2 Diciembre 2022

117ª Reunión de la Territorial Valenciana de la SEAP

Tumores de pulmón y pleura. Novedades y revisión de la 5° edición de OMS

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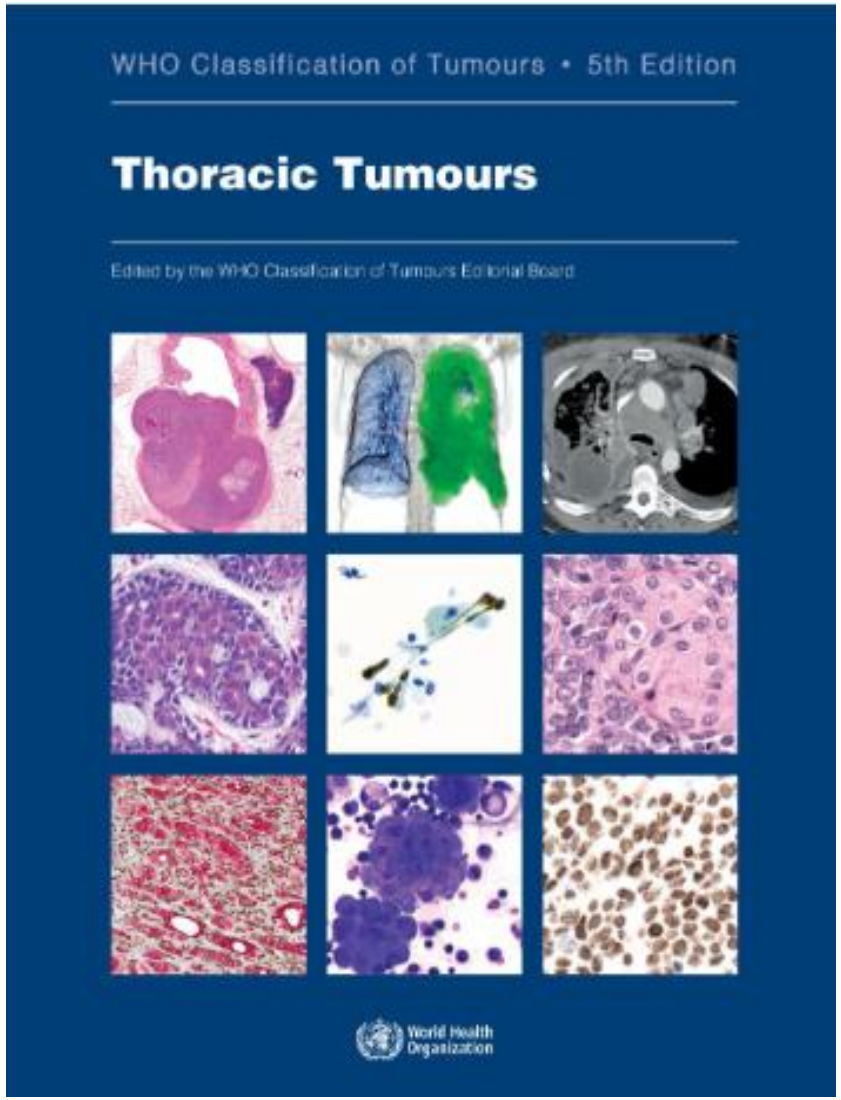


Table 1. Main Chapters in the Fifth Edition (2021) WHO Classification of Thoracic Tumors

1. Tumors of the lung
2. Tumors of the pleura and pericardium
3. Tumors of the heart
4. Mesenchymal tumors of the thorax NEW!
5. Tumors of the thymus
6. Germ cell tumors of the mediastinum NEW!
7. Hematolymphoid tumors of the mediastinum NEW!
8. Ectopic tumors of the thyroid and parathyroid origin NEW!
9. Metastases NEW!
10. Genetic tumor syndromes involving the thorax NEW!

Tsao MS et al. *J Thorac Oncology*. 2022;17:337-340.

Nuevas secciones

Diagnostic molecular pathology

Detection of driver alterations is not necessary for diagnosis.

Essential and desirable diagnostic criteria

Essential:

Circumscribed peribronchiolar lung nodule of papillary and/or flat glandular epithelium A bilayered cellular proliferation of luminal epithelial cells and subjacent basal cells Luminal cells consisting of mainly mucous cells and ciliated cells in proximal-type areas, but mainly type II pneumocytes and club cells in distal-type areas Lack of nuclear atypia and inconspicuous or absent mitoses

Desirable:

p40 and CK5/6 expression in basal layer TTF1-positive luminal cells with more-diffuse staining in distal-type areas and either focal or negative staining in proximal-type areas positive BRAF immunohistochemistry or *BRAF* mutation may be confirmatory in the appropriate morphological context

Novedades en tumores pulmonares

1. Sección únicamente dedicada a la clasificación de la **biopsia diagnóstica pequeña**.
2. Recomendaciones en el uso de porcentajes de los patrones histológicos para determinar el **grado de diferenciación de los adenocarcinomas invasivos no mucinosos.**
3. Reconocimiento de **STAS** (diseminación a través de espacios aéreos) como característica histológica de significado pronóstico.
4. Reconocimiento del **carcinoma linfoepitelial** como carcinoma de células escamosas.
5. **Adenoma bronquiolar/ tumor papilar muconodular ciliado**, nueva entidad dentro del subgrupo de adenomas.
6. **Tumor indiferenciado torácico deficiente en SMARCA4**.
7. **Carcinoma hialinizante de células claras, mioepitelioma y carcinoma mioepitelial**, nuevos subtipos de tumores tipo de glándula salival.
8. Actualización en **clasificación de neoplasias neuroendocrinas pulmonares**.

Biopsia pequeña

Table 2. Guidelines for Good Practice of Small Biopsies and Cytologic Preparations

1. For small biopsies and cytology, NSCC should be further classified into a more specific type, such as ADC or SQCC, whenever possible.
2. The term "non-small cell lung carcinoma-NOS (NSCLC-NOS)" should be used as little as possible, and only when a more specific diagnosis is not possible.
3. When a diagnosis is made in a small biopsy or cytology specimen in conjunction with special studies, it should be clarified whether the diagnosis was established on the basis of light microscopy alone or if special stains were required.
4. The term "non-squamous cell carcinoma (non-SQCC)" should not be used by pathologists in diagnostic reports. This categorization is used by clinicians to define groups of patients whose tumors comprise several histological types and who can be treated in a similar manner; in small biopsies/cytology, pathologists should classify NSCLC as ADC, SQCC, NSCLC-NOS, or other terms.
5. The above-mentioned classification of ADC versus other histologies and the terminology in Table 3 and 4 should be used in routine diagnosis, future research, and clinical trials, to ensure a uniform classification of disease cohorts in relation to tumor subtypes, stratified according to diagnoses made by light microscopy alone versus diagnoses requiring special stains.
6. When paired cytology and biopsy specimens exist, they should be reviewed together to achieve the most specific and concordant diagnosis.
7. The terms AIS and minimally invasive ADC should not be used for diagnosis of small biopsies or cytology specimens. If a noninvasive pattern is present in a small biopsy, it should be referred to as a lepidic growth pattern. Similarly, if a cytology specimen has the attributes of AIS, then the tumor should be diagnosed as an ADC, possibly with a comment that this may represent, at least in part, AIS.
8. The term large cell carcinoma should not be used for diagnosis in small biopsy or cytology specimens and should be restricted to resection specimens where the tumor is thoroughly sampled to exclude a differentiated component.
9. In biopsies of tumors that reveal sarcomatoid features (marked nuclear pleomorphism, malignant giant cells, or spindle cell morphology), these should be initially classified as mentioned previously in relation to ADC; NSCC, favor ADC; SQCC; or NSCC favor SQCC, as this is apt to influence management, with additional statement that giant and/or spindle cell features (depending on what feature) are present. If such features are not present, the term NSCC-NOS should be used, again with comment on the sarcomatoid features.
10. Neuroendocrine immunohistochemical markers should be performed only in cases where there is suspected neuroendocrine morphology.

Reprinted from WHO Classification of Tumours, Thoracic Tumours, 5th Edition. Travis WD, Al Dayel FH, Bubendorf L, Chung JH, Rekhtman N and Scagliotti G. Tumours of the lung. Page 29, IARC, 2021.

ADC, adenocarcinoma; AIS, adenocarcinoma in situ; IARC, International Agency for Research on Cancer; NOS, not otherwise specified; NSCC, nonsmall cell carcinoma; SQCC, squamous cell carcinoma

Nicholson AG et al. *J Thorac Oncology*. 2022;17:362-387.

Table 3. Terminology in Small Biopsy and Cytology Versus Resection Specimens for Adenocarcinoma and Squamous Cell Carcinoma

Morphology/Stains	Terminology for Small Biopsies and Cytology Specimens	Terminology for Resection Specimens
Morphologic squamous cell patterns clearly present	Squamous cell carcinoma	Squamous cell carcinoma
Morphologic adenocarcinoma patterns clearly present		
	Adenocarcinoma (list the patterns in the diagnosis)	Adenocarcinoma Predominant pattern: Lepidic Acinar Papillary Solid Micropapillary
	Adenocarcinoma with lepidic pattern (if pure, list the differential diagnosis on the right and add a comment that an invasive component cannot be excluded)	Minimally invasive adenocarcinoma, adenocarcinoma in situ, or an invasive adenocarcinoma with a lepidic component
	Invasive mucinous adenocarcinoma (list the patterns; use the term "mucinous adenocarcinoma with lepidic pattern" if pure lepidic pattern and mention the differential diagnosis listed on the right)	Invasive mucinous adenocarcinoma
		Minimally invasive adenocarcinoma or adenocarcinoma in situ, mucinous type
	Adenocarcinoma with colloid features	Colloid adenocarcinoma
	Adenocarcinoma with fetal features	Fetal adenocarcinoma
	Adenocarcinoma with enteric features[a]	Enteric adenocarcinoma
Morphologic squamous cell patterns not present, but supported by stains (i.e., p40+)	Nonsmall cell carcinoma, favor squamous cell carcinoma[b]	Squamous cell carcinoma (nonkeratinizing pattern may be a component of the tumor)[b]
Morphologic adenocarcinoma patterns not present, but supported by special stains (i.e., TTF1+)	Nonsmall cell carcinoma, favor adenocarcinoma[b]	Adenocarcinoma (solid pattern may be just one component of the tumor)[b]
No clear adenocarcinoma, squamous, or neuroendocrine morphology or staining pattern	Nonsmall cell carcinoma NOS[a,c]	Large cell carcinoma

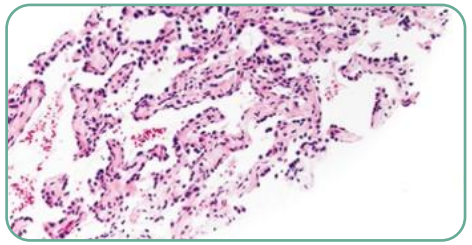
Nicholson AG et al. *J Thorac Oncology*. 2022;17:362-387.

