Radiology / Pathology Conference

June 4, 2010

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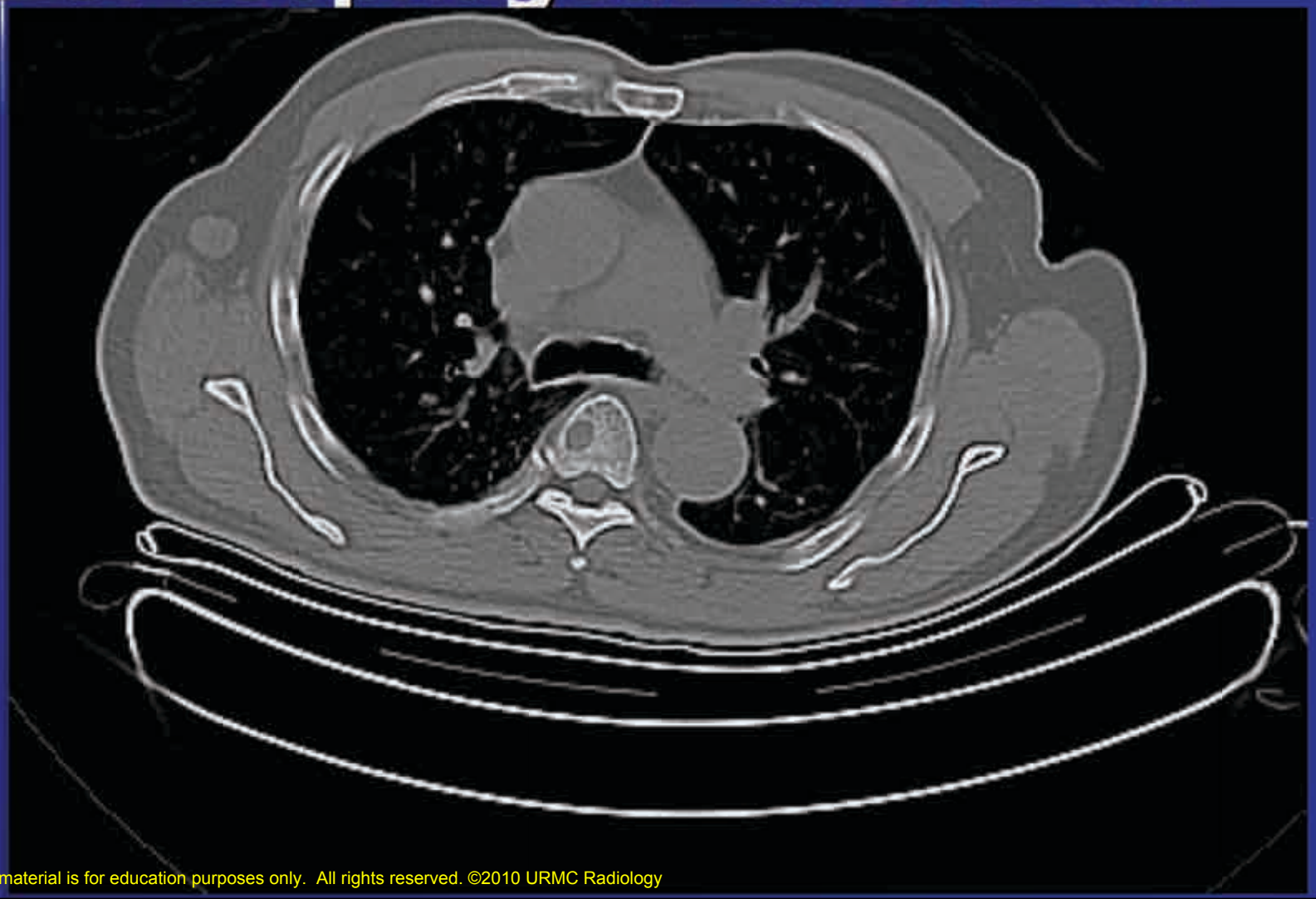
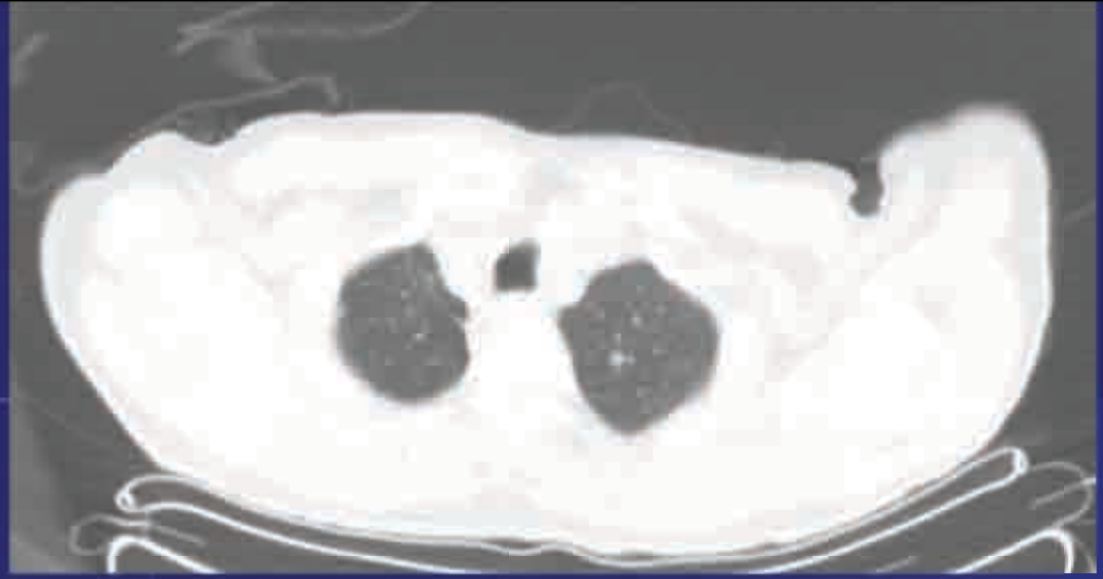
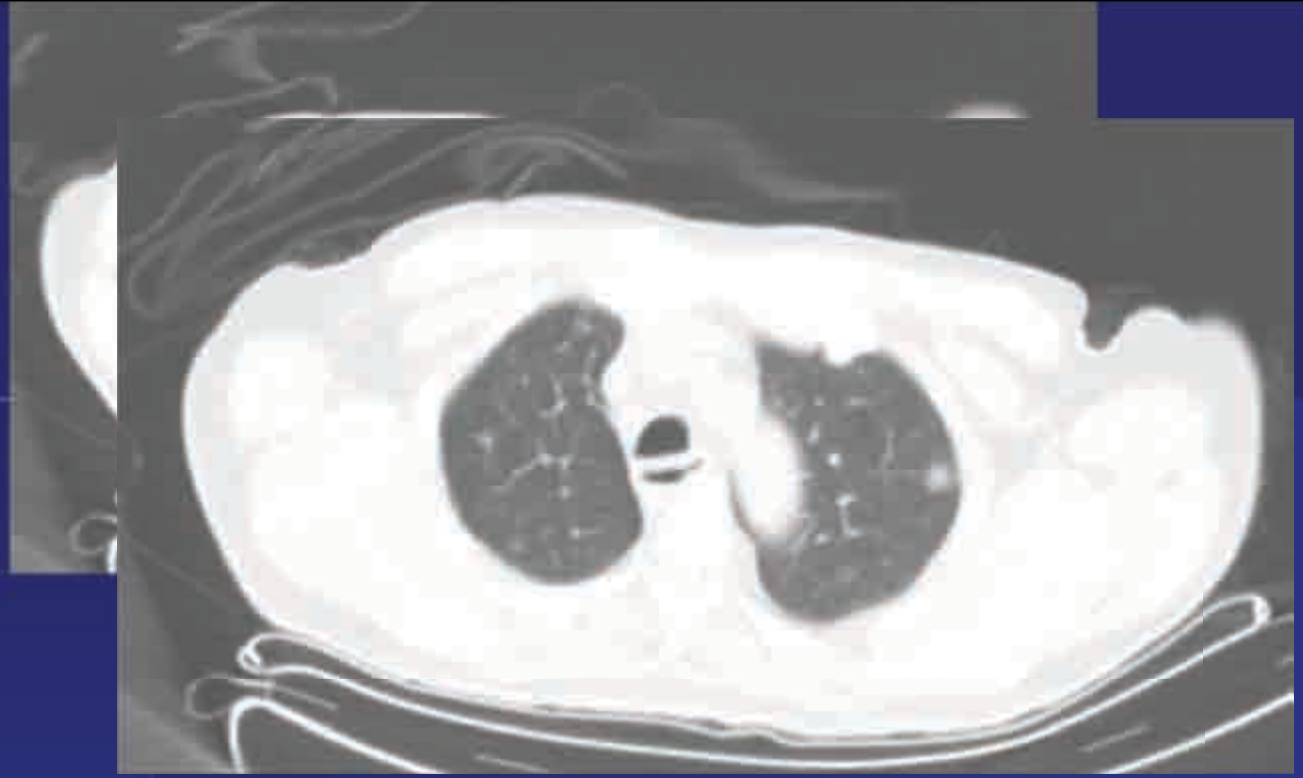
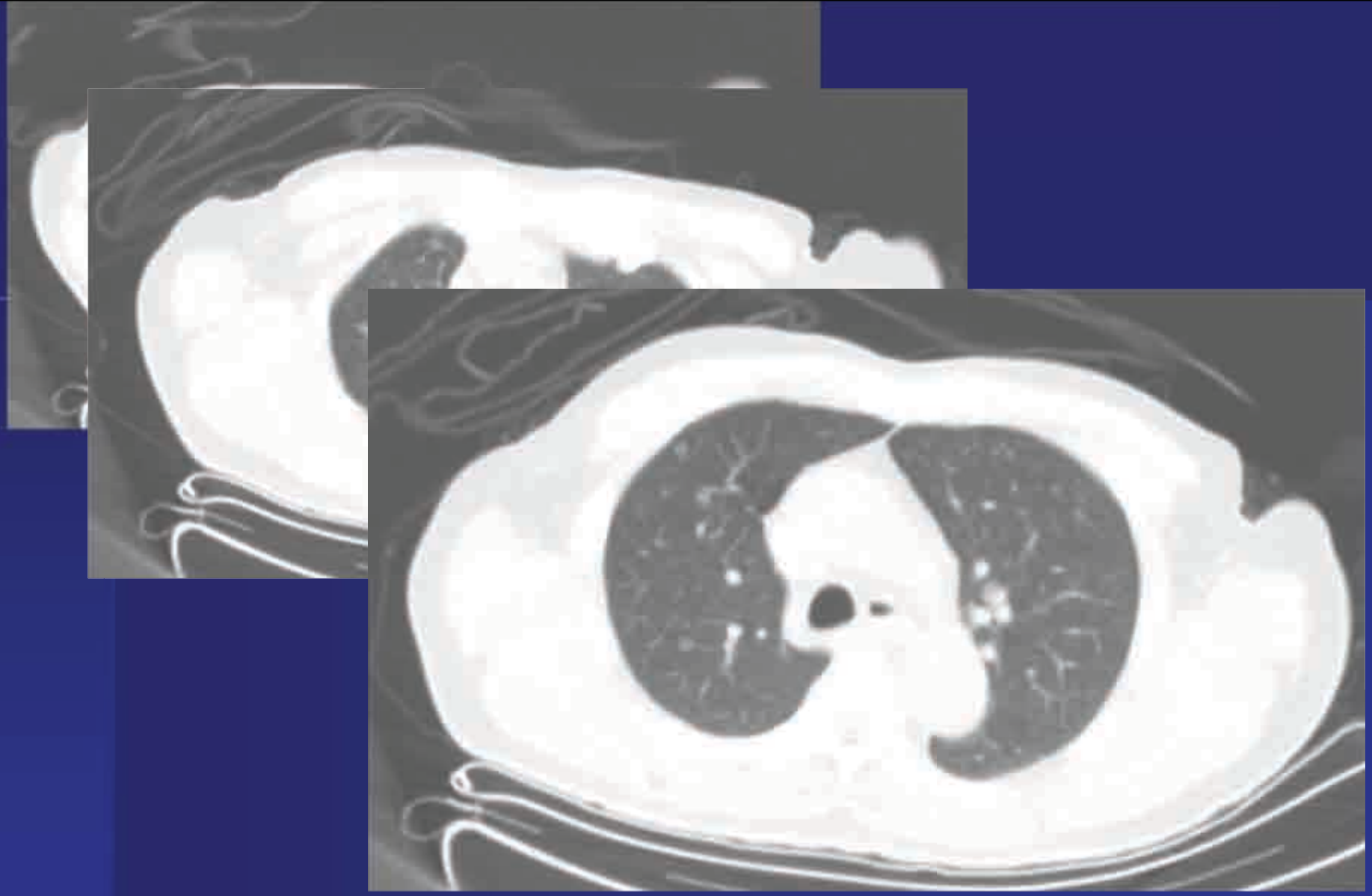
Case 1

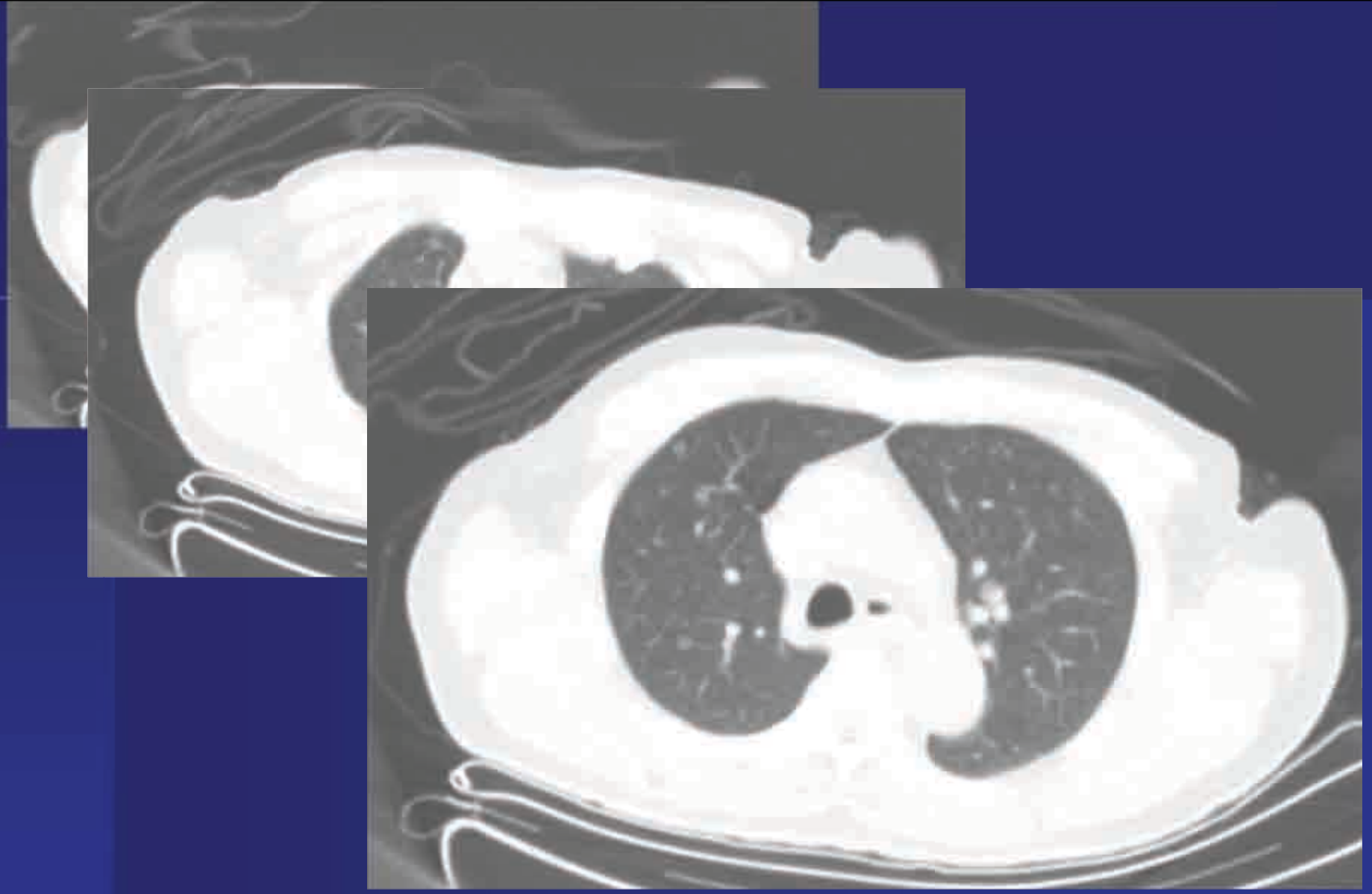
76 year old M, hx of lung carcinoma 5 yr prior, new dx of esophageal carcinoma



