116 REUNIÓN DE LA TERRITORIAL VALENCIANA DE LA

SEAP-IAP
[Sociedad Española de Anatomía Patológica]
[International Academy of Pathology]

En Denia, a 10 de junio de 2022

Jesús Javier Sola Gallego

Marta Atienza Robles

Carlos Miguel Ruiz

Hospital San Pedro

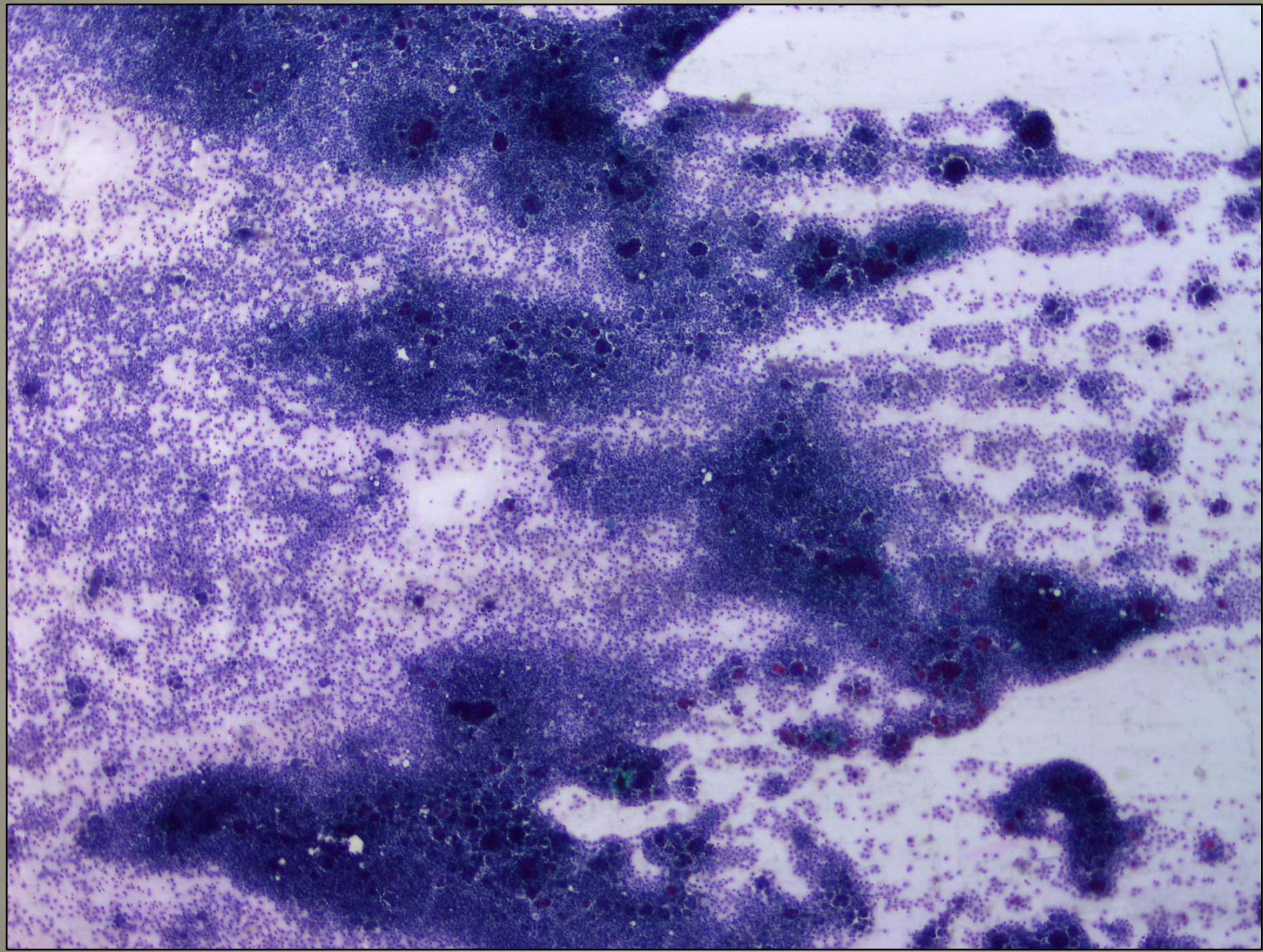
- Mujer 52 años
- Ex-fumadora
- Tiroiditis autoinmune
- Dolor en hipogastrio
- Sensación de hinchazón abdominal de varias semanas de evolución, que ha empeorado progresivamente

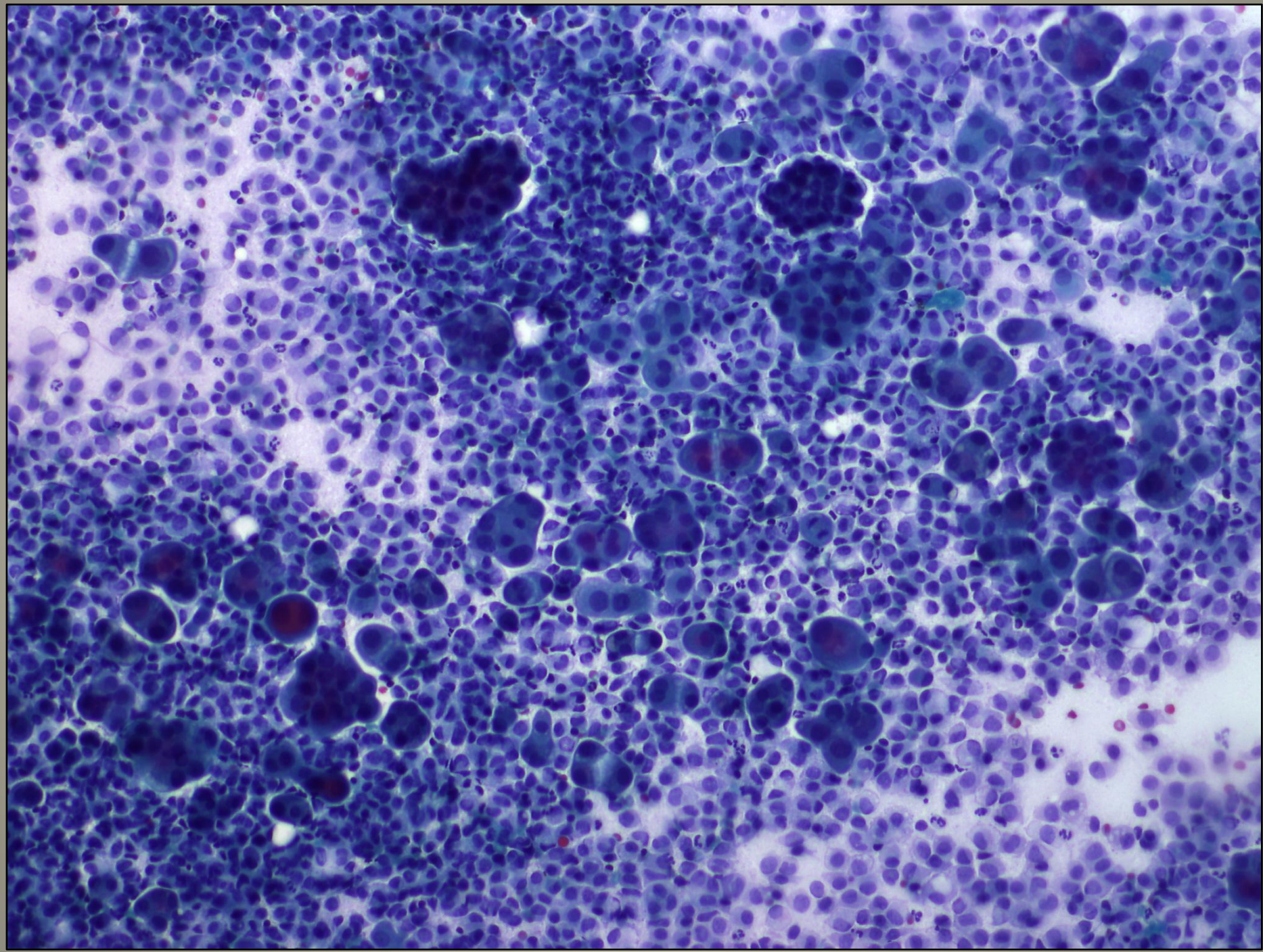
…durante su ingreso…

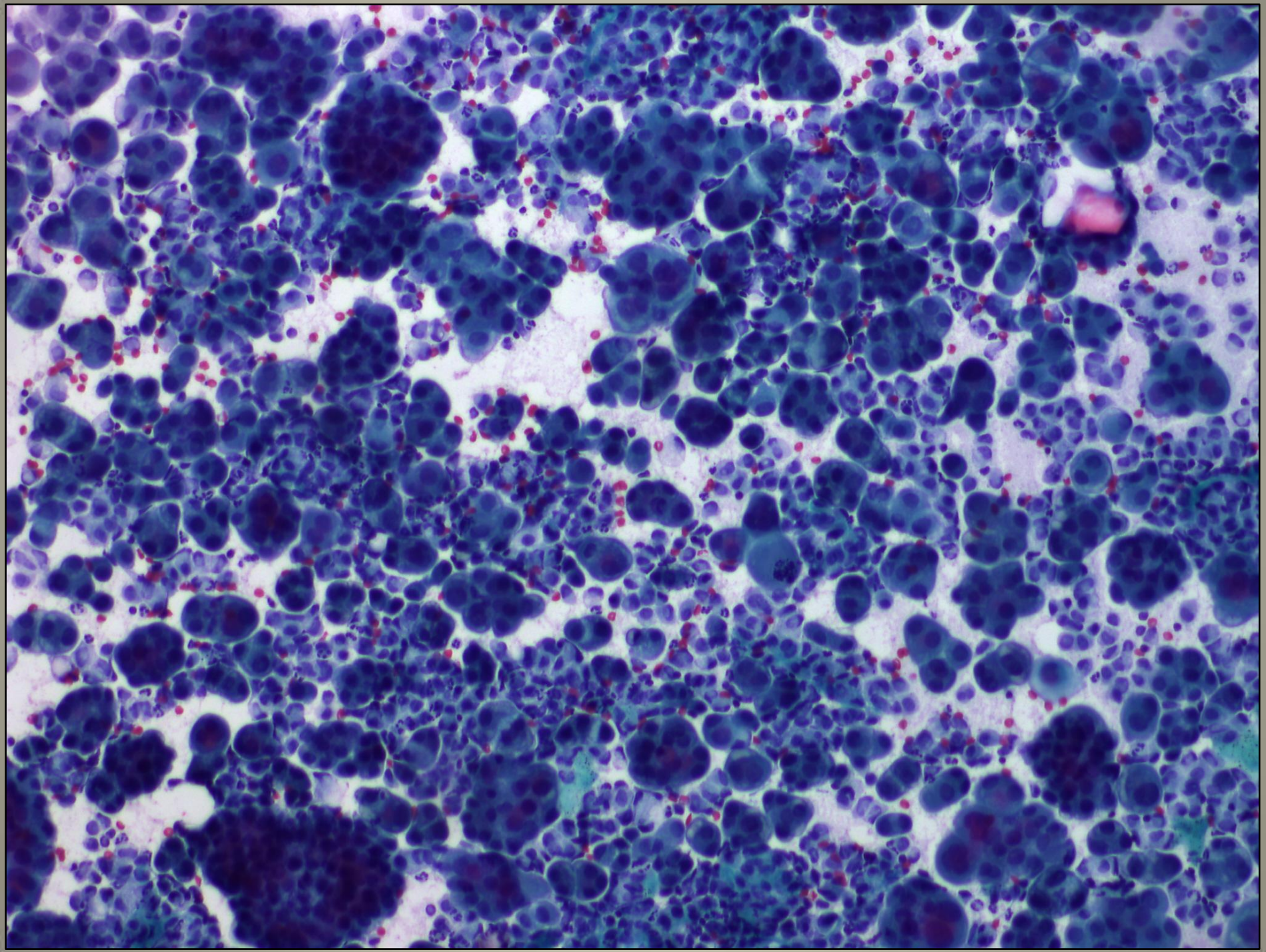
El TC revela:

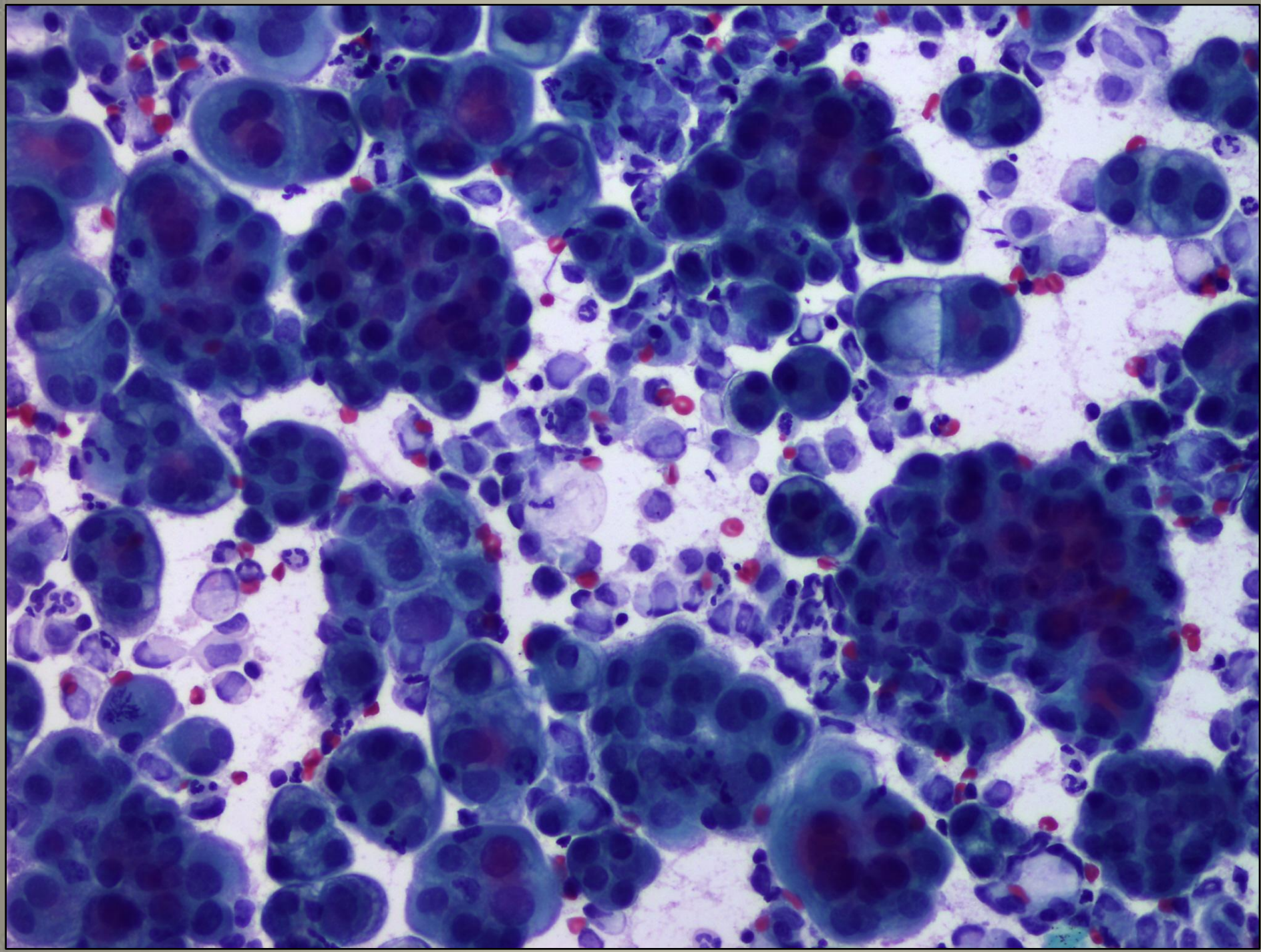
- engrosamiento de 5’6cm a nivel del colon sigmoide
- lesión de 4’5cm de posible aunque dudoso origen ovárico (recomienda estudio ecográfico)
- imágenes de carcinomatosis peritoneal

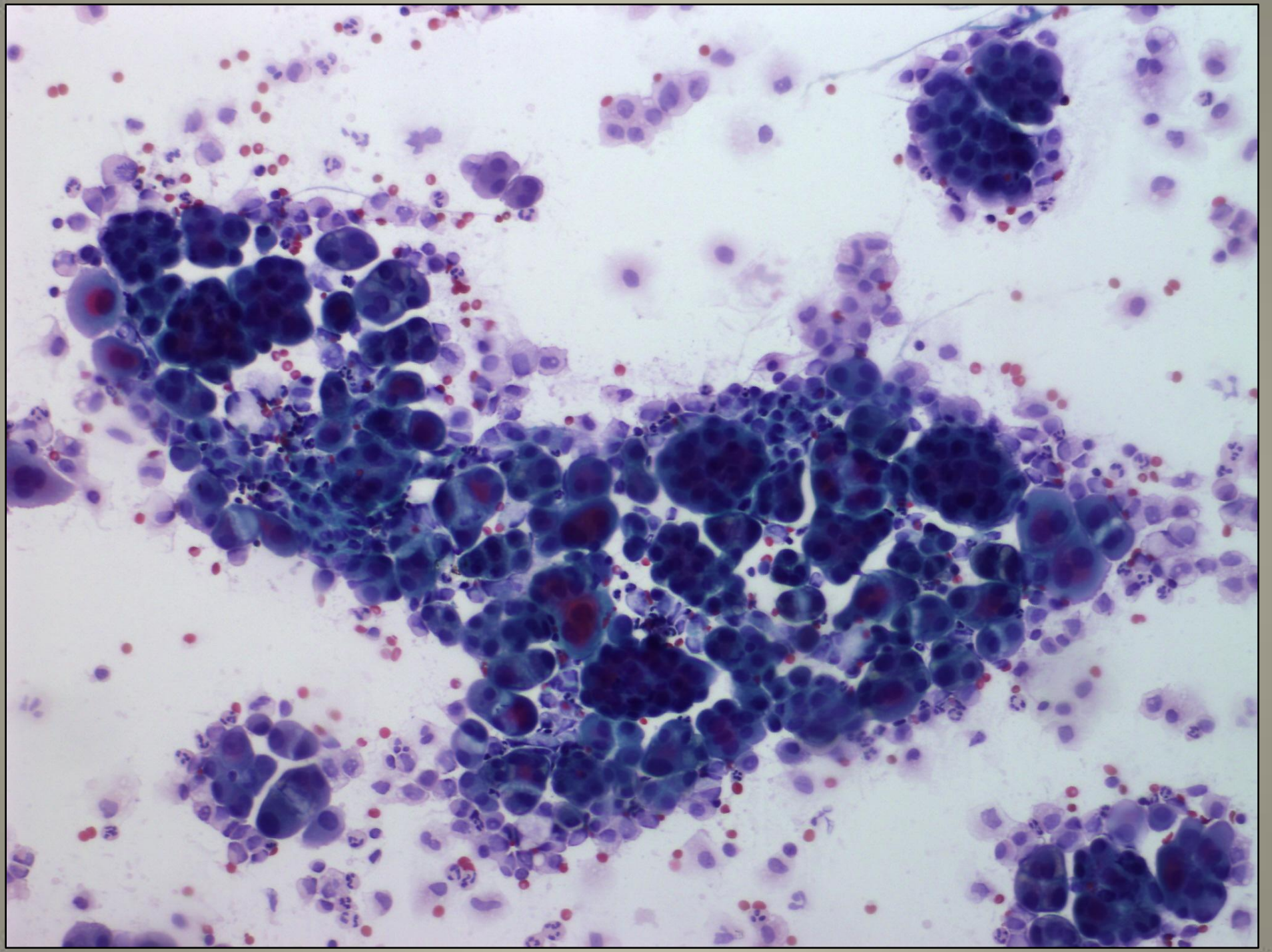
Se punciona la cavidad abdominal con extracción de líquido ascítico turbio…

