

# MESOTELIOMAS MALIGNOS PLEURALES

Revisión de los últimos 11 años

XXV Congreso de la Sociedad Española de Anatomía Patológica  
y División Española de la International Academy of Pathology.  
Zaragoza Mayo 2011.

Dra. A. Capdevila Puerta  
Servicio de Anatomía Patológica  
CHUAC. A Coruña



**Monasterio Moldovita**

# MESOTELIOMA MALIGNO PLEURAL DIFUSO

Clasificación OMS 2004

## DEFINICION:

TUMOR MALIGNO ASENTANDO EN LA PLEURA DE CELULAS MESOTELIALES MOSTRANDO UN PATRON DE CRECIMIENTO DIFUSO EN LA SUPERFICIE PLEURAL

## TIPOS HISTOLÓGICOS

**-EPITELIOIDE** (TUBULO-PAPILAR, SOLIDO, DECIDUOIDE, CELS.

CLARAS, CELS. ANILLO DE SELLO, PLEOMORFICO.

**-SARCOMATOIDE** (LINFOHISTIOCITICO, ZONAS OSTEOSARCOMATOSAS O CONDROSARCOMATOSAS..)

**-DESMOPLASICO**

**-BIFASICO**

# MESOTELIOMA MALIGNO DIFUSO

- TUMOR RARO. Pero en aumento.
- INCIDENCIA VARIABLE EN DIFERENTES PAISES despues de que Wagner y cols demostraran su relación con Asbestos en mineros de Sud-Africa
- 2,8/millon habit/ **VARONES**
- 0,7 millon habit/ **MUJERES.**
- 3 veces mas frecuente en varones que en mujeres.
- EDAD: ADULTOS (entre 50-70 a)
- Evidente relación con exposición a **ASBESTOS** con tiempo de latencia de al menos 15-20 años. Todos los tipos de fibras son capaces de causar M.M.
- Existe correlación entre intensidad y duracion de exposición/riesgo M.M
- **Otras causas:** Radiacion terapéutica torax, (linfomas, Ca. Mama, pulmón) Inflamacion cron. Pleural, Predisposición genética tras exposición Erionita (Turquía),
- Virus SV-40: Controvertido (cancerigeno? Co-factor con asbesto?).
- 30-40% son espontáneos.

**Table 1. Worldwide Trends in the Epidemiologic Features of Malignant Mesothelioma.<sup>⊘</sup>**

Country or Region	Incidence <i>cases/million population</i>	Predicted Peak Year	Predicted No. of Deaths in Next 40 Yr <sup>†</sup>	Predicted Cost <sup>‡</sup> <i>billions of U.S. dollars</i>
United States	15	2004	72,000	200
Europe	18§	2015–2020	250,000	80
Japan	7	2025	103,000	—
Australia	40	2015	30,000	5–10

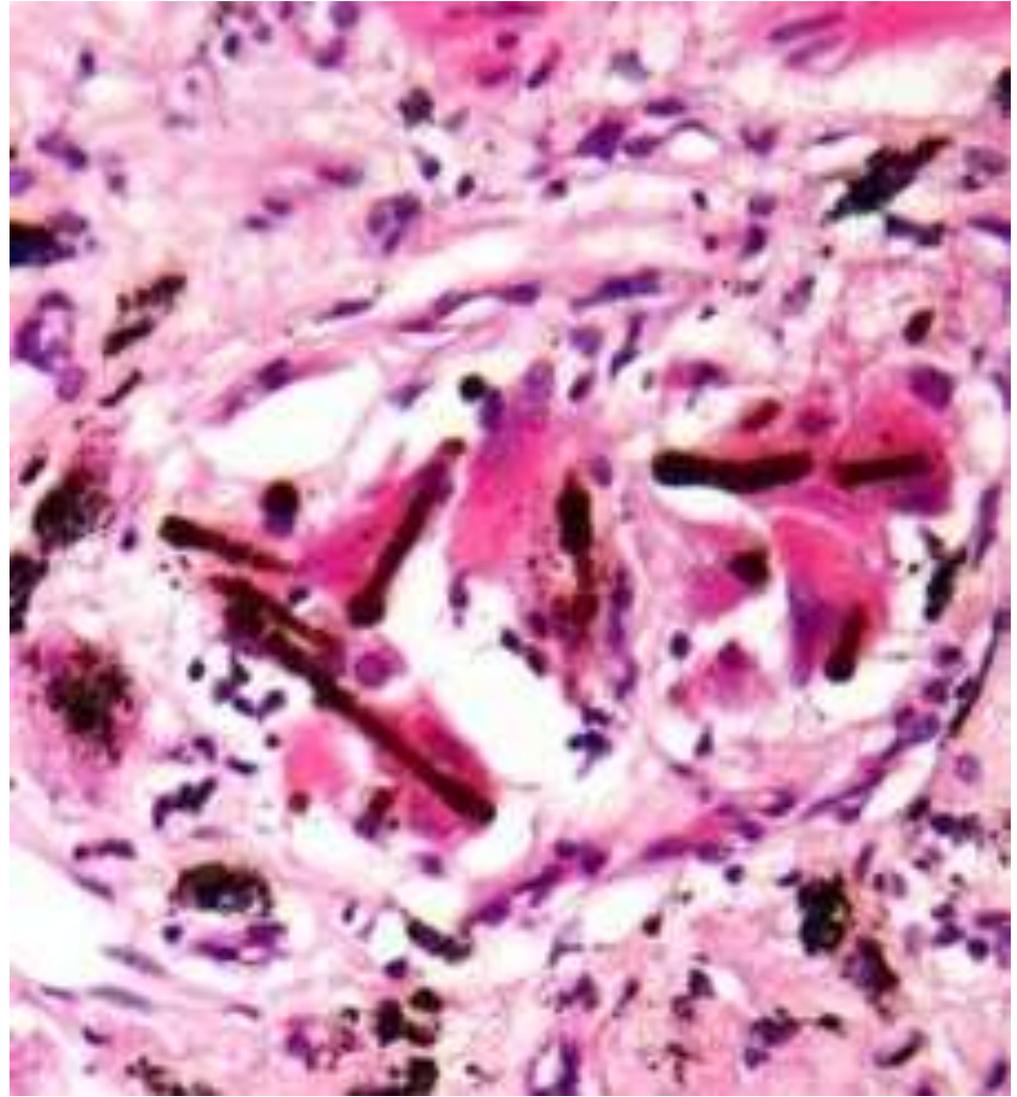
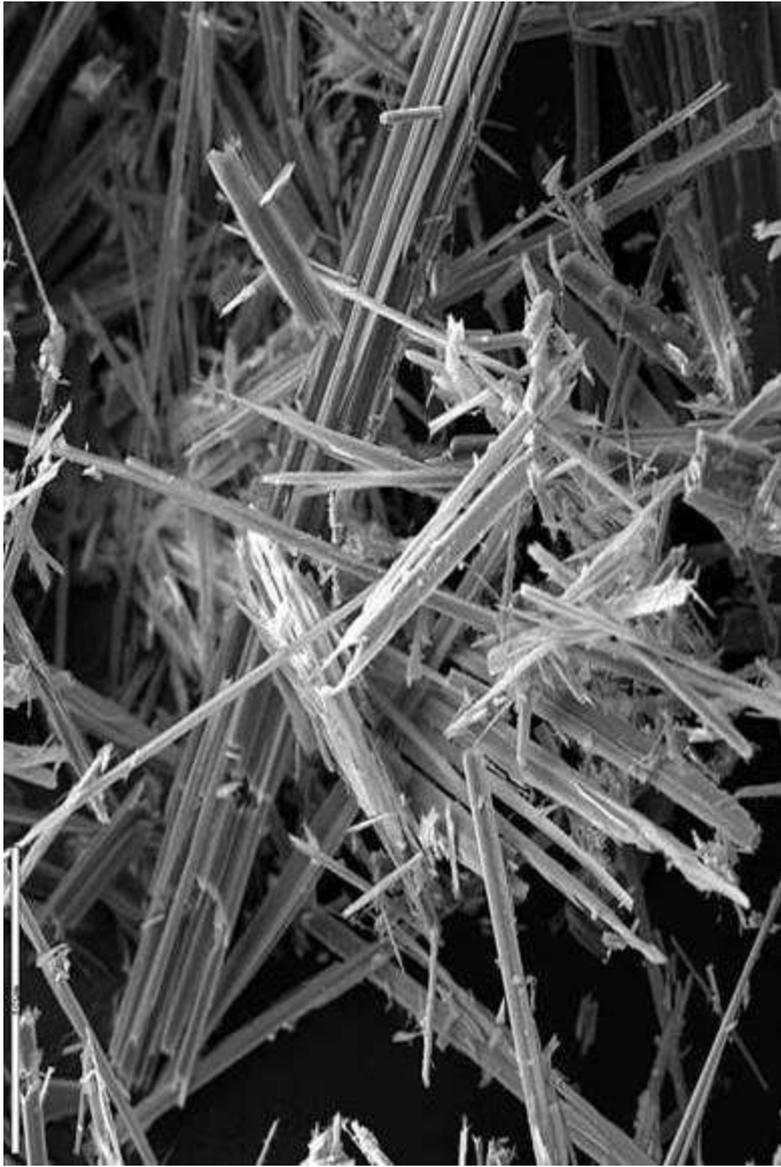
<sup>⊘</sup> The sources of the data on the incidence (most recent figures), predicted peak year, and predicted number of deaths in the next 40 years are as follows: United States, Roushdy-Hammady et al.<sup>2</sup>; Europe, Pelin et al.<sup>3</sup>; Japan, Sebastien et al.<sup>4</sup>; and Australia, Wagner et al.<sup>5</sup> The sources of the data on predicted cost are as follows: United States, Shah and Williams<sup>6</sup>; Europe, Lee et al.<sup>7</sup>; and Australia, Wagner et al.<sup>5</sup> Costs for Japan are unknown.

<sup>†</sup> The predicted number of deaths is estimated from data on annual incidence and predicted peak year.

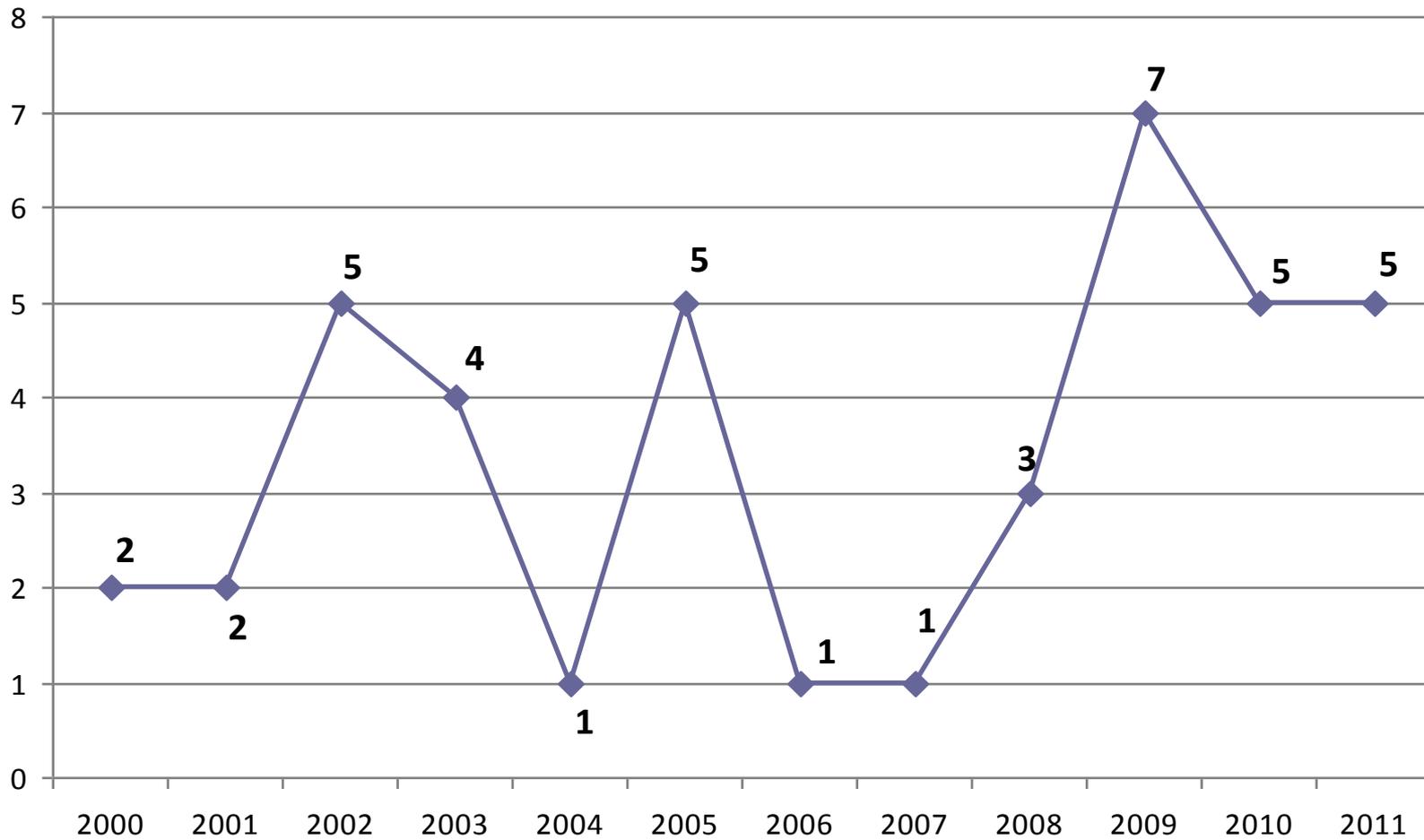
<sup>‡</sup> The costs shown are for compensation only; health care costs are excluded.

<sup>§</sup> The incidence, in number of cases per million population, is 33 in Great Britain, 30 in the Netherlands, 15 in Germany, 16 in France, and 19 in Italy (range in Europe, 15 to 33).

Robinson BW, Lake RA. Advances in malignant mesothelioma.  
N Engl J Med 2005;353:1591-1603



# Mesoteliomas Malignos Pleurales CHUAC

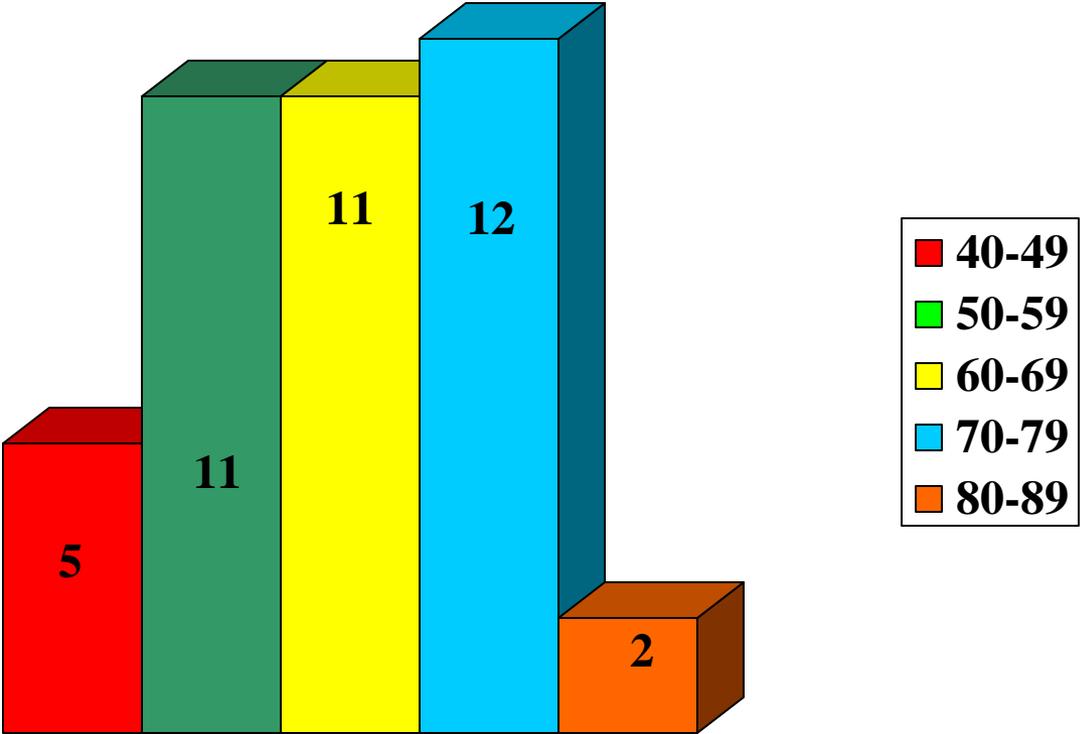


# Mesotelioma Maligno Difuso.

## Revision de los ultimos 11 años CHUAC

- N° de casos: 41 casos.
- 37 varones/4 mujeres (9:1)
- Edad: 43-82. Edad media 64.35 años.
  - EM mujeres: 62.07
  - EM Varones: 62.5
- Historia exposición asbestos: 14 casos.
- 13 fumadores o exfumadores.
- 1 paciente Tx. Hepatico, 1 Ca pene, 1 GIST gastrico
- Clínica de Disnea, Dolor torácico y derrame pleural.  
1 caso neumotórax
- 21 lado dcho/20 lado izq.

# MESOTELIOMA MALIGNOS. EDADES



# Mesotelioma malignos.

## Tipos histologicos

- Epitelioide.....24 casos.
- Bifásicos.....9 casos.
- Sarcomatoide (Desm.).....8 casos.



**Monasterio de Voronet**

# MESOTELIOMA MALIGNO PLEURAL

## Problemas que plantea al Patólogo:

- A.- DIFERENCIAR HIPERPLASIAS BENIGNAS REACTIVAS - MESOTELIOMA.
- B.- DIFERENCIAR MESOTELIOMA EPITELIOIDE- METASTASIS CARCINOMA.
- C.- DIFERENCIAR MESOTELIOMA SARCOMATOIDE-SARCOMAS

# **Diferencial Diagnosis of Benig and Malignant Mesothelial Proliferations on pleural biopsies**

Cagle PL and Churg A.

Arch. Pathol Lab Med. 2005;129:1421-1427

**Inmunohistoq.** Tiene escaso valor

Puede usarse CKs para confirmar invasion.

P53 y EMA pueden ayudar, pero no son  
especificos ni sensibles.

**INVASION ES EL CRITERIO DE MAS VALOR**

**Oncofetal Protein IMP3, a new Diagnostic Biomarker to distinguish M.M. from  
Reactive Mesothelial Proliferation.**

Shi M., Fraire A.E., Chu P, Cornejo K, Woda B.A., Dresser K., Rock K.L. and Jiang Zh.

Am J Surg Pathol 2011.

# **The Immunohistochemical Diagnosis of Mesothelioma A Comparative Study of Epithelioid Mesothelioma and Lung Adenocarcinoma**

Nelson G.Ordoñez

The American Journal of Surgical Pathology 2003,27(8):  
1031-1051

Estudian 60 mesoteliomas epitelioides y 50 AdenoCa. De Pulmon empleando una batería de 19 anticuerpos.

**CONCLUSIONES Y RECOMENDACIONES:  
POSITIVOS :CALRETININA, CK5/6 (O WT1)  
NEGATIVOS:CEA Y MOC-31(B72.3 O Ver-EP4)**

**Sarcomatoid mesothelioma and its histological mimics:  
a comparative immunohistochemical study.**

**Lucas DR y cols**

**Histopathology 2003,42, 270-279**

**CONCLUSIONES: La IMHQ juega un papel limitado en diag.  
Diferencial de m. sarcomatoide vs sarcomas fusocelulares vs Ca  
Sarcomatoide.**

**Datos clinico-radiologicos del tumor ayudan para un diagnostico.**

# Guidelines for Pathologic Diagnosis of Malignant Mesothelioma.

A consensus statement from the International Mesothelioma Interest Group.

Husain A.N, Colby T.V., Ordoñez N.G- Krausz Th,  
Borczuk A; Cagle P.T., Chirieac L.R., Churg A., Galateau-Salle F., Gibbs A.R. Gown A.M.  
Hammar S.P. Litzky L.A., Roggli V.L. Travis W.D., Wick R.M.

**Arch. Pathol lab. Med. 2009; 1317-31**

# RECOMENDACIONES GENERALES

- El diagnóstico de MM siempre debe basarse en el resultado de:
  - Biopsia adecuada, (VTC)
  - Clínica apropiada, hallazgos radiológicos y quirúrgicos adecuados
- Historia de exposición a Asbestos NO debe tenerse en consideración.

## Diagnóstico diferencial:

- 1- Proliferaciones mesoteliales benignas/malignas
  - a: Hiperplasia mesotelial reactiva/MM Epiteliode.
  - b: Pleuritis fibrosa/ MM Sarcomatoide-Desmoplásico
- 2- MM Epiteliode/ Carcinomas metastásicos.
- 3- MM Sarcomatoide/ Sarcomas y tumores fusocelulares.
- 4- MM Bifásico/ S. Sinovial

## CONCLUSIONES

- **Diagnóstico debe hacerse con criterios Histológicos e IMHQ.**
- **Realizar Paneles de anticuerpos positivos MM y Negativos adecuados al caso**
- **La Citología, M. Electronica y Biología Molecular son de escasa ayuda.**

## **1. A: HIPERPLASIA MESOTELIAL REACTIVA/ M.M. EPITELIOIDE**

ASPECTOS HISTOLOGICOS CLASICOS (atipia, mitosis...) No utiles.

DETERMINANTE: DEMOSTRACIÓN DE INVASION estromal, grasa, musculo.  
ayudan PANCITOQUERATINAS.

INMUNOHISTOQUIMICA: EMA, p53 positivas frecuentemente en MM.

Desmina generalmente negativa en M.M.

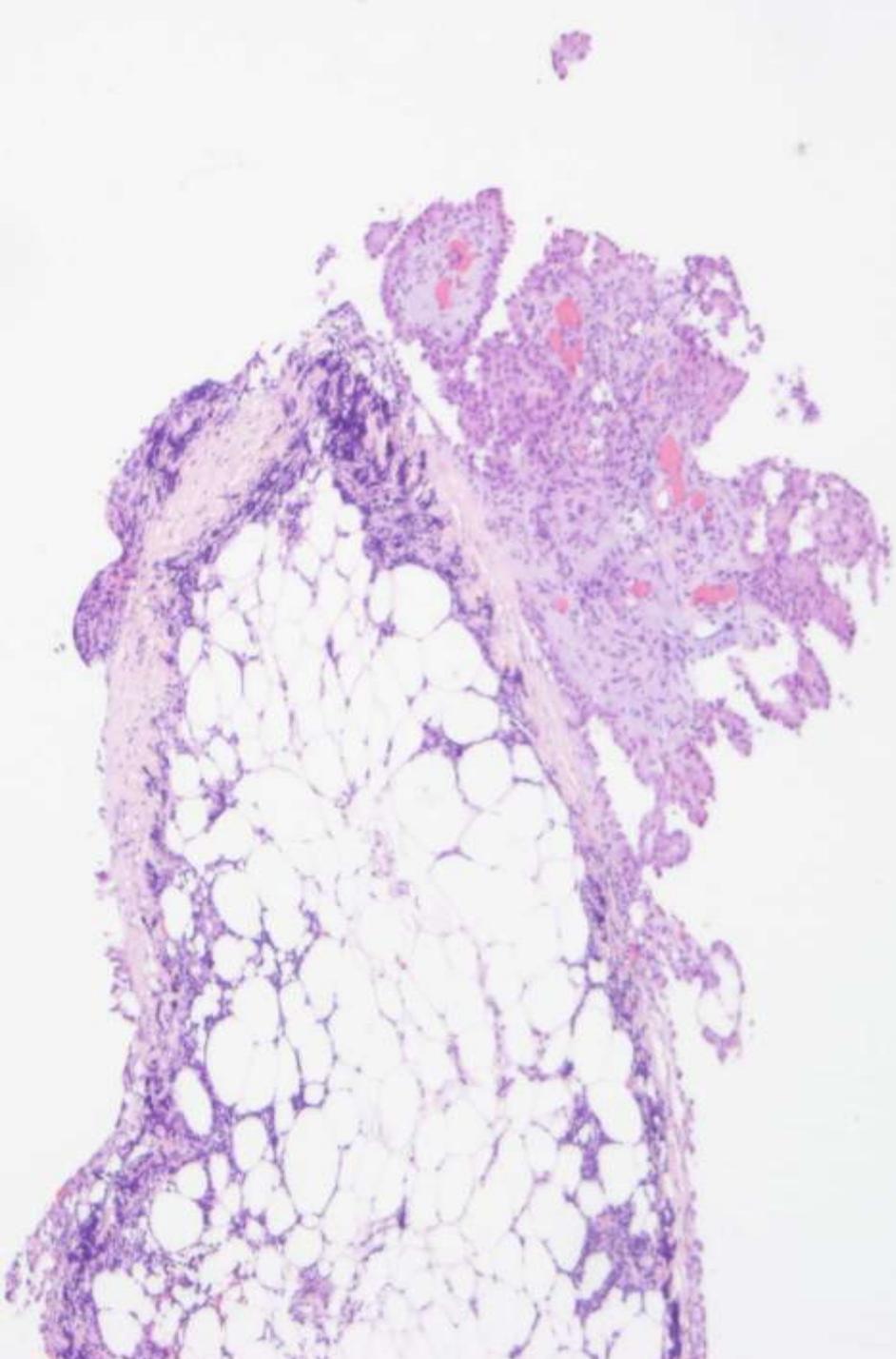
GLUT-1: Si positivo diagn. M.M.

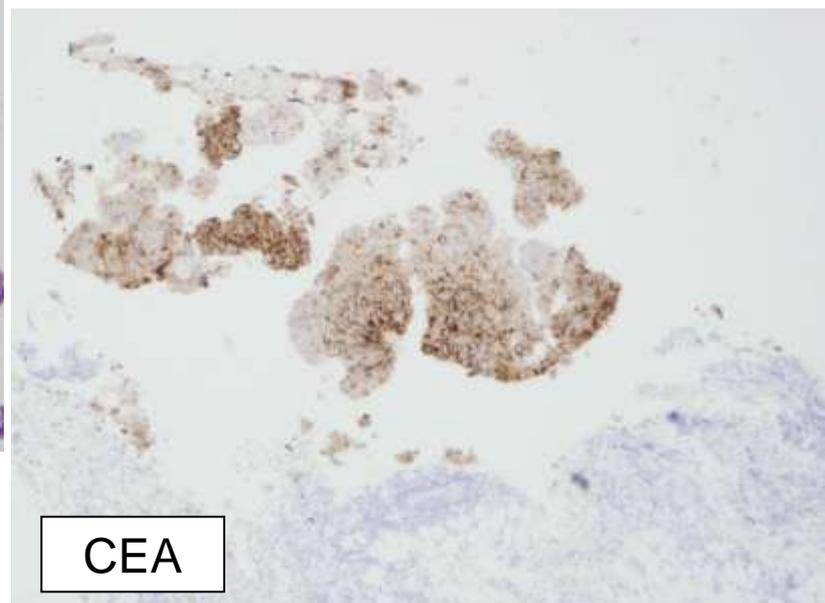
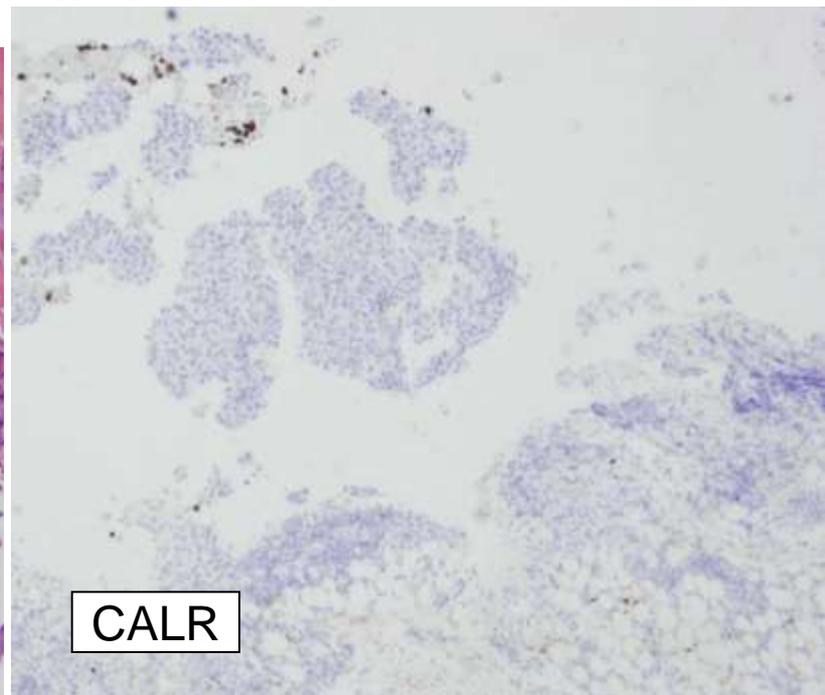
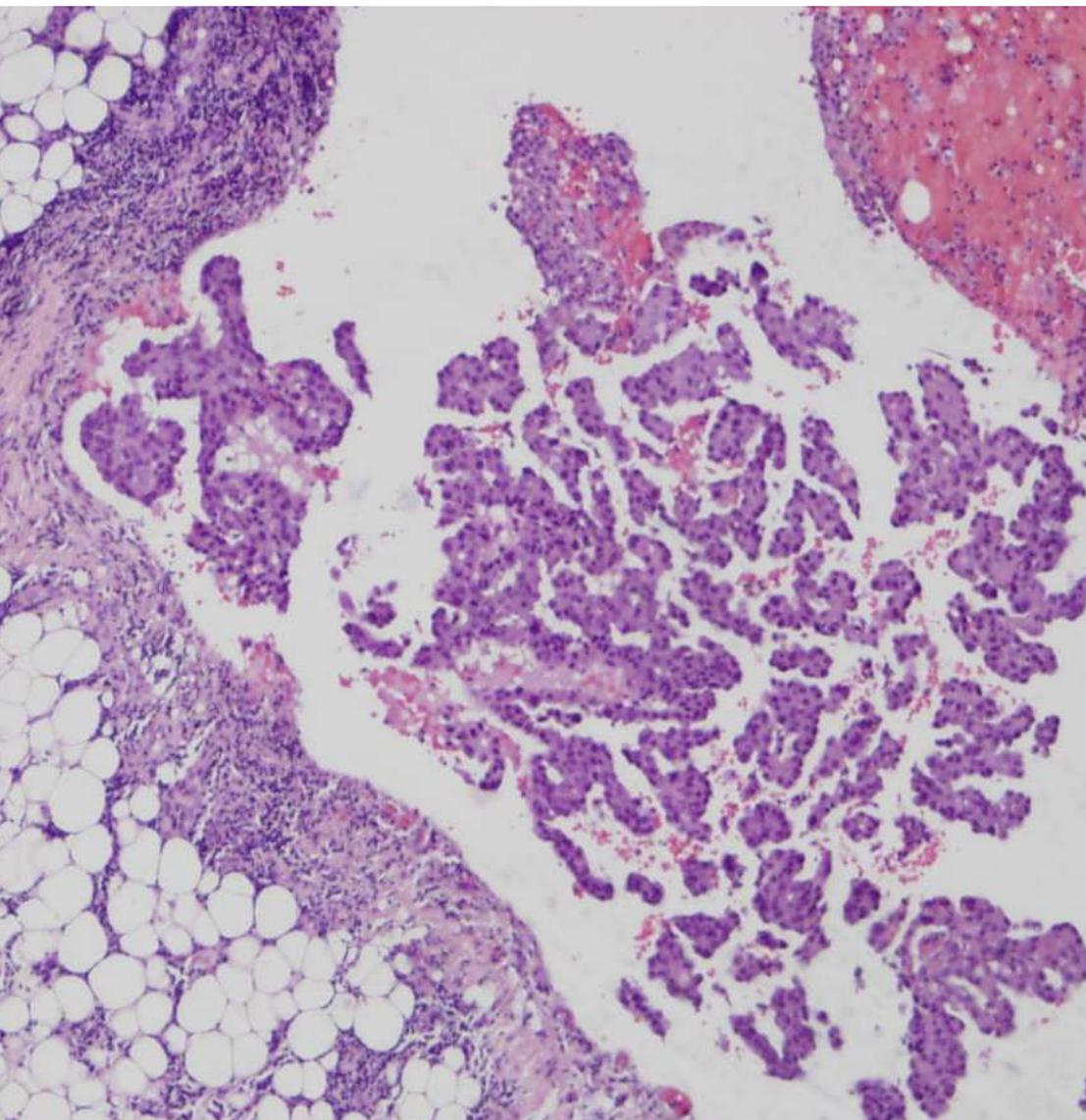
## **- B: PLEURITIS FIBROSA/ M.M. DESMOPLASICO**

DEMOSTRACION DE INVASION → PANCITOQUERATINAS.