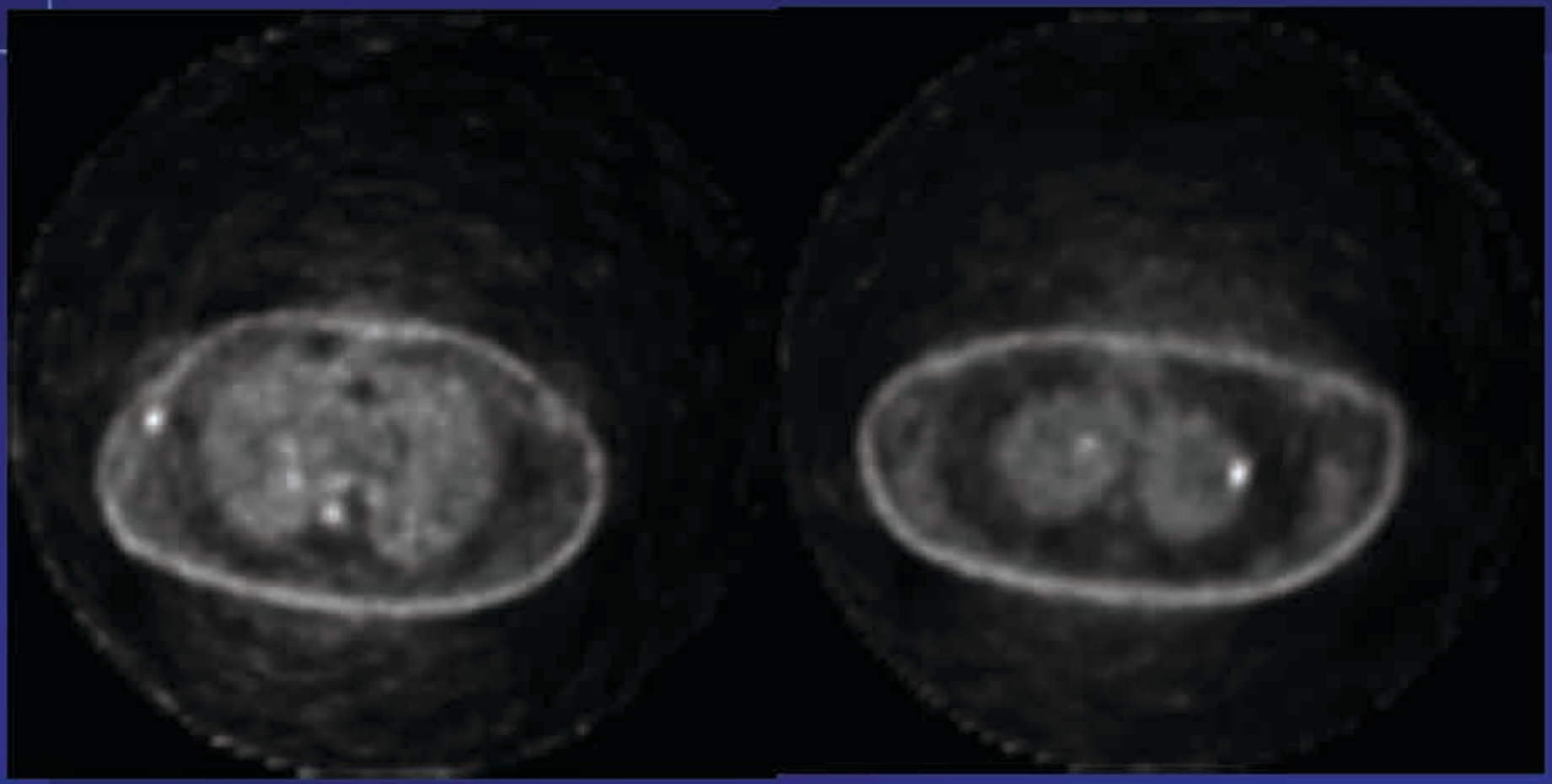


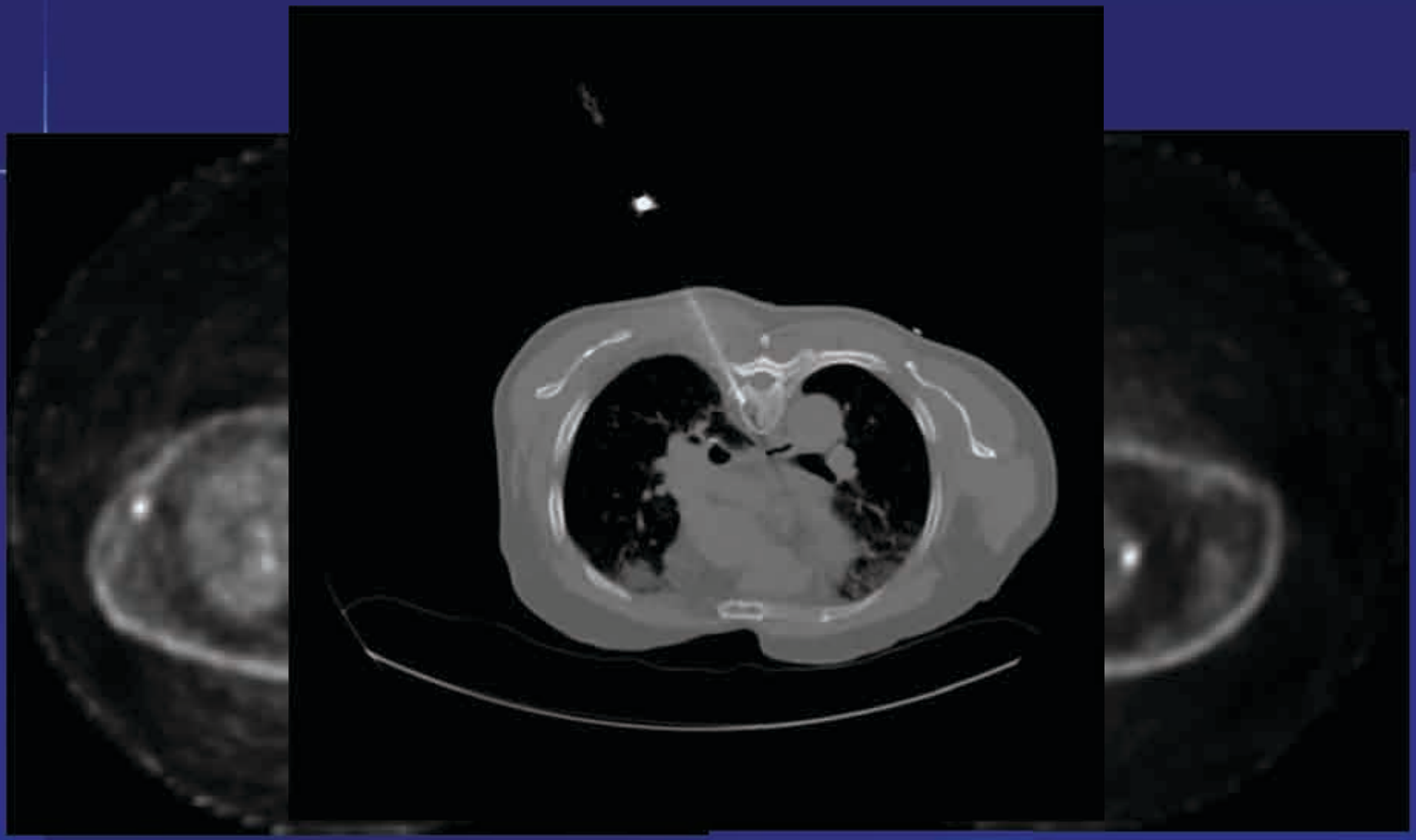






Differential? Next step?

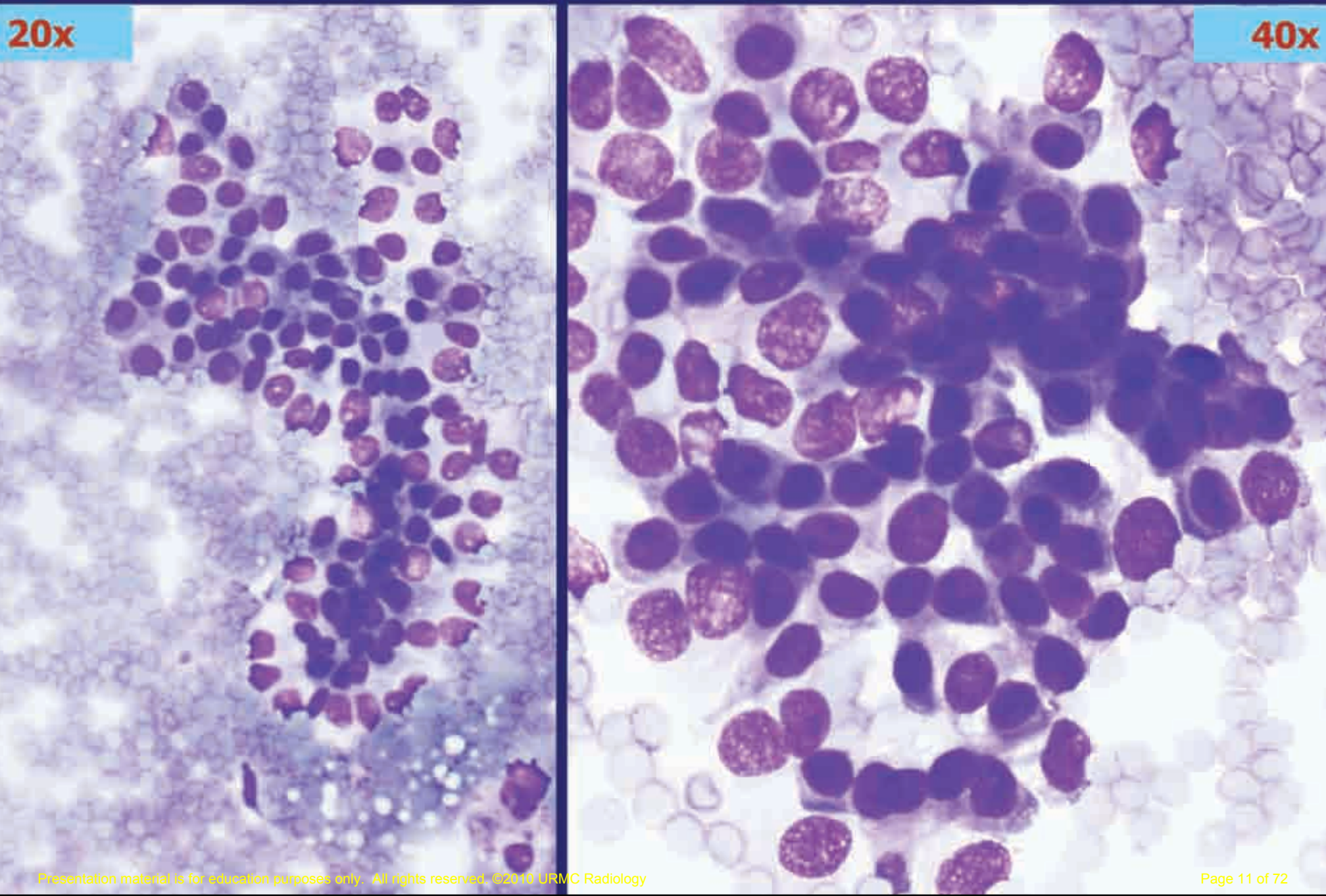




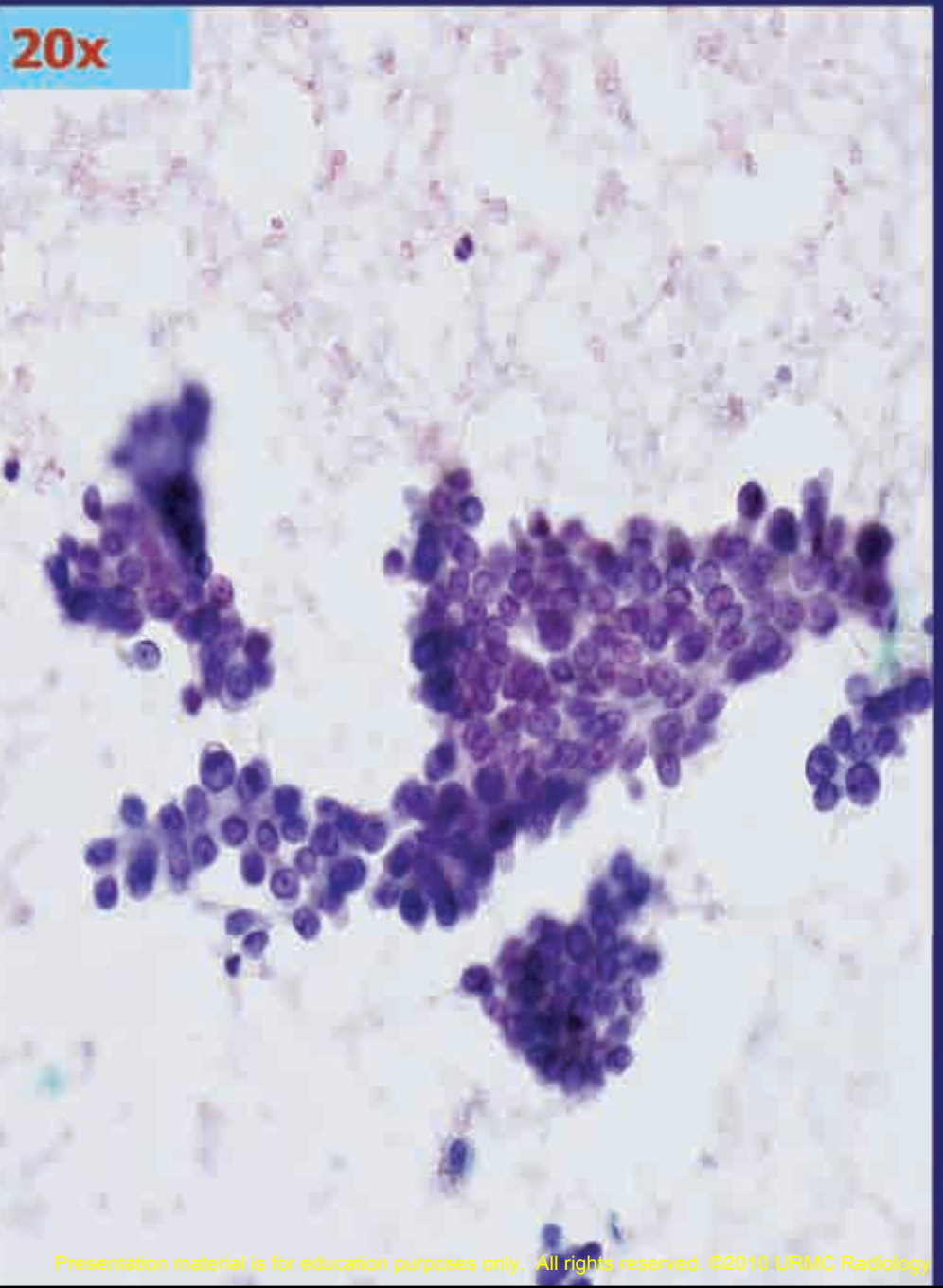
Multiple pulmonary nodules

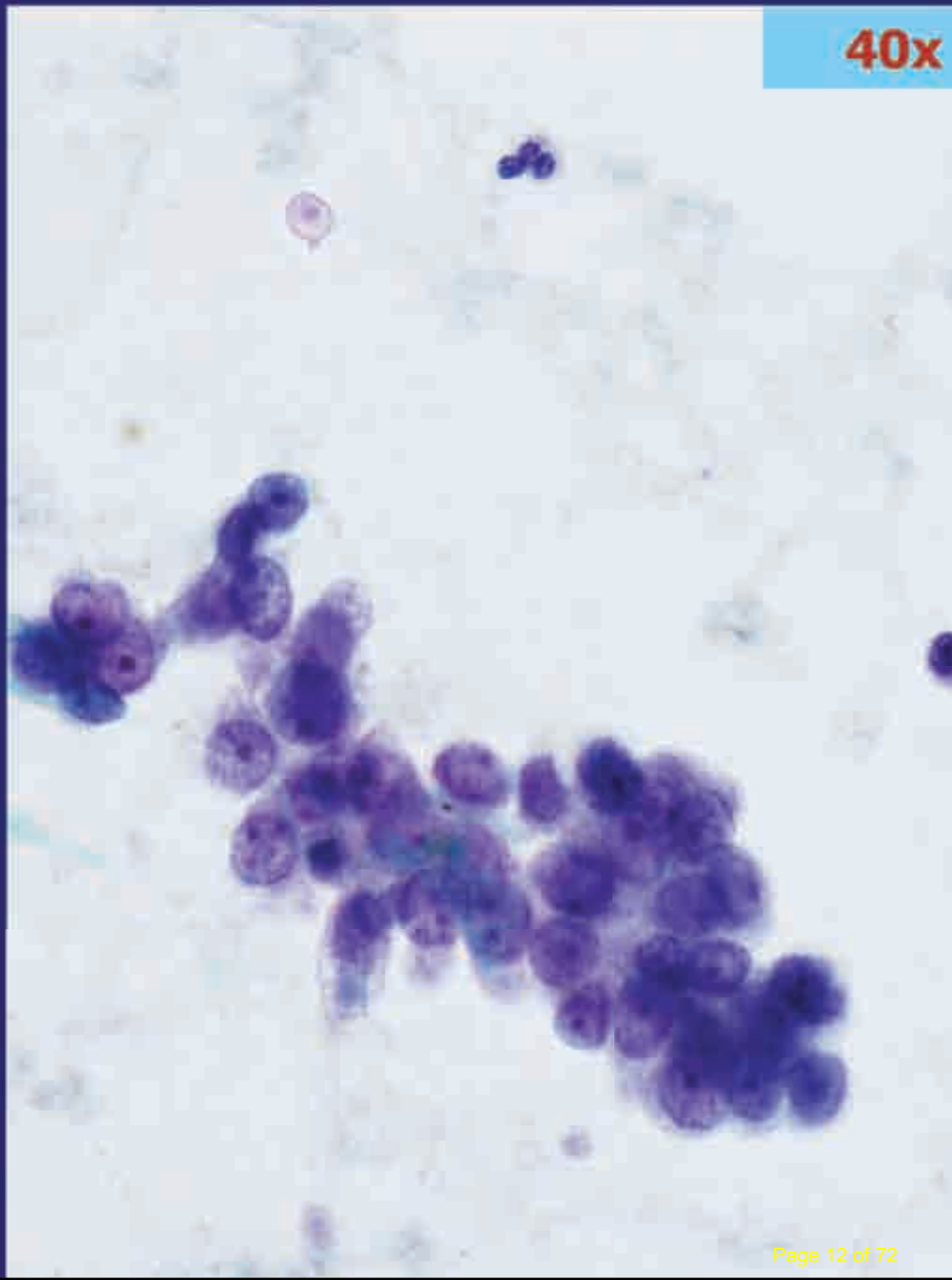
- Metastatic disease is the most common cause.
  - Melanoma, sarcoma, renal, thyroid, gastrointestinal, breast, testis, ovary.
- Bronchioloalveolar carcinoma
- Lymphoma
- PTLD
- Septic emboli (cavitate)
- Fungal infection (histoplasmosis, aspergillosis, coccidiomycosis, cryptococcosis)
- TB
- Sarcoid
- Pneumoconioses
  - Silicosis, asbestosis
- Rheumatoid nodules
- Wegener's granulomatosis (cavitates)
- AVM
- Multiple pulmonary hamartomas

