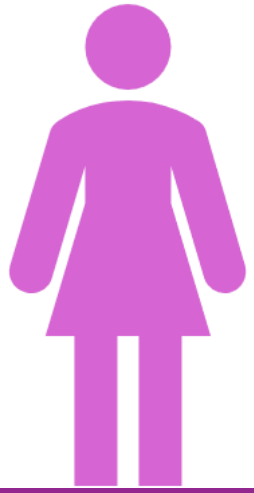
Adenopatía supraclavicular izquierda en paciente con carcinomatosis peritoneal

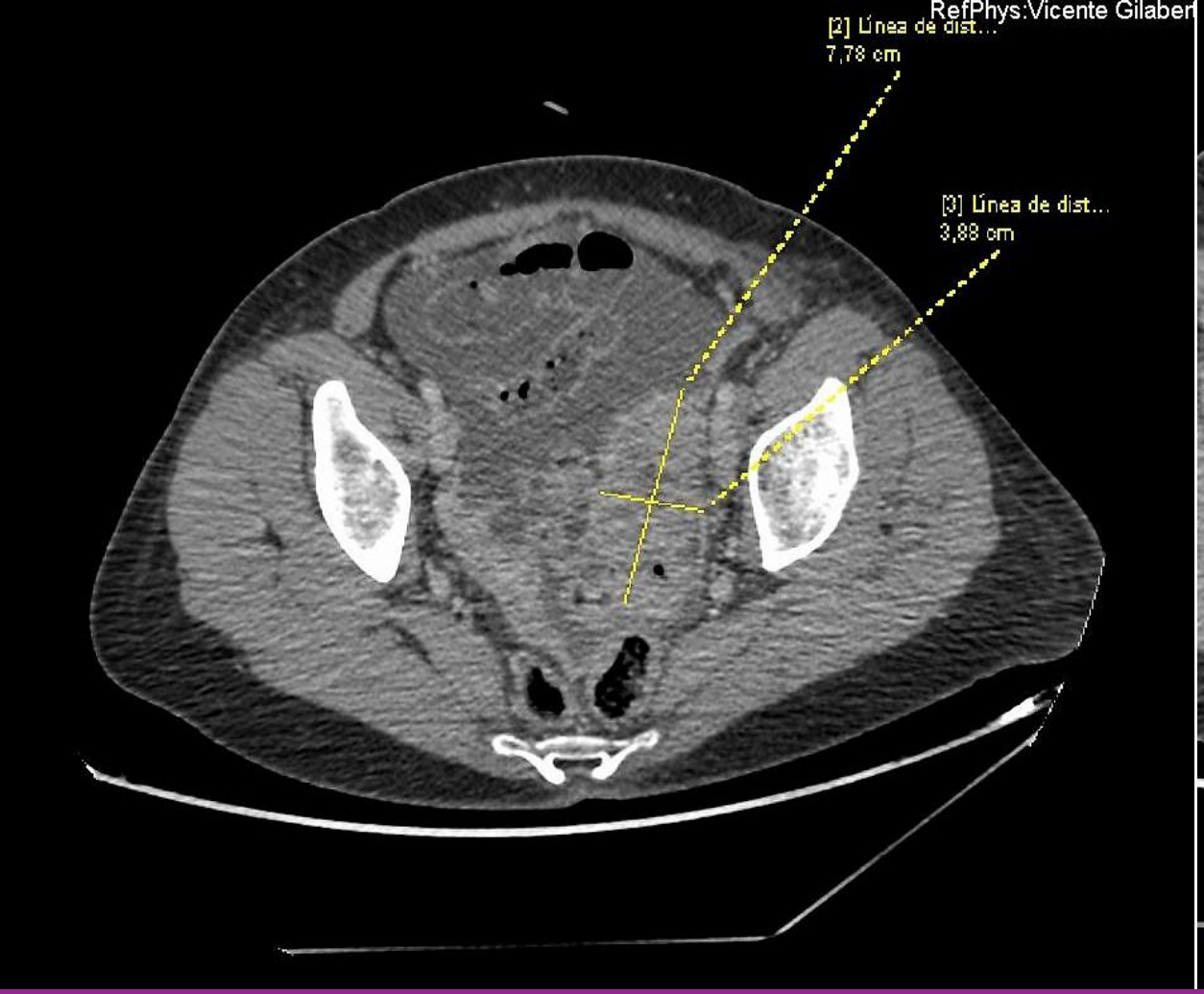
PRESENTACIÓN DE UN CASO

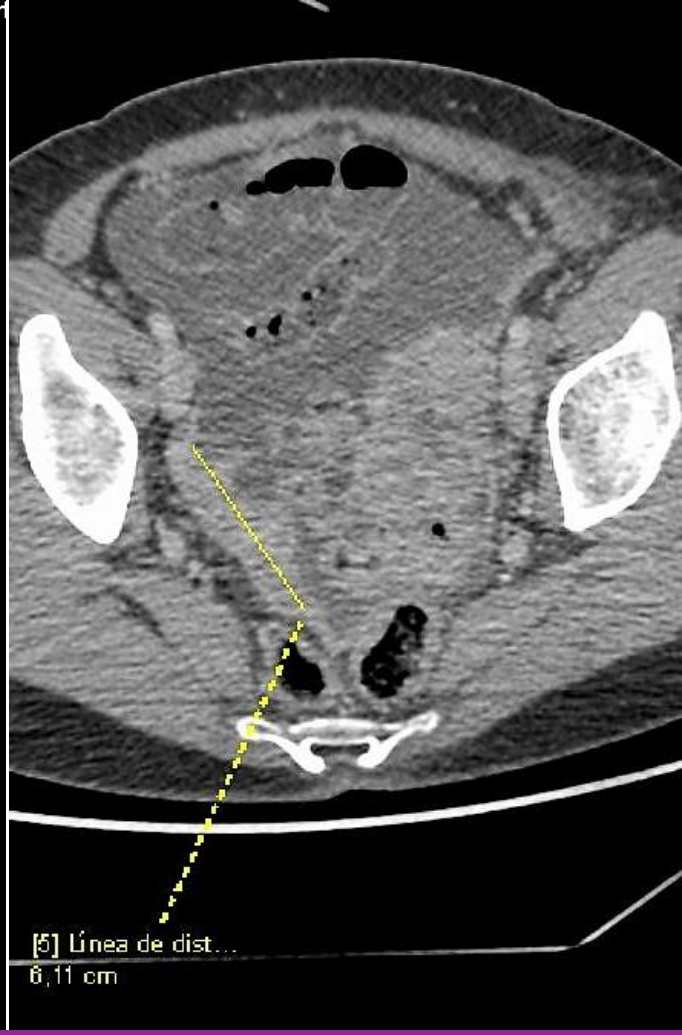
Autores: Albert Caballero Illanes, Laura Barona García, Alejandro Nicolás Salazar, Alejandro Garzón Arana, María Amparo Torroba Carón, José Antonio Ruiz Maciá

Presentación del caso

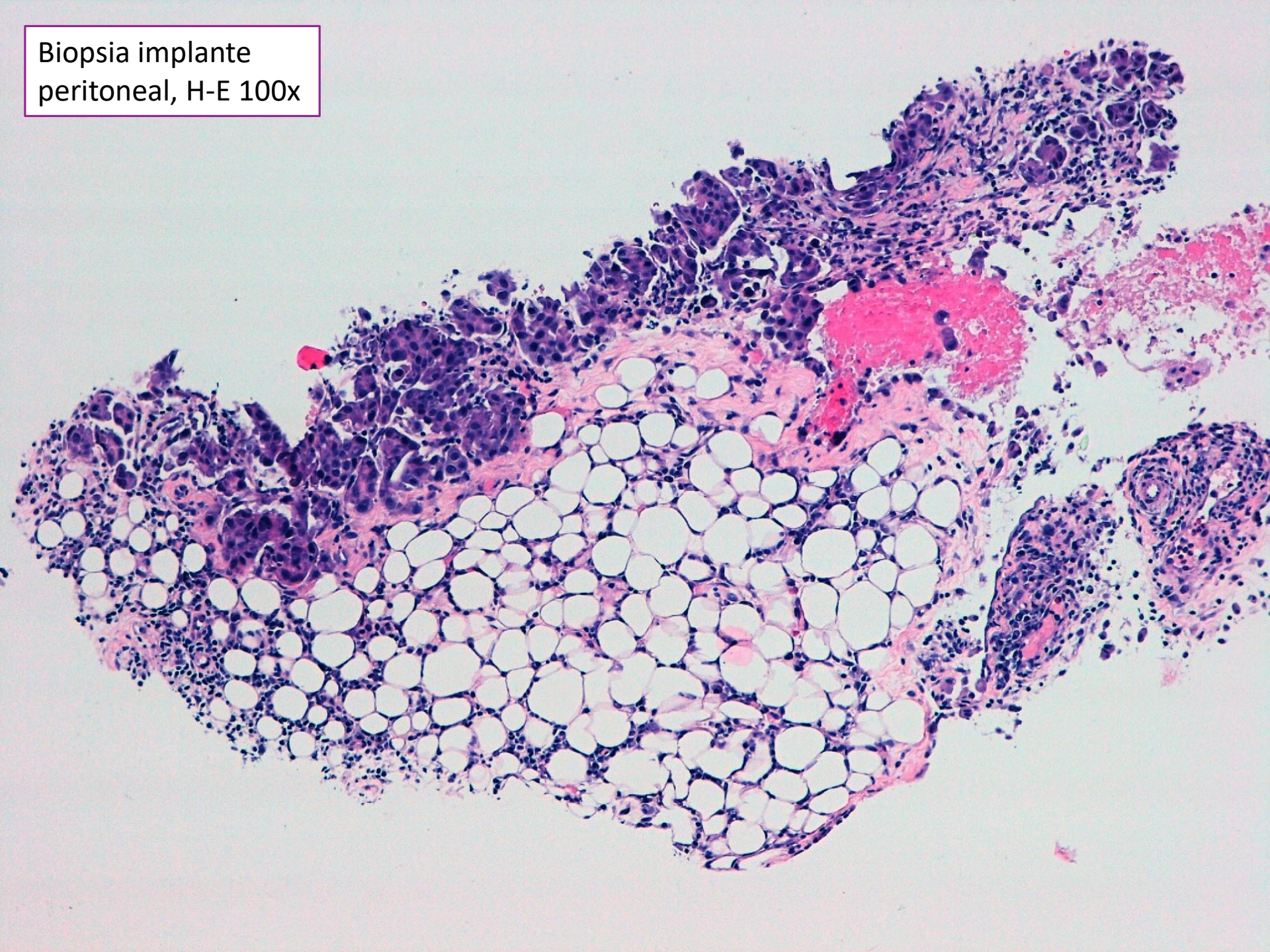
- Mujer de 51 años con carcinomatosis peritoneal de origen no filiado.