ZONAS DE NECROSIS ACELULAR, AREAS FRANCAMENTE SARCOMATOSAS,  
PRESENCIA DE METASTASIS → **MESOTELIOMA.**

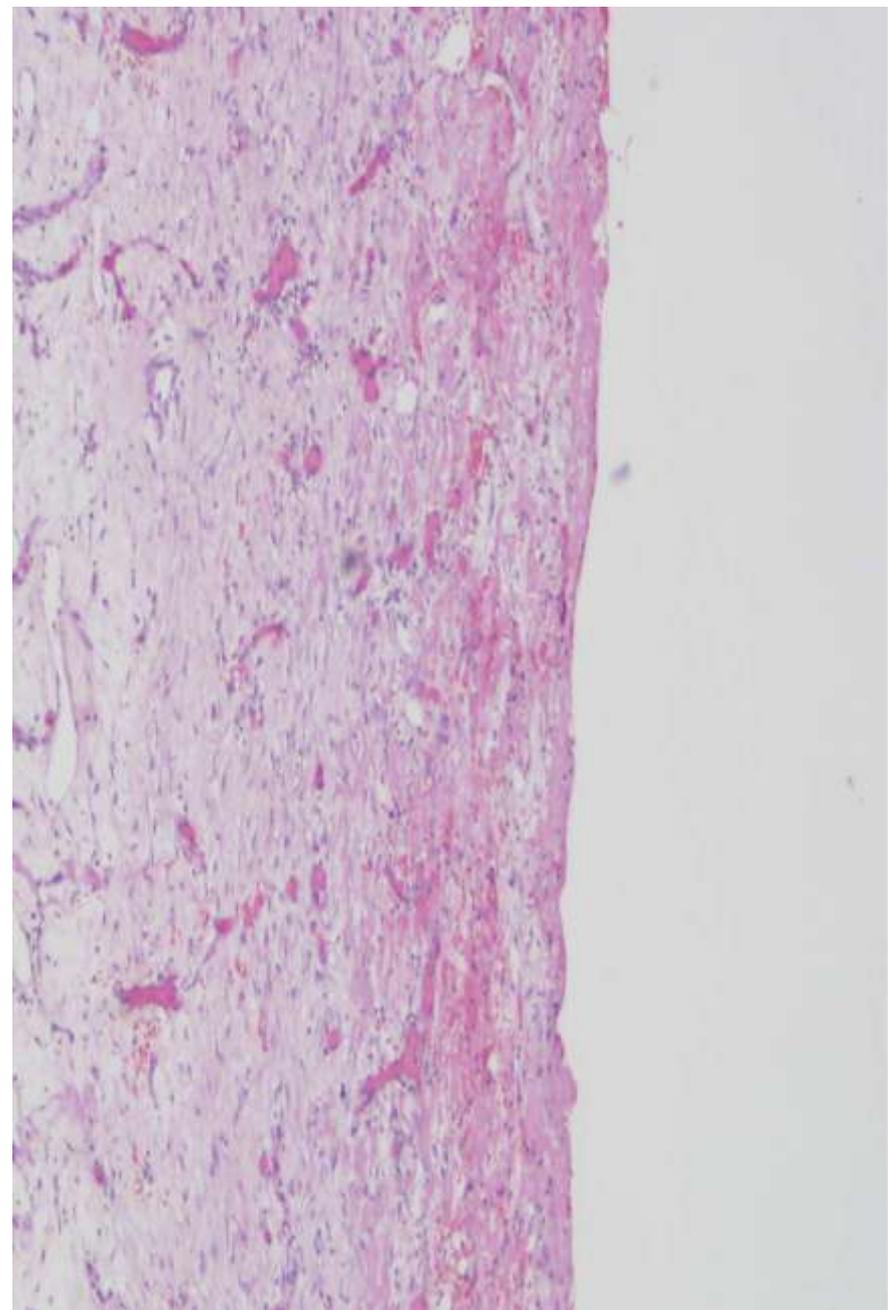
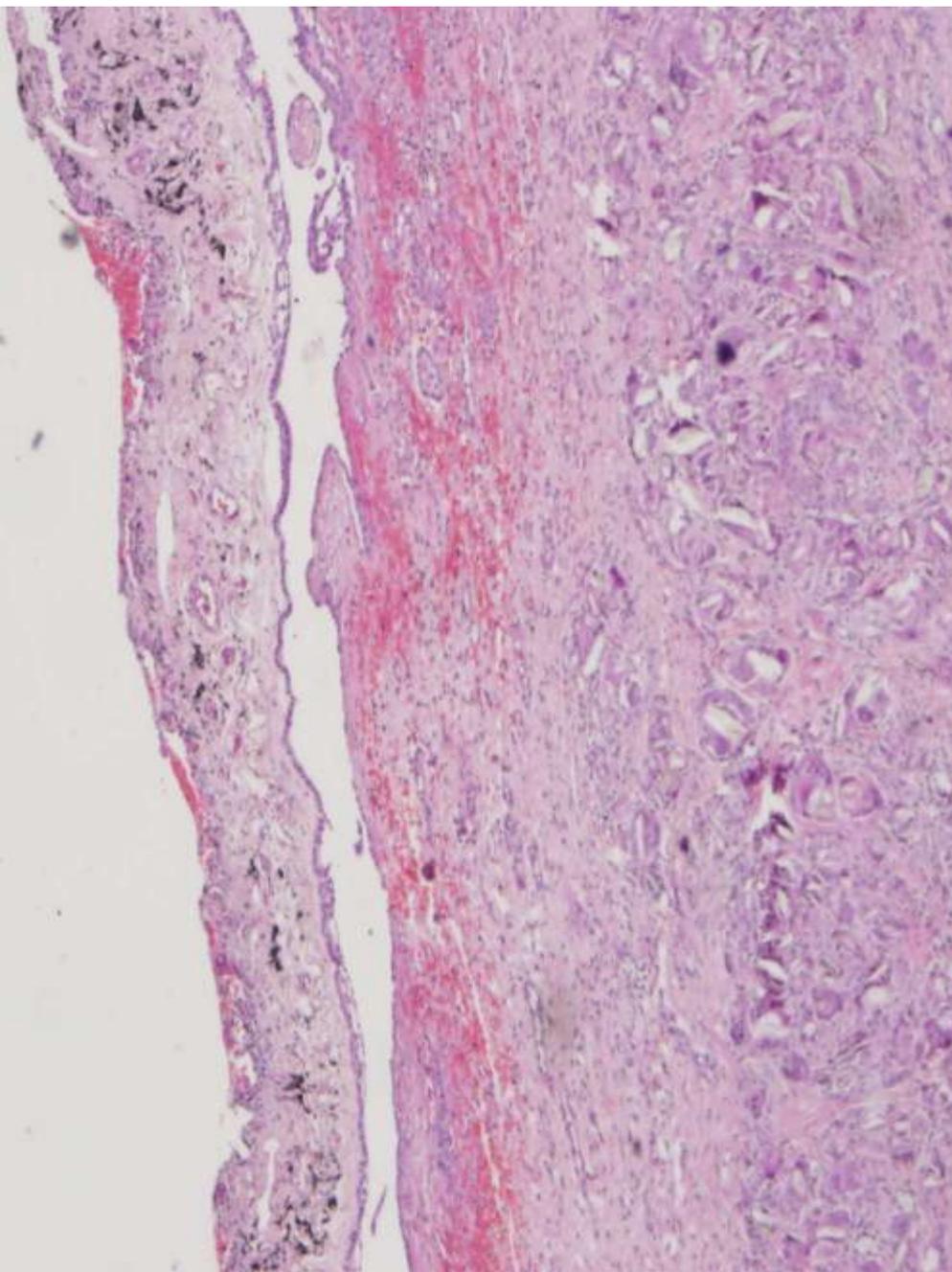
UNIFORMIDAD DEL CRECIMIENTO, MADURACION EN PROFUNDIDAD,  
VASOS FINOS PERPENDICULARES A SUPERFICIE → **PLEURITIS FIBROSA**

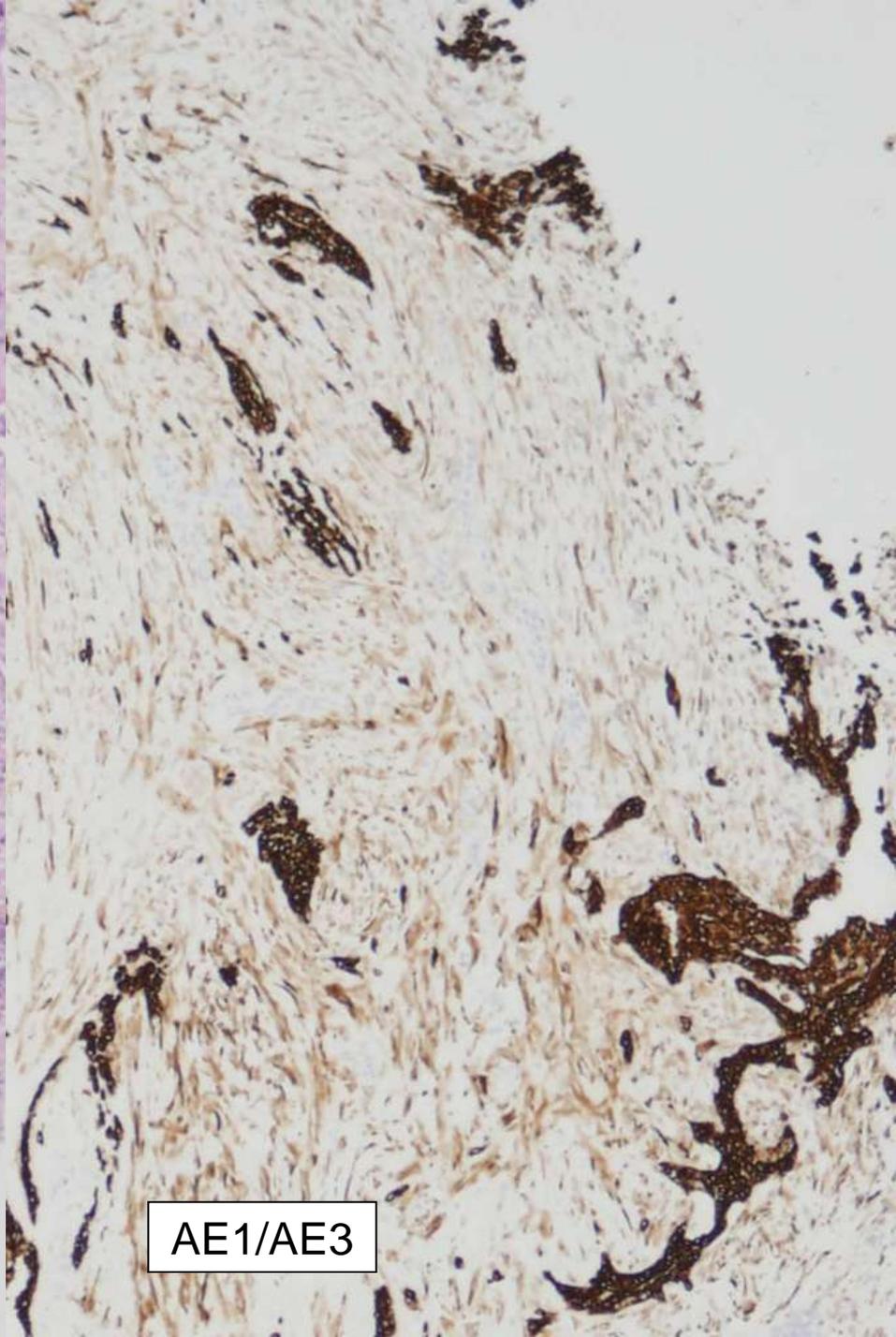
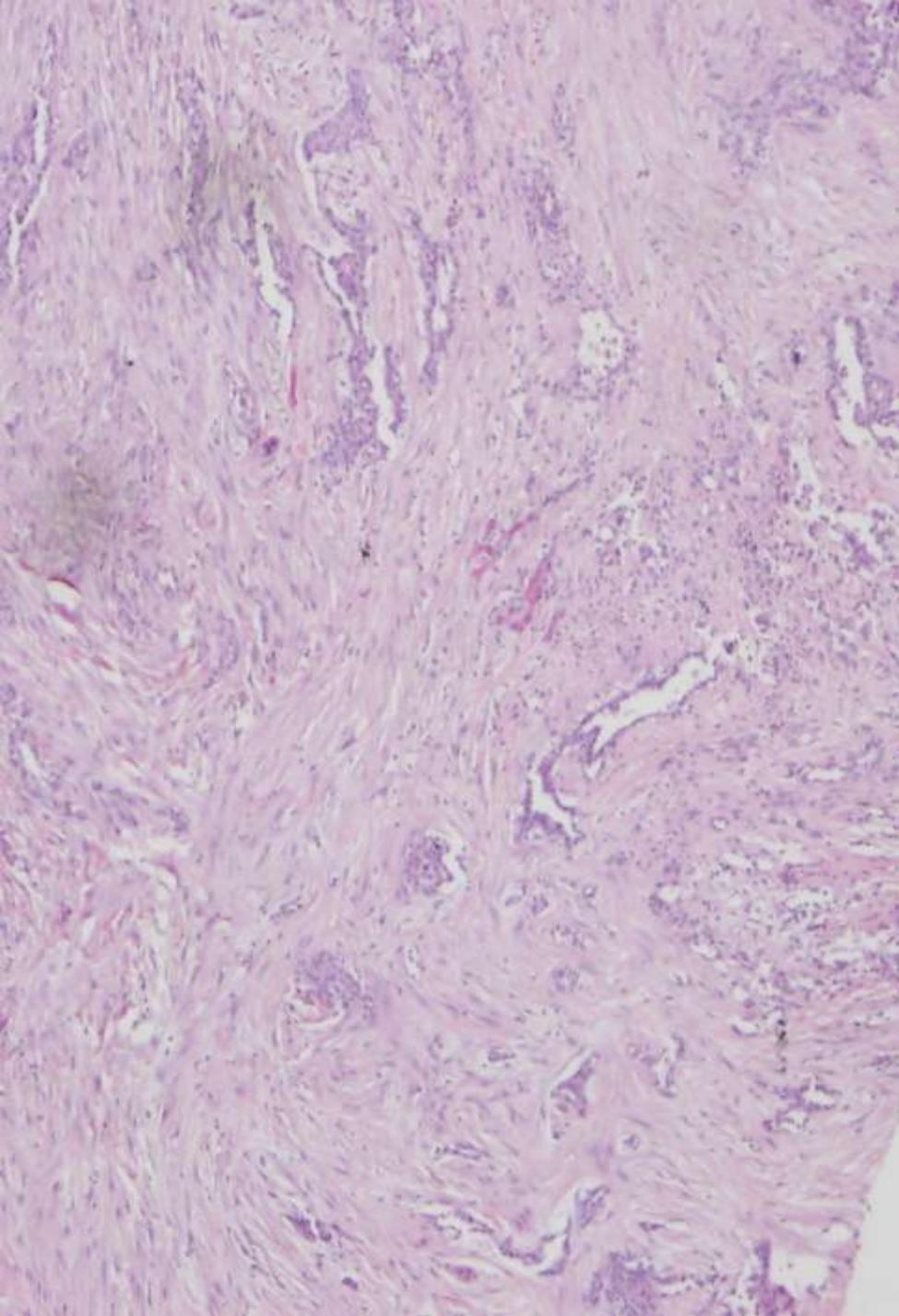




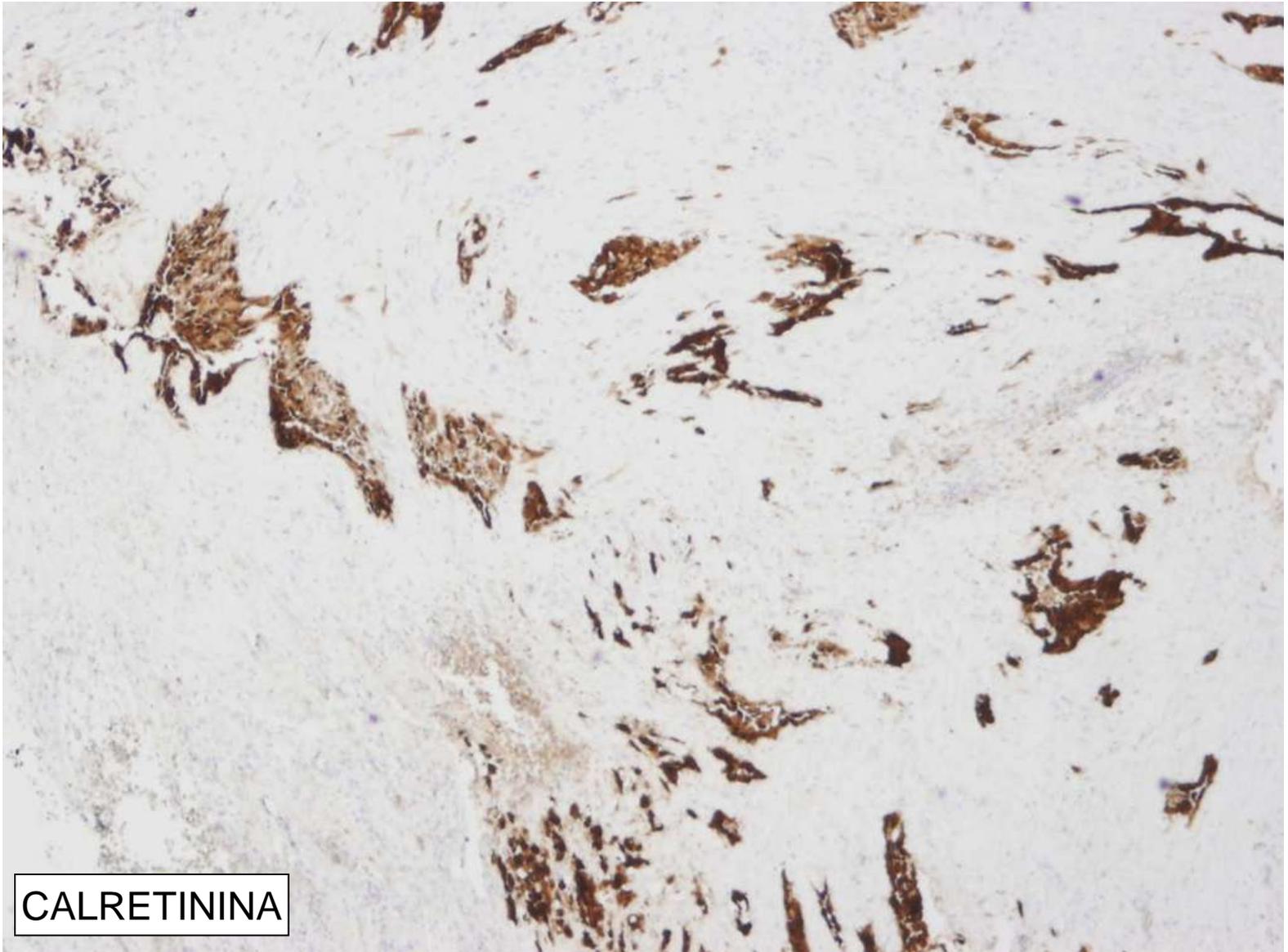


**Monast Sucevita**  
**El arbol de Jesé**





AE1/AE3

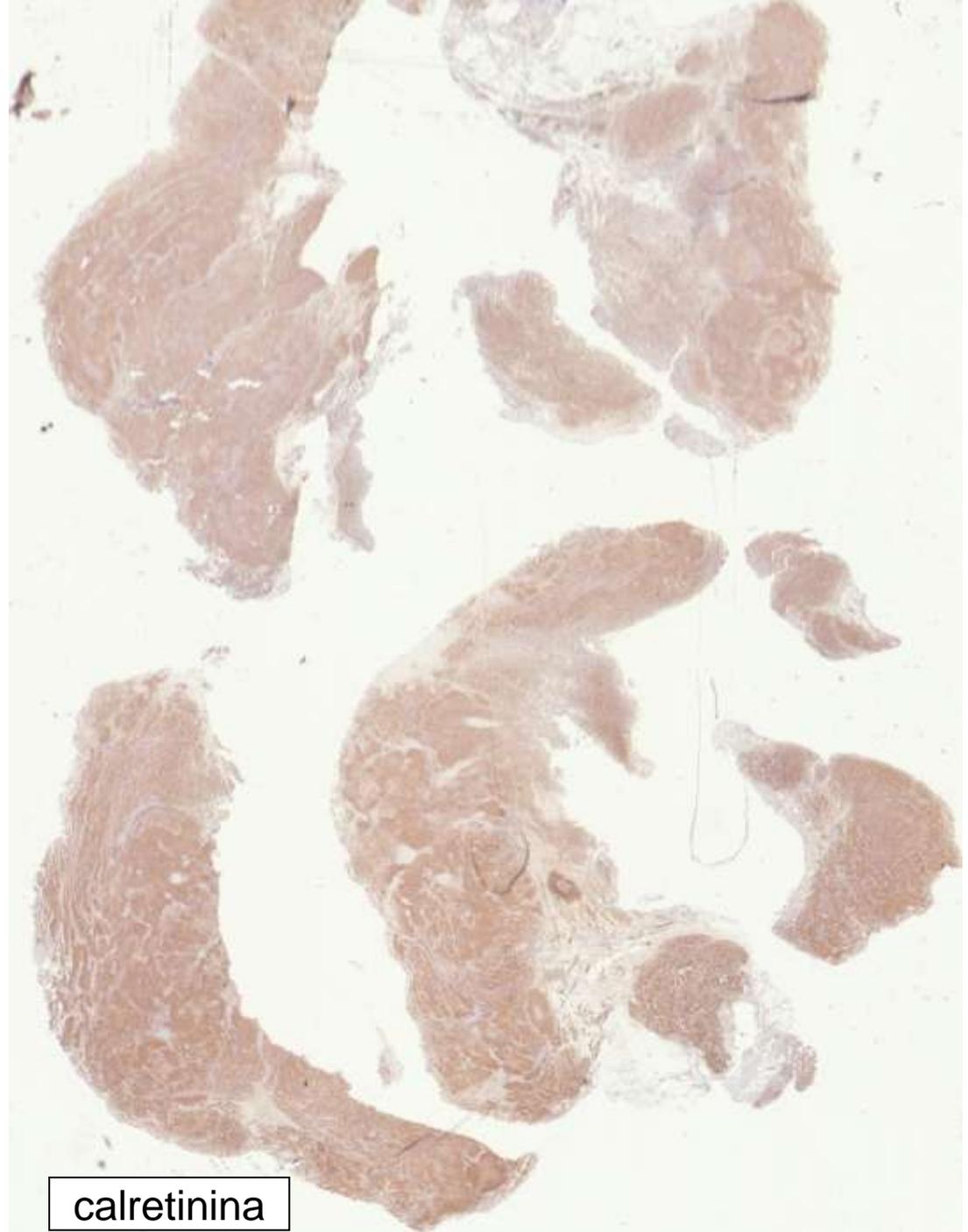


CALRETININA

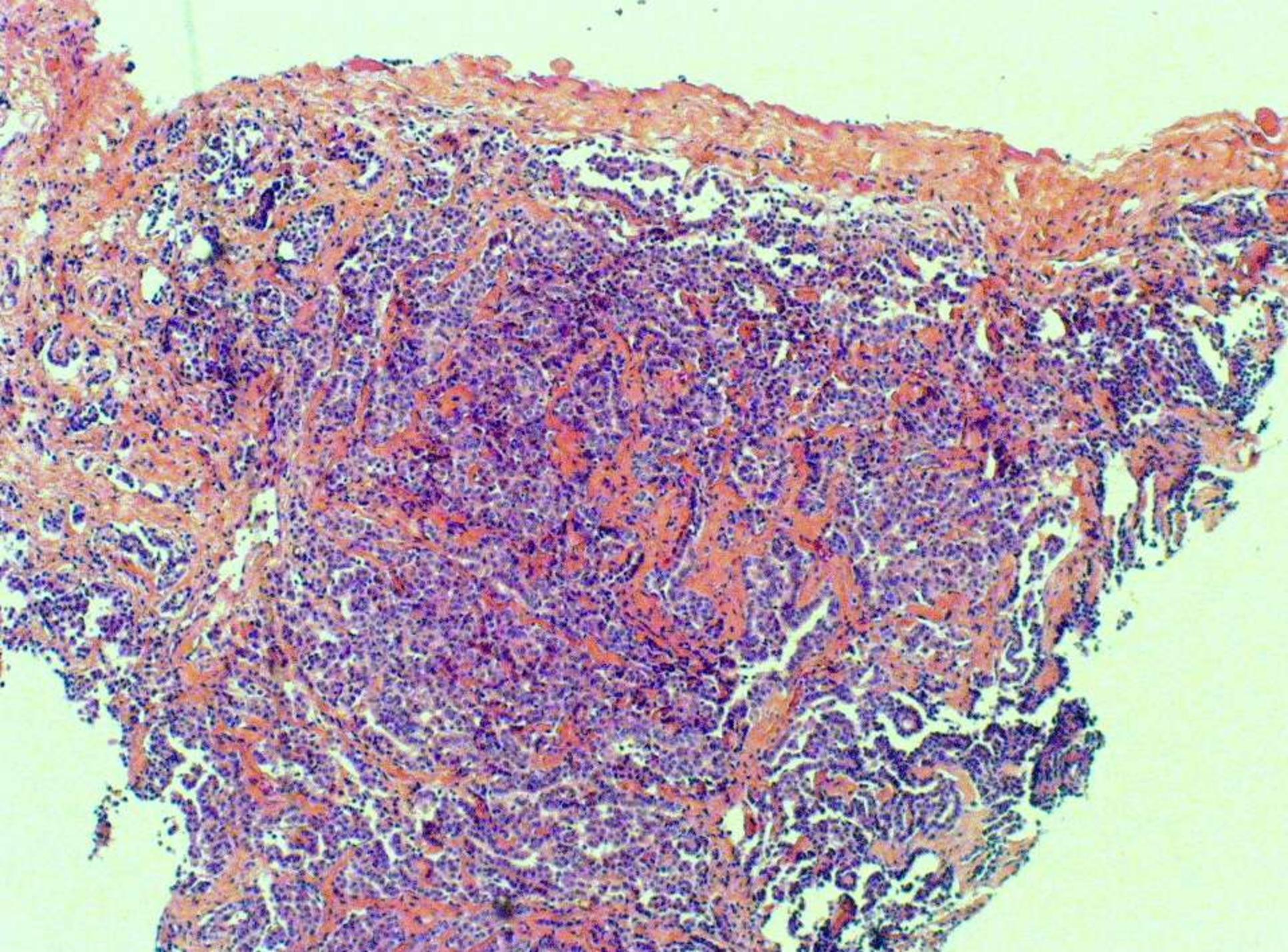
## **2.- MESOTELIOMA EPITELIOIDE /ADENOCa. METASTATICO**

