Advances in Cytology and Small Biopsies

# Challenges and Lessons Learned - Virtual Microscopy 2

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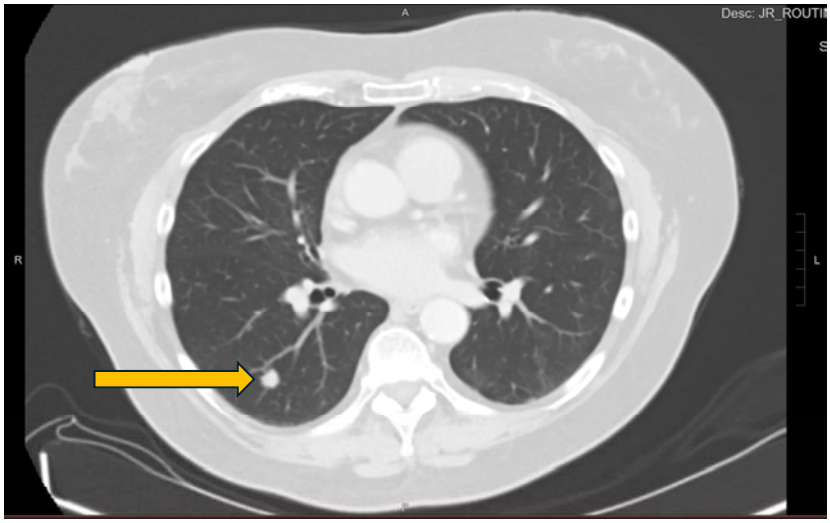
## Clinical History

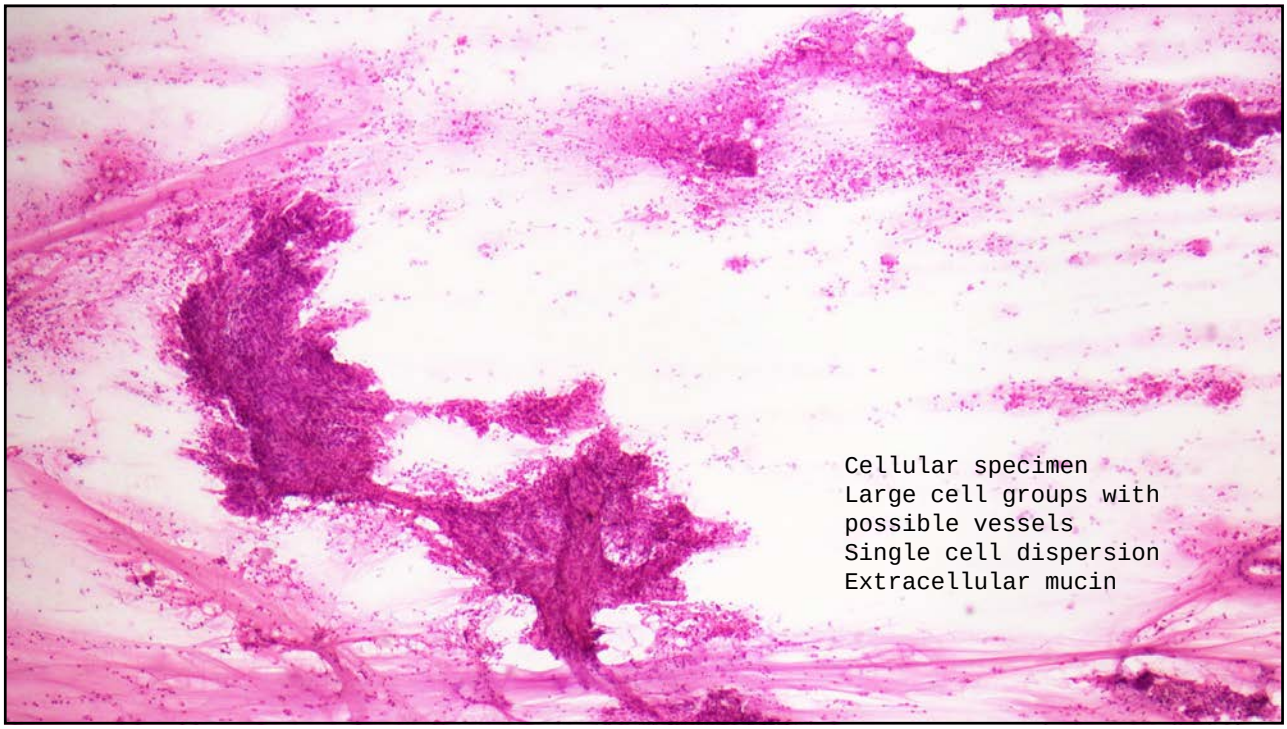
- 71 year old woman
- Former smoker (15 pack years)
- No cancer history
- Screening lung CT:
  - 10mm RLL noncalcified solid pulmonary nodule
  - Several additional 2-3mm and 3-4mm RLL nodules
  - Moderate FDG uptake (SUV 3.4)

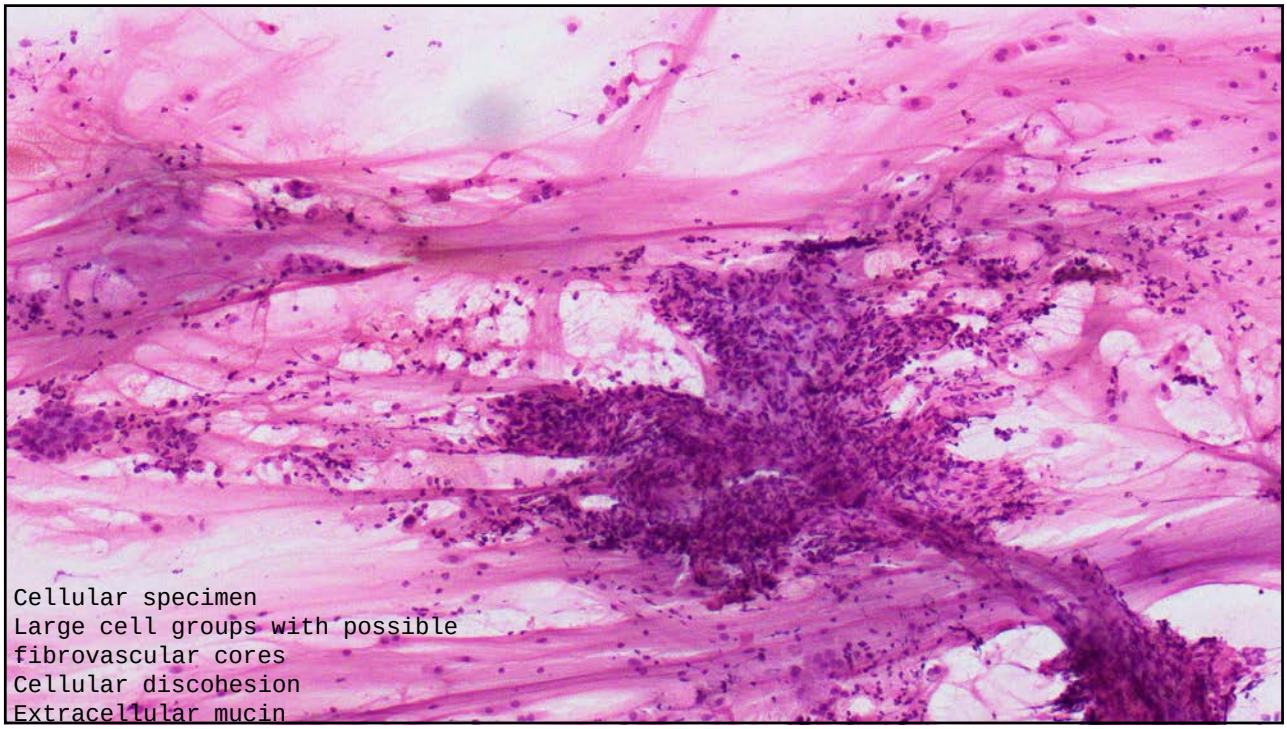
## Lung PET-CT Scan

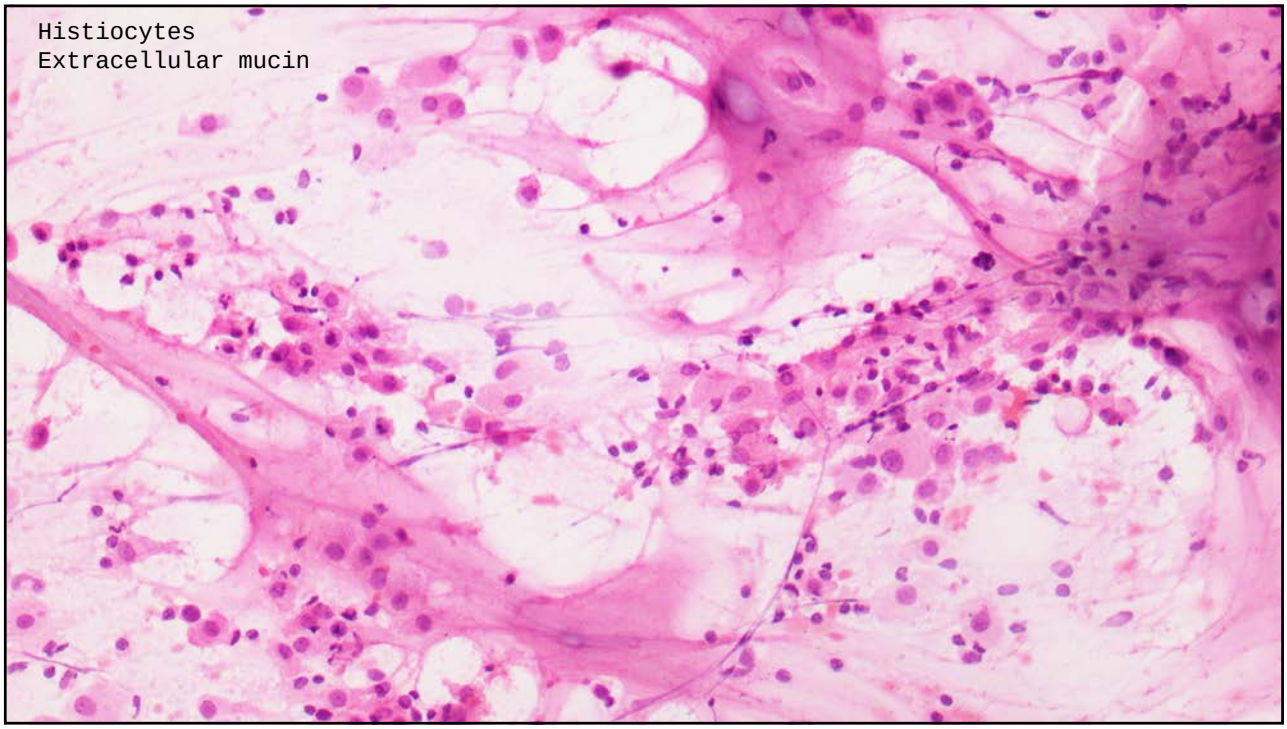


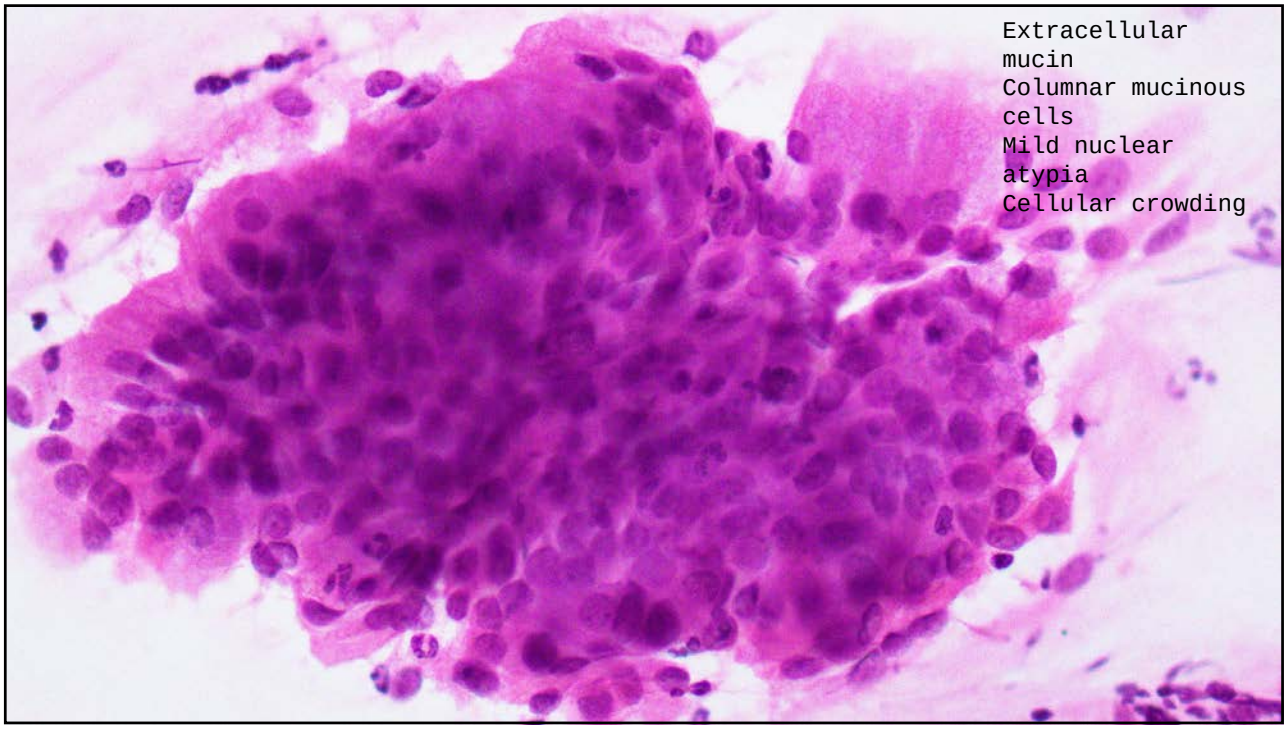

# FNA performed of Lung Mass

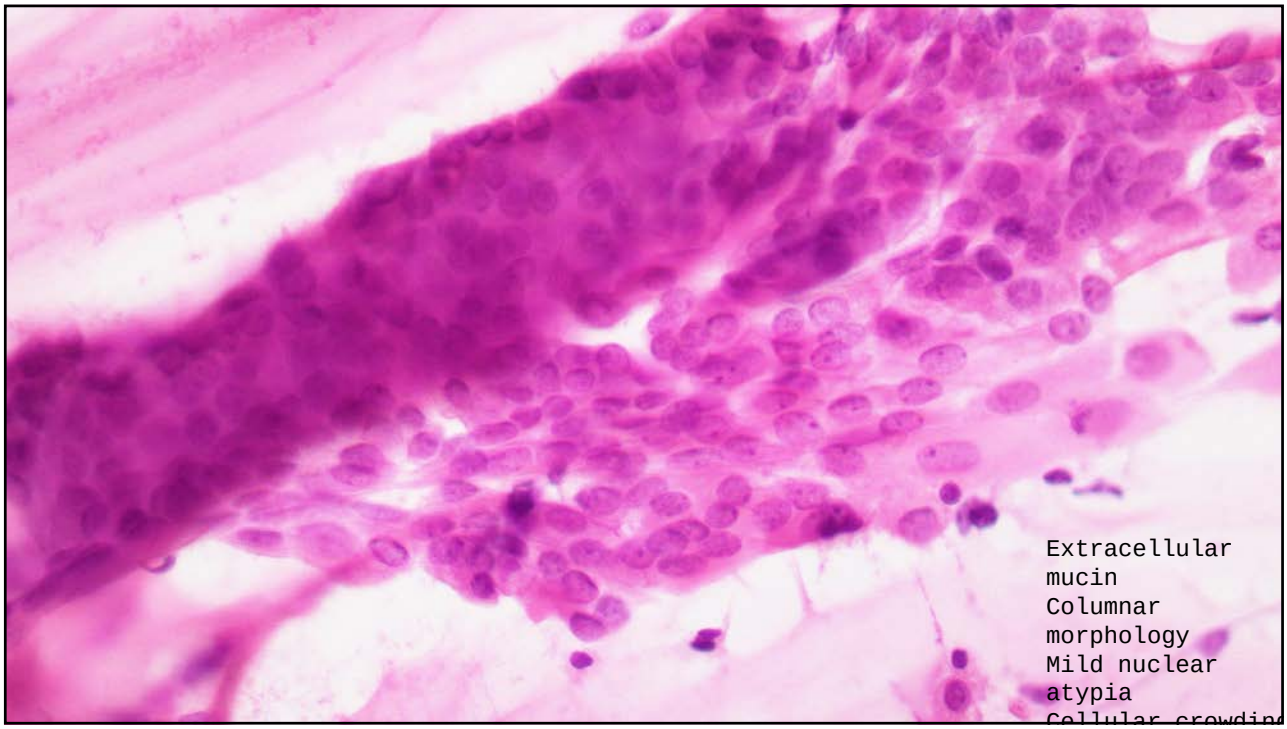
ROSE requested on Rapid H&E stains

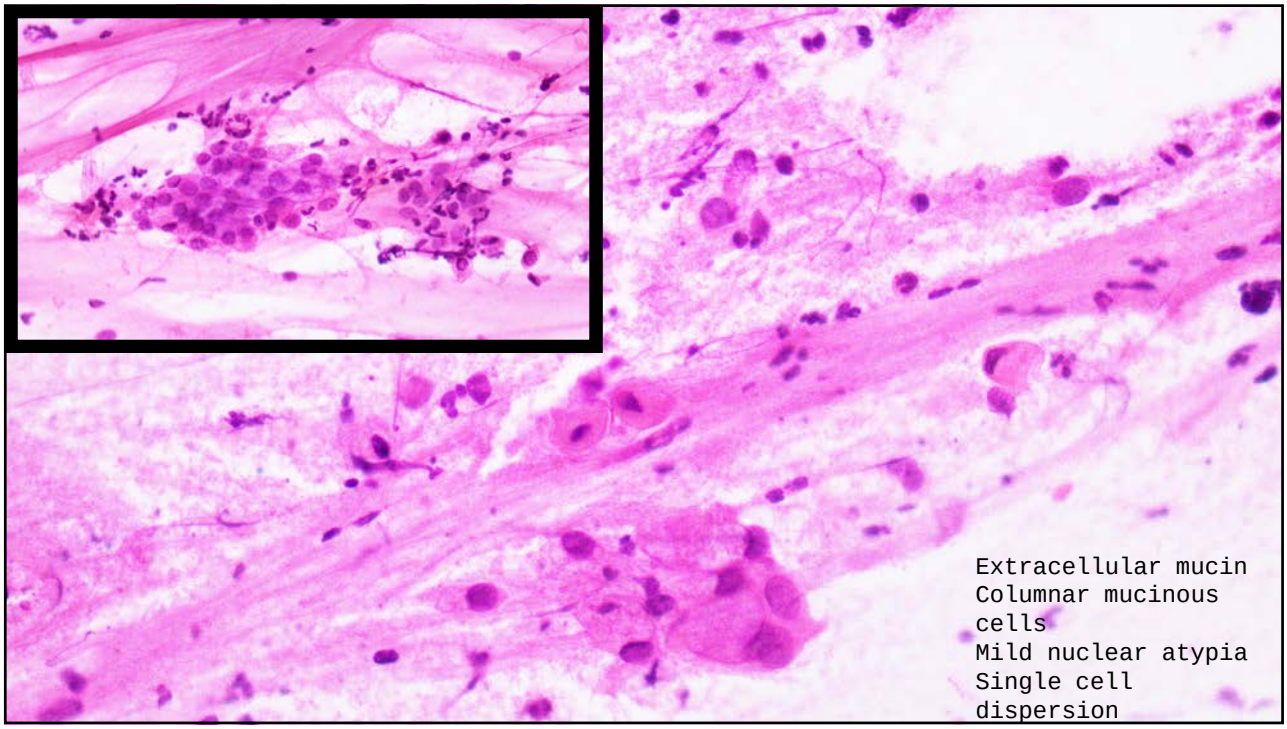

Cellular specimen
Large cell groups with
possible vessels
Single cell dispersion
Extracellular mucin