Bone, T7, CT-guided FNA: Diff-Quik stain

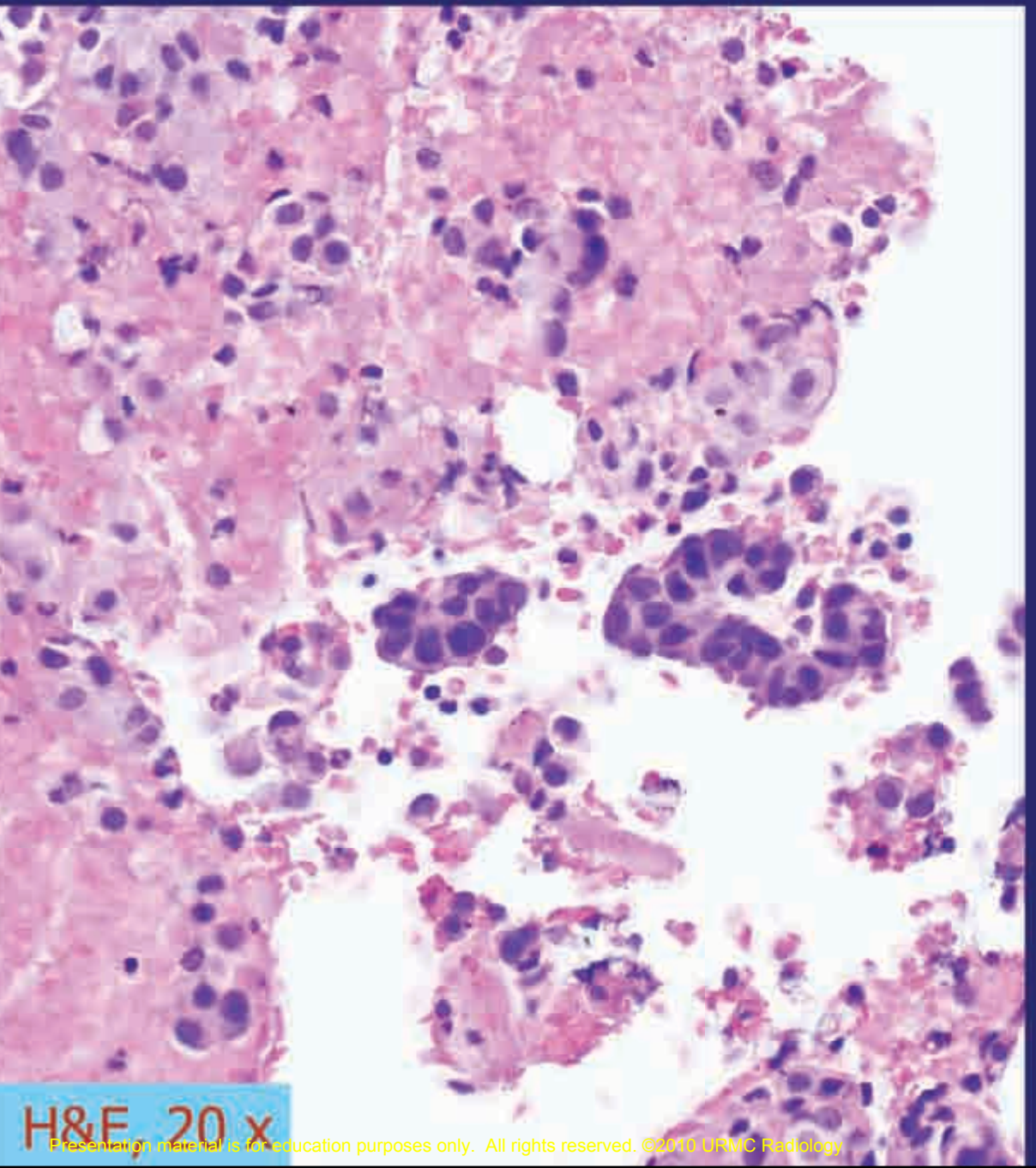


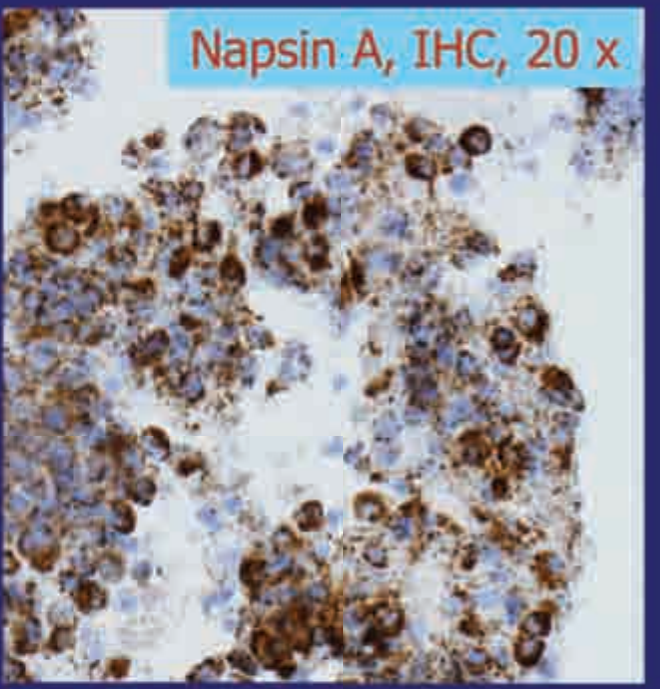
Bone, T7, CT-guided FNA: Papanicolaou stain

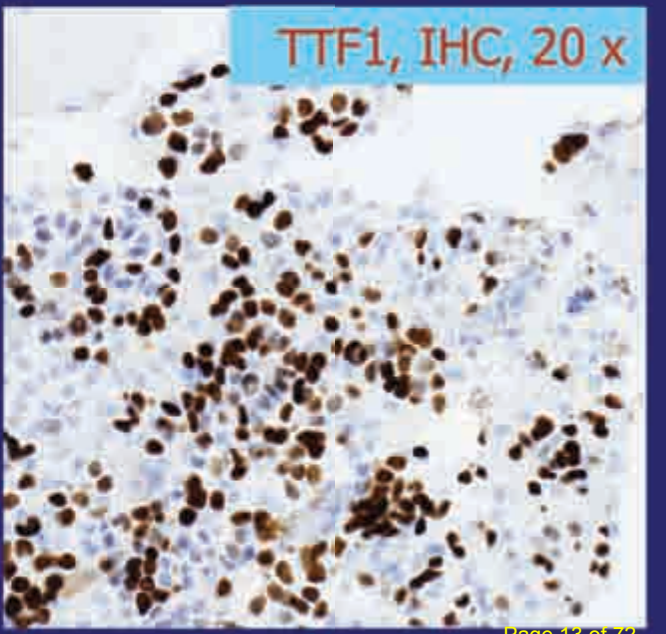




Bone, T7, CT-guided FNA: Cell block







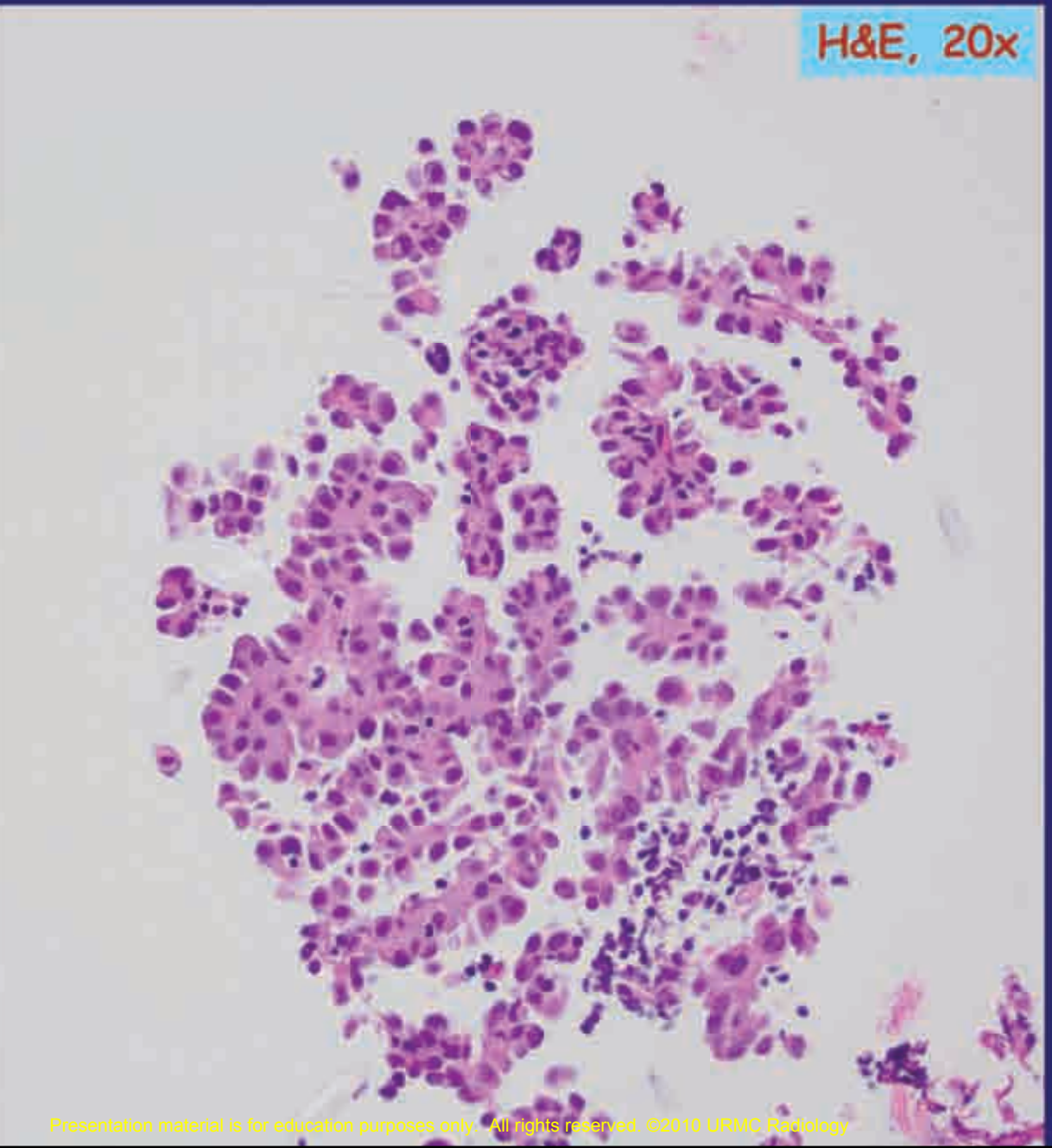
Bone, T7, CT-guided fine needle aspiration:

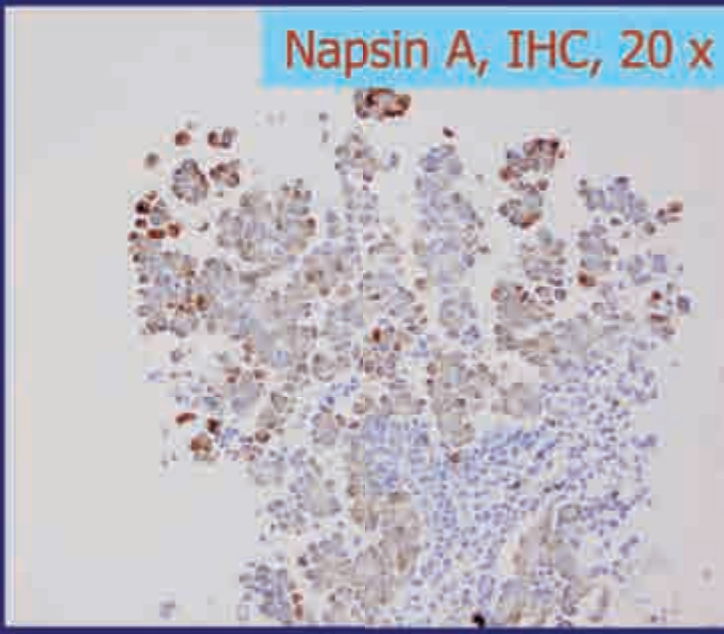
- Malignant tumor cells present derived from adenocarcinoma consistent with pulmonary primary. See comment.
- Comment: Immunohistochemical stains show that the tumor cells mark strongly with TTF-1 and Napsin A. These staining results support pulmonary origin.

Lymph node, right axillary, core biopsy with immunophenotyping:

- Metastatic adenocarcinoma with papillary pattern, consistent with pulmonary primary (see comment).
- The specimen consists of minute fragments of metastatic adenocarcinoma with papillary/pseudopapillary pattern. According to the immunohistochemical studies, the tumor cells are positive for CK7, TTF-1 and napsin A. The results support the diagnosis of metastatic adenocarcinoma with papillary pattern, consistent with pulmonary primary.

Lymph node, right axillary, core biopsy :



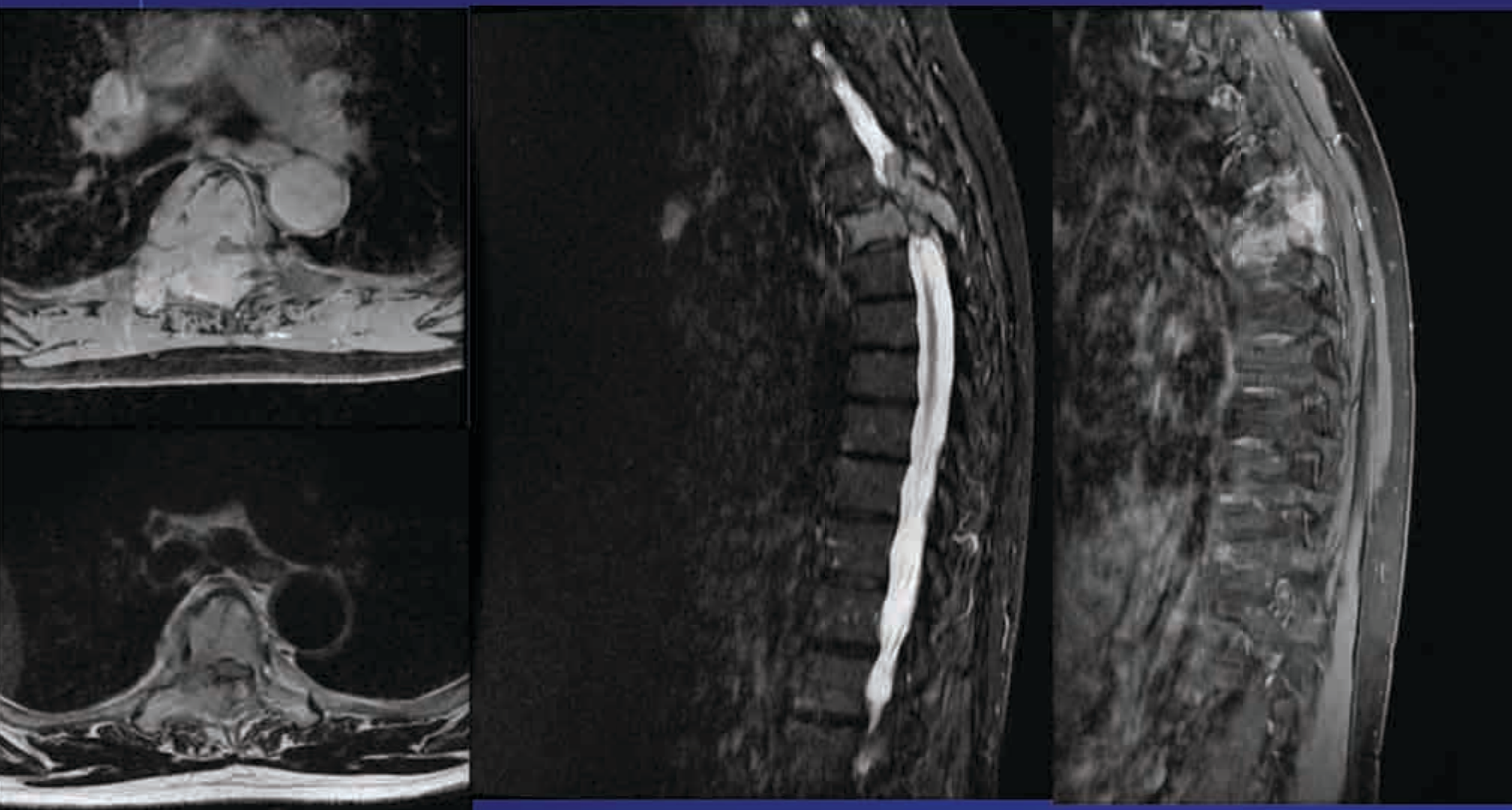


Pulmonary adenocarcinoma

- **Broad classification is non-small cell carcinoma (80%) versus small cell carcinoma (20%)**
  - **50% of non-small cell carcinomas are metastatic at diagnosis vs. 80% of small cell carcinomas**
    - **Many have mixed histologic subtypes**
      - **Favorable: non mucinous bronchioloalveolar, well differentiated squamous cell**
- **Metastases:**
  - 50% have nodal involvement at resection (usually hilar, mediastinal and supraclavicular);
  - metastases to adrenals (50%), liver (30%), brain, bone; also opposite lung, pericardium, kidneys
- **Positive stains:** mucin, CK7, EMA, CEA, TTF1 (72%), surfactant apoprotein (50%), mesothelin (50%), vimentin (9%), S100 (Langerhans cells), p53, CD57/Leu7 (50% of well/moderately differentiated tumors), calretinin (11%)
  - **Negative stains:** CK20, vimentin (usually), keratin 5 (usually), P504S

Case 2

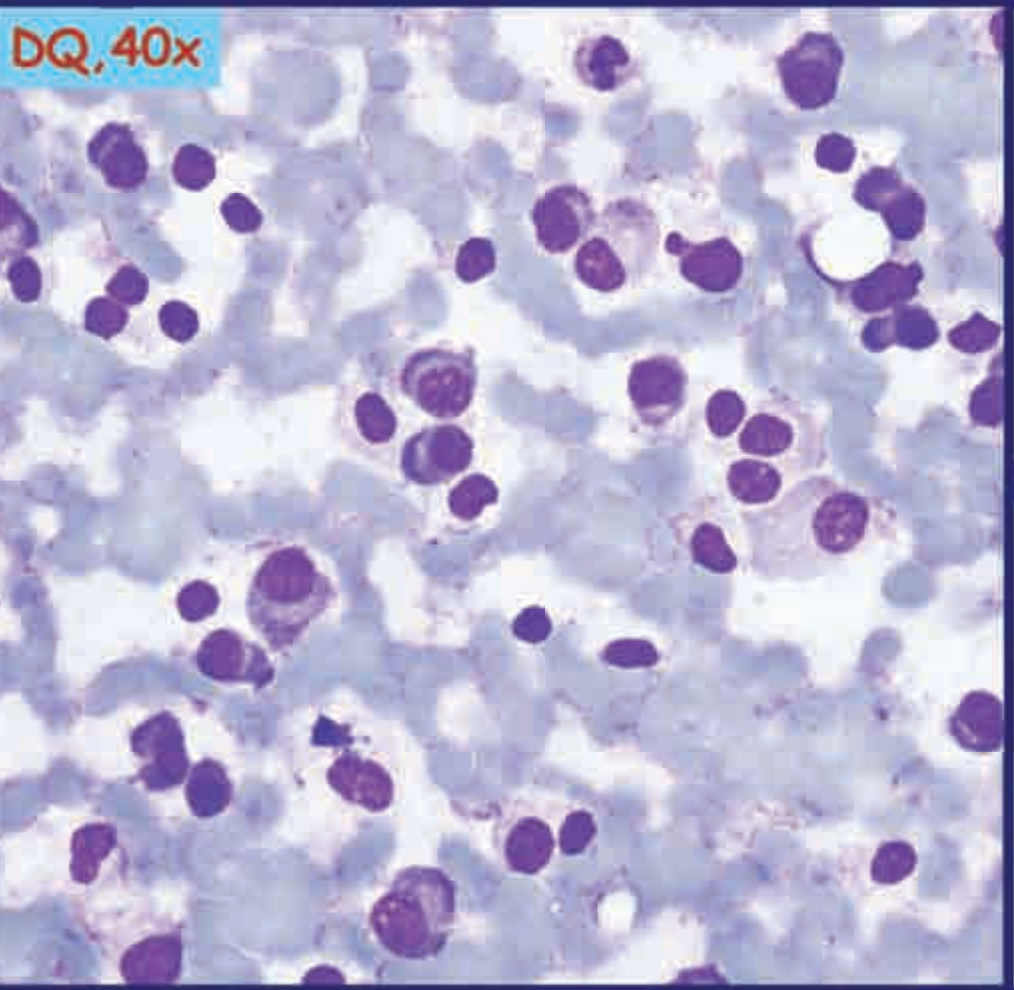
74 year old F, back pain

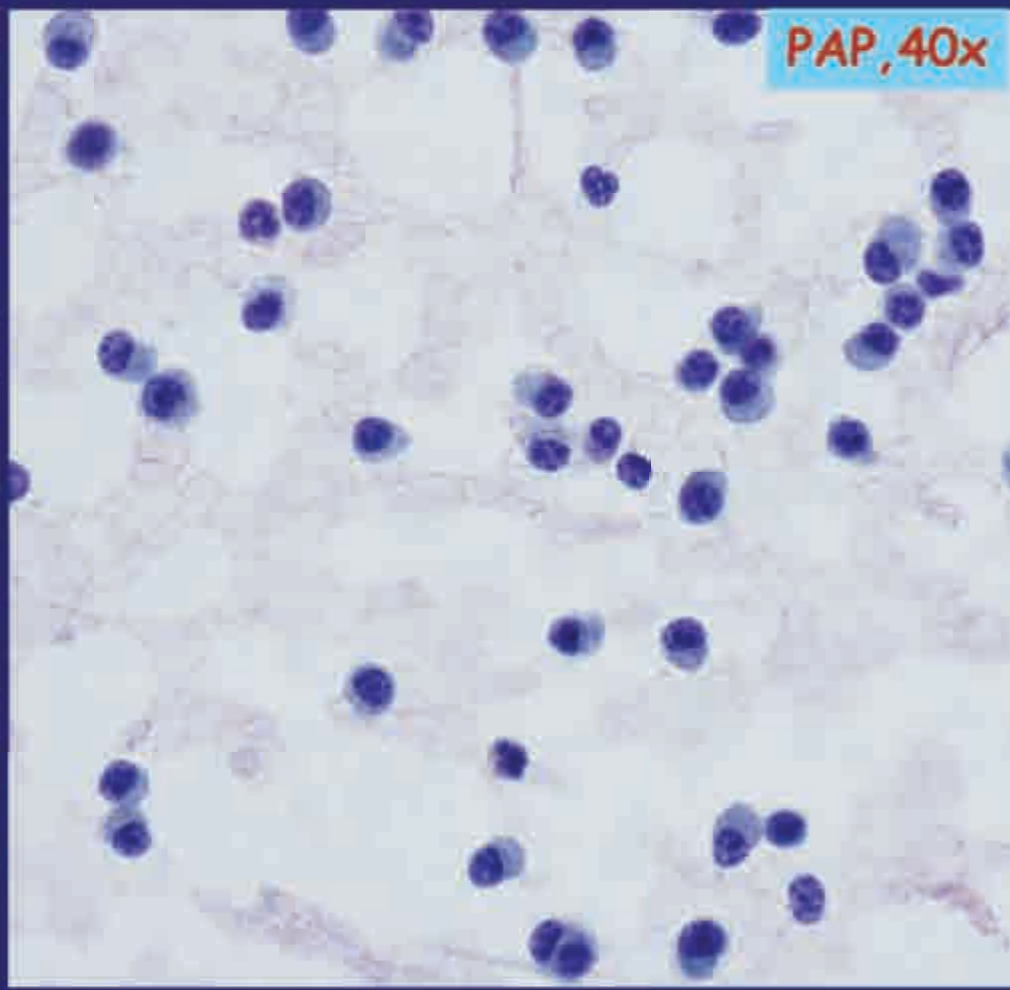


Vertebral body mass

- Metastasis
  - Breast, lung, prostate, thyroid, kidney
- Plasmacytoma
- Lymphoma
- Multiple myeloma
- Chondrosarcoma
  - Lobulated growth pattern, chondroid mineralization (flocculent or arcs & whorls)
- Osteosarcoma