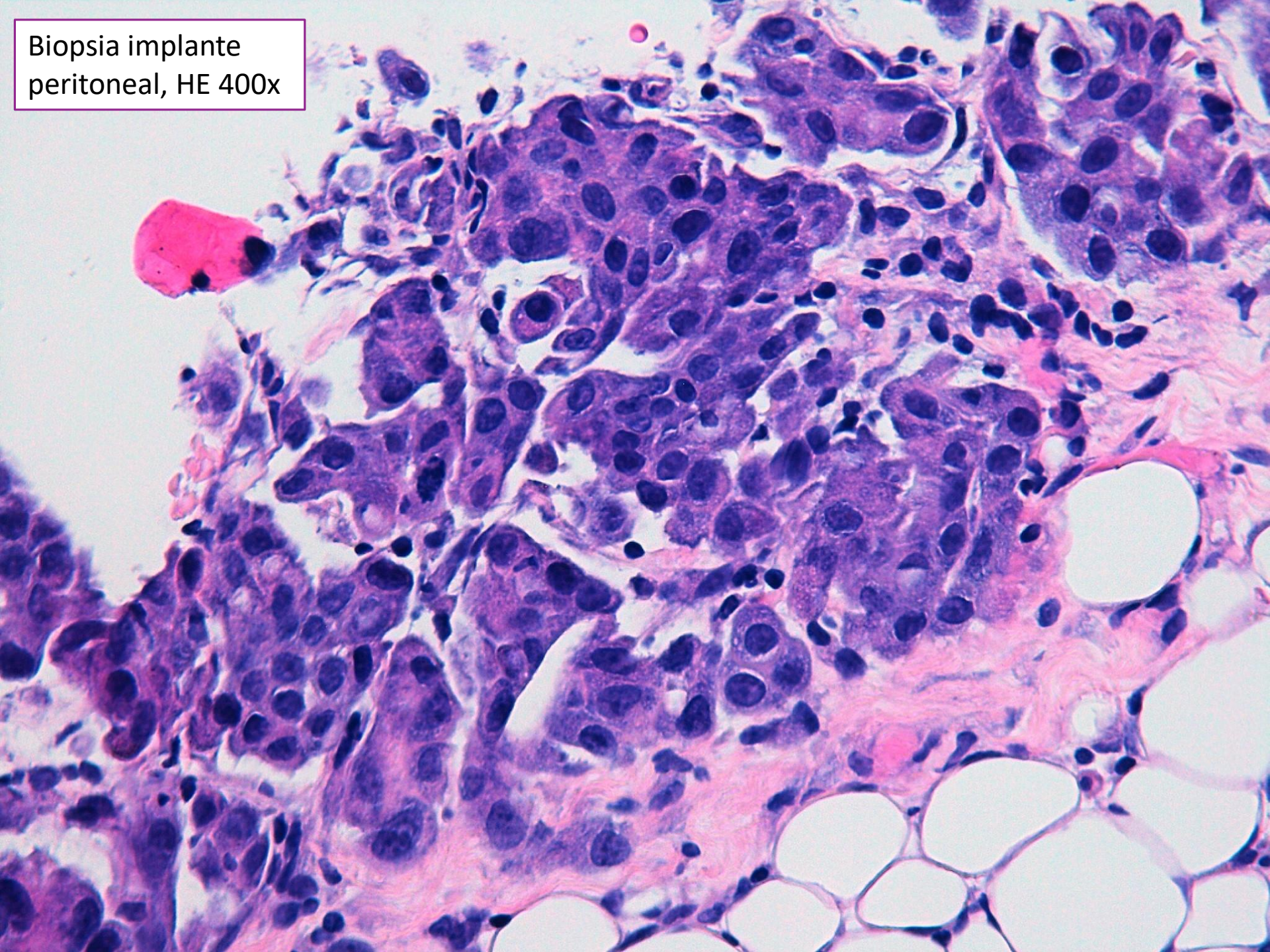


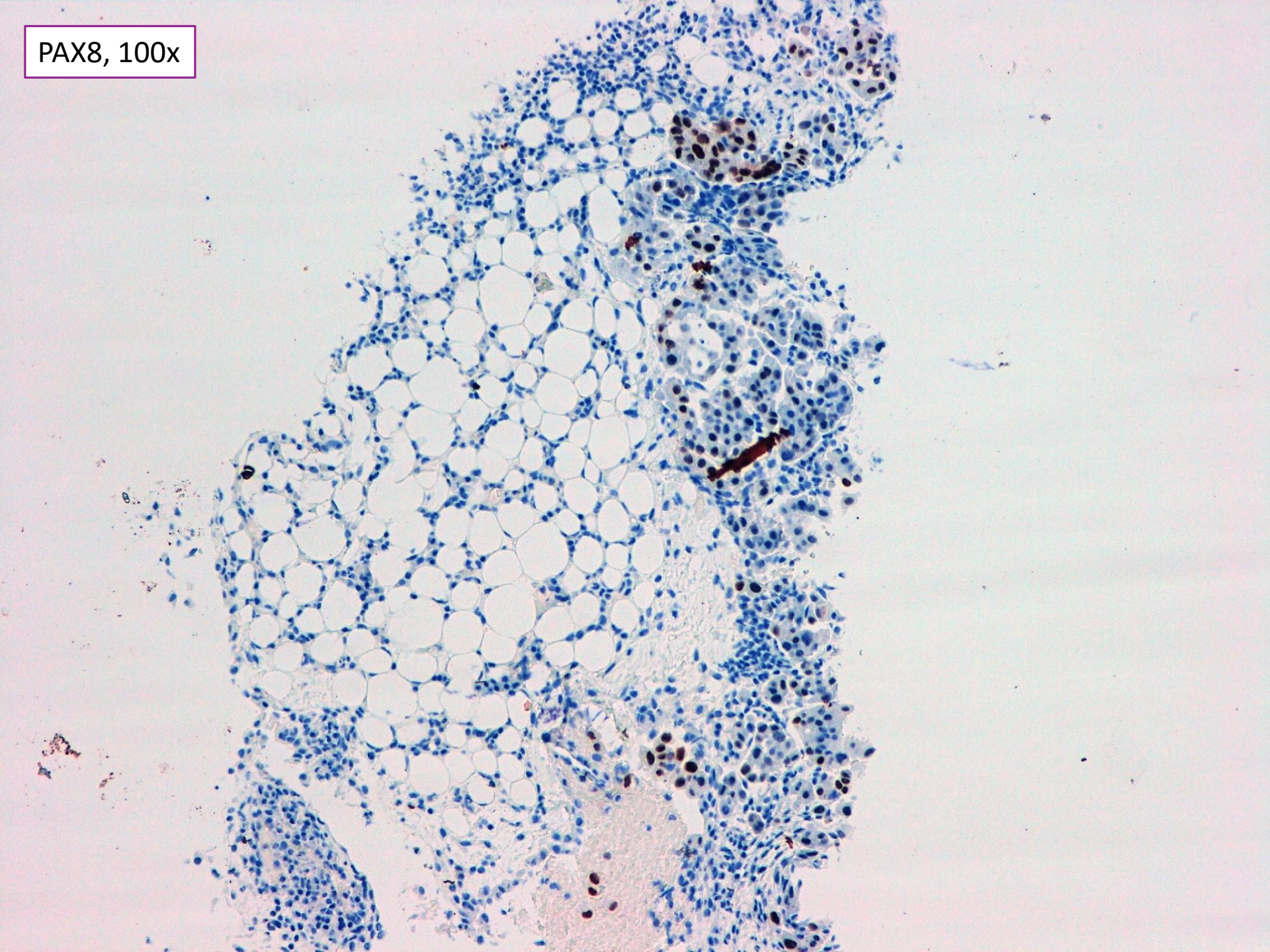


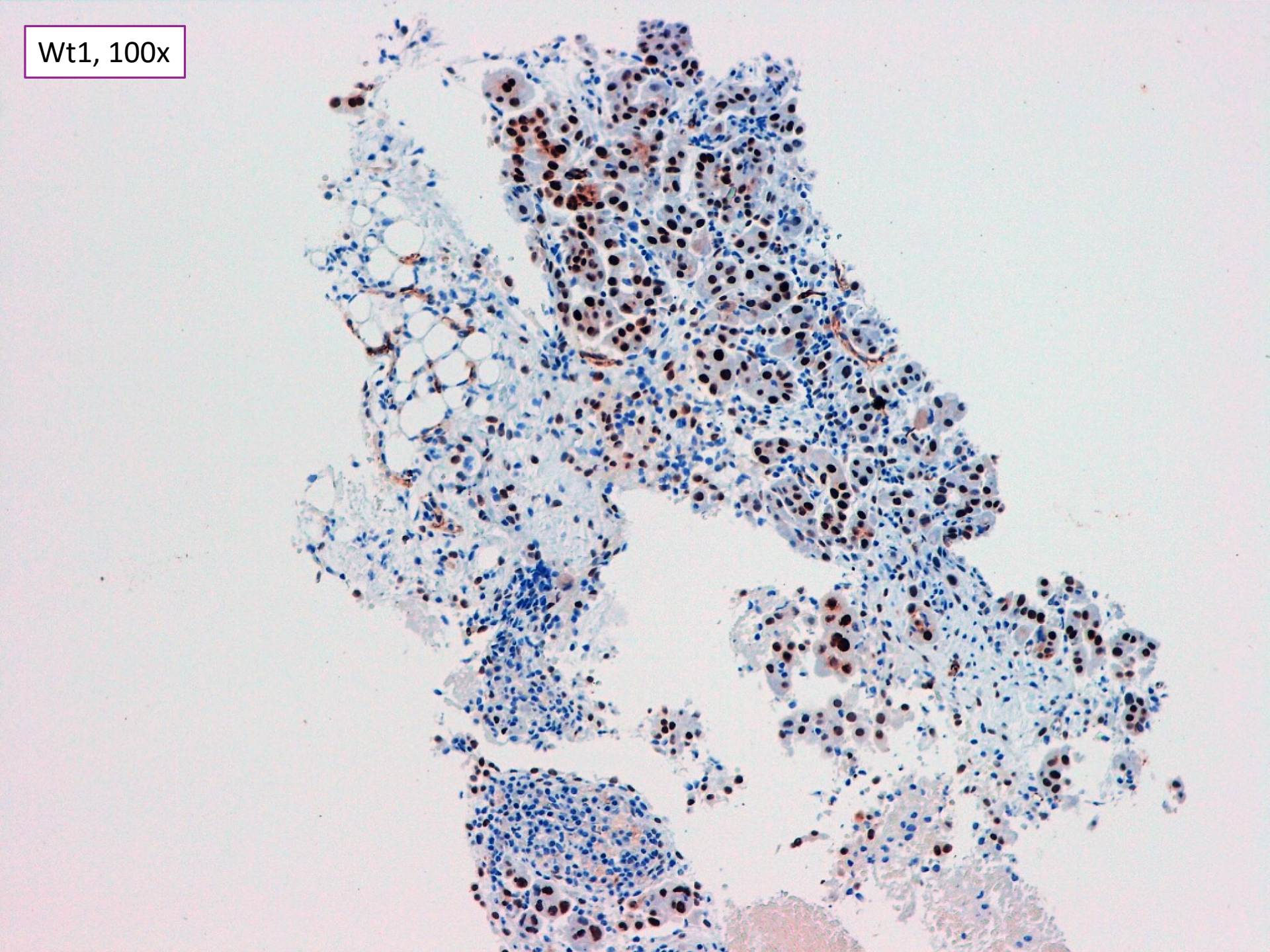