Cellular specimen
Large cell groups with possible
fibrovascular cores
Cellular discohesion
Extracellular mucin


Histiocytes
Extracellular mucin


Extracellular mucin
Columnar mucinous cells
Mild nuclear atypia
Cellular crowding


Extracellular mucin
Columnar morphology
Mild nuclear atypia
Cellular crowding


Extracellular mucin
Columnar mucinous cells
Mild nuclear atypia
Single cell dispersion

## What is your ROSE assessment?

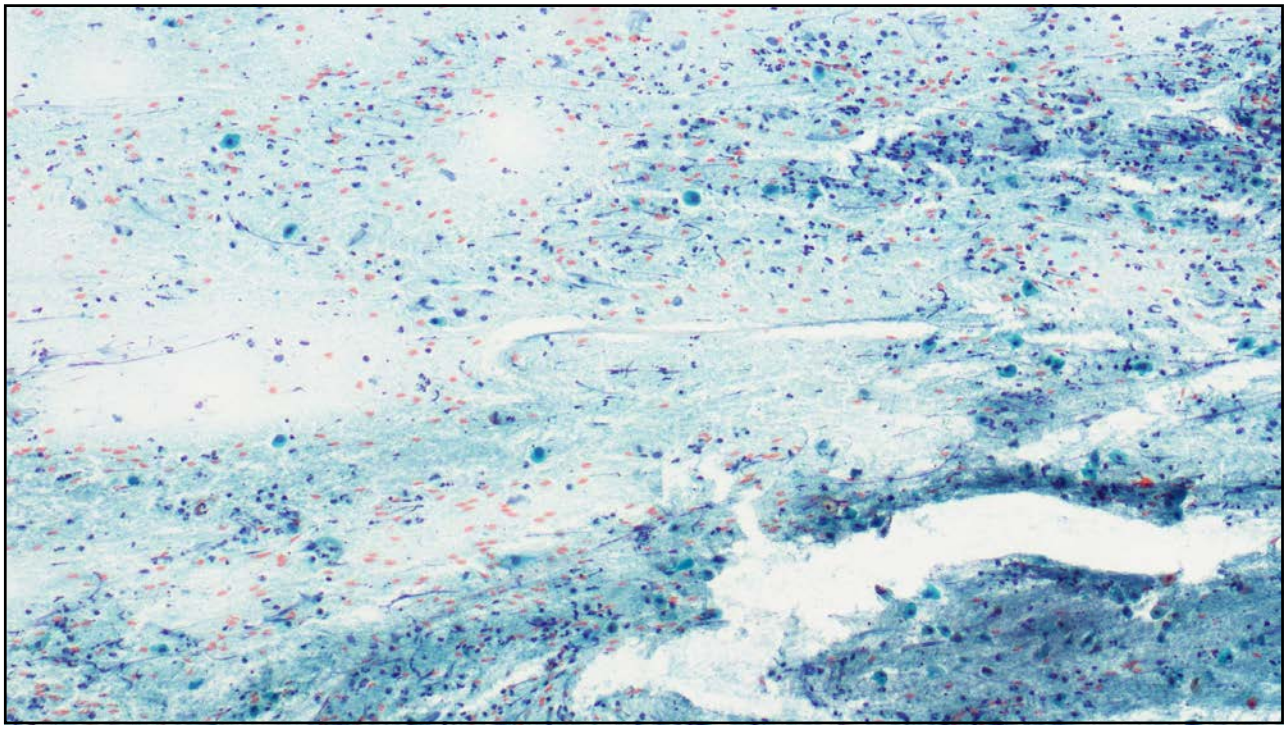
A. Inadequate

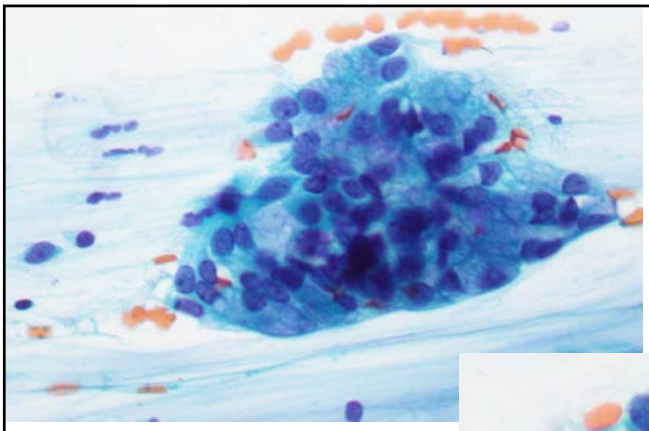
B. Adequate
- Mucinous metaplasia (benign)
- Invasive mucinous adenocarcinoma, lung primary
- Metastatic adenocarcinoma (e.g. pancreatic primary)
- Other

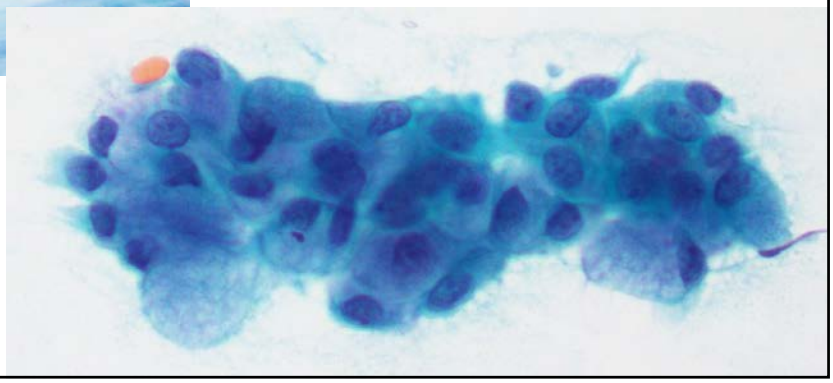
## ROSE Diagnosis

“POSITIVE FOR MALIGNANCY
Consistent with mucinous adenocarcinoma”