Vertebra, T5, CT-guided FNA:

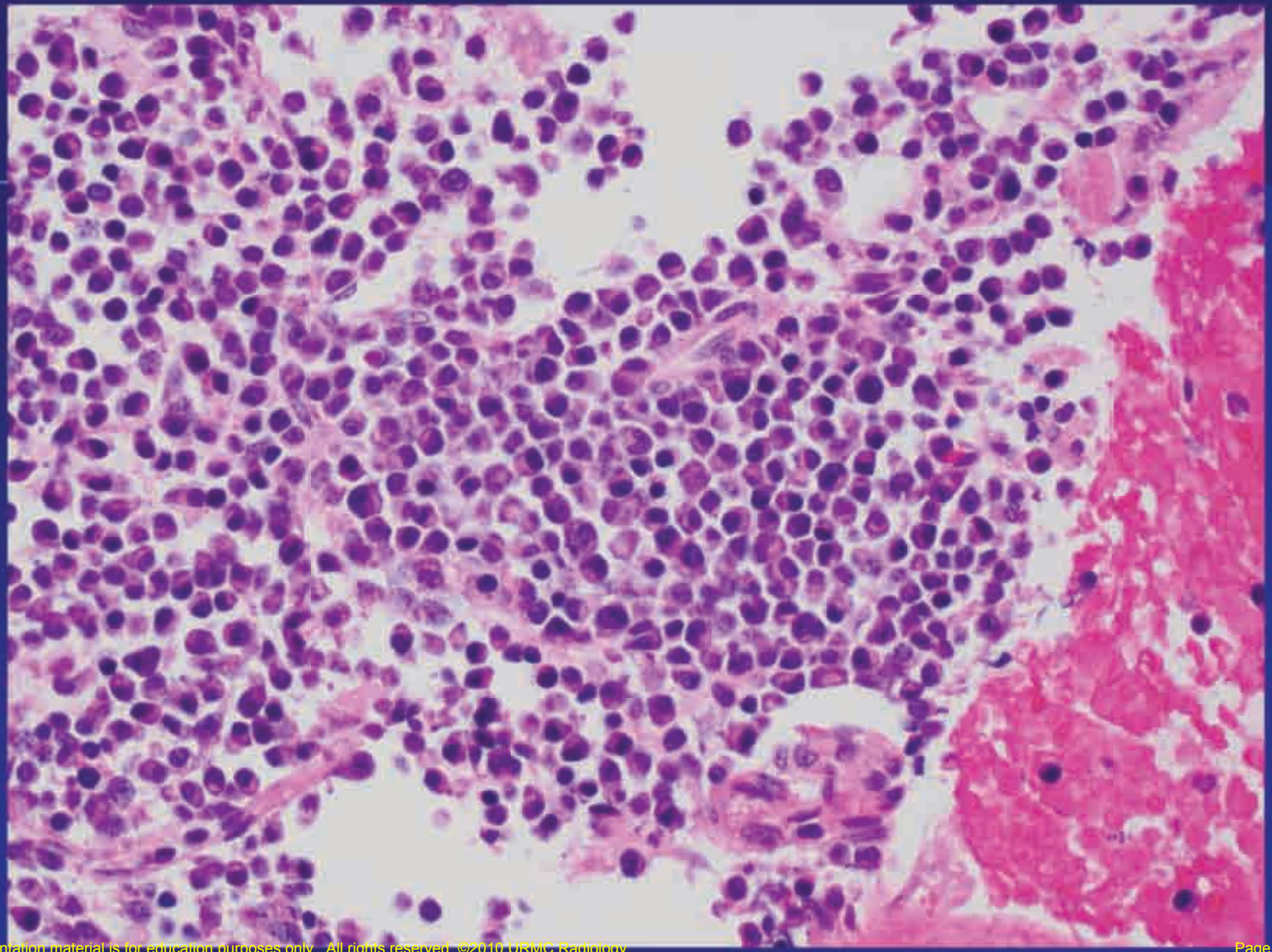




Vertebra, T5, CT-guided fine needle aspiration:

- Malignant plasmacytoid cells present derived from possible plasmacytoma or multiple myeloma. Clinical correlation is recommended (See also concurrent biopsy 10-SSP11212 and flow cytometry 10-SHE688)

Vertebra, T5, CT-guided core biopsy:



Bone Biopsy, T5

- Plasmacytoma

Bone, T5, fine needle aspirate with flow cytometry:

- Monoclonal Plasma Cell population detected
  - The cytospin slide shows many plasma cells (few with atypical features,) lymphocytes, neutrophils, and red blood cells.

Flow Cytometry:

  - Antigens tested: CD19, CD38, CD45, CD56, CD138, surface and cytoplasmic kappa and lambda. Gating using side and forward light scatter shows few CD19+ B-cells that are polyclonal. The low-moderate side scatter, bright CD38 plasma cell gate contains 28% of total cells. Within this gate is a monotypic population that is:
  - CD38+/CD56+/CD138+(40%)/CD117-/CD19-/cytoplasmic kappa

WHO classification of plasma cell neoplasms:

- Plasma cell myeloma
- Plasmacytoma
- Heavy chain disease
- Monoclonal immunoglobulin deposition diseases

Diagnostic Criteria for Multiple Myeloma

Major criteria

I. Plasmacytoma on tissue biopsy

II. Bone marrow plasma cell > 30%

III. Monoclonal M spike on electrophoresis IgG > 3,5g/dl,
IgA > 2g/dl, light chain > 1g/dl in 24h urine sample

Minor criteria

a. Bone marrow plasma cells 10-30%

b. M spike but less than above

c. Lytic bone lesions

d. Normal IgM < 50mg, IgA < 100mg, IgG < 600mg/dl

Diagnosis:

- I + b, I + c, I + d
- II + b, II + c, II + d
- III + a, III + c, I II + d
- a + b + c, a +b + d

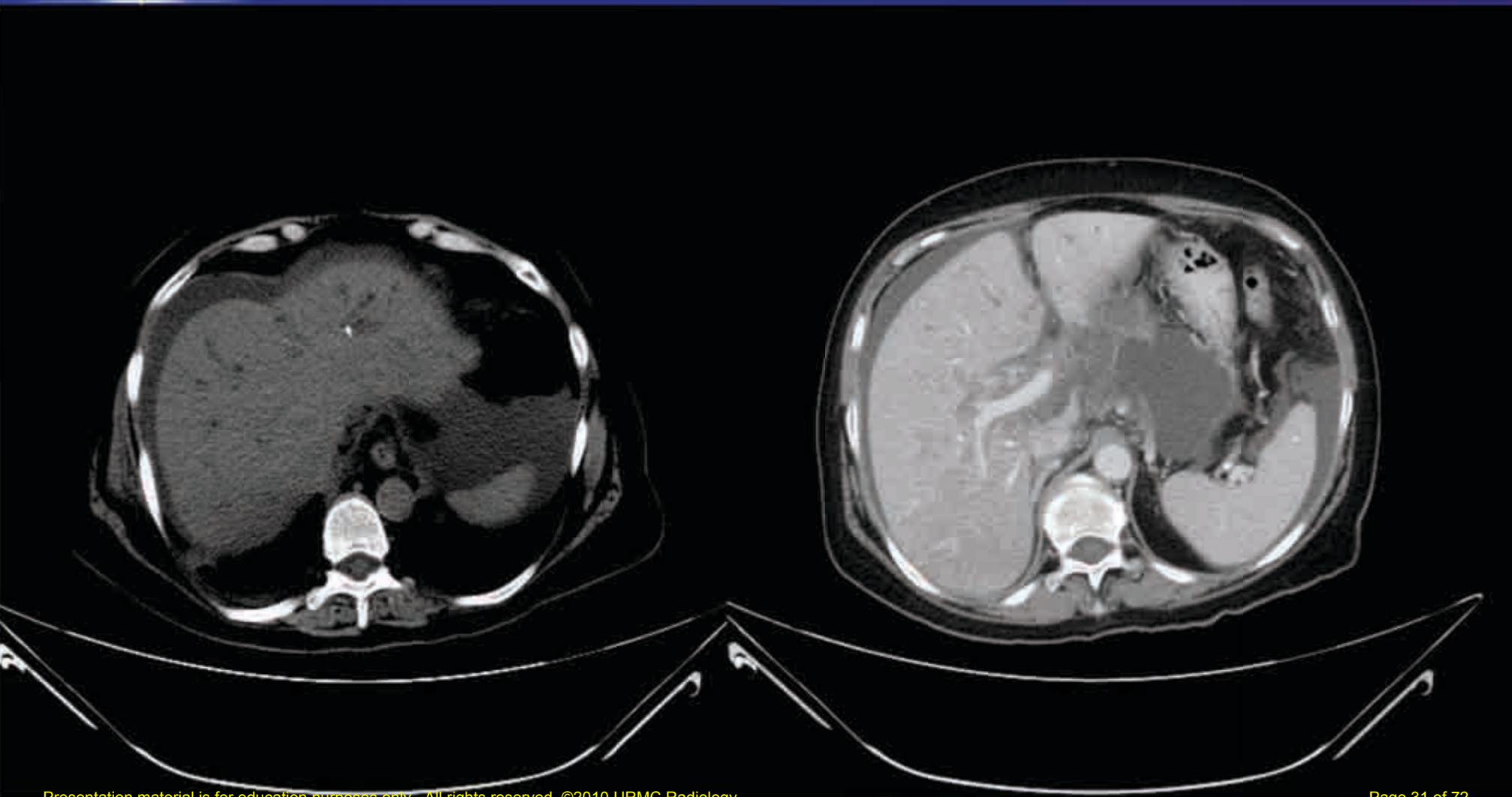
Monoclonal gammopathy of undetermined significance (MGUS)

- M protein presence, stable
  - levels of M protein: <30g/l
- Marrow plasmacytosis < 10%
- No end organ damage
  - complete blood count - normal
  - no lytic bone lesions
  - no signs of disease

- MGUS is diagnosed in 67% of patients with an M protein
  - 3% of people > 70 years, 15% of people > 90 years
  - 10% of patients with MGUS develop multiple myeloma, 1-2%/year

Case 3

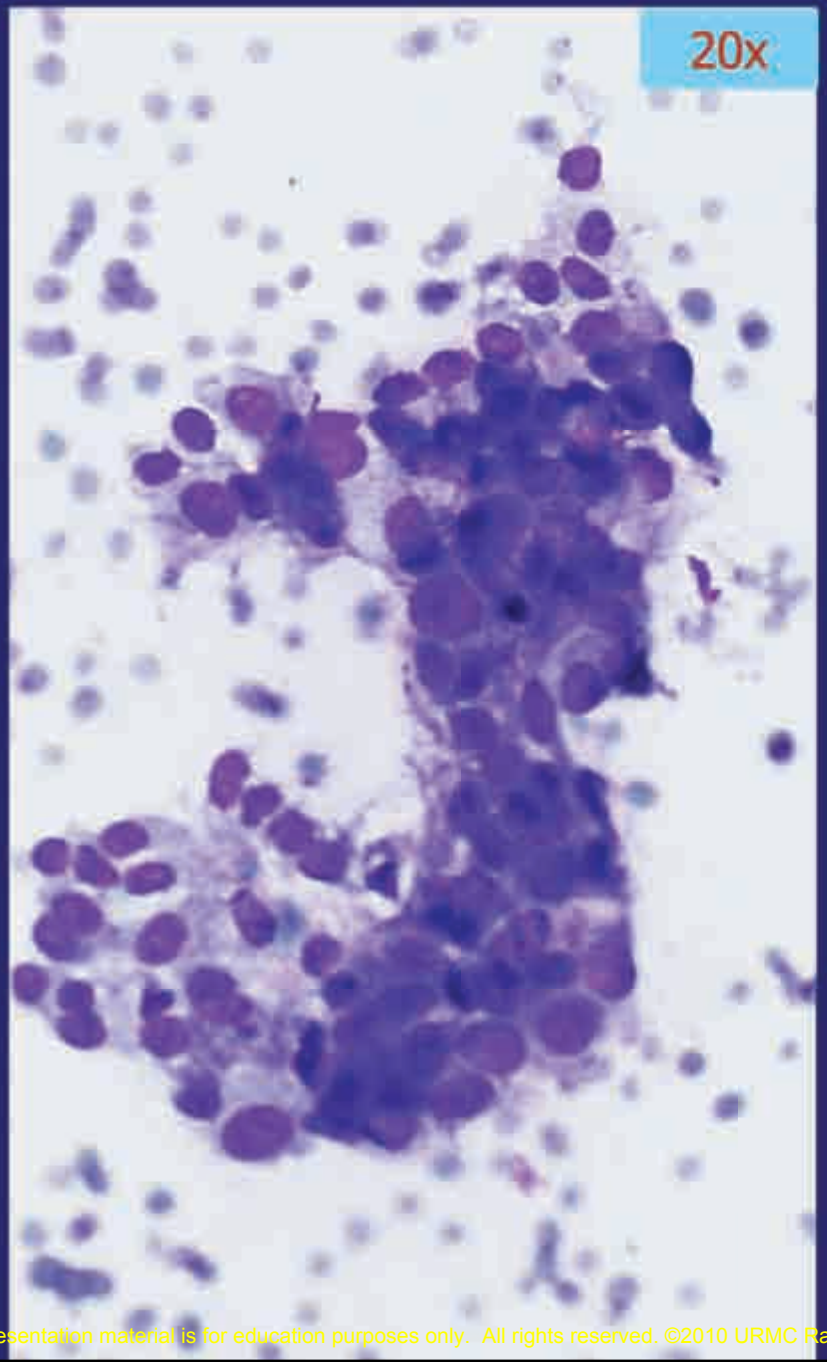
65 year old F with jaundice and abdominal pain