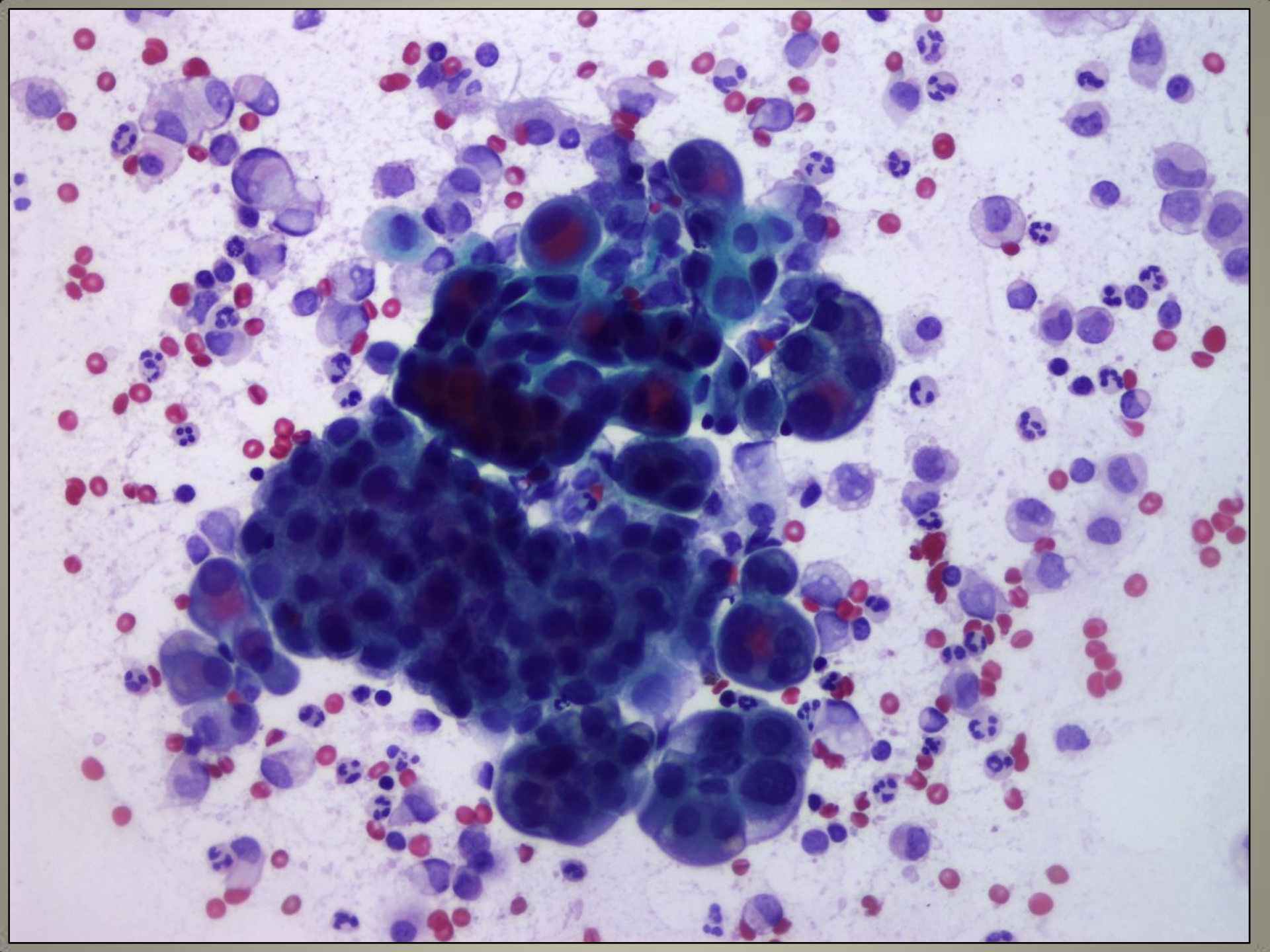


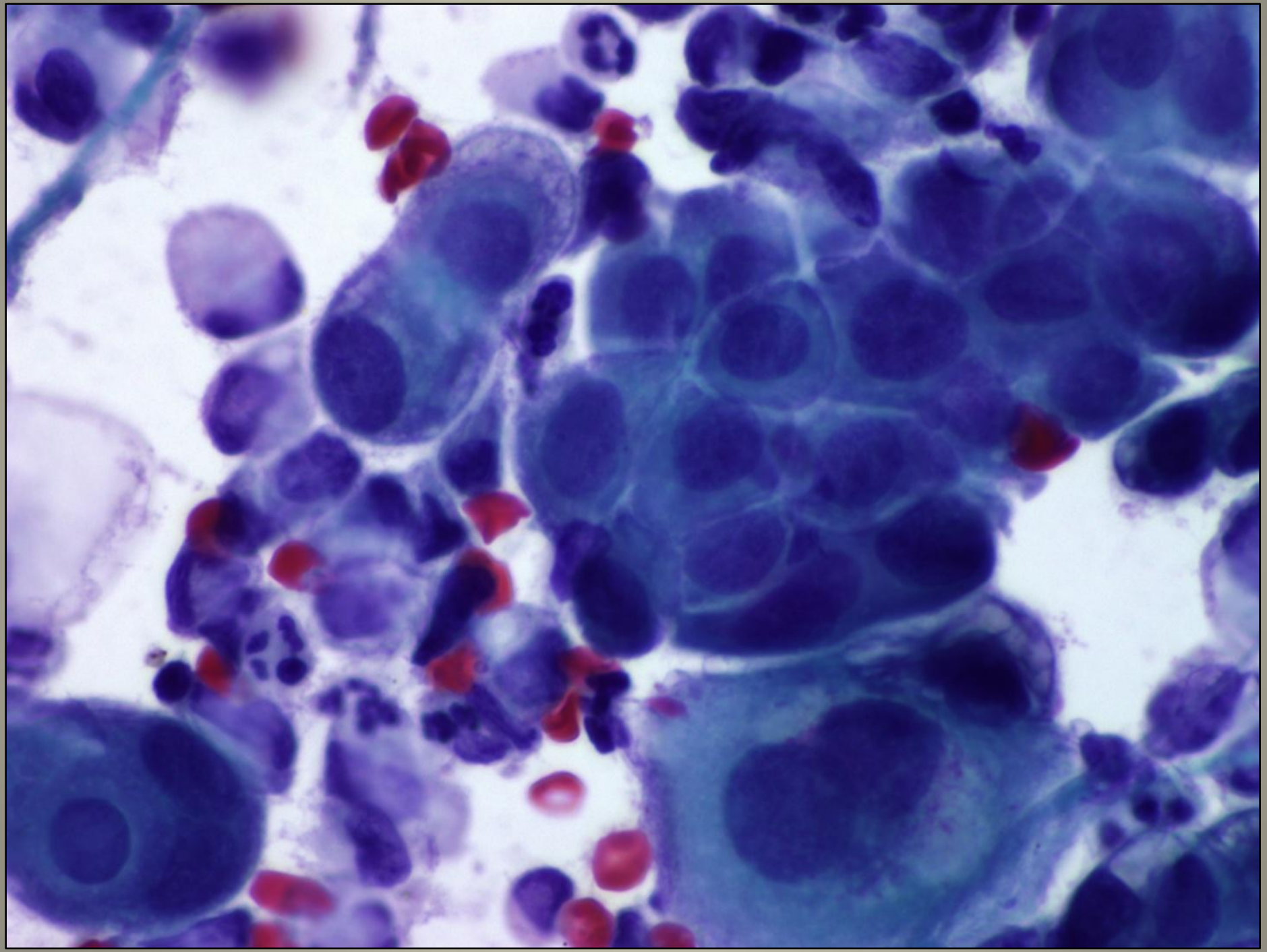


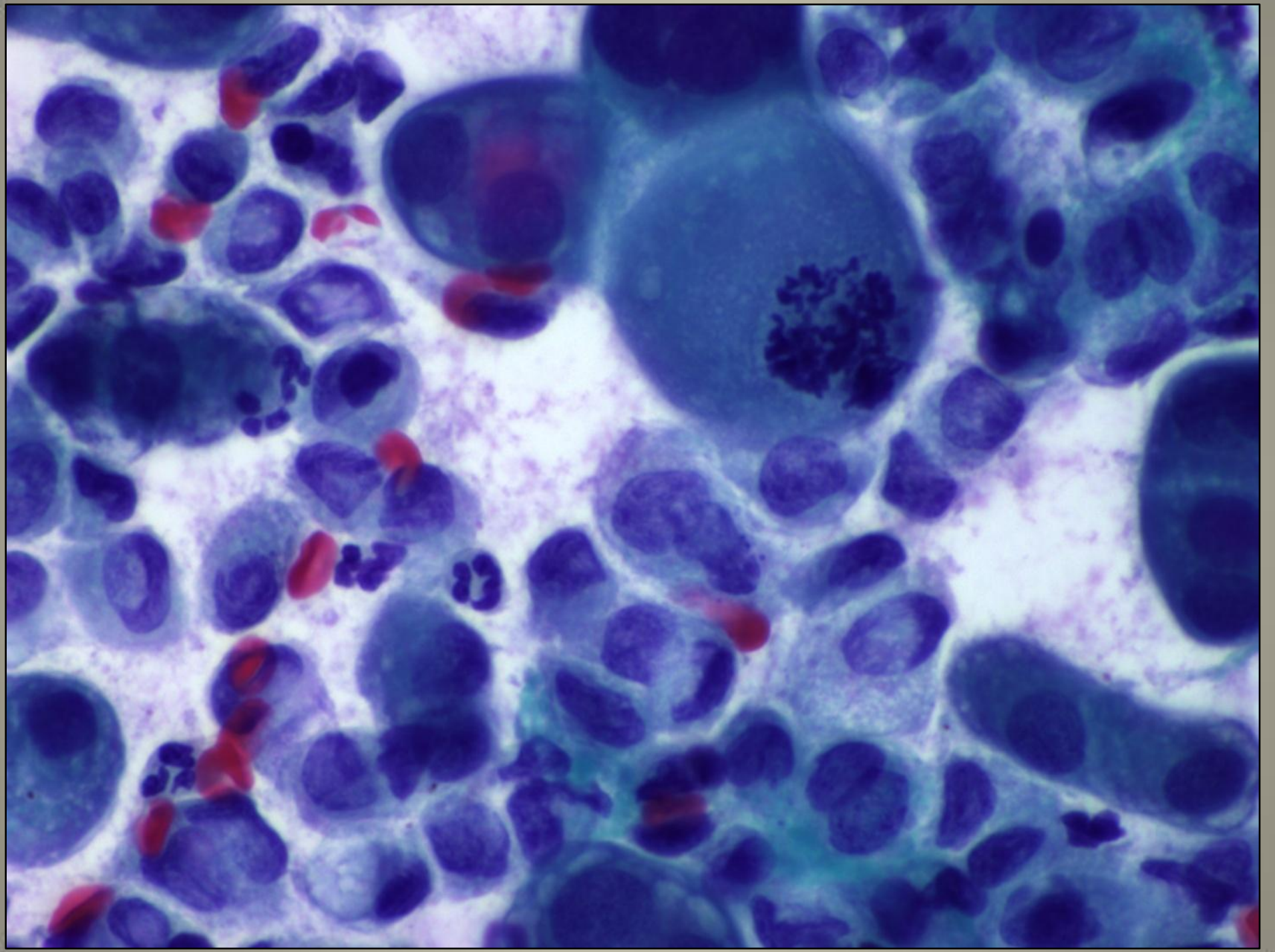


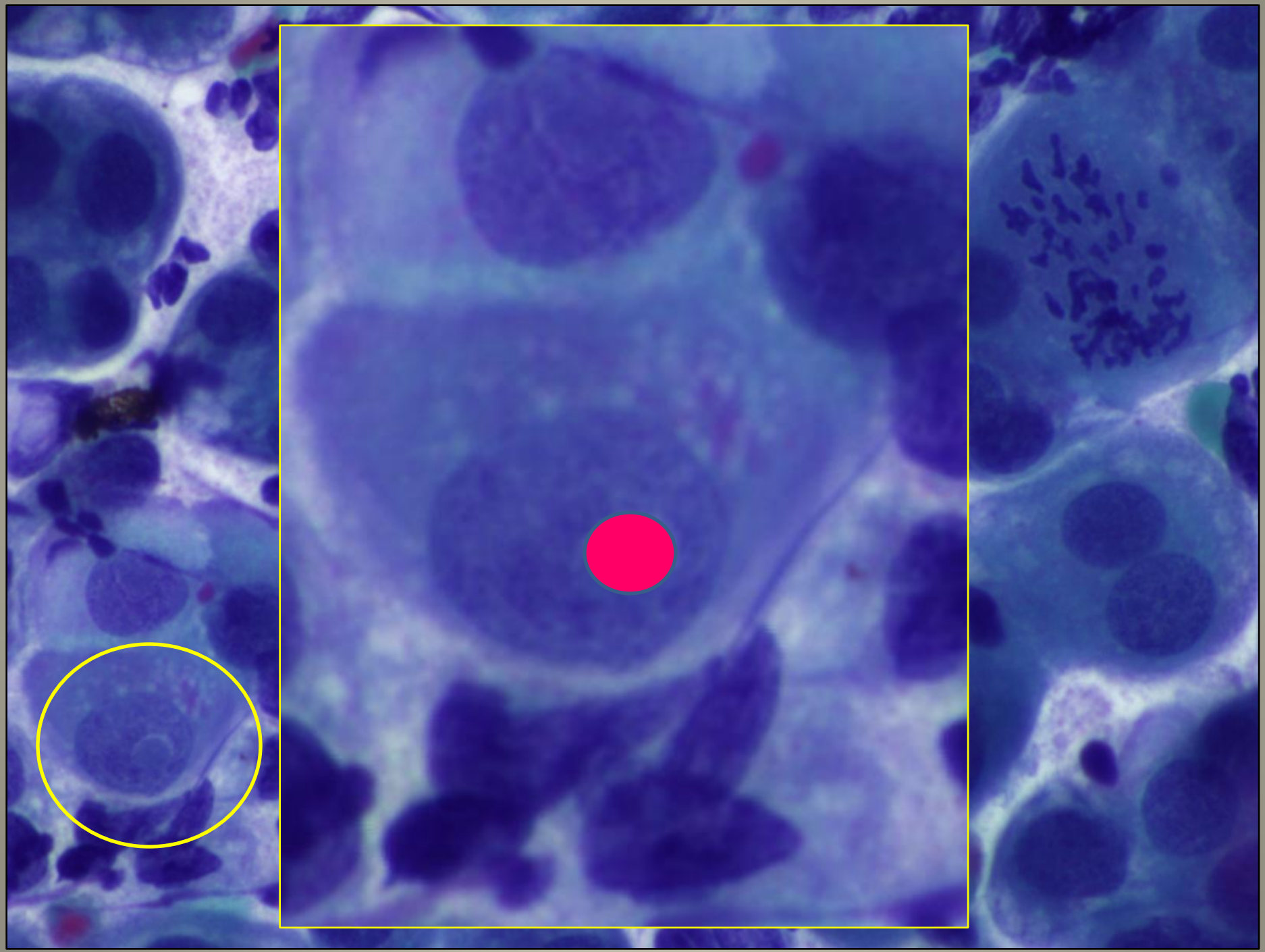




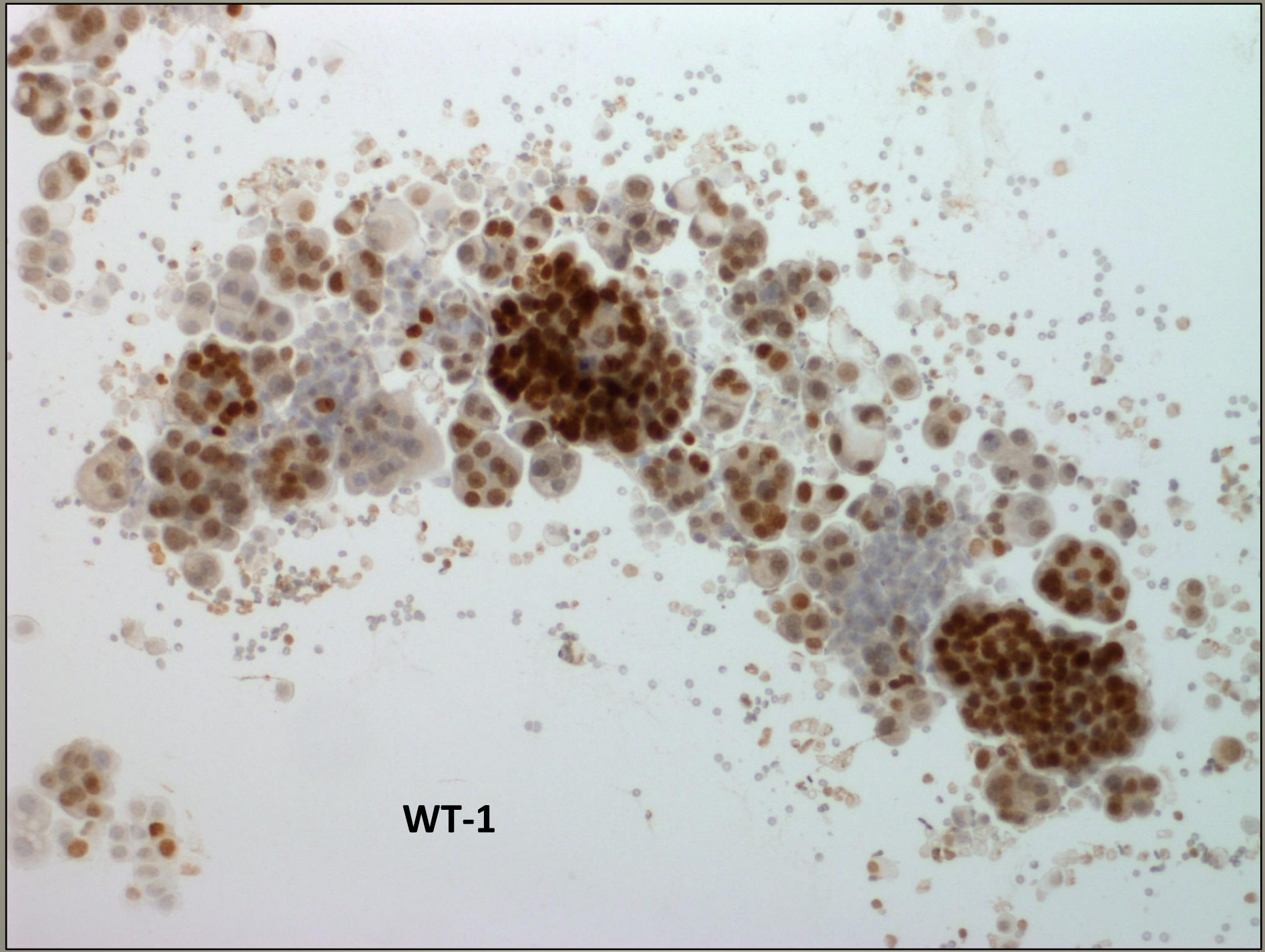


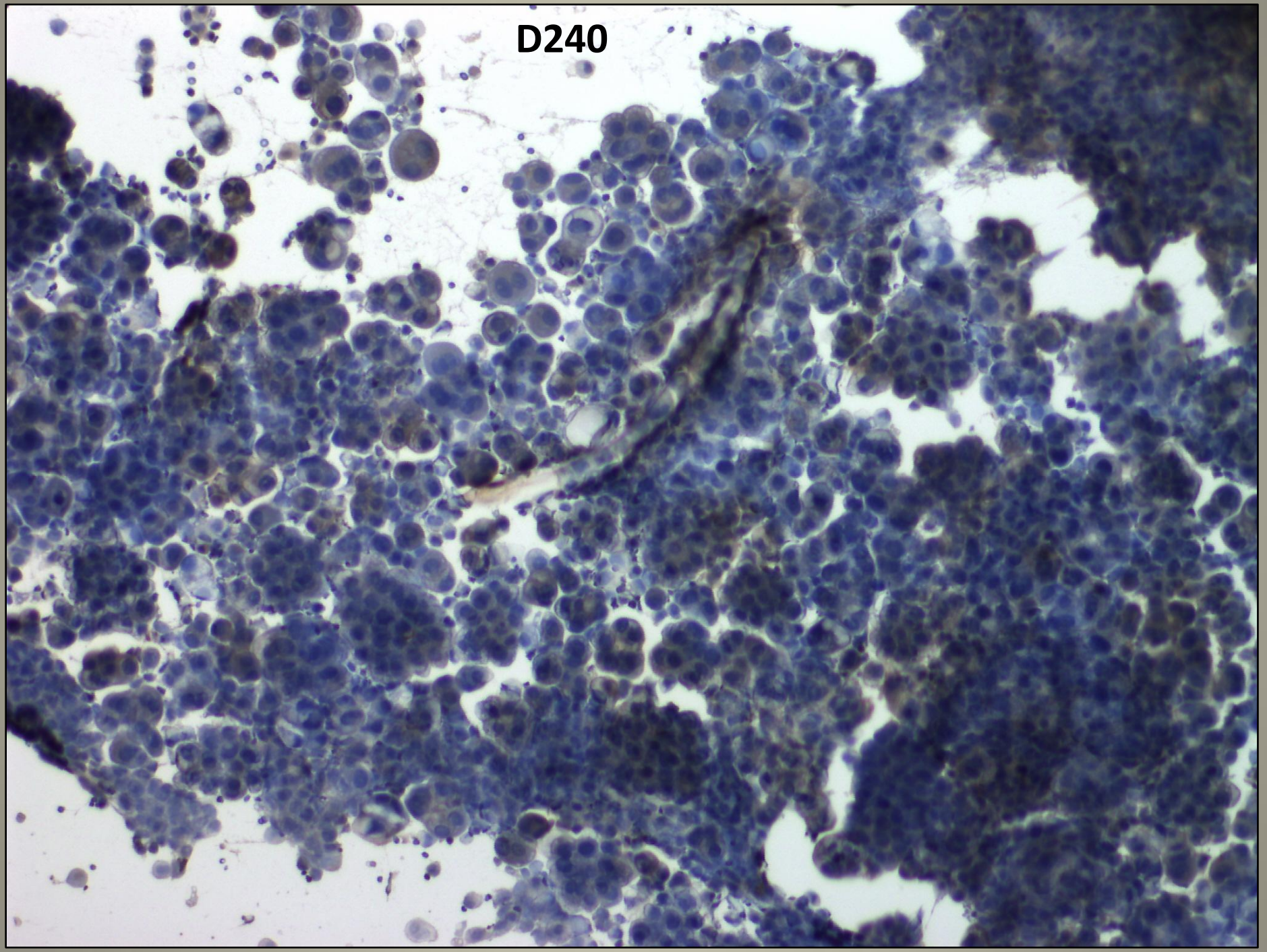


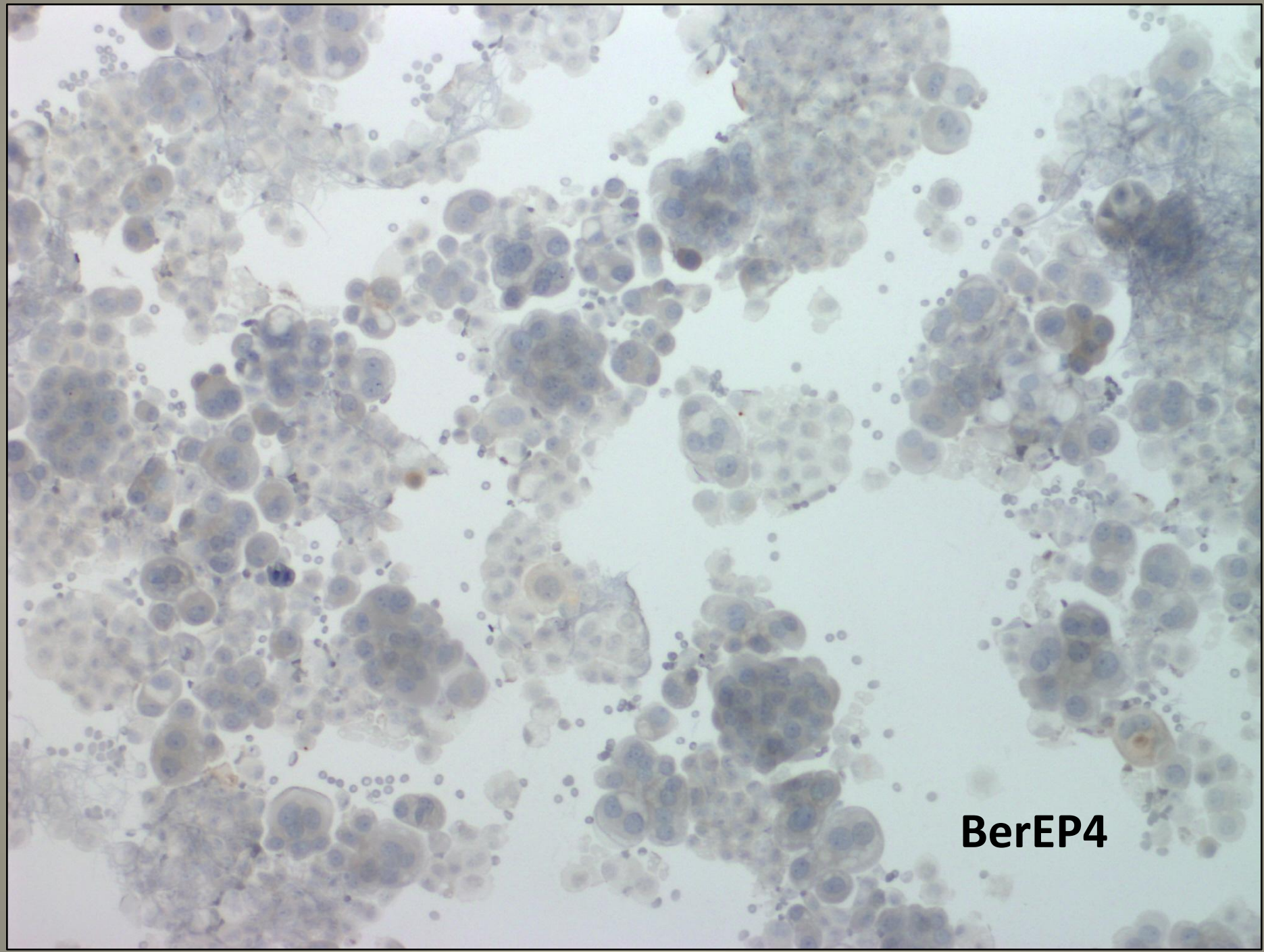


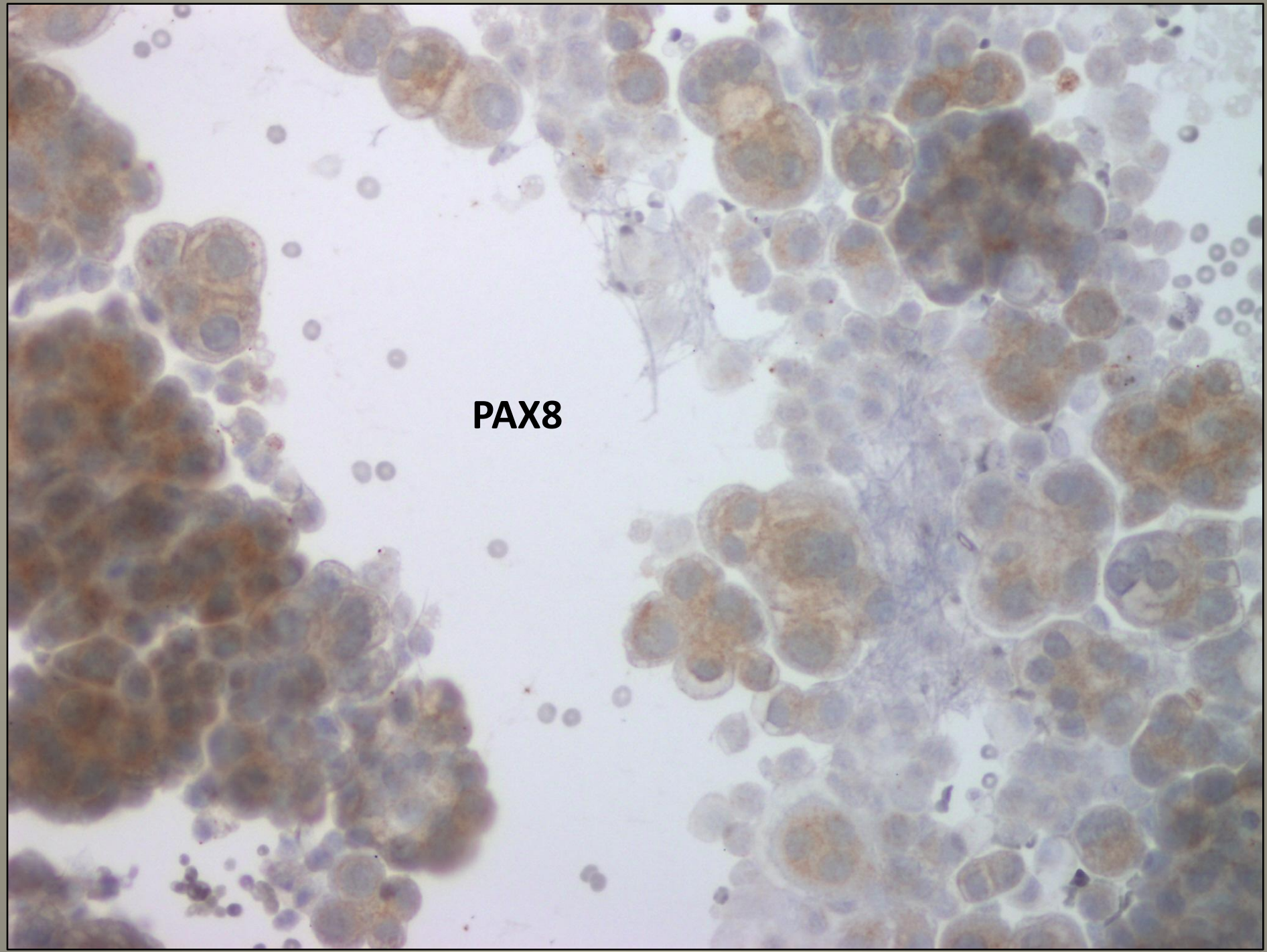


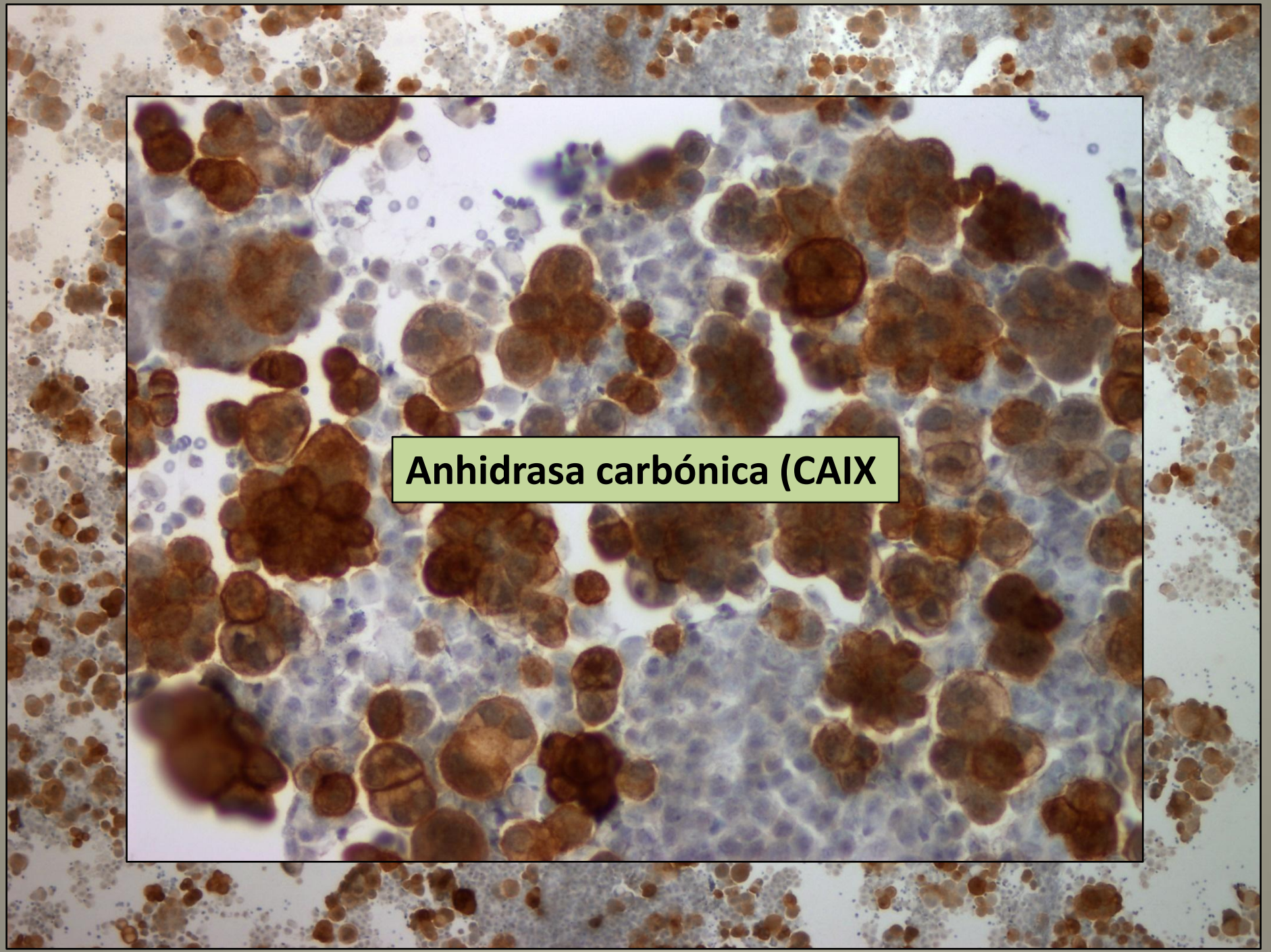
sigma