# Additional smears prepared with Pap stain

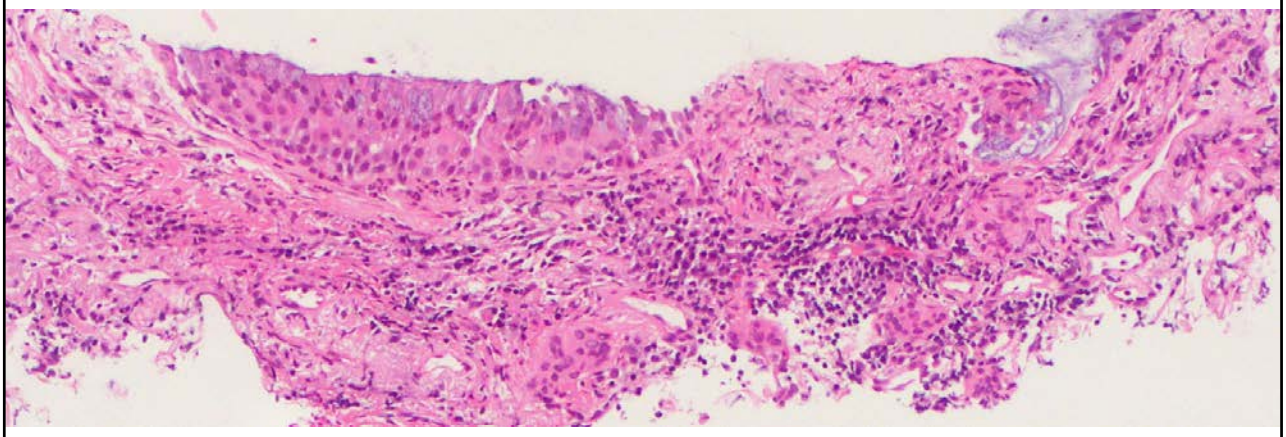






Columnar mucinous
cells
Mild nuclear atypia

## RLL nodule, concurrent core biopsy

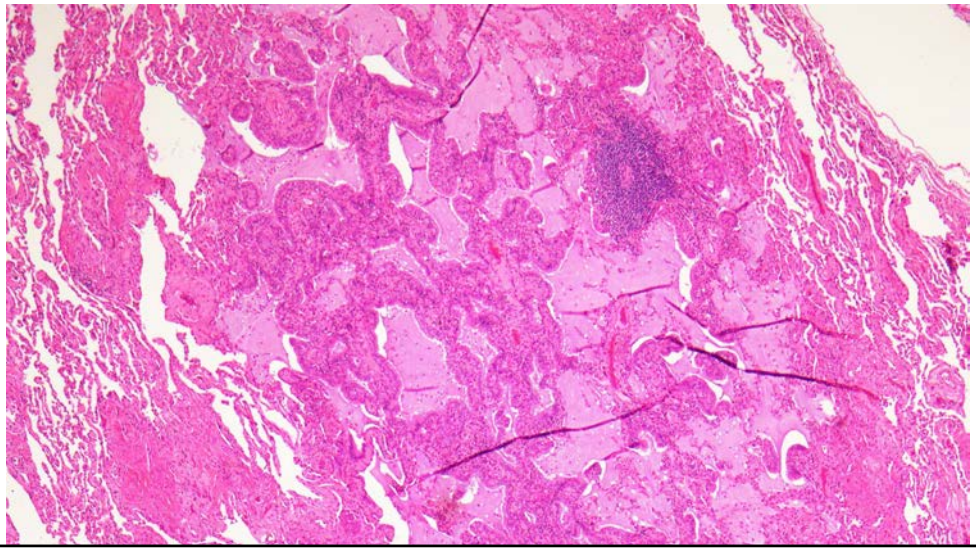


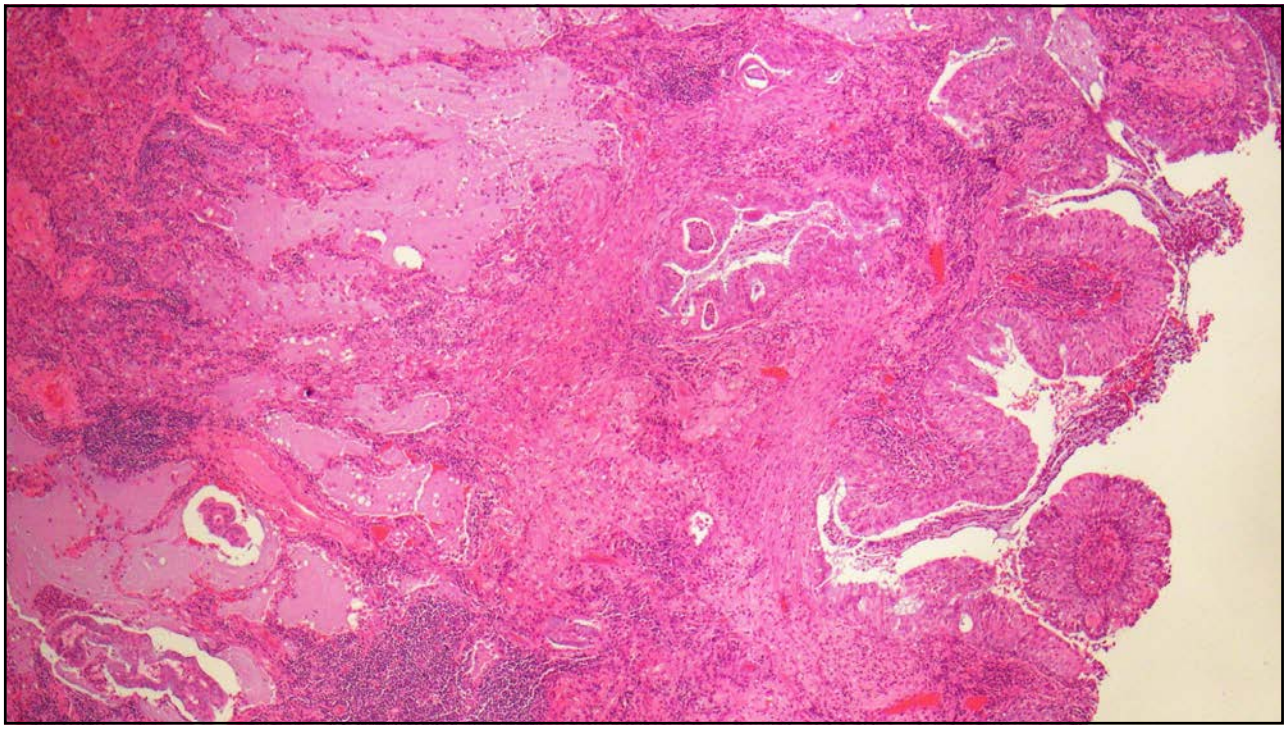
# RLL nodule Final Diagnosis

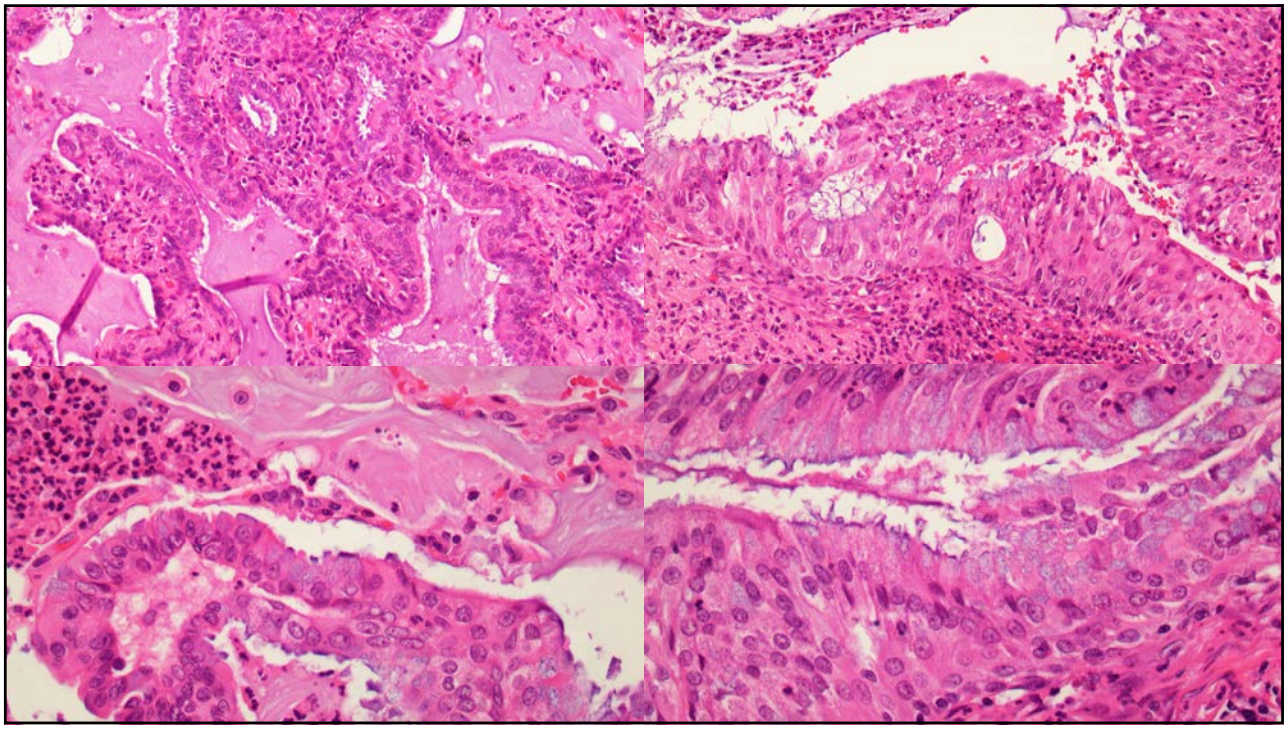
MALIGNANT

Mucinous adenocarcinoma

# Subsequent Lobectomy: Bronchiolar adenomas (4 foci)

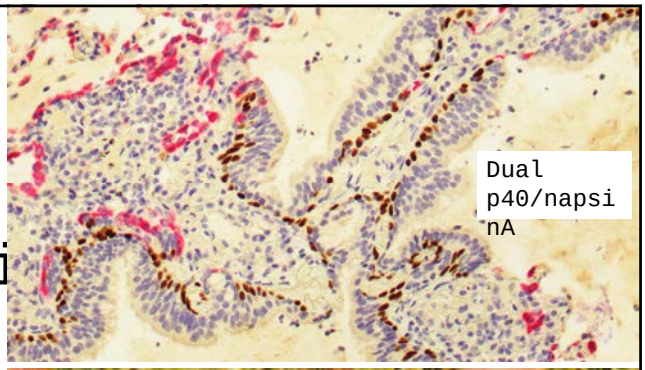


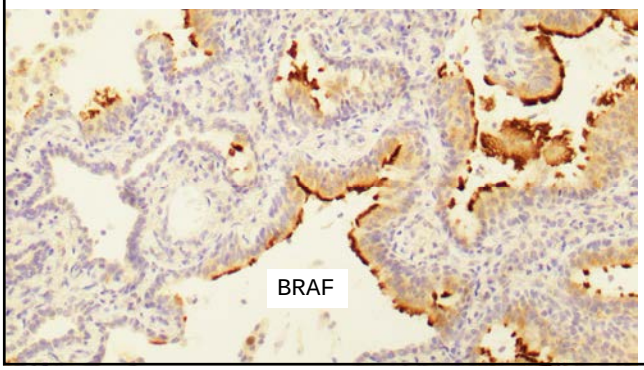


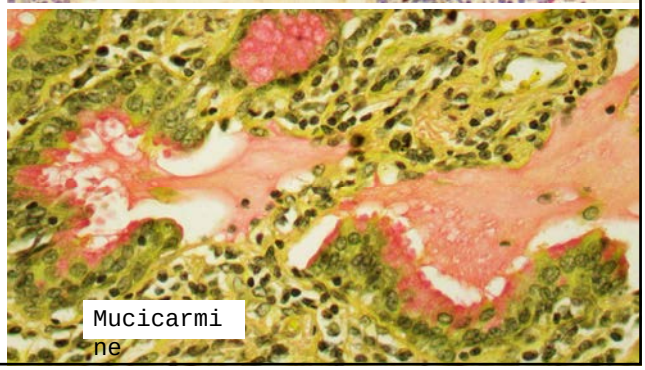


# Lobectomy
# IHC Stains

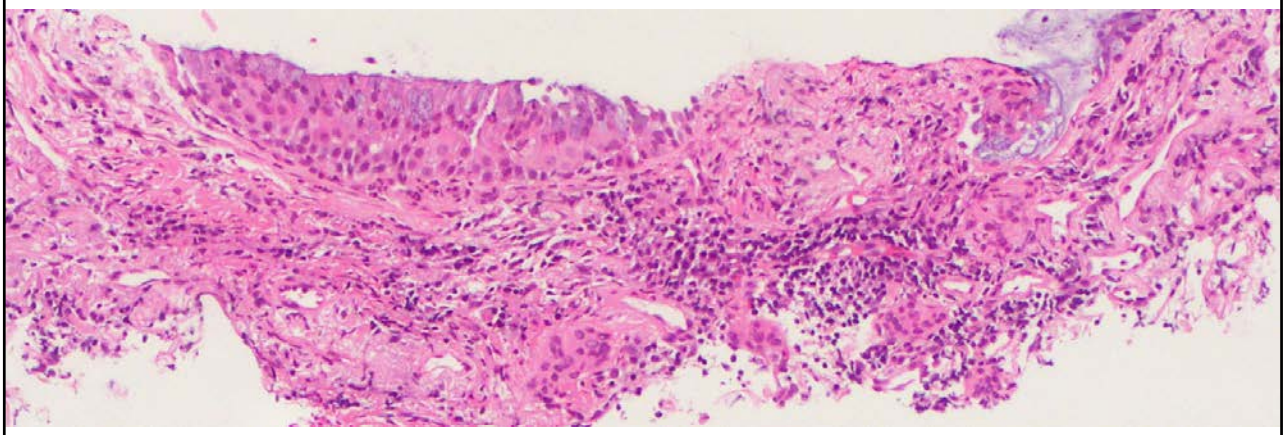
All nodes negati



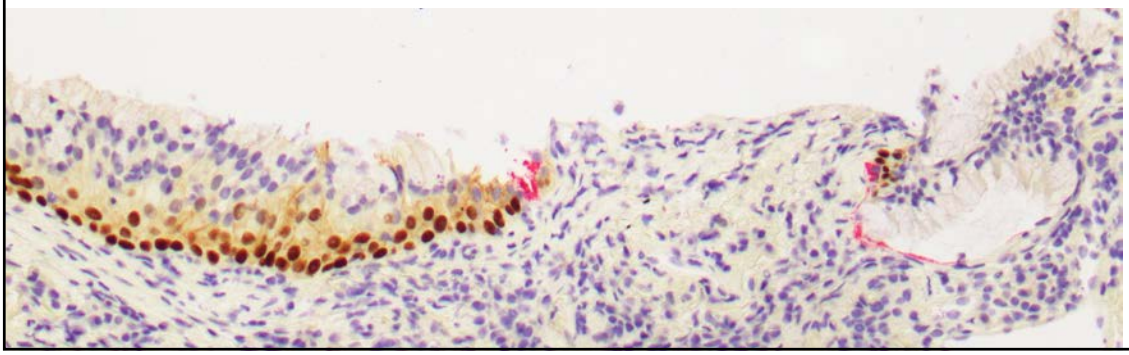

# RLL nodule, concurrent core biopsy



# RLL nodule

Dual immunohistochemistry

- p40 (brown)
- Napsin A (red)



# RLL nodule

Revised Final Diagnosis

- FNA: ATYPICAL

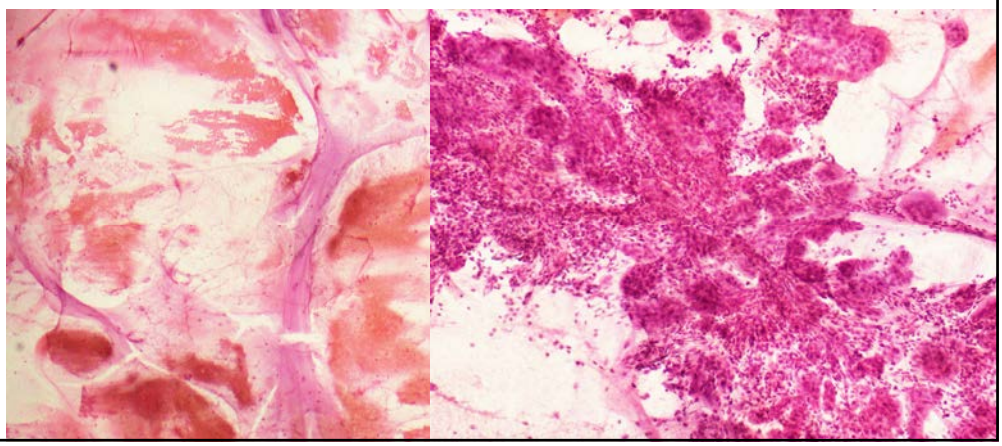
Numerous epithelial cells with mucinous differentiation

- Core biopsy: Findings suggestive of bronchiolar adenoma

# Pitfalls: low grade mucinous neoplasms

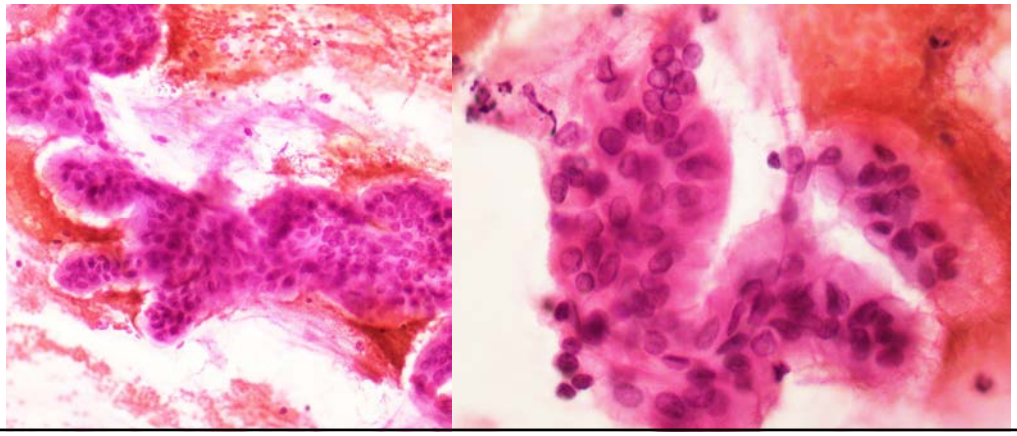
- Bronchiolar adenoma (ciliated muconodular papillary tumor) may mimic invasive or metastatic mucinous adenocarcinoma on FNA

Mucinous adenocarcinoma, lung (KRAS mutant); TTF1 negative



# Mucinous adenocarcinoma, lung (KRAS mutant)

- Morphology not high grade, no mitoses/necrosis

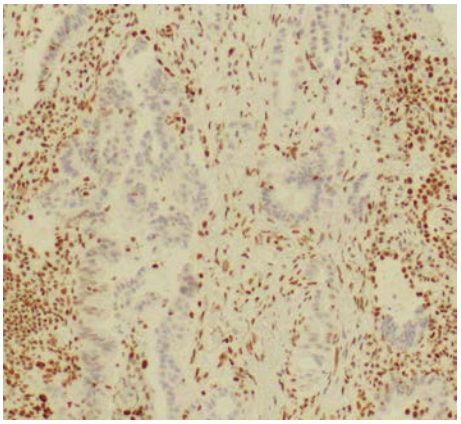


# Diagnostic Pitfalls

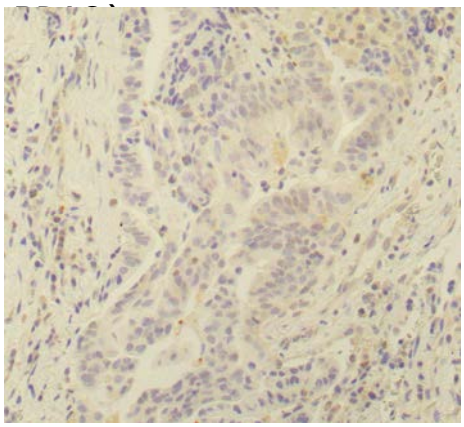
- TTF-1/napsinA negativity in a mucinous tumor does not rule out primary lung, especially when:
  - CK7 positive
  - CDX2/SATB2 negative/weak
  - No known GI/panc primary
  - Lung tumor is solitary and peripheral
- Correlate with available histologic tissue biopsies (and consider signing out together)
- Perform immunohistochemical stains for basal cells (e.g. p40) and cilia (e.g. BRAF)
- Currently no marker is specific for mucinous lung adenocarcinoma

# Staining for known mutations: Pancreatic adenocarcinoma spread to lung

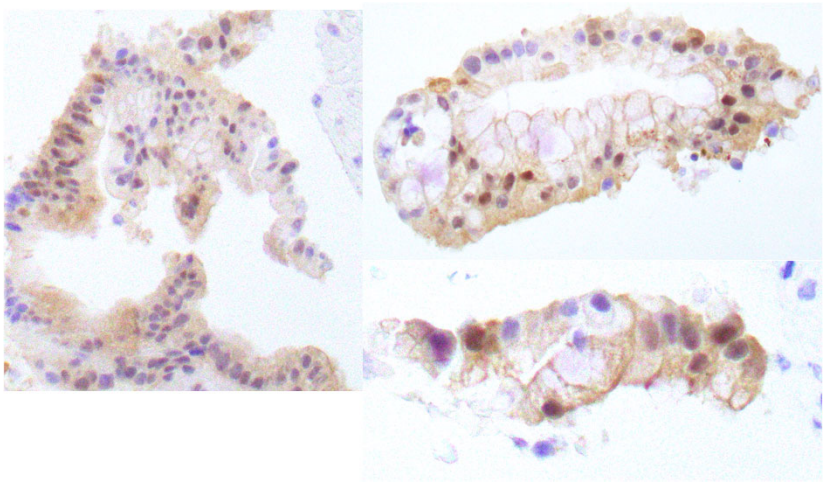
ARID1A (BAF250a) loss



SMAD4 (lost in ~50%



# Marker for pancreas: Annexin



Staining pattern
nuclear and
cytoplasmic
Sensitivity high for
gastric/panc (80-90%)
Not specific enough
to use alone
Use in a panel

# References


- Mao TL, Shih IeM. The roles of ARID1A in gynecologic cancer. J Gynecol Oncol. 2013 Oct;24(4):376-81. doi: 10.3802/jgo.2013.24.4.376. Epub 2013 Oct 2. PMID: 24167674; PMCID: PMC3805919.
- Mikubo M, Maruyama R, Kakinuma H, Yoshida T, Satoh Y. Ciliated muconodular papillary tumors of the lung: Cytologic features and diagnostic pitfalls in intraoperative examinations. Diagn Cytopathol. 2019 Jul;47(7):716-719. doi: 10.1002/dc.24169. Epub 2019 Mar 8. PMID: 30848550.

Mass General Brigham

# Advances in Cytology and Small Biopsies

## Jaw mass in a 23-year-old male patient

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Cytopathology fellow, Mass General Brigham – Harvard Medical School

### Clinical history:

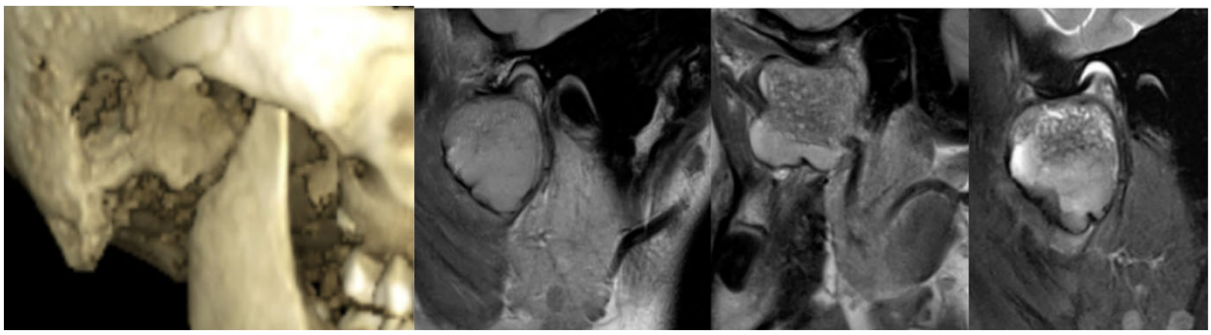
23-year-old male with no significant past medical history.

May 2024: Patient noticed an open bite of the left posterior dentition. 2D radiograph at an outside facility did not pick up any abnormalities.

December 2024: Patient developed pain and sudden swelling in the right temporomandibular joint area.

Patient was referred to maxillofacial surgery at MGH by his dentist.

## Imaging



Imaging: 3.6 x 3.0 x 2.9 cm expansile heterogeneously enhancing mass with multi-cystic and solid components centered in the right mandibular ramus and extending to the condyle.

A benign radiologic differential diagnosis (ameloblastoma vs. giant cell tumor of bone) was favored.



The patient was referred to the FNA clinic at MGH.

After communicating with the clinicians and radiologists, it was agreed that the mass has a bony cortex that is thin enough for FNA biopsy.

Physical examination revealed a well-defined, non-tender, irregular, firm, fixed swelling/mass lesion in the right temporomandibular joint region, measuring approximately 3 cm in greatest dimension.

## Bedside ultrasound at FNA clinic

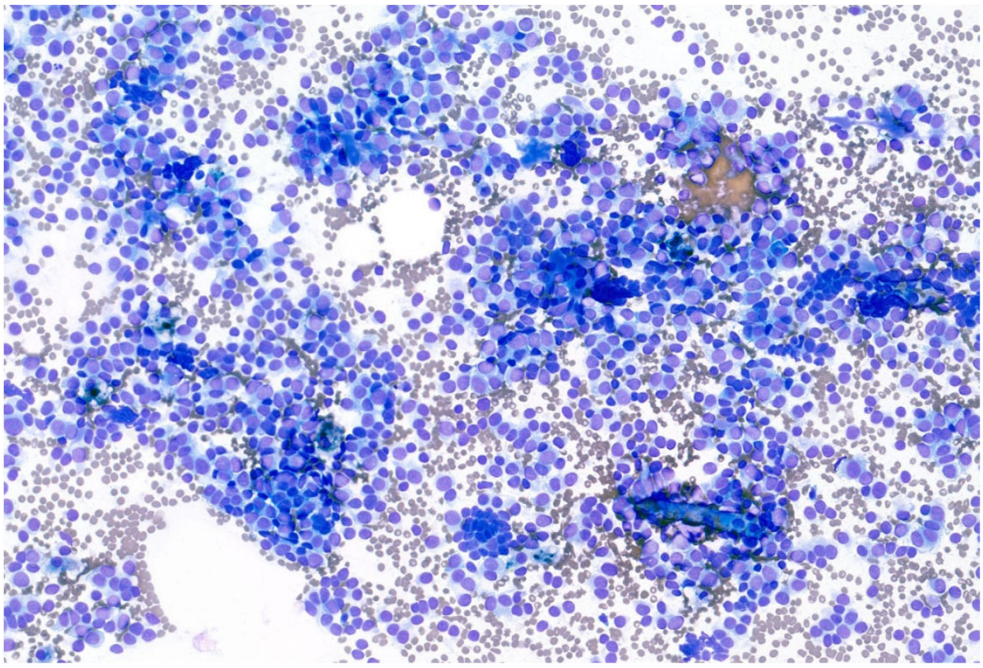
3.0 x 2.28 cm well-defined, solid and cystic mass lesion with irregular borders.

The lesion was heterogeneously hyperechoic and hypoechoic without significant internal vascularity and with minimal peripheral vascularity.

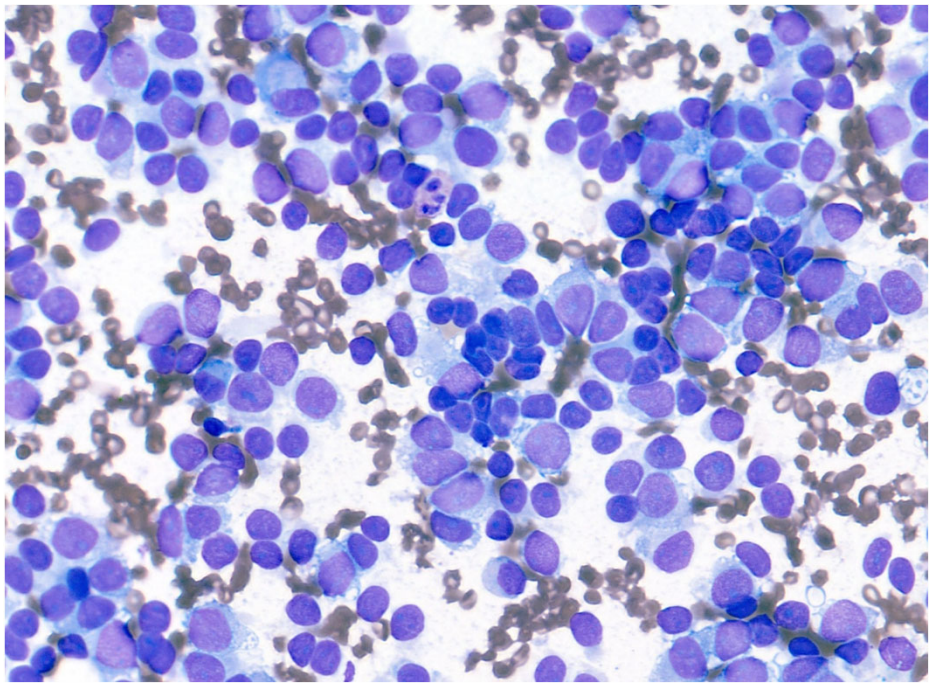


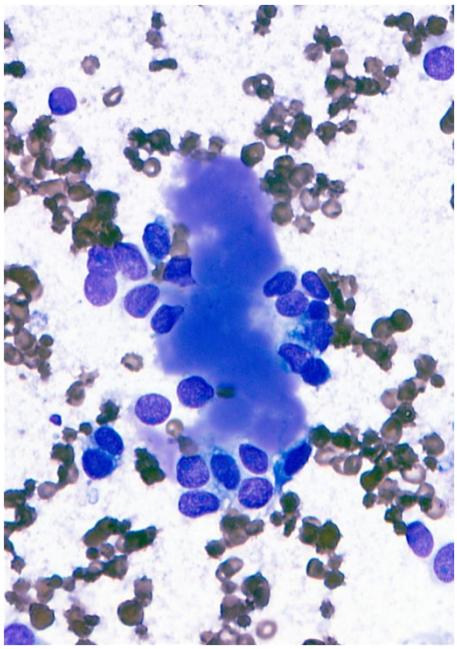
# On-site smears (Air dried – Diff Quick)

