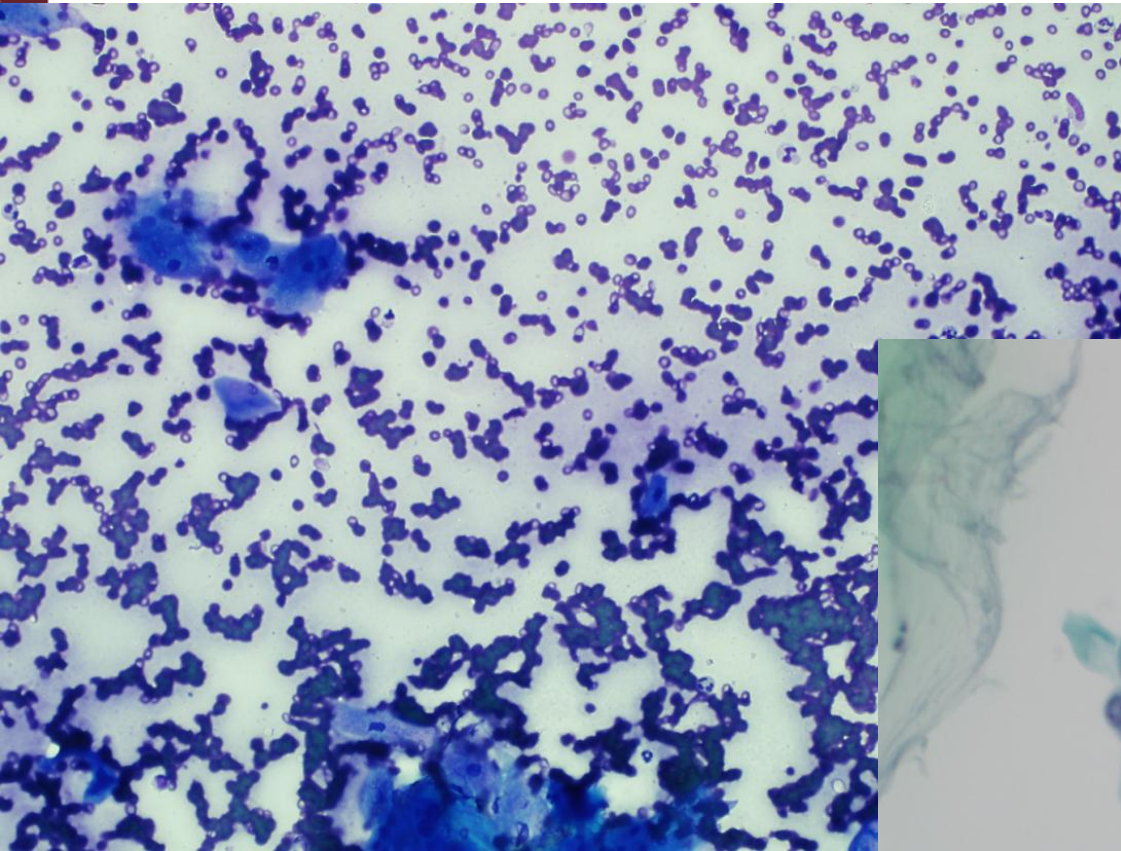


Inflamed EIC

Lymph Nodes: Differentiating SCCA from Benign Epithelial Cysts



Well-Differentiated SCCA



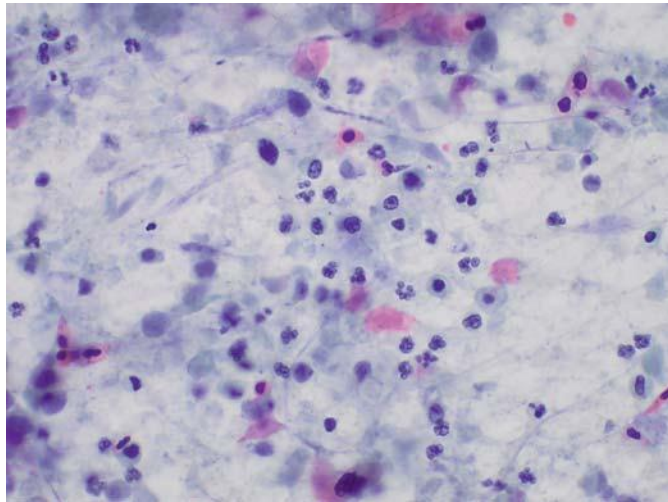
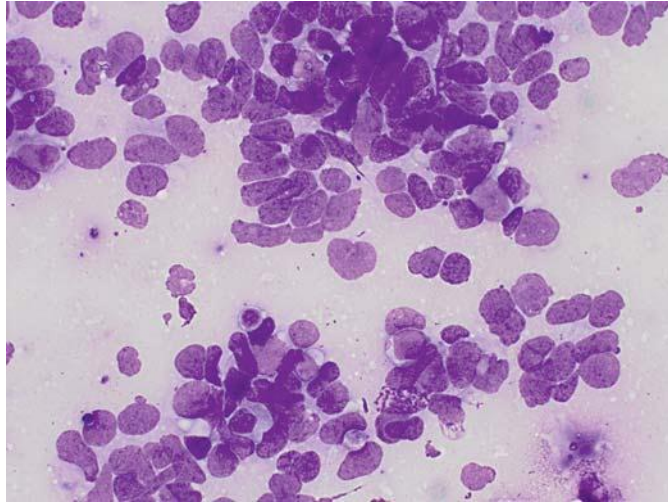
Options for Needle Rinse

- Patients with FNAs showing SCCA with no clinical evidence of a head and neck primary might benefit from HPV testing
- Patient's with HPV-related tumors show a greater response to radiation and overall improved survival compared to patients with non-HPV tumors

Jarboe EA et al. Diagnostic
Cytopathology.
2012;40(6):491-497



HPV-Associated SCCA of the Head and Neck



- Most commonly HPV driven carcinomas are poorly differentiated non-keratinizing tumors
- They may less frequently demonstrate cystic change with keratinization
- Many cases may share morphology with nasopharyngeal carcinoma (EBV ISH testing on a cell block may be of value)

Options for Needle Rinse to Assess for HPV Status

- Rinse for cell block with immunohistochemical staining for p16 or DNA in situ hybridization (ISH)
- Rinse into Thin-Prep[®] Pap Test PreservCyt[®] solution for either Hybrid Capture II or Cervista[™] HPV HR testing



Limitations of HPV Testing

- p16 is highly sensitive (near 100%) for the presence of HPV infection but with specificity of ~80%.
- p16 overexpression has been found in a subset of non-HPV associated SCCA, small cell carcinoma and sinonasal undifferentiated carcinoma
- p16 may be expressed in normal tonsillar crypt epithelium as well as within the benign epithelium of a branchial cleft cyst
- DNA ISH testing has a lower sensitivity with a higher specificity for HPV
- Neither p16 nor DNA ISH has a consensus standard guideline for the interpretation of a positive

Krane JF. *Acta Cytologica*.
2013;57:117-126.



Recommendations

- Positive HPV testing in the presence of SCCA morphology can function as a standard part of cytologic workup
- Positive HPV testing can be used in FNAs of lung SCCAs as evidence of metastatic involvement from a head and neck primary
- Positive HPV testing in cases that are nondiagnostic on cytomorphology should be treated with caution
- Adult patients with aspirates showing squamous elements; recommend excision liberally
- Don't forget about other metastatic sources (approximately 50% of supraclavicular metastases originate from primary carcinomas below the diaphragm)

Krane JF. Acta Cytologica.
2013;57:117-126.

Layfield LJ. Diagnostic Cytopathology.
2007; 35(12):798-805

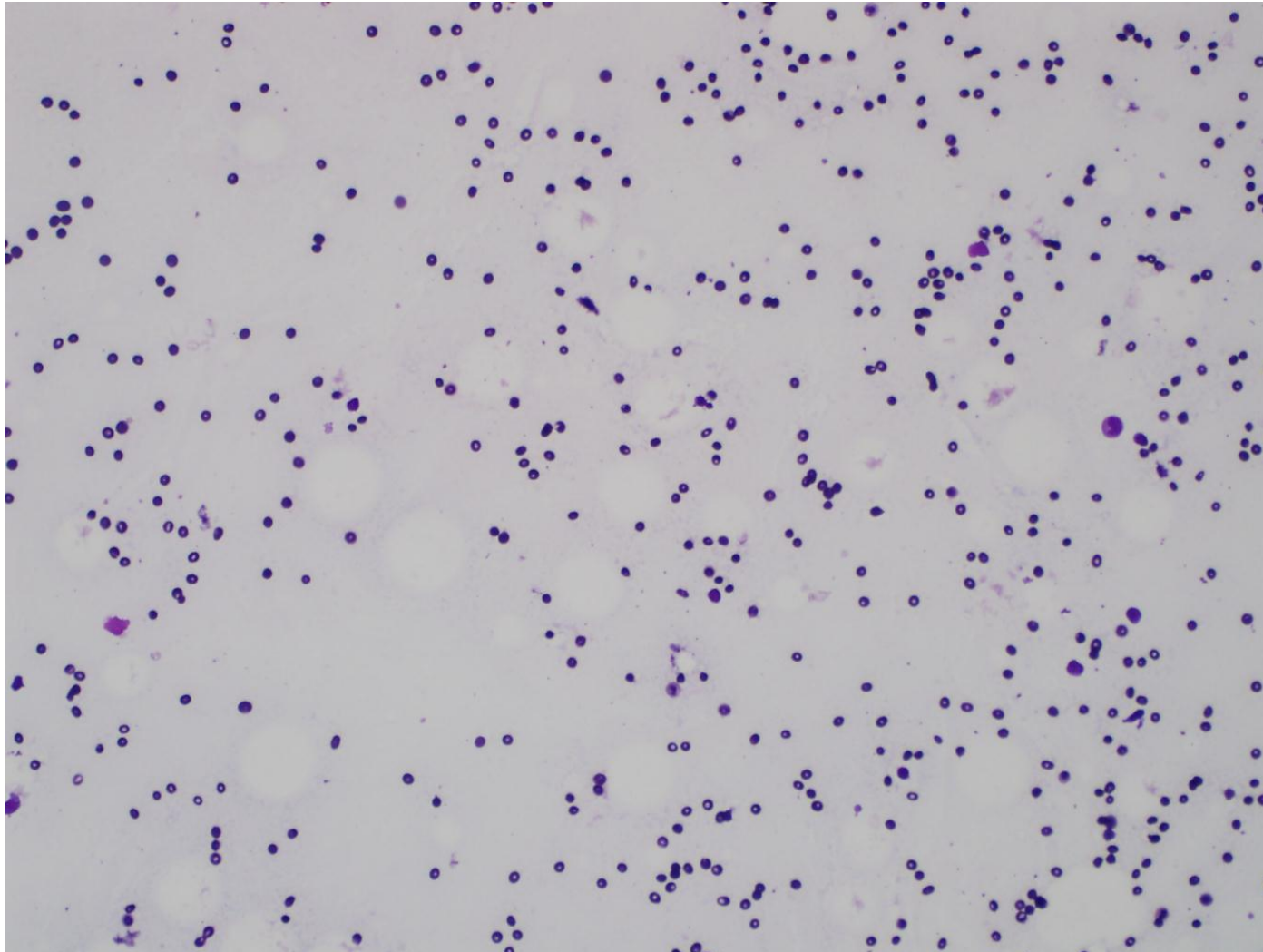


Reactive/Reparative Versus Mesenchymal Neoplasm

- Many patients evaluated for head and neck FNAs have had prior surgery or chemo-radiation treatment
- A variety of benign and malignant mesenchymal neoplasms involve the soft tissues of the head and neck
- Thus a common diagnostic dilemma occurs with respect to spindle cell lesions