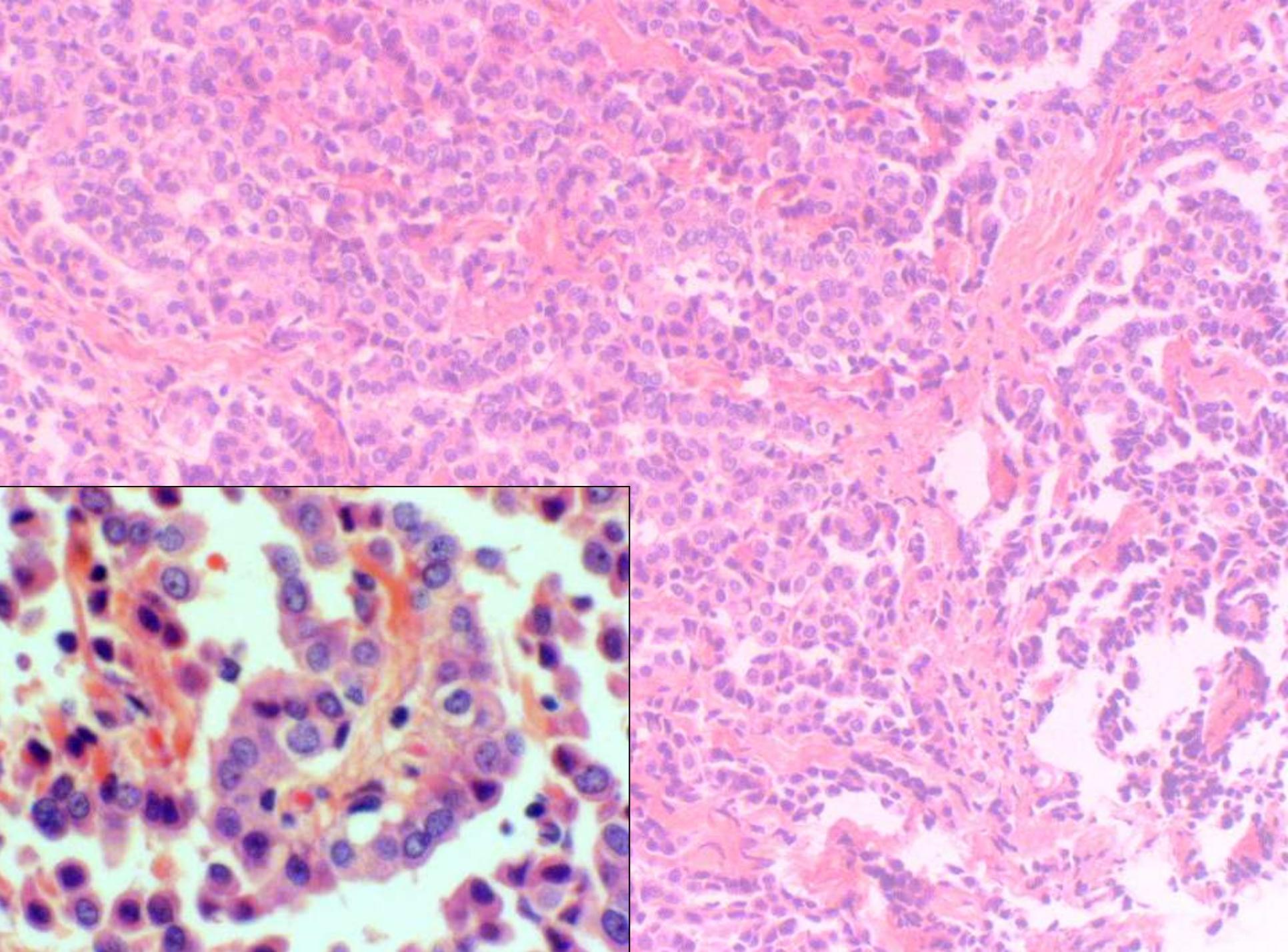
- NO SE HA IDENTIFICADO UN MARCADOR ESPECIFICO PARA MESOTELIOMAS.
- EL DIAGNOSTICO I.H.Q. SE BASA EN EL USO DE “BATERIAS” DE MARCADORES.
- LAS BATERIAS DEBEN ESTAR COMPUESTAS POR AL MENOS 2 MARCADORES POSITIVOS Y 2 NEGATIVOS (SENSIBILIDAD>80%)
  - POSITIVOS: CALRETININA, C.K 5/6, WT-1, PODOPLANIN (D2-40)
  - NEGATIVOS: CEA, MOC-31, TTF-1, Ber-EP4, BG8.
- SI LOS RESULTADOS SON CONCORDANTES CON CLINICA Y Rx EL DIAGNOSTICO QUEDA ESTABLECIDO. SI ES DISCORDANTE SE AMPLIA EL PANEL DE ANTICUERPOS, SEGÚN DIAG. DIFERENCIAL

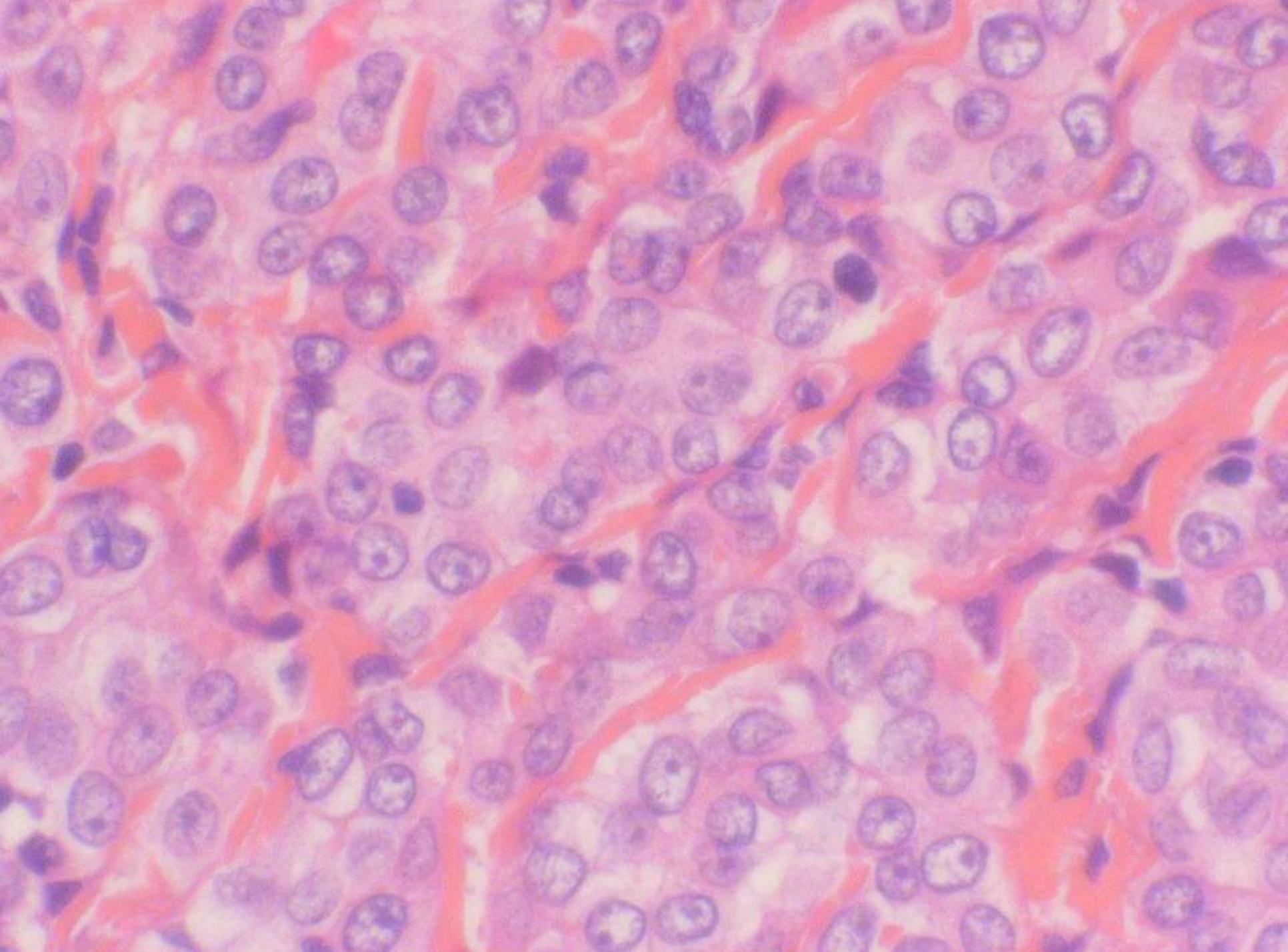
B02-7347  
Varon 58 años.  
Exposicion a amianto  
Engrosamiento pleural

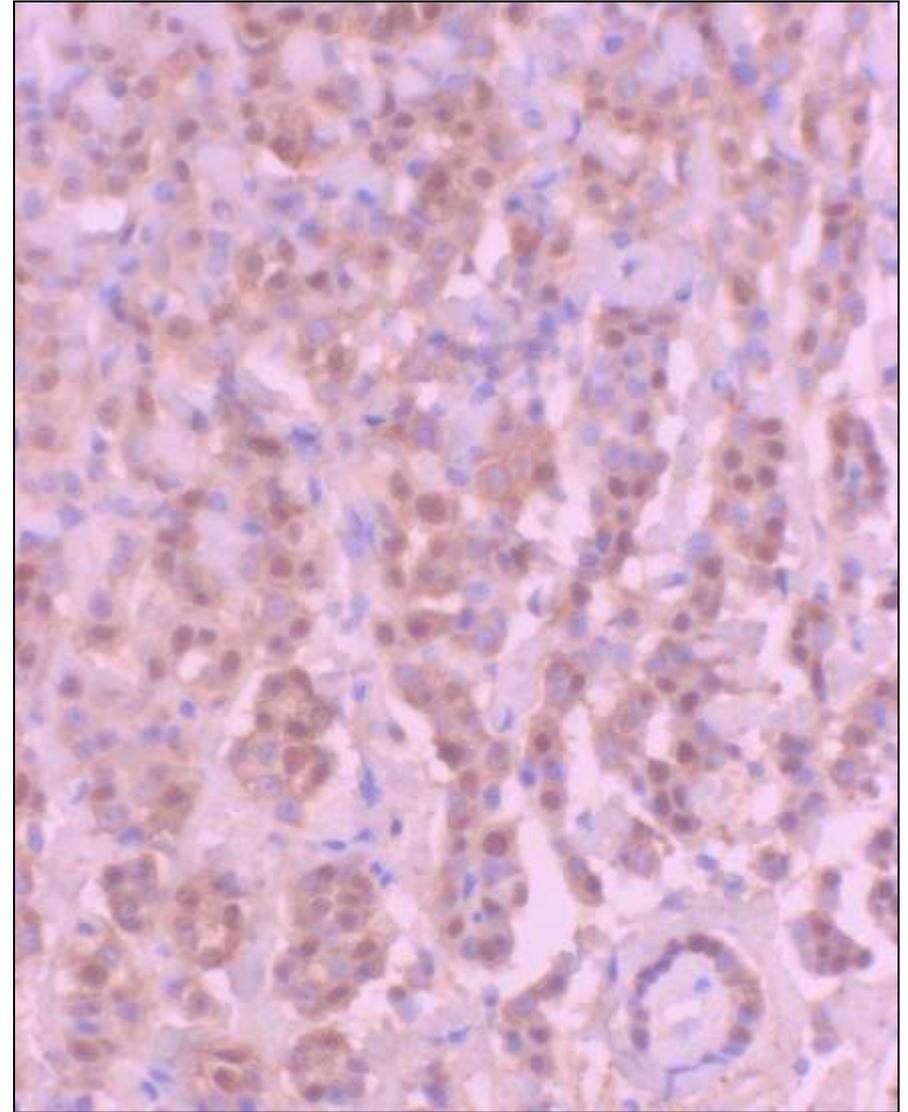
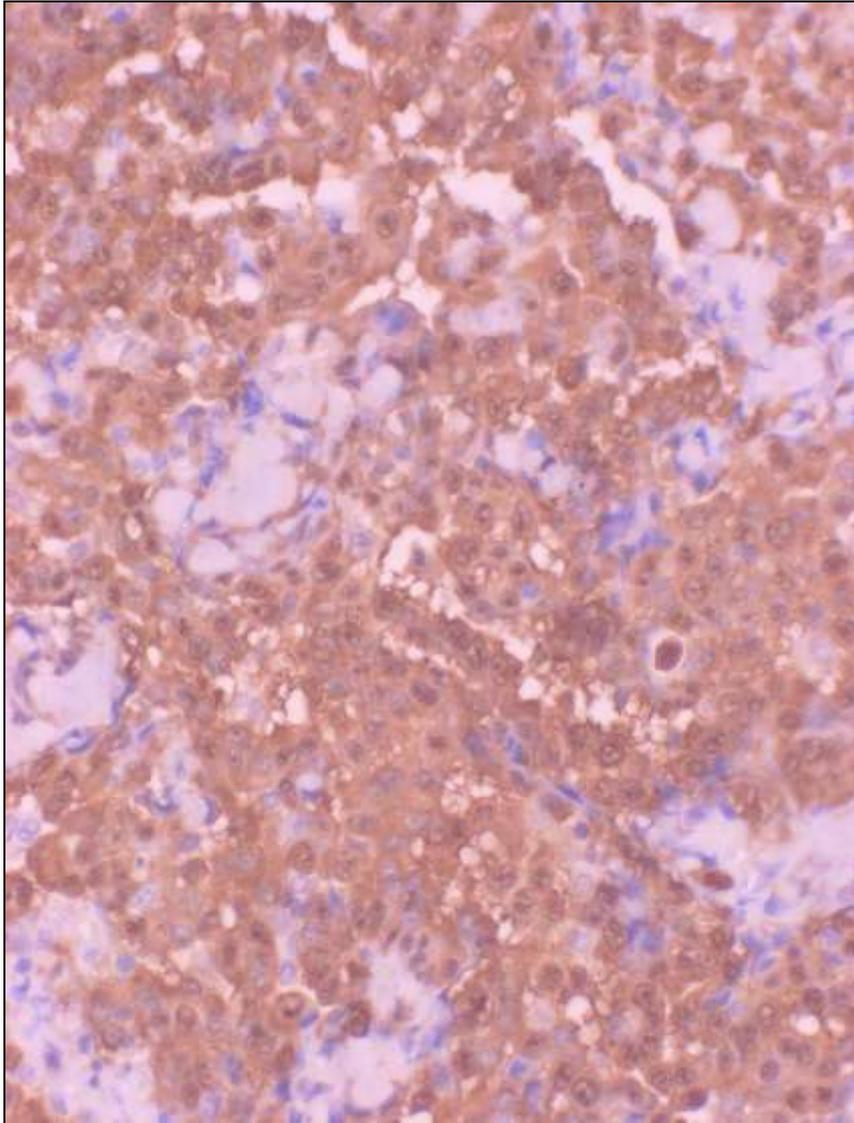


calretinina

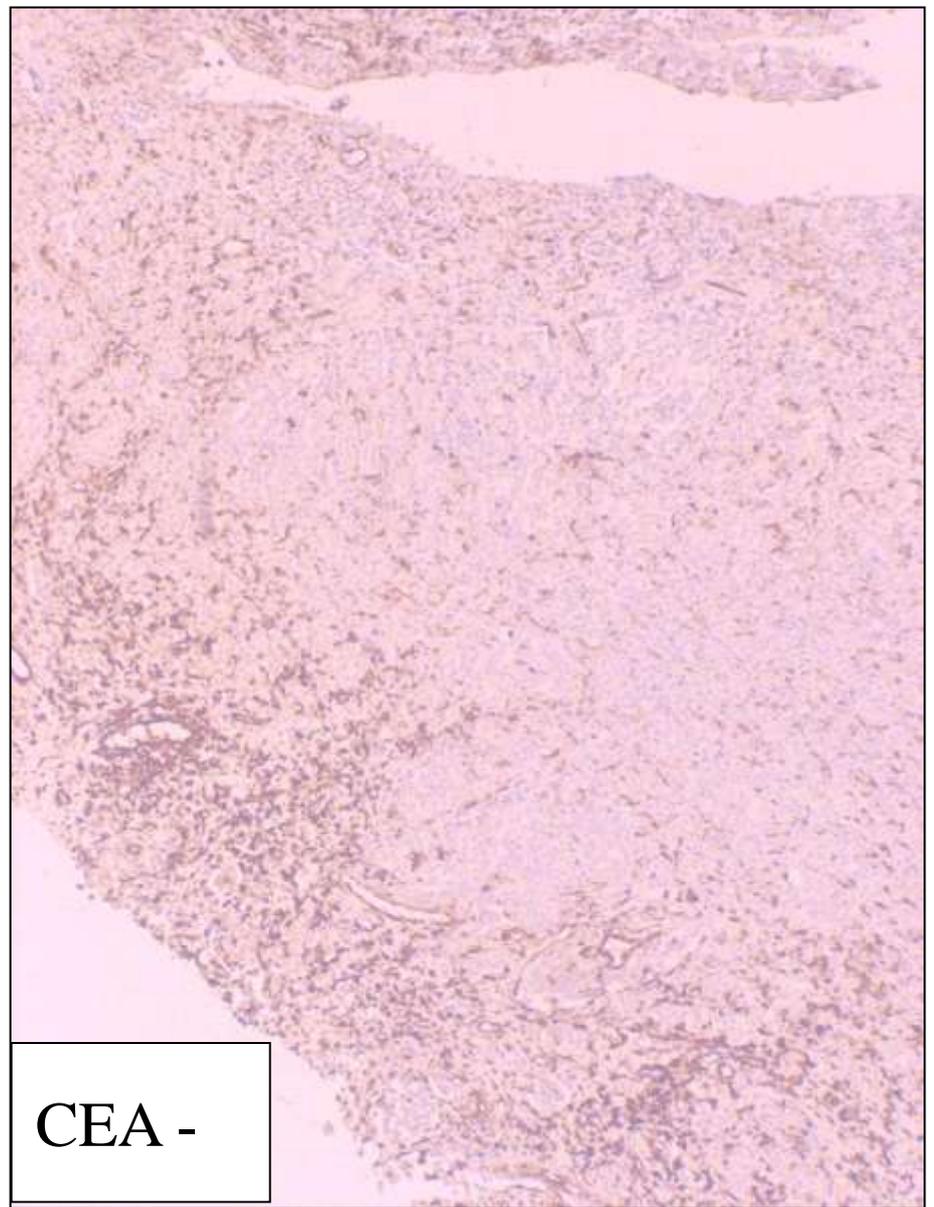
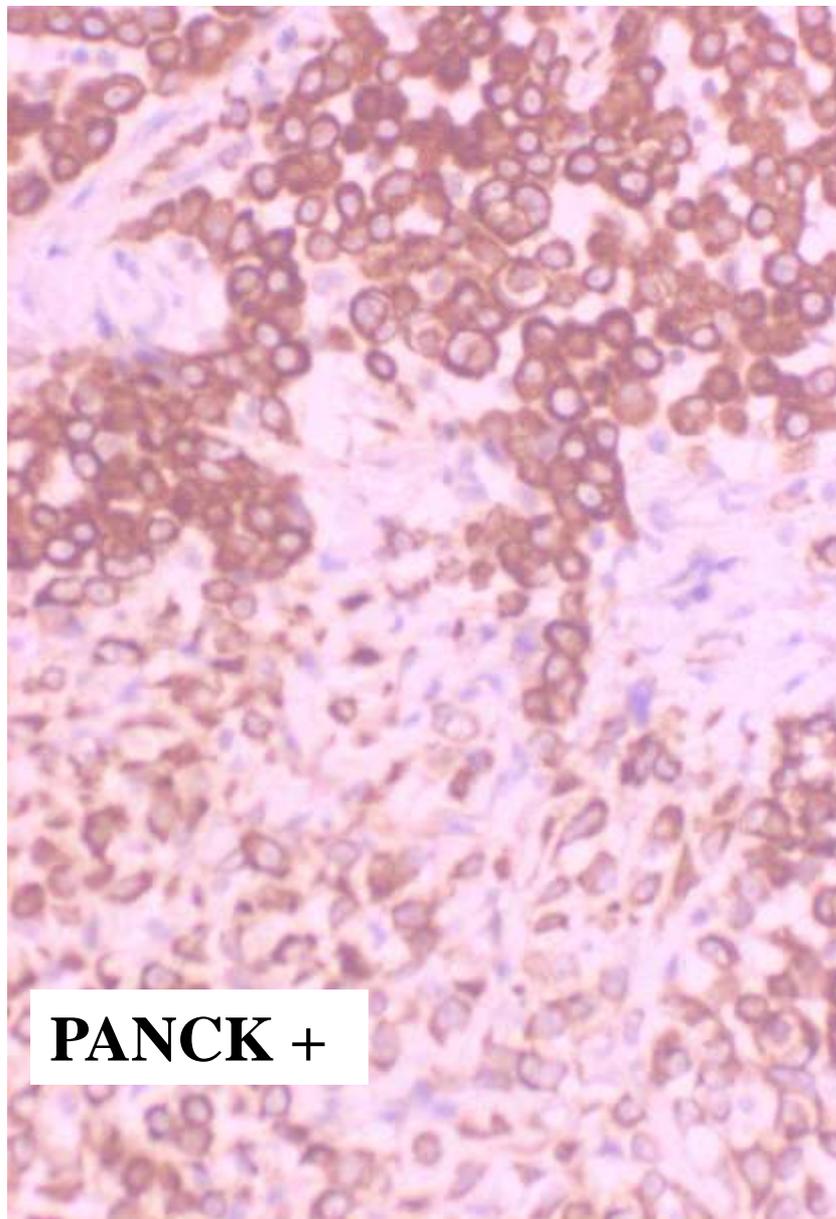




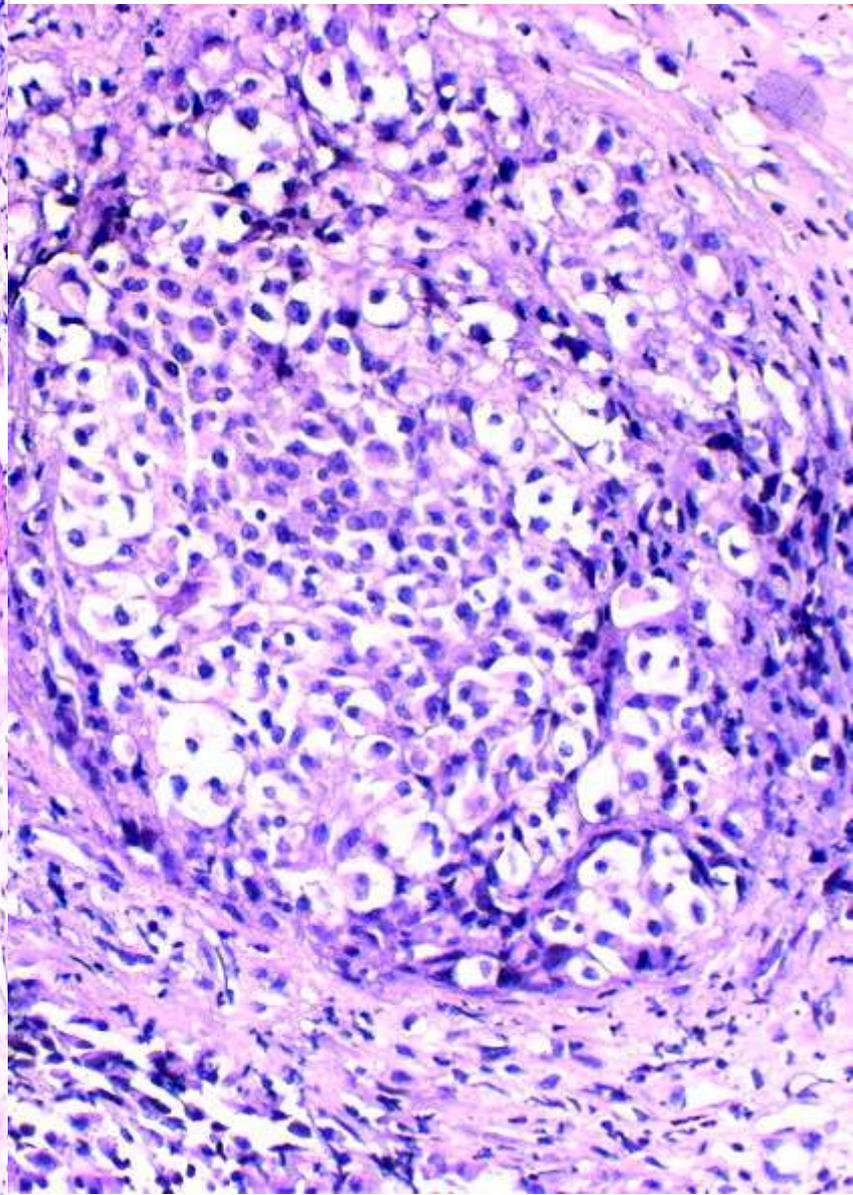
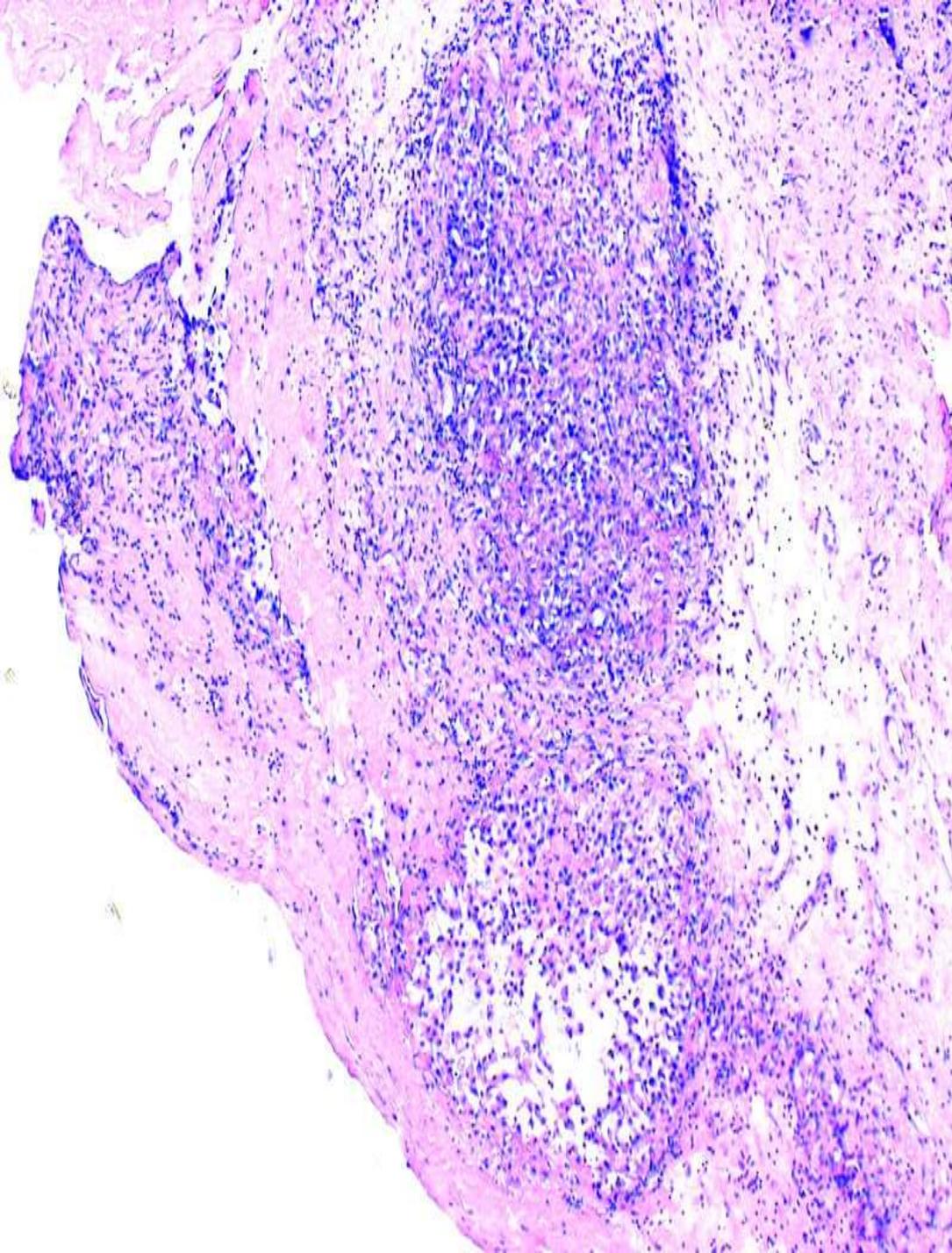