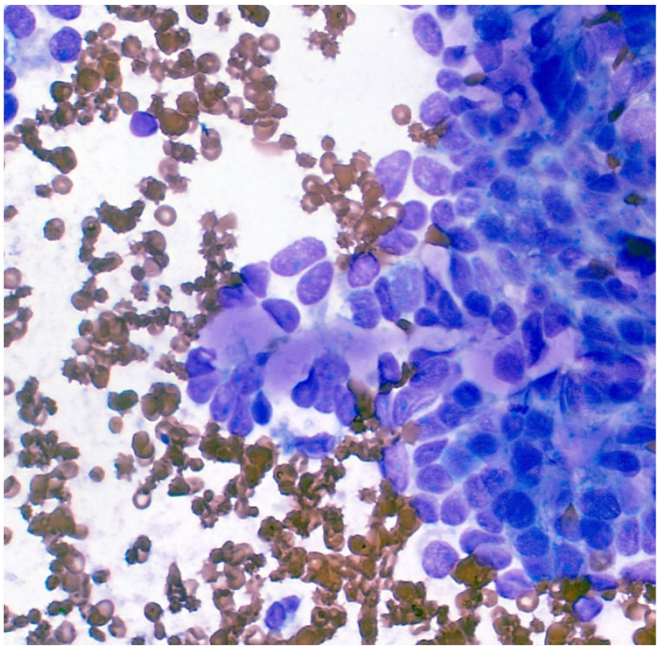
Favor ameloblastoma, awaiting permanents





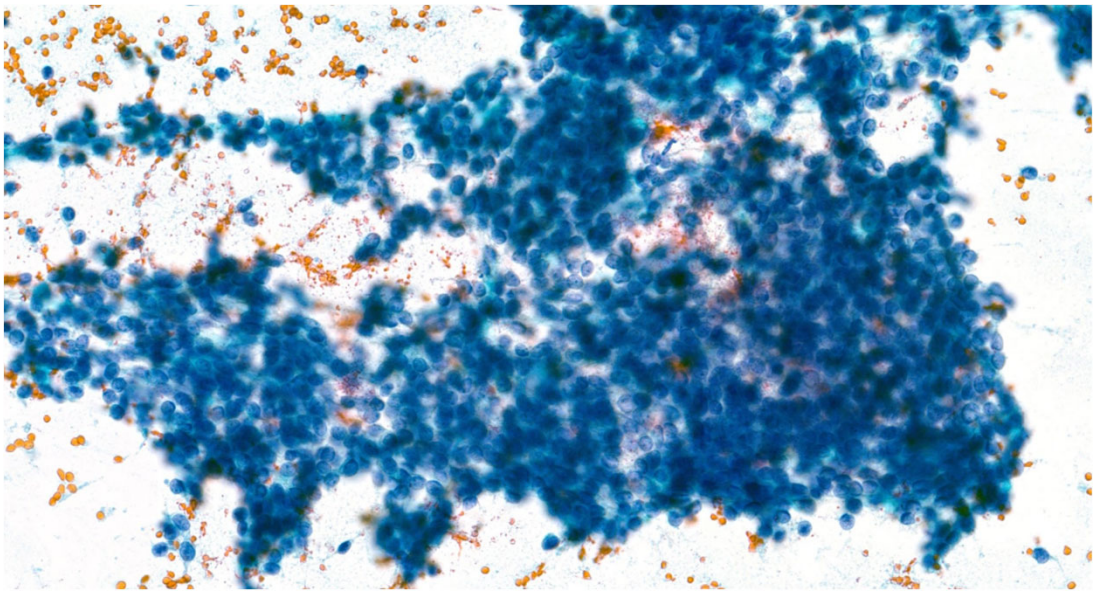








## Alcohol fixed smears (Pap stain) and cell block



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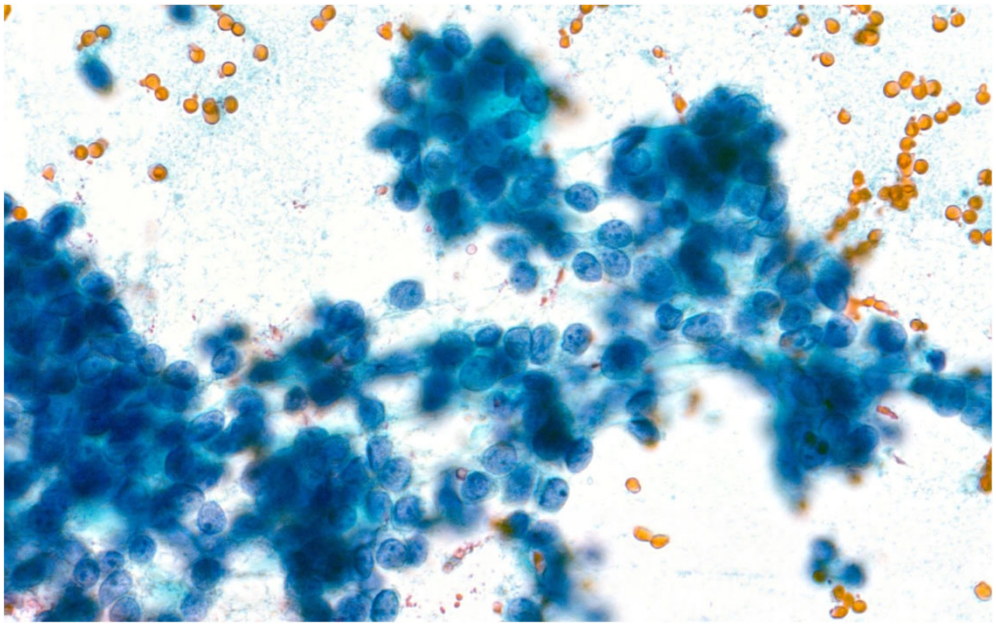

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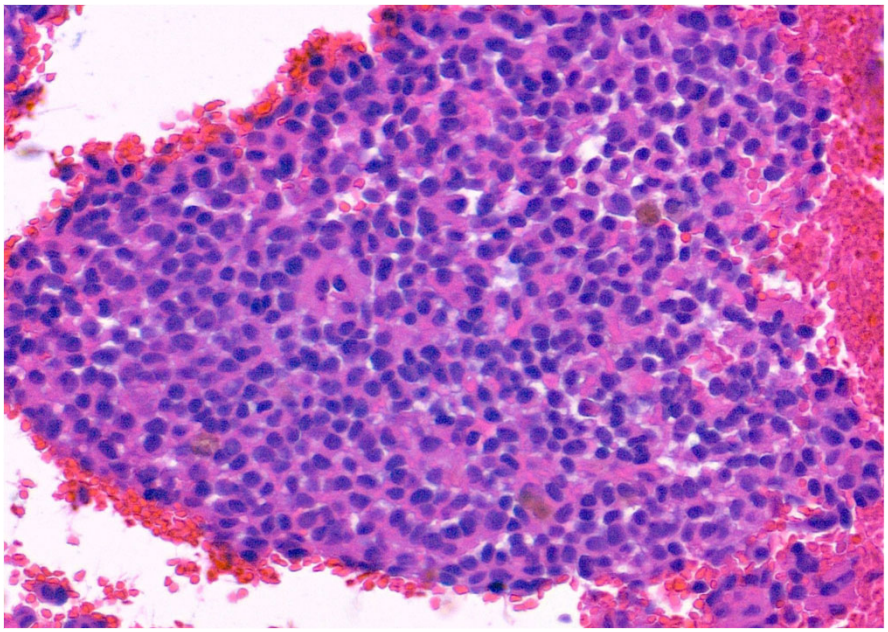
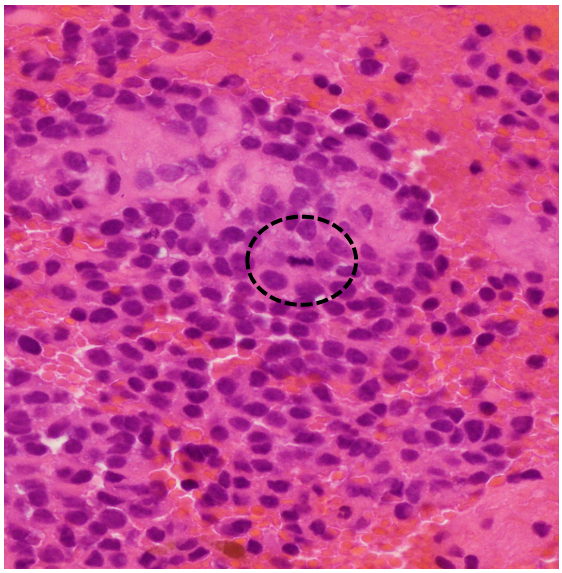
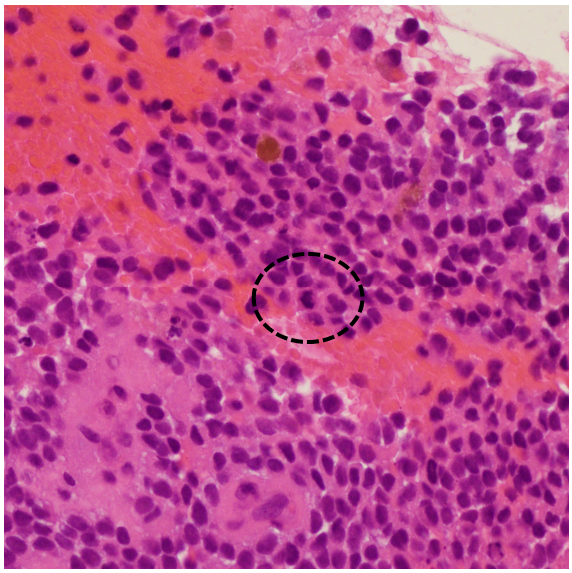








## Mitoses

## Summary of cytologic findings:

Cellular smears.
Groups of small round monomorphic tumor cells with finely granular chromatin, inconspicuous (and some pinpoint) nucleoli.

Moderate amount of cytoplasm, eosinophilic to clear

Globular and band-like matrix material as well as some cells with possibly squamous features are also present.

Scattered mitotic figures are identified.

No giant cells are present.
No necrosis is seen.



## Differential diagnosis

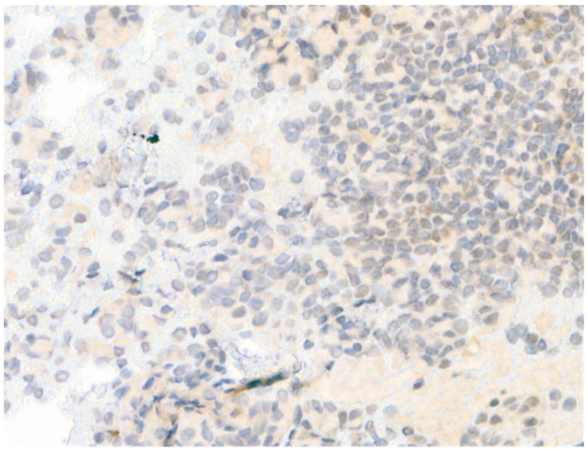
Ameloblastoma.

Small round blue cell tumors:
- Ewing sarcoma.
- Rhabdomyosarcoma and subtypes.
- Lymphoma.

Metastasis: Melanoma, neuroblastoma, Wilm's tumor, poorly differentiated carcinoma

## Immunohistochemistry…

**CK MNF 116**
**(Neg)**



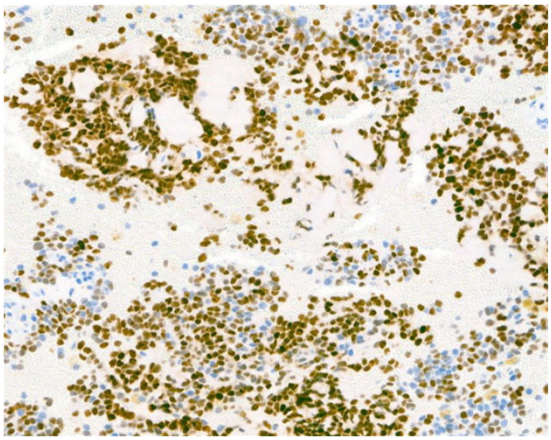
**BRAF**
**(Neg)**



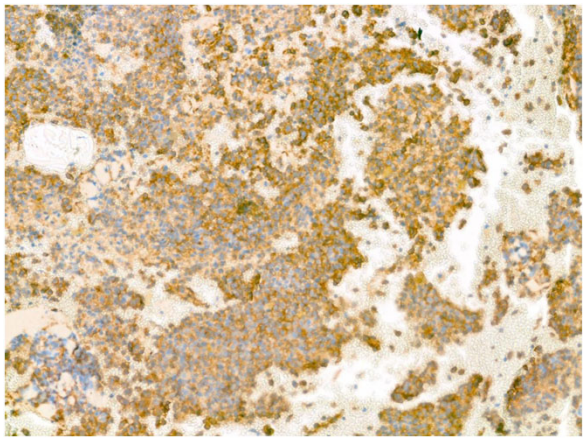
## Solid Fusion Assay (Molecular testing)

RESULTS:
A fusion transcript was identified involving EWSR1 exon:7 (NM_005243.4) and FLI1 exon:9 (NM_002017.5).
No other reportable fusion transcripts were identified.

INTERPRETATION:
POSITIVE for EWSR1::FLI1 gene fusion

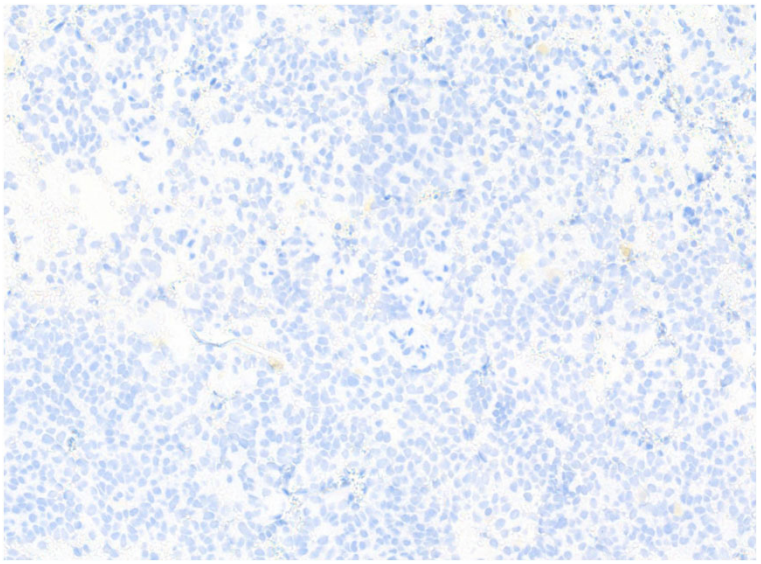


NKX2.2
(Pos)



CD99
(Pos)





Desmin
(Neg)

## Final diagnosis:

Ewing Sarcoma



## Ewing sarcoma

Second most common malignant bone tumor in children/young adults.

Peak incidence in second decade of life. (nearly 80% of patients are younger than 20 years of age).

Overall male predilection (M:F ratio: 3:2).

More common in individuals of European descent (compared to individuals of African or Asia descent).

Most are sporadic.

Vast majority occur in bone.
12% are extra-skeletal.

## Ewing sarcoma of the head and neck

PMID: 19841575
PMID: 28056517
PMID: 28056517
PMID: 26304893

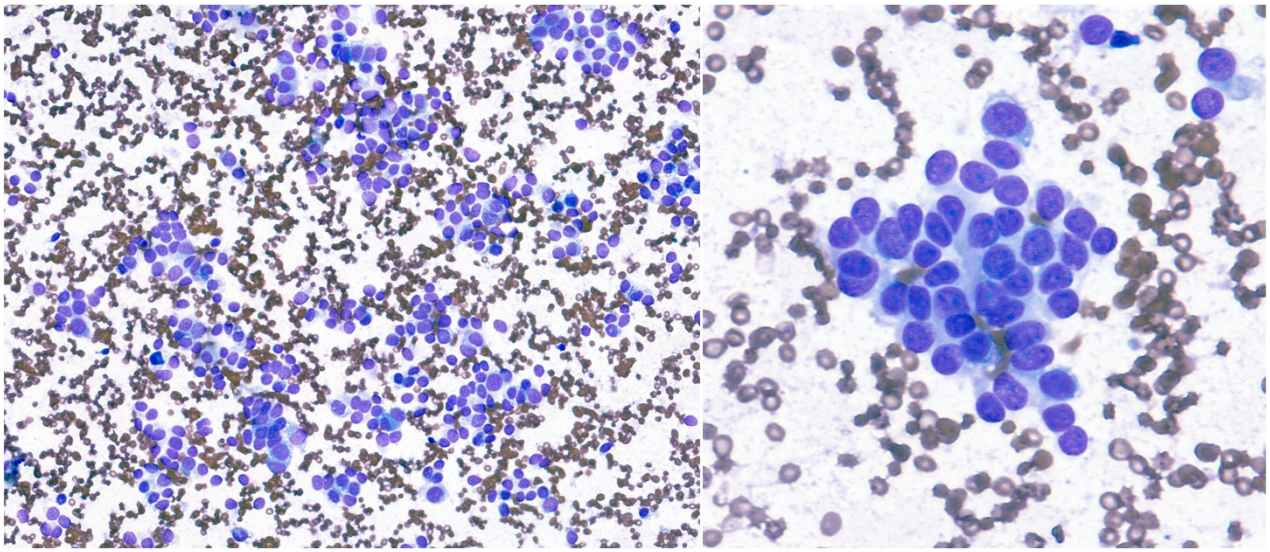
1-9% of Ewing sarcoma cases.
- 40% in skull and facial bones.
- 30% centered in soft tissue
- 9% in mandible (0.09-0.81 %)

~ 50% of head and neck Ewing sarcomas arise in patients aged < 18 years
85% occur in the first four decades of life.

Slight male predominance.

Prognosis better than that of other tumor sites (smaller size, lower metastatic rate)
5-year survival is 70% for localized disease and 30% for metastasis at presentation.





## **Immunohistochemistry**:

**CD99** typically shows strong diffuse membranous reactivity (Not specific).
**NKX2.2** shows nuclear staining (high sensitivity, moderate specificity)

**FLI1 and ERG** are often expressed in cases with the corresponding gene fusion.

Cytokeratins expressed in 30% of cases
Neuroendocrine markers expressed in 50% of cases

+/- S100 and TRK proteins.