Table 4. Terminology for Small Biopsies and Cytology Versus Resection Specimens for Small Cell Carcinoma, Large Cell Neuroendocrine Carcinoma, Adenosquamous Carcinoma, and Pleomorphic Carcinoma

Terminology for Small Biopsies and Cytology Specimens	Terminology for Resection Specimens
Small cell carcinoma	Small cell carcinoma
Nonsmall cell carcinoma with neuroendocrine morphology and positive neuroendocrine markers, possible large cell neuroendocrine carcinoma	Large cell neuroendocrine carcinoma
Morphologic squamous cell and adenocarcinoma patterns both present: nonsmall cell carcinoma-NOS Comment that adenocarcinoma and squamous components are present, and that this could represent adenosquamous carcinoma	Adenosquamous carcinoma (if both components ≥10%)
Morphologic squamous cell or adenocarcinoma patterns not present, but immunohistochemical stains favor separate squamous and adenocarcinoma components: nonsmall cell carcinoma-NOS Specify the results of the immunohistochemical stains and the interpretation, and comment that this could represent adenosquamous carcinoma, but that diagnosis requires a resection specimen	Adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma, or large cell carcinoma with unclear immunohistochemical features
Nonsmall cell carcinoma with spindle cell and/or giant cell carcinoma Mention if adenocarcinoma or squamous carcinoma is present. Comment that this could represent a pleomorphic carcinoma; however, that diagnosis requires a resection specimen.	Pleomorphic, spindle cell, and/or giant cell carcinoma

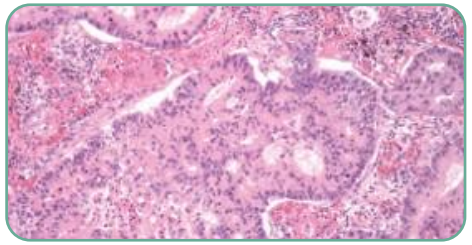
Nicholson AG et al. *J Thorac Oncology*. 2022;17:362-387.

Adenocarcinoma invasivo no mucinoso



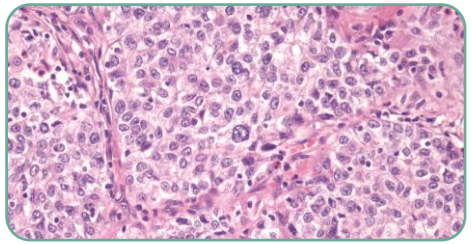
Grado 1 - Bien diferenciado

- Patrón **lepídico** predominante con **< 20% de patrón de alto grado**



Grado 2 – Moderadamente diferenciado

- Predominio de patrón **acinar** o **papilar** con **< 20% de patrón de alto grado**



Grado 3 – Pobremente diferenciado

- Cualquier tumor con **> 20% de patrón de alto grado** (sólido, micropapilar, cribiforme o patrón glandular complejo).

STAS

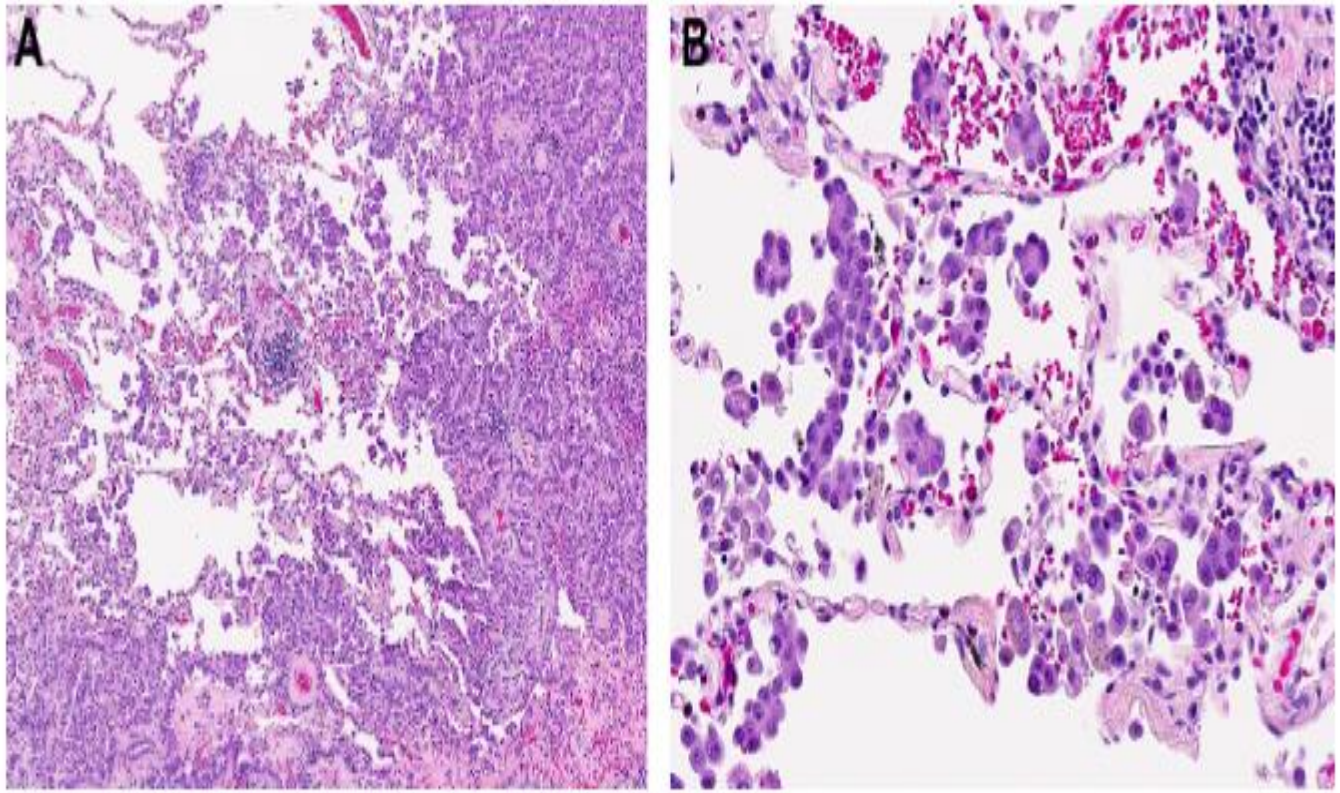


Figure 5. Tumor STAS. (*A*) This adenocarcinoma has tumor cells in airspaces beyond the edge of the main tumor, a feature associated with poor prognosis. (*B*) At high power, the atypical morphology distinguishes the cells from alveolar macrophages. STAS, spread through air spaces.

No confundir con :

Grupos tumorales en el borde tumoral

Neumocitos o células bronquiales con características citológicas benignas y/o cilios

Fragmentos de pared alveolar

Nicholson AG et al. *J Thorac Oncology*. 2022;17:362-387.

Carcinoma linfoepitelial

- En la 4° edición estaba en grupo “otros y carcinomas inclasificables”
- Tipo de carcinoma de células escamosas

Essential and desirable diagnostic criteria

Essential:

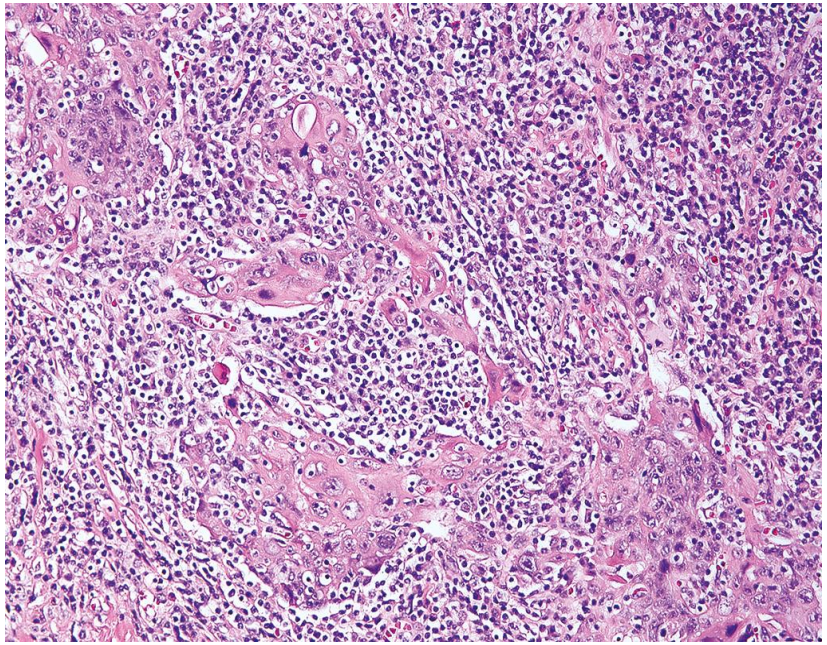
Non-keratinizing SCC with syncytial-appearing tumour cells, vesicular nuclei, and distinct nucleoli