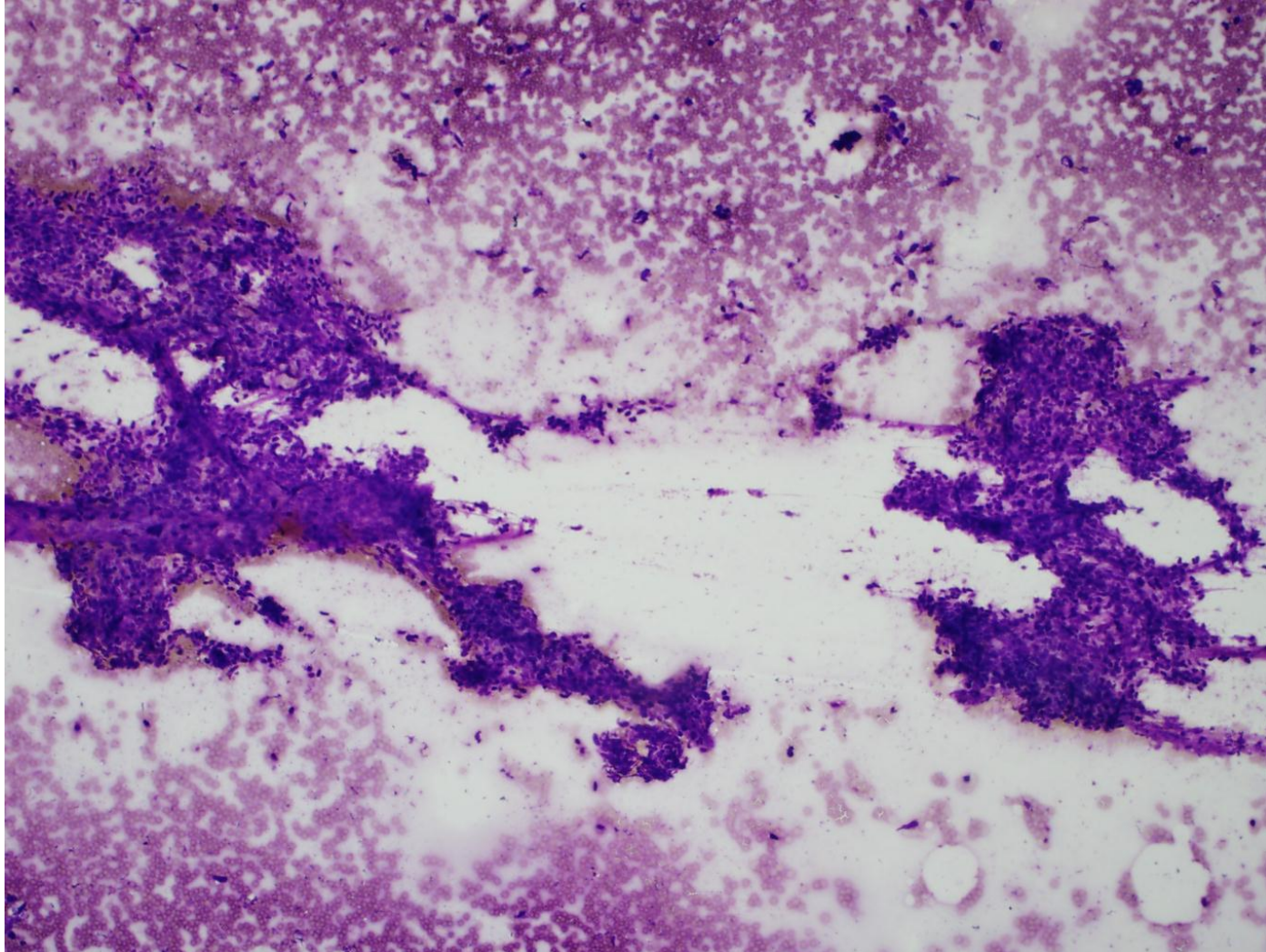


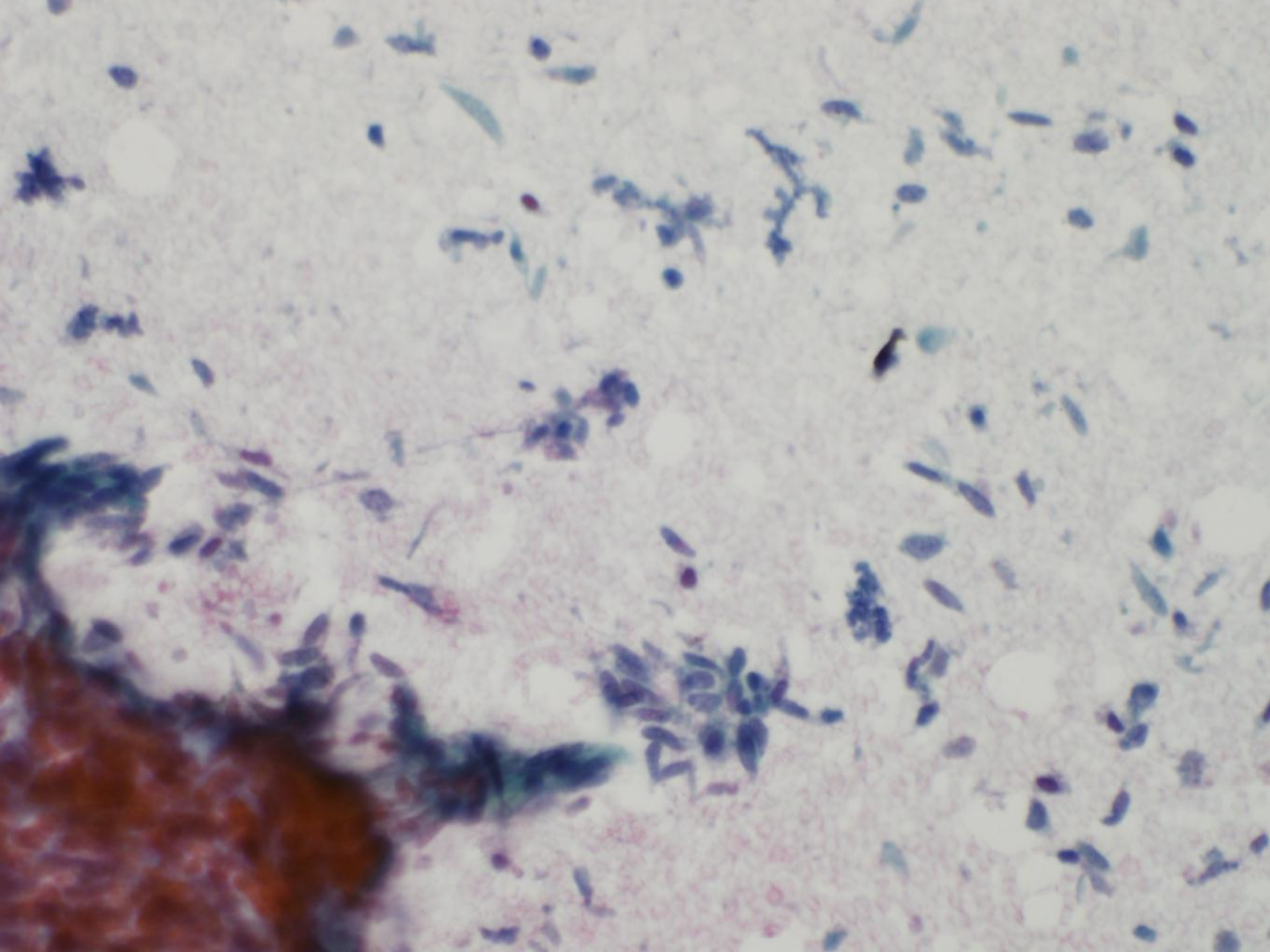
Sometimes it Really is Nothing: 2 cm nodule 10 days postoperative

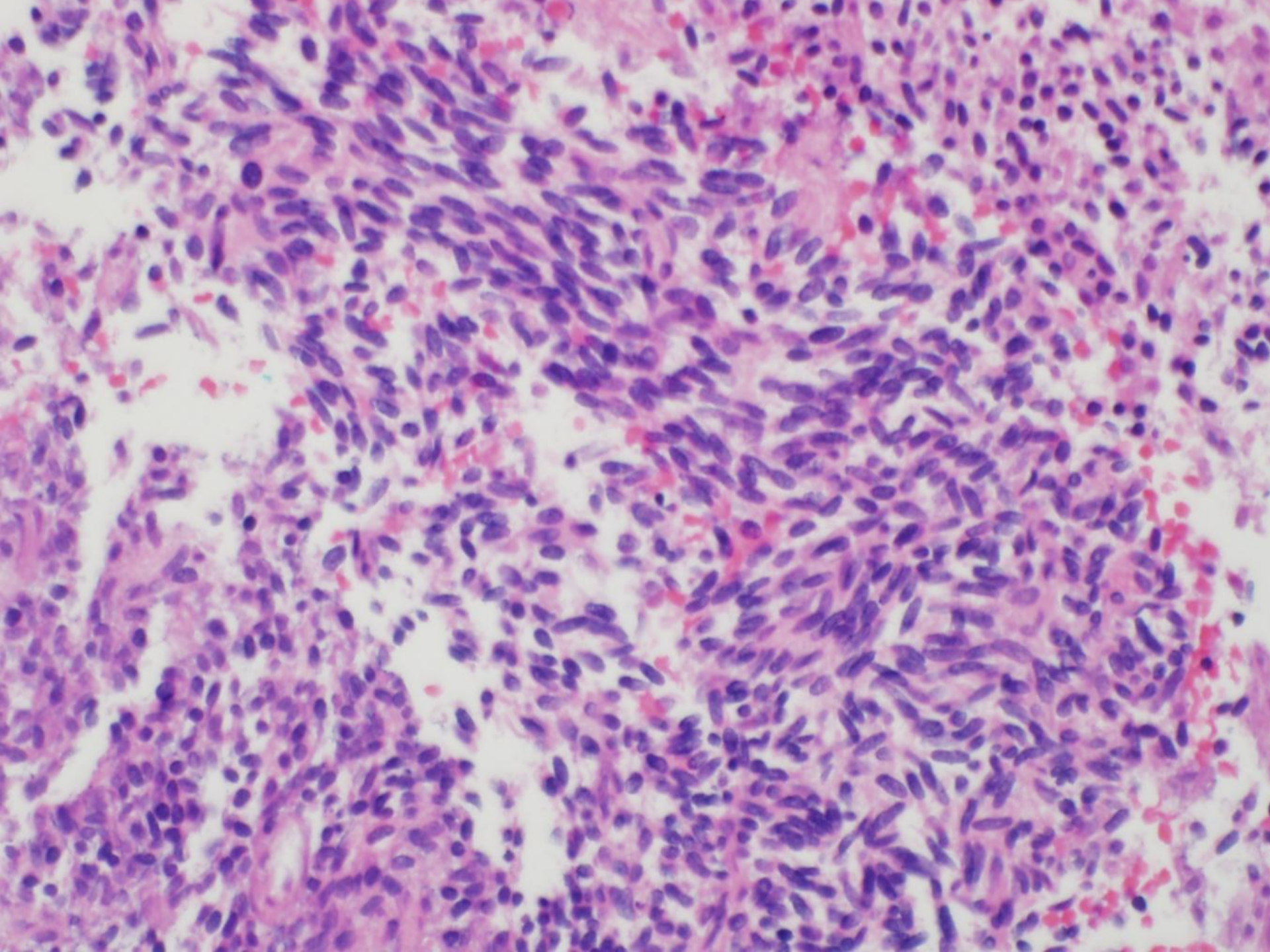


Seroma

30 year old male with left parapharyngeal neck mass







Synovial Sarcoma

- 9% present in the head and neck (AFIP series); second most common site after the extremities
- Hypercellular smears demonstrating both cohesive and dispersed patterns
- Majority are monophasic in appearance with a uniform proliferation of spindled to rounded cells
- Chromatin is finely granular and cell size is small to medium
- Single stripped, unipolar or bipolar cells are common
- +/- hemangiopericytomas-like vessels
- Look for mitoses