## **Molecular testing:**

Gene fusion involving a FET gene (*FUS*, *EWSR1*, or *TAF15*) and an ETS gene.
*Most common fusion is EWSR1::FLI1 - t(11;22)(q24;q12), present in 85% of cases.*

Second most common fusion is EWSR1::ERG - t(21;22)(q22;q12)

Other less common reported fusions:
*EWSR1*::*ETV1*, *EWSR1*::*ETV4*, *EWSR1*::*FEV*, *FUS*::*ERG* , and *FUS*::*FEV*

**Adverse prognostic factors:**
Presence of metastasis (most important)
Anatomical location.

**Favorable prognostic factors:**
Complete pathological response to neoadjuvant chemotherapy



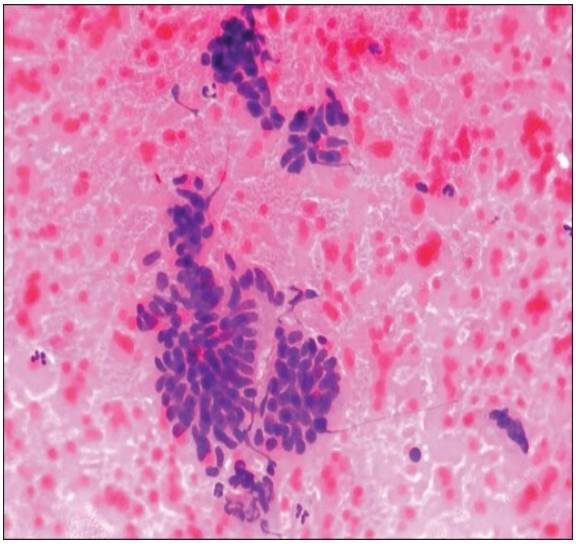
PMID: 19787372

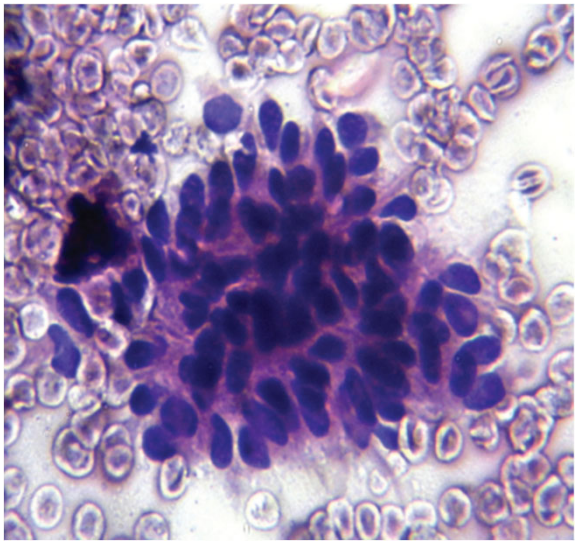
## Small round blue cell tumor workup

| | Histochemical staining | Immunohistochemistry | Molecular diagnostics |
|---|---|---|---|
| Ewing sarcoma/PNET | PAS positive | CD99+ | Translocation EWSR1 |
| Neuroblastoma | – | CD99−, CD56+ | MYCN amplification |
| Alveolar rhabdomyosarcoma | – | MYF4 (myogenin)+, Desmin+ | Translocation FKHR (FOXO1A) |
| Non-Hodgkin lymphoma/leukemia | PAS negative | CD45+ | Depending on subtype |
| Small cell carcinoma | – | Keratin+, neuroendocrine markers | – |
| (Poorly differentiated) synovial sarcoma | – | CD99+, BCL-2+ | Translocation SS18 (SYT) |
| Small cell osteosarcoma | Deposition of bone (alkaline phosphatase) | – | – |
| Mesenchymal chondrosarcoma | Deposition of cartilage | – | – |
| Desmoplastic small round cell tumor | – | Coexpression keratin and desmin | Translocation EWSR1 |
| Melanoma | – | Melanocytic markers+ | – |

## Ameloblastoma cytology

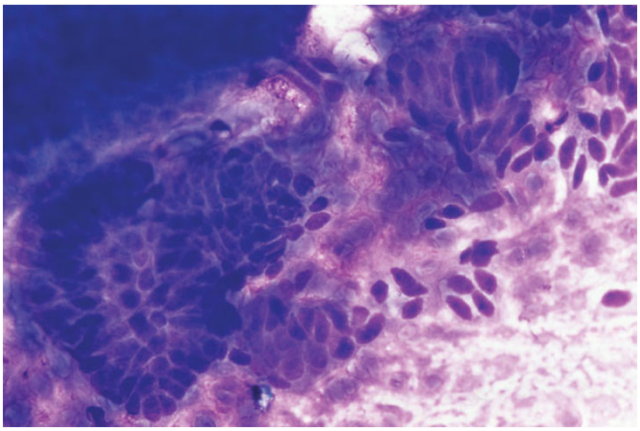
PMID: 25538387
PMID: 29937671



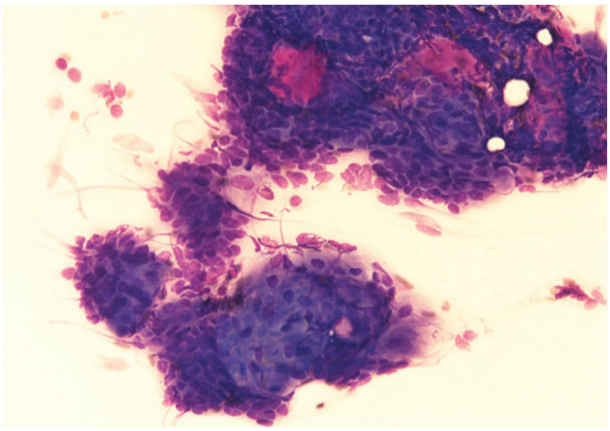




PMID: 21965020



Palisading



Squamous metaplasia

Not a common specimen in cytology

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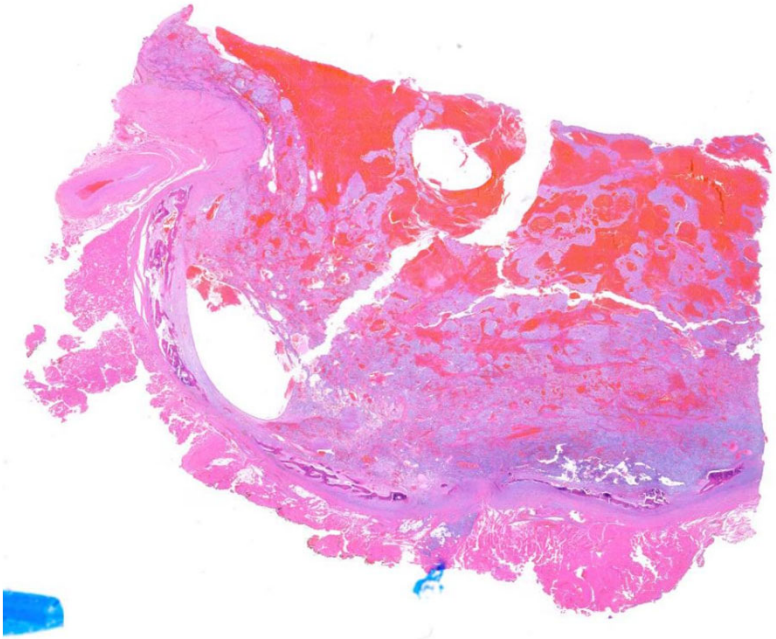

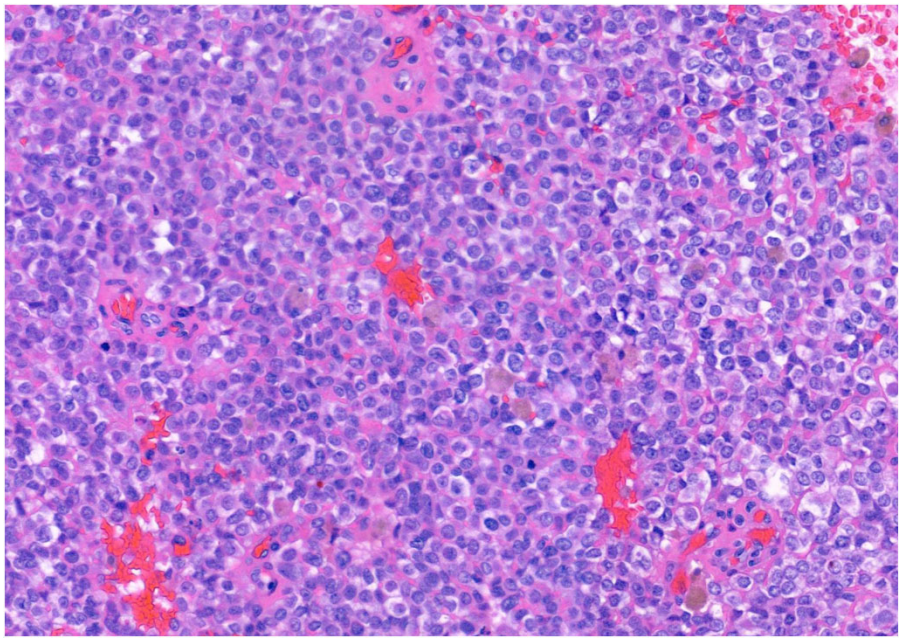



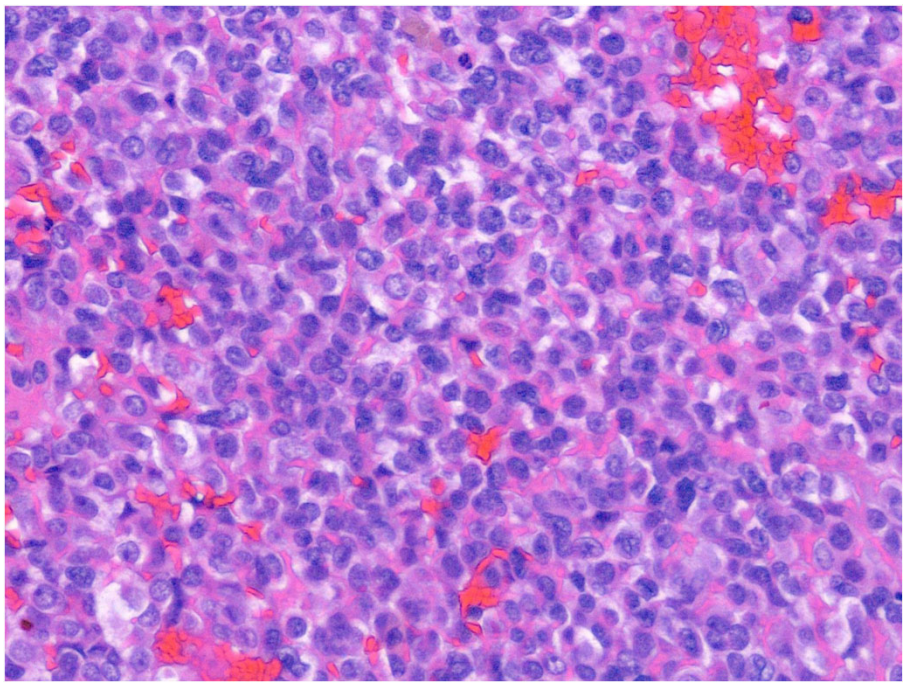

## Lessons I learned as a trainee

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2- Cytomorphologic overlap between different SRBCTs, and between Ewing sarcoma and ameloblastoma.

*On-site diagnosis is preliminary and subject to change.*

3- Typical features aren't always present!

4- Triaging samples with minimal tissue amount should start with tests that are most likely to yield a definitive diagnosis.

5- FNA by a pathologist vs. radiologist vs. clinician.



## Thank you

Mass General Brigham

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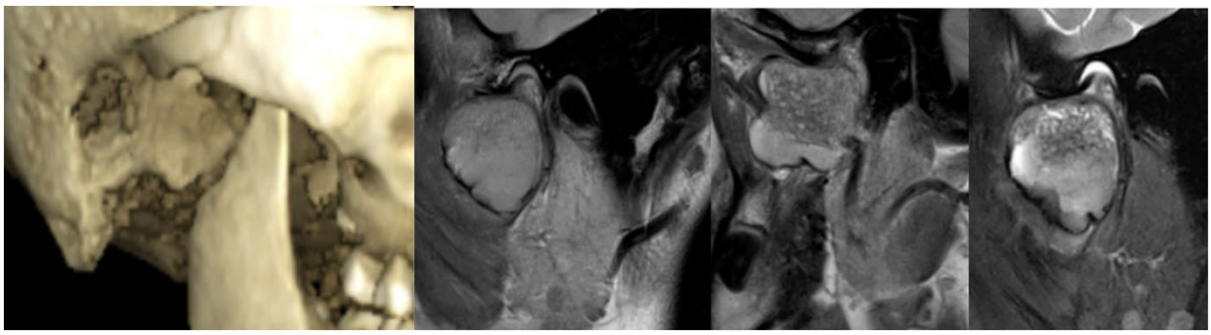
Dr. Bayan AlZumaili

## Imaging



Imaging: 3.6 x 3.0 x 2.9 cm expansile heterogeneously enhancing mass with multi-cystic and solid components centered in the right mandibular ramus and extending to the condyle.

A benign radiologic differential diagnosis (ameloblastoma vs. giant cell tumor of bone) was favored.



The patient was referred to the FNA clinic at MGH.

After communicating with the clinicians and radiologists, it was agreed that the mass has a bony cortex that is thin enough for FNA biopsy.

Physical examination revealed a well-defined, non-tender, irregular, firm, fixed swelling/mass lesion in the right temporomandibular joint region, measuring approximately 3 cm in greatest dimension.

## Bedside ultrasound at FNA clinic

3.0 x 2.28 cm well-defined, solid and cystic mass lesion with irregular borders.

The lesion was heterogeneously hyperechoic and hypoechoic without significant internal vascularity and with minimal peripheral vascularity.

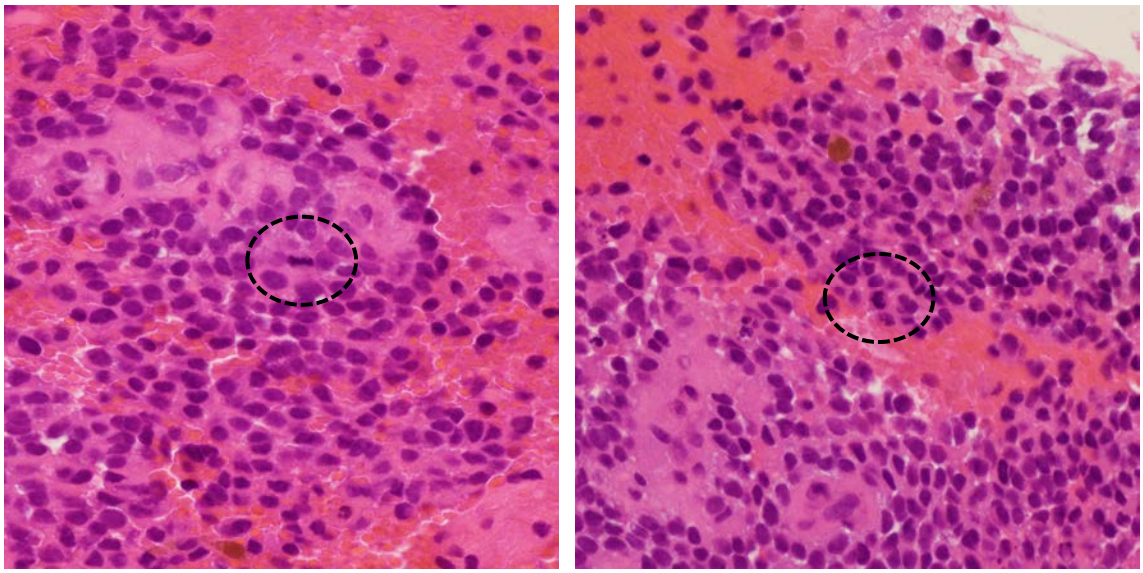


# On-site smears (Air dried – Diff Quick)

Favor ameloblastoma, awaiting permanents

## Alcohol fixed smears (Pap stain) and cell block





**Mitoses**

## Summary of cytologic findings:

Cellular smears.
Groups of small round monomorphic tumor cells with finely granular chromatin, inconspicuous (and some pinpoint) nucleoli.

Moderate amount of cytoplasm, eosinophilic to clear

Globular and band-like matrix material as well as some cells with possibly squamous features are also present.

Scattered mitotic figures are identified.

No giant cells are present.
No necrosis is seen.



## Differential diagnosis

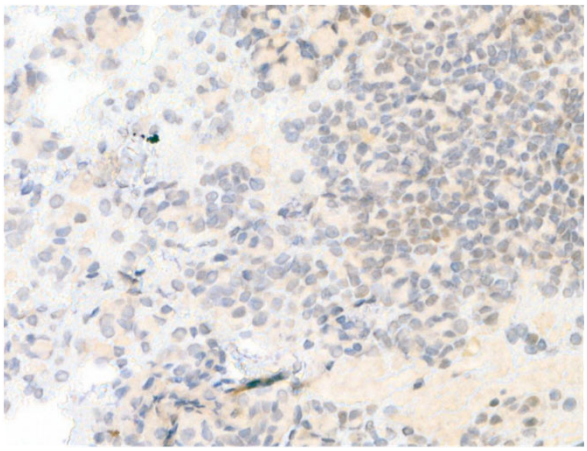
Ameloblastoma.

Small round blue cell tumors:
- Ewing sarcoma.
- Rhabdomyosarcoma and subtypes.
- Lymphoma.

Metastasis: Melanoma, neuroblastoma, Wilm's tumor, poorly differentiated carcinoma

## Immunohistochemistry…

**CK MNF 116**
**(Neg)**



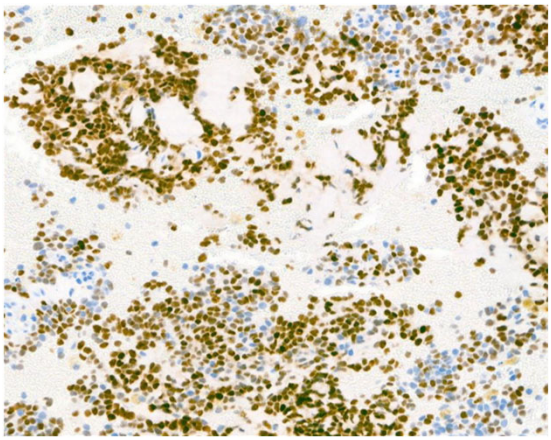
**BRAF**
**(Neg)**



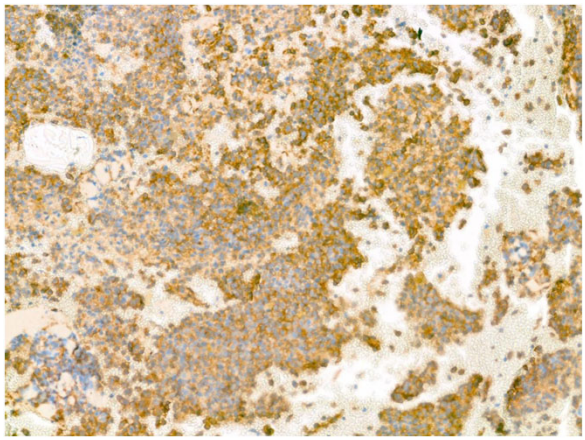
## Solid Fusion Assay (Molecular testing)

RESULTS:
A fusion transcript was identified involving EWSR1 exon:7 (NM_005243.4) and FLI1 exon:9 (NM_002017.5).
No other reportable fusion transcripts were identified.