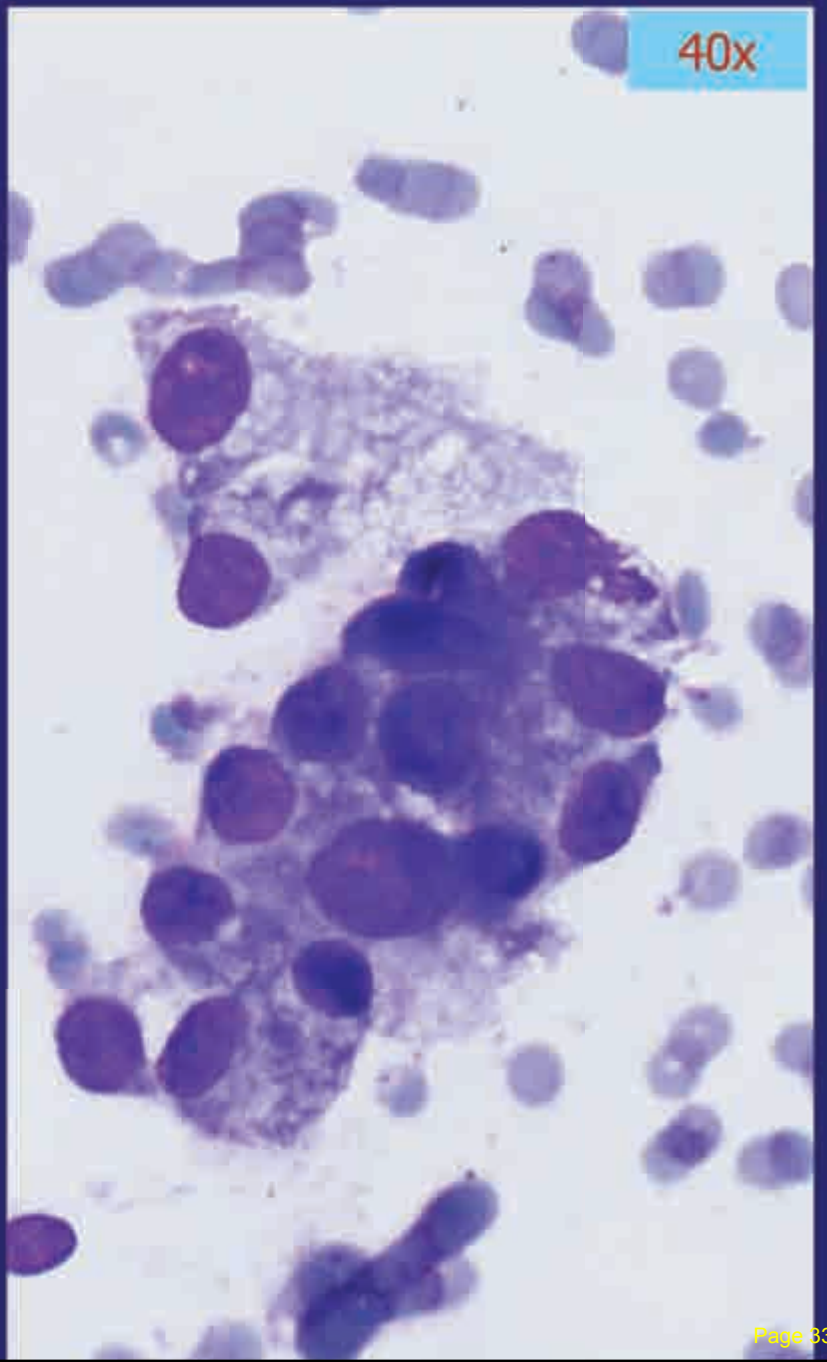


Intrahepatic biliary dilatation/mass

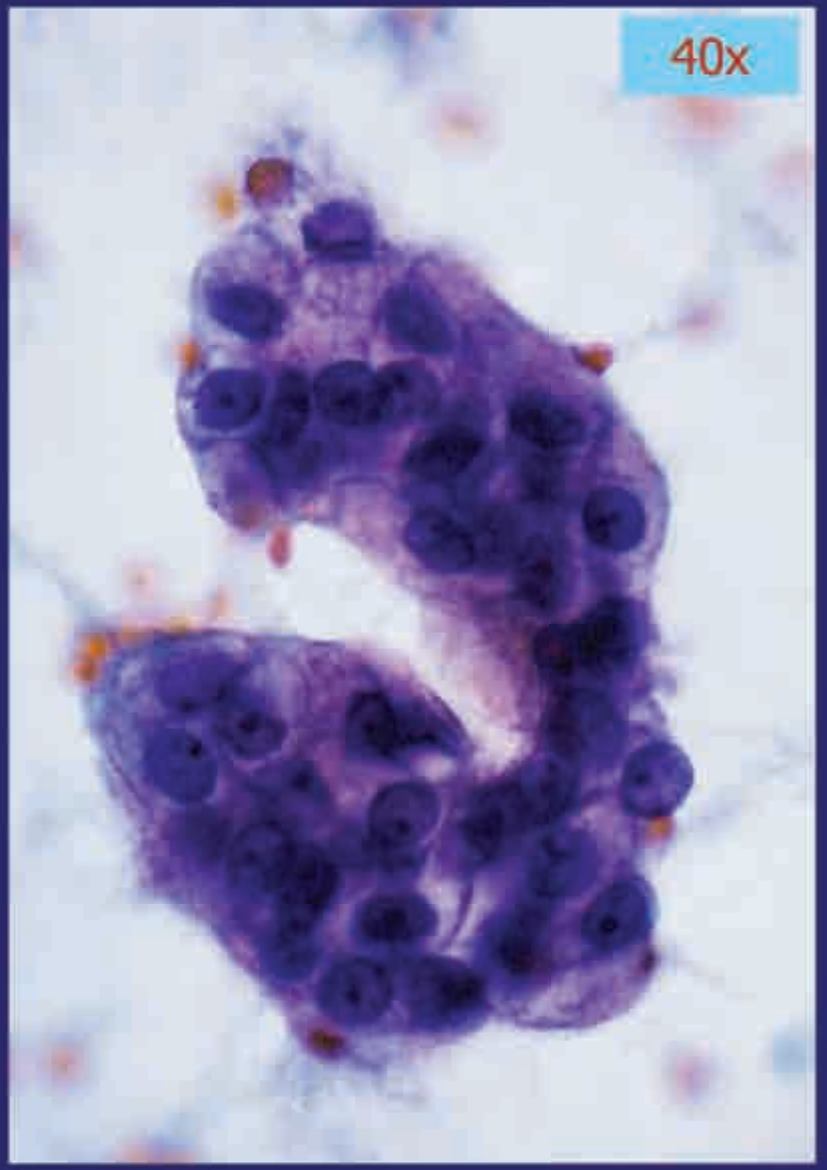
- Cholangiocarcinoma (Klatskin tumor)
- Pancreatic adenocarcinoma
- HCC
- Metastasis

Pancreas, CT-guided FNA: Diff-Quik stain

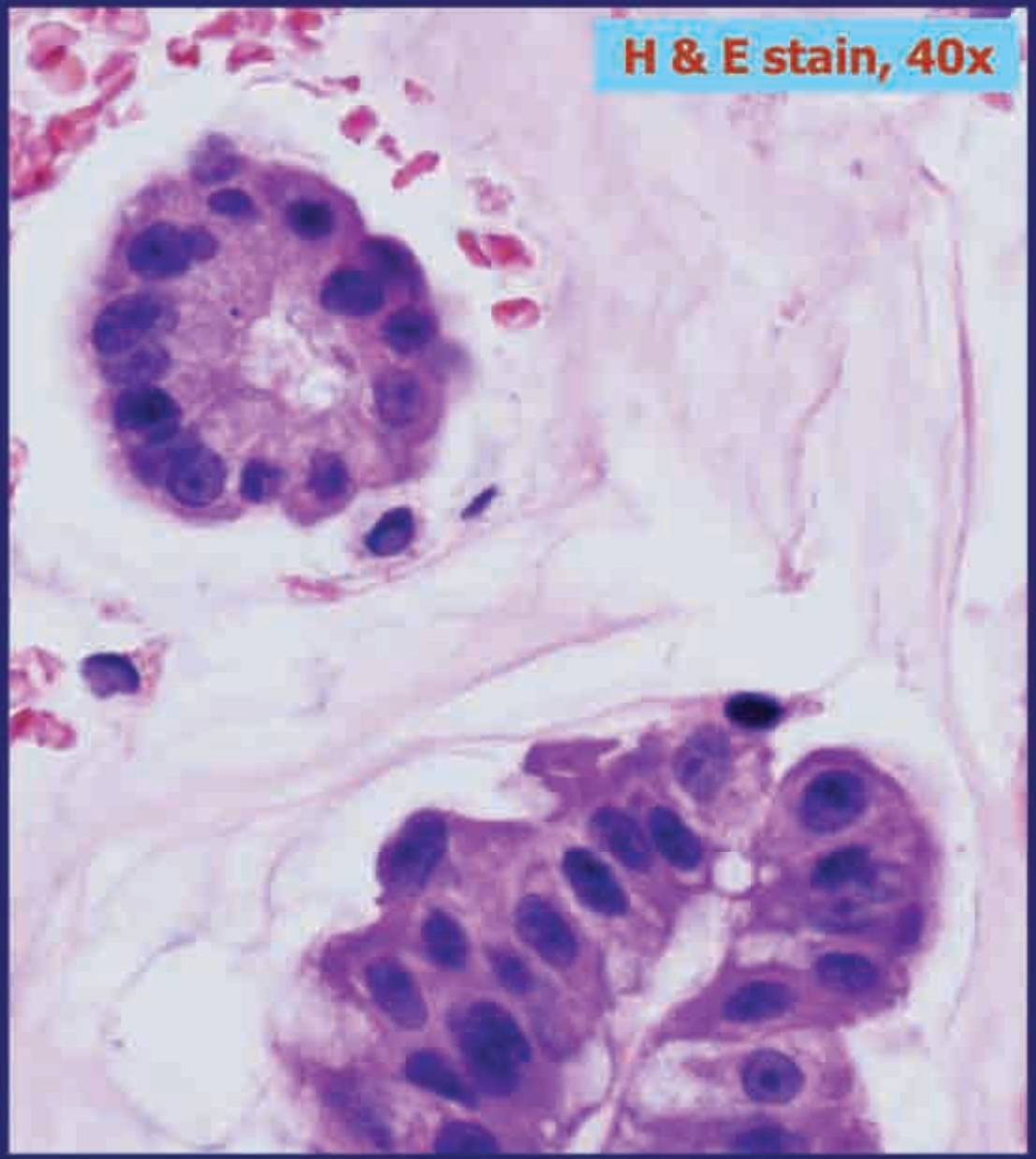


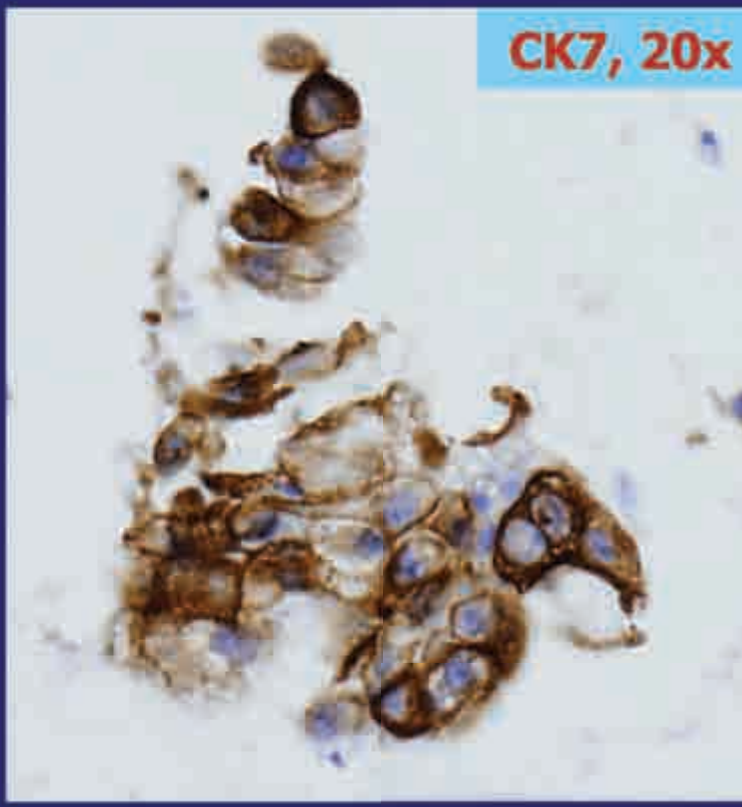


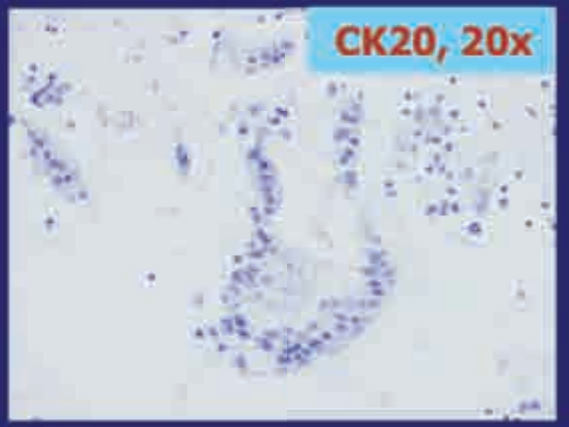
Pancreas, CT-guided FNA: Papanicolaou stain, 20x



Pancreas, CT-guided FNA: Cell block



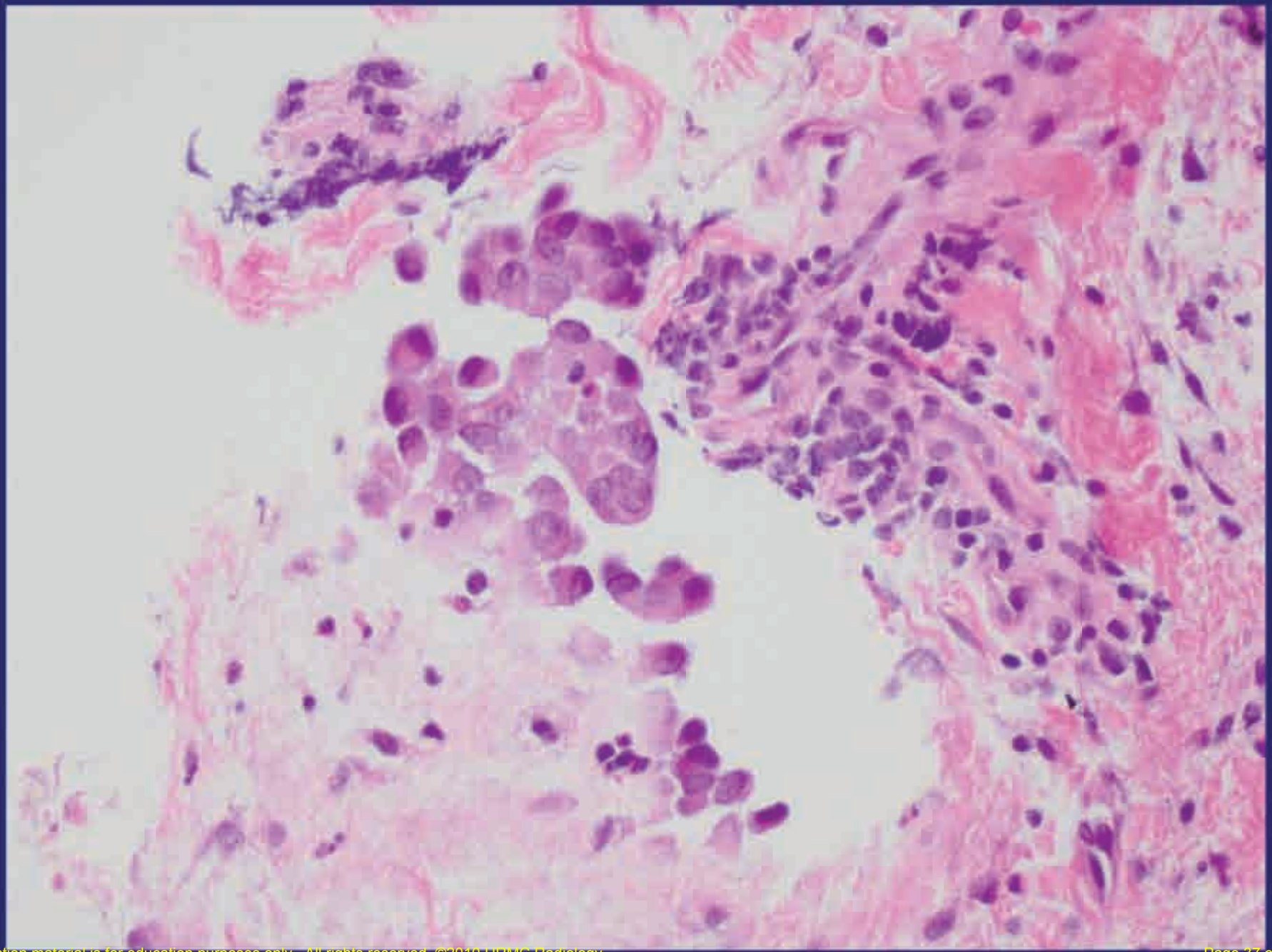




Pancreas, Head, mass CT-guided fine needle aspiration:

- Malignant tumor cells present derived from well differentiated adenocarcinoma.
- Comment: Immunohistochemical stains show that the tumor cells do not mark with TTF-1 and cytokeratin 20. They do mark with cytokeratin 7. This staining pattern does not confirm a primary site. Clinical correlation is recommended.

Pancreas, core biopsy:
H&E, 40x



Pancreas and liver, mass, core biopsy:

- Mucinous lesion, suspicious for adenocarcinoma

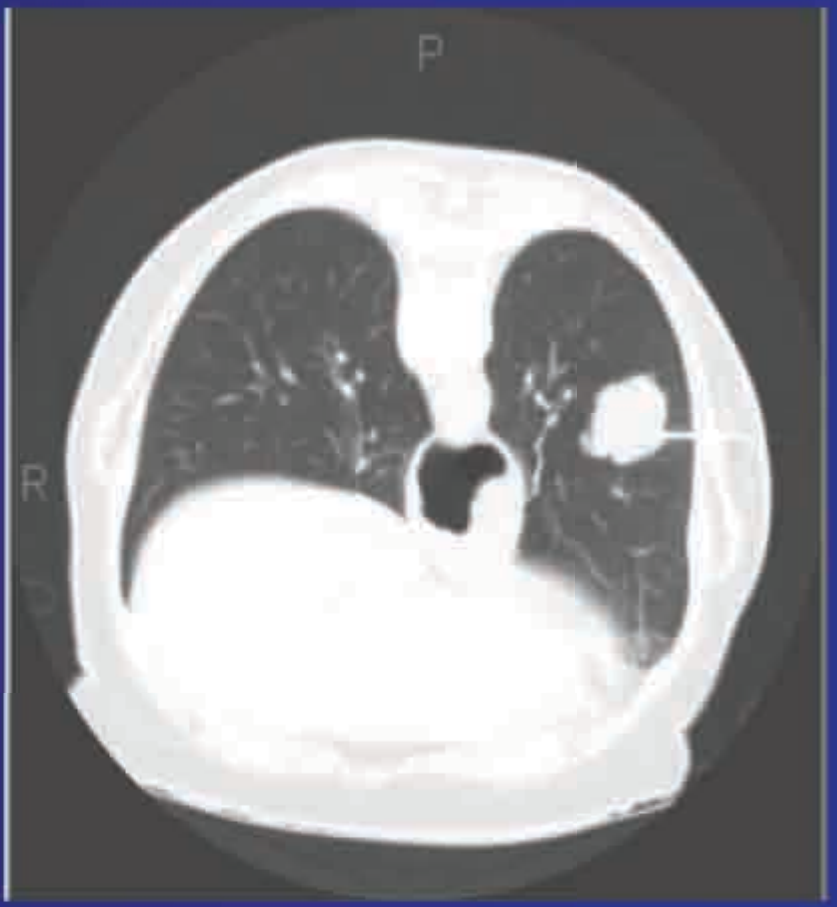
Pancreatic Adenocarcinoma

- 85% of pancreatic cancers are ductal adenocarcinoma not otherwise specified (NOS)
  - #5 cause of cancer death in US after lung, colon, breast, prostate
  - 60% of tumors are in head, 15% in body, 5% in tail, 20% diffusely involve pancreas
- Metastases:
  - Local: lymph nodes (microscopic metastases found in 75% with T1, T2 disease)
  - Distant: liver, lung, peritoneum, adrenal, bone, distal nodes

Would you recommend PET/CT for this patient?