WT-1

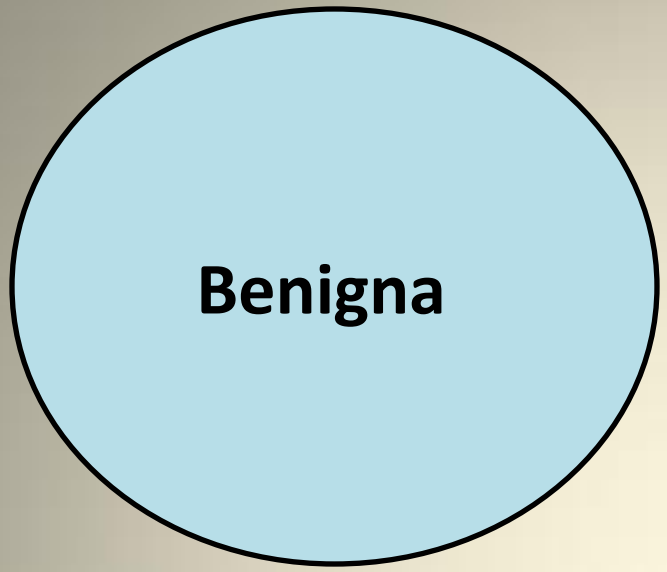

D240

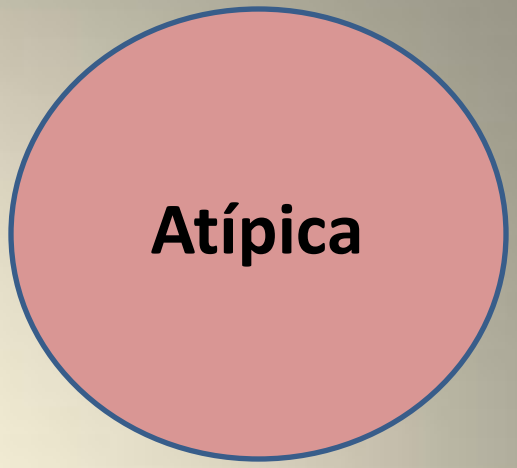

BerEP4


PAX8

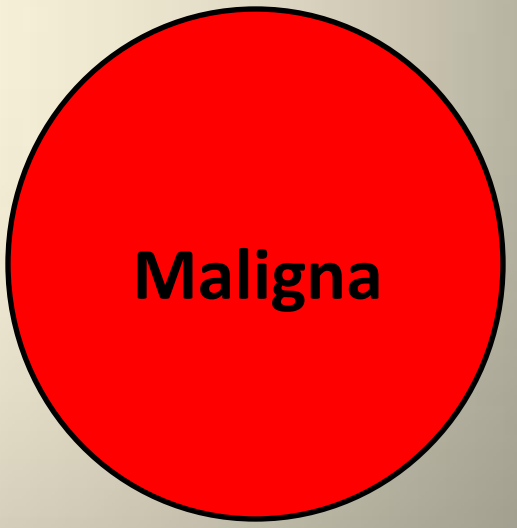

Anhidrasa carbónica (CAIX

benigno
maligno


Benigna


Atípica

Sospechosa


Maligna

mesotelial

No-mesotelial

El TC revela:

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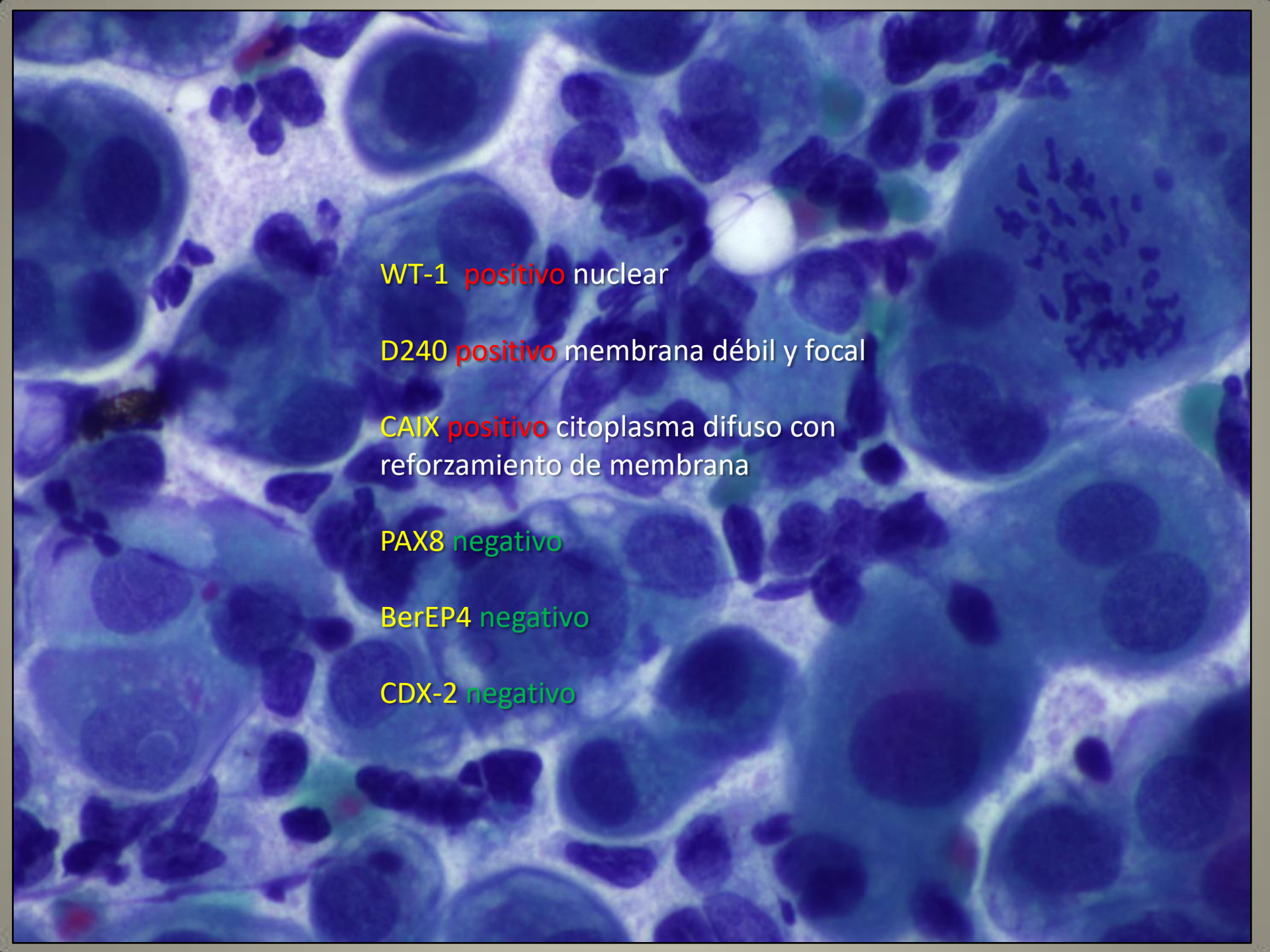
Ecografía ginecológica