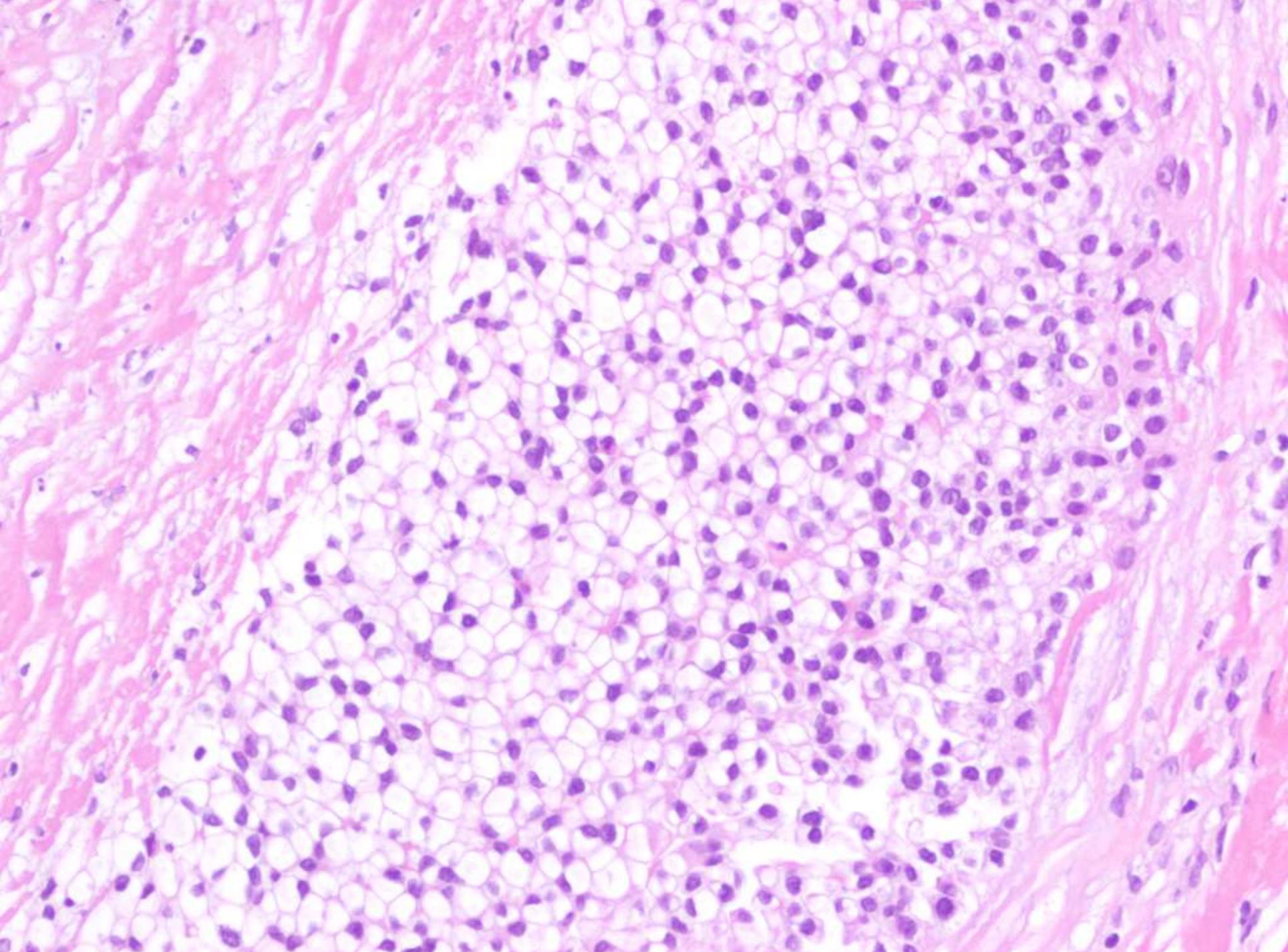
**CALRETININA**



TTF-1 -, CD-15 -, CK-5/6 +, WT-1 + MIB-1:+35%



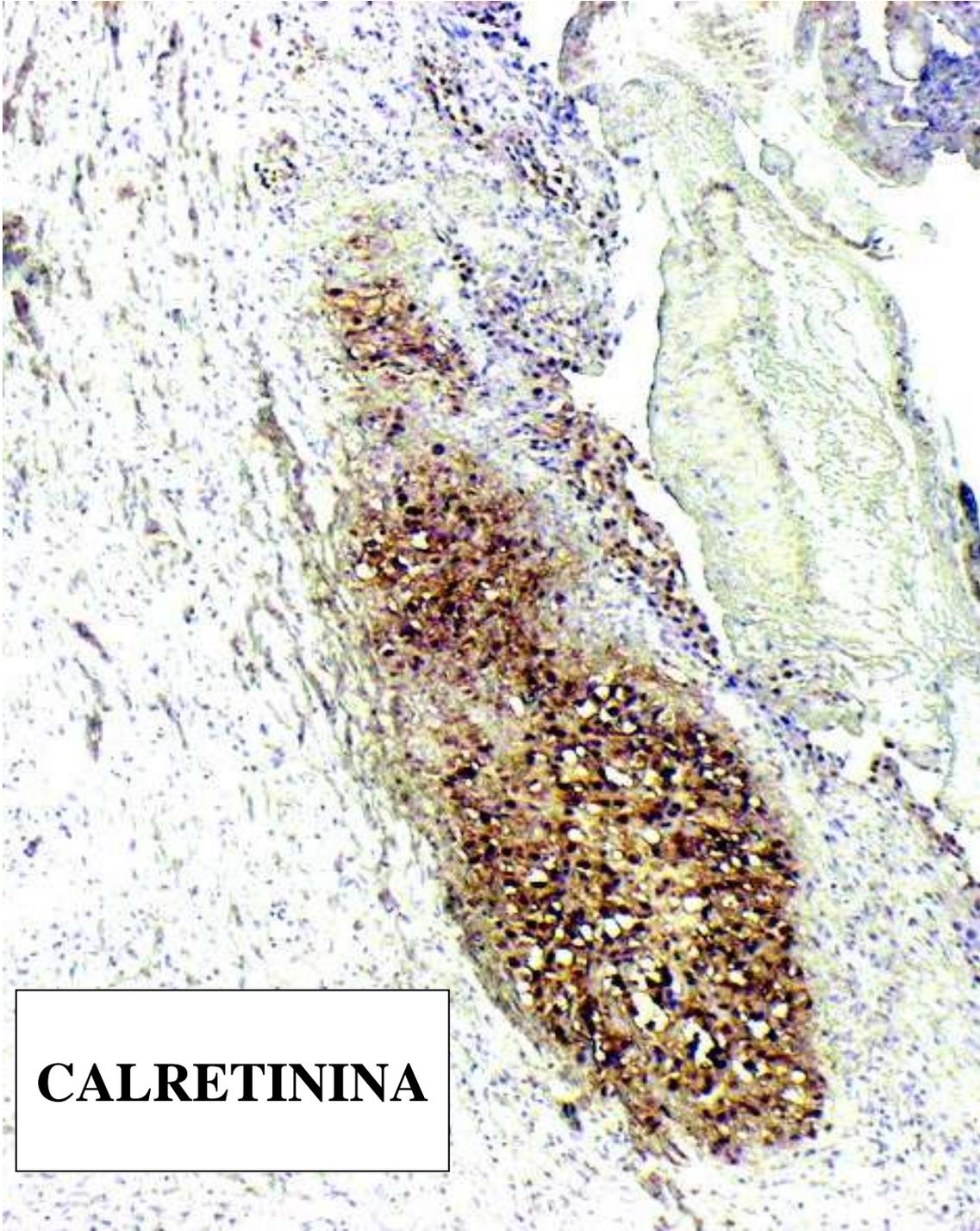
**Varon 61<sup>a</sup>.exposic asbestos  
Derrame pleural dcho.**



Mesothelioma with clear cell  
Features: an ultrastructural  
And immunohistochemical  
Study of 20 cases.

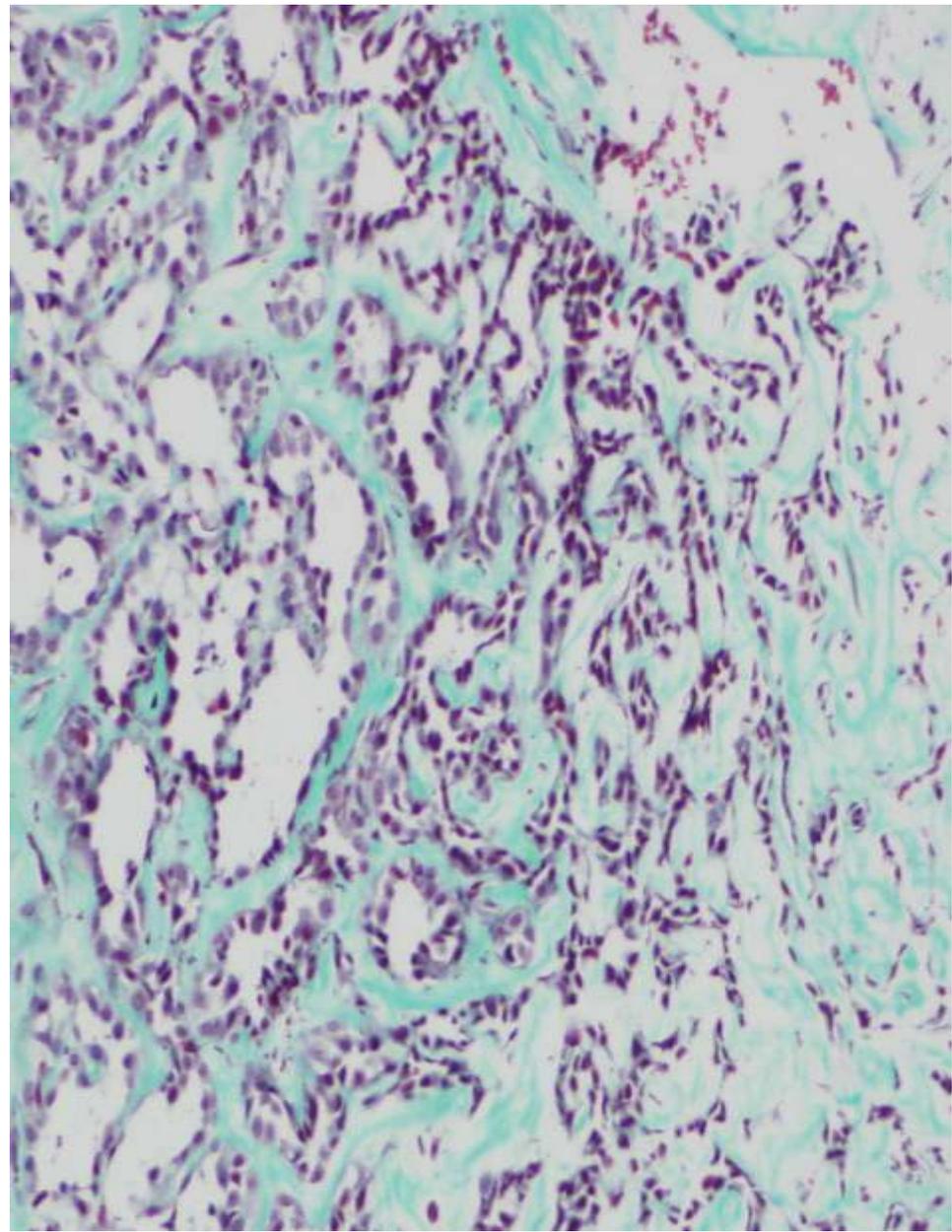
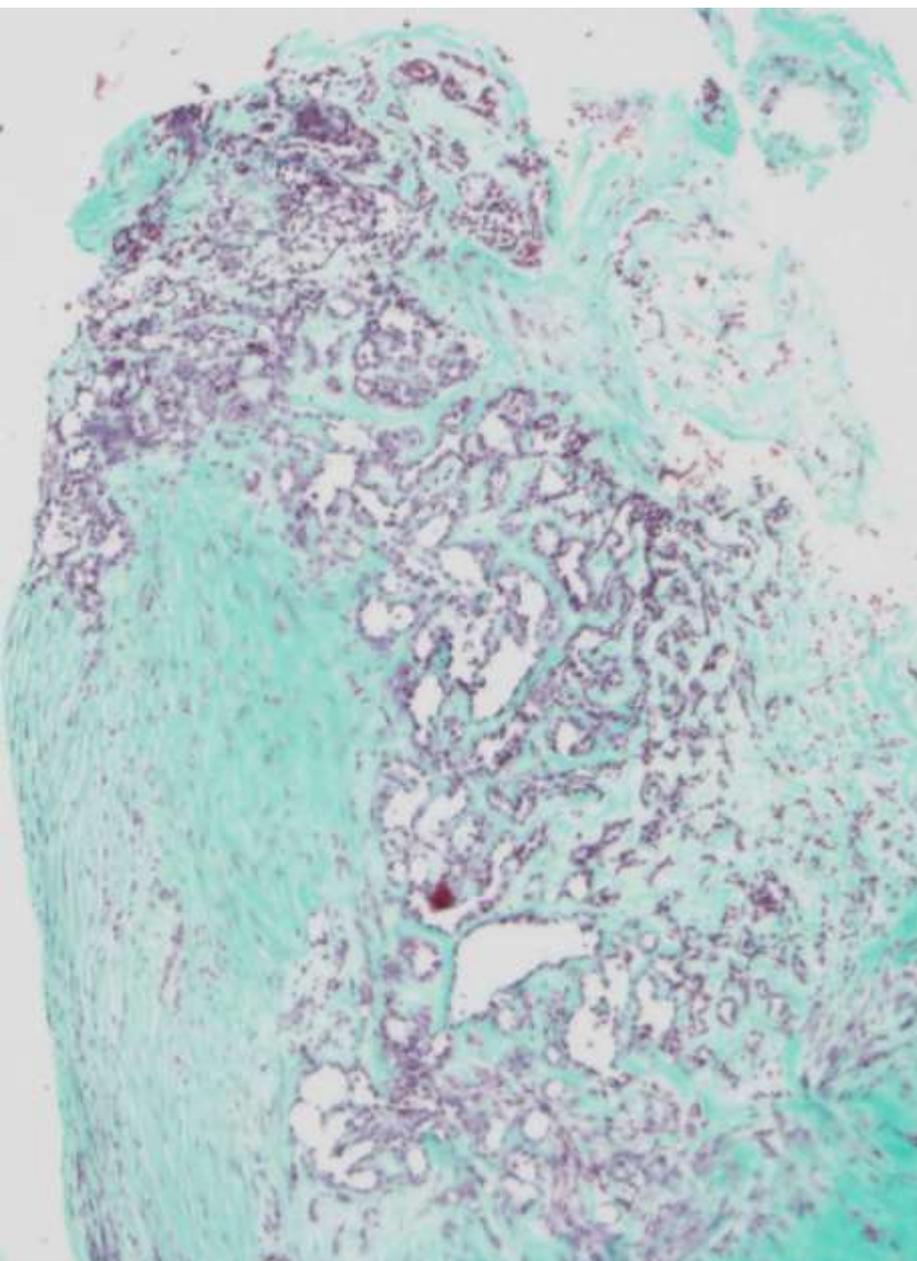
Ordoñez N.G.

Human Pathology 2005,36,465

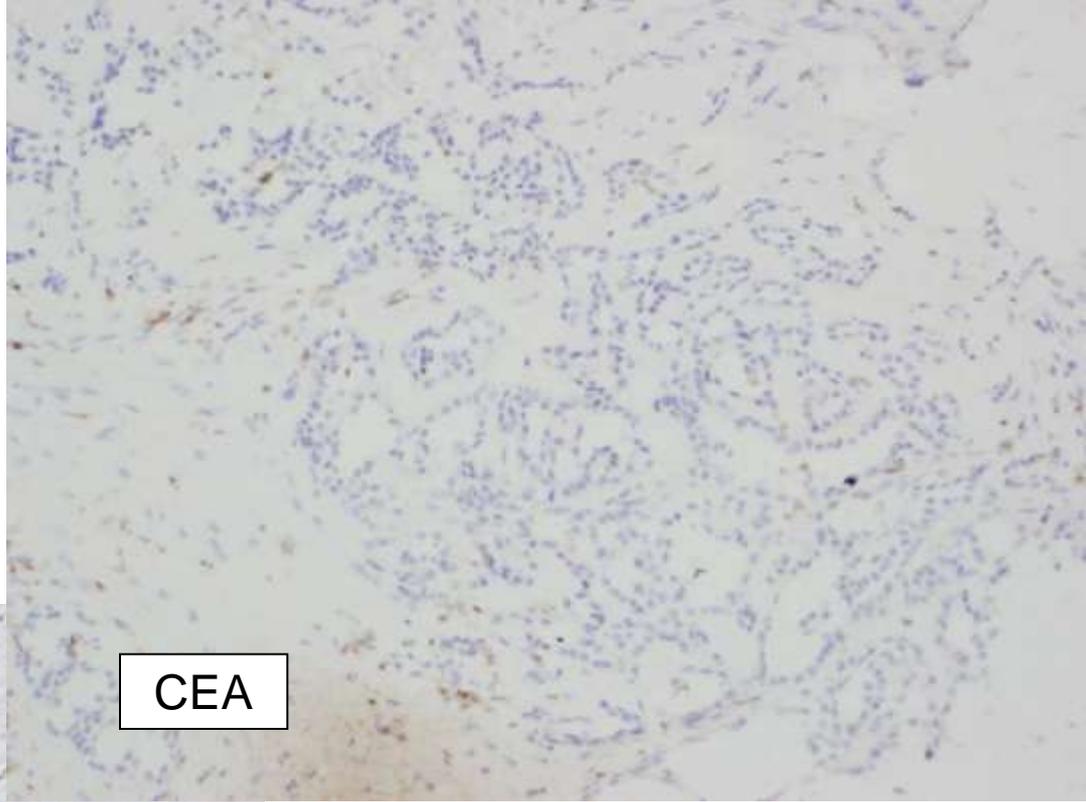


**CALRETININA**

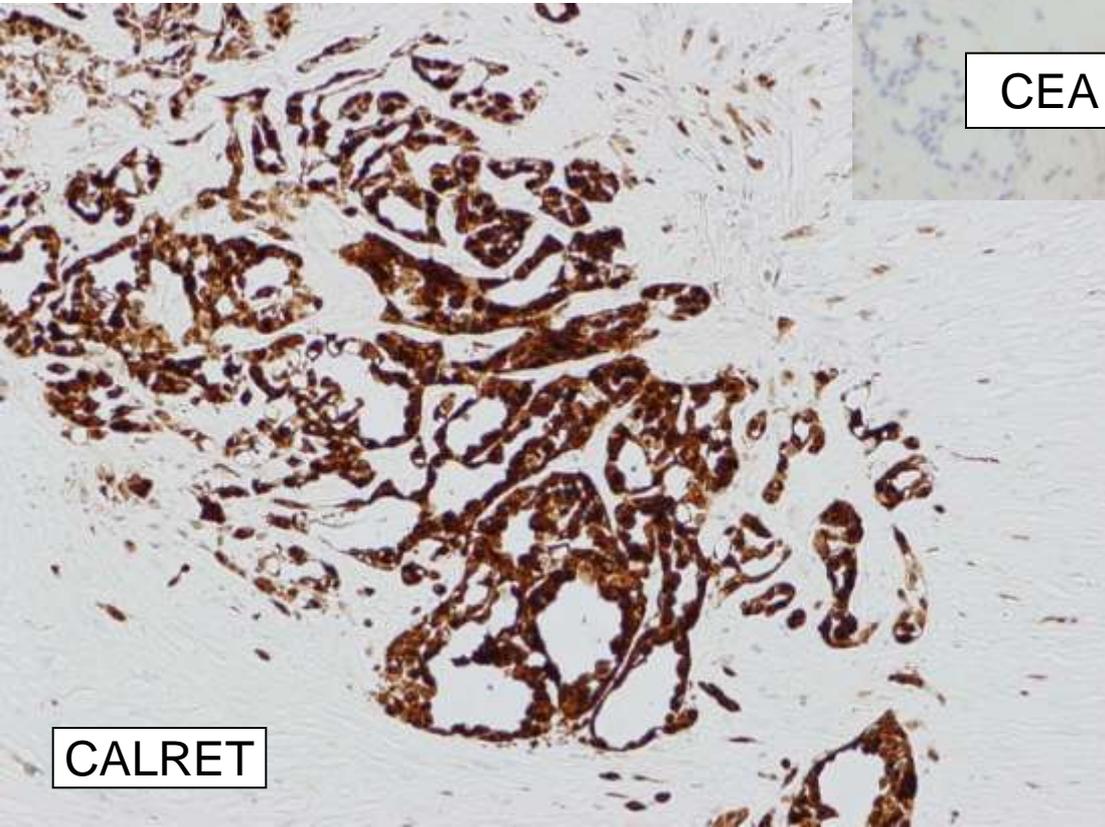
The image shows a histological section of tissue stained for Calretinin. The tissue exhibits a dense, elongated structure with a central region showing strong brown immunohistochemical staining, indicating the presence of Calretinin. The surrounding tissue is stained with hematoxylin and eosin, showing a mix of purple nuclei and pink cytoplasm/extracellular matrix. The overall appearance is consistent with a clear cell mesothelioma.



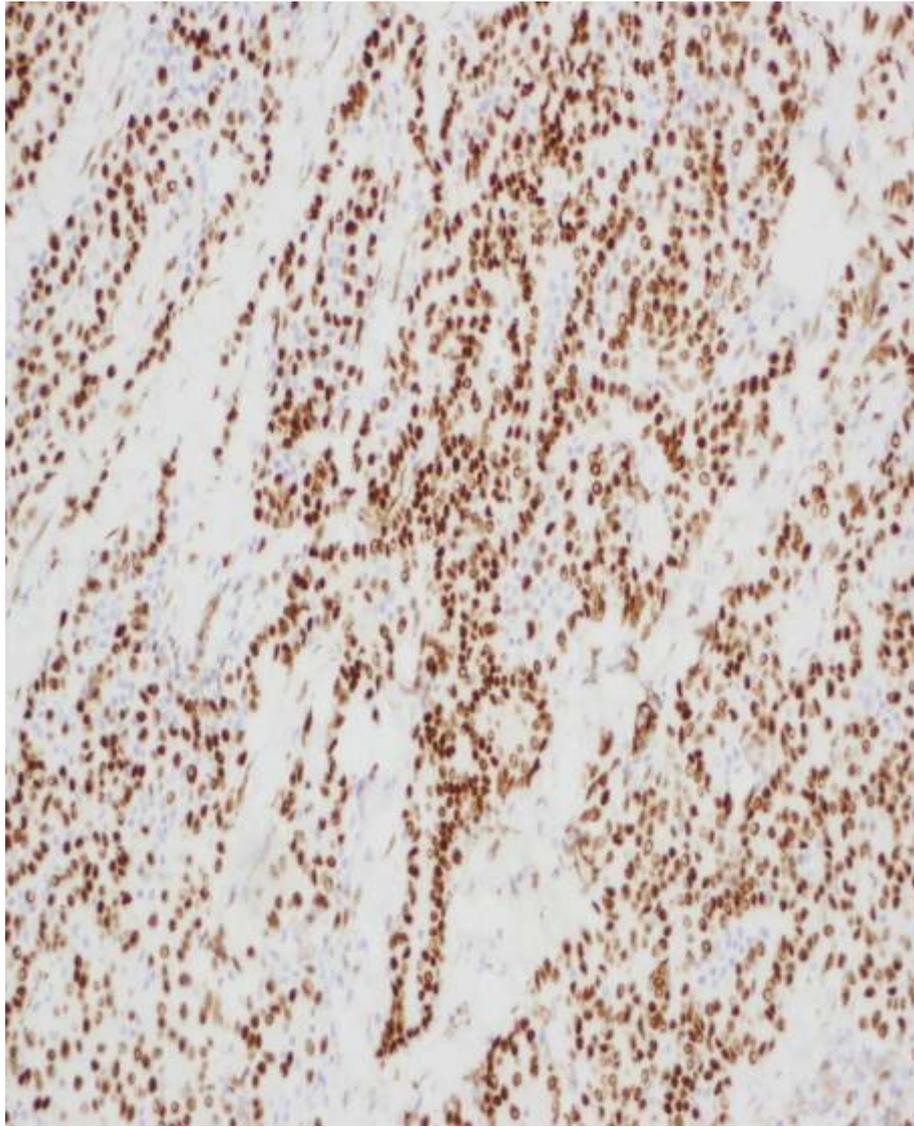
N10-27628 Varon 75<sup>a</sup>. Exposicion Amianto. Dolor y Derrame pleural