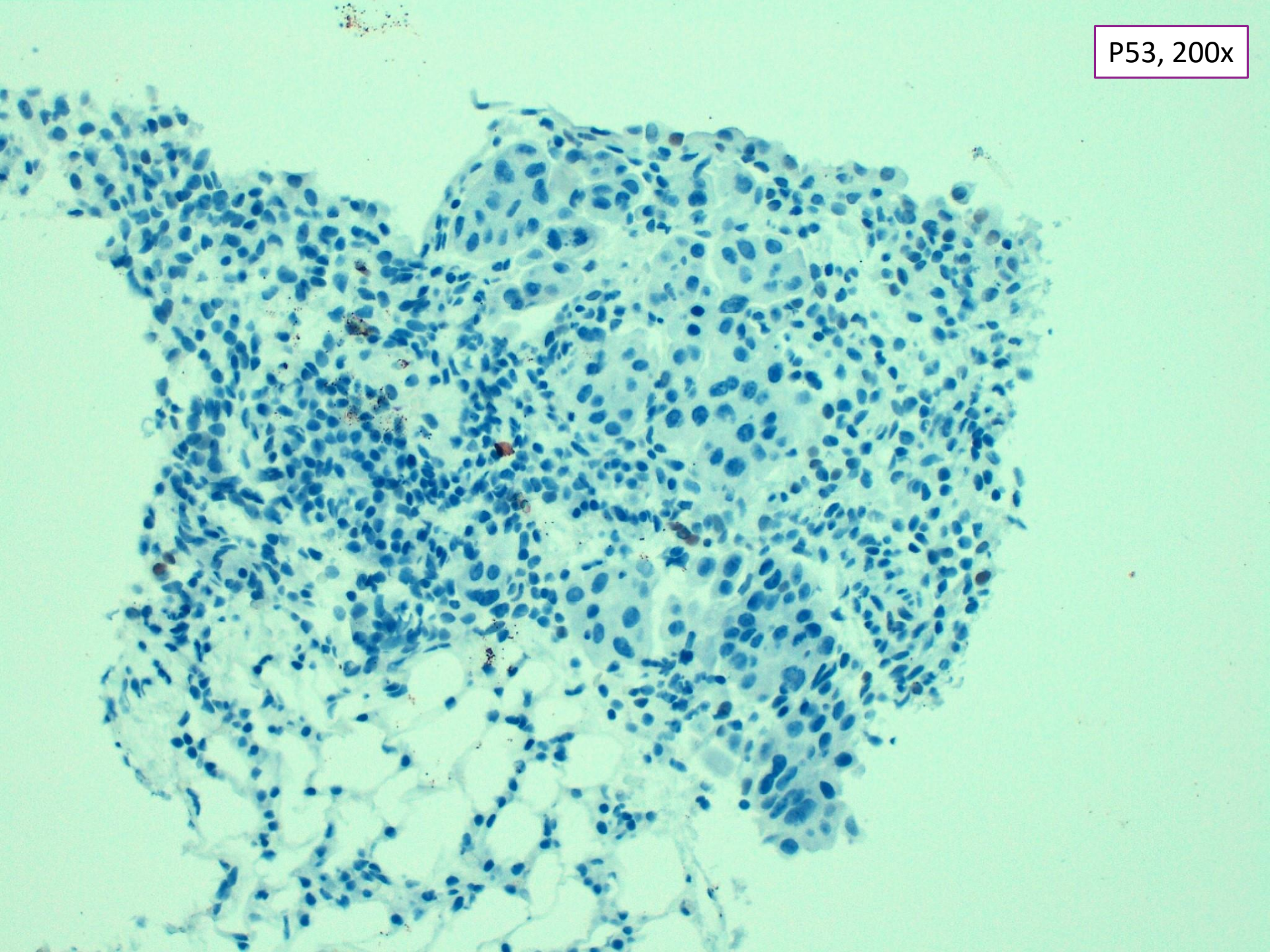
Masa en parametrio izquierdo de 8x4cm e implante peritoneal pararectal de 6x2cm.