Different patient: risk for FALSE NEGATIVE PET

- Most of lesion filled with mucin(mucinous colon carcinoma)



Different patient: risk for FALSE NEGATIVE PET

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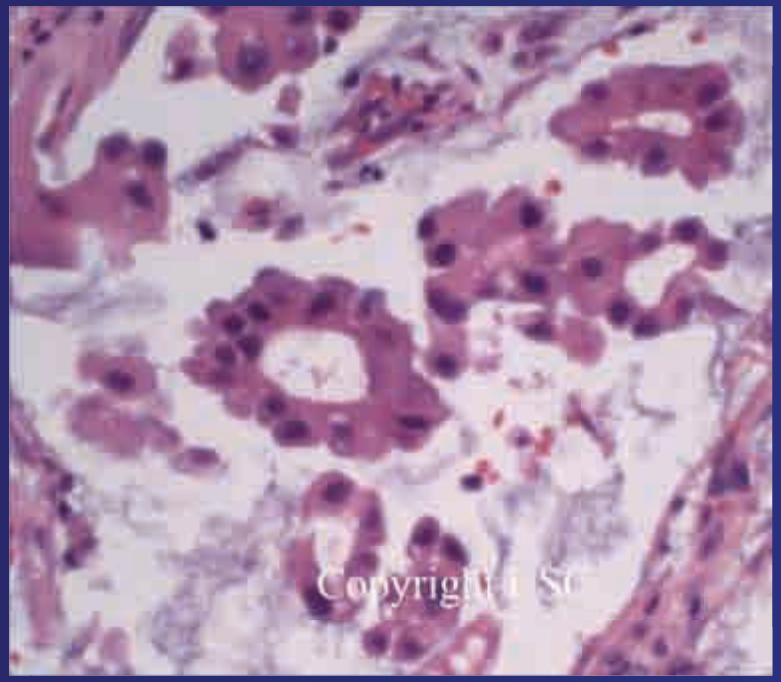
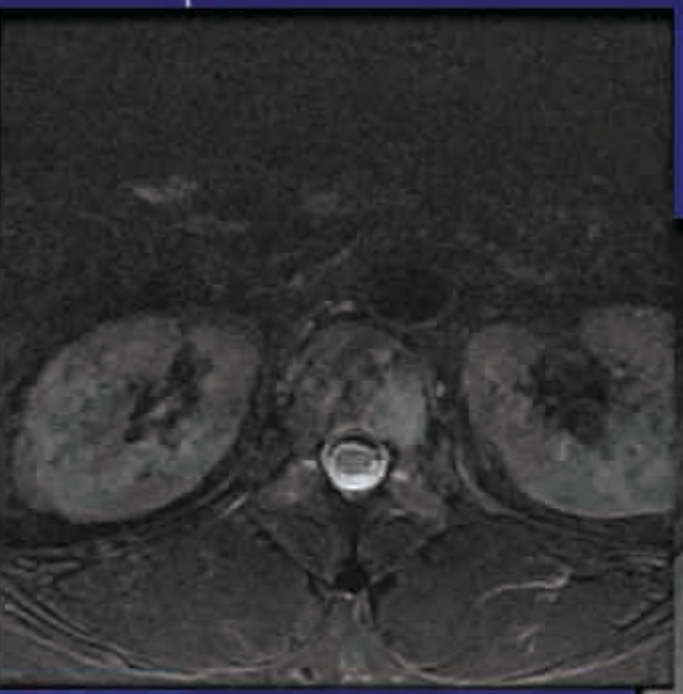
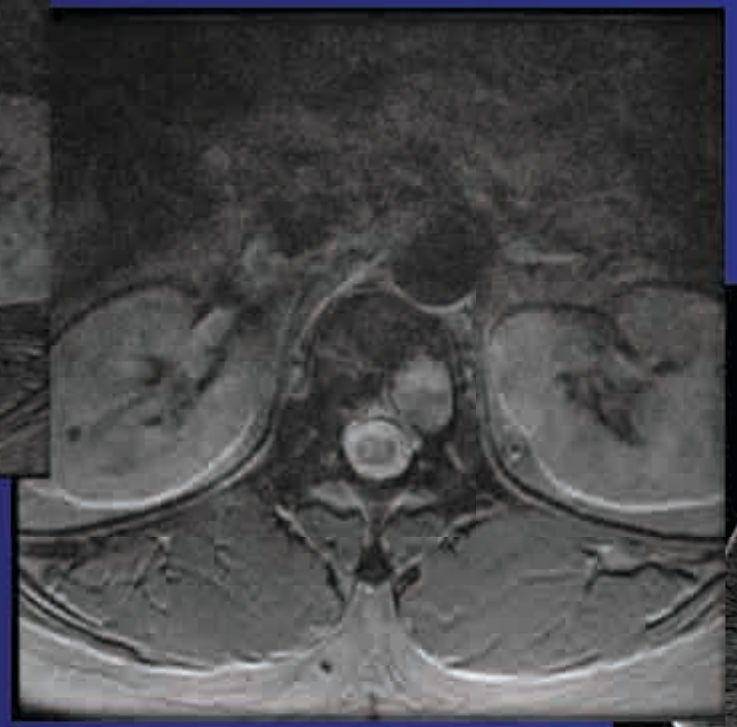
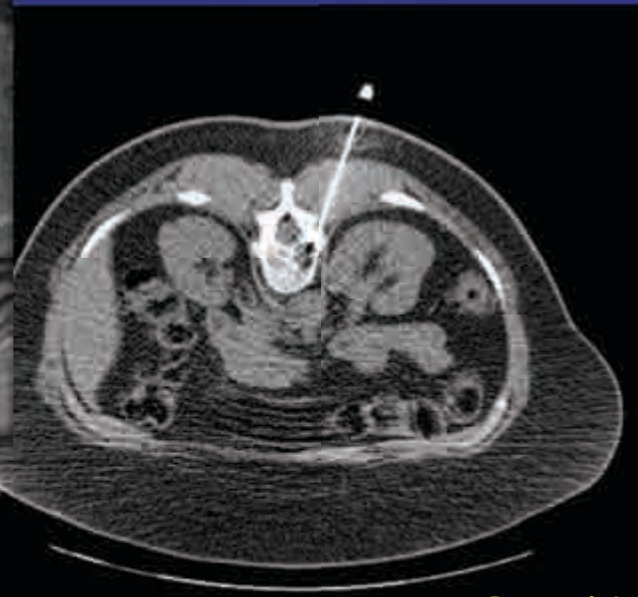


Case 4

51 year old F



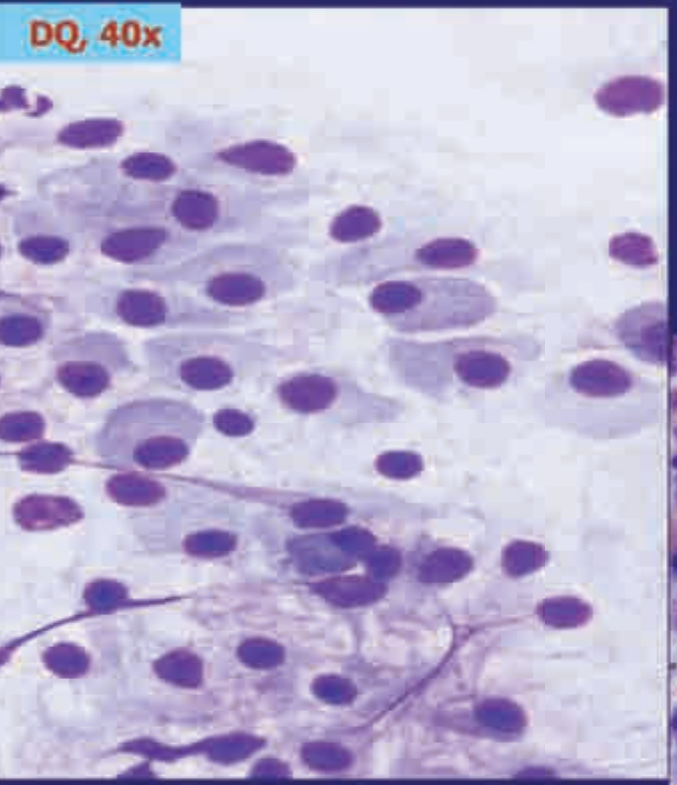


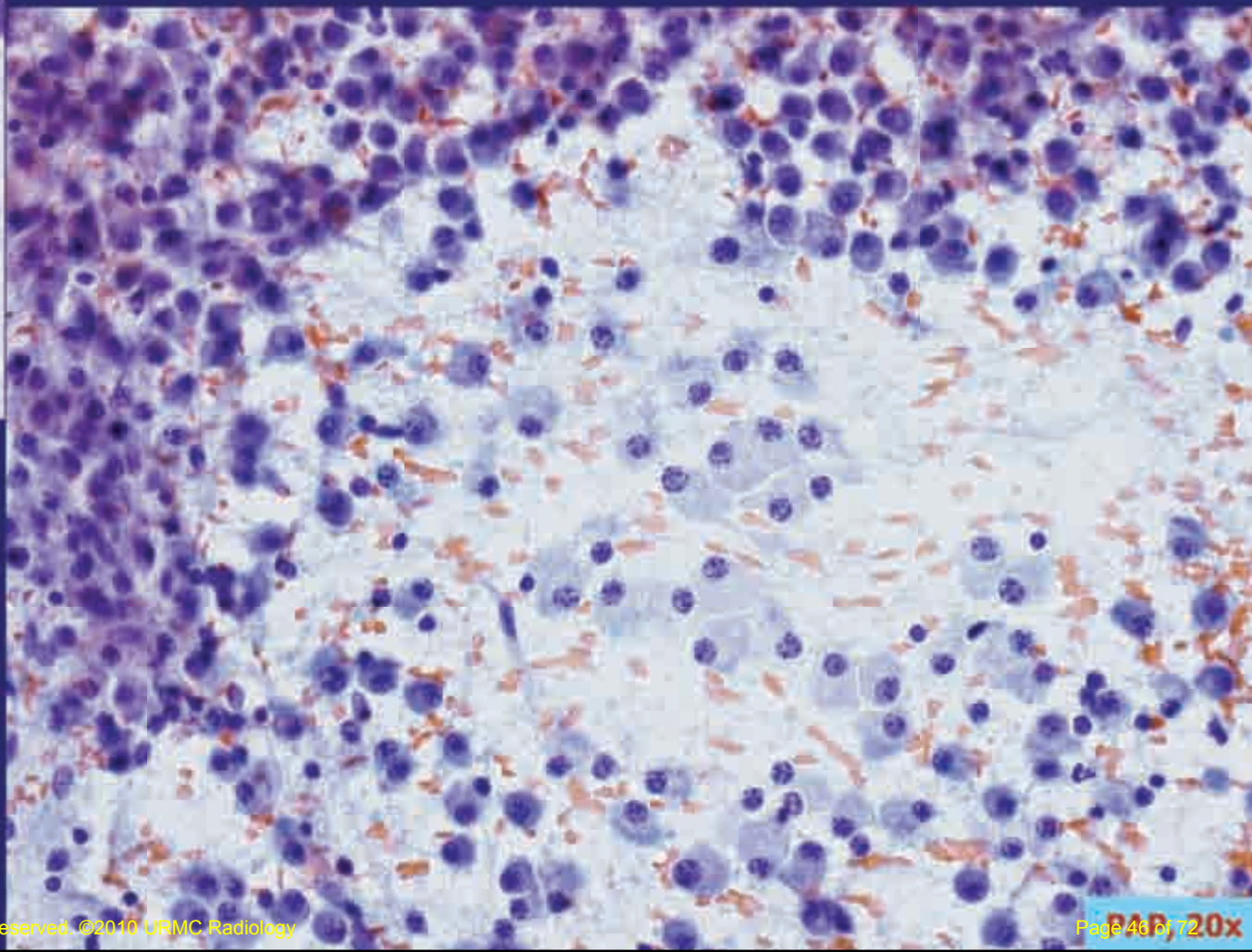


Vertebral body lytic lesion

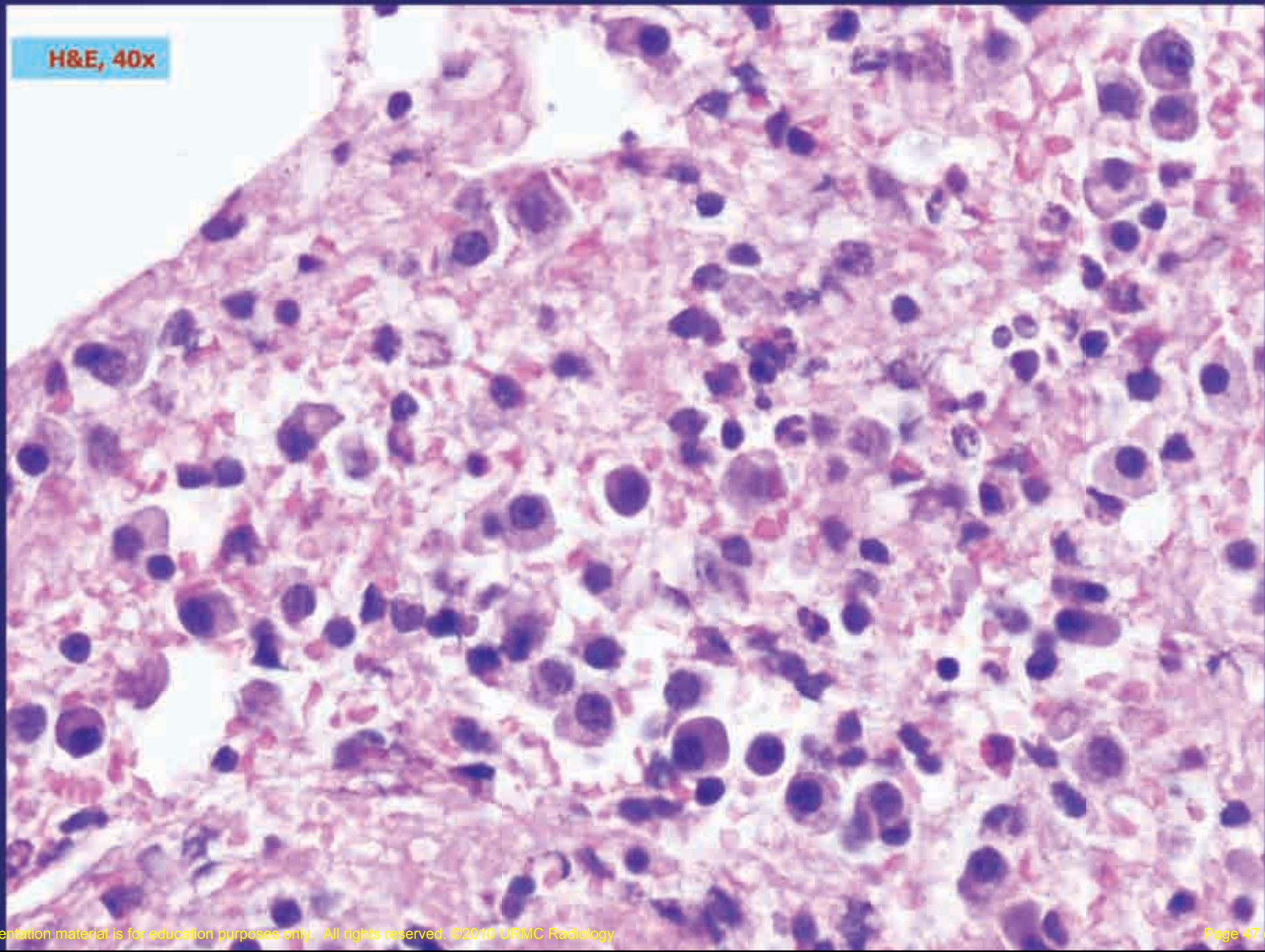
- Metastasis
  - Breast, lung, prostate, thyroid, kidney
- Plasmacytoma
- Lymphoma
- Multiple myeloma
- Chondrosarcoma
  - Lobulated growth pattern, chondroid mineralization (flocculent or arcs & whorls)
- Osteosarcoma

Bone, spine, T-12, CT-guided, FNA:





Bone, spine, T-12, CT-guided,FNA: Cell block, 40x



Bone, spine, T-12, CT-guided, fine needle aspiration:

- Abundant plasma cells are identified. Consistent with Plasma Cell Neoplasm.

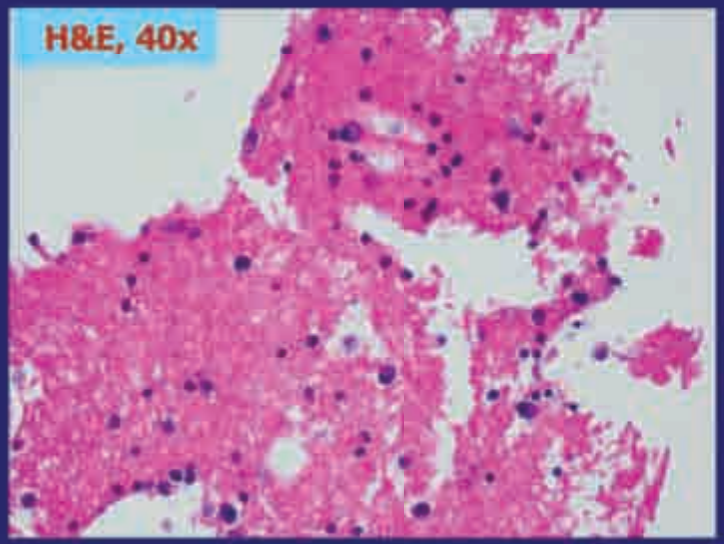
Bone, T12 vertebral body, biopsy:

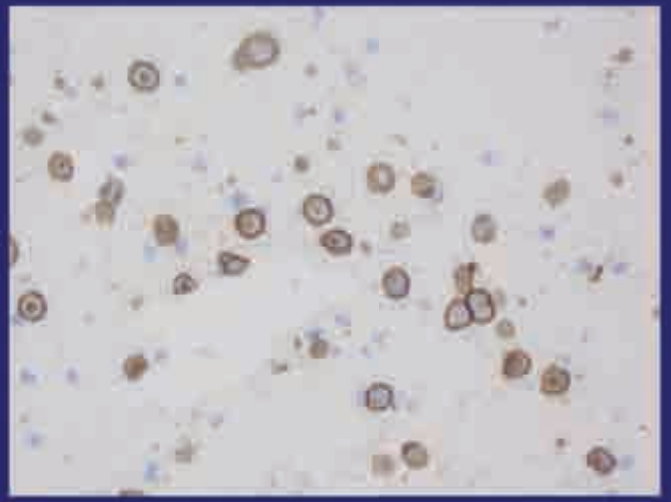
- Blood clot containing Kappa light chain clonal neoplastic plasma cells
- No tissue or bone/bone marrow evident

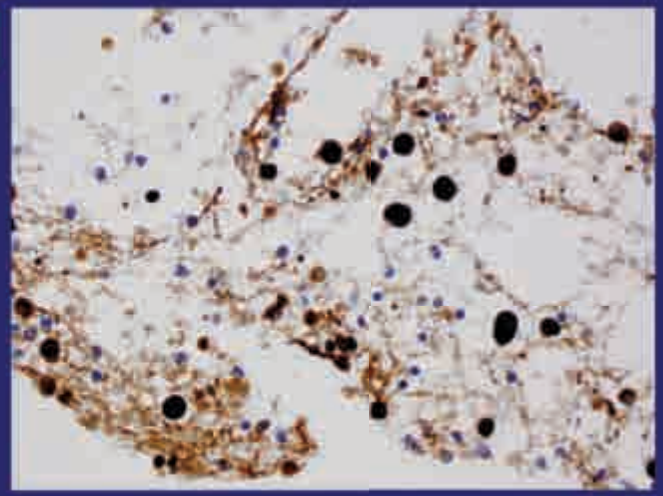
- COMMENT: The specimen consists of peripheral blood with suspended plasma cells demonstrating the same Kappa light chain clonality as that noted on the prior bone marrow biopsy

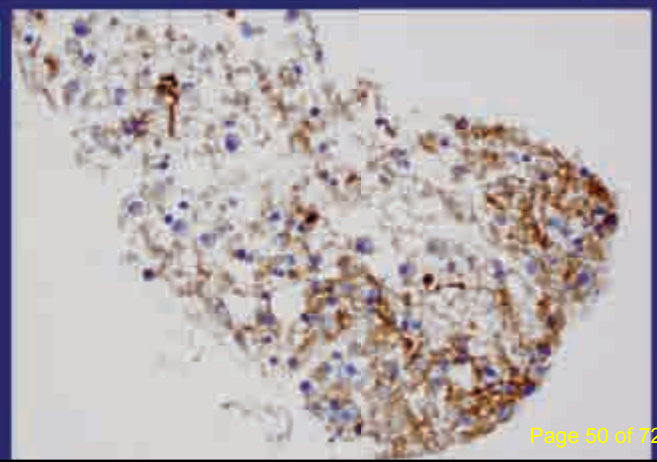
- IMMUNOHISTOCHEMICAL STAINS: CD138 highlights the moderate number of suspended plasma cells. Nearly all the plasma cells stain for Kappa light chain with relatively few staining for Lambda light chain.