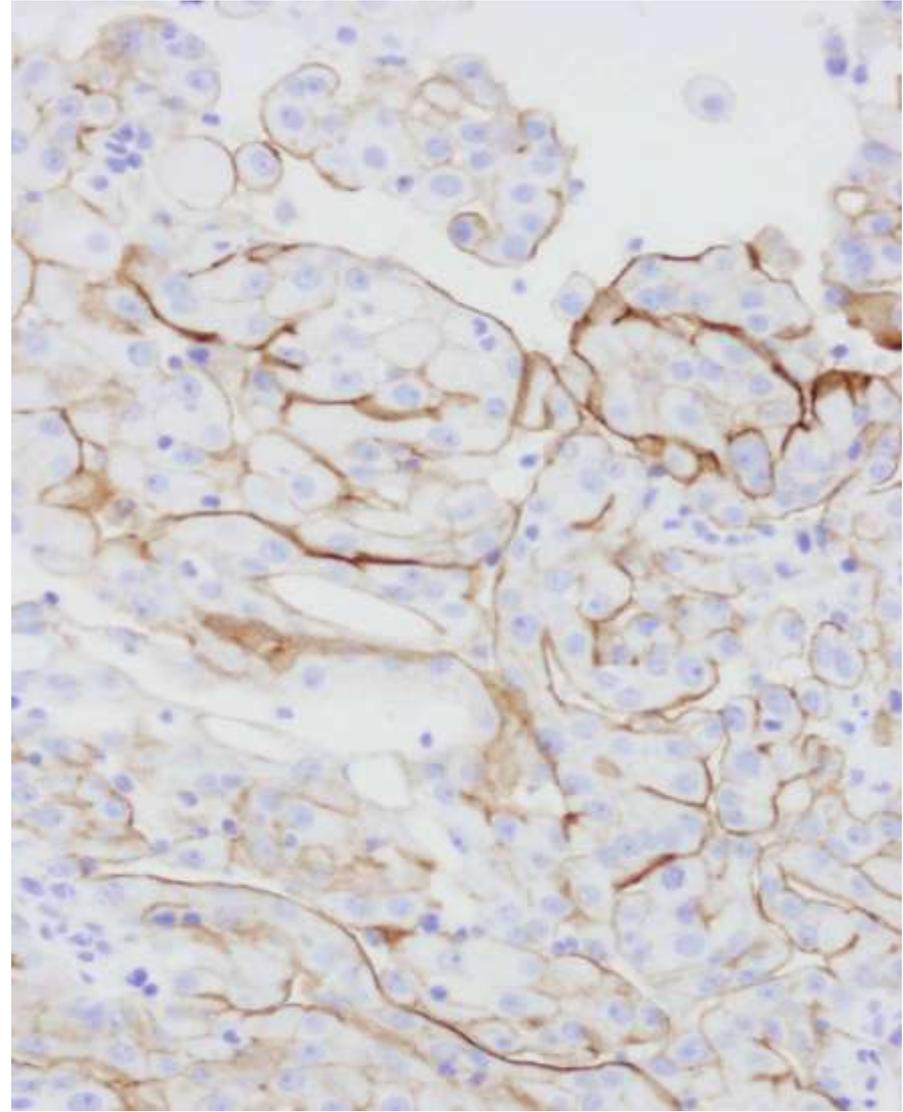
CEA



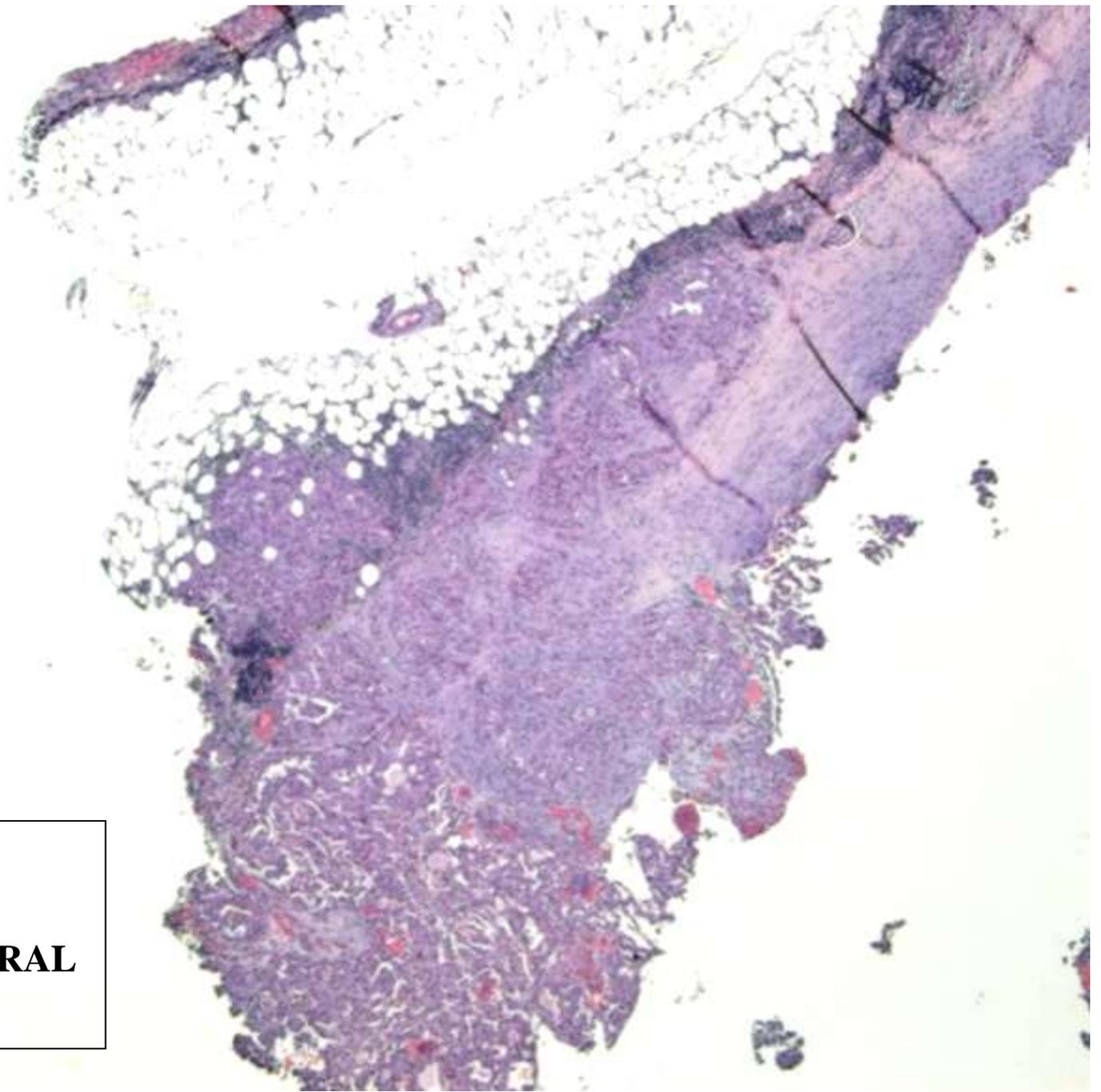
CALRET



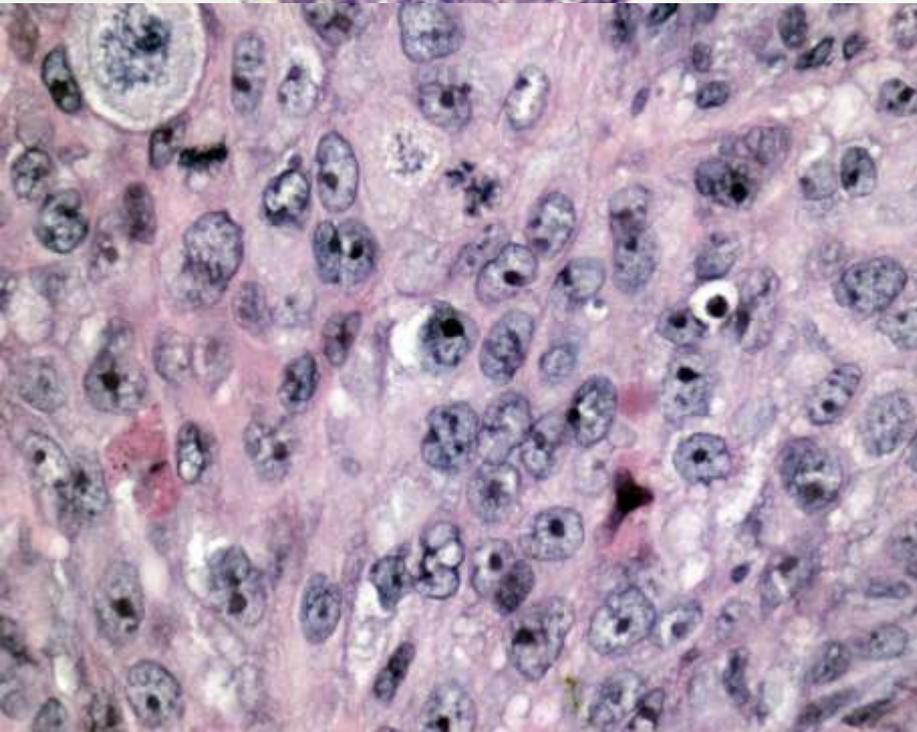
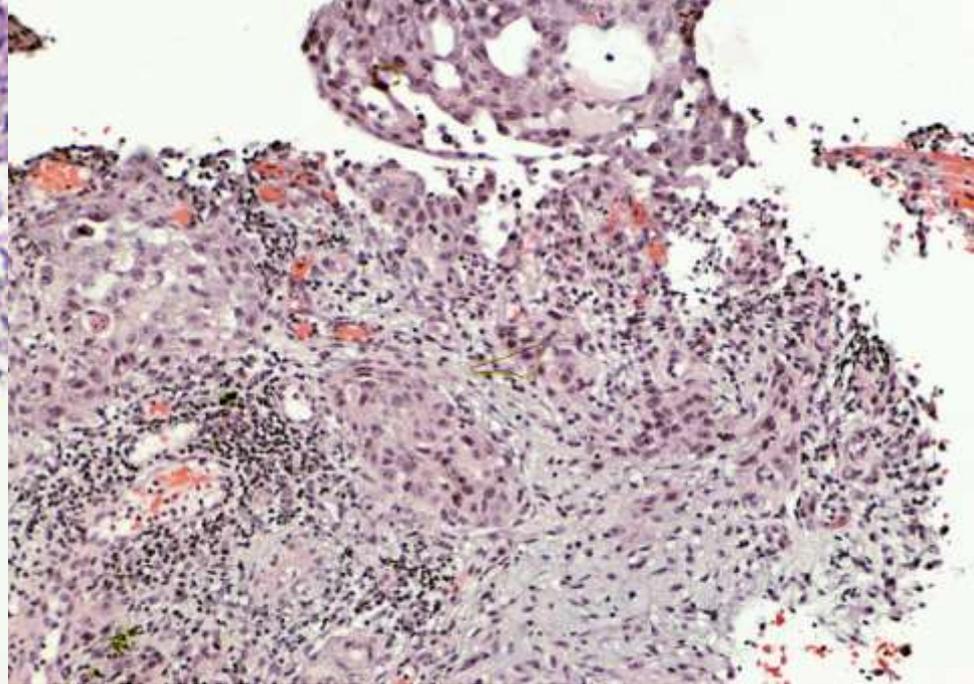
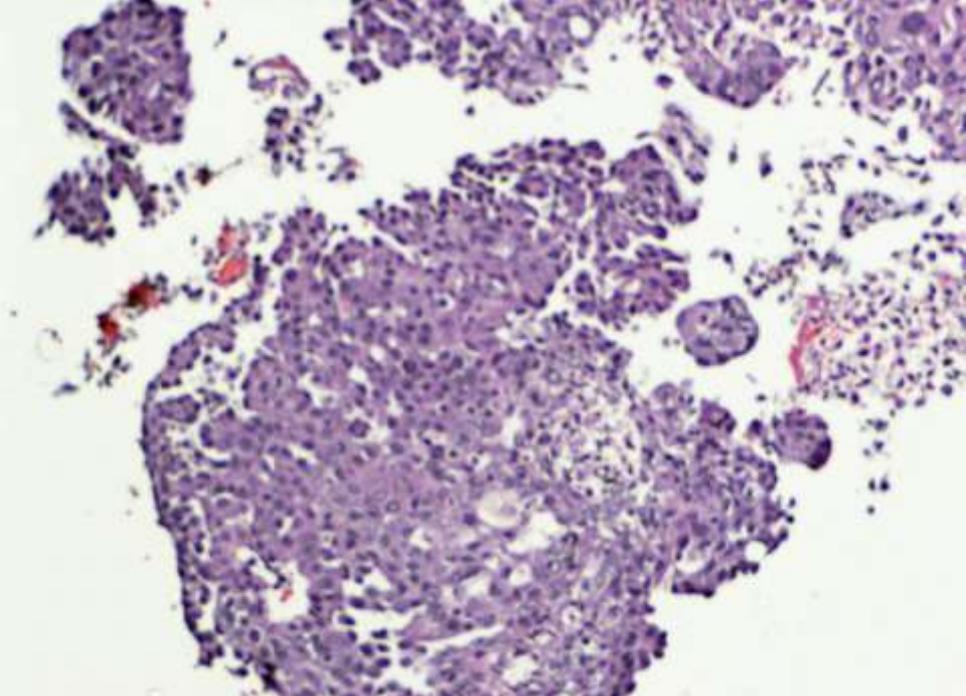
WT-1



PODOPLANIN (D2-40)

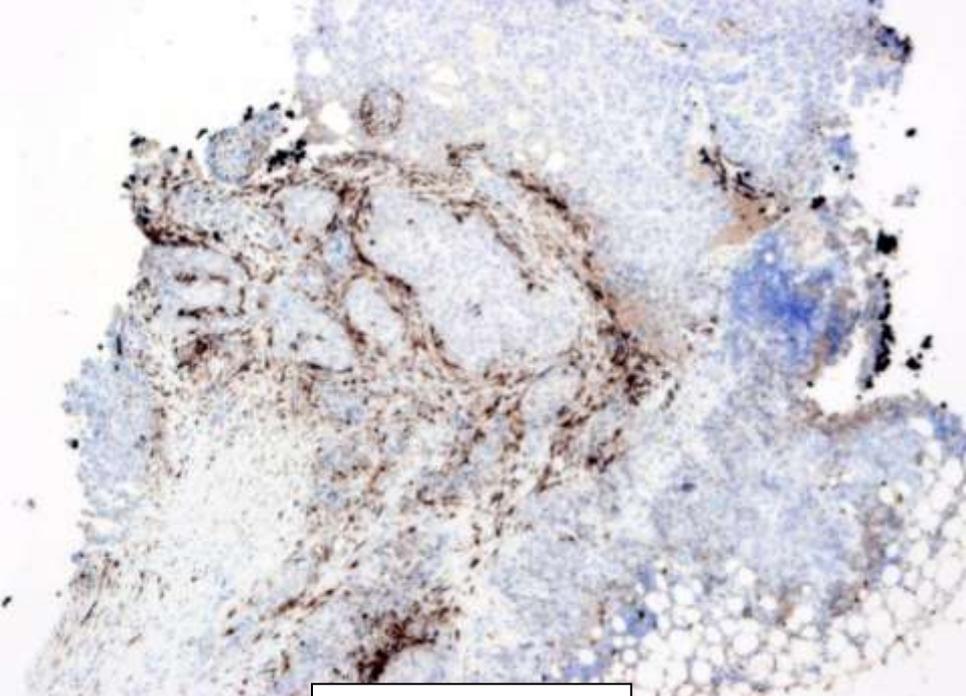


**MUJER 46<sup>a</sup>**  
**DERRAME PLEURAL**

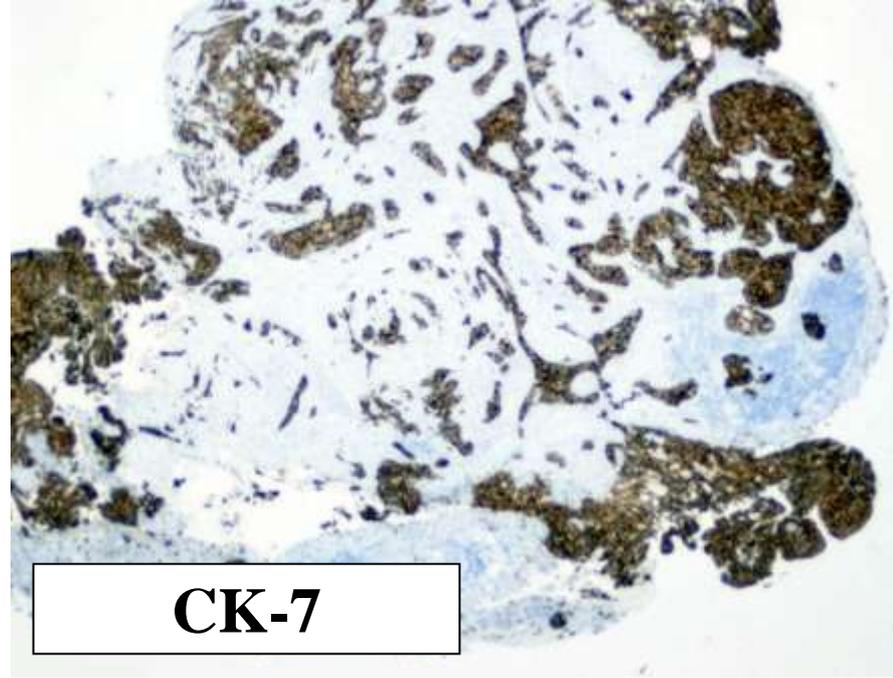
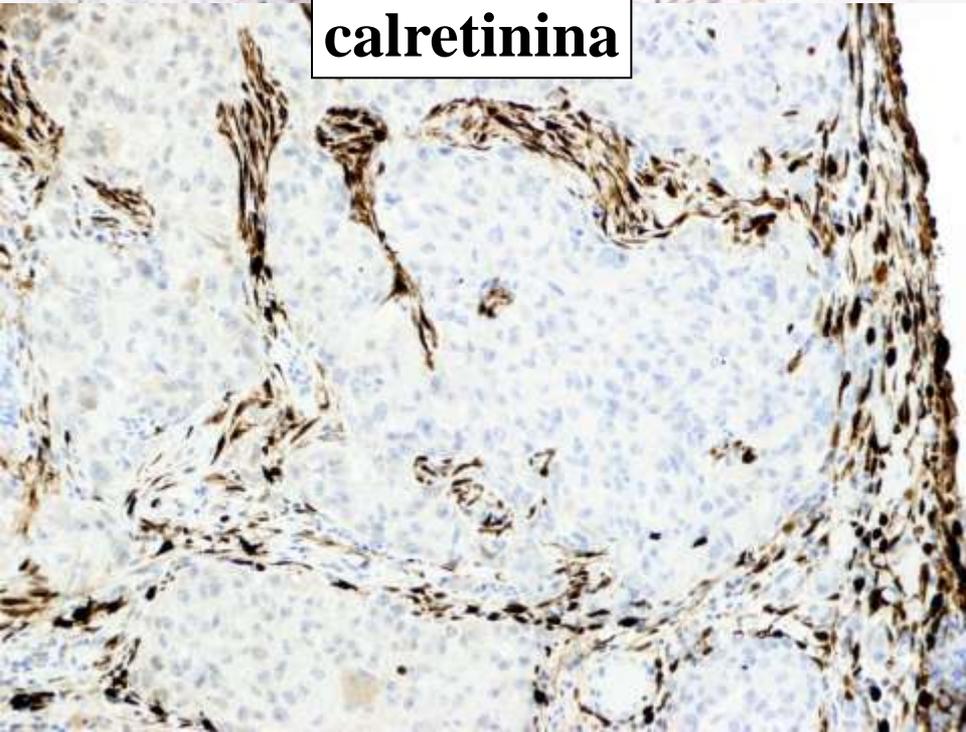


**B07-20476**

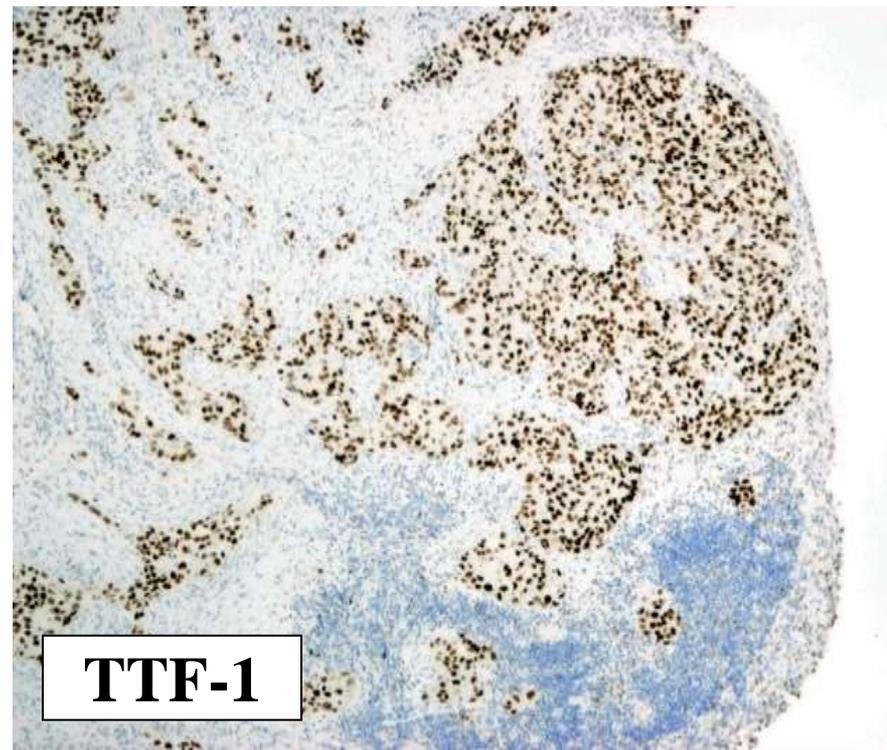
**Ca. Adenoescamoso**



**calretinina**



**CK-7**



**TTF-1**



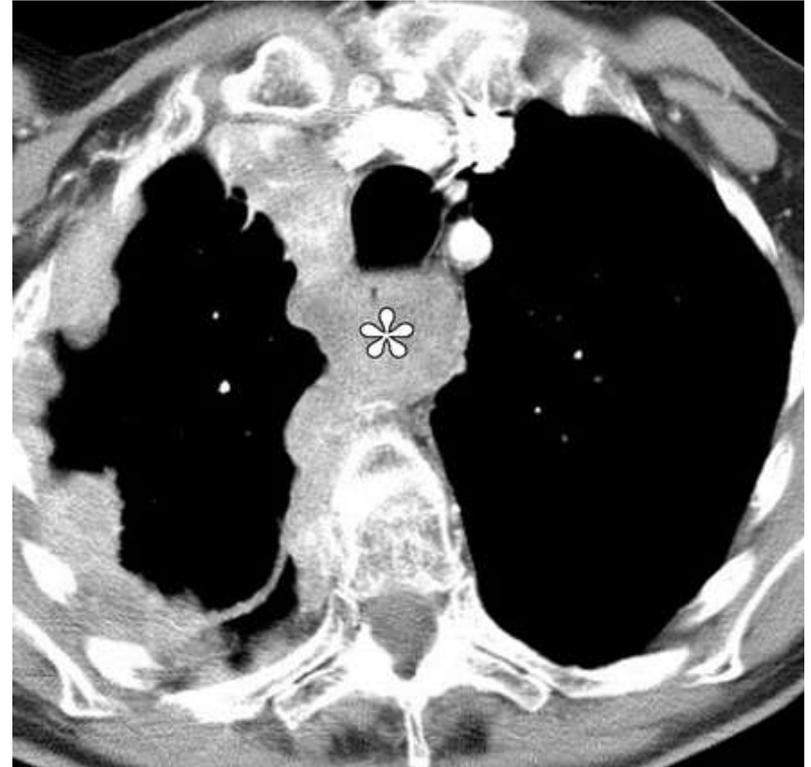
**Escala de las virtudes  
Monast Sucevita. Moldavia**

## **3.- MM SARCOMATOIDE/SARCOMAS**

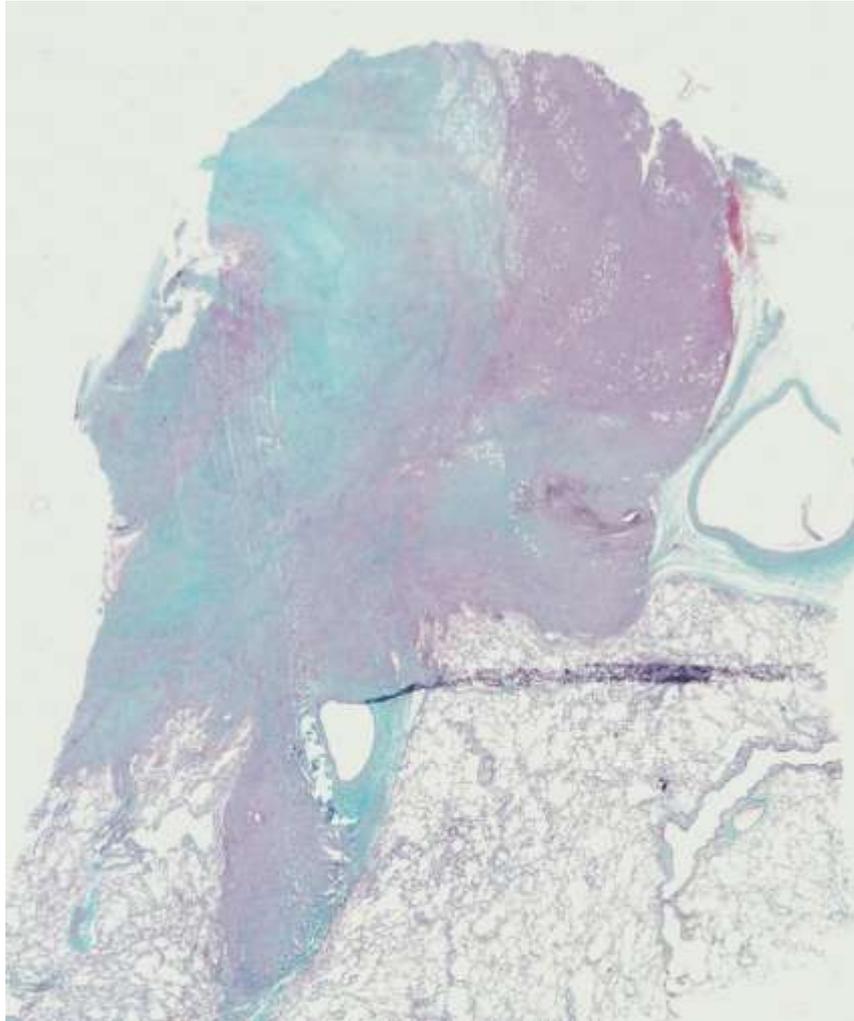
**POOL CITOQUERATINAS +  
CALRETININA, D2-40. MARCADORES POSITIVOS  
DESMINA, S-100, VIM. CD-34 MARCADORES NEGATIVOS**

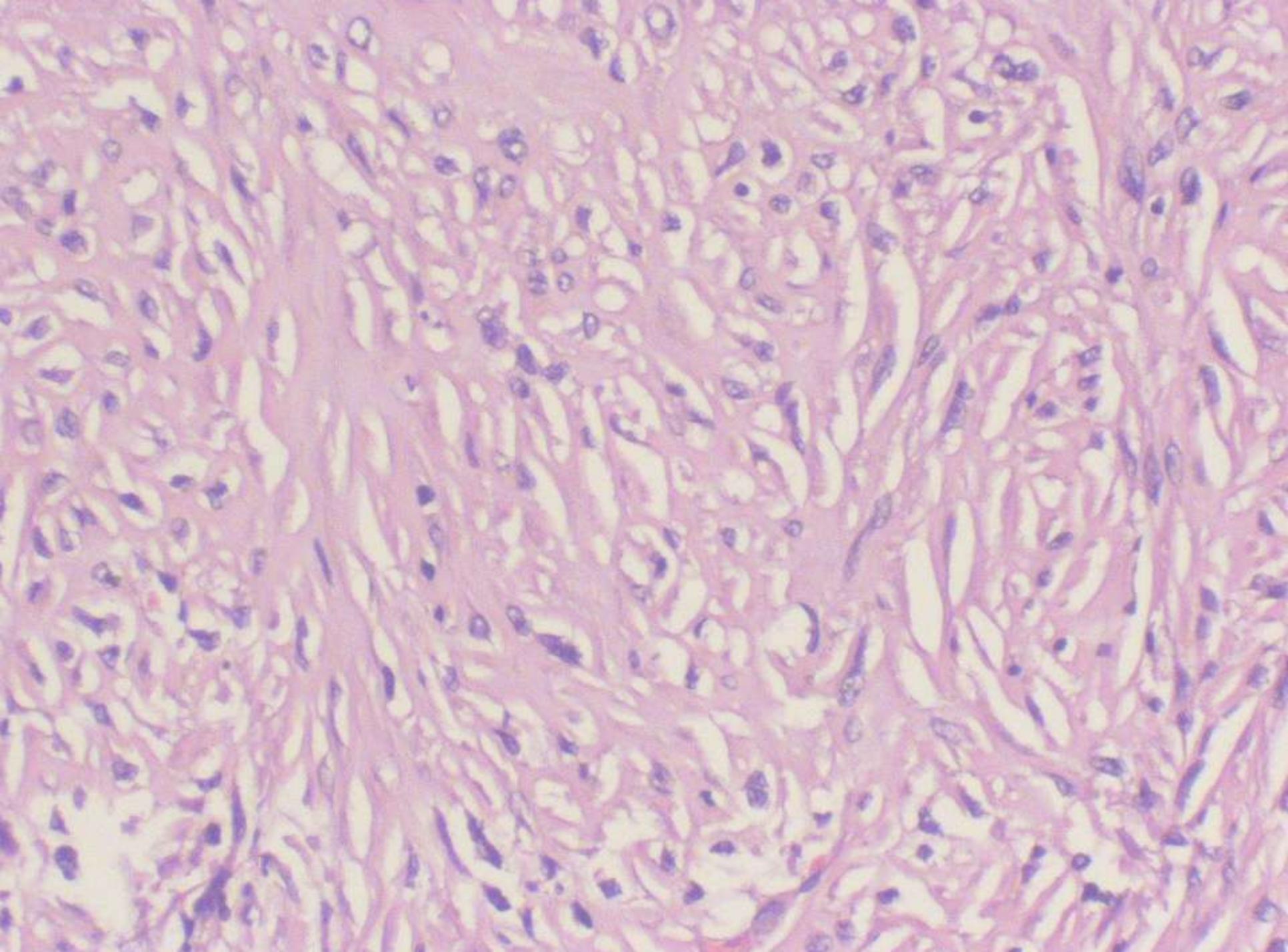
**VARON 54a ENGROSAMIENTO PLEURAL DERECHO CON MASAS QUE SE INTRODUCEN EN CISURA.**