- Útero normal
- Endometrio atrófico
- Mioma intramural de 13mm en cara post
- Ovarios no-identificables
- Engrosamiento del peritoneo parietal en Douglas a modo de placas
- Carcinomatosis sin masas anexiales identificables

PET

- Incremento de actividad metabólica en:
  - Pared abdominal ant. y lateral (SUVmax=8’6) y fondos de saco pélvicos
  - Implantes metastásicos en cúpula hepática, hilio esplénico, senos costodiafragmáticos y pararrectal
  - No descarto tumoración anexial primaria ante la dificultad de identificar ambos anejos


WT-1 positivo nuclear
D240 positivo membrana débil y focal
CAIX positivo citoplasma difuso con reforzamiento de membrana
PAX8 negativo
BerEP4 negativo
CDX-2 negativo

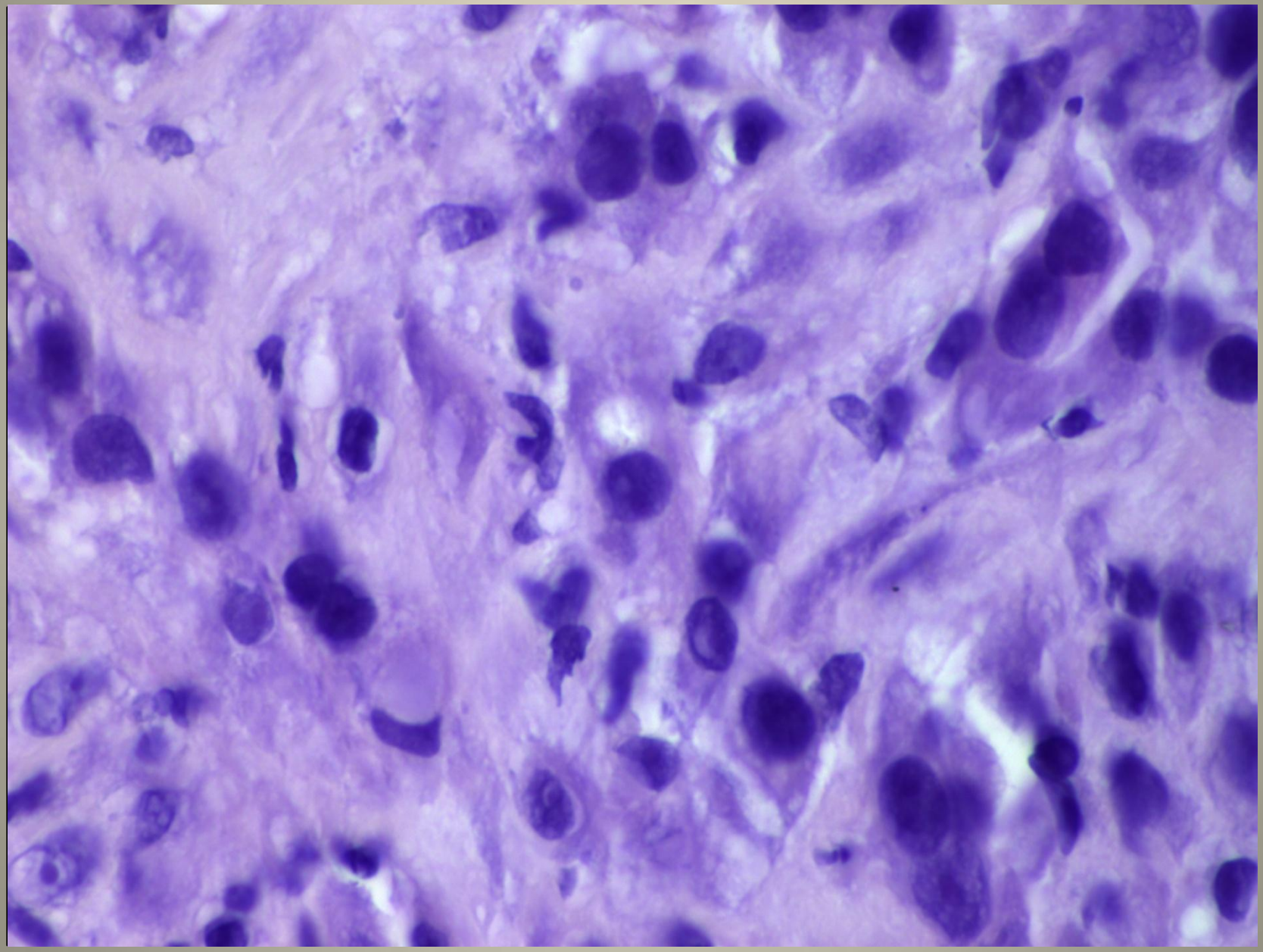
Diagnóstico líquido ascítico:

- Citología **POSITIVA** para malignidad
- Compatible con **MESOTELIOMA**

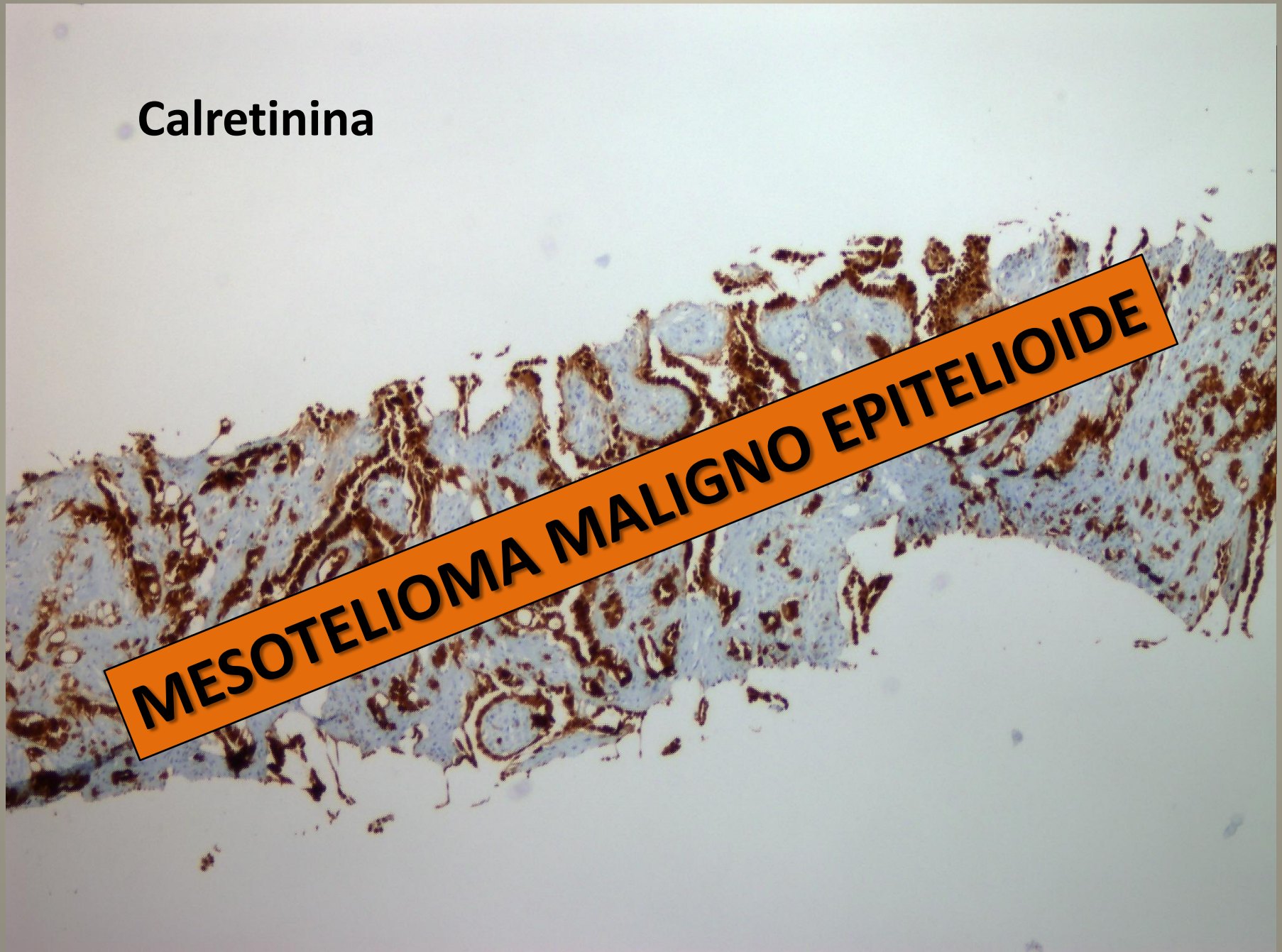
"Este perfil inmunohistoquímico sugiere que el origen más probable de la lesión es el mesotelio, y que probablemente se trata de un mesotelioma

Se recomienda **biopsia** de la lesión para confirmar el diagnóstico morfológico y los fenómenos de infiltración si los hubiere"

BAG fondo de saco de Douglas…



BAG fondo de saco de Douglas…



CISPLATINO - PEMETREXED

TC >>> Progresión con gran masa en pelvis 14’5cm

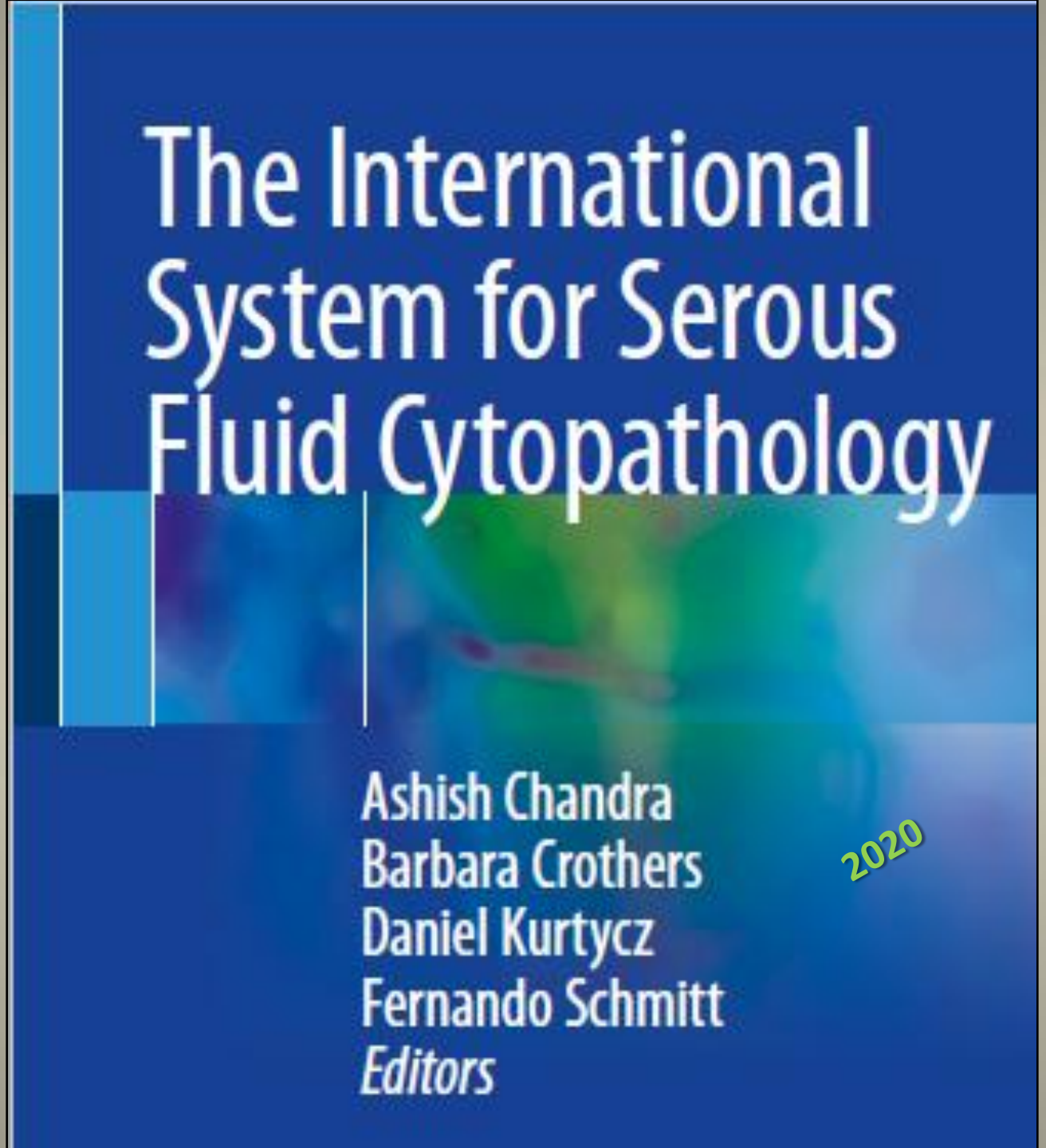
GEMCITABINA + VINORELBINA

Enfermedad estable (5 ciclos)

9 meses

Paracentesis evacuadoras (4l.)