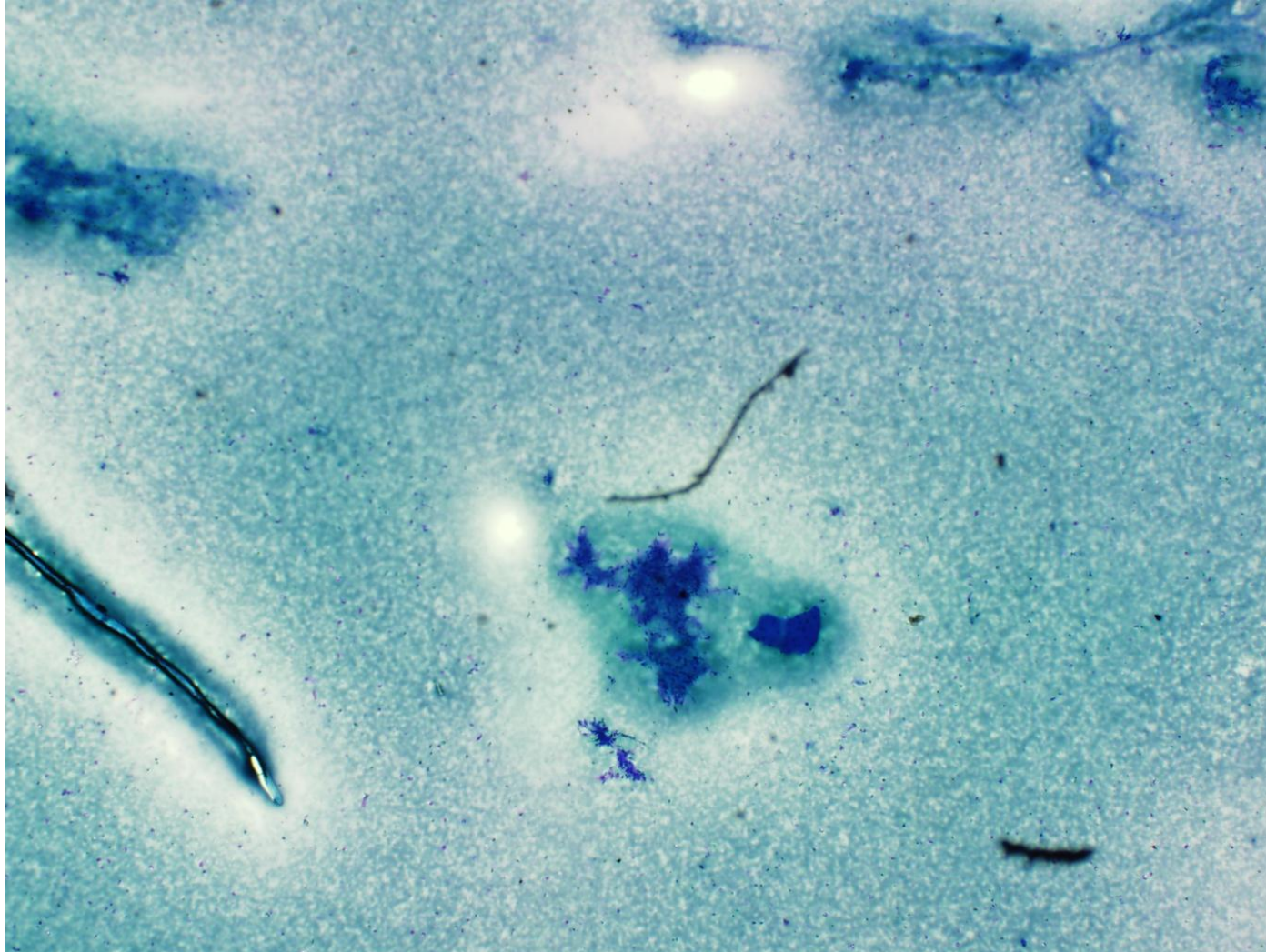
Synovial Sarcoma Rinse Options

- Cell block material is optimal
- Immunohistochemical assessment:
 - Majority show focal positivity for EMA and cytokeratins (CK7 is particularly consistent)
 - CD99 positive in 60-70%
 - Diffuse Bcl2 positivity
 - TLE1 is positive in >90% of synovial sarcomas
 - Note up to 30% of synovial sarcomas show focal S100 positivity
- Molecular diagnostics yields the characteristic t(X;18) SYT-SSX translocation

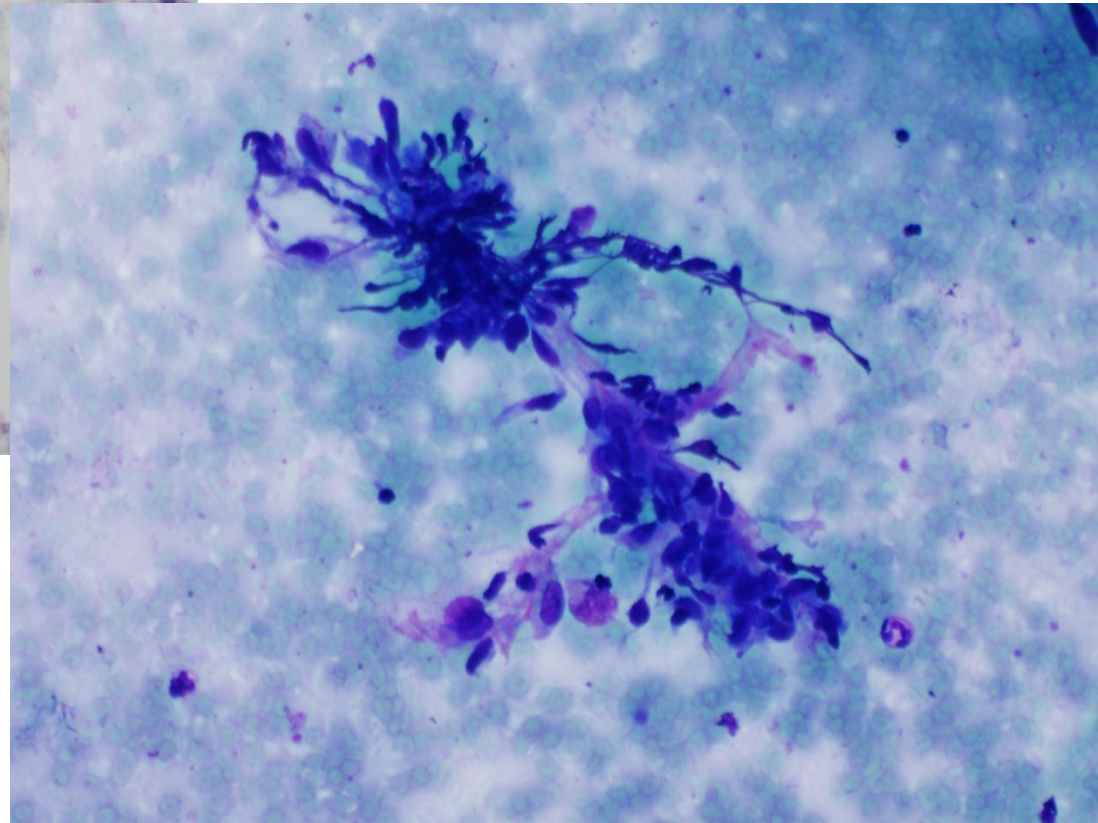
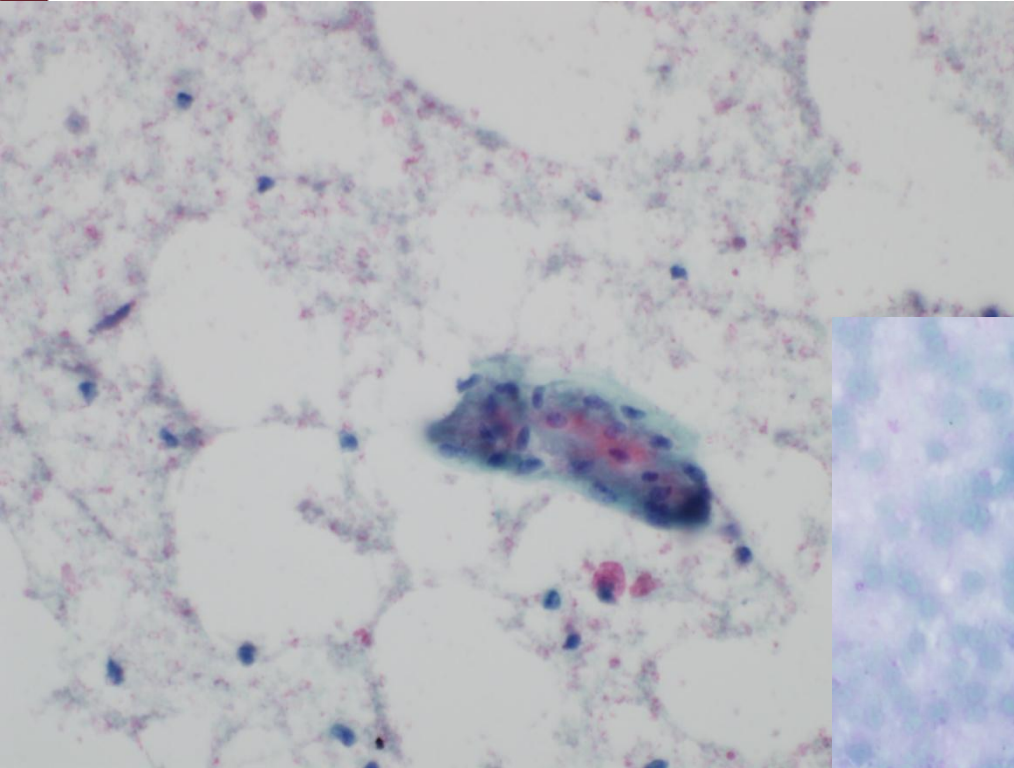
Sharon Weiss and John Goldblum. Enzinger & Weiss's Soft Tissue Tumors. 2008.