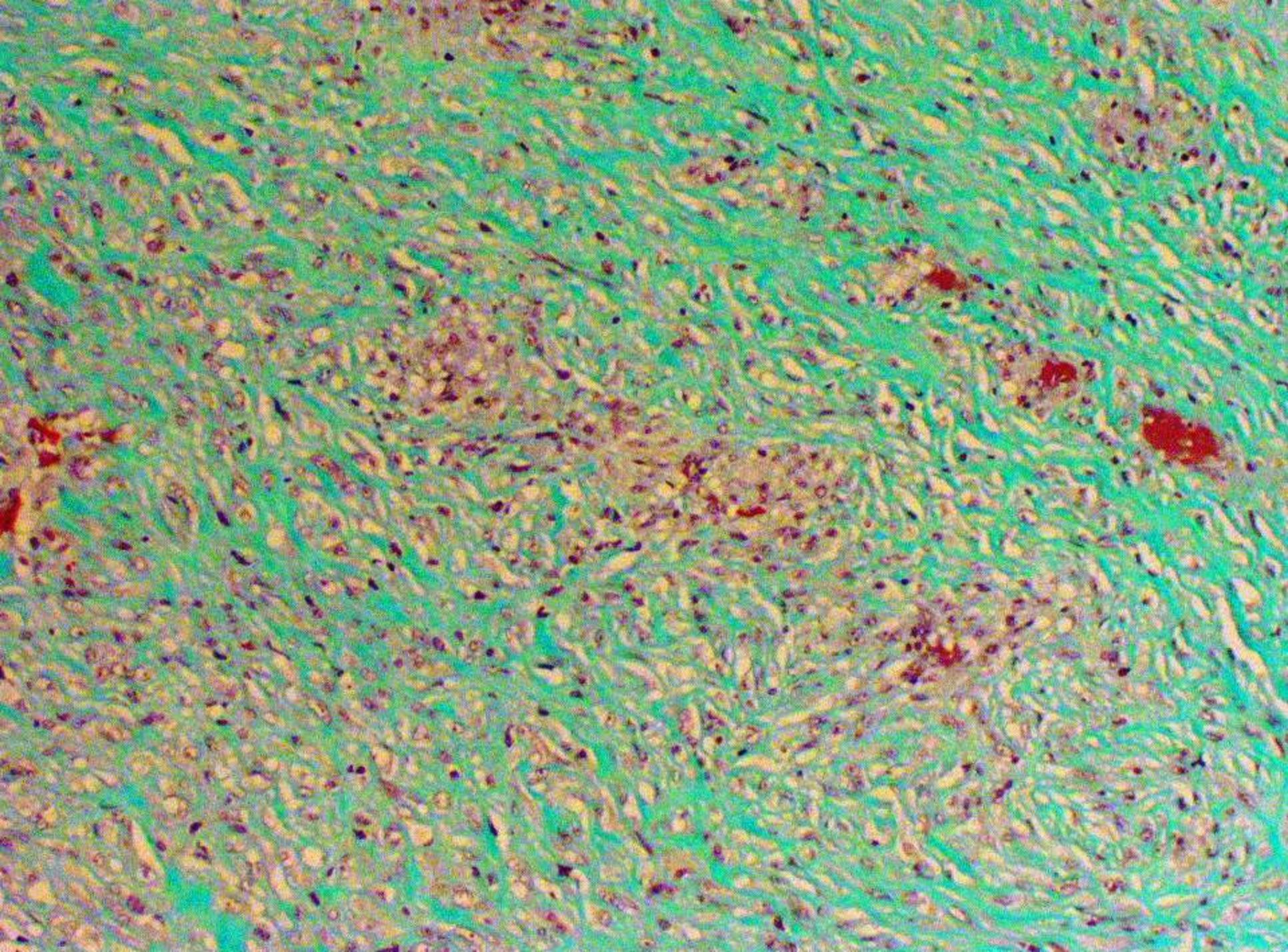
**SOSPECHA: MESOTELIOMA**

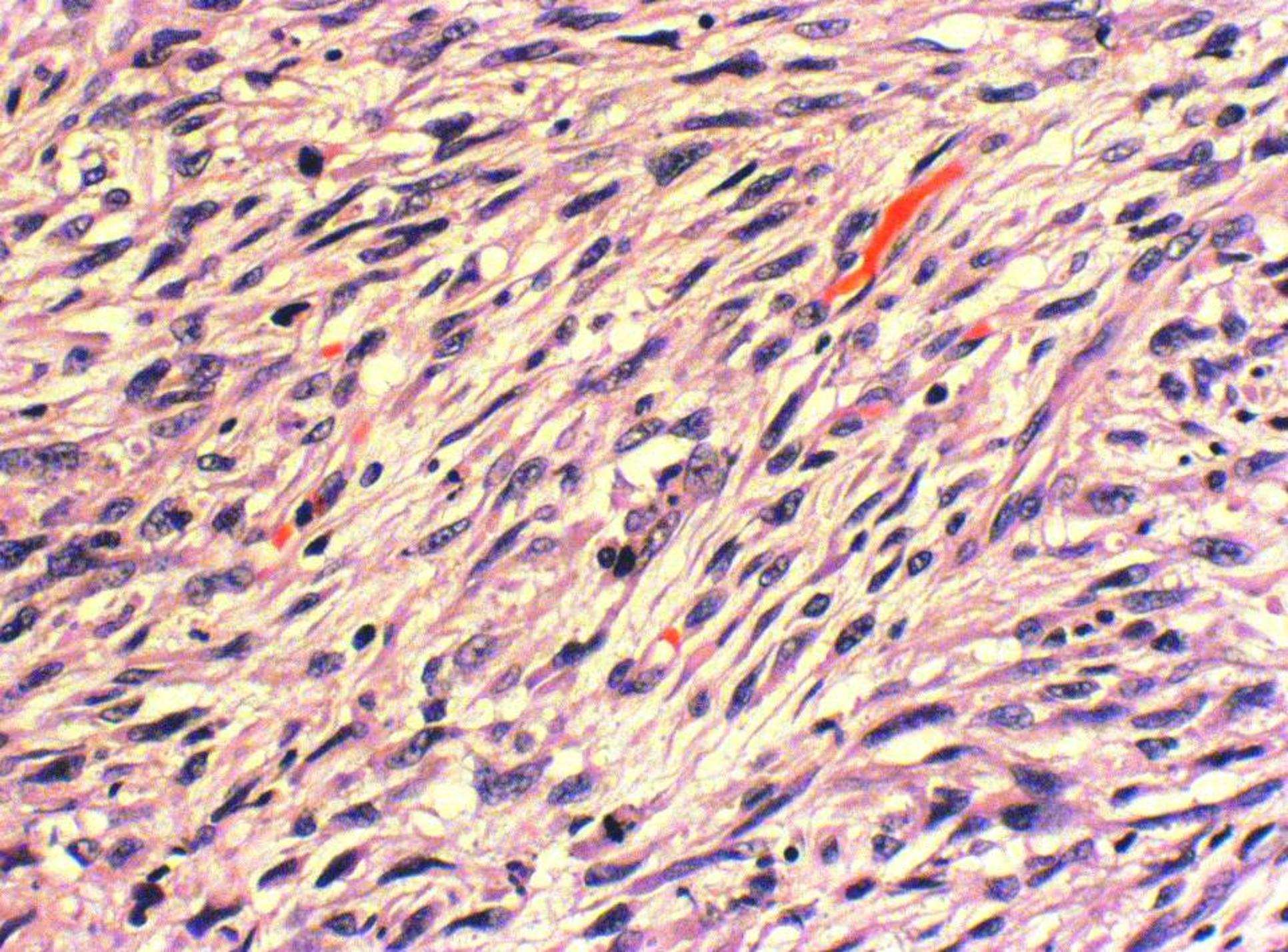


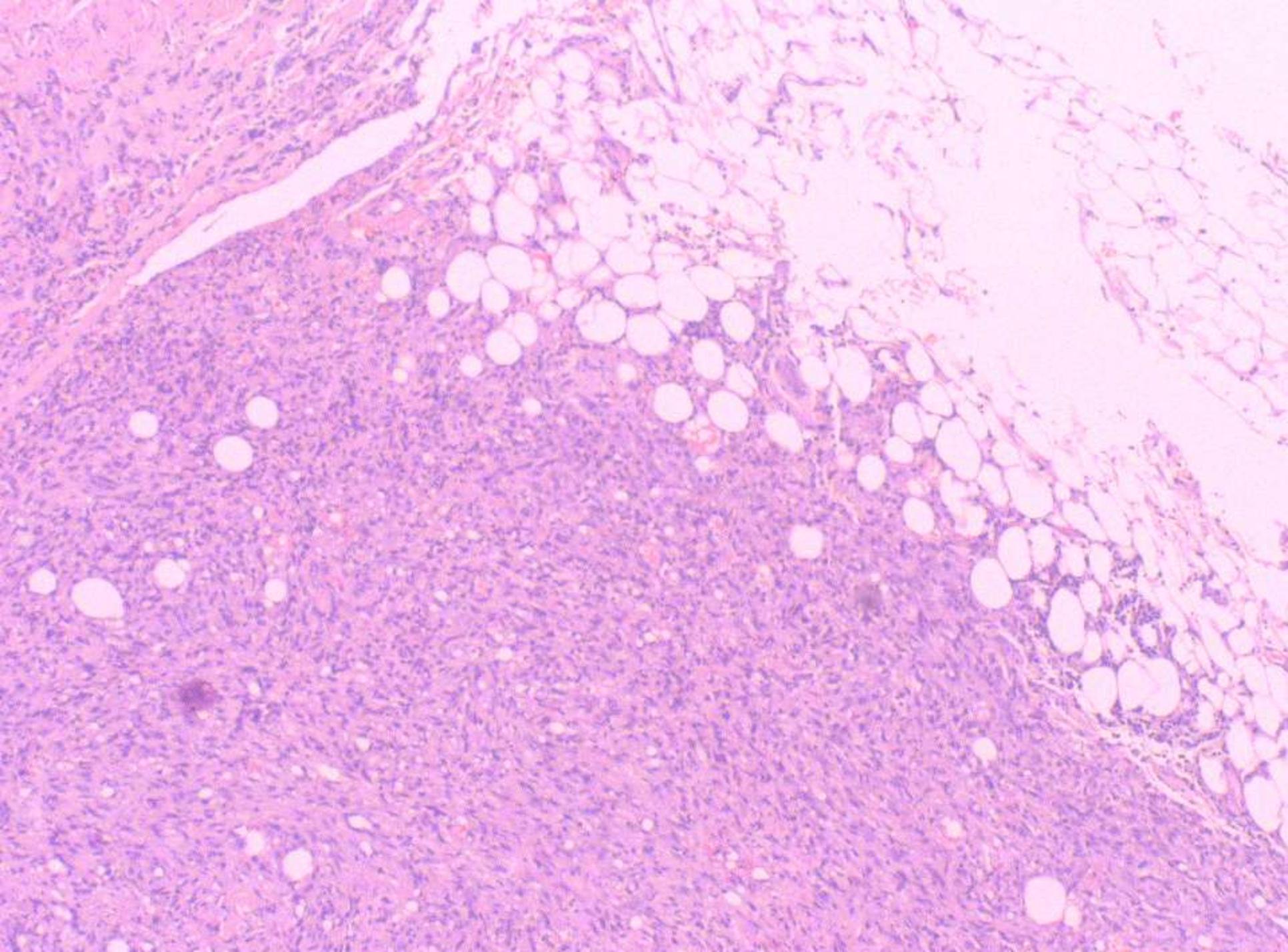


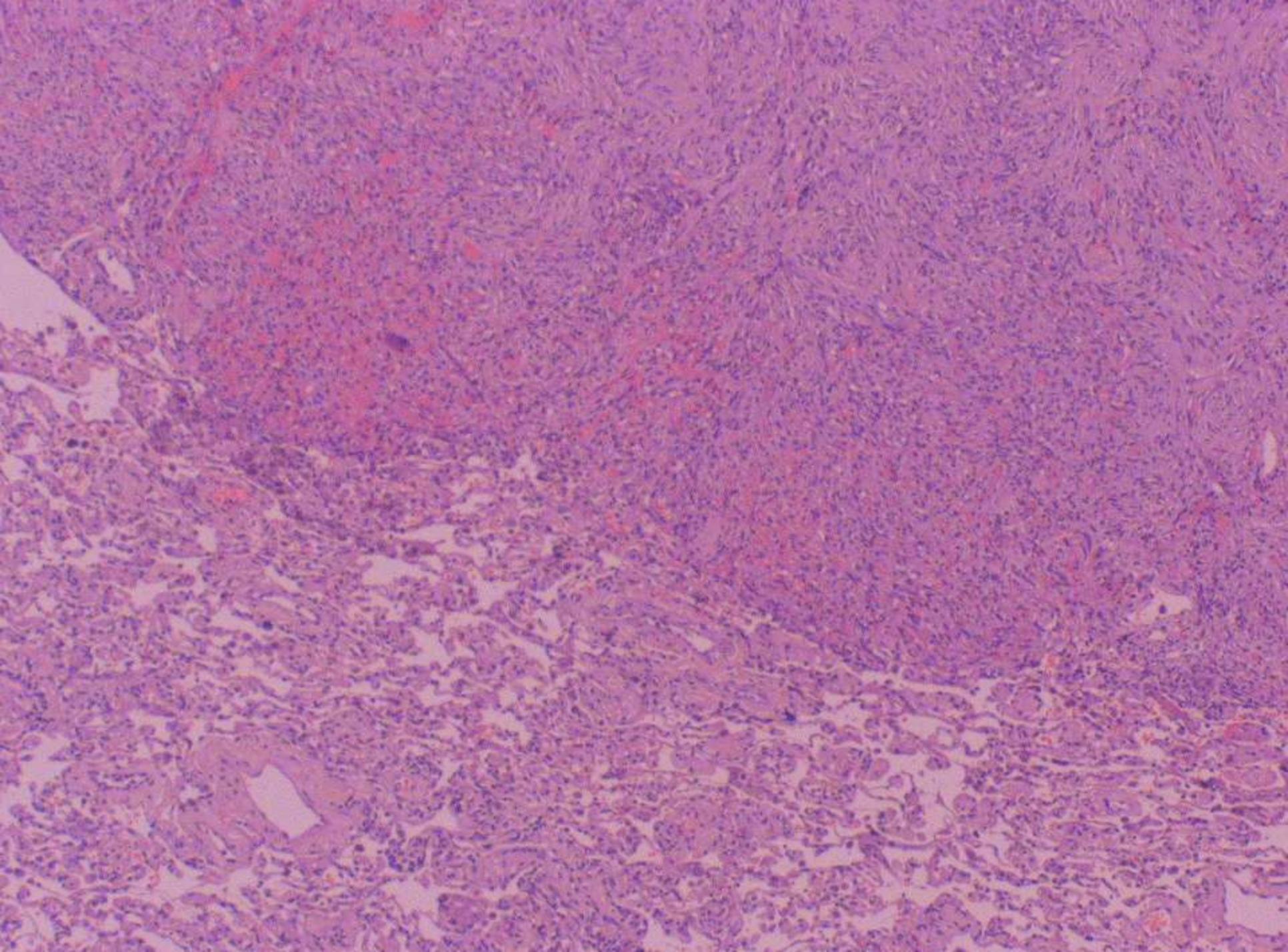


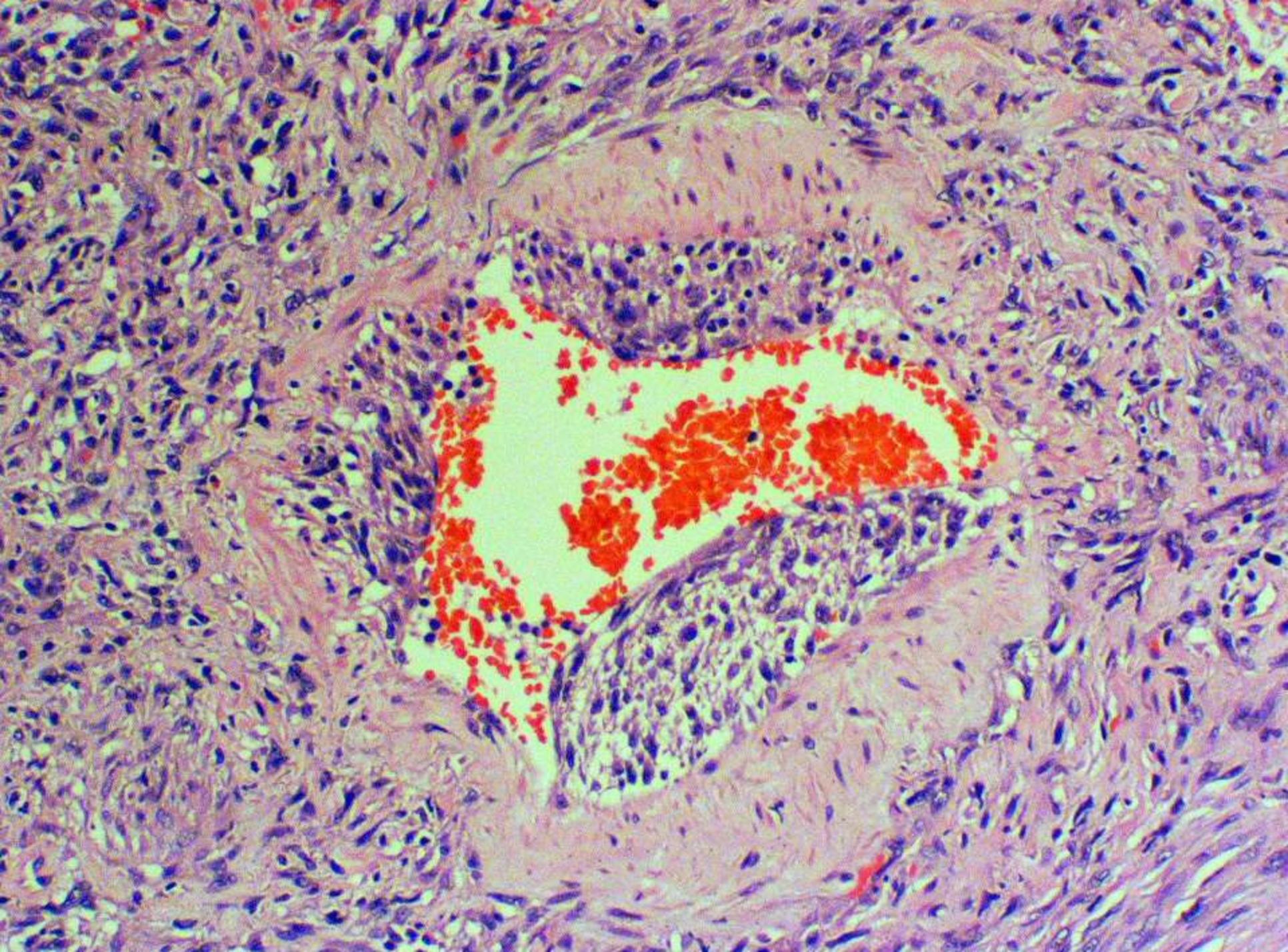


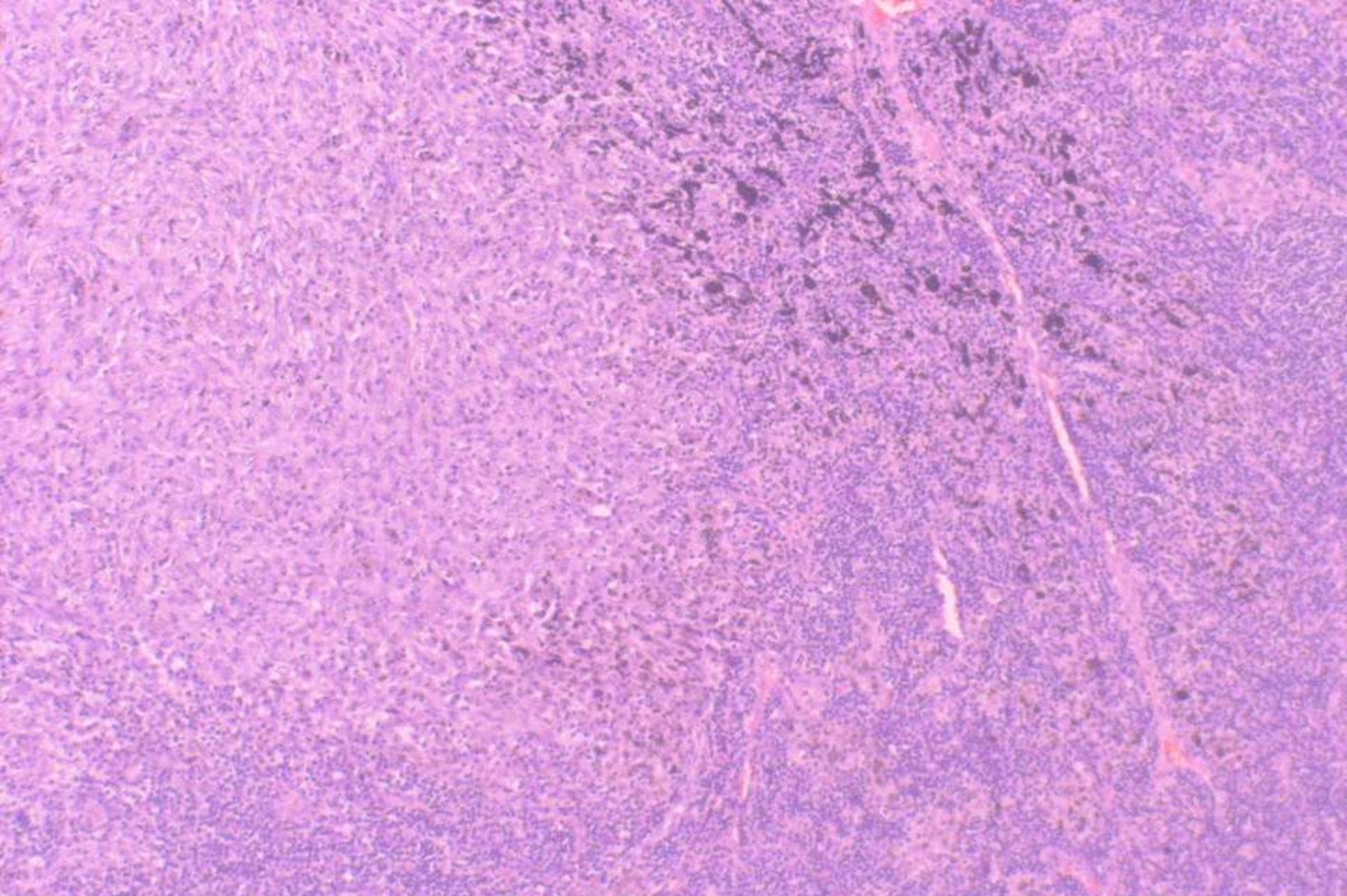




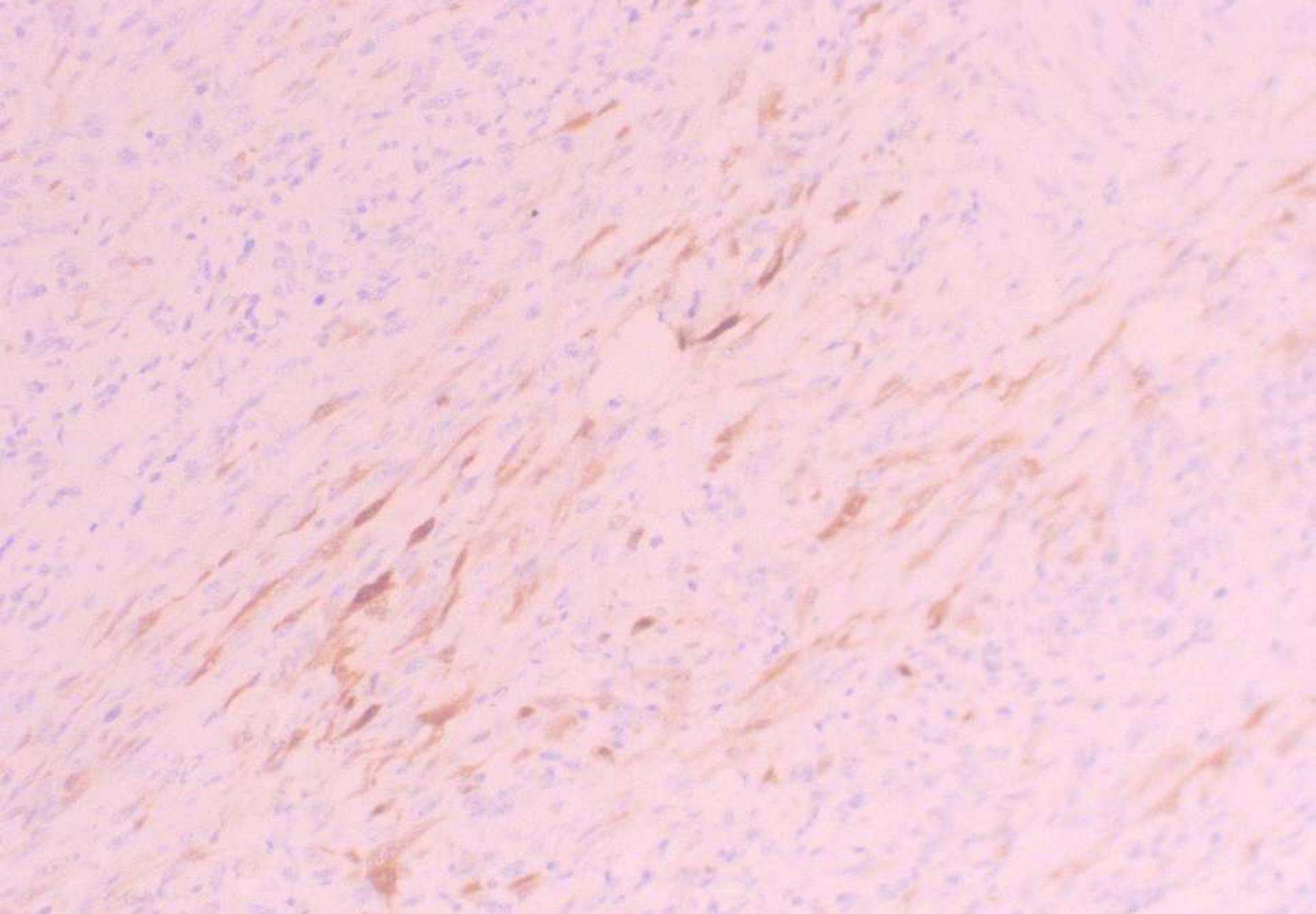




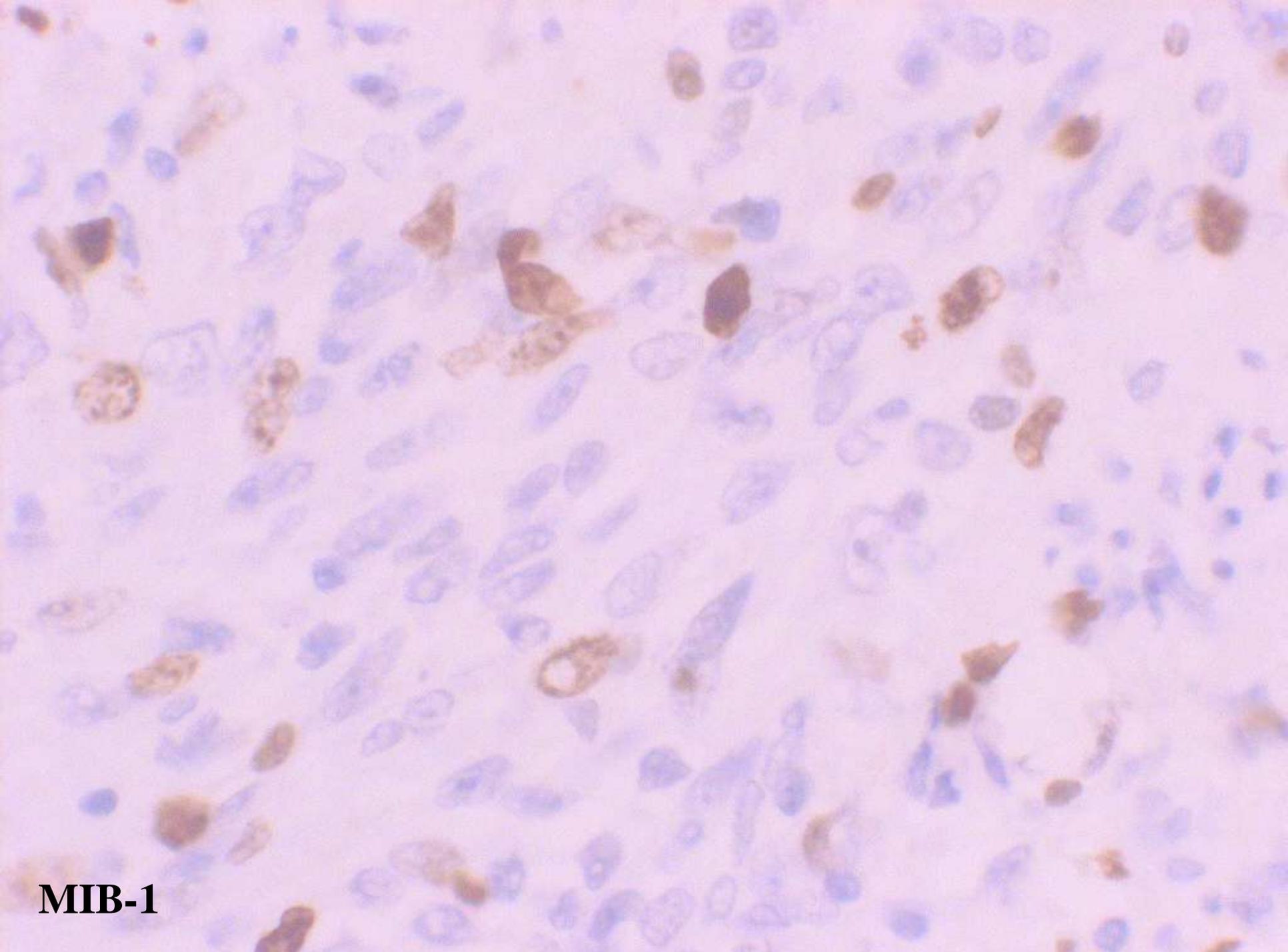




**GANGLIO HILIO**



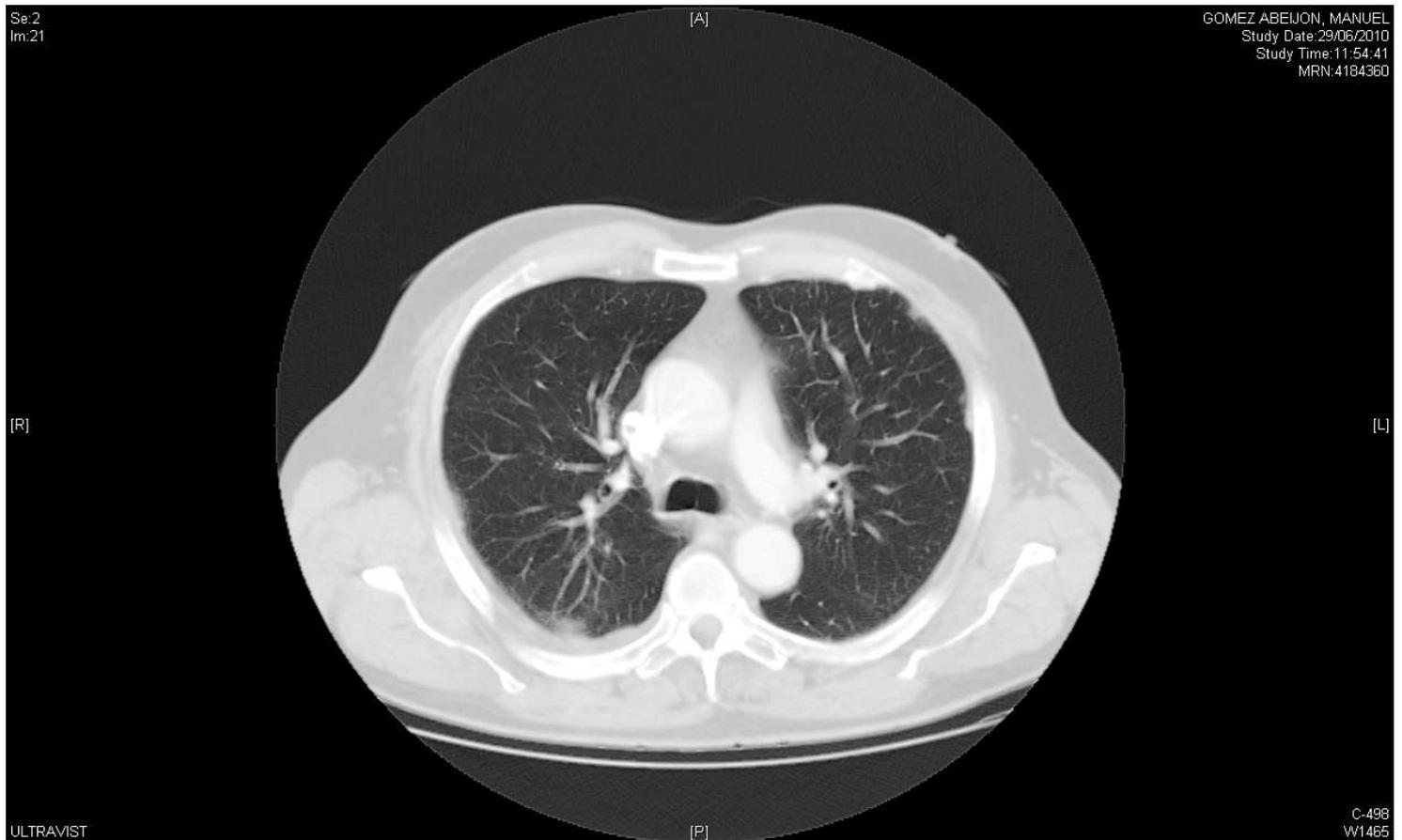