Lymphoplasmacytic infiltrate between and within tumour islands

Exclusion of metastatic nasopharyngeal carcinoma clinically

Desirable:

EBER in situ hybridization positive in EBV-associated tumours, but negative in EBV-independent tumours



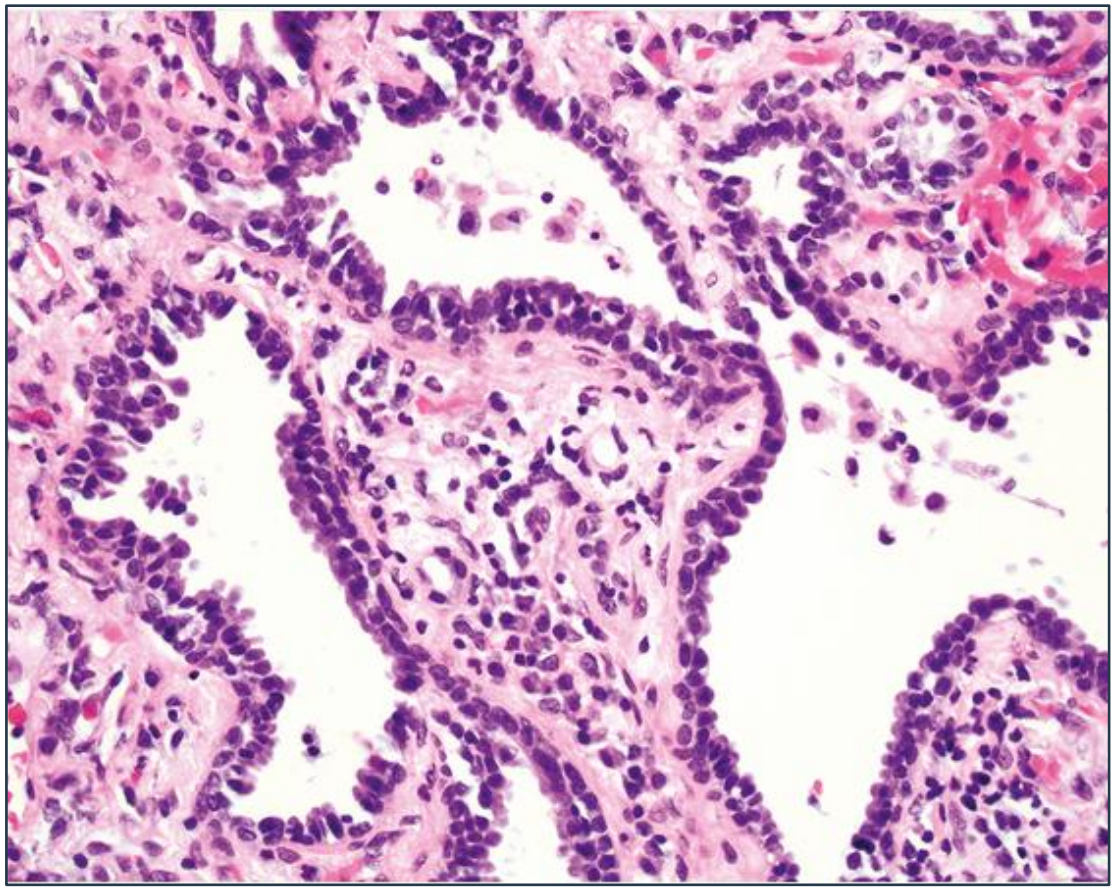
Adenoma bronquiolar (tumor papilar muconodular ciliado)

Localización:
Periférico, peribronquiolar

Clínica:
Hallazgo incidental.

Patogénesis:

Mutaciones en BRAF (más frec.), EGFR, KRAS, HRAS y ALK.

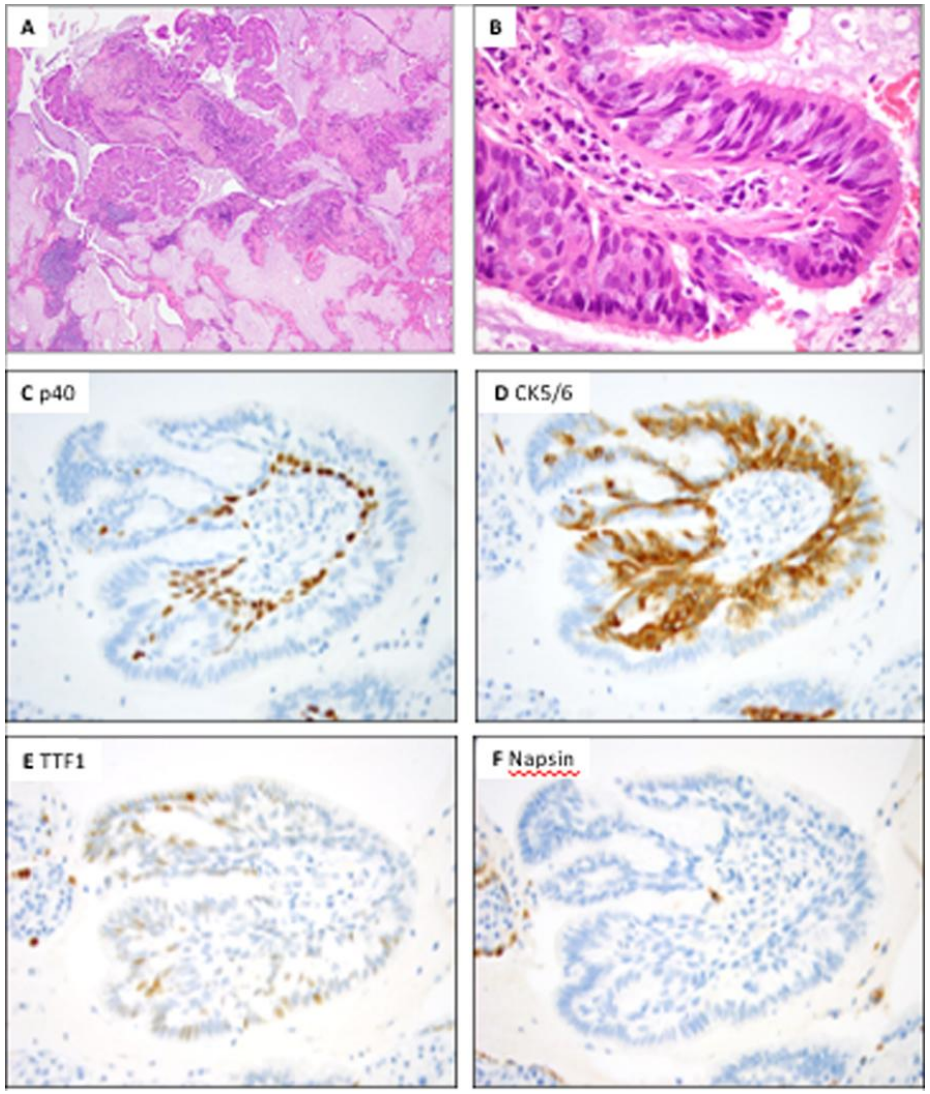


Subtipos histológicos:
-Tipo proximal o CMPT clásico

- Tipo distal o CMPT no clásico

Diagnóstico diferencial:
-ADC in situ
-Papilomas
-Metaplasia peribronquiolar

Adenoma bronquiolar tipo proximal



Células luminales:

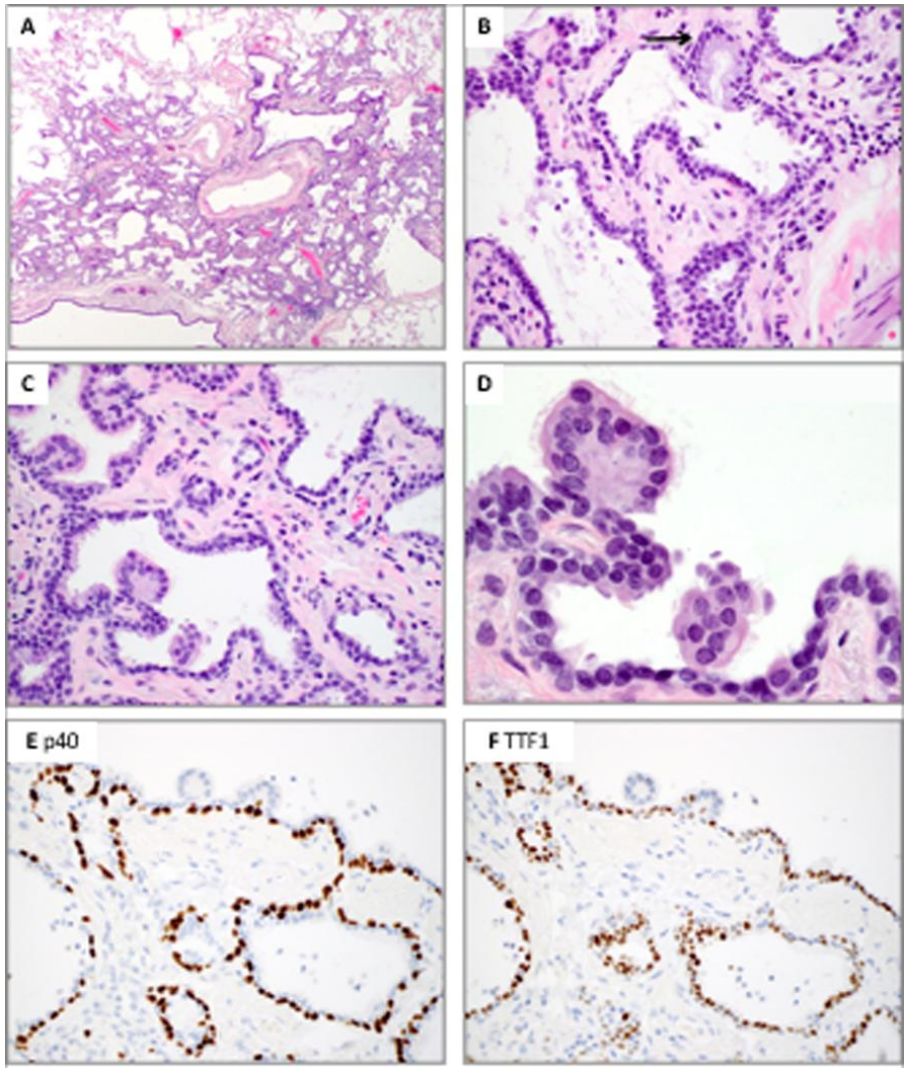
-Arquitectura papilar o plana

-Mucosecretoras y ciliadas

-Expresión de TTF-1 focal o son negativas

Chang JC et al. Am J Surg Pathol. 2018 Aug; 42(8): 1010–1026

Adenoma bronquiolar tipo distal



Células luminales:

-Arquitectura plana

-Cuboidales tipo neumocitos tipo II y células Clara

-Expresión difusa de TTF-1

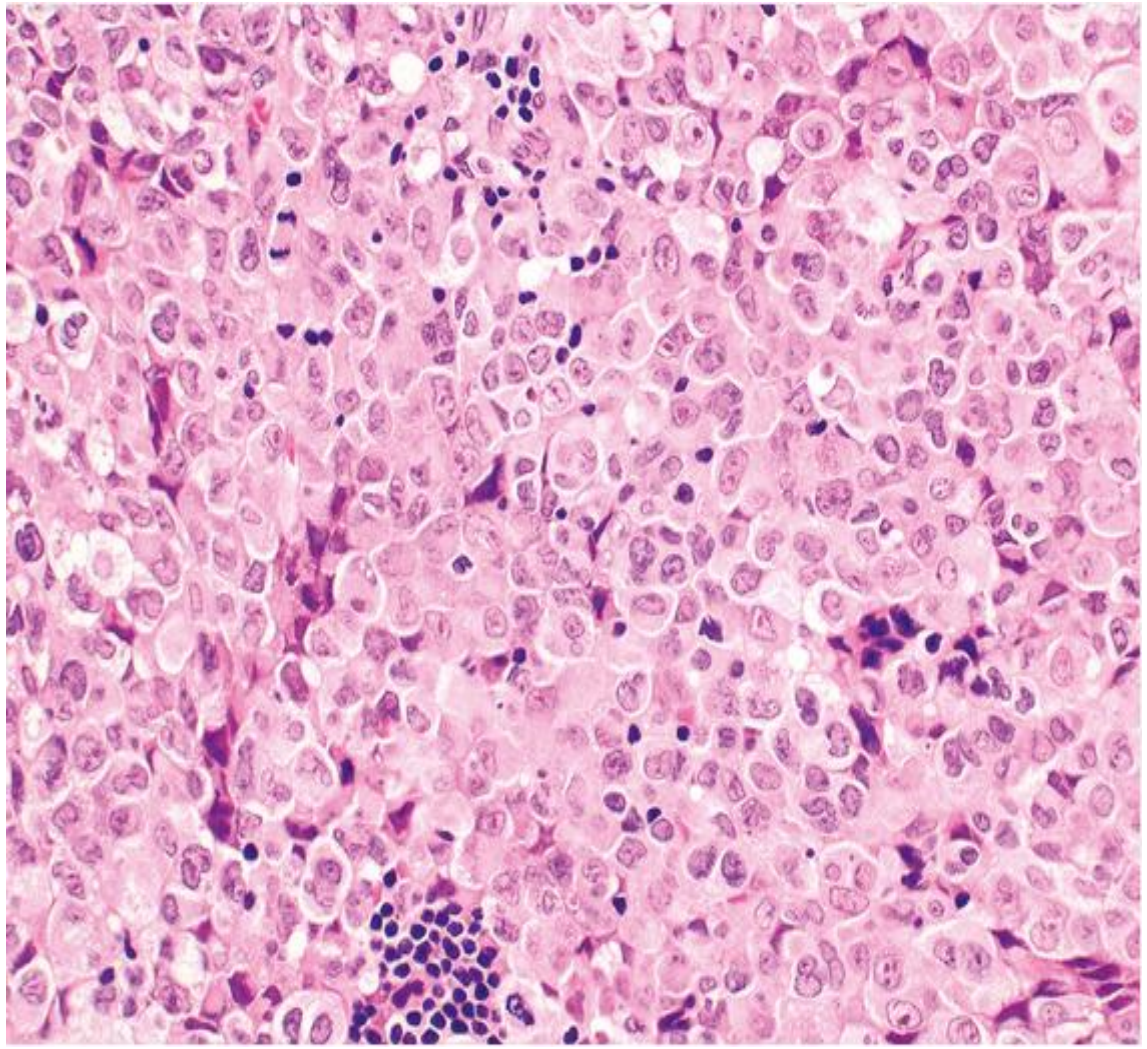
Chang JC et al. Am J Surg Pathol. 2018 Aug; 42(8): 1010–1026

Tumor indiferenciado torácico SMARCA4 deficiente

Localización:
Mediastino, hilio pulmonar, pulmón y/o pleura con/sin invasión de pared torácica

Clínica:
Metastásico al diagnóstico

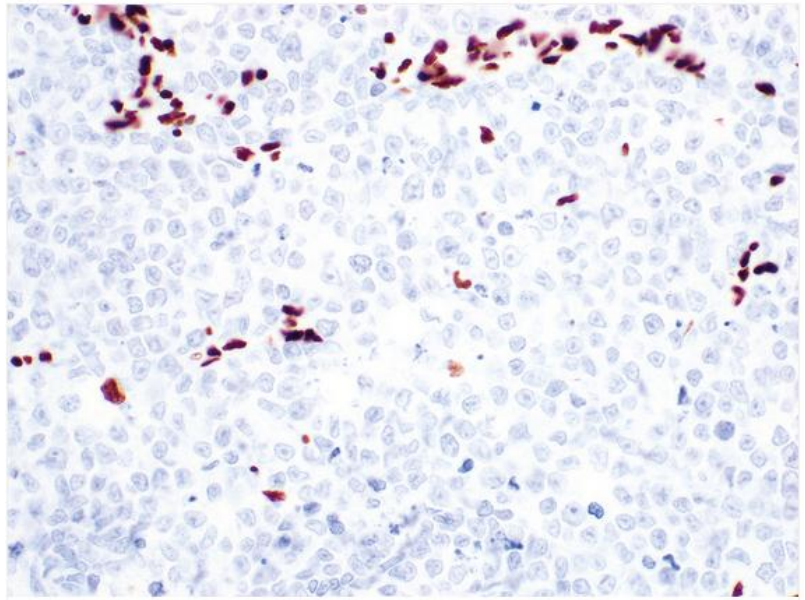
Epidemiología:
-Predominio en hombres
-Media 48 años
-Fumadores



Patogénesis:
Inactivación bialélica de SMARCA-4 y también de TP53

Diagnóstico diferencial:
-Linfoma
-Carcinoma NUT
-Tumores germinales
-Ca. Neuroendocrino de cel. Grandes
-Melanoma
-Sarcomas

Tumor indiferenciado torácico SMARCA4 deficiente



Perfil IHQ:

-Pérdida completa de expresión de SMARCA-4 (BRG1).
-Expresión de CD34, SOX-2, SALL-4 y sinaptofisina.
-Expresión focal o ausencia de expresión de CK, claudina-4, TTF-1, p63, p40 o WT1
-Expresión de INI1 conservada
-Sobreexpresión de p53

Essential and desirable diagnostic criteria

Essential:

- Tumour in adults, with significant thoracic involvement
- Diffuse sheets of variably discohesive, round to epithelioid, relatively monotonous cells with vesicular nuclei and prominent nucleoli
- No clear evidence of epithelial differentiation (except juxtaposed carcinoma in combined cases)
- SMARCA4 (BRG1) deficiency by immunohistochemistry

Desirable:

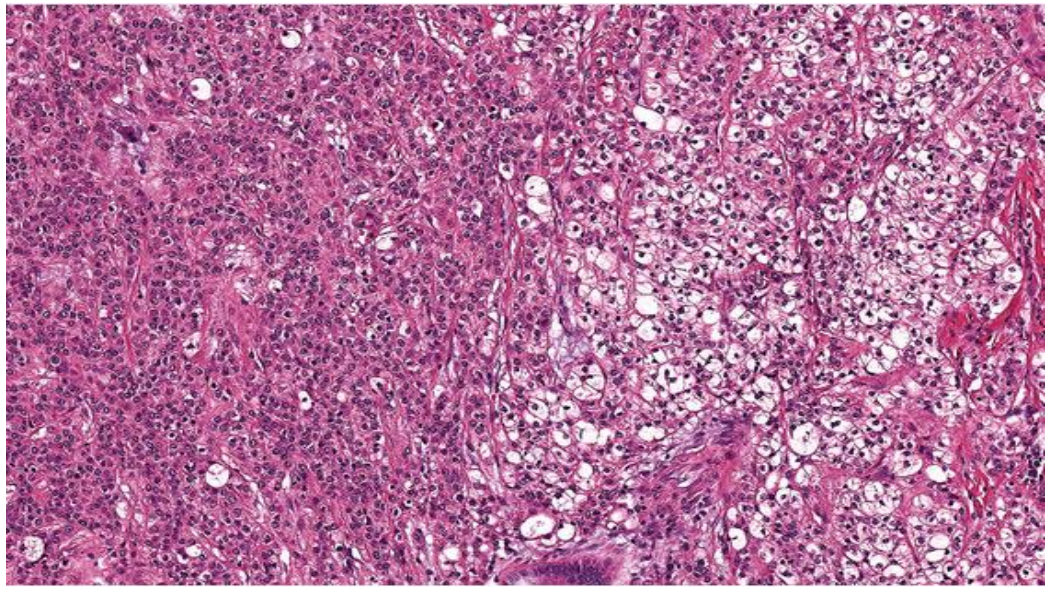
- SMARCA2 (BRM) deficiency by immunohistochemistry
- Expression of CD34, SOX2, and/or SALL4
- Absent or focal claudin-4 expression