37 year old male with central neck mass adjacent to central line



37 year old male with central neck mass adjacent to central line



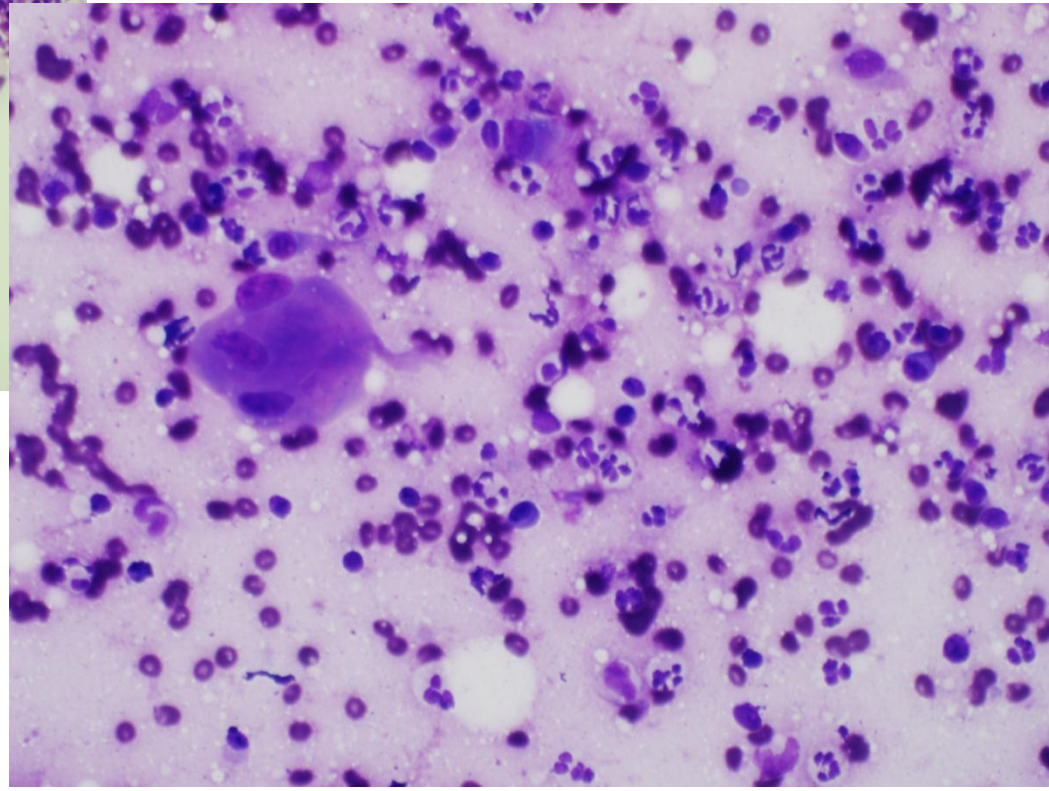
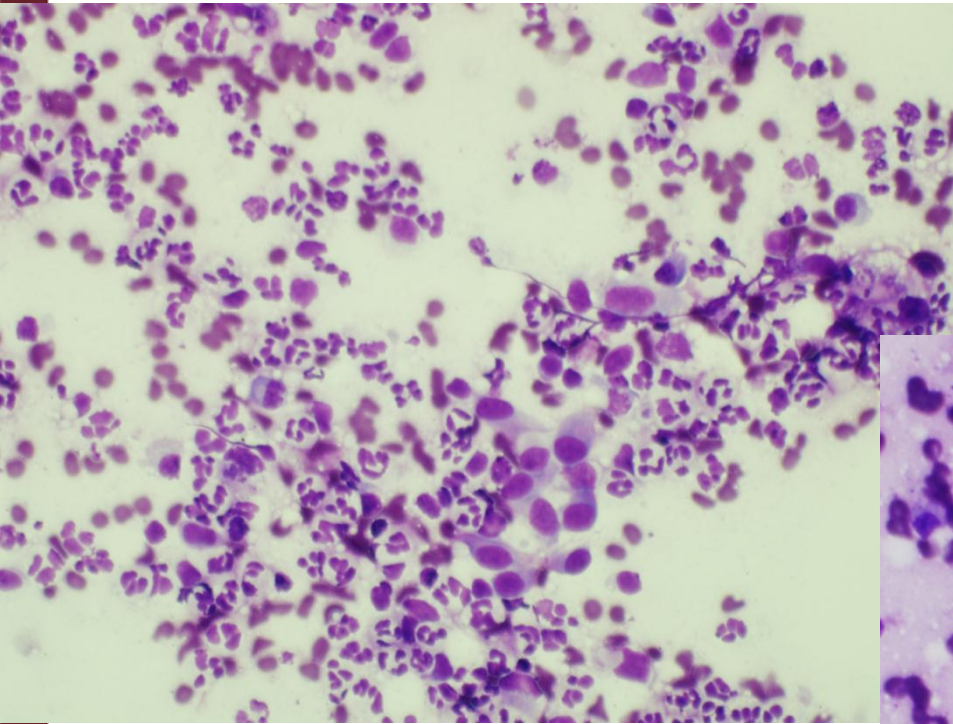
Nodular Fasciitis

- Relatively common fibrous proliferation typically occurring in subcutaneous tissue
- Head and neck (including the salivary gland) is among the most common sites
- Typical cytomorphology:
 - moderately cellular smears
 - often a myxoid background
 - numerous grouped/dispersed spindled myofibroblasts
 - abundant cytoplasm with tapering ends and ill-defined cell borders
 - **lack of hyperchromasia**
 - **inflammatory cells**
 - branching vessels
- The key to diagnosis is often suggested by the clinical presentation (rapidly growing subcutaneous mass smaller than 2 cm)

Edmund S. Cibas and Barbara Ducatman. *Cytology Diagnostic Principles and Clinical Correlates*. 2009.



38 year old female s/p thyroidectomy and radiation for PTC; now central neck lesion



Radiation/reparative changes
and suture granuloma

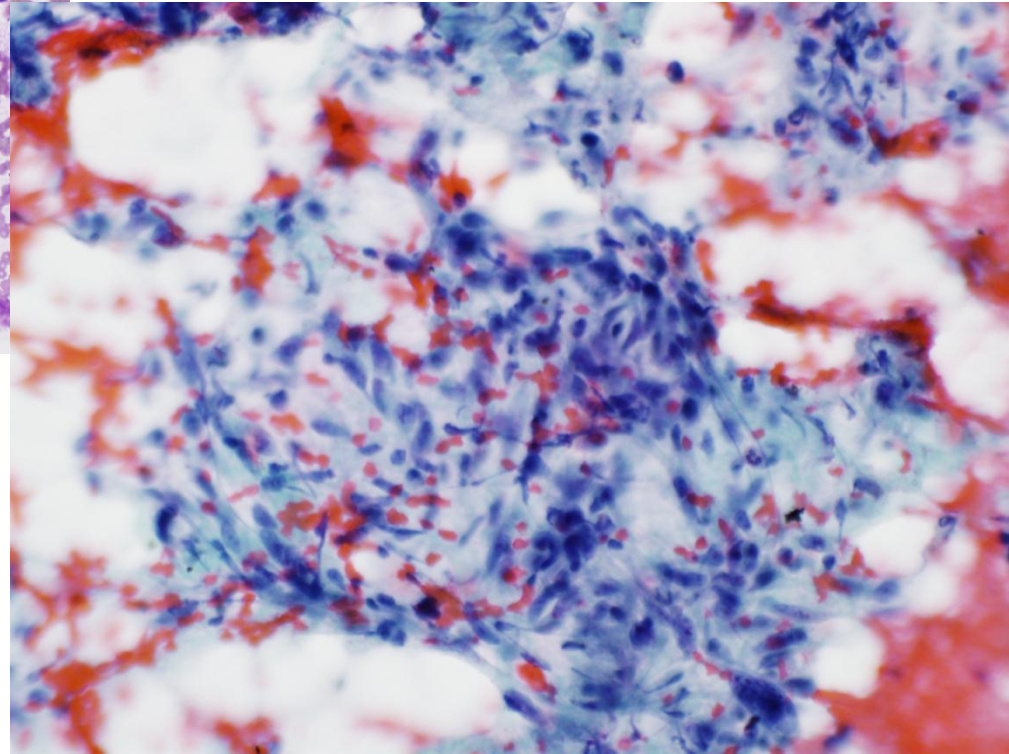
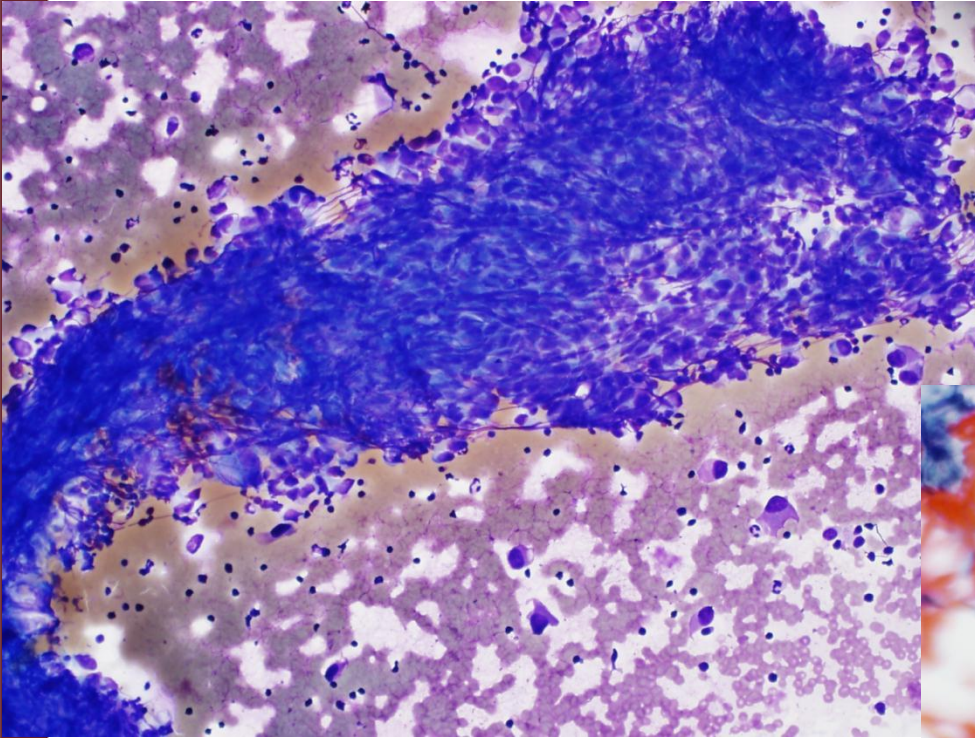
Reactive/Reparative Changes

- Benign fibrous proliferations can have a spectrum of appearance
- If prior radiation may have large cells with irregular nuclei, multinucleation, **with retention of a low N/C ratio**
- With resolution the inflammatory background may diminish
- Over time (healing) the plump myofibroblasts become slender with less conspicuous nucleoli
- **The presence of significant pleomorphism, hyperchromasia, and atypical mitotic figures suggests malignancy**
- An excision in this case showed a suture granuloma with surrounding reactive radiation-type fibroblasts

Richard M. Demay. The Art & Science of Cytopathology.