**CALRETININA**



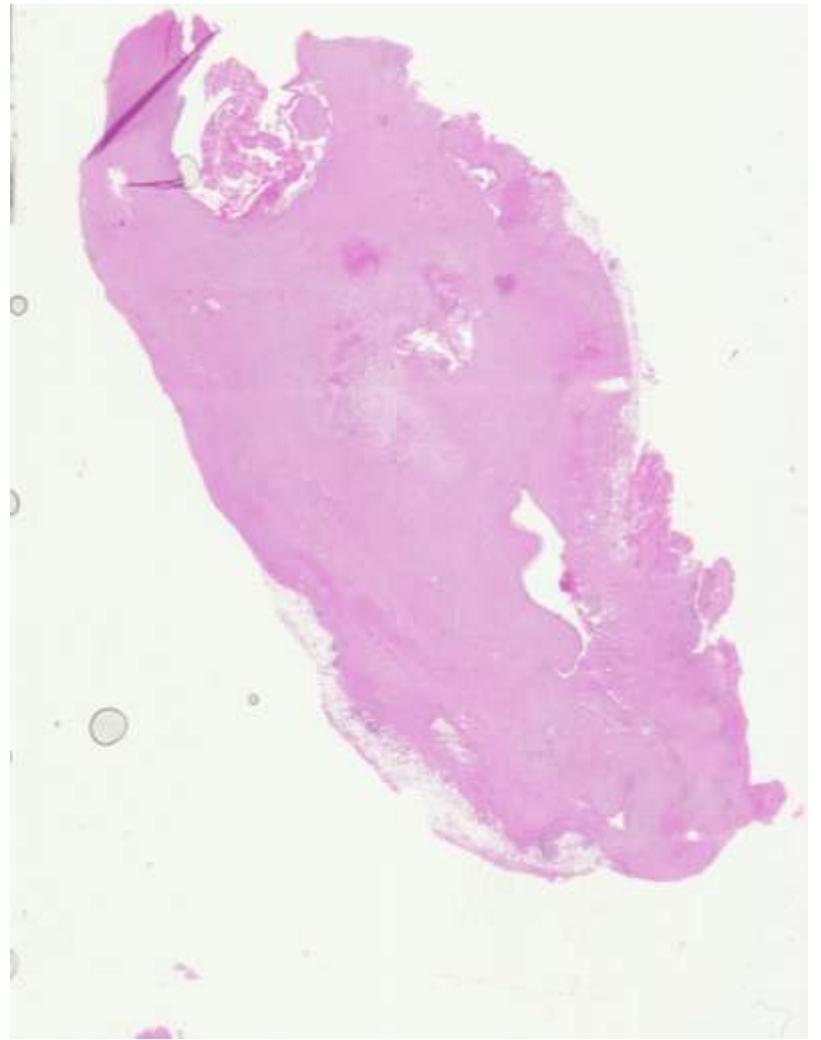
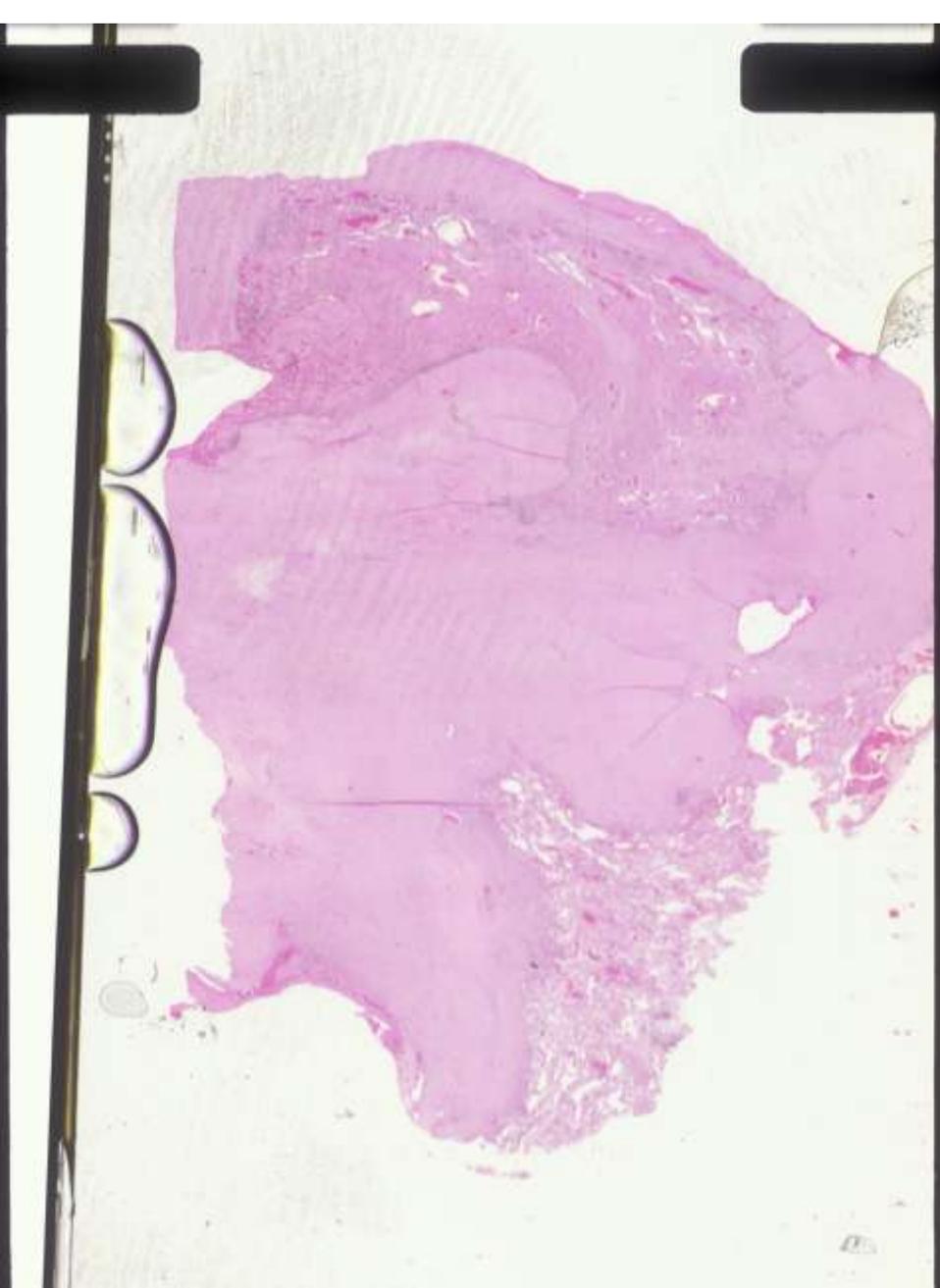
**MIB-1**

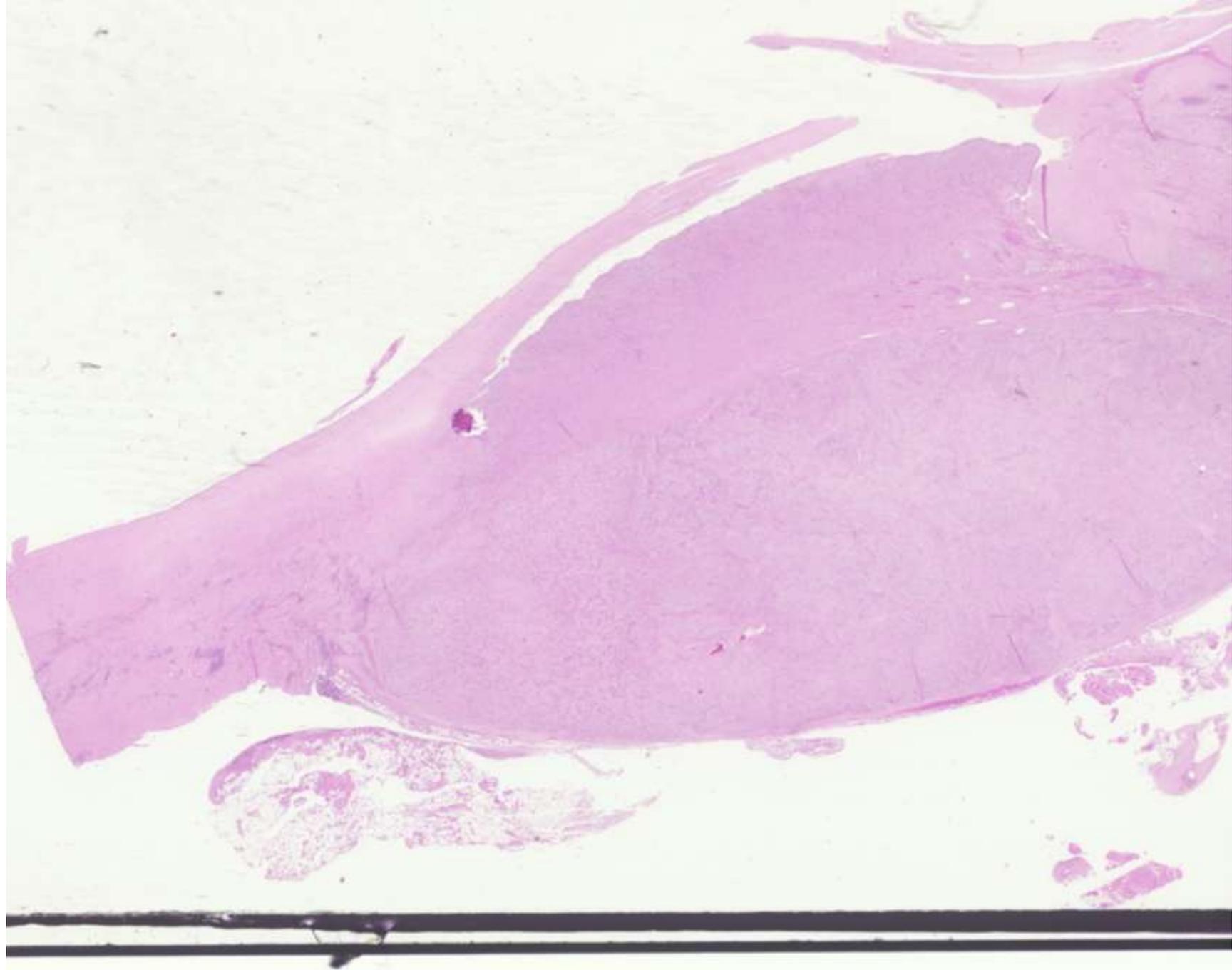
B11-9884

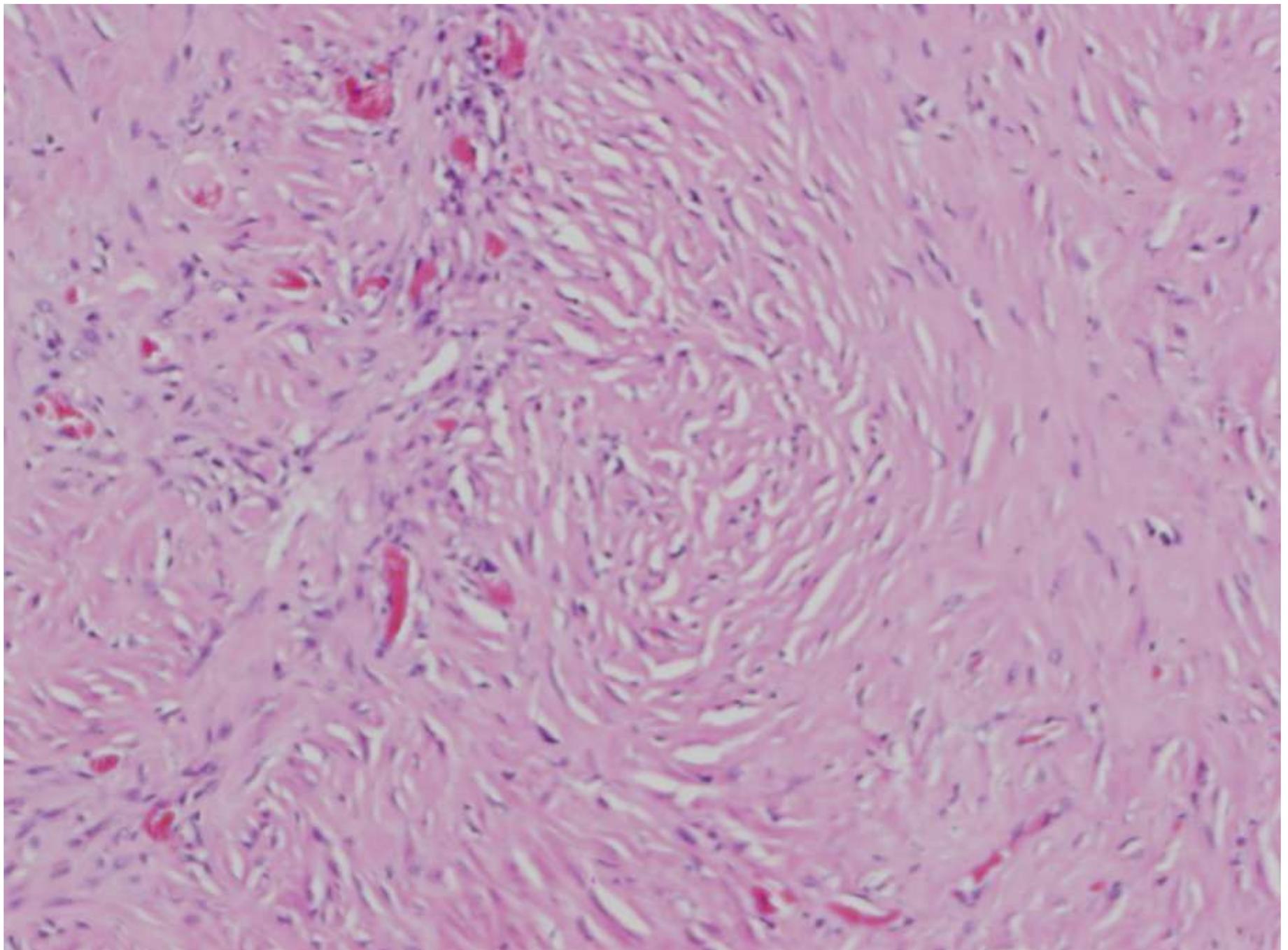
- VARÓN 71 AÑOS
- DERRAME PLEURAL DERECHO
- CONTACTO CON ASBESTOS

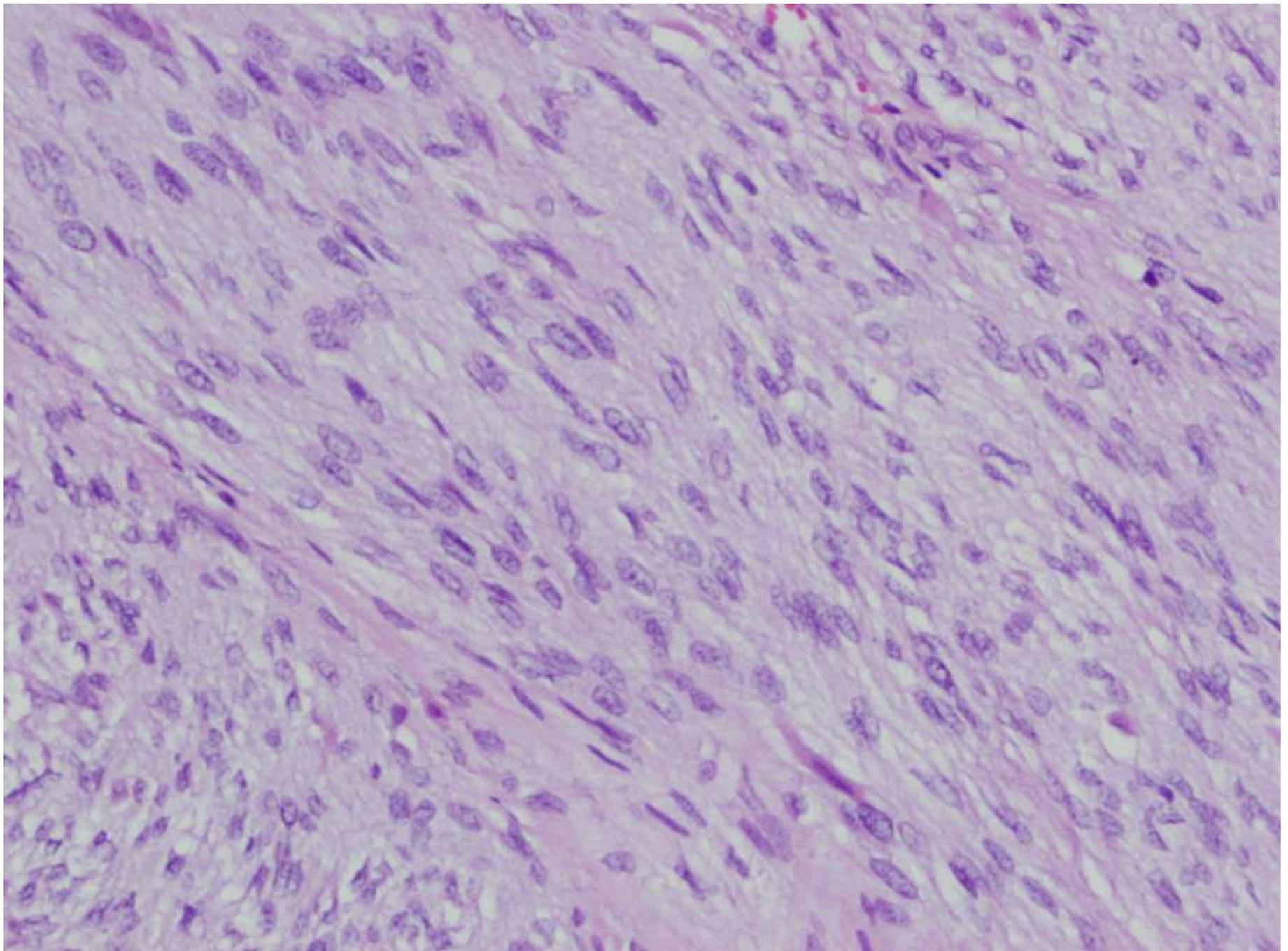


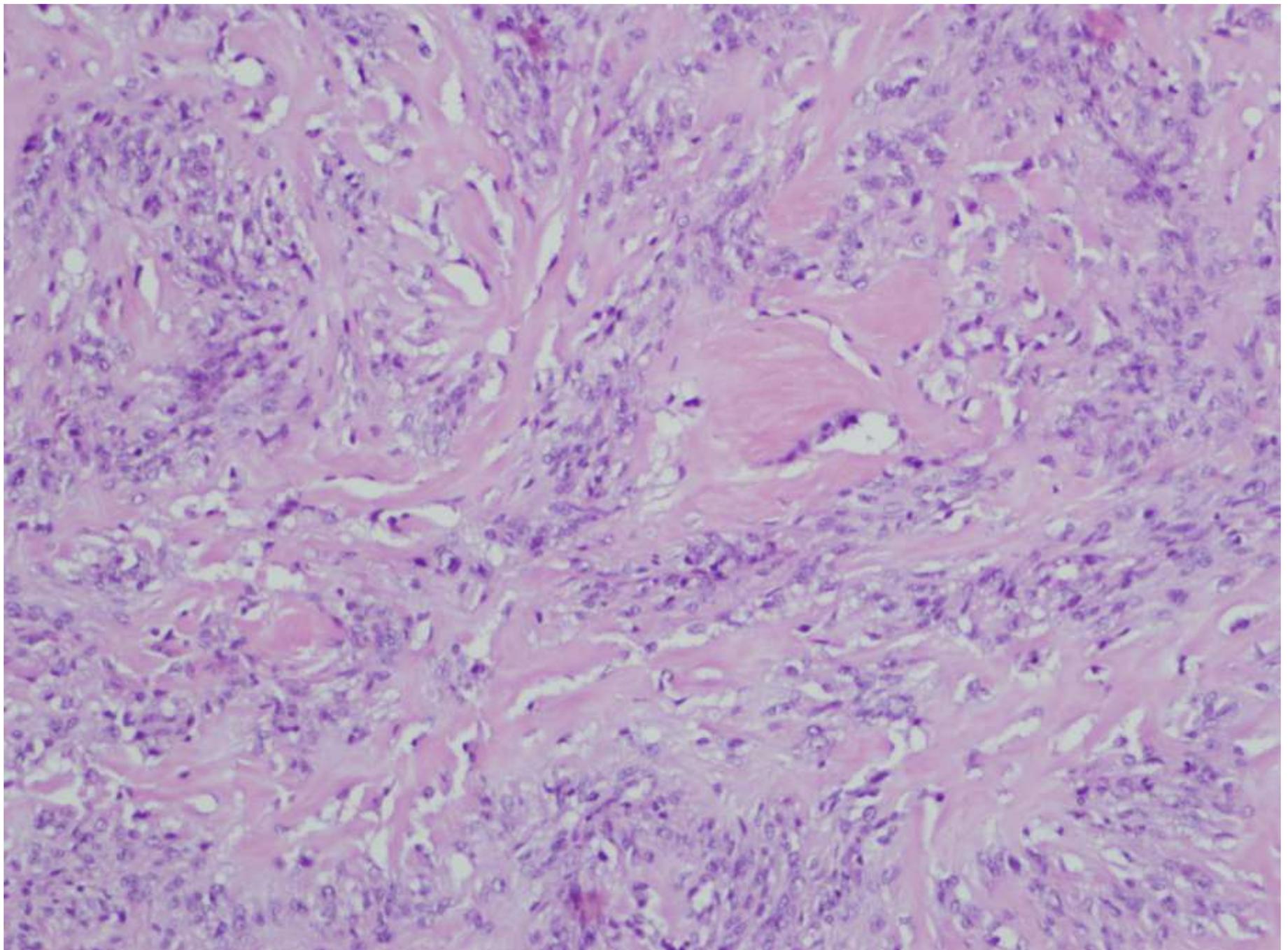


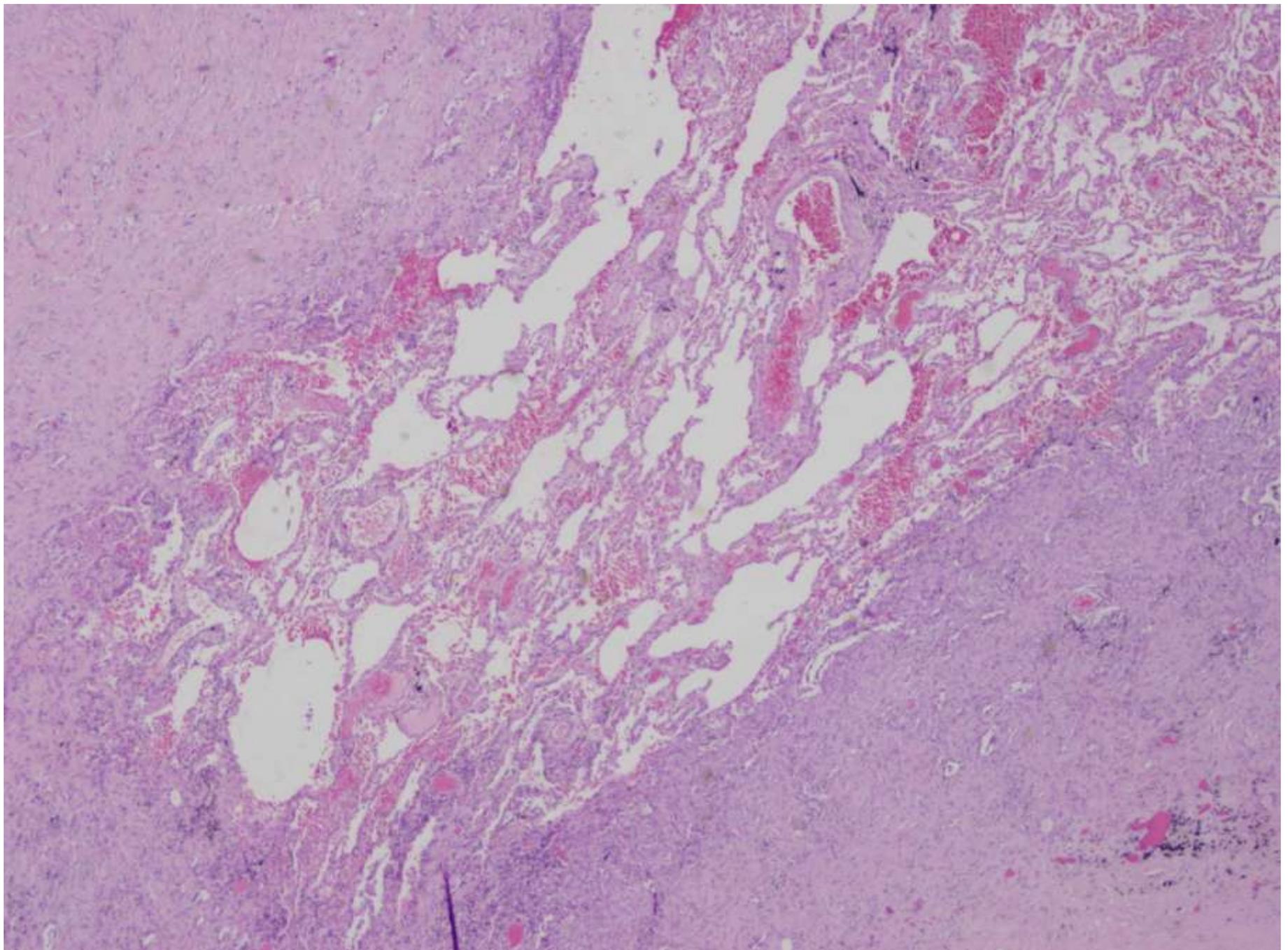












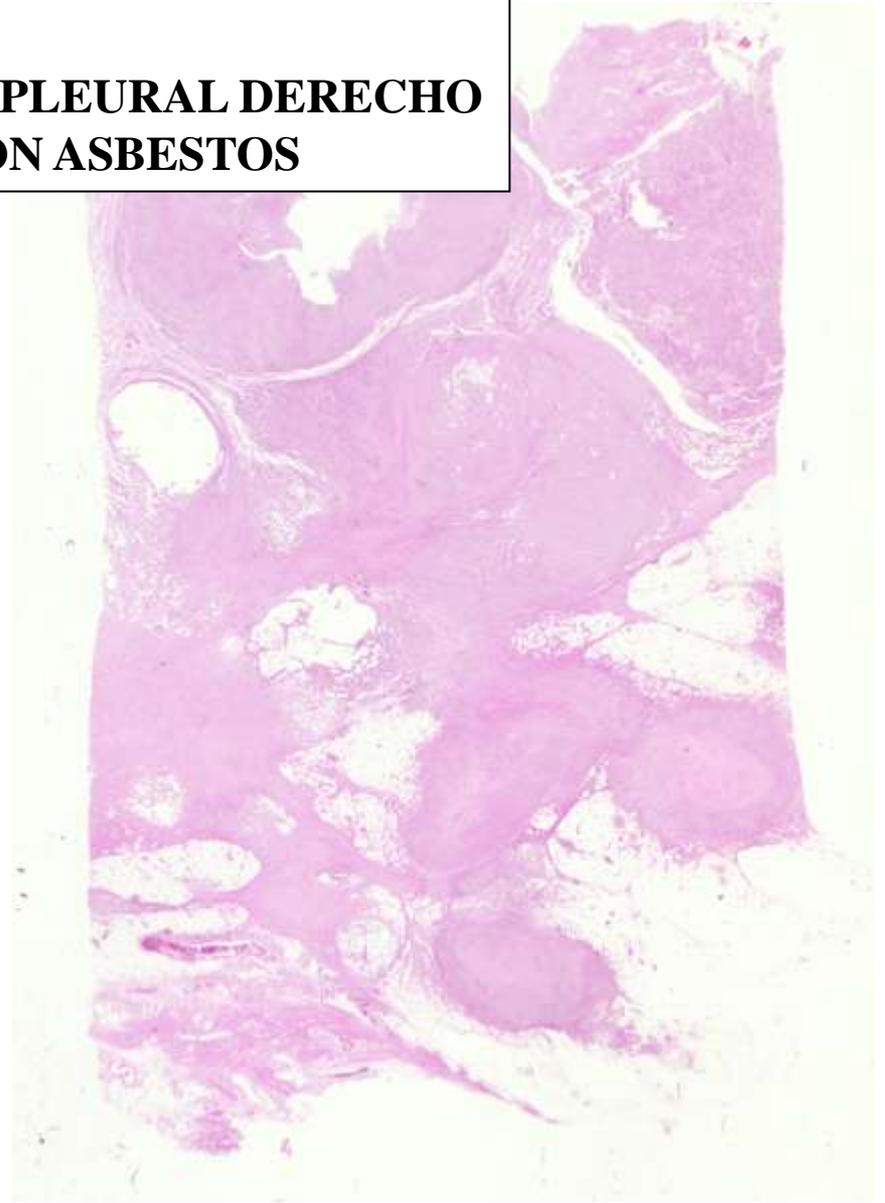
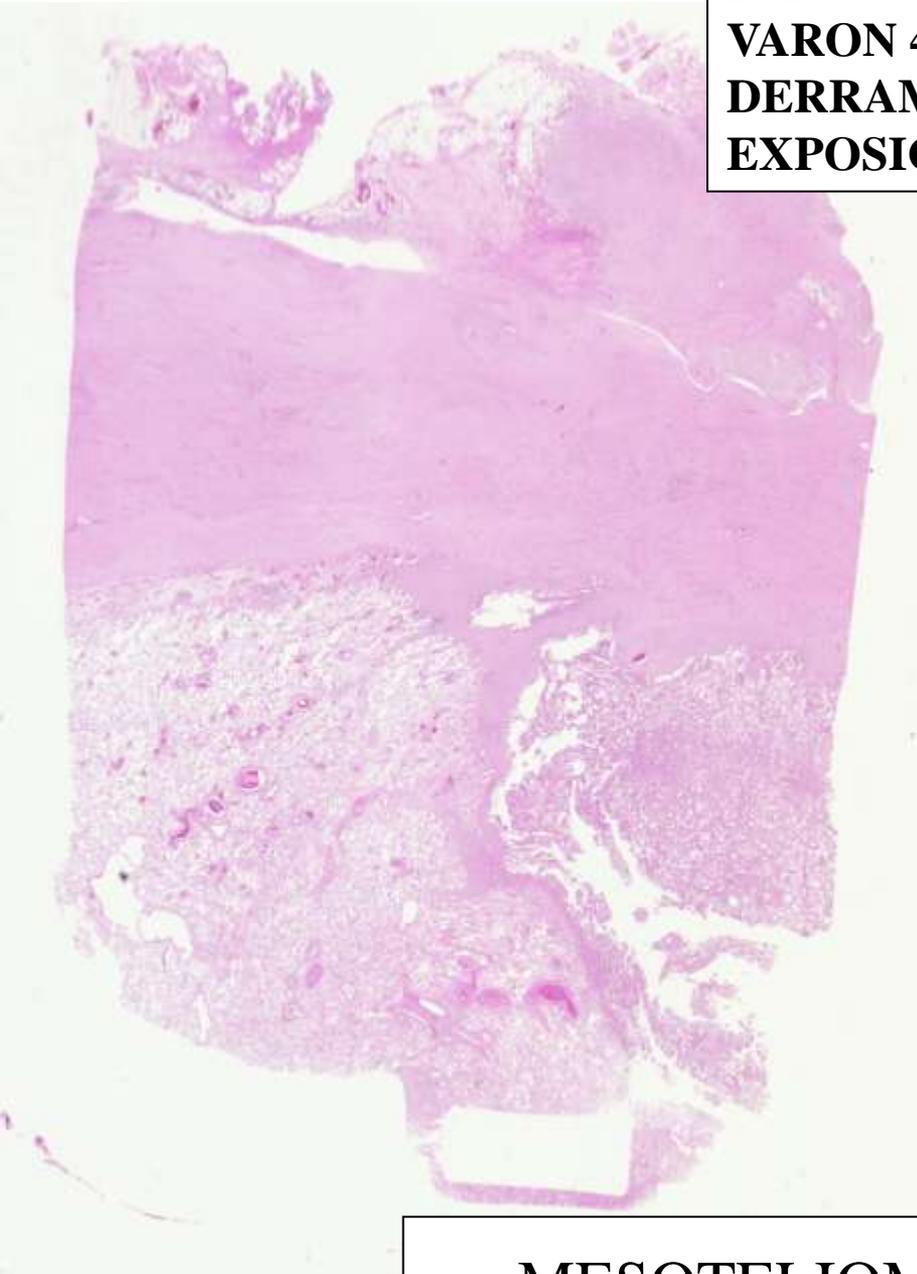