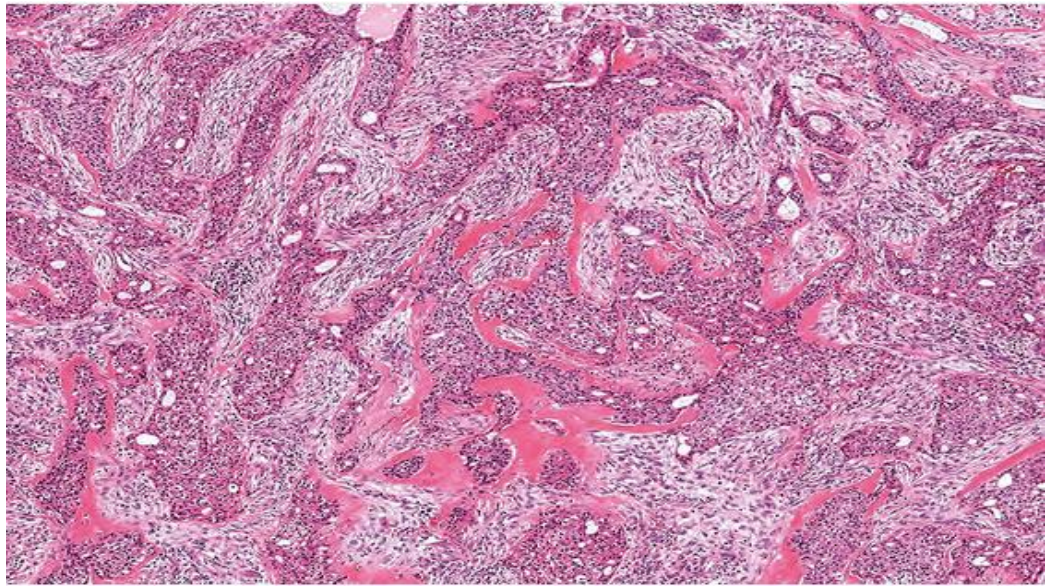
Carcinoma hialinizante de células claras

Localización:
Endobronquial

Epidemiología:
-Leve predominio en mujeres.
-Rango de edad 30-66 años

Clínica:
Síntomas obstructivos, tos y disnea





Perfil IHQ:
+ : CK7, CK34bE12, CK5/6, p63 y p40

+/- : EMA, CAM 5.2, CK19 y CK14

- : TTF-1, napsina A, CK20, S100, SMA, sinaptofisina y cromogranina

Molecular:
Fusión de EWSR1 – ATF1

Neoplasias neuroendocrinas pulmonares

Major clinicopathological features of lung neuroendocrine tumours

	Typical carcinoid	Atypical carcinoid	LCNEC	SCLC
Average age	Sixth decade	Sixth decade	Seventh decade	Seventh decade
Sex predominance	Female	Female	Male	Male
Diagnostic criteria				
Mitoses per 2 mm^2	< 2	2–10	> 10 (median: 70)	> 10 (median: 80)
Necrosis	No	Focal, if any	Yes	Yes
Neuroendocrine morphology	Yes	Yes	Yes	Yes
Ki-67 proliferation index	Up to 5%	Up to 30%	30–100%	30–100%
TTF1 expression	Mostly positive in peripheral, mostly negative in central tumours	Mostly positive in peripheral, mostly negative in central tumours	Positive (70%)	Positive (85%)
p40 expression	Negative	Negative	Negative	Negative
Combined with NSCC component	No	No	Up to 25% of resected LCNEC	Up to 25% of resected SCLC

LCNEC, large cell neuroendocrine carcinoma; NSCC, non-small cell carcinoma; SCLC, small cell lung carcinoma.

Bajo grado

Grado intermedio

Alto grado

NET grado 1

NET grado 2

NEC grado 3

Carcinoide NOS

Se debe usar cuando **no es posible distinguir carcinoide típico de carcinoide atípico**.

1. Biopsia pequeña o citología
2. Carcinoides metastásicos
3. Sección no representativa del tumor resecado (casos consulta)

Se debe especificar **índice mitótico**, presencia o no de **necrosis** y si es posible el índice de **Ki67**.

Novedades en tumores pleurales

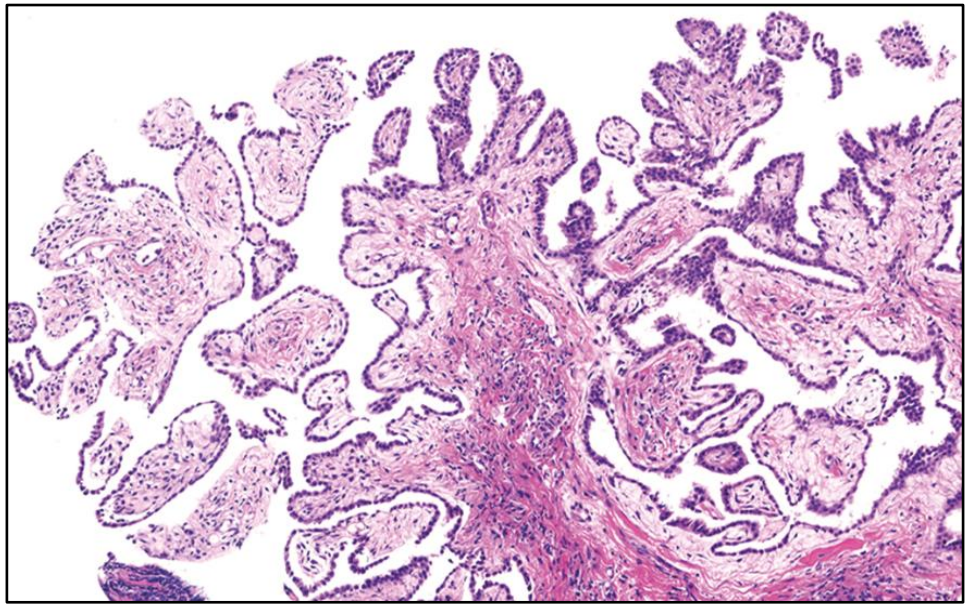
1. Tumores pleurales y pericárdicos en el mismo capítulo.
2. Mesotelioma papilar bien diferenciado pasa a llamarse **Tumor mesotelial papilar bien diferenciado**.
3. **Mesotelioma** ~~maligno~~ **localizado y difuso**.
4. **Mesotelioma in situ**.
5. Incorporación de **patrón arquitectural** y **características citológicas y estromales**.
6. Incorporación del **grado nuclear** en el mesotelioma epiteloide difuso.
7. Mesotelioma bifásico se puede diagnosticar en biopsia pequeña.

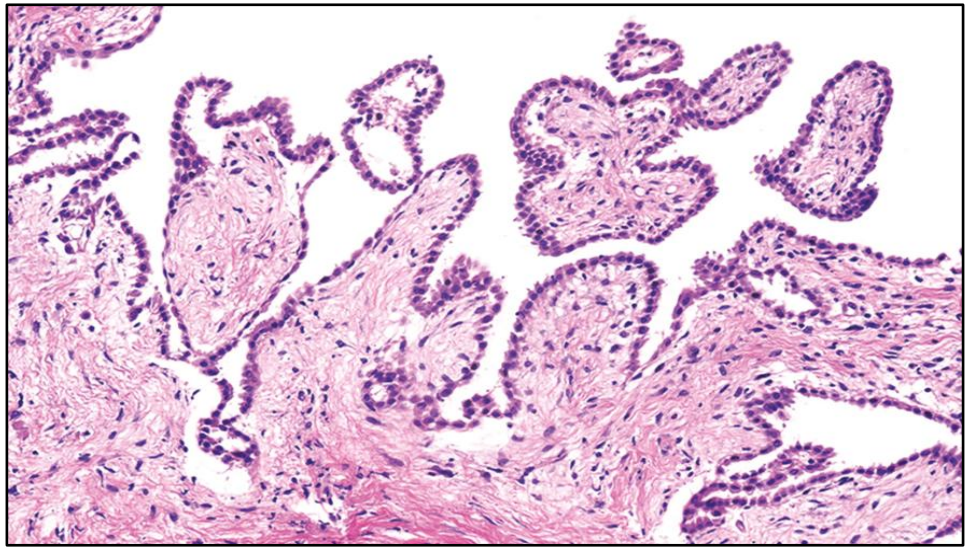
Tumor mesotelial papilar bien diferenciado

Clínica:

-Disnea

-Derrame pleural unilateral recurrente





Macroscopía:

-Masa arborescente

-Múltiples nódulos <10 mm.

IHQ y molecular:

-No hay pérdida de expresión BAP1

-No deleción homocigota de CDKN2A.