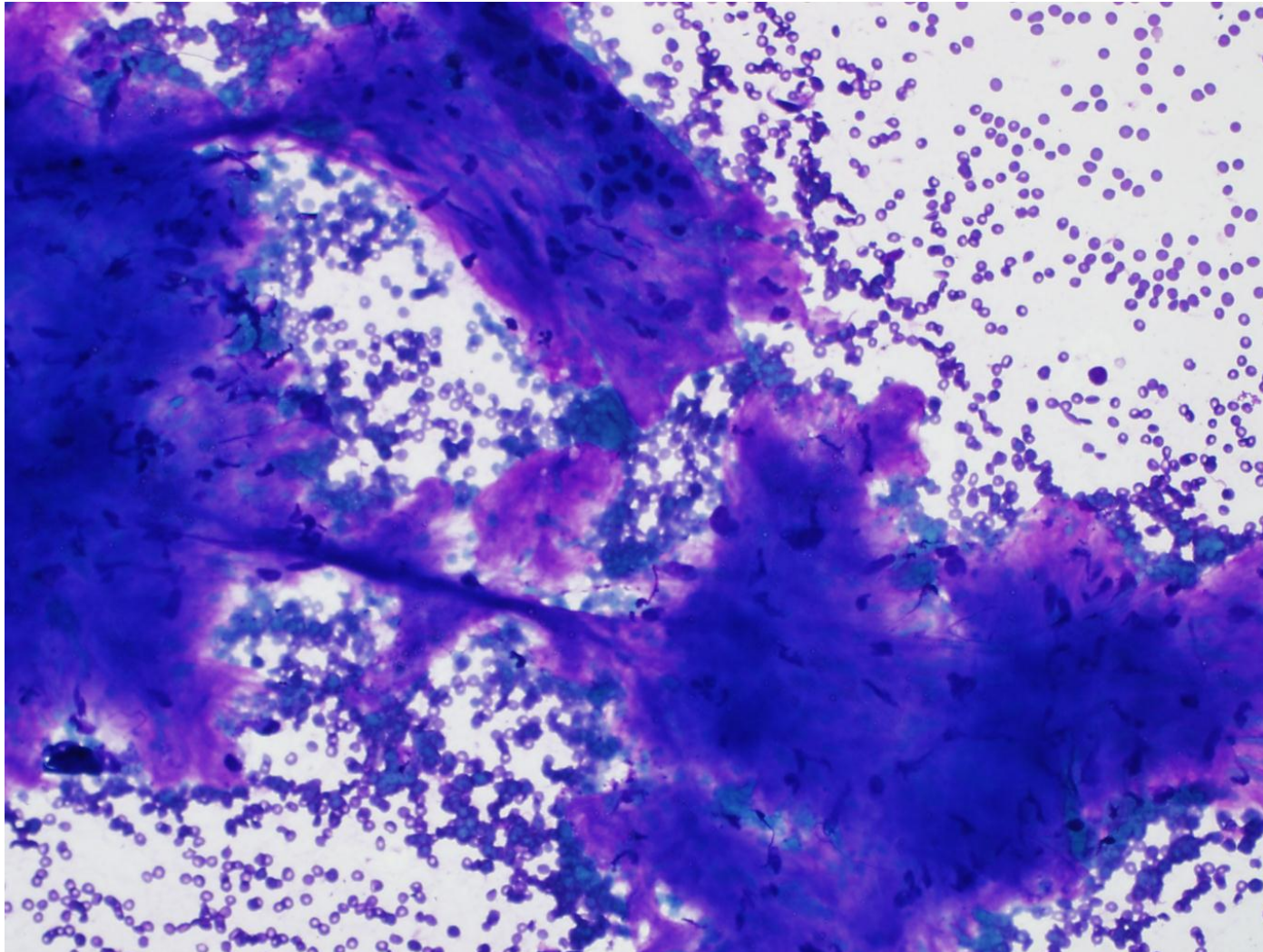


77 year old male with a 3.0 cm blue nodule behind the right ear

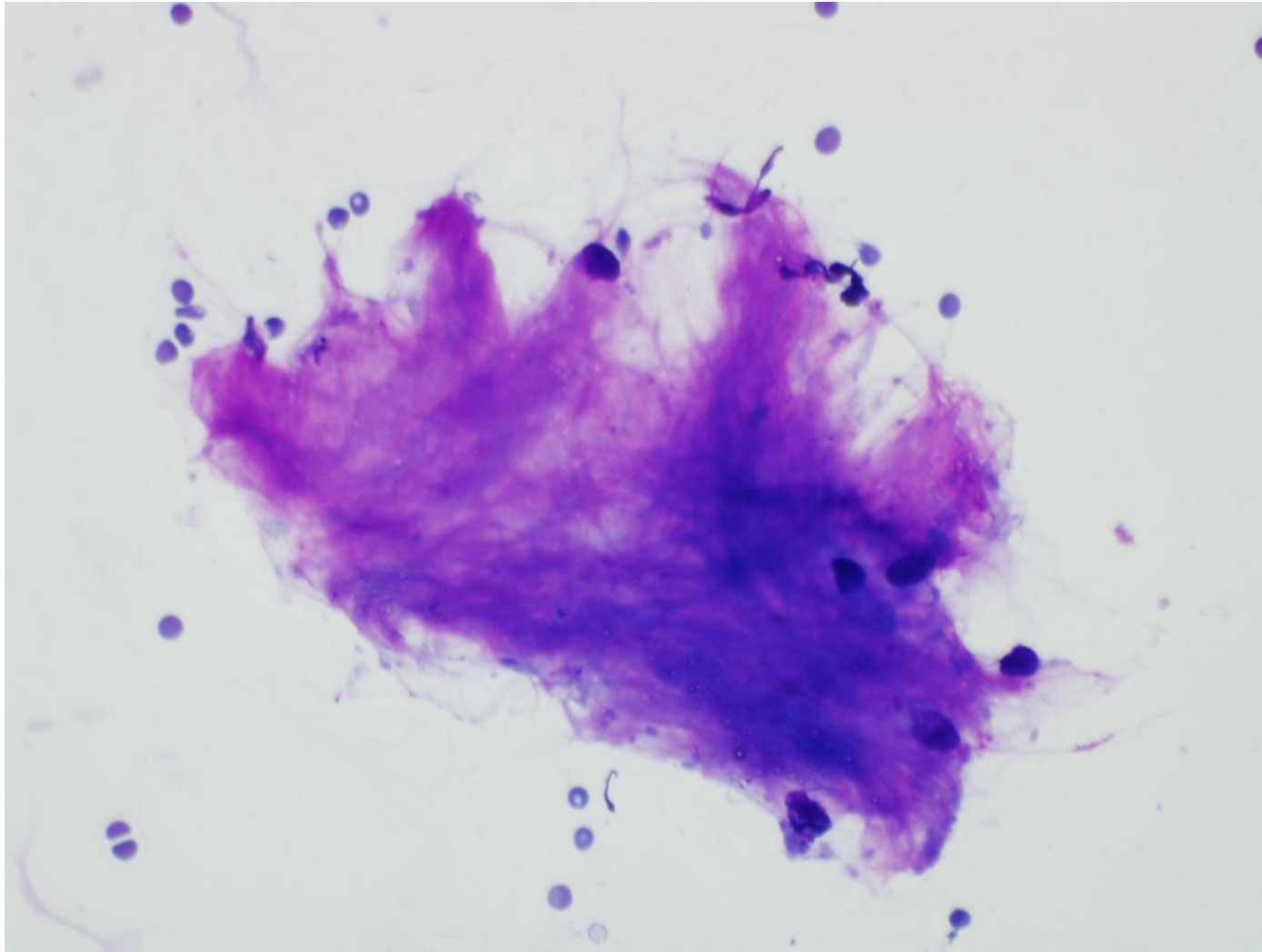


Angiosarcoma

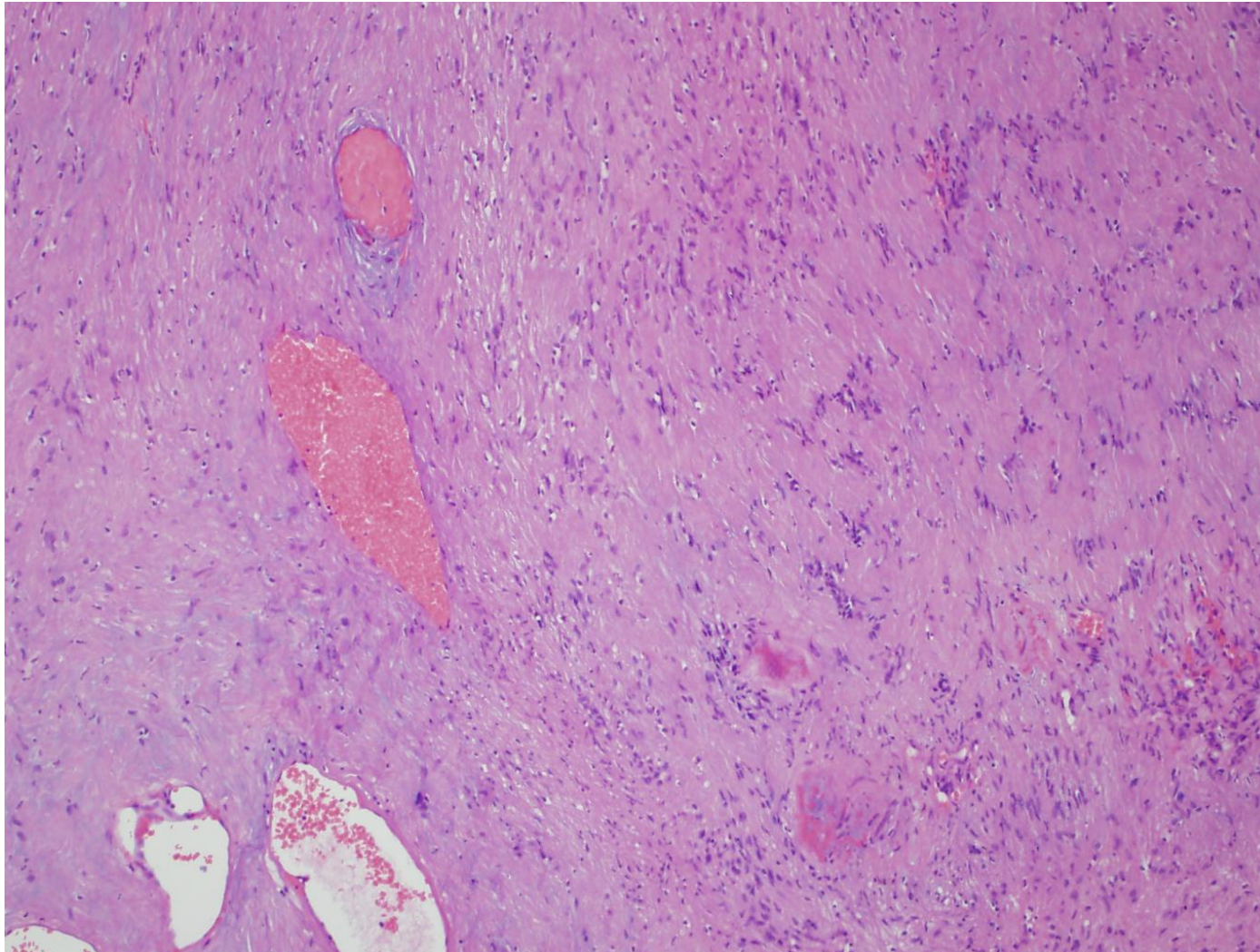
24 year-old with a 4 cm paratonsillar mass