Bone, T12 vertebral body, biopsy:







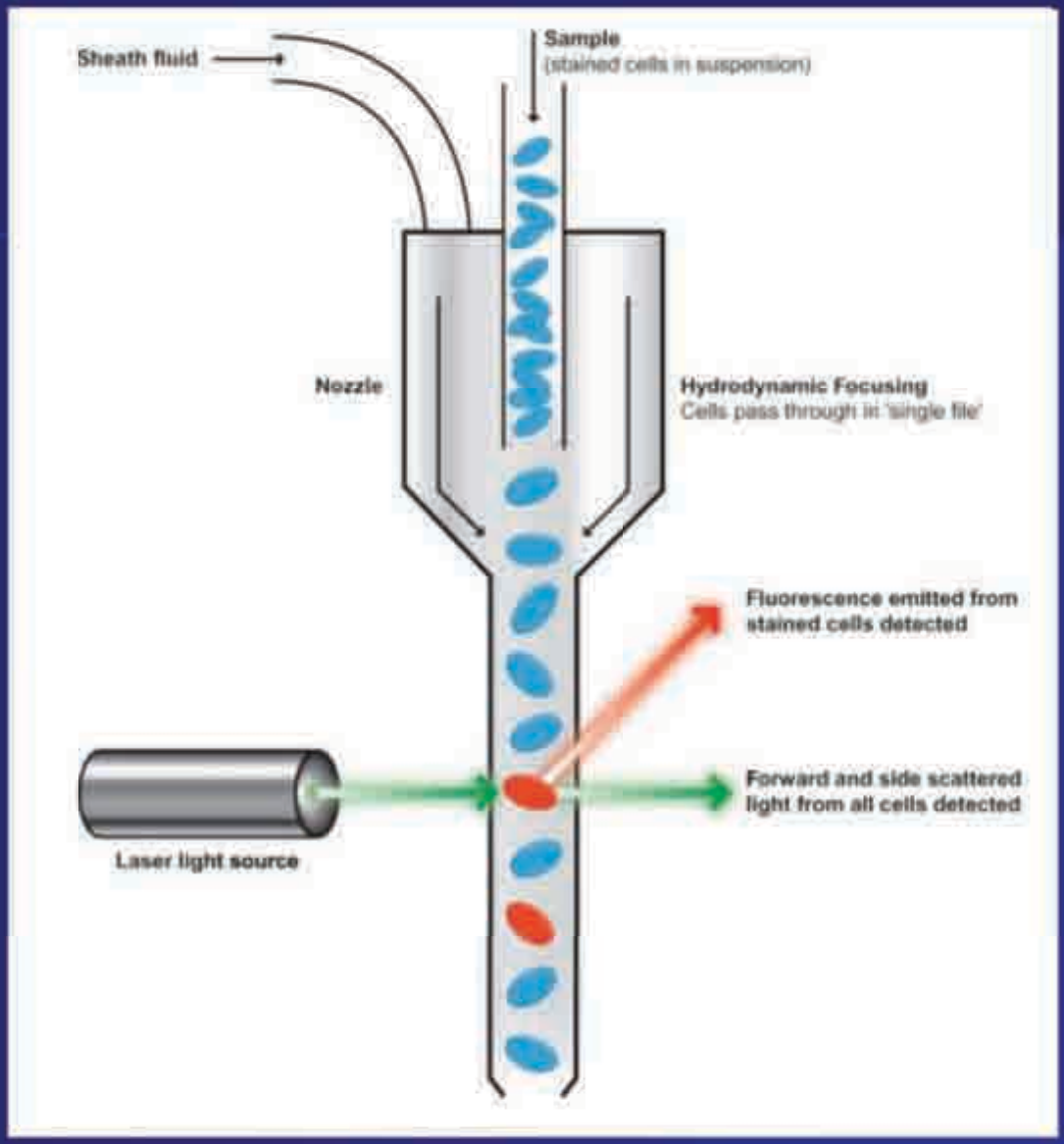


Bone, T12 vertebra, fine needle aspiration, flowcytometry:

- Plasmacytoma/consistent with plasma cell myeloma.
  - Cytospin preparations show predominantly atypical plasma cells in clusters. There are scattered neutrophils, monocytes and lymphocytes present.
  - Flow cytometry: The following antigens were evaluated: cytoplasmic and surface kappa and lambda, CD19, CD38, CD45, CD56, CD117, and CD138. Plasma cells comprise 45% of total cells. They are CD56, CD117 and kappa positive. CD19 is negative.
  - Sample viability was 95.8%.

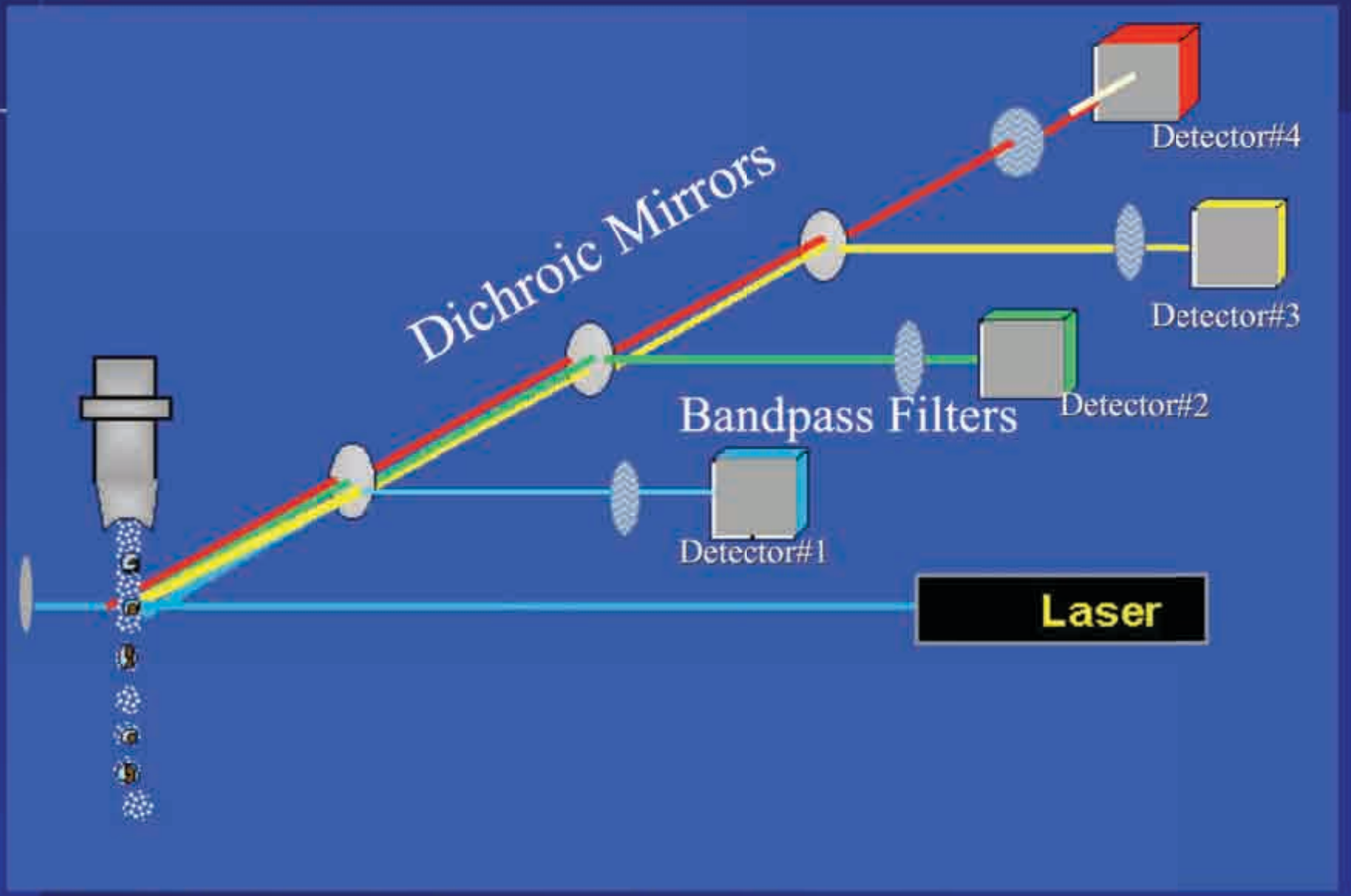
Flow Cytometry

- Flow Cytometry is a technique used to measure the physical and chemical properties of cells or cellular components.
  - Cells are measured individually, but in large numbers.



http://www.sonyinsider.com/wp-content/uploads/2010/02/Flow-Cytometry-Diagram2.jpg

Example Channel Layout



Original from Purdue University Cytometry Laboratories

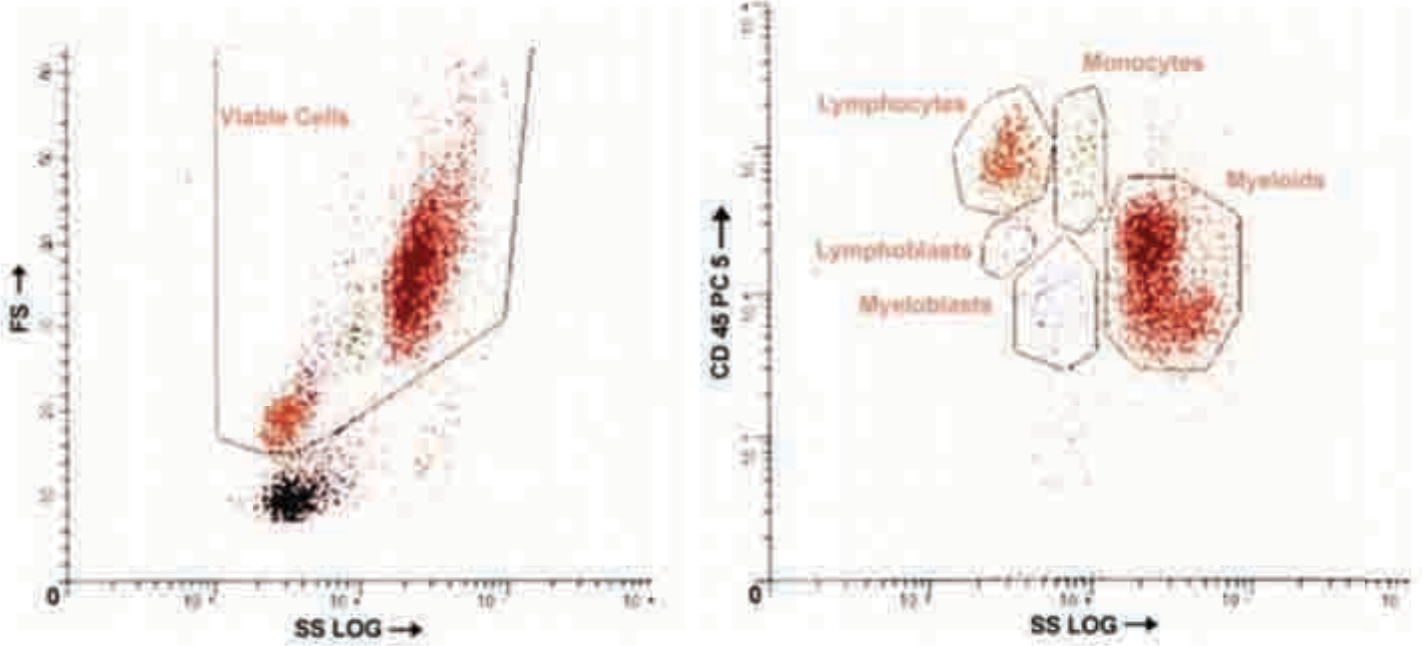


Figure 6.3 Cell population identification by forward versus side scatter (FS/SS) gating in normal peripheral blood (*left*), and by CD45 expression versus side scatter (45/SS) gating in normal bone marrow. FS typically is measured on a linear scale. SS can be measured on linear (not shown) or logarithmic scales. Measuring the dark red, high-SS neutrophils on a log scale enables a more compressed view of the data than does SS measurement on a linear scale. Antibody-specific fluorescence typically is measured on a log scale. Although the constituents of low- to moderate-complexity specimens, such as blood or lymph node, can be adequately separated for analysis using FS versus SS gating, CD45 versus SS gating is more effective for a high-complexity specimen such as bone marrow, enabling more reliable identification of the blasts.

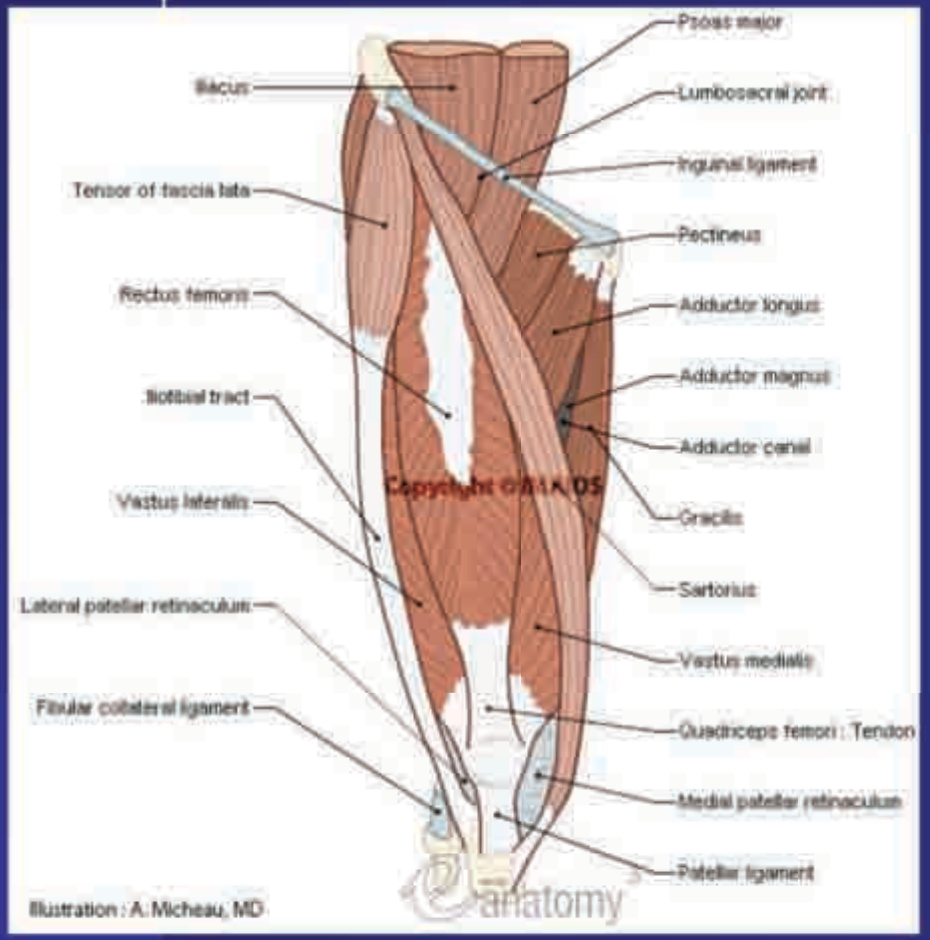
Wintrobe's Atlas of Clinical Hematology, by Douglas C. Thachuk and Jan V. Hirschmann.