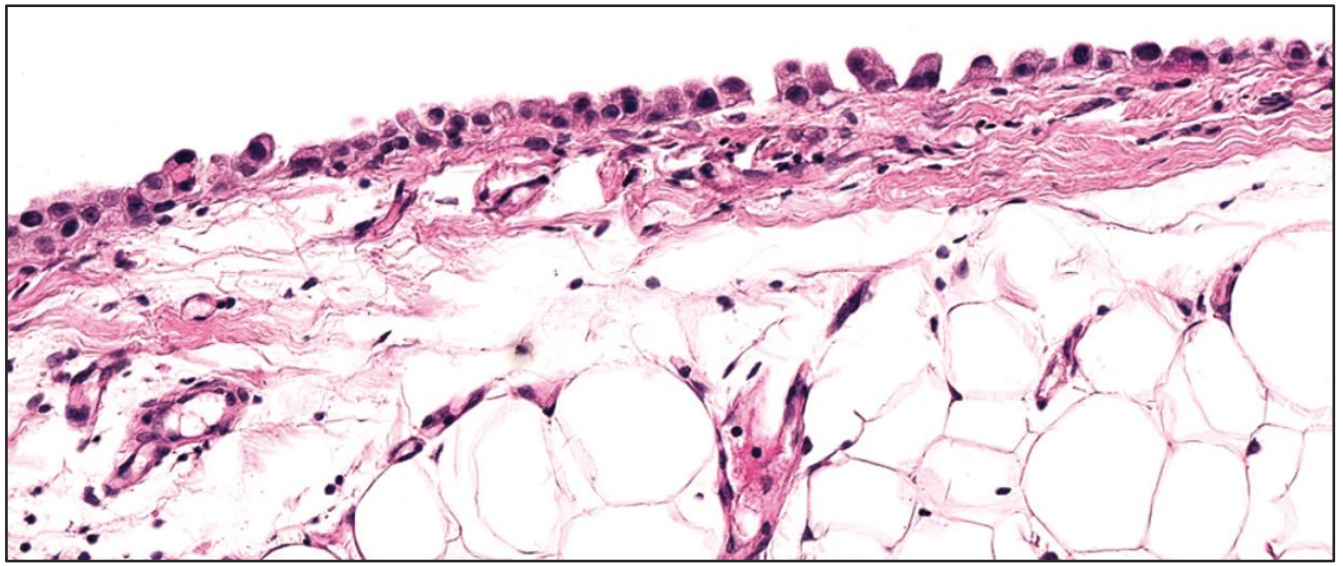
Diagnóstico diferencial:

-Hiperplasia mesotelial con pleuritis reactiva

-Mesotelioma epiteloide difuso con patrón papilar de bajo grado

Mesotelioma in situ

Clínica:
-Derrame pleural recurrente
-Antecedente de exposición a asbesto, irradiación o predisposición familiar.



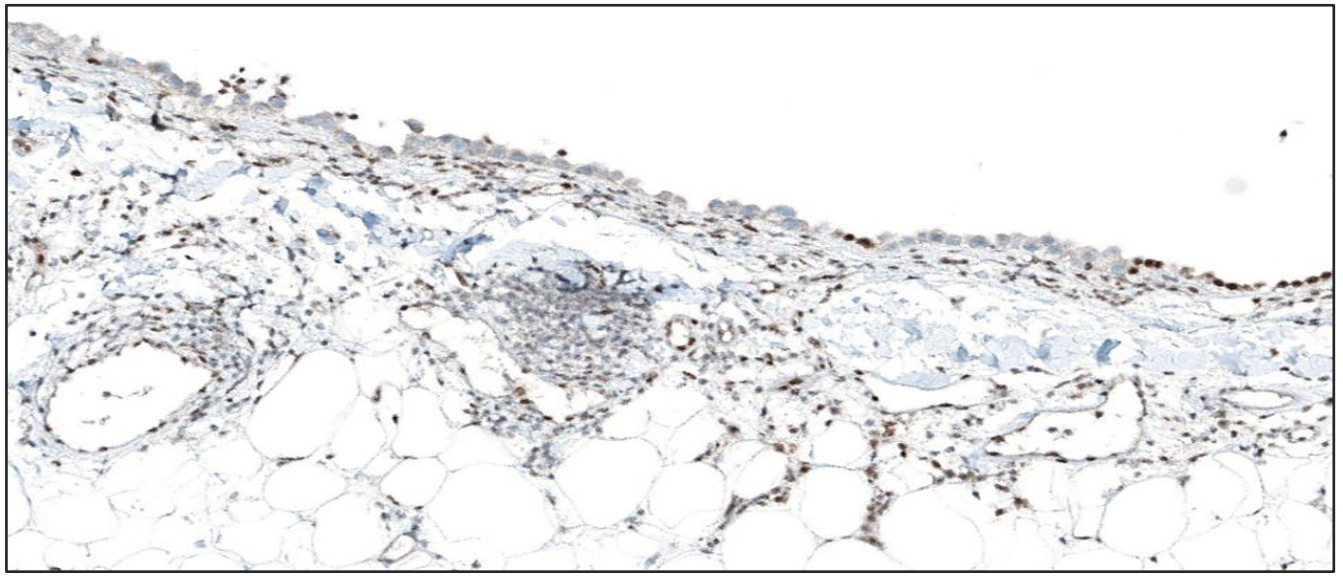
Ausencia de masas en pruebas de imagen y toracoscopia.

Diagnóstico multidisciplinar clínico, radiológico y anatomopatológico

IHQ y molecular:

-Pérdida de expresión de BAP1 y/o MTAP.

-Deleción homocigota de CDKN2A por FISH.

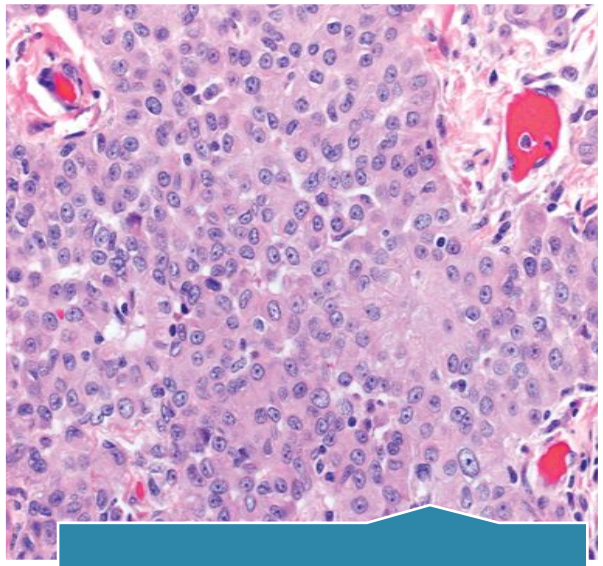


Diagnóstico Diferencial:

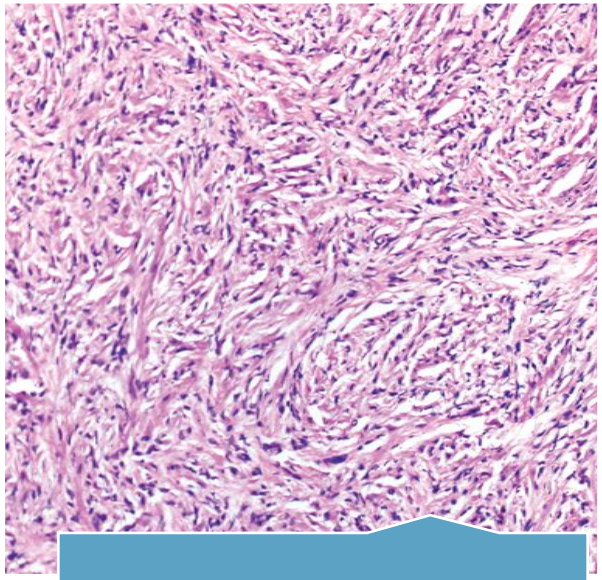
-Proliferación mesotelial reactiva

-T. Mesotelial papilar bien diferenciado

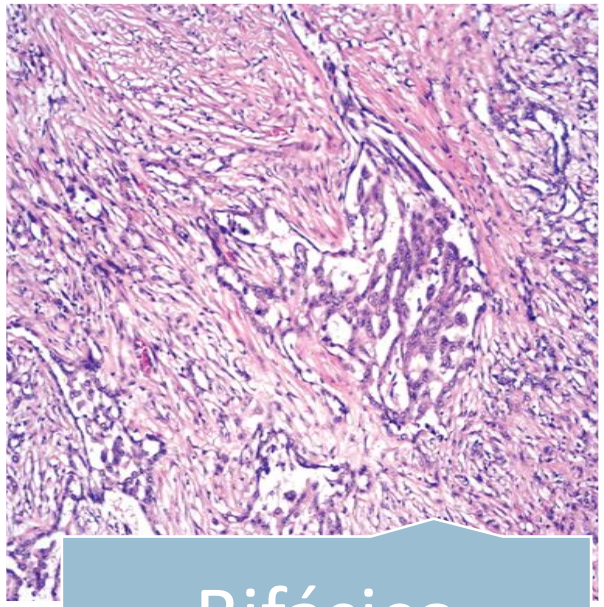
Mesotelioma difuso



Epiteloide



Sarcomatoide



Bifásico

Table 3. 2021 World Health Organization Classification of Diffuse Pleural Mesothelioma

Type	Description	Features/Patterns	Favorable	Unfavorable	Reporting
Epithelioid mesothelioma	Composed of round, epithelioid cells, usually with cohesive architecture, but single cells within a fibrous stroma may also be seen	**Architectural patterns:** Tubulopapillary Trabecular Adenomatoid Solid Micropapillary **Cytologic features:** Rhabdoid Deciduoid[a] Small cell[a] Clear cell[a] Signet ring[a] Lymphohistiocytoid Pleomorphic **Stromal features:** Myxoid	**Architectural patterns:** Tubulopapillary Trabecular Adenomatoid **Cytologic features:** Lymphohistiocytoid Low nuclear grade[b] **Stromal features:** Myxoid (if predominant, i.e., when ≥50% of tumor with <50% solid pattern contains myxoid stroma)	**Architectural patterns:** Solid (≥50%) Micropapillary **Cytologic features:** Rhabdoid Pleomorphic High nuclear grade[b] **Necrosis** (included in grading)	Grade (high or low), architectural patterns present (and in definitive resection specimens, such as EPD and EPP, percentages of each pattern; for all other specimens, indicate "with … patterns/features")
Sarcomatoid mesothelioma, including desmoplastic pattern	Composed of elongated/spindle cells (>2 times longer than wide) arranged in solid sheets or within a fibrous stroma	**Cytologic features:** Lymphohistiocytoid Transitional Pleomorphic **Stromal features:** Desmoplastic With heterologous differentiation	**Cytologic features:** Lymphohistiocytoid	**Cytologic features:** Transitional	
Biphasic mesothelioma	Composed of both epithelioid and sarcomatoid components (in definitive resection specimens, namely EPD and EPP, ≥10% of each component is required for diagnosis); for smaller samples, including biopsy and cytology specimens, the diagnosis of biphasic mesothelioma can be rendered regardless of percentages of each component present				Percentage of sarcomatoid component should be reported regardless of specimen type