24 year-old with a 4 cm paratonsillar mass



Schwannoma

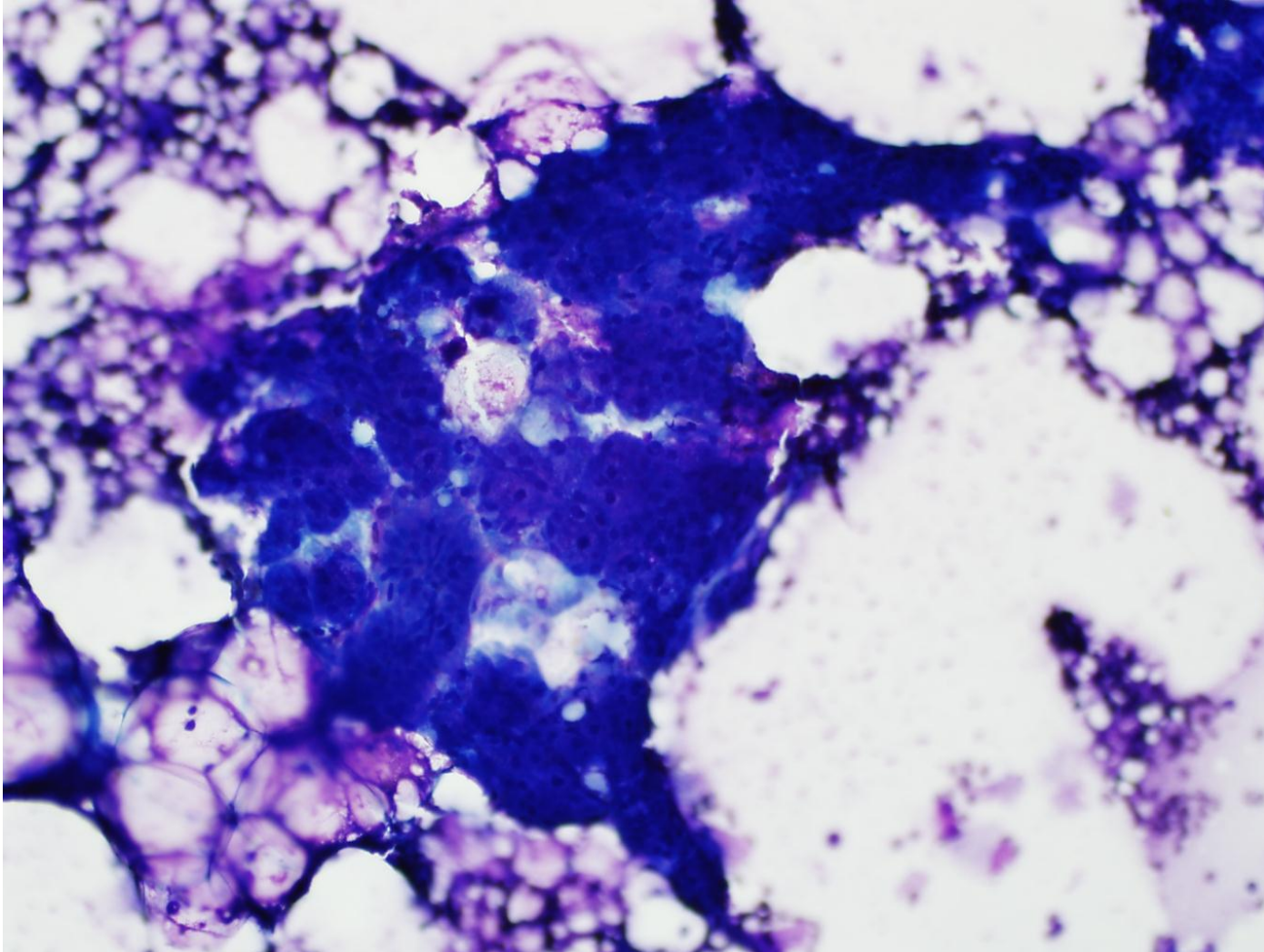


Schwannoma

- The tumors have a predilection for the head and neck, as well as the flexor surfaces of the upper and lower extremities
- Cytomorphology:
 - Variable cellularity
 - Tissue fragments of cohesive cells (Antoni A)
 - Dispersed cells with myxoid background (Antoni B)
 - **Most typical is the fibrillar appearance of the stroma in fragments**
 - Nuclei are long, slender, with pointed ends or are bent (fishhook)
 - Can be moderate pleomorphism but chromatin is open and bland
 - Pain during FNA procedure can be a good clue to nerve sheath tumor



Salivary Gland Lesions



FNA and Salivary Gland Lesions

- Cytologic diagnoses of malignant tumors were confirmed histologically in 93%
- Cytologic diagnoses of benign tumors were confirmed on histology in 95%
- Cytologic diagnoses of inflammatory lesions were confirmed histologically in 73%
- Cytologic diagnoses of benign salivary gland tissue confirmed histologically in 18%

Collela G et al. J Oral Maxillofac Surg. 2010;68: 2146-2153



Salivary Gland: Malignant Neoplasms

- Acinic cell carcinoma
- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Adenocarcinoma NOS
- Squamous cell carcinoma
- Malignant lymphomas
- Metastatic tumors
 - Account for 359/415 malignant tumors (86%)

Collela G et al. J Oral Maxillofac Surg. 2010;68: 2146-2153



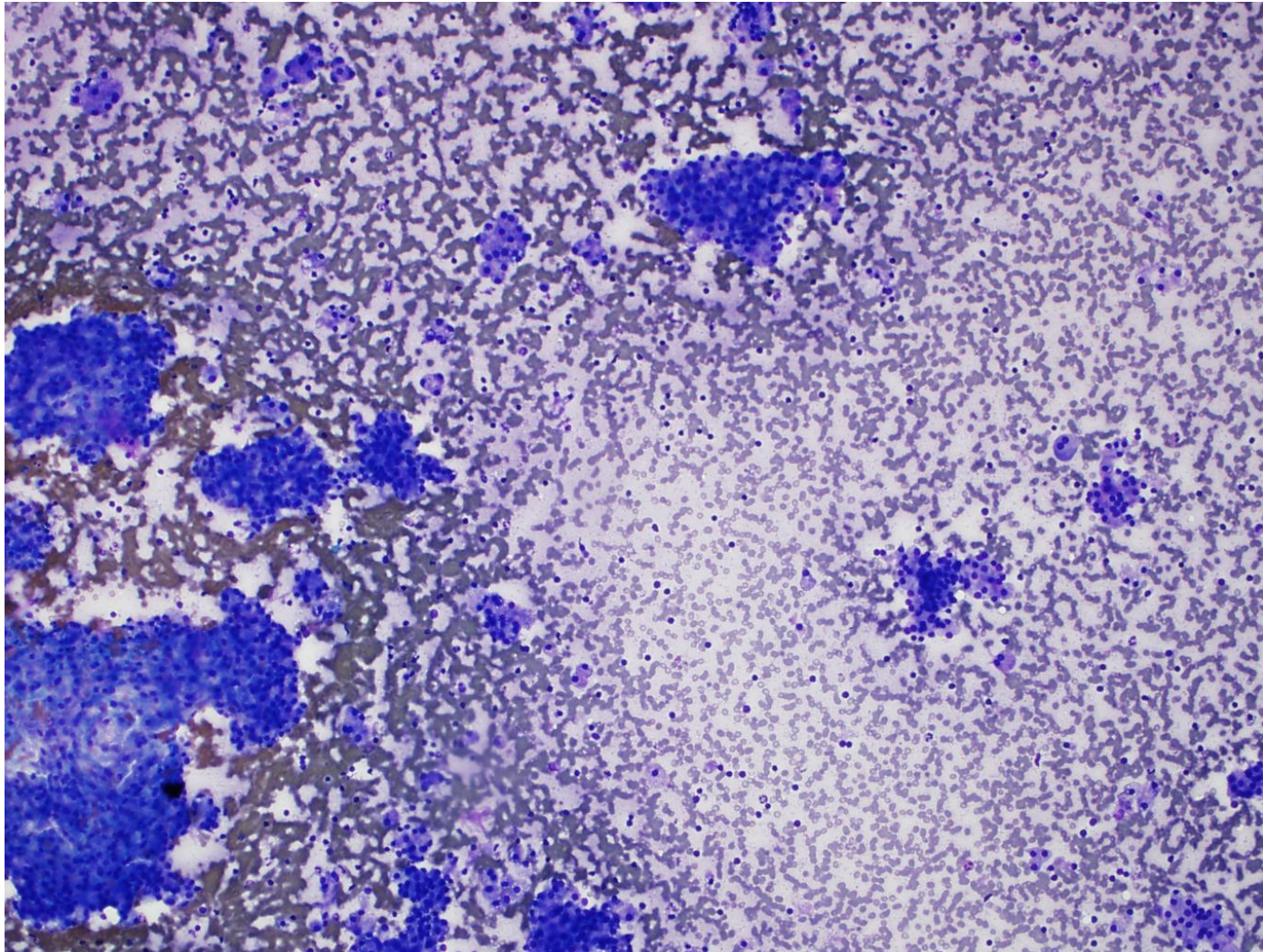
Salivary Gland: Benign Neoplasms

- Pleomorphic adenoma
- Warthin's tumor
 - Account for 1233/1278 benign tumors (96%)

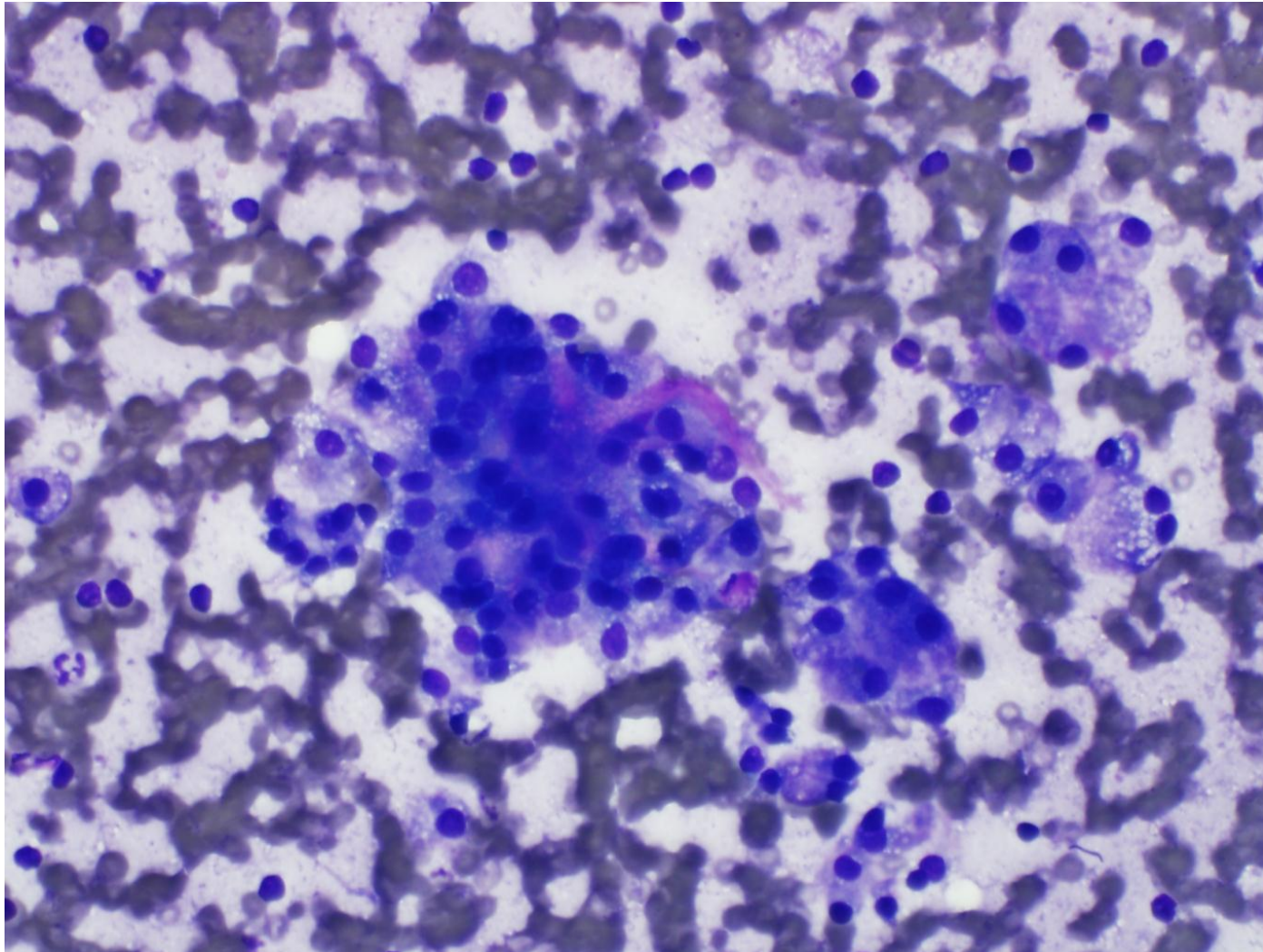
Collela G et al. J Oral Maxillofac Surg. 2010;68: 2146-2153



25 year old female with preauricular 2cm nodule



25 year old female with preauricular 2cm nodule



Acinic Cell Carcinoma

- Malignant epithelial neoplasm characterized by cytologic differentiation toward serous acinar cells (distinctive zymogen type secretory granules)
- Second most common epithelial malignancy of the salivary gland (about half as frequent as mucoepidermoid carcinoma)
- 80% arise in the parotid gland

Gary L. Ellis and Paul L. Auclair. Tumors of the Salivary Glands. AFIP Atlas of Tumor Pathology, Series 4, 2008.