INTERPRETATION:
POSITIVE for EWSR1::FLI1 gene fusion

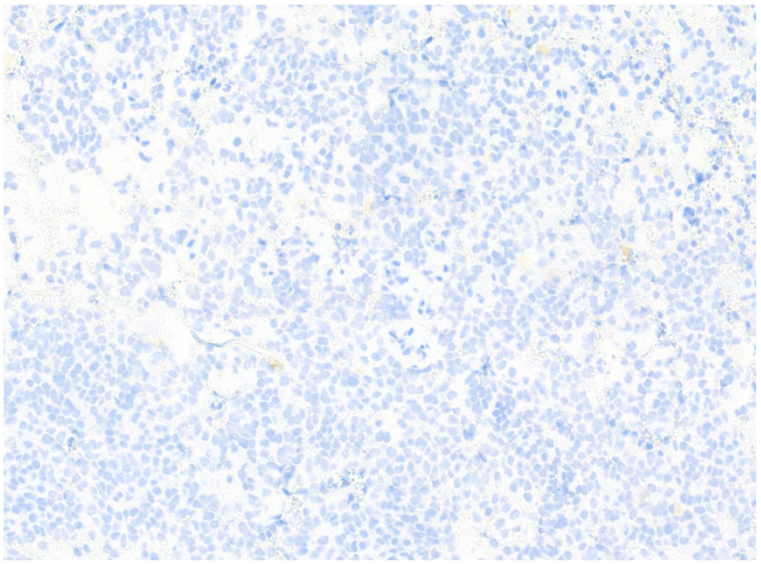


NKX2.2
(Pos)



CD99
(Pos)





Desmin
(Neg)

## Final diagnosis:

Ewing Sarcoma



## Ewing sarcoma

Second most common malignant bone tumor in children/young adults.

Peak incidence in second decade of life. (nearly 80% of patients are younger than 20 years of age).

Overall male predilection (M:F ratio: 3:2).

More common in individuals of European descent (compared to individuals of African or Asia descent).

Most are sporadic.

Vast majority occur in bone.
12% are extra-skeletal.

## Ewing sarcoma of the head and neck

PMID: 19841575
PMID: 28056517
PMID: 28056517
PMID: 26304893

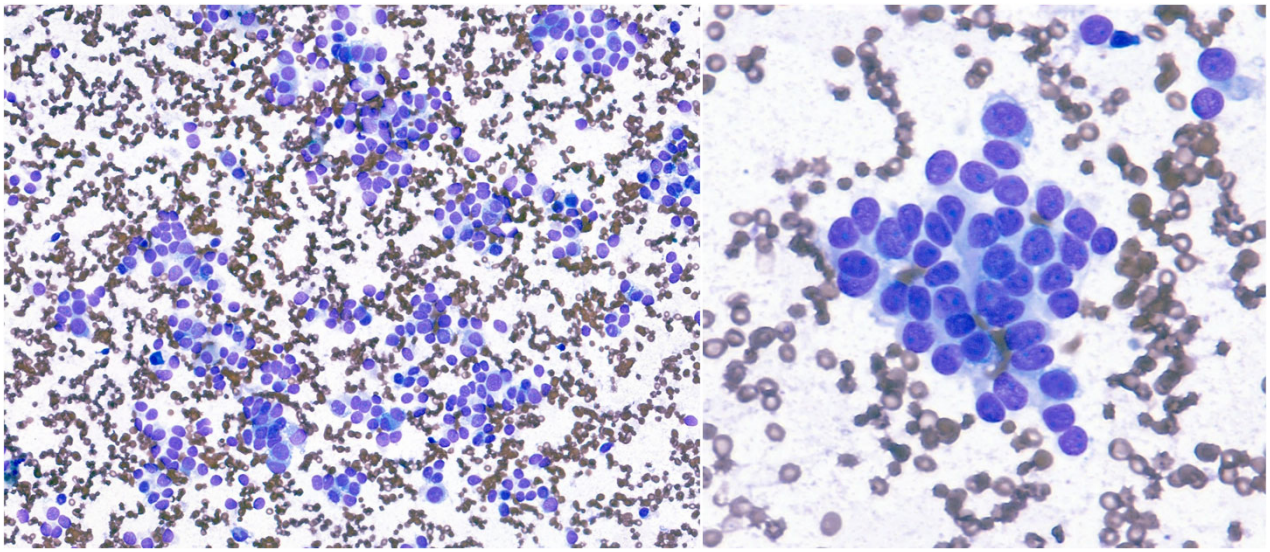
1-9% of Ewing sarcoma cases.
- 40% in skull and facial bones.
- 30% centered in soft tissue
- 9% in mandible (0.09-0.81 %)

~ 50% of head and neck Ewing sarcomas arise in patients aged < 18 years
85% occur in the first four decades of life.

Slight male predominance.

Prognosis better than that of other tumor sites (smaller size, lower metastatic rate)
5-year survival is 70% for localized disease and 30% for metastasis at presentation.





## **Immunohistochemistry**:

**CD99** typically shows strong diffuse membranous reactivity (Not specific).
**NKX2.2** shows nuclear staining (high sensitivity, moderate specificity)

**FLI1 and ERG** are often expressed in cases with the corresponding gene fusion.

Cytokeratins expressed in 30% of cases
Neuroendocrine markers expressed in 50% of cases

+/- S100 and TRK proteins.



## **Molecular testing:**

Gene fusion involving a FET gene (*FUS*, *EWSR1*, or *TAF15*) and an ETS gene.
*Most common fusion is EWSR1::FLI1 - t(11;22)(q24;q12), present in 85% of cases.*

Second most common fusion is EWSR1::ERG - t(21;22)(q22;q12)

Other less common reported fusions:
*EWSR1*::*ETV1*, *EWSR1*::*ETV4*, *EWSR1*::*FEV*, *FUS*::*ERG* , and *FUS*::*FEV*

**Adverse prognostic factors:**
Presence of metastasis (most important)
Anatomical location.

**Favorable prognostic factors:**
Complete pathological response to neoadjuvant chemotherapy



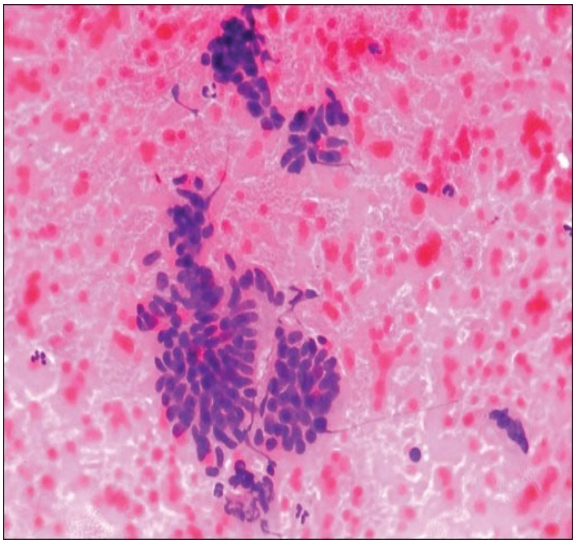
PMID: 19787372

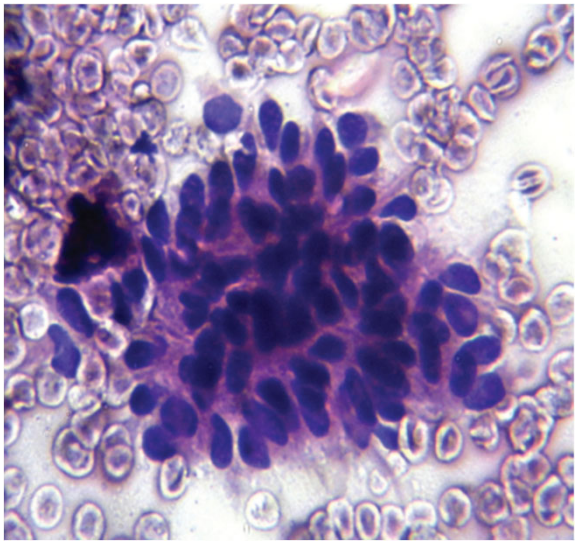
## Small round blue cell tumor workup

| | Histochemical staining | Immunohistochemistry | Molecular diagnostics |
|---|---|---|---|
| Ewing sarcoma/PNET | PAS positive | CD99+ | Translocation EWSR1 |
| Neuroblastoma | – | CD99−, CD56+ | MYCN amplification |
| Alveolar rhabdomyosarcoma | – | MYF4 (myogenin)+, Desmin+ | Translocation FKHR (FOXO1A) |
| Non-Hodgkin lymphoma/leukemia | PAS negative | CD45+ | Depending on subtype |
| Small cell carcinoma | – | Keratin+, neuroendocrine markers | – |
| (Poorly differentiated) synovial sarcoma | – | CD99+, BCL-2+ | Translocation SS18 (SYT) |
| Small cell osteosarcoma | Deposition of bone (alkaline phosphatase) | – | – |
| Mesenchymal chondrosarcoma | Deposition of cartilage | – | – |
| Desmoplastic small round cell tumor | – | Coexpression keratin and desmin | Translocation EWSR1 |
| Melanoma | – | Melanocytic markers+ | – |

## Ameloblastoma cytology

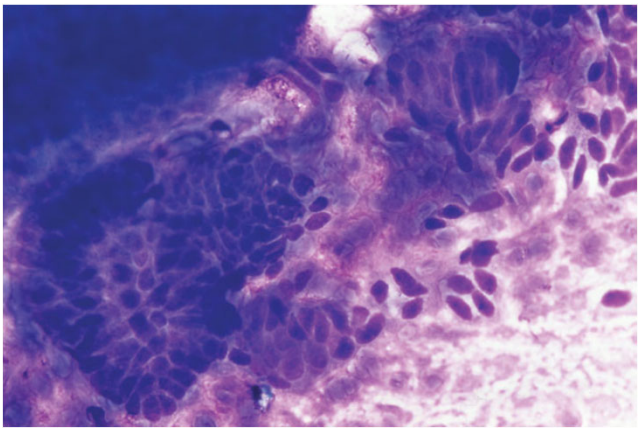
PMID: 25538387
PMID: 29937671







PMID: 21965020



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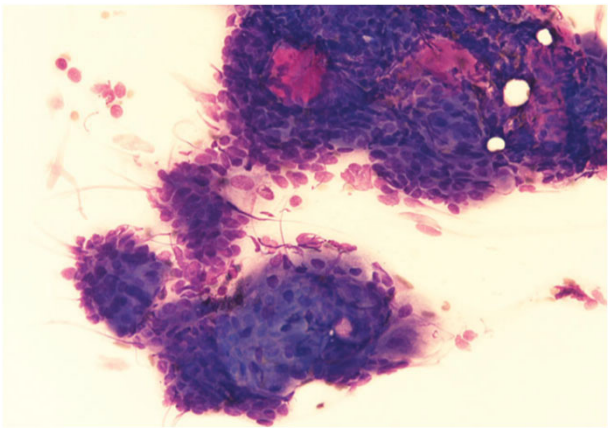

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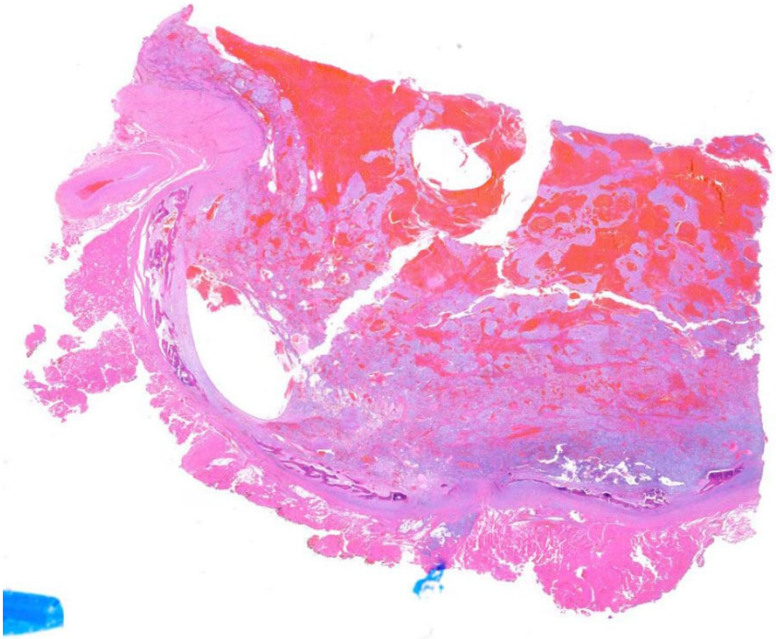

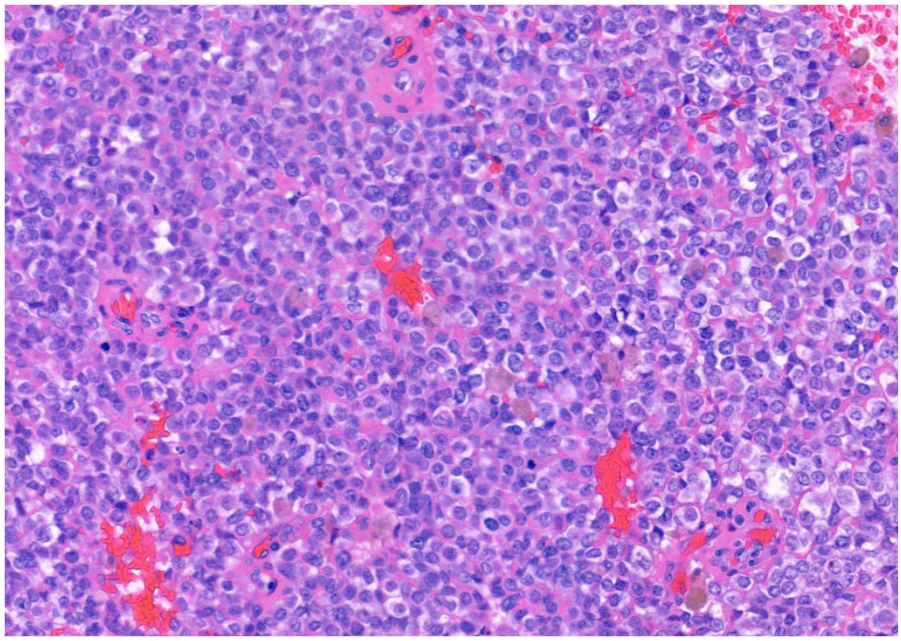



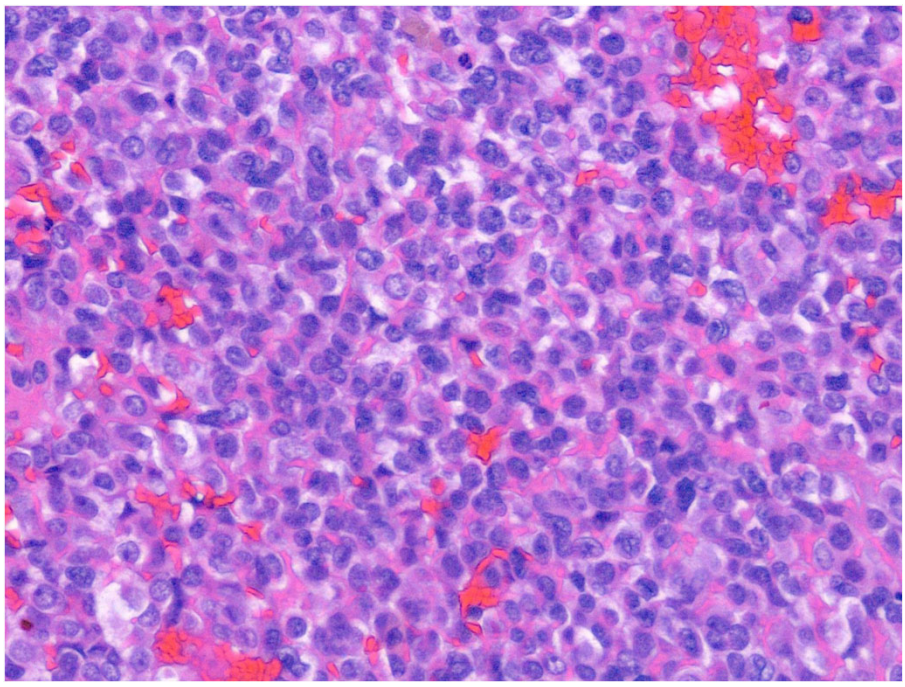

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Dr. Bayan ALZumaili

Mass General Brigham

# Challenges and Lessons Learned Virtual Microscopy 2

Ruhani Sardana MD.
Cytopathology Fellow
Mass General Brigham Hospitals

06/10/2025 4:30-6:00 pm EST



## Disclosure

I have no disclosure or conflict of interest in relation to this presentation

# CASE 1



## Clinical History

70 years female with chronic kidney disease found to have incidental multiple pancreatic cysts

# Imaging

**MRCP**

Pancreatic head shows a conglomerate of simple appearing cysts
Measuring approx. 7.3 x 4.3 cm, stable from prior studies.
Findings may represent IPMN

Pancreatic body shows a 6.2x5.6x5.4 cm circumscribed
mixed solid-cystic mass with multiple enhancing internal septation.
Differential diagnosis includes primary pancreatic neoplasm
cannot rule out adenocarcinoma. Recommend sampling.

**EUS**

A well-defined mass was identified in pancreatic body which was solid and cystic measuring 5.8x5.1 cm.