Biopsia implante
peritoneal, H-E 100x


Biopsia implante
peritoneal, HE 400x


PAX8, 100x

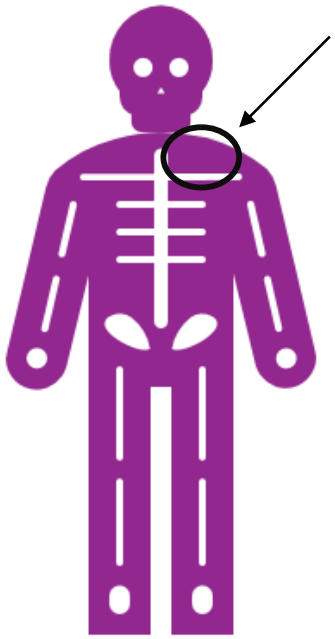

Wt1, 100x

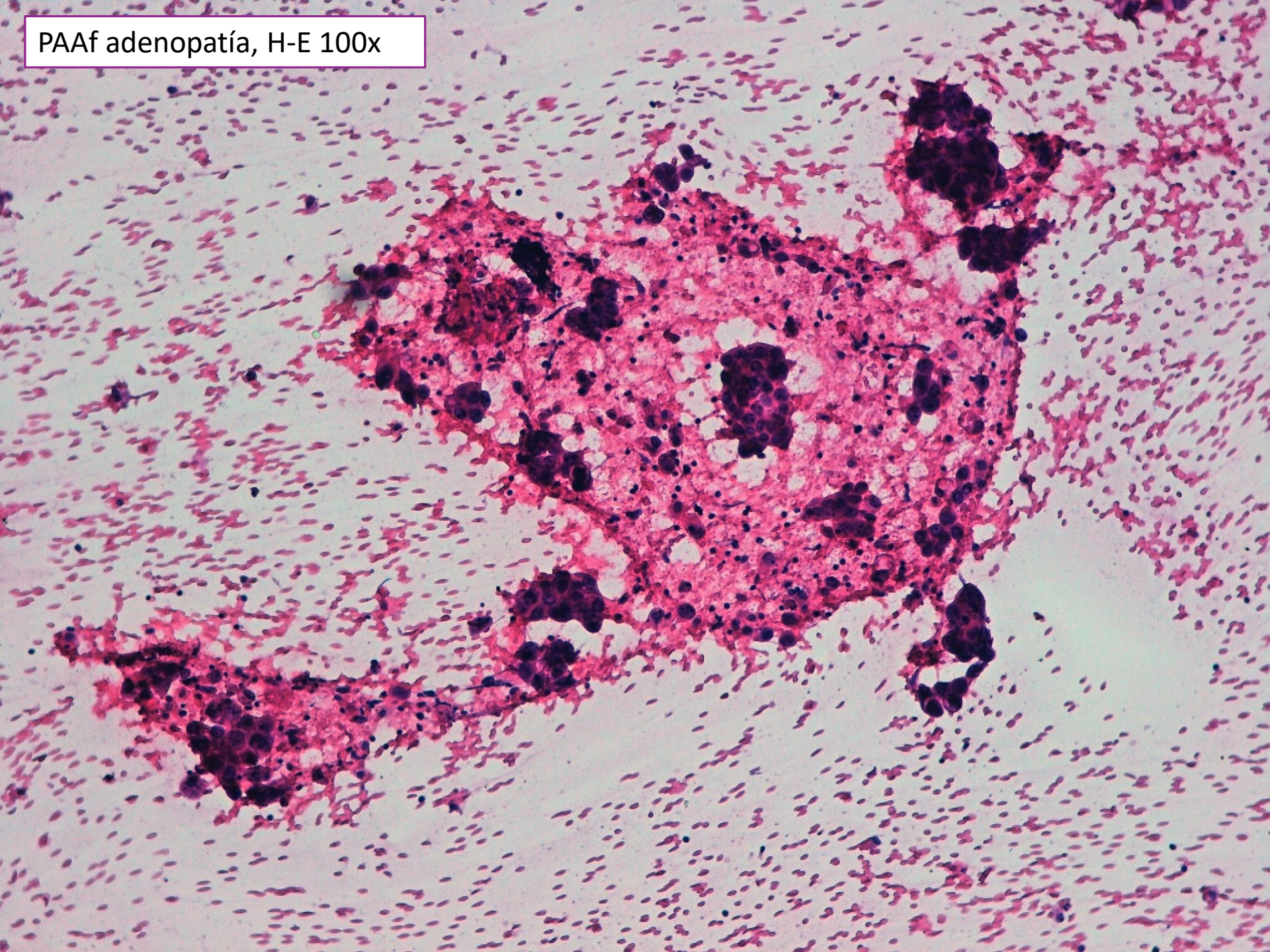

P53, 200x

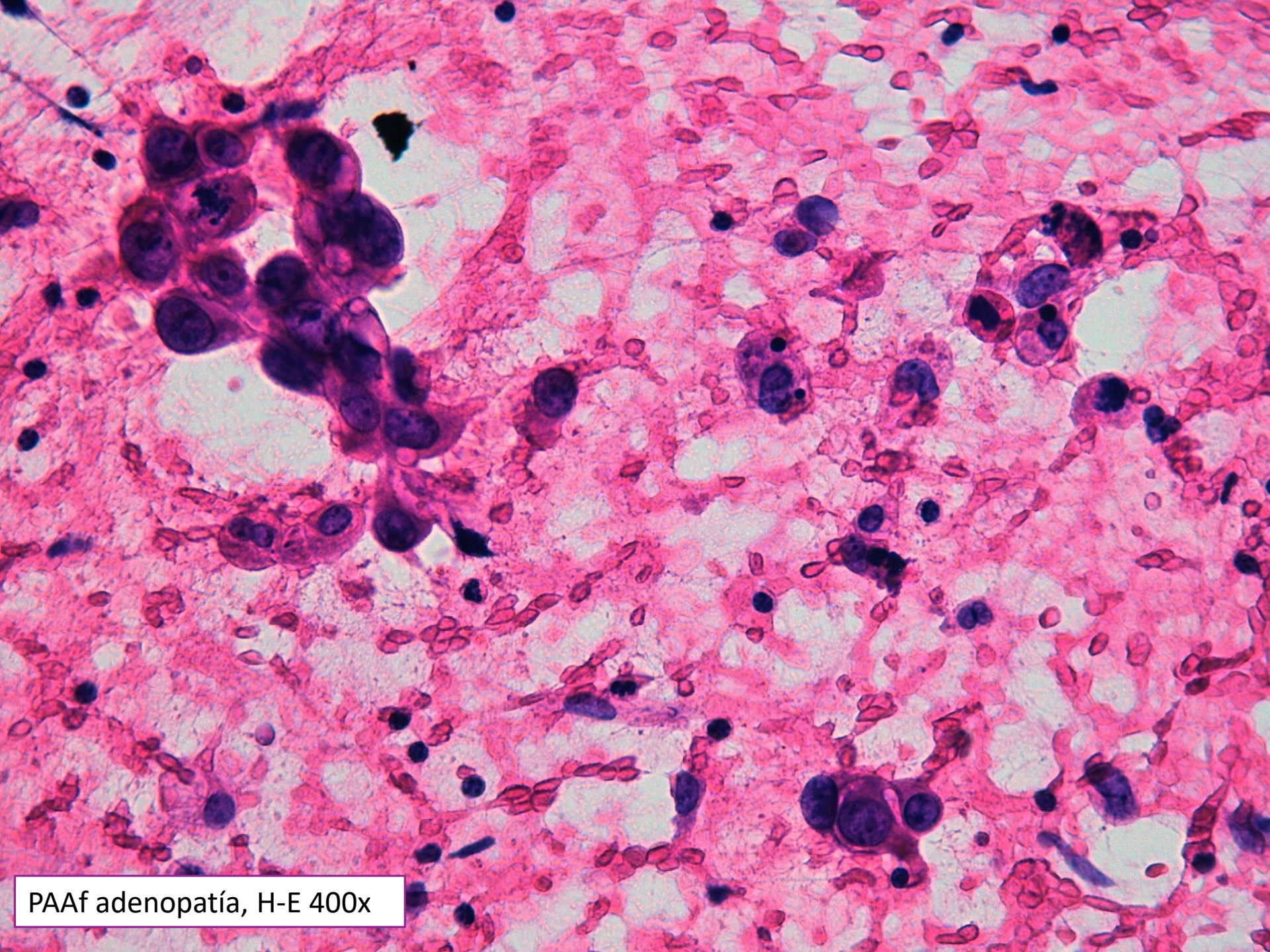
Exploración

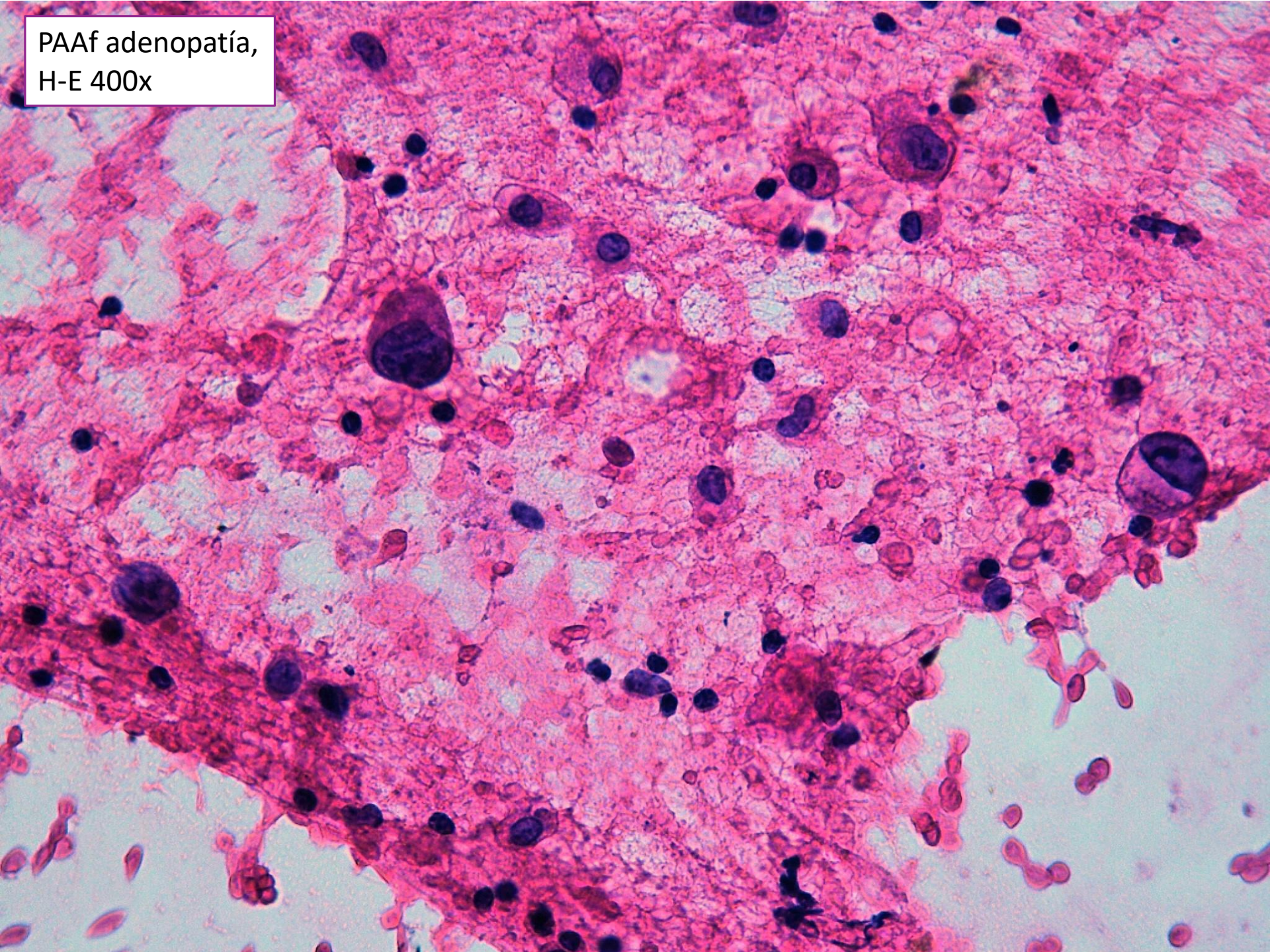
- PET-TC revela positividad para adenopatía supraclavicular izquierda.