Acinic Cell Carcinoma

- Hypercellular aspirates with a clean background
- Cells are in disorganized clusters with loss of discrete round groupings and no associated ductal epithelium
- Cells are uniform and resemble normal serous acinar cells
- Their cytoplasm is foamy or bubbly some with fine dark granules
- Naked nuclei are frequent



Acinic Cell Carcinoma (Ddx)

- Normal salivary gland tissue
- Sialadenosis
- Oncocytic tumors
- Clear cell tumors
 - RCC (vascular pattern, more nuclear pleomorphism, nucleoli)
 - Epithelial-myoepithelial carcinoma (usually biphasic)
 - Low grade mucoepidermoid carcinoma

Orell & Sterrett's. Fine Needle Aspiration Cytology 5th Edition. 2012.



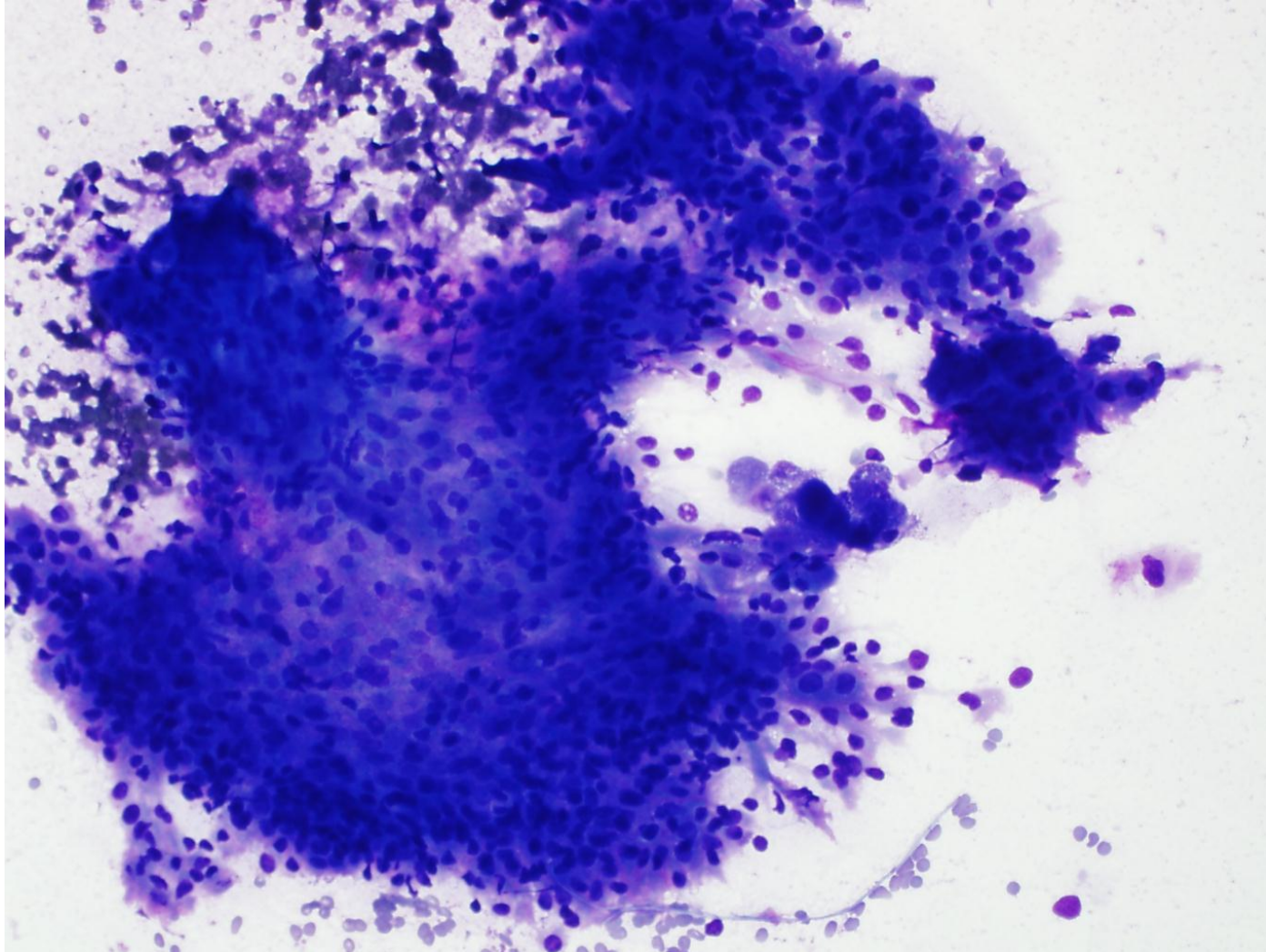
Pitfalls in FNA Sampling of Acinic Cell Carcinoma

- The papillary cystic variant can be almost entirely cystic and yield only benign cyst fluid
- US guidance for any residual mass may solve this issue

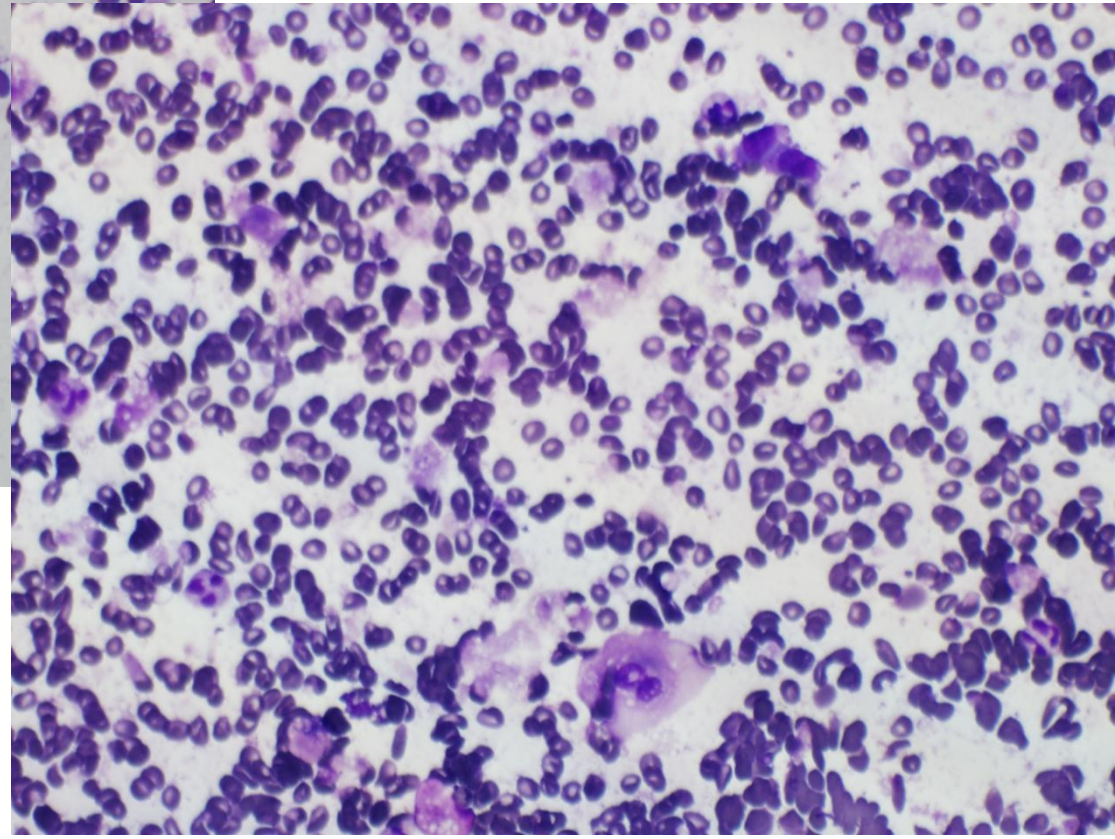
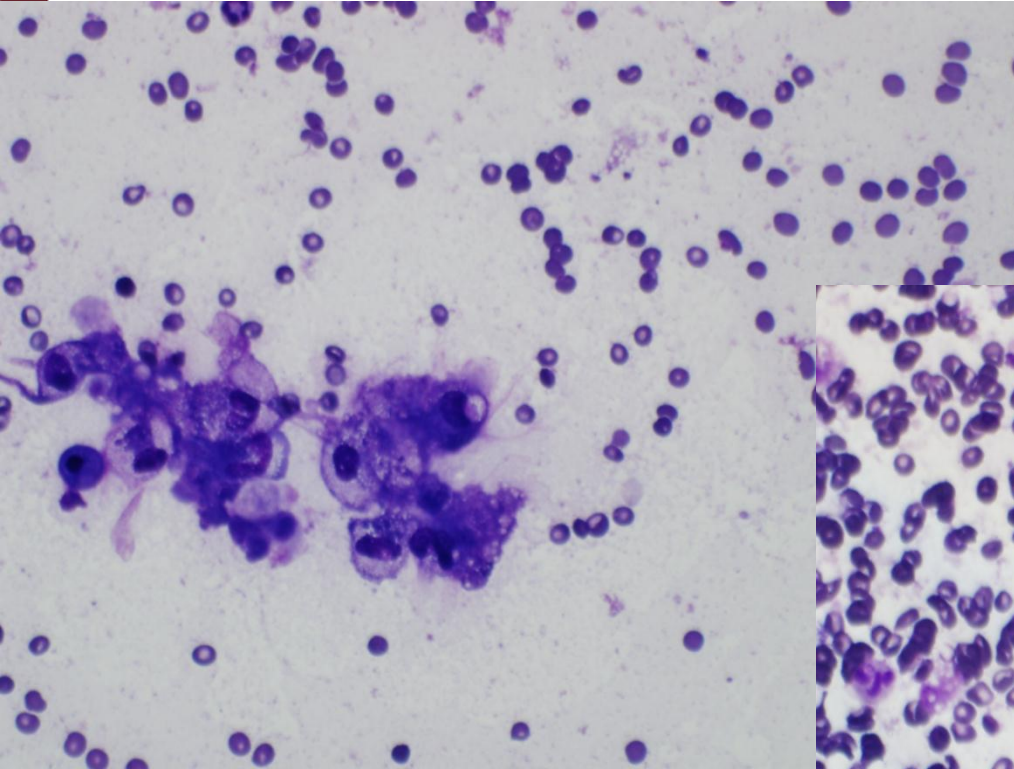
Orell & Sterrett's. Fine Needle Aspiration Cytology 5th Edition. 2012.