Suspender tratamiento
Regreso a país de origen


The International System for Serous Fluid Cytopathology
Ashish Chandra
Barbara Crothers
Daniel Kurtycz
Fernando Schmitt
Editors
2020

Cellularity: Super-cellular / high / moderate / low cellularity

Cell type: mesothelial / non-mesothelial / both

Cellular atypia: malignant / suspicious / atypical / benign

Mesotelioma: Criterios citológicos de malignidad

- Definitivo Criteria of Malignancy

Supportive Criteria of Malignancy

- Significantly enlarged mesothelial cells with abundant (metachromatic or two-tone) cytoplasm
- Large nuclei with subtle atypia
- Prominent nucleoli often variable in size and number
- Wide variation in cellular size, from normal-appearing mesothelial cell to gigantic
- Numerous multinucleated cells
- Tissue fragments or papillary groups with collagen or basement membrane cores
- Pyknotic, eosinophilic, or orangeophilic cells (pseudokeratotic cells)
- Numerous perinuclear lipid vacuoles on MGG, confirmed by oil-red O stain on fresh fluid
- Pink or red granular background on MGG (representing high hyaluronan concentrations)

cellular clusters

- The cytologic diagnosis in a mesothelial proliferative effusion depends primarily on the morphologic findings

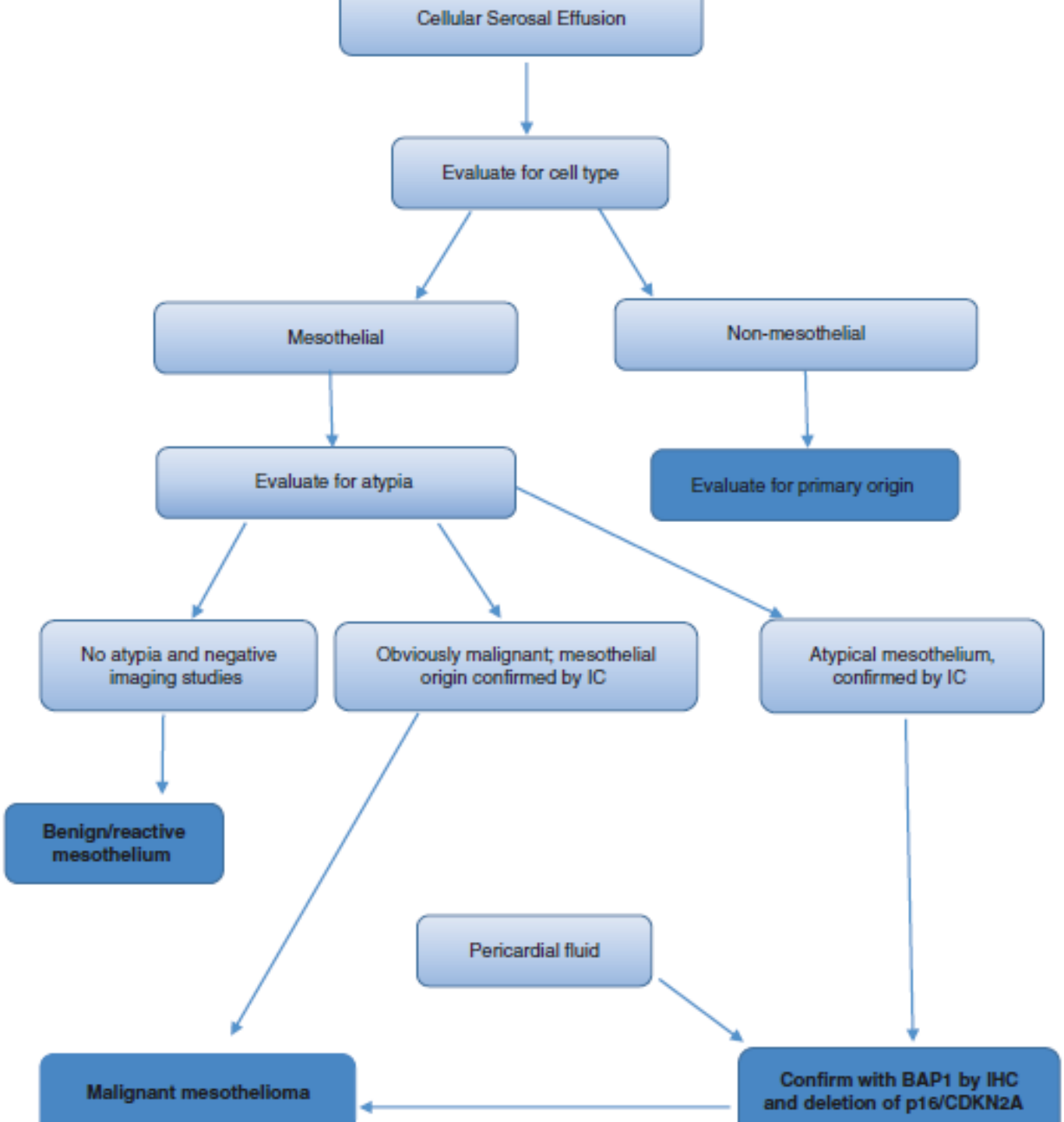
- The diagnosis of malignant mesothelioma can be issued in cases where overtly malignant features are identified

- Cases presenting with subtle atypia and many of the additional supportive criteria of malignancy can be diagnosed as malignant mesothelioma if confirmed by ancillary tests such as loss of BAP1 expression and/or deletion of p16/CDKN2A by fluorescence in situ hybridization (FISH)

- The diagnosis of atypical mesothelial cells (AUS) should be used judiciously and avoided whenever possible

	Reactive mesothelium	Malignant mesothelioma
Desmina	+	-
EMA (E29 clone)	-	+
BAP1	+	Lost in 60% of cases
P16/CDKN2A (FISH) deletion	Not deleted	Homozygous deletion in up to 80%

	Malignant mesothelioma	Metastatic carcinoma
Calretinin	Positive	Negative (most cases)
D2–40	Positive	Negative
WT-1	Positive	Variable
CK5/6	Positive	Negative (most cases)
Claudin 4	Negative	Positive
GATA-3	Positive	Positive in breast, urothelial and some squamous carcinoma
MOC-31 and BerEp4	Negative	Positive
Broad spectrum epithelial markers	Positive	Positive
p40 and p63	Negative	Positive in squamous and urothelial carcinoma


Cellular Serosal Effusion
Evaluate for cell type
Mesothelial
Non-mesothelial
Evaluate for atypia
Evaluate for primary origin
No atypia and negative imaging studies
Obviously malignant; mesothelial origin confirmed by IC
Atypical mesothelium, confirmed by IC
Benign/reactive mesothelium
Pericardial fluid
Malignant mesothelioma
Confirm with BAP1 by IHC and deletion of p16/CDKN2A

AME Publishing Company
ATM ANNALS OF TRANSLATIONAL MEDICINE
Malignant peritoneal mesothelioma: a review
Joseph Kim, Shanel Bhagwandin, and Daniel M. Labow
Ann Transl Med. 2017 junio; 5(11): 236.
doi: 10.21037/atm.2017.03.96
PMID: 28706904

•Commonly presents with diffuse, extensive spread throughout the abdomen with rare metastatic spread beyond the abdominal cavity

• Due to its rarity and nonspecific symptoms, it is usually diagnosed late when the disease burden is extensive

• Most research has been on the pleural variant and extrapolated for peritoneum

• Mesothelioma has been linked to industrial pollutants and mineral exposure. The most common carcinogen identified for pleural mesothelioma has been asbestos, with approximately 80% of cases linked to asbestos exposure (7,8). While asbestos is also the best defined risk factor for MPM, the link is weaker (33-50%)

• Time and duration of exposure do not directly correlate with disease development, with some long-term exposures yielding no disease while some short-term exposures leading to significant tumor burden

• While there is a significant predominance of men diagnosed with pleural mesothelioma, of the 300–400 new cases of MPM a year, the prevalence between men and women is equal in the U.S.

IASLC

The 2021 WHO Classification of Tumors of the Pleura: Advances Since the 2015 Classification

Jennifer L. Sauter, MD,[a,*] Sanja Dacic, MD, PhD,[b] Francoise Galateau-Salle, MD,[c,d] Richard L. Attanoos, M.B.B.S., FRCPath.,[e] Kelly J. Butnor, MD,[f] Andrew Churg, MD,[g] Aliya N. Husain, MD,[h] Kyuichi Kadota, MD, PhD,[i] Andras Khoor, MD, PhD,[j] Andrew G. Nicholson, MD,[k] Victor Roggli, MD,[l] Fernando Schmitt, MD, PhD,[m,n] Ming-Sound Tsao, MD,[o] William D. Travis, MD[a]

[a]*Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York*
[b]*Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania*
[c]*MESOPATH Centre Leon Berard, Lyon, France*
[d]*Unit of Cancer Research Center INSERM U1052-CNRS5286R, Lyon, France*
[e]*Department of Cellular Pathology, University Hospital of Wales and School of Medicine, Cardiff University, Cardiff, Wales, United Kingdom*
[f]*Department of Pathology & Laboratory Medicine, The University of Vermont Medical Center, Burlington, Vermont*
[g]*Department of Pathology and Laboratory Medicine, Vancouver General Hospital and The University of British Columbia, Vancouver, British Columbia, Canada*
[h]*Department of Pathology, The University of Chicago, Chicago, Illinois*
[i]*Department of Pathology, Faculty of Medicine, Shimane University, Izumo, Japan*
[j]*Department of Laboratory Medicine and Pathology, Mayo Clinic, Jacksonville, Florida*
[k]*Royal Brompton and Harefield Hospitals, and National Heart and Lung Institute, Imperial College, London, United Kingdom*
[l]*Department of Pathology, Duke University Medical Center, Durham, North Carolina*
[m]*RISE@CINTESIS, Medical Faculty of Porto University, Porto, Portugal*
[n]*Unit of Molecular Pathology of IPATIMUP, Porto University Medical School, Porto, Portugal*
[o]*Department of Pathology, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada*

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“Carbonic anhydrase IX (CAIX) does not differentiate between benign and malignant mesothelium”

Vijayalakshmi Ananthanarayanan et al.

Am J Clin Pathol. 2014 Jul;142(1):82-7
doi: 10.1309/AJCP8BJ8CJXUEHZD PMID: **24926090**

- **Objectives:** To examine carbonic anhydrase IX (CAIX), a marker of renal cell carcinoma that recently has been described in malignant effusions.
- **Methods:** Pleural and peritoneal fluids with the following diagnoses-reactive (n = 23), carcinoma (n = 17), and "suspicious for mesothelioma" (n = 4)-were immunostained for CAIX, calretinin, Ber-EP4, and MOC31. A tissue microarray of epithelioid (n = 27) and sarcomatoid (n = 8) mesotheliomas and three cases of benign mesothelium were also immunostained for CAIX.
- **Results:** Mesothelial cells in both reactive (18/23) and malignant effusions (18/21) were positive for CAIX (P > .05). In carcinomatous effusions, CAIX expression was restricted to the mesothelial cells. Agreement between CAIX and calretinin expression was present in 89% of cases. In tissues, CAIX was positive in 100% of benign and 91% of malignant mesothelium.
- **Conclusions:** CAIX can be a useful ancillary marker for identifying mesothelial cells. There is no difference in CAIX expression between benign and malignant mesothelium. Caution should be exercised while evaluating for metastasis from renal cell carcinoma