[a]These cytologic features carry no prognostic significance but are important to recognize to avoid misdiagnosis with other entities in the differential diagnosis.
[b]See Table 4 for nuclear grading.
EPD, extended pleurectomy/decortication; EPP, extrapleural pneumonectomy.
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Sauter JL et al. *J Thorac Oncology*. 2022;17:608-622

Type	Description	Features/Patterns	Favorable	Unfavorable	Reporting
Epithelioid mesothelioma	Composed of round, epithelioid cells, usually with cohesive architecture, but single cells within a fibrous stroma may also be seen	**Architectural patterns:** Tubulopapillary Trabecular Adenomatoid Solid Micropapillary **Cytologic features:** Rhabdoid Deciduoid[a] Small cell[a] Clear cell[a] Signet ring[a] Lymphohistiocytoid Pleomorphic **Stromal features:** Myxoid	**Architectural patterns:** Tubulopapillary Trabecular Adenomatoid **Cytologic features:** Lymphohistiocytoid Low nuclear grade[b] **Stromal features:** Myxoid (if predominant, i.e., when ≥50% of tumor with <50% solid pattern contains myxoid stroma)	**Architectural patterns:** Solid (≥50%) Micropapillary **Cytologic features:** Rhabdoid Pleomorphic High nuclear grade[b] **Necrosis** (included in grading)	Grade (high or low), architectural patterns present (and in definitive resection specimens, such as EPD and EPP, percentages of each pattern; for all other specimens, indicate "with … patterns/features")

Sarcomatoid mesothelioma, including desmoplastic pattern	Composed of elongated/spindle cells (>2 times longer than wide) arranged in solid sheets or within a fibrous stroma	**Cytologic features:** Lymphohistiocytoid ← Transitional Pleomorphic ← **Stromal features:** Desmoplastic With heterologous differentiation	**Cytologic features:** Lymphohistiocytoid	**Cytologic features:** Transitional	
Biphasic mesothelioma	Composed of both epithelioid and sarcomatoid components (in definitive resection specimens, namely EPD and EPP, ≥10% of each component is required for diagnosis); for smaller samples, including biopsy and cytology specimens, the diagnosis of biphasic mesothelioma can be rendered regardless of percentages of each component present				Percentage of sarcomatoid component should be reported regardless of specimen type

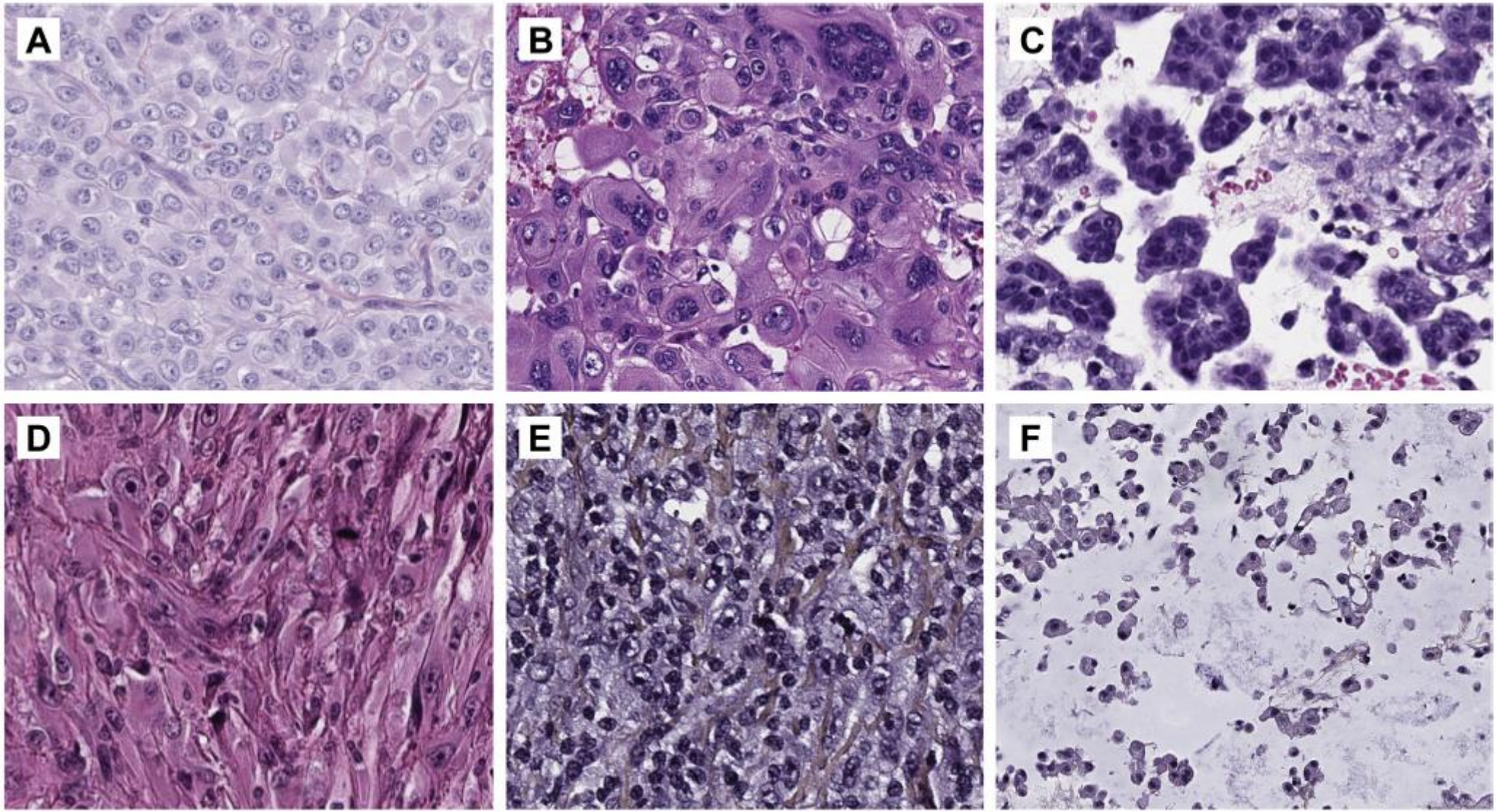

Figure 3. Poor prognostic histologic features in epithelioid diffuse pleural mesothelioma include (*A*) solid architectural pattern, (*B*) pleomorphic cytologic features, and (*C*) micropapillary architectural pattern. Pleural mesotheliomas with (*D*) transitional cytologic features are now classified as sarcomatoid mesothelioma because transitional cytologic features are associated with worse prognosis than epithelioid and biphasic mesothelioma. Pleural mesotheliomas with (*E*) lymphohistiocytoid cytologic features can be classified as epithelioid or sarcomatoid mesothelioma, and the presence of lymphohistiocytoid cytologic features is associated with better prognosis when seen in an otherwise sarcomatoid mesothelioma. The presence of (*F*) abundant myxoid stroma in more than or equal to 50% of an epithelioid mesothelioma with less than 50% solid pattern is associated with better prognosis.

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Mesotelioma pleural difuso epiteloide – grado nuclear

Atipia nuclear

- 1 – leve
- 2 – moderada
- 3 - severa

Índice mitótico

- 1- bajo (≤ 1 mitosis/ 2mm²)
- 2 -intermedio (2-4 mitosis/2mm²)
- 3 -alto (≥ 5 mitosis/2mm²)

Suma

- 2 o 3 = grado nuclear I
- 4 o 5 = grado nuclear II
- 6 = grado nuclear III

Necrosis

- Presente
- Ausente

Grado nuclear

- Bajo
  - Grado nuclear I y II sin necrosis
- Alto
  - Grado nuclear III con o sin necrosis
  - Grado nuclear II con necrosis

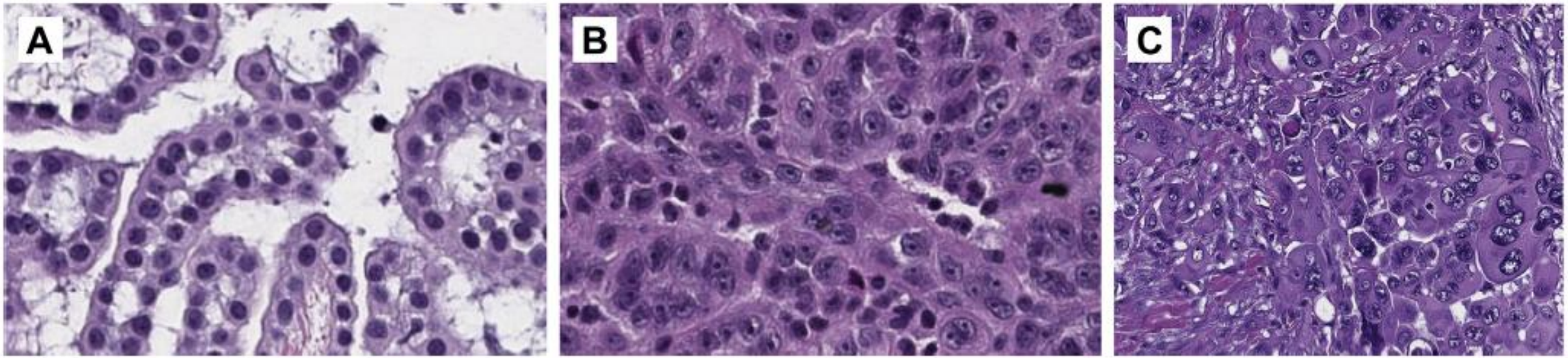

Figure 4. The 2021 WHO two-tiered nuclear grading incorporates nuclear atypia. Examples of diffuse pleural mesothelioma with nuclear atypia scores of (*A*) mild, 1; (*B*) moderate, 2; and (*C*) severe, 3, are found.