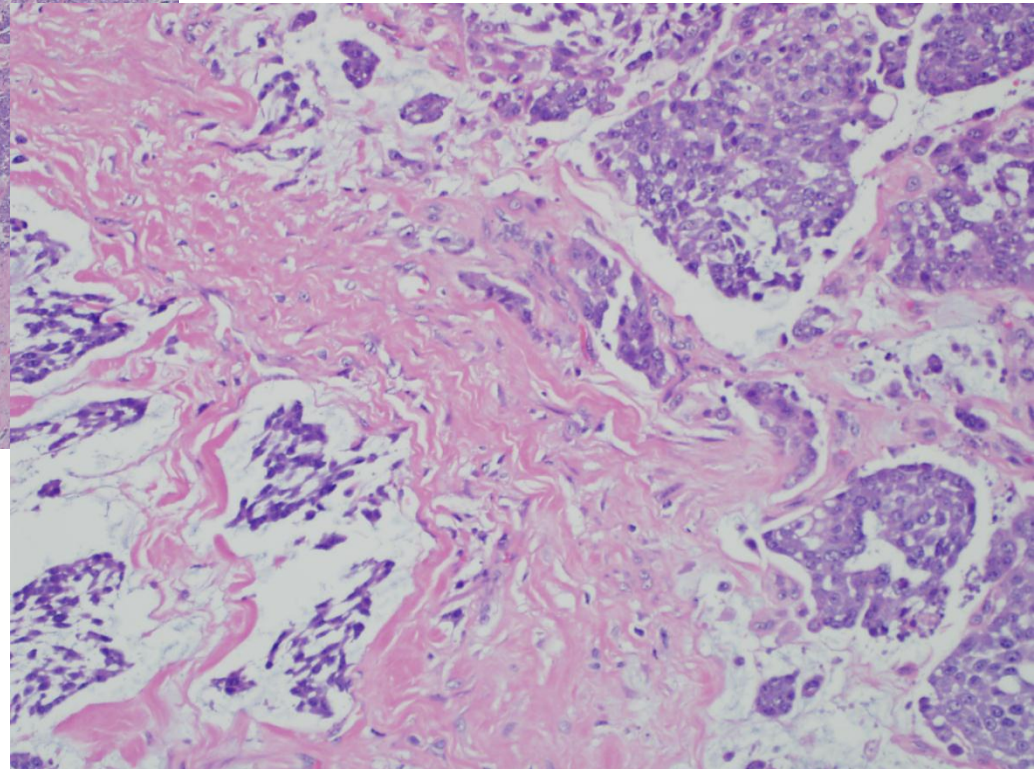
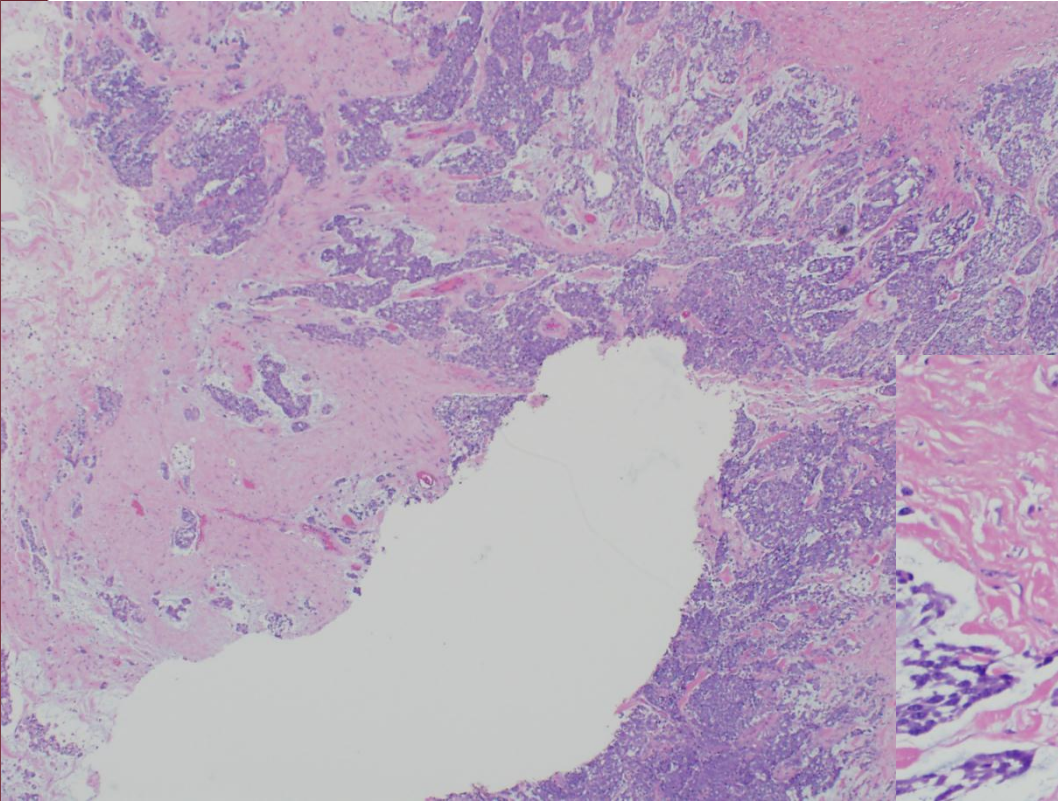
19 year old male with nodule in submandibular gland



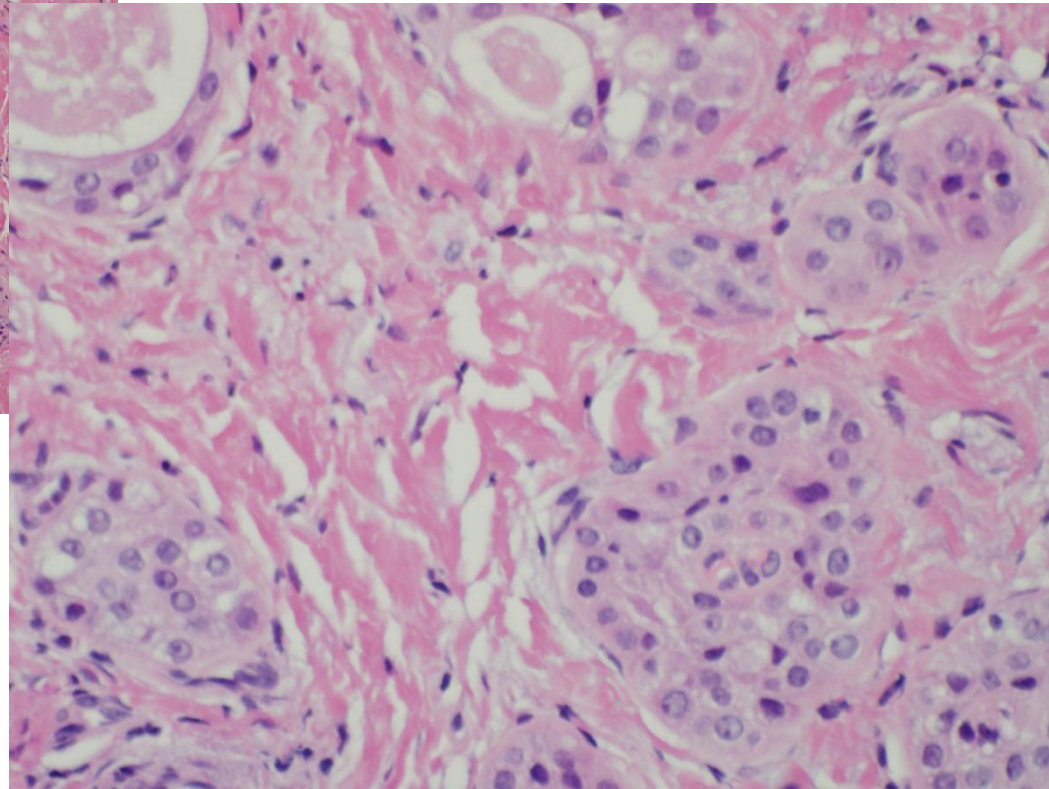
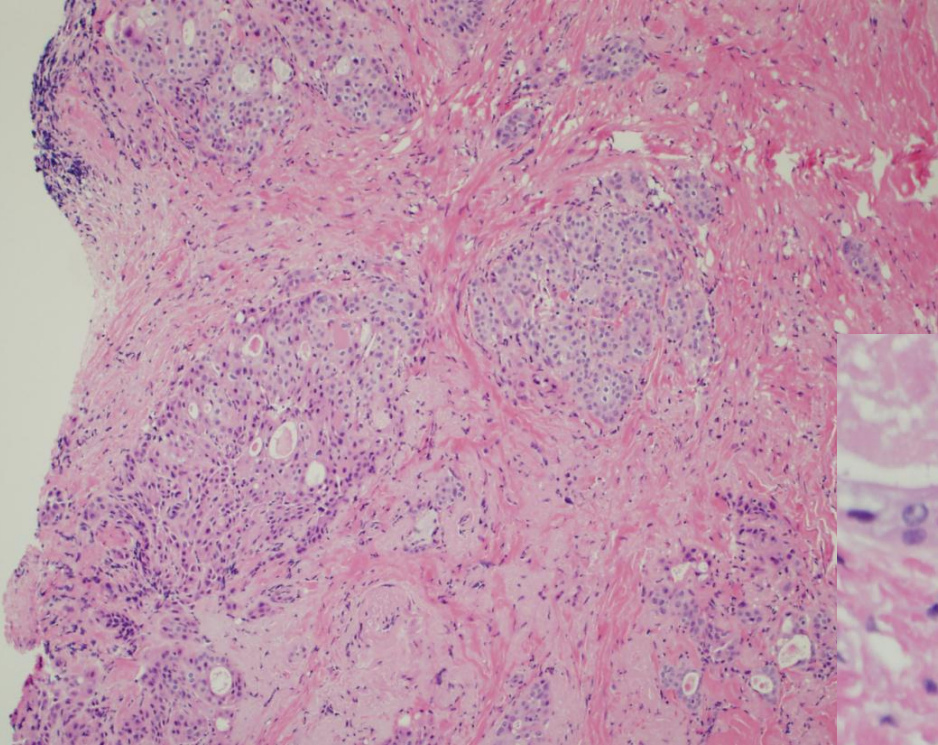
19 year old male with nodule in submandibular gland



Mucoepidermoid Carcinoma



Mucoepidermoid Carcinoma



Mucoepidermoid Carcinoma

- The most common malignant salivary gland tumor
- Represents about 30% of all malignant tumors originating in both major and minor salivary glands
- About half occur in the major salivary glands

Gary L. Ellis and Paul L. Auclair. Tumors of the Salivary Glands. AFIP Atlas of Tumor Pathology, Series 4, 2008.



Mucoepidermoid Carcinoma

- Smears are usually of low cellularity with a dirty background (mucin and debris)
- Scattered cell clusters of intermediate cells (resembling squamous metaplastic cells on Pap test)
- Some mucin secreting cells (resembling goblet cells)
- Infrequently squamous epithelial cells
- Nuclear features are generally bland in low grade tumors
- **The coexistence of cells showing squamous differentiation and mucin secreting cells cannot always be found**

Orell & Sterrett's. Fine Needle Aspiration Cytology 5th Edition. 2012.



Mucoepidermoid Carcinoma: Difficulties at FNA

- Frequently problematic on FNA sampling
- Often is cystic and yields only acellular or hypocellular mucoid material
- The low grade subtype far outnumbered the high grade type
- Extracellular mucin is often abundant and mimics the fibrillary stroma seen in PAs (mucin stains less intensely and is not fibrillar)
- The presence of extracellular or intracellular mucin in FNA specimens may not be reliable in distinguishing from WT
- Squamous metaplasia is common in other lesions (Warthin's tumor, pleomorphic adenoma)

Goonewardene SA. Acta Cytol. 2002;46(4): 704-8.



Mucoepidermoid Carcinoma: Cytomorphologic Clues

- 3 cytologic features selected as most predictive of mucoepidermoid carcinoma (in a series of 34 histologically confirmed tumors):
 - Intermediate cells
 - Squamous cells
 - Overlapping epithelial groups

Cohen MB, et al. *Acta Cytol.*
1990. 34(1):43-49.



Mucoepidermoid Carcinoma: Tips for Equivocal Cases

- In equivocal cases only a tentative differential diagnosis can be offered
- Smears from non-neoplastic cysts (retention cysts and lymphoepithelial cysts) can mimic low grade MEC with mucus, debris, metaplastic squamous cells
- High grade squamous cell carcinoma may not be distinguishable from high grade MEC
 - Obvious mucinous component (MEC)
 - Keratinization is present (SCCA)



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