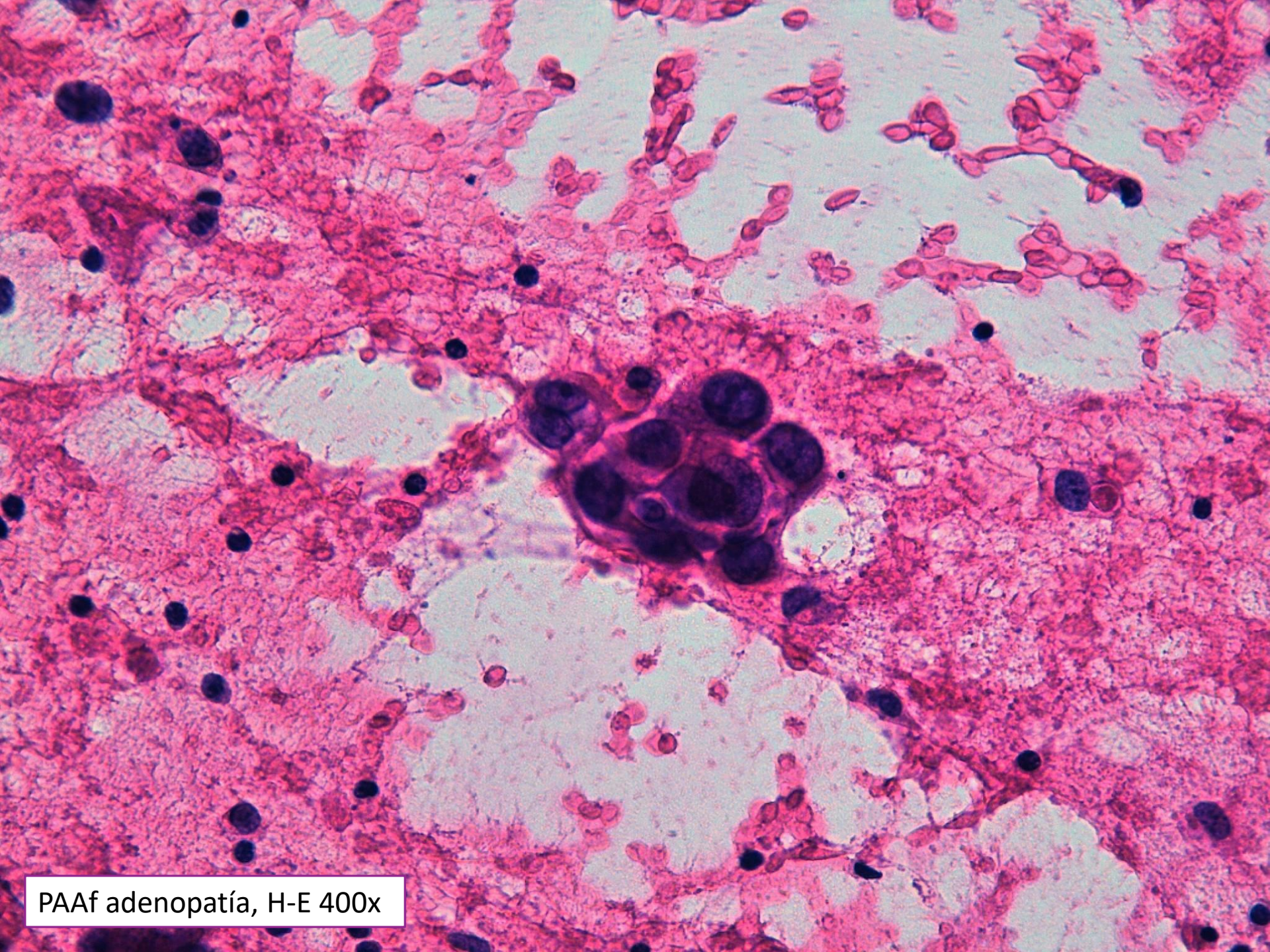
- Ecografía: imagen heterogénea con cortical engrosada y ausencia de hilio graso.




PAAf adenopatía, H-E 100x


PAAf adenopatía, H-E 400x


PAAf adenopatía,
H-E 400x



PAAf adenopatía, H-E 400x

cancers

MDPI

Review

Rare Distant Metastatic Disease of Ovarian and Peritoneal Carcinomatosis: A Review of the Literature

Nikolaos Thomakos [1], Michail Diakosavvas [1], Nikolaos Machairiotis [2,*], Zacharias Fasoulakis [1], Paul Zarogoulidis [3] and Alexandros Rodolakis [1]

Received: 9 June 2019; Accepted: 22 July 2019; Published: 24 July 2019

- *Supraclavicular Lymphadenopathy*

To date, only a few cases of supraclavicular lymphadenopathy due to primary ovarian cancer have been reported in the international literature [95,96]. Patel et al. reported, in 1999, five patients with supradiaphragmatic spread from epithelial ovarian cancer. In another study of 100 autopsies of ovarian cancer patients, Dvoretsky et al. reported supraclavicular metastases in only 4% while the total lymph nodes metastases were present in 70% of the patients examined [30–32]. Subperitoneal, infradiaphragmatic, and diaphragmatic lymphatic vessels are all connected and thus, the lymphatic fluid route explains supradiaphragmatic metastatic lymph nodes in ovarian cancer [31,97]. Pelvic and para-aortic lymph nodes are present in approximately 40–70% of epithelial ovarian cancers. The left supraclavicular lymph node (LSCLN), the Virchow's node, collects lymph fluid of the thoracic duct which percolates many organs of the abdomen. [98]. Thus, cancer cells are able to reach and metastasize through lymphatic vessels there.

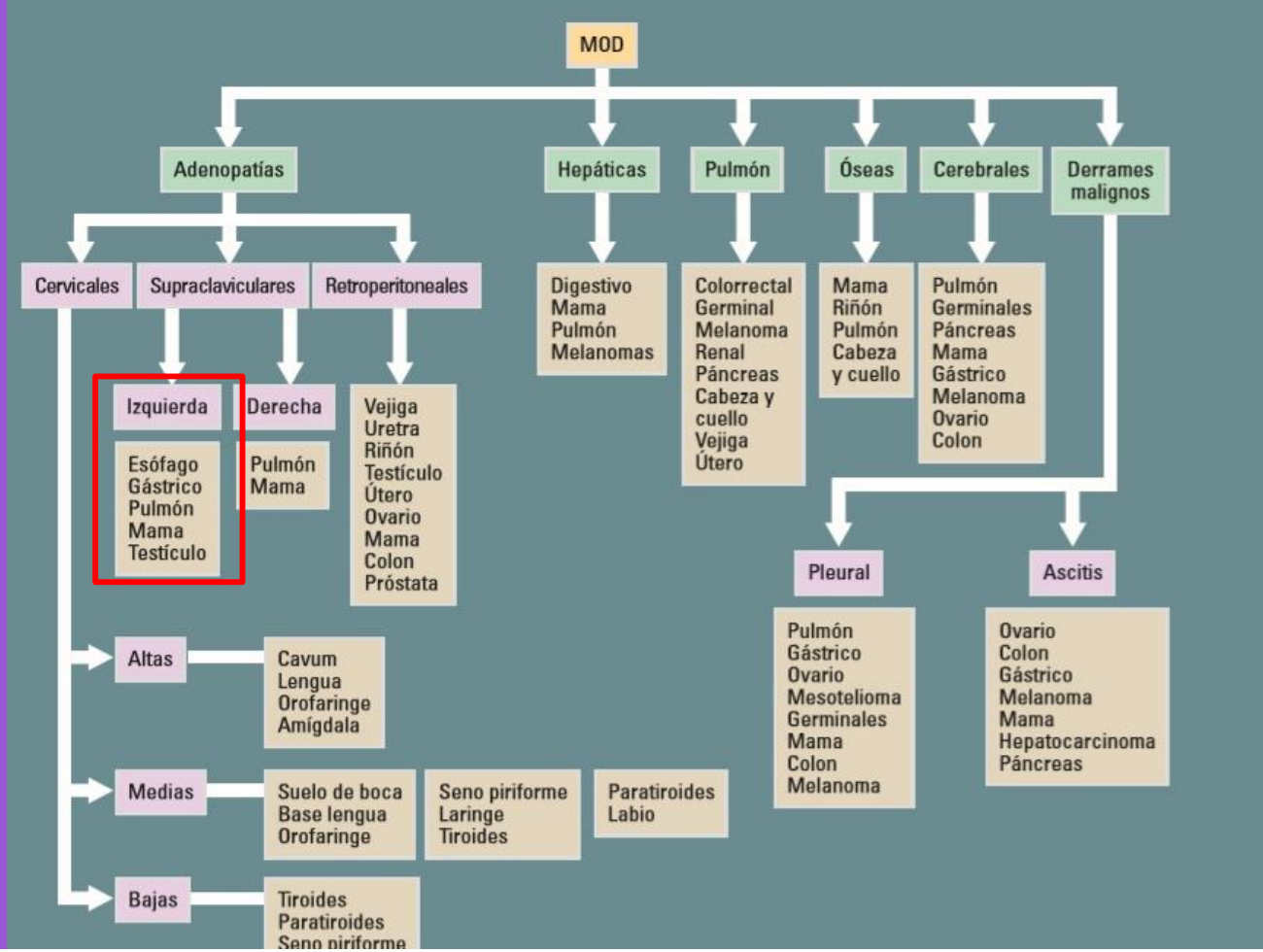
Figure 1. Rare distant metastatic sites of ovarian cancer and their route of metastasis.

Table 1. Metastatic sites, frequency and prognosis and peritoneal carcinomatosis.

Metastatic Site		Frequency	Prognosis (Median Survival)	Ref.
CNS		0.3–12%	8.2 months	[9–13]
Eye		9 cases reported until 2009	6.5–16 months	[14–21]
Skin		1.2%	12 months (1–41 months)	[22–27]
Bones		<3.74%	7.5 months	[28,29]
Lymph nodes	Supraclavicular	4%	NR	[30–39]
	Inguinal	0.8–3%	NR	
	Mediastinal-Cardiophrenic	2.3%	68.9–72.3 months	
Breast		0.03–0.6%	16 months (13 days–3.5 months)	[40–43]
Rare intra-abdominal	Spleen	2%–3% in epithelial ovarian cancer	NR	[44–47]
	Gastrointestinal	Depends on type and stage of diagnosis	<15 months	
Bronchus and Trachea		10 reports until 2018	6–24 months	[5,48,49]
Heart		2.4–4%	3–72 months	[22,32,50,51]
Placenta and Fetus		3 cases reported until now to placenta 0 to fetus	NR	[52–54]

CNS: Central Nervous System, NR: Not Reported.

Localización del tumor primario en metástasis de origen desconocido según la localización metastásica.