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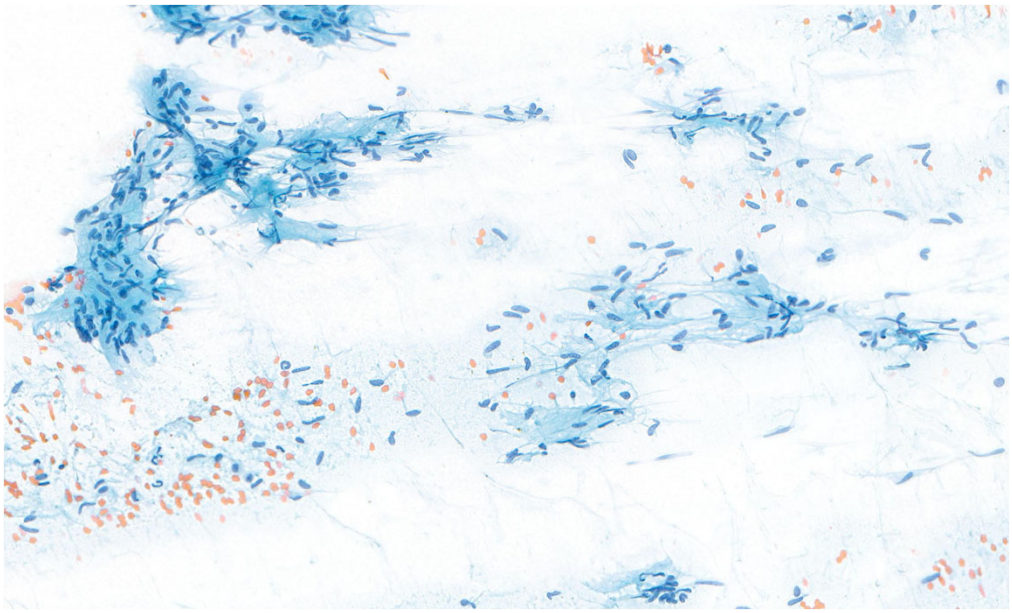

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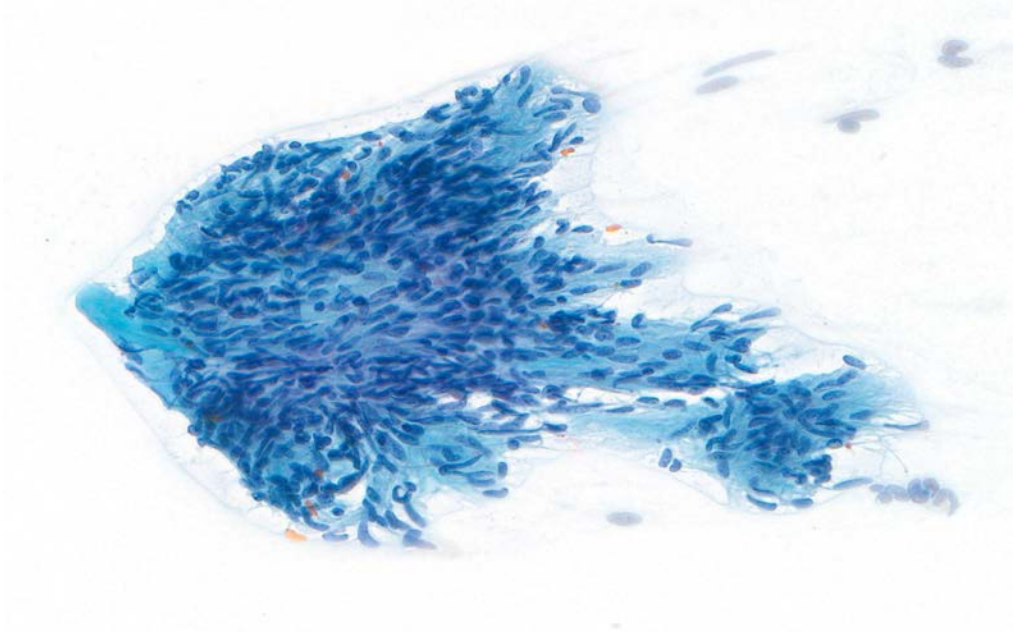

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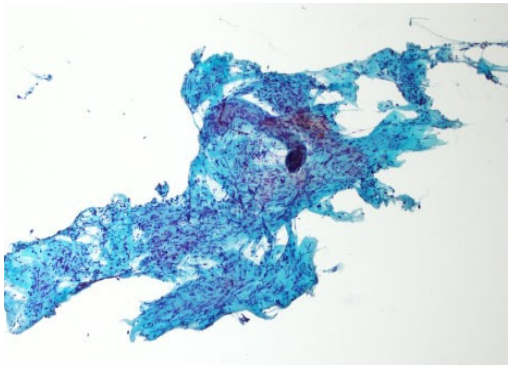
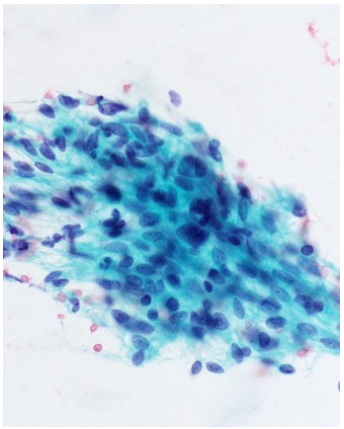
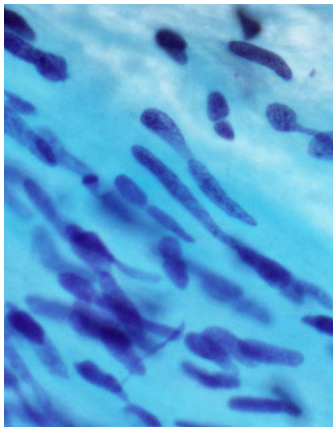
Whole slide images available

# Schwannoma facts



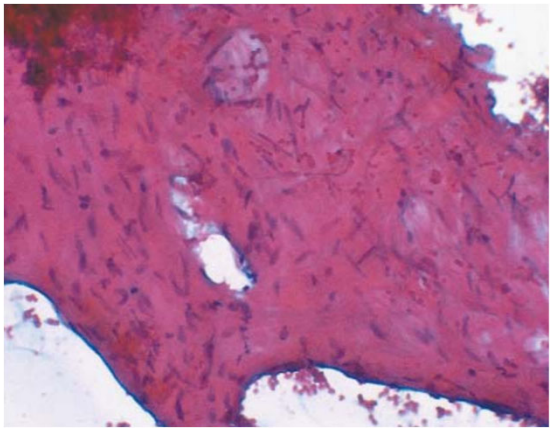


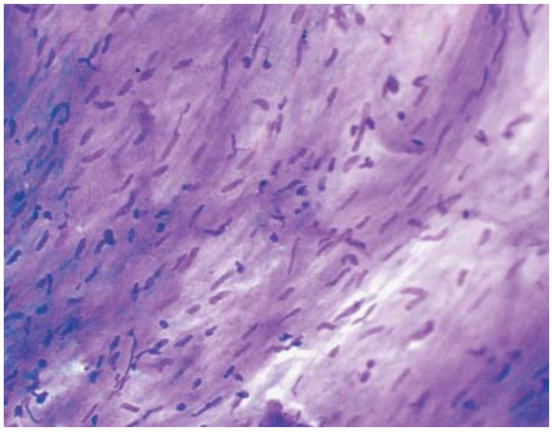


Spindle cell neoplasm showing large cohesive cluster (Pap stain x40, x100), with cells arranged in fascicles haphazardly in dense fibrillary stroma. There is anisonuceolsis with pointed nuclear tips (Pap stain x400)

Chebib, Ivan et al. "Cytomorphologic features that distinguish schwannoma from other low-grade spindle cell lesions." *Cancer cytopathology* vol. 123,3 (2015): 171-9. doi:10.1002/cncy.21506

# Leiomyoma facts



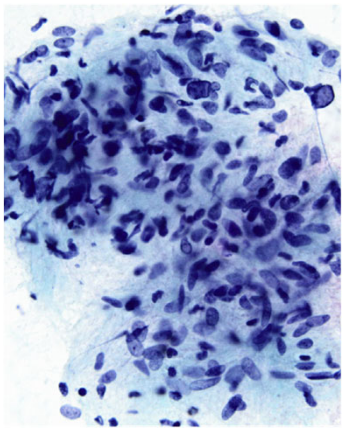


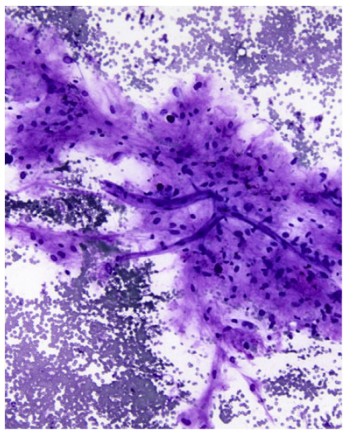
Spindle cell neoplasm forming fascicles with relatively low cellularity and monomorphic spindle cells with eosinophilic cytoplasm, vesicular nuclei

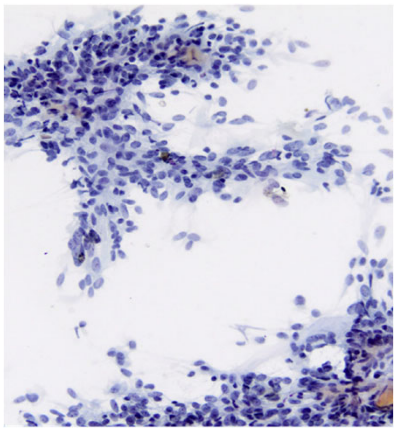
Garg, Karuna et al. "Morphologic features of uterine leiomyomas associated with hereditary leiomyomatosis and renal cell carcinoma syndrome: a case report." *The American journal of surgical pathology* vol. 35,8 (2011): 1235-7. doi:10.1097/PAS.0b013e318223ca01



# Solitary Fibrous Tumor Facts





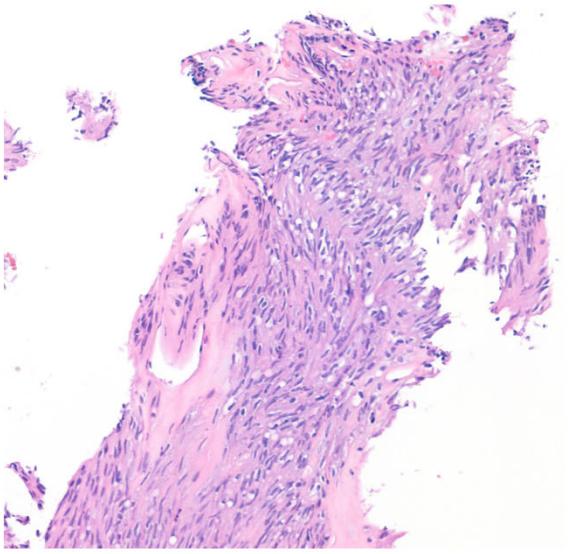


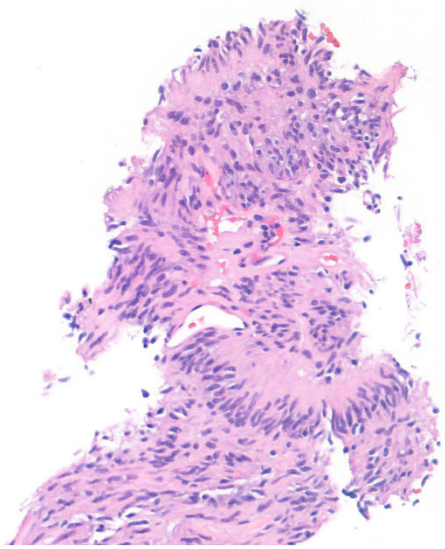
Severely tight clustered jagged clusters contain euchromatic elongated nuclei. Spindle cells are arranged along collagenous core, with cells at the edge appear to be loose and detach themselves

Wakely PE Jr, Rekhi B. Cytopathology of solitary fibrous tumor: a series of 34 cases. *J Am Soc Cytopathol.* 2021;1
doi:10.1016/j.jasc.2021.03.005

# Let's work up !

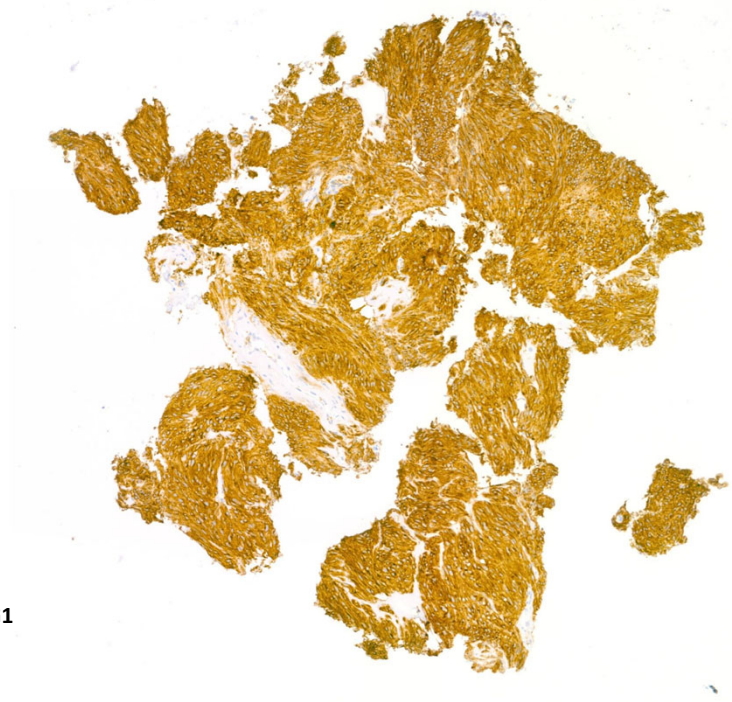






Whole slide images available

CD117



DOG1

# Diagnosis

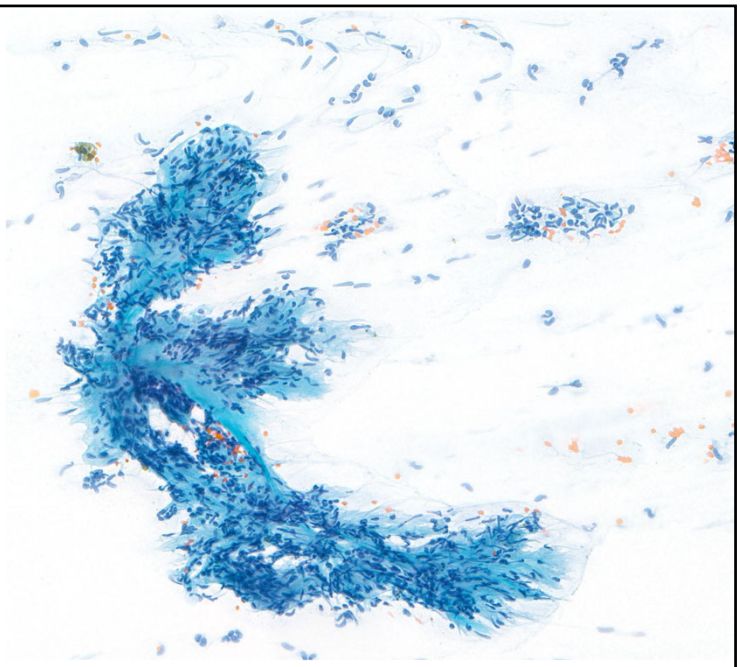
**Gastrointestinal Stromal Tumor**

- High cellularity, elongated monomorphic spindle cells

- Large sized clusters in a non-fascicular growth pattern with fibrillary stroma

- Prominent single cells in background

- Blunted nuclear ends



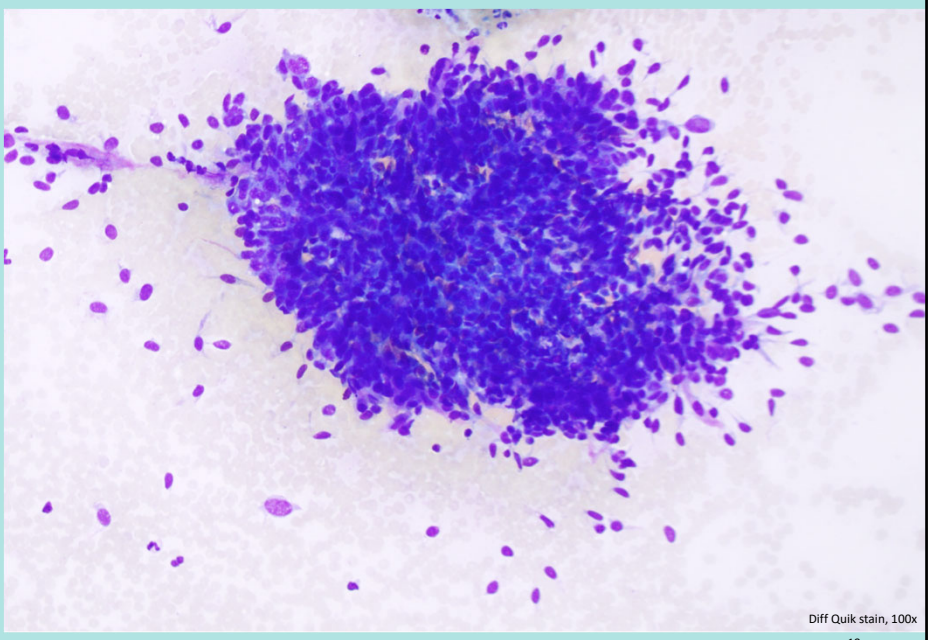


# Helpful clues

| | GIST | Schwannoma | Leiomyoma | Solitary Fibrous Tumor |
|---|---|---|---|---|
| **Cellularity** | High | High | Low | Moderate |
| **Pattern** | Non-fascicular, Fibrillary | Cohesive, haphazard | Fascicular | Ragged, shedding at edge |
| **Background** | Stripped nuclei | Lymphocytes +/- | - | Stripped nuclei |
| **Stroma** | Fibrillary | Fibrillary, Metachromatic (Diff-Quik) | - | Collagenous core |
| **Nuclear detail** | Blunted ends | Pointed ends Anisonucleosis +/- | Vesicular, bland | Elongated, euchromatic |
| **IHC** | DOG-1, c-KIT/CD117 | S100 | Desmin | CD34, STAT6 |

# Bonus Case for Curious Minds!

3.2 cm mass arising in the oral cavity



Diff Quik stain, 100x

# CASE 2



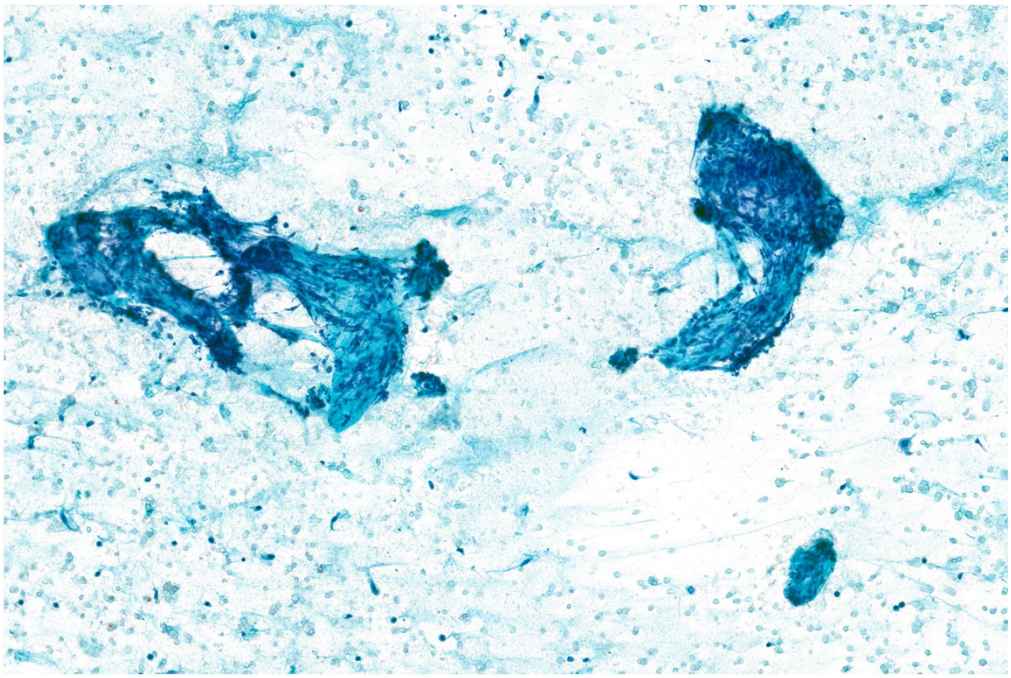
## Clinical History

80 years old man noted swelling and redness in in his left foot. This was treated with antibiotics and compression stockings. DVT was ruled out.