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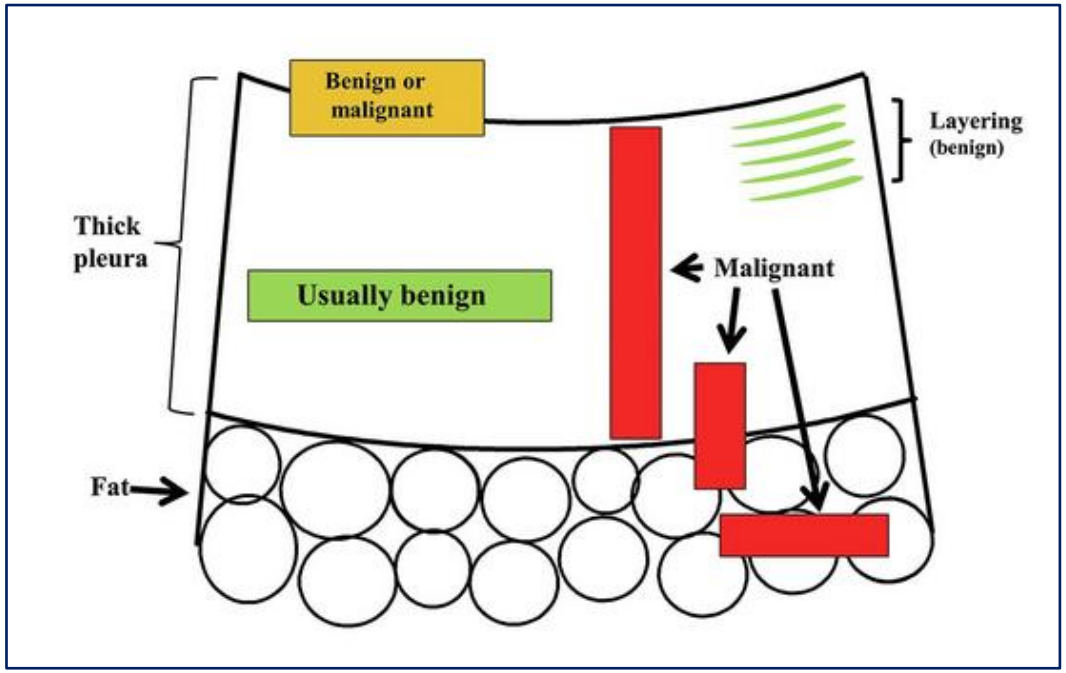
Table 5. Examples of Pathology Reporting a Diffuse Pleural Mesothelioma in Biopsy and Resection Specimens (i.e., Extended Pleurectomy/Extrapleural Pneumonectomy)

Specimens
Small specimens (i.e. biopsy and cytology specimens):
Tumor site, specimen type: Histologic type (epithelioid, biphasic,[a] or sarcomatoid; if desmoplastic features are present, include "with desmoplastic features") High/low grade (use only for epithelioid) List all architectural patterns (do not give a percentage) and any cytologic or stromal features present (do not give a percentage)
Example of a pathology report for a biopsy specimen:
Pleura (biopsy): epithelioid mesothelioma, high grade. Solid pattern and with rhabdoid cytologic features
Resection specimens (i.e., extended pleurectomy/extrapleural pneumonectomy):
Tumor site, specimen type: Histologic type (epithelioid, biphasic,[a] or sarcomatoid/desmoplastic) High/low grade (use only for epithelioid) List all architectural patterns present (give a predominant pattern and percentages for each pattern listed) and any cytologic and/or stromal features present Staging[b]
Example of a pathology report for a resection specimen:
Extended pleurectomy: Epithelioid mesothelioma, high grade. Predominantly tubulopapillary pattern (80%), also with micropapillary pattern (20%) and pleomorphic features (20%). AJCC[b] stage (eighth edition): pT1pN0

Adapted with permission from Nicholson et al.[20]

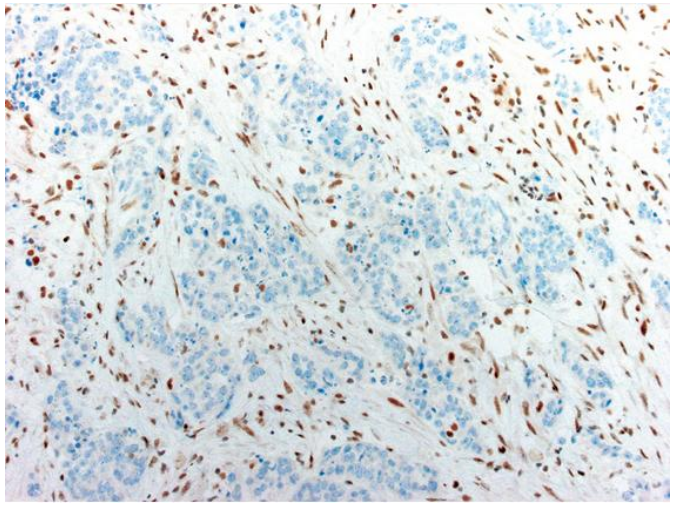
[a]When a diagnosis of biphasic mesothelioma is made, a comment should be included to indicate the percentage of sarcomatoid component present.
[b]Using the TNM staging system.
AJCC, American Joint Committee on Cancer.

Mesotelioma vs. Proliferación mesotelial reactiva

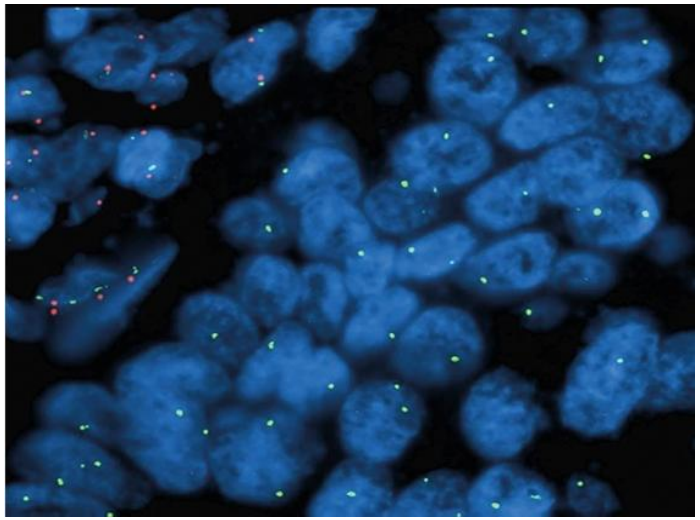


MESOTELIOMA

- Pérdida de expresión nuclear de **BAP1** por IHQ (+ frecuente en M. Epiteloides)
- **Deleción homocigota de CDKN2A** (9p21 / p16) por FISH (+frecuente en M. Sarcomatoides)
- Pérdida de expresión citoplasmática de MTAP por IHQ
- Sobreexpresión de EZH2 por IHQ



BAP1



FISH
CDKN2A

IASLC

Journal of Thoracic Oncology

Introduction to 2021 WHO Classification of Thoracic Tumors

Ming-Sound Tsao, MD,[a,*] Andrew G. Nicholson, DM,[b,c] Joseph J. Maleszewski, MD,[d] Alexander Marx, MD,[e] William D. Travis, MD[f]

The 2021 WHO Classification of Lung Tumors: Impact of Advances Since 2015

Andrew G. Nicholson, DM,[a,*] Ming S. Tsao, MD,[b] Mary Beth Beasley, MD,[c] Alain C. Borczuk, MD,[d] Elisabeth Brambilla, MD,[e] Wendy A. Cooper, PhD,[f] Sanja Dacic, MD,[g] Deepali Jain, MD,[h] Keith M. Kerr, MD,[i] Sylvie Lantuejoul, PhD,[e,j] Masayuki Noguchi, MD,[k] Mauro Papotti, MD,[l] Natasha Rekhtman, MD,[m] Giorgio Scagliotti, PhD,[l] Paul van Schil, PhD,[n] Lynette Sholl, MD,[o] Yasushi Yatabe, PhD,[p] Akihiko Yoshida, PhD,[p] William D. Travis, MD[m]

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]

The 2021 WHO Classification of Tumors of the Thymus and Mediastinum: What Is New in Thymic Epithelial, Germ Cell, and Mesenchymal Tumors?

Alexander Marx, MD,[a,*] John K. C. Chan, MD,[b] Lara Chalabreysse, MD,[c] Sanja Dacic, MD, PhD,[d] Frank Detterbeck, MD,[e] Christopher A. French, MD,[f] Jason L. Hornick, MD, PhD,[g] Hiroshi Inagaki, MD, PhD,[h] Deepali Jain, MD,[i] Alexander J. Lazar, MD, PhD,[j] Mirella Marino, MD,[k] Edith M. Marom, MD,[l] Andre L. Moreira, MD, PhD,[m] Andrew G. Nicholson, MD,[n] Masayuki Noguchi, MD,[o] Daisuke Nonaka, MD,[p] Mauro G. Papotti, MD,[q] Stefan Porubsky, MD,[r] Lynette M. Sholl, MD,[s] Hisashi Tateyama, MD,[t] Vincent Thomas de Montpréville, MD,[u] William D. Travis, MD,[v] Arun Rajan, MD,[w] Anja C. Roden, MD,[x] Philipp Ströbel, MD[y]

The 2021 WHO Classification of Tumors of the Heart

Joseph J. Maleszewski, MD,[a,b,*] Cristina Basso, MD,[c] Melanie C. Bois, MD,[a] Carolyn Glass, MD,[d] Kyle W. Klarich, MD,[b] Charles Leduc, MD,[e] Robert F. Padera, MD, PhD,[f] Fabio Tavora, MD[g]

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