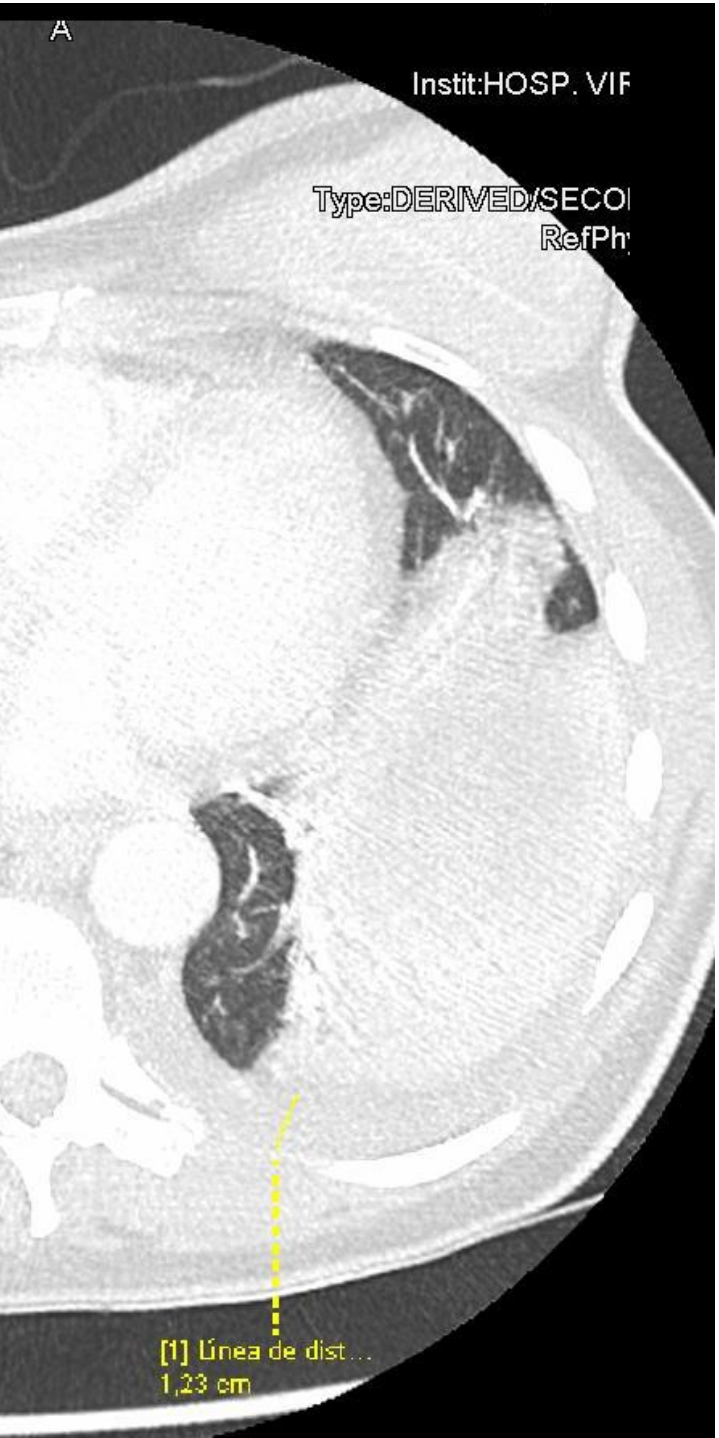


Protocolo de actuación clínica en las metástasis de origen desconocido

A. García García. S. González-Santiago y M.J. Méndez Vidal

Servicio de Oncología Médica. Hospital Universitario Reina Sofía. Córdoba.

Medicine 2005; 9(25): 1652-1654



Otros hallazgos

- Adenopatías cadena mamaria interna y retroesternal con hallazgos BIRADS 2 en mamografía. Portadora de prótesis bilateral.
- Derrame pleural bilateral e incremento metabólico en pulmón derecho.
- Engrosamiento de paredes gástricas con incremento metabólico difuso.
- Adenopatías tronco celíaco y retroperitoneales.

Serous Carcinoma of the Ovary and Peritoneum With Metastases to the Breast and Axillary Lymph Nodes

A Potential Pitfall

Monica A. Recine, MD, Michael T. Deavers, MD, Lavinia P. Middleton, MD, Elvio G. Silva, MD, and Anais Malpica, MD

Key Words: serous carcinoma, ovary, peritoneum, breast, axillary lymph node, metastasis

(*Am J Surg Pathol* 2004;28:1646–1651)

Ovarian serous carcinoma usually presents at an advanced stage, but with disease confined to the peritoneal cavity in 85% of patients. Distant metastases are unusual at presentation and during the course of the disease. Metastases of ovarian or peritoneal primary serous carcinomas to the breast and/or axillary lymph nodes are uncommon with only isolated cases reported thus far. These metastases may represent a pitfall for the pathologist because they can mimic primary breast carcinoma. The correct diagnosis in these cases is of utmost importance for proper treatment and prognosis. In this study, we present the clinicopathologic features of 18 cases of ovarian or peritoneal serous carcinoma that metastasized to the breast and/or axillary lmph nodes seen at the University of Texas M.D. Anderson Cancer Center during a 14-year period. Two (11%) patients, whose primary diagnosis was ovarian serous tumor of low malignant potential, developed metastases after 102 and 135 months.

These findings are similar to those previously published. Patients with breast involvement secondary to ovarian cancer generally have a known history of advanced-stage ovarian or peritoneal intraabdominal disease and develop the breast metastases after a relatively short period of time (2–3 years). Breast metastases concurrent with initial presentation occurred in 24% of the reported cases. In addition, synchronous axillary lymph node involvement is seen in more than 60% of these patients.[7,35] Few cases of isolated axillary lymph node metastases have been reported.[12,21] In our series, 8 patients (44%) had simultaneous breast and axillary lymph node involvement and 6 (33%) developed only lymph node metastases.

Generally, metastatic tumors in the breast are unilateral, solitary, superficial, oval, well-circumscribed, firm nodules and are unlikely to be fixed to the surrounding structures.[20,41,43] There is usually no skin retraction or peau d'orange. Radiographically, metastatic tumors are more likely to be dense, well-circumscribed lesions compared with the irregular outlines seen in primary tumors. Calcifications are usually absent.[3,32] However, upon careful review of published cases of

Metastatic gastric cancer arising from ovarian cancer

Using the key words "gastric metastasis", "metastatic tumor" and "ovarian cancer (carcinoma)" on Medline found only nine reports published in the English literature between 1970 and 2013 [7, 14–16, 18–22]. The data regarding age, gender, tumor location, tumor size, metastases to other organs, the IPM, treatment method and outcomes were collated for each patient (Table 3). The median age of the patients with metastatic gastric tumors arising from ovarian cancer was 62 years (range 42–71 years). Two patients had lesions in the upper third of the stomach, two had lesions in the middle third of the stomach and five had lesions in the lower third of the stomach. The median tumor size was 4 cm (range 1.2–7.0 cm). One patient was found to have multiple metastatic tumors in the stomach, in addition to metastases in the peritoneum and spleen [9]; all other patients had solitary gastric lesions. An examination of the tumors revealed submucosal tumors (SMT) in six patients, ulcerated tumors in two patients and a protruding tumor in one

"Clinopathological features and treatment outcomes of metastasic tumors in the stomach"

Surg Today (2.014)

Clinicopathological features and treatment outcomes of metastatic tumors in the stomach

Tsutomu Namikawa · Kazuhiro Hanazaki

Received: 21 February 2013 / Accepted: 13 June 2013

Table 1 Review of the case series of patients with metastatic tumors in the stomach

Study	Years	No. of cases	Median age (years)	Primary lesion	Tumor size (cm)	No. of solitary lesions (%)	No. of multiple lesions (%)	IPM (months)	Median survival time (months)
Antler et al. [8]	1982	10	ND	Lung	ND	5 (50.0)	5 (50.0)	ND	ND
Saito et al. [9]	1985	35	62 (42–80)	Esophagus	ND	27 (77.1)	8 (22.9)	ND	8.3 (1–31)
Green [10]	1990	67	58	Lung, pancreas, esophagus, colon, liver, melanoma, kidney, prostate, testis, head and neck	ND	ND	ND	ND	ND
Taal et al. [5]	2000	51	56 (35–73)	Breast	ND	14 (27.5)	37 (72.5)	50 (2–210)	10 (2–67.2)
Oda et al. [3]	2001	54	56 (28–82)	Lung, esophagus, breast, melanoma	ND	35 (65.0)	19 (35.0)	ND	ND
Kobayashi et al. [1]	2004	9	60 (50–78)	Esophagus, lung, breast, liver, kidney, uterus, melanoma	5 (3–20)	3 (33.3)	6 (66.7)	20 (0–74)	5.7 (0.5–29.7)
Palma et al. [2]	2006	64	56 (28–82)	Breast, lung, melanoma, head and neck, uterus, colorectum, kidney, soft tissue	ND	40 (62.5)	24 (37.5)	25.7 (1–40)	ND
Campoli et al. [11]	2006	20	58.1 (31–95)	Esophagus, melanoma, lung, cervix, breast, colon, testis	ND	10 (50.0)	10 (50.0)	16 (0–56)	4.75 (0–14)
Ayantunde et al. [12]	2007	9	71 (57–90)	Breast	ND	0 (0)	9 (100)	78 (34–394)	20 (2.1–96.6)
Namikawa et al. [4]	2012	22	68 (48–83)	Kidney	3 (1–8)	7 (31.8)	15 (68.2)	75.6 (12–276)	19 (1–36)
Our study	2013	9	62 (42–71)	Ovary	4 (1.2–7.0)	7 (77.8)	2 (22.2)	30 (0–84)	Not reached

Unless indicated otherwise, the data show either median values, with the range given in parentheses, or the number of patients in each group, with percentages in parentheses

IPM the interval between the treatment of the primary tumor and the diagnosis of the metastatic tumor in the stomach, *ND* not described

Preguntas

¿Origen ovárico?