**Detalle monasterio moldavo**

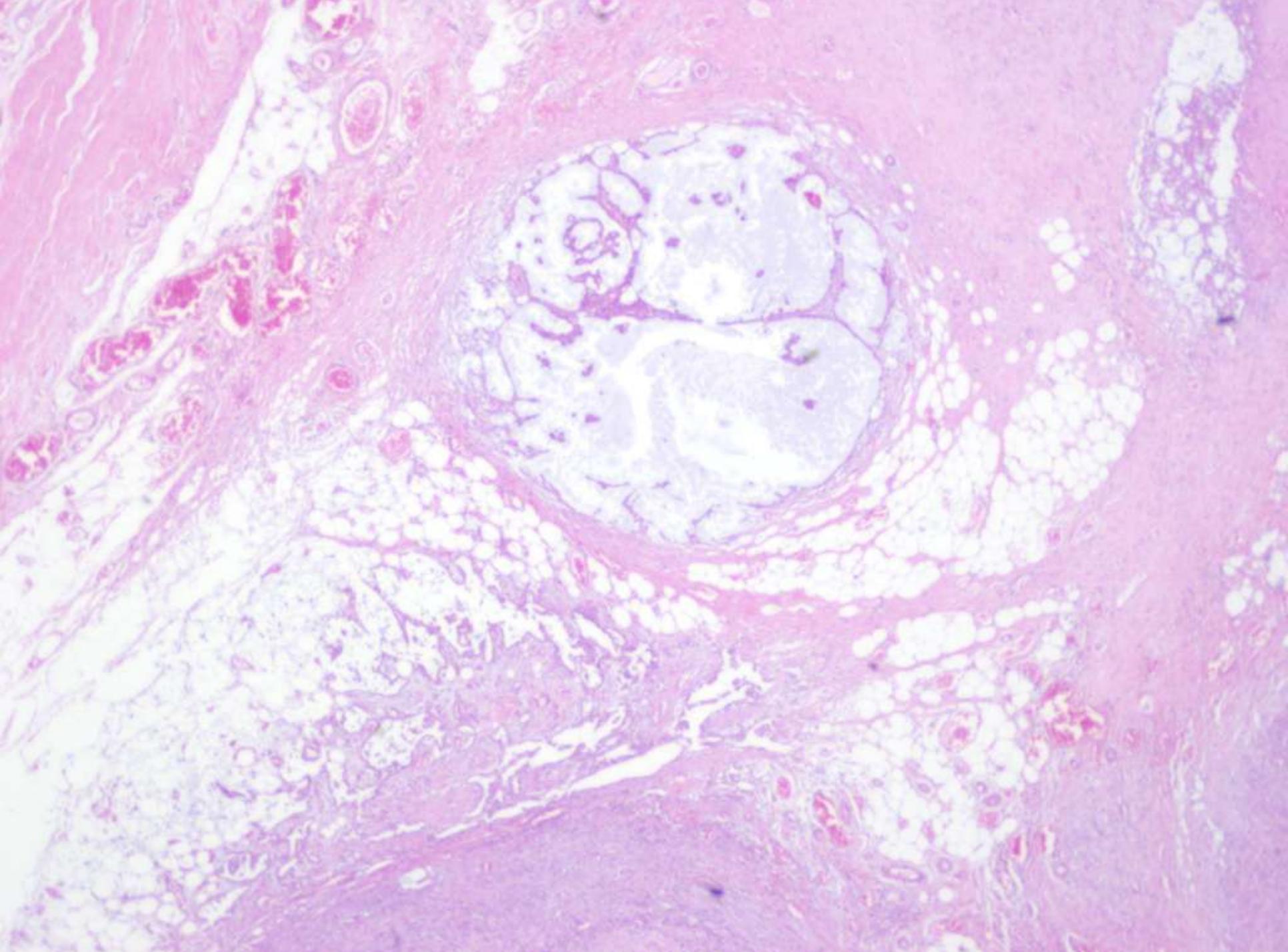
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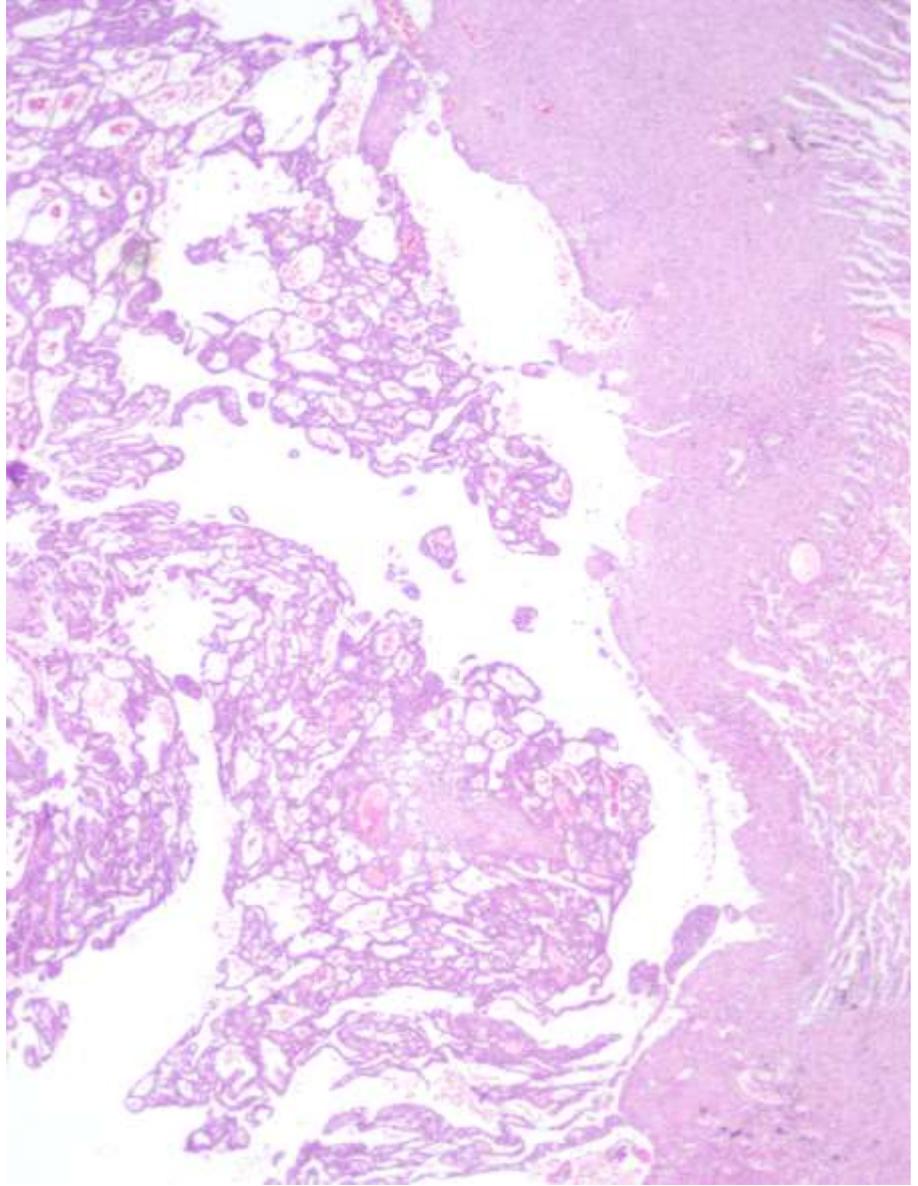
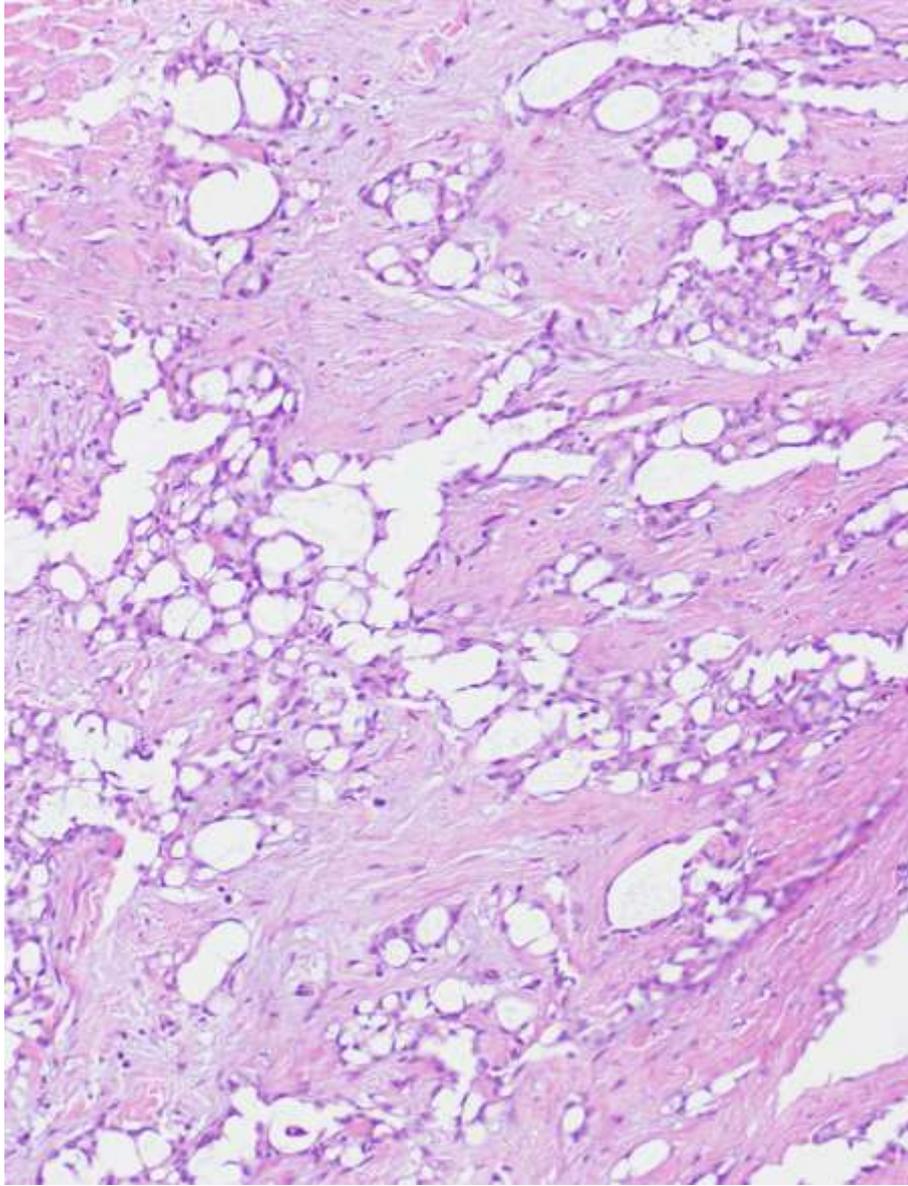
**VARON 47**

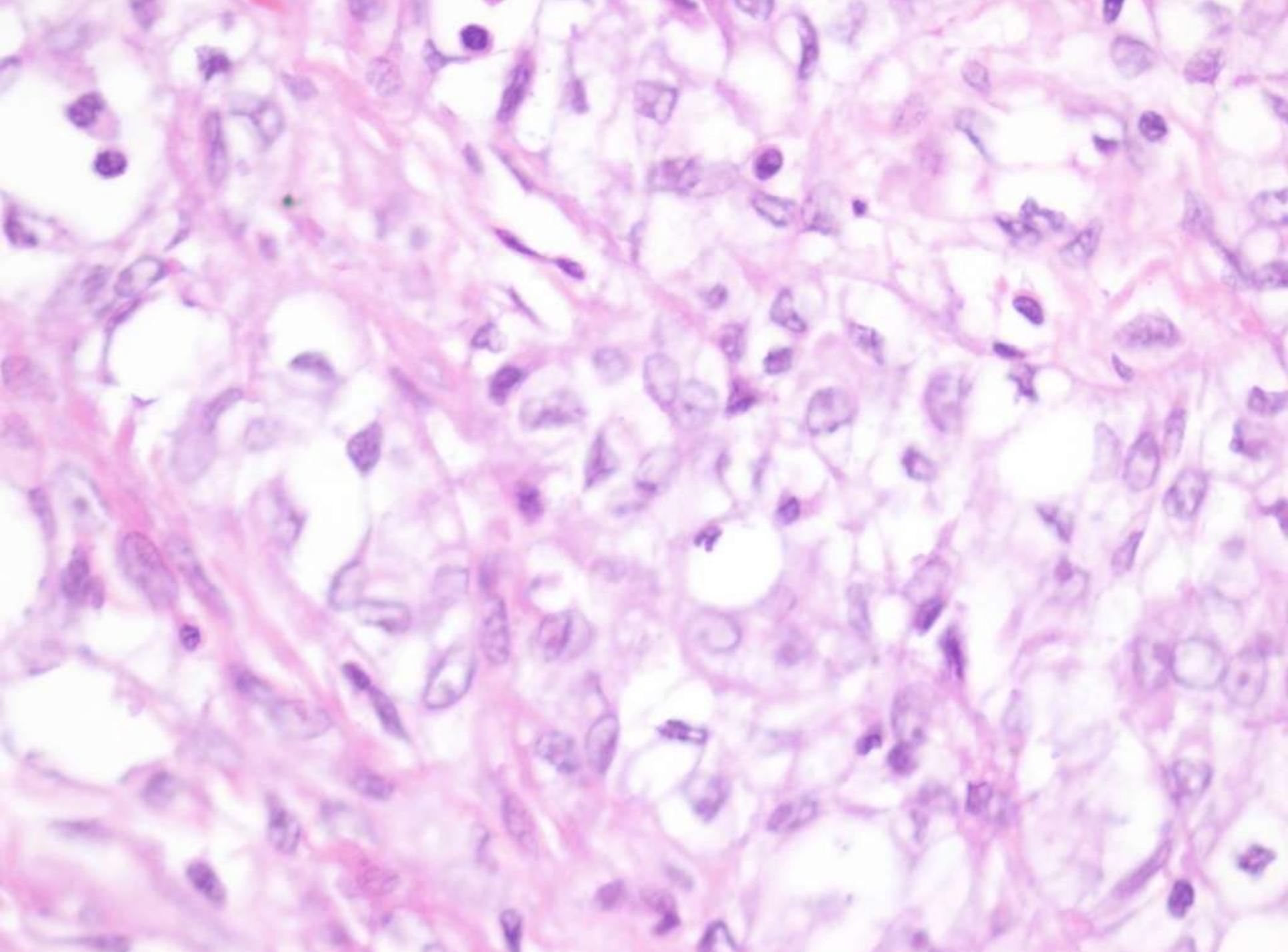
**DERRAME PLEURAL DERECHO  
EXPOSICION ASBESTOS**

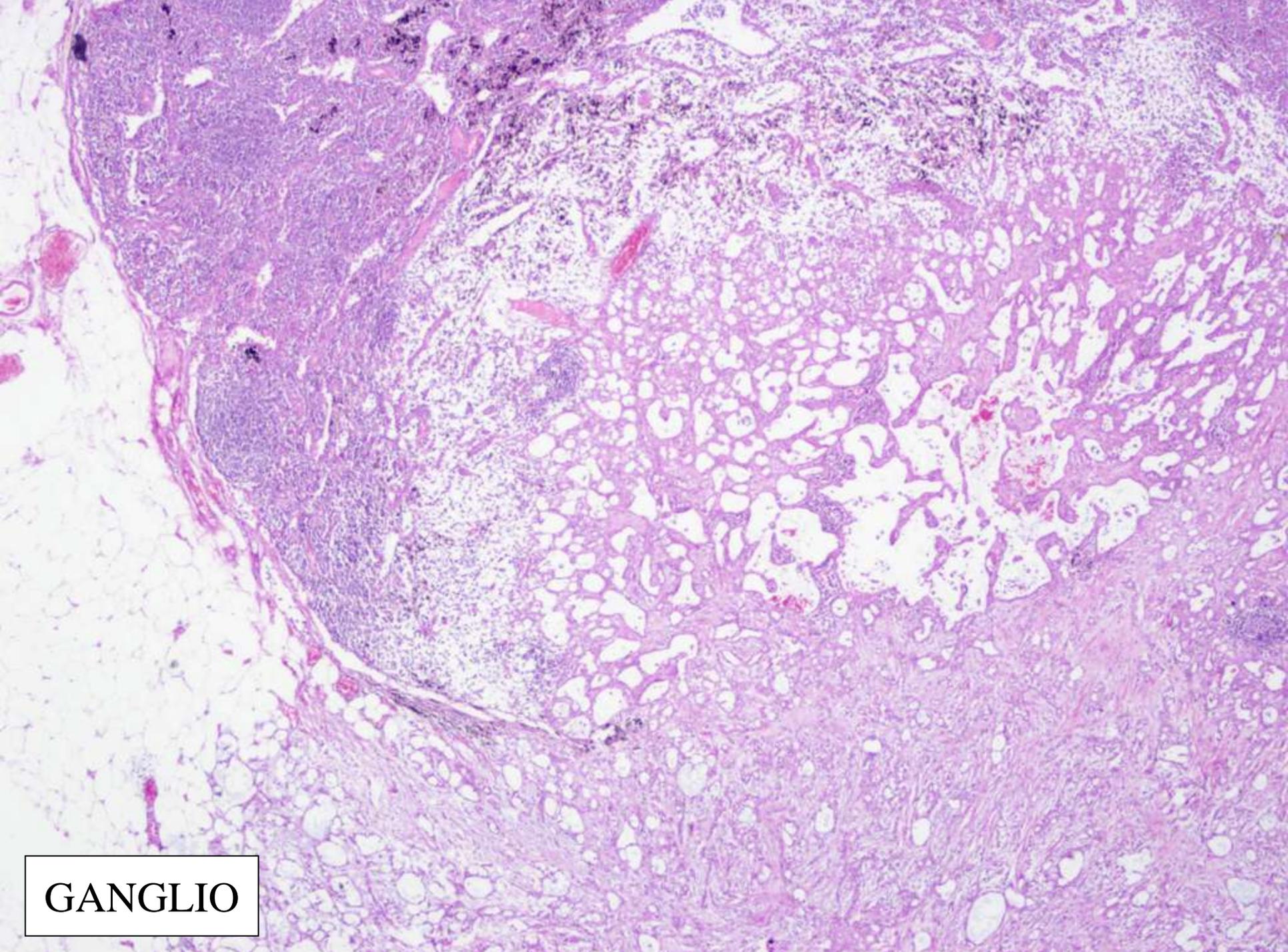


**MESOTELIOMA BIFÁSICO**

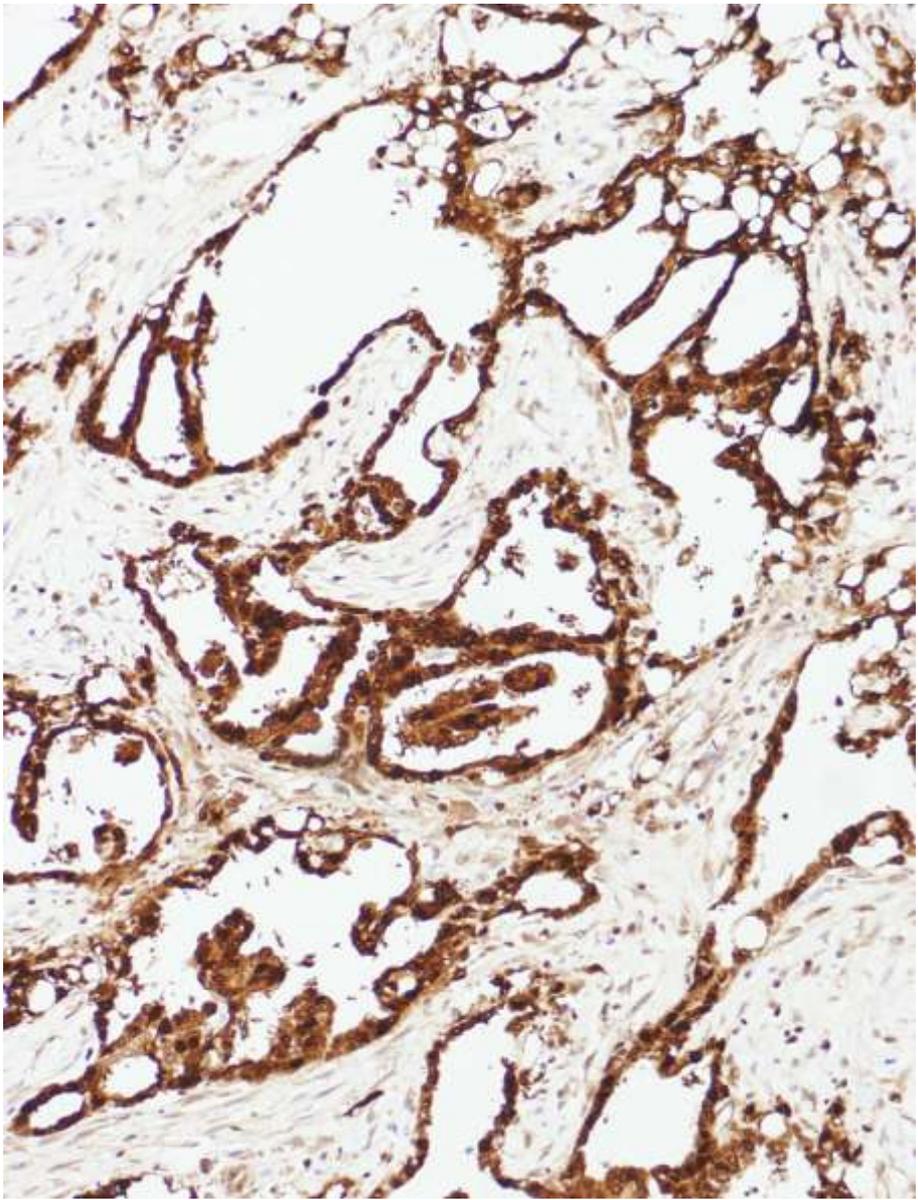




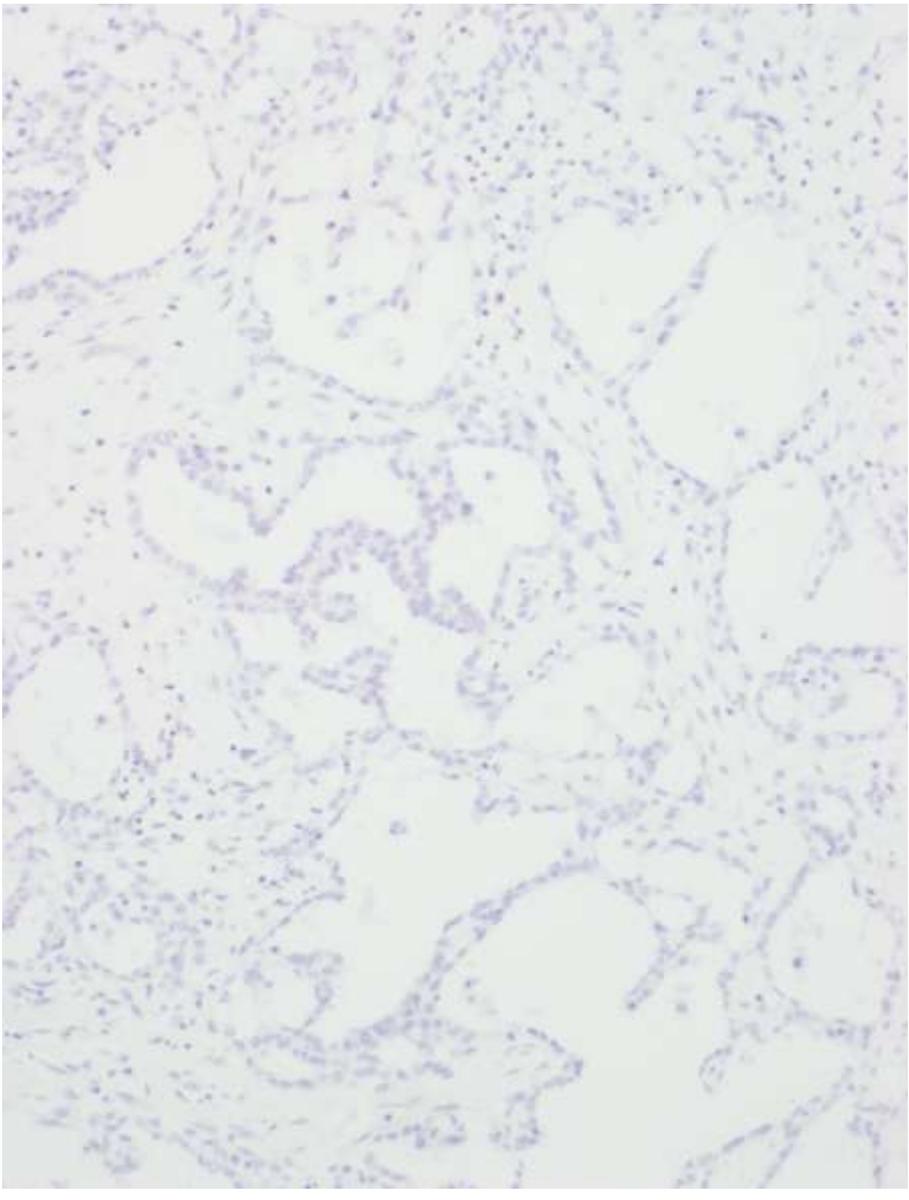




GANGLIO



CALRETININA



CEA -, MOC-31 -, TTF-1 -

# **Survival and Prognostic Factors in Malignant Pleural Mesothelioma: A Retrospective study of 314 patients in the West Part of Japan**

Nojiri S, Gemba K, Aoe K, Kato K, Yamaguchi T, Soto T, Kubota K, Kishimoto T  
Japanese Journal of Clinical Oncology 2001: 41(1);32-39

- **Conclusiones:**

Del estudio de 314 casos de Mesotelioma maligno pleural estudiados buscando posibles factores pronósticos encuentran que algunas condiciones básicas como edad avanzada, mal estado general, así como tipo histológico NO epitelioide, Leucocitosis y elevación de la proteína C reactiva son determinantes de mal pronóstico.

De sus 314 pacientes la supervivencia media fue de 308 días.

# MESOTELIOMA MALIGNO (CHUAC)

## TRATAMIENTO:

- 6 PLEURONEUMONECTOMÍA
- QUIMIO (Pemetrexed + Platino) Y RADIOTERAPIA

## EVOLUCIÓN: MALA

## EXITUS: 31 CASOS

- 20 pacientes en el 1º año, 8 en el 2º , 2 en el 3º , y 1 en el 4º año.

## VIVEN :10 CASOS. (El más antiguo 1 año y 9 meses)



**Monast Voronet. El juicio final**