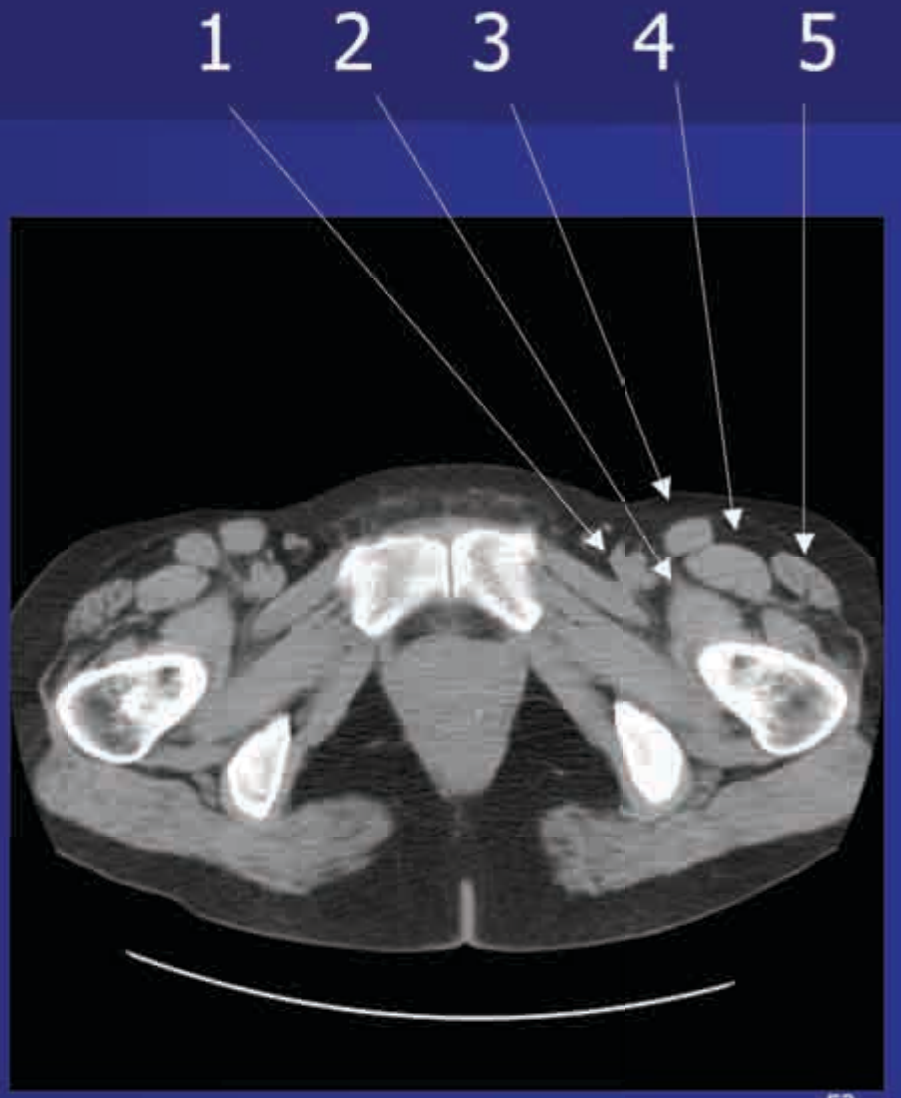
Case 5

38 year old F

38 year old F

anatomy





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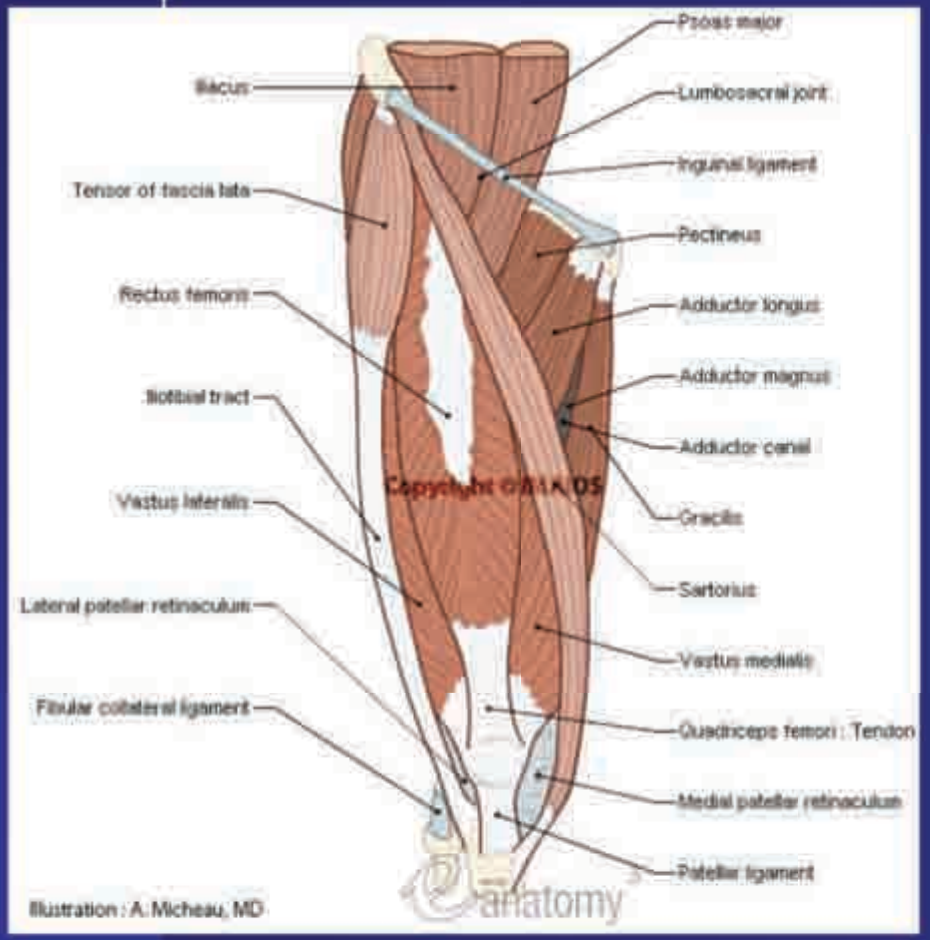
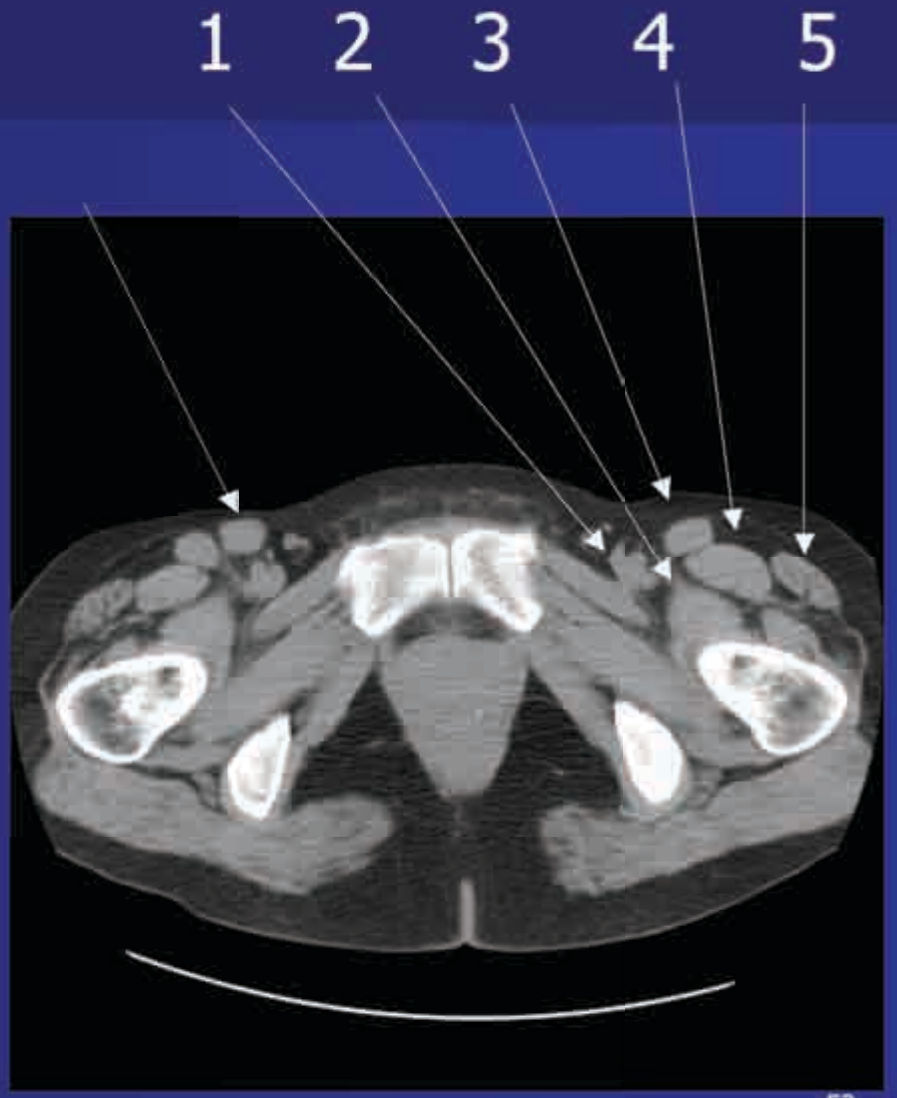




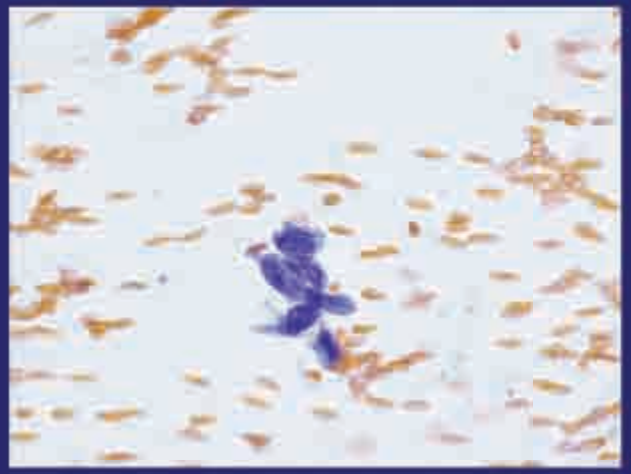
38 year old F

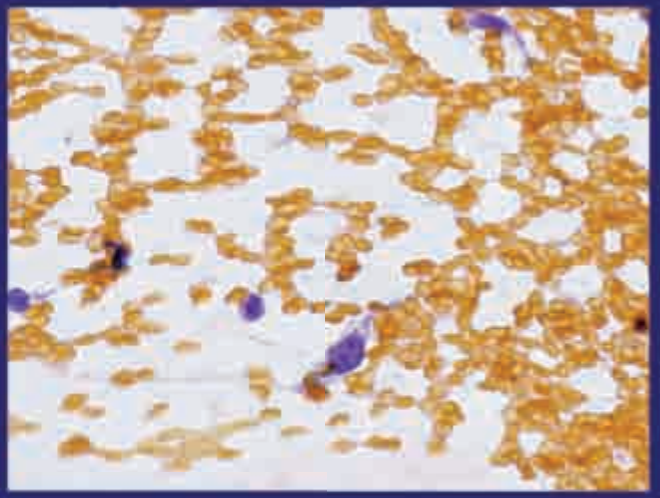
Unilateral inguinal adenopathy

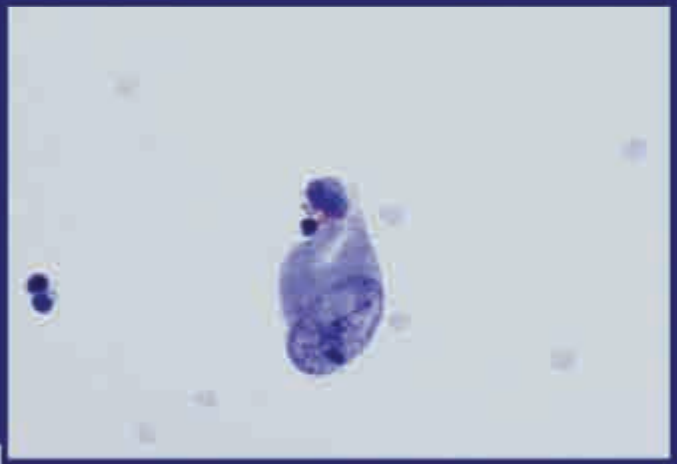
- Reactive
- Metastatic
- Partially visualizing lymphoma

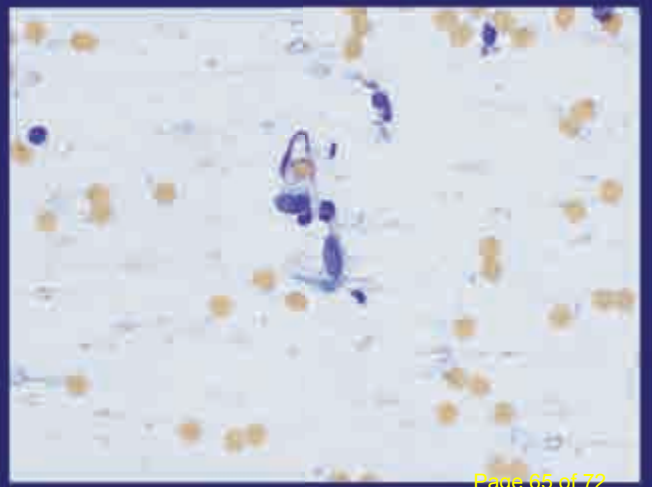
8 yr earlier

Lymph node, inguinal, right, CT-guided FNA: PAP stain, 40x





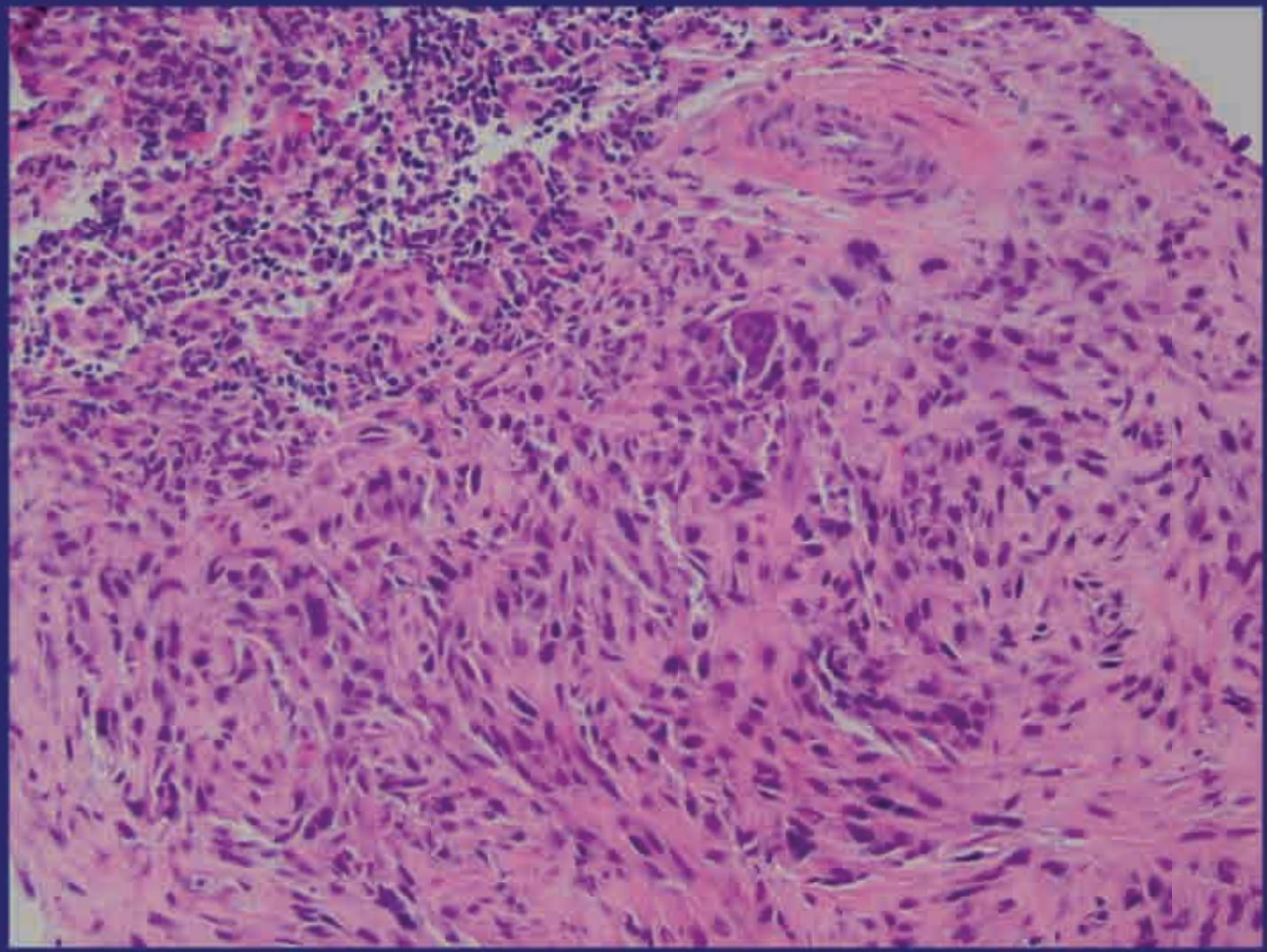




Lymph node, inguinal, right, ultrasound -guided, fine needle aspiration:

- **Malignant tumor cells present consistent with metastatic osteosarcoma.**

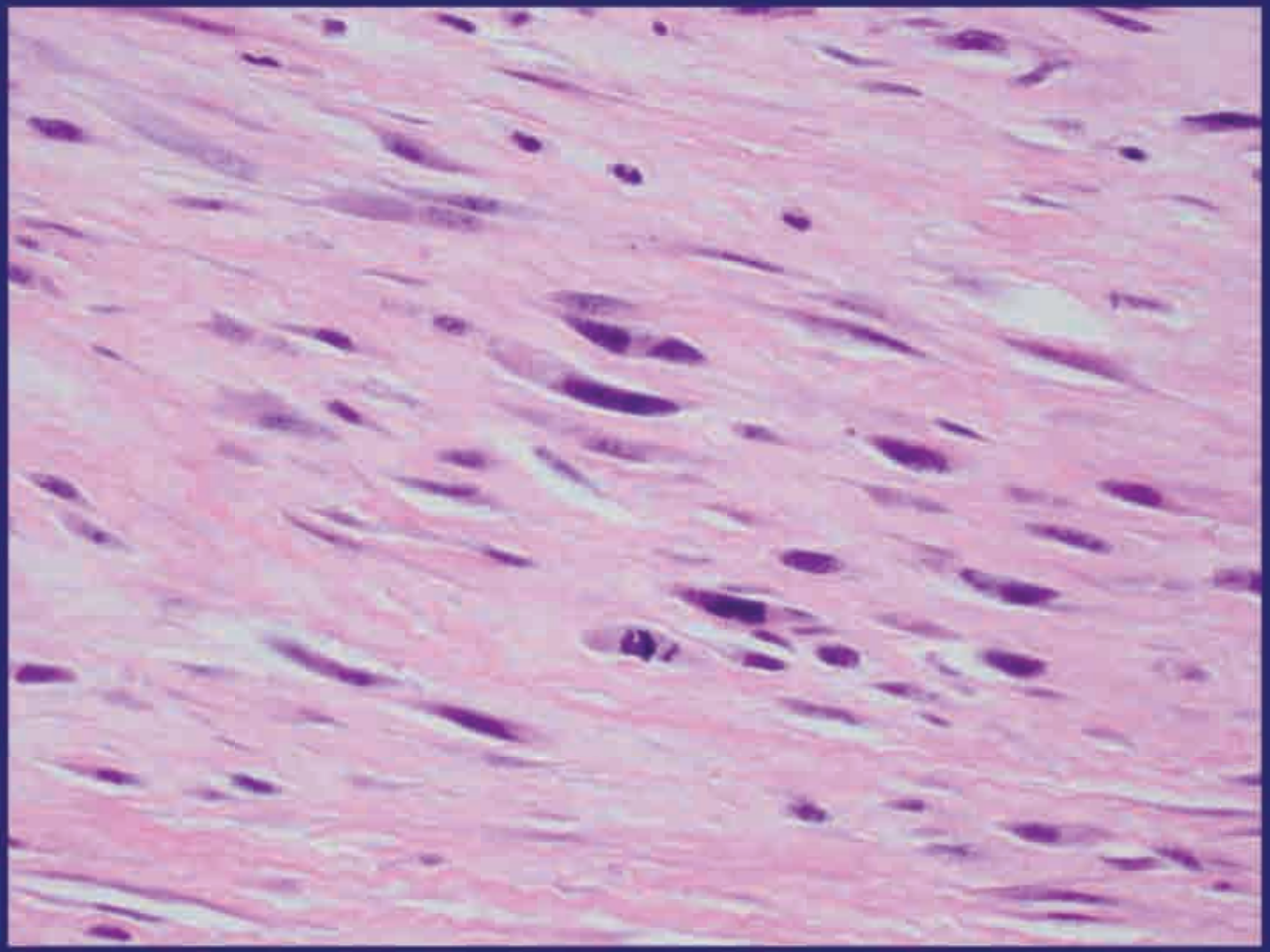
Lymph node, right groin, CT-guided Core biopy, 40x



Lymph node, right groin, core biopsy:

- High grade sarcoma, consistent with metastatic osteosarcoma, fibroblastic variant.

Soft tissue, distal right thigh, reexcision: 40x



Soft tissue, distal right thigh, reexcision:

- Recurrent osteosarcoma, fibroblastic variant, with necrosis and fibrosis.

Osteosarcoma

- Most common primary bone tumor after myeloma
  - Associated with Paget's disease after age 40 years, post-radiation exposure, Thorotrast administration, chemotherapy in children, fibrous dysplasia, osteochondromatosis, chondromatosis, rarely with hip implants
- May have ***osteoblastic***, ***fibroblastic*** or ***chondroblastic*** predominance
- **Sites of metastasis:** lung (98%, 20-80% at diagnosis, rarely within pulmonary arteries), other bones , pleura , heart
  - Rarely to lymph nodes, GI tract, liver, brain

Suggested Panels for the Classification of Various Tumors

Tumor Type	Common Immunomarkers
Carcinomas (Epithelial Tumors)	Pankeratin, CK 7 and CK 20, TTF-1, Napsin-A, CDX-2, CalR, CK 5/6, CEA, EMA, B72.3, Hep-Par1
Lymphomas	CD45, CD 3, CD 20, CD 30, CD 15, Kappa, Lambda, CD138 (plasma cell)
Sarcomas (Mesenchymal Tumors)	S-100, Myogenin, MSA, SMA, Vimentin CD 99, CD 31, CD 34, C-kit
Melanoma	S-100, HMB-45, Melan-A, Cytokeratin (-)
Neural/NE	Chromogranin, Synaptophysin, CD 56, GFAP