¿Otro origen? (v.g estómago)

¿Más de un tumor?

cancers

MDPI

Review

Immunohistochemistry for Diagnosis of Metastatic Carcinomas of Unknown Primary Site

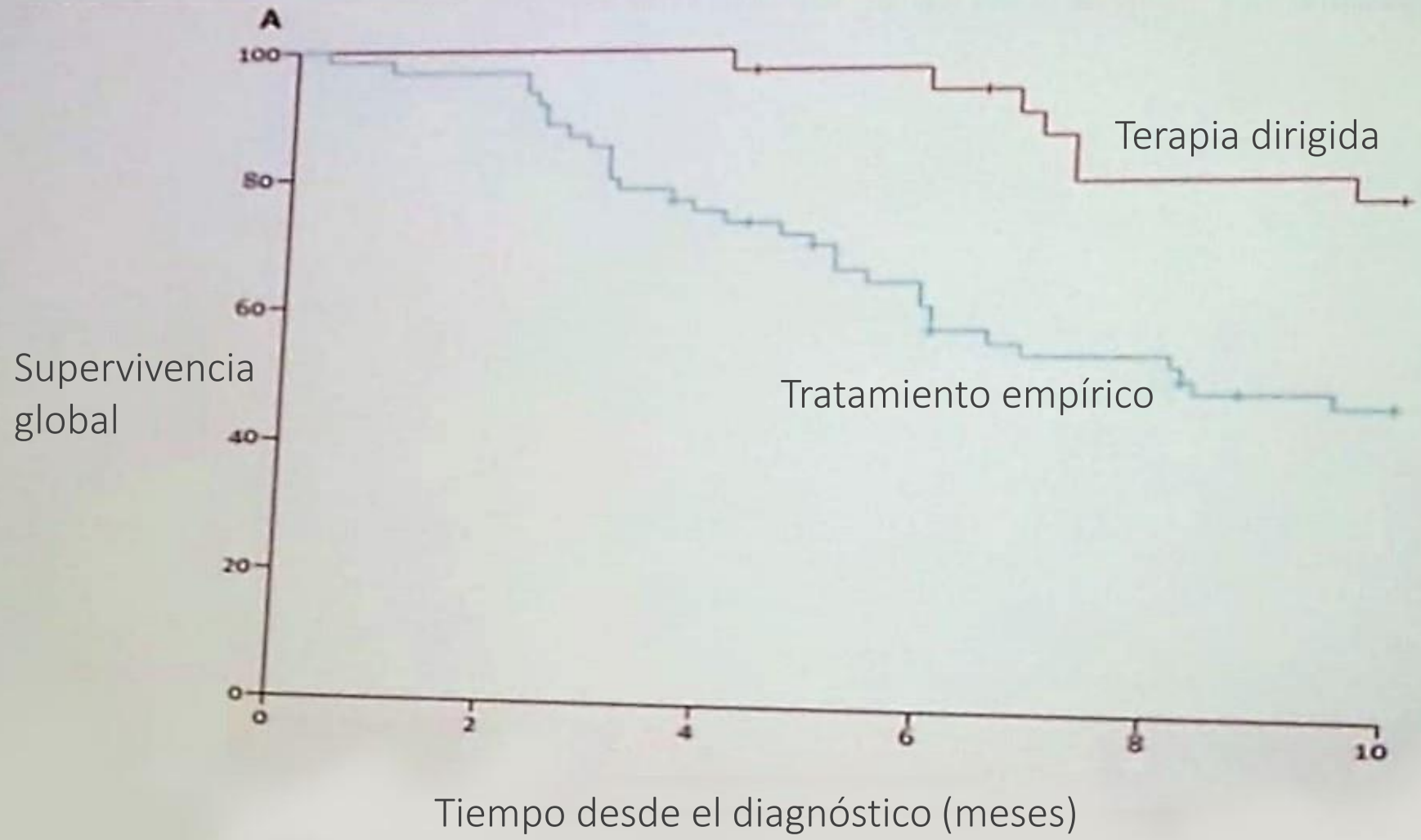
Janick Selves [1], Elodie Long-Mira [2], Marie-Christine Mathieu [3], Philippe Rochaix [1] and Marius Ilié [2,*]

Received: 10 February 2018; Accepted: 2 April 2018; Published: 5 April 2018

1. Introduction

In the absence of an identifiable primary tumour site, despite extensive multidisciplinary investigations, carcinomas of unknown primary site (CUPs) are characterized as metastatic carcinomas [1]. Diagnosis is intended essentially to identify the subsets of CUPs sensitive to specific treatment. Beside these clinical entities, the identification of the primary tumour has no prognostic or therapeutic effect and a comprehensive systematic review is unnecessary and costly [2]. However, the therapeutic choice, and several favourable subsets of CUPs, warrants further histopathological characterization, which is often performed with immunohistochemistry (IHC) and, more recently, using molecular analyses [3,4]. In practice, four primary sites (breast, ovarian, prostate and thyroid) involving specific effective treatment options and a better prognosis should first be investigated [5]. In addition, the development of targeted therapies must eliminate a pulmonary or colorectal origin.

IHC provides diagnostic guidance in approximately 90% of undifferentiated malignant tumours but usually at the end of a fastidious and expensive algorithm based on both morphology and IHC. However, identification of the primary site of origin may represent a difficult challenge for the pathologist when dealing with a small sample size along with increased generation of tumour-specific primary antibodies and the need for complementary molecular analysis.



Fuente: II Simposio organizado por GECOD en Madrid (2019). Foto de JA R. Maciá

Tratamiento empírico vs. tratamiento dirigido

cancers

MDPI

Review

Immunohistochemistry for Diagnosis of Metastatic Carcinomas of Unknown Primary Site

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Diagnóstico diferencial

Panel IHQ

Table 2

Immunohistochemistry (IHC) tumour staining patterns in the differential diagnosis of CUPs expressing CK7+/CK20− [7].

Primary Site of Origin	Immunostaining Profile
Breast [8,14,15,16,17]	ER+/PgR+, GATA3+, GCDFP15−/+, MGB+/−, TFF1−
Ovary (serous) [17,18,19,20,21]	PAX8+, ER+, WT1+, TTF1−, TFF3−, GATA3−
Ovary (clear cell) [17,18,19,20,21]	pVHL+, HNF-1β+, Napsin A+, AFP−, WT1−, ER−, GPC3−
Endometrium [17,18,19,20,21]	ER+, PAX8+, Vimentin+
Uterine cervix [17,18,19,20,21]	p16+, HPV+, CEA+, PR−, PAX2−, PAX8+/−
Lung [22,23,24]	TTF1+, Napsin A+, GATA3−
Thyroid (papillary/follicular) [23,24,25]	TTF1+, Thyroglobulin+, PAX8+
Thyroid (medullary) [23,24,25]	TTF1+, Calcitonin+, CEA+
Stomach [26,27,28,29]	CEA+, CDX2−/+, MUC1−/+, MUC5AC−/+, CDH17+/−, TTF1−
Oesophagus [26,27,28,29]	CDX2+/−, CEA+, CDH17+, MUC1−/+, MUC5AC−/+, SATB2−
Pancreas [26,27,28,29]	DPC4−/+, CK17+/−, pVHL−, Maspin+, S100P+, MUC5AC+
Urinary bladder [17,18,19,20,21]	GATA3+, p63+, CK5/6+, p40+, S100P+, CK903+, UPII+/−
Thymus [19,20,21]	CD5+/−, p63+/−, PAX8+/−, CD117+/−, Glut1+/−
Salivary (ductal) [16,17,30]	GATA3+, AR+, GCDFP-15+
Mesothelioma [30,31,32,33,34]	Calretinin+, WT1+, CK5/6+, TTF1−, CEA−, BerP4−

Abbreviations: AR, androgen receptor; calretinin; AFP, α-fetoprotein; CD5, cluster of differentiation 5; CDH17, cadherin-17; CDX2, caudal type homeobox 2; CEA, carcinoembryonic antigen; CK, cytokeratin; D2-40, podoplanin; DPC4, SMAD family member 4; ER, oestrogen receptor; GATA3, GATA binding protein 3; GCDFP-15, gross cystic disease fluid protein 15; HNF-1b, hepatocyte nuclear factor 1b; HPV, human papillomavirus; MGB, mammaglobin; MUC, mucin; PAX, paired box gene; CEA, carcinoembryonic antigen; PgR, progesterone receptor; pVHL, von Hippel-Lindau tumour suppressor; S100P, placental S100; TFF, trefoil factor; TFF3, trefoil factor 3; TM, thrombomodulin; TTF1, thyroid transcription factor 1; UPII, uroplakin II; WT1, Wilms tumour 1.

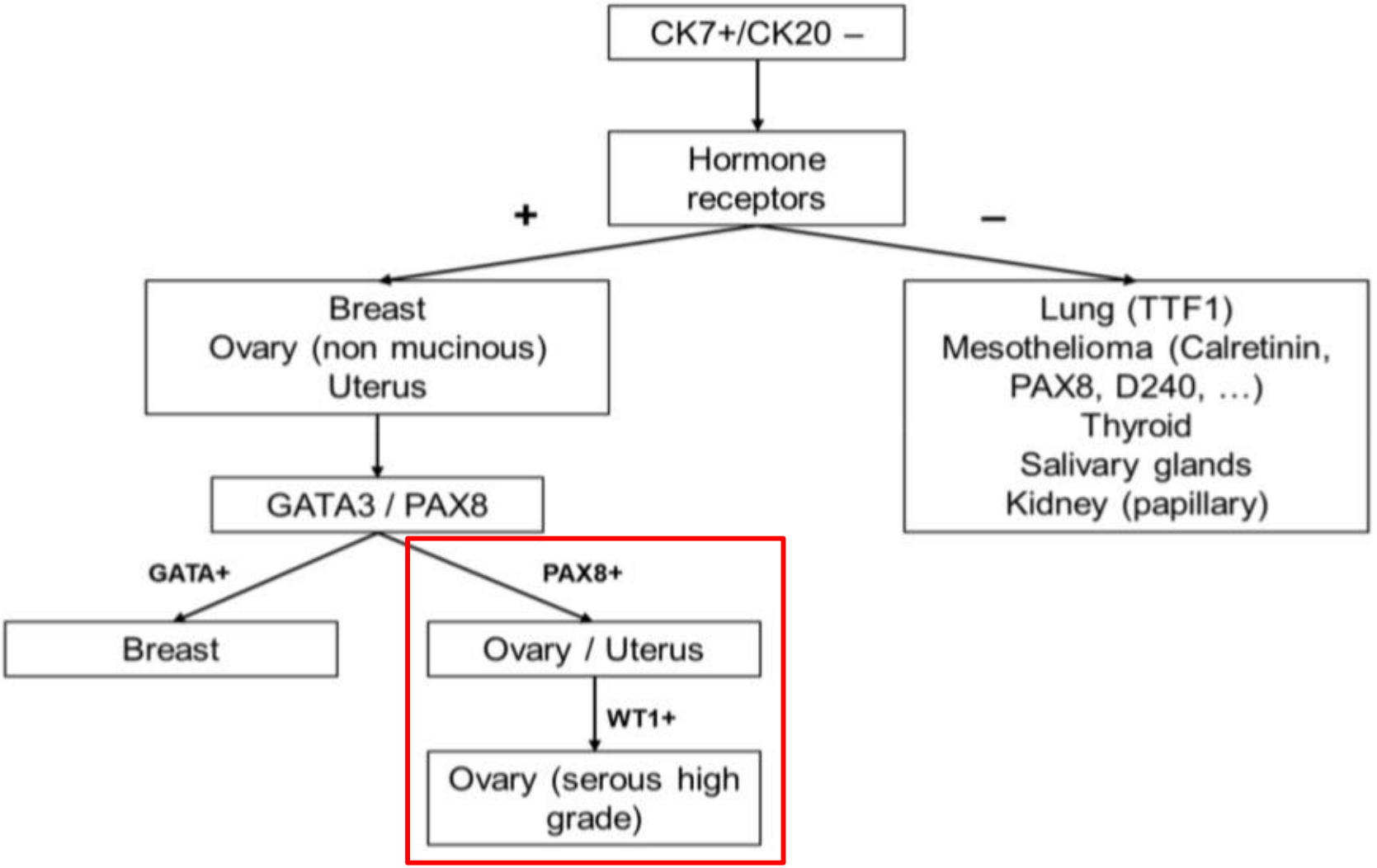


Figure 3. The diagnostic algorithm in female patients with CK7+/CK20– CUPs.

Algoritmo diagnóstico frente a metástasis adenocarcinoma de origen desconocido

MODERN PATHOLOGY (2011) 24, 751–764

PAX 8 expression in non-neoplastic tissues, primary tumors, and metastatic tumors: a comprehensive immunohistochemical study

Ayhan Ozcan[1,2,3], Steven S Shen[1,2,4], Candice Hamilton[1], Kundu Anjana[1], Donna Coffey[1,2,4], Bhuvaneswari Krishnan[5] and Luan D Truong[1,2,4,5]

Factor de transcripción que participa en el desarrollo de órganos derivados de estructuras wolffianas y Müllerianas, tiroides, ojo, riñón y SNC.

Table 1 PAX 8 expression in normal or non-neoplastic tissues

Renal tubular cells	*189/189 (100%)*
Glomeruli	0/189 (0%)[a]
Ovarian surface epithelial cells	5/8 (62%
Ovarian epithelial inclusion cyst	45/45 (100%)
Fallopian tubal epithelial cells	14/14 (100%)
Endocervical epithelial cells	20/20 (100%)
Endometrial epithelial cells	35/35 (100%)
Adenomyosis/endometriosis	8/8 (100%)
Endosalpingiosis	22/22 (100%)
Ovarian stromal cells	0/52 (0%)
Exocervical squamous cells	0/20 (0%)
Endometrial stromal cells	0/35 (0%)
Cervical stromal cells	0/20 (0%)
Seminal vesicle epithelial cells	17/17 (100%)
Epidydimal epithelial cells	27/27 (100%)
Seminiferous tubule cells	0/18 (0%)
Sertoli cells	0/18 (0%)
Leydig cells	0/13 (0%)
Prostatic epithelial cells	0/54 (0%)
Regenerative bile duct cells	4/35 (11%)
Hepatocytes	0/84 (0%)
Native bile duct cells	0/39 (0%)
Parathyroid epithelial cells	5/14 (35%)
Thyroid epithelial cells	80/80 (100%)
Brain cells	1/23 (4%)[b]
Urothelial cells	1/27 (6%)
Lymphoid cells	65/65 (100%)
Breast epithelial cells	0/57 (0%)
Pulmonary epithelial cells	0/ 69 (0%)
Adrenal cortical cells	0/24 (0%)
Adrenal medullary cells	0/10 (0%)
Gastrointestinal epithelial cells	0/56 (0%)
Pancreatic acinar cells	0/33 (0%)
Pancreatic ductal cells	0/33 (0%)
Pancreatic islet cells	19/27 (70%)
Salivary gland parenchymal cells	0/12 (0%)
Squamous epithelial cells	0/25 (0%)
Mesothelial cells	0/25 (0%)
Muscle cells (smooth, skeletal, and cardiac)	0/82 (0%)
Connective tissue cells (including fibroblasts)[c]	0%
Total	556/1601(35%)

En tejidos normales: Negativo en pulmón, mama y estómago.

Muy sensible y especifico. En tejidos normales su expresividad se va perdiendo a medida que los tejidos maduran. Sin embargo vuelve a expresarse en las transformaciones neoplásicas.

Table 3 PAX 8 expression in metastatic neoplasms

	Primary site	*Metastatic sites*	*Positive/total cases (%)*
Renal cell carcinoma	Kidney, all histological types	Lung, node, liver, brain, pancreas, bone, pleura, skin, soft tissue, spleen	90/102 (88%)
	Clear cell		75/80 (93%)
	Papillary		10/10 (100%)
	Collecting duct		4/5 (80%)
	Chromophobe		1/1 (100%)
	Sarcomatoid		0/6 (0%)
All Müllerian tumors			57/63 (90%)
Endometrioid carcinoma	Uterus	Node, omentum, liver	7/7 (100%)
Undifferentiated carcinoma	Ovary	Omentum	4/8 (50%)
Serous carcinoma	Ovary	Omentum, pleura, node, liver	44/46 (95%)
Clear cell carcinoma	Ovary	Lung	2/2 (100%)
Neuroendocrine carcinoma	Pancreas, GI tract	Node, liver	1/9 (11%)[a]
Small cell carcinoma	Lung	Node, bone, liver	1/15 (7%)[a]
Thyroid papillary carcinoma	Thyroid	Node	6/6 (100%)
Adenocarcinoma	Stomach	Node, small bowel, omentum, liver	0/5 (0%)
	Prostate	Node, bone, testis, brain, seminal vesicle	0/44 (0%)
	Colon	Node, liver, brain, lung, bladder, kidney	0/39 (0%)
	Appendix	Peritoneum	0/1 (0%)
	Breast	Node	0/62 (0%)
	Pancreas	Liver, kidney, omentum	0/8 (0%)
	Lung	Bone, brain, kidney, liver	0/9 (0%)
	Bile duct	Omentum, node	0/6 (0%)
Squamous cell carcinoma	Lung	Bowel, brain, node	0/6 (0%)
Urothelial carcinoma	Bladder	Liver, lung, node, bone	0/10 (0%)
Hepatocellular carcinoma	Liver	Node	0/1 (0%)
Malignant melanoma	Skin	Node, liver	0/6 (0%)
Adrenal cortical carcinoma	Adrenal cortex	Liver	0/2 (0%)
Total			245/496 (49%)

Node, lymph node.

[a]Less than 5% of cell nuclei were stained.

PAX 8 Expression in Metastatic Neoplasms

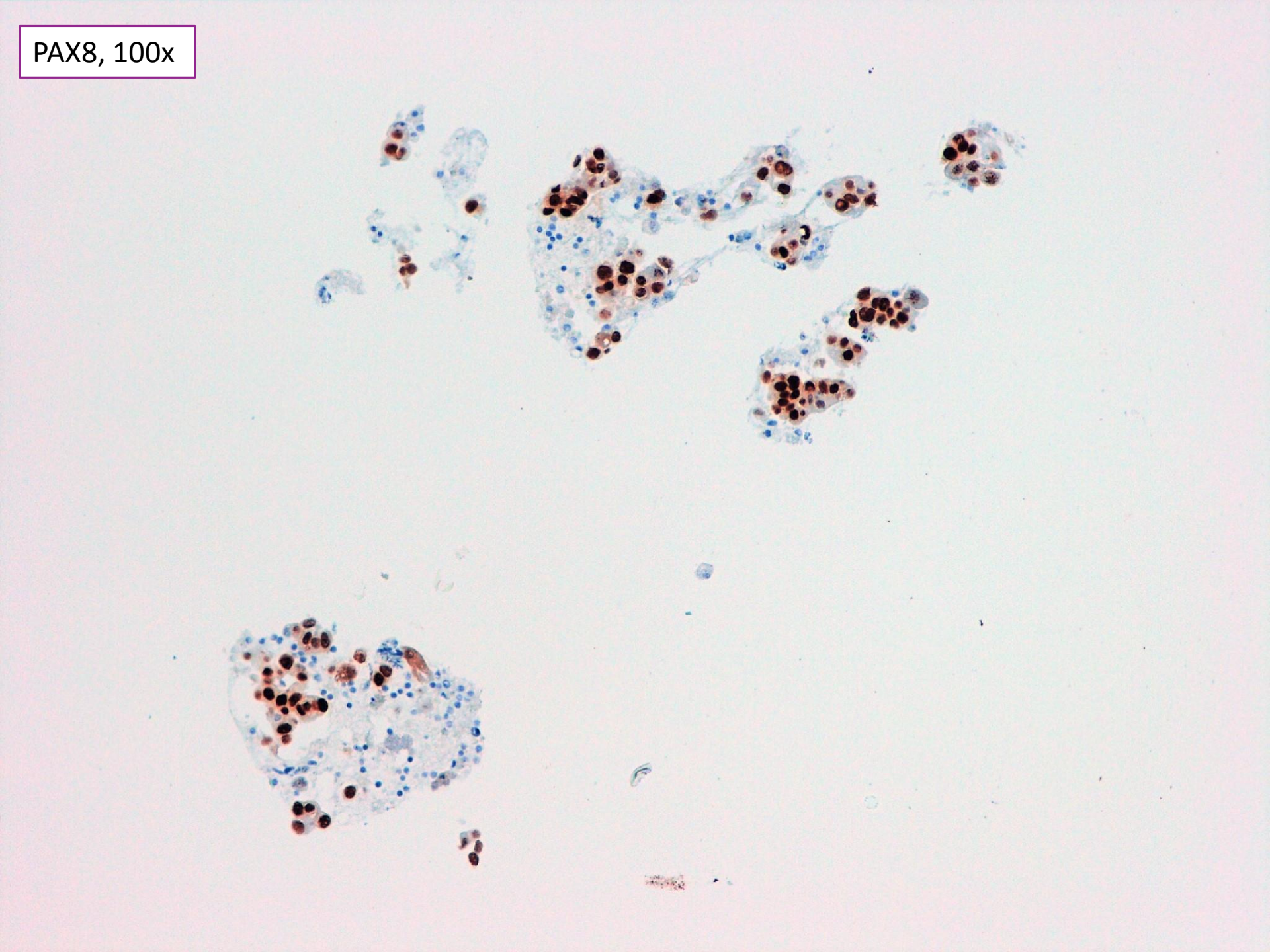
PAX 8 expression in the metastatic context has not been systematically evaluated. Yet, this matter is important for