Multiple PET avid, enlarged lymph nodes were seen bilaterally in lower extremities ranging from 0.5 to 1.2 cm in largest dimensions

No significant neoplastic history

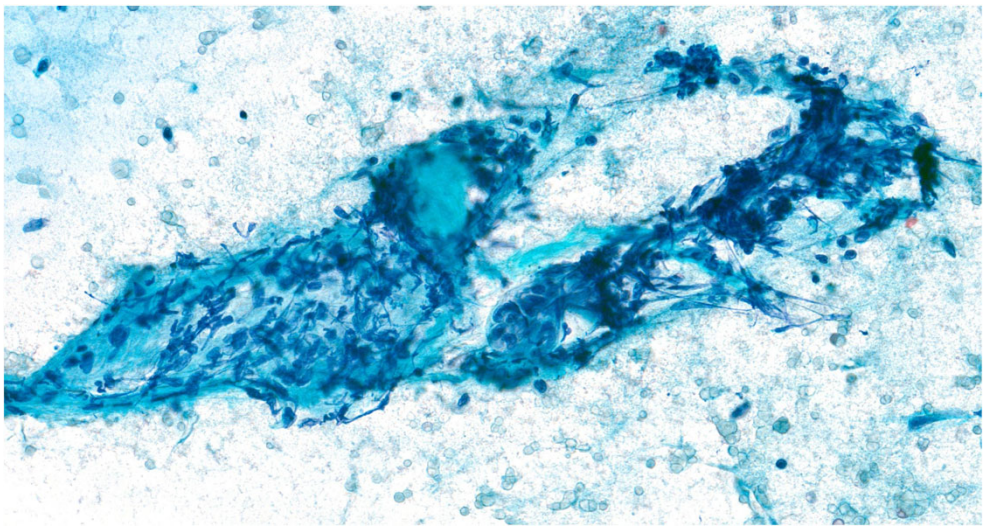
Patient presented to our FNA clinic for sampling of the lymph node in the left popliteal fossa



Whole slide images available

Pap stain, 10x

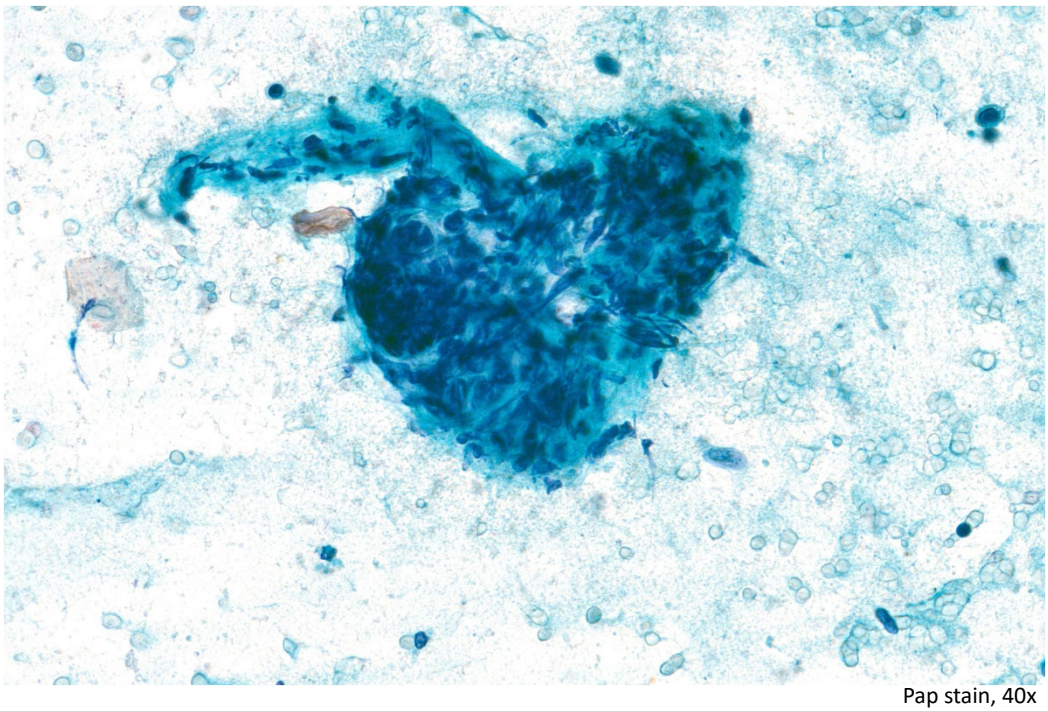
23



Whole slide images available

Pap stain, 40x

24



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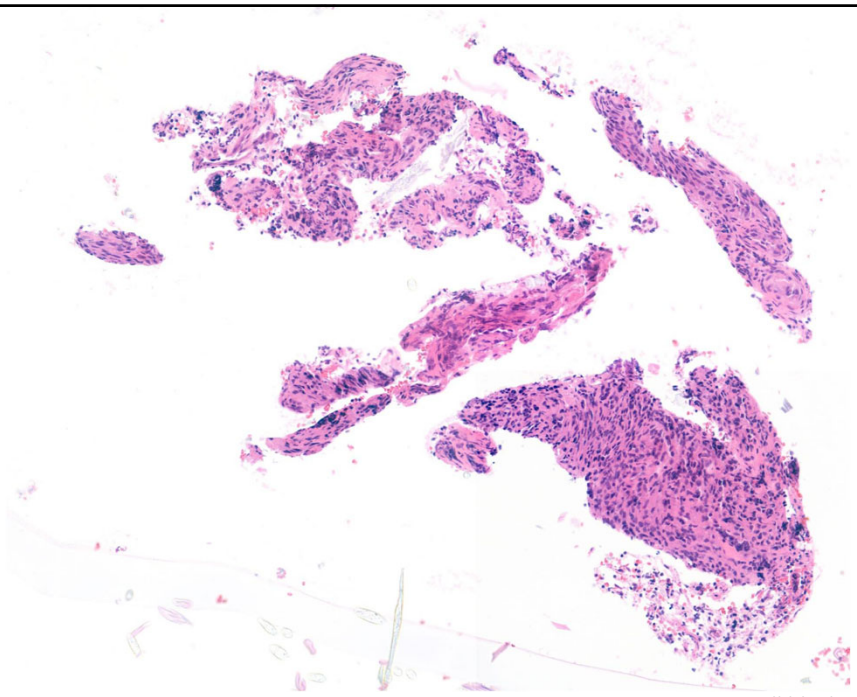
Pap stain, 40x



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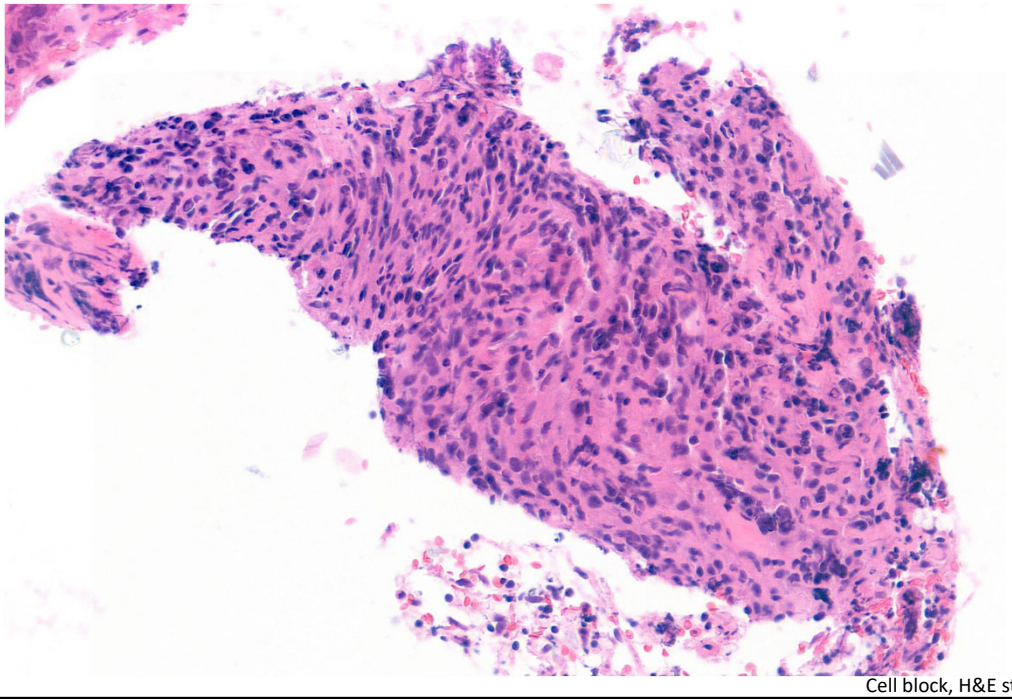
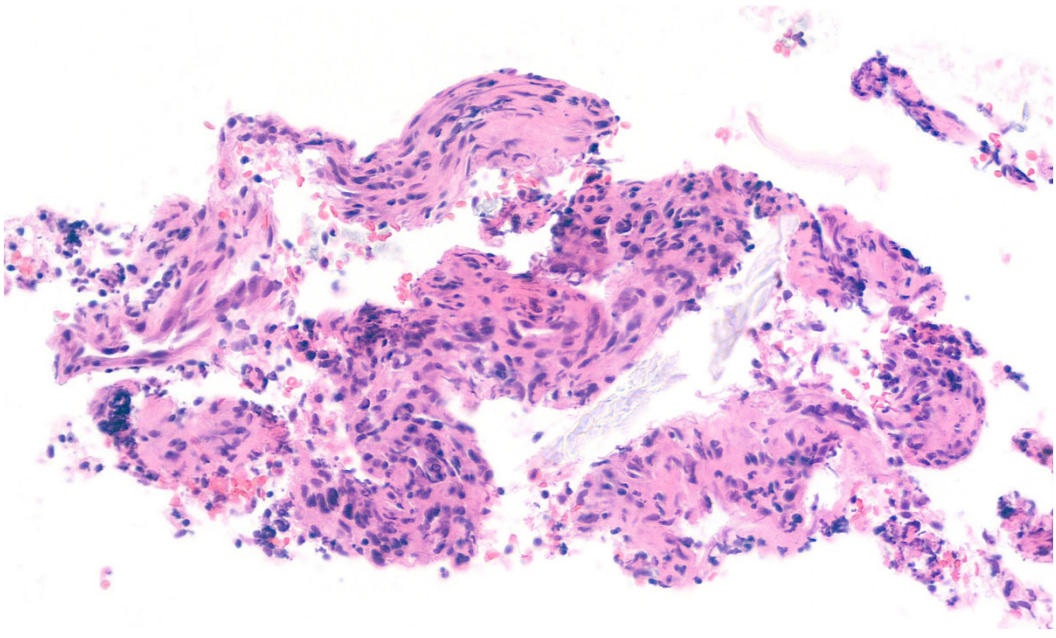
Whole slide images available

Cell block, H&E stain, 10x



27

Cell block, H&E stain, 40x

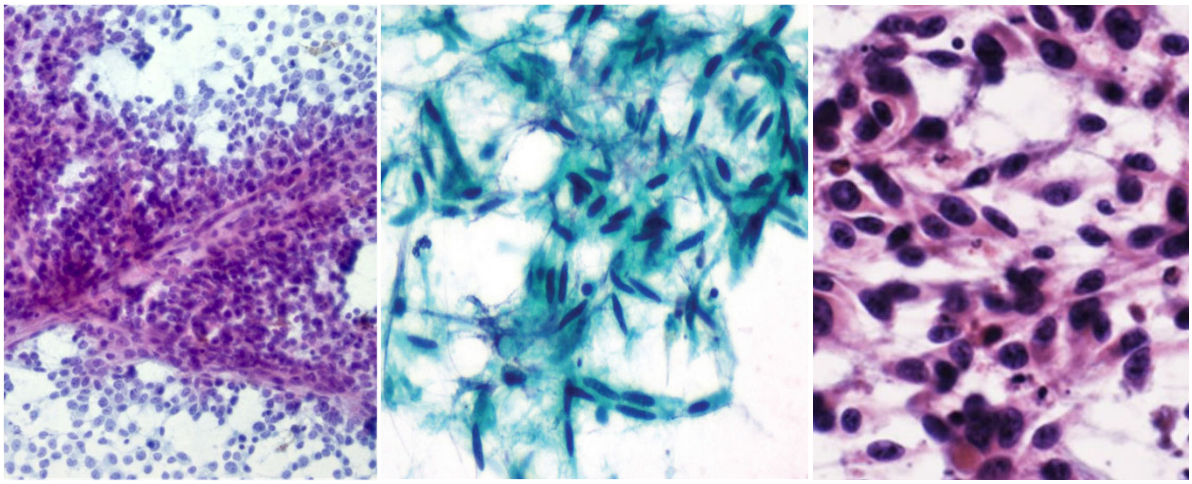


28

Whole slide images available

Cell block, H&E stain, 10x

## Melanoma Facts

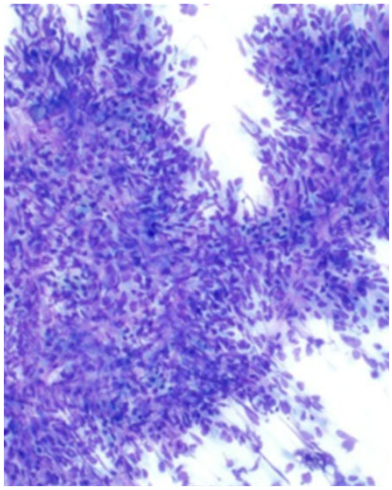


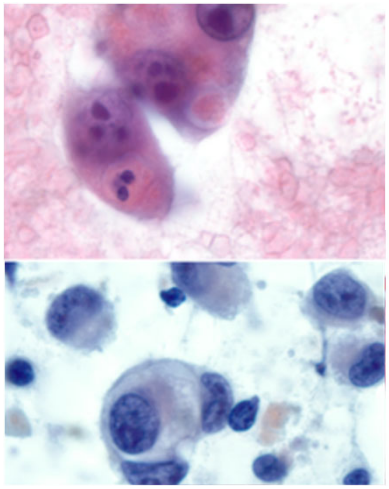
Predominantly interlacing fascicles and whorls of spindle cells. Prominent macro-nucleoli, pseudoinclusion, binucleate cells are rare

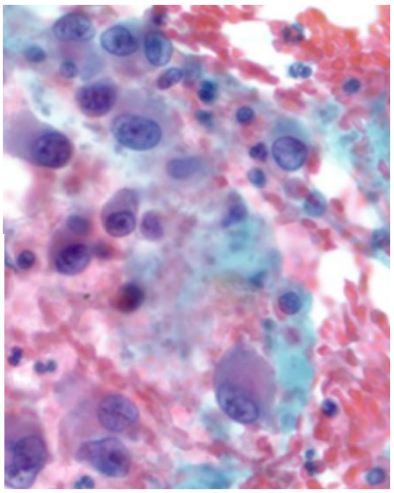


Ronchi, Andrea et al. "Cytologic diagnosis of metastatic melanoma by FNA: A practical review." *Cancer cytopathology* vol. 130,1 (2022): 18-29. doi:10.1002/cncy.22488

# Angiosarcoma Facts





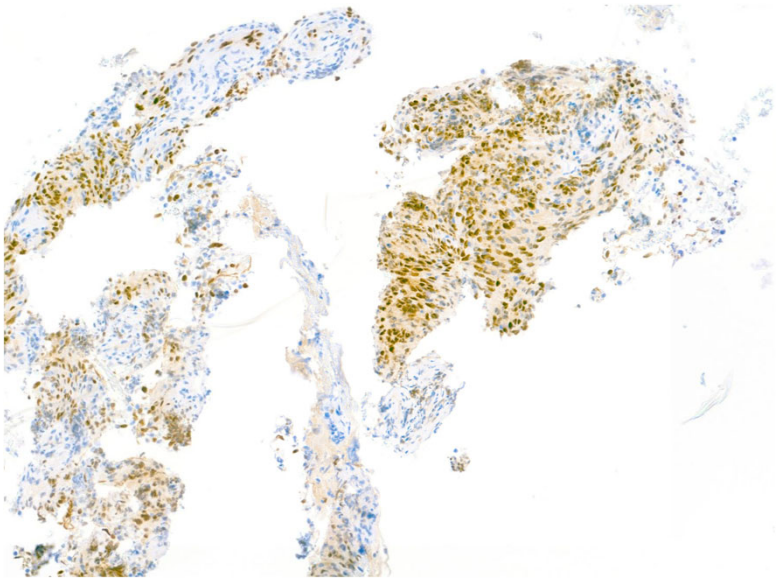


Prominent papillary groups with central fibrovascular cores surrounded by pleomorphic spindled tumor cells (Diff-Quik stain, ×200), Vaso-formative features, endothelial wrapping of tumor cells



Geller, Rachel L et al. "Cytologic features of angiosarcoma: A review of 26 cases diagnosed on FNA." *Cancer cytopathology* vol. 124,9 (2016): 659-68. doi:10.1002/cncy.21726

# Let's work up !



ERG



HHV8

# Diagnosis

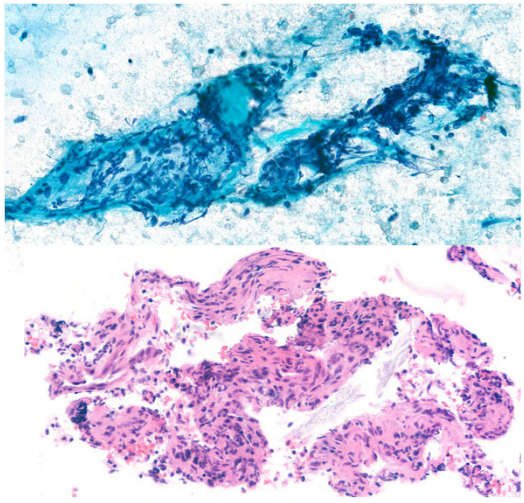
**Kaposi sarcoma**

- Hypercellular smear

- Atypical spindle cells with moderate amount of cytoplasm with minimal nuclear atypia

- Hemorrhagic background +/-

- Cell block:
  - Vaso-formative architecture, slit like spaces
  - Extravasated RBCs, hemosiderin
  - Uniform cells with mild nuclear atypia
  - Eosinophilic globules “Dorf Balls”
  - Plasma cells





# Helpful clues

- Melanoma:
  - Eccentric nuclei, prominent nucleoli, “demons” binucleation
  - Peritheliomatous pattern
  - Cytoplasmic melanin pigment
  - Positive: Sox10, Melan A, HMB45  Negative: ERG, SMA

- Angiosarcoma:
  - Epithelioid to spindle cells, hob nailing, lose clusters
  - Marked nuclear atypia, atypical mitotic figures, necrosis
  - Cytoplasmic vacuoles
  - Positive: ERG  Negative: HHV8

- Poorly differentiated carcinoma:
  - Diverse morphologic spectrum; clusters, discohesive pleomorphic spells
  - Positive: Keratins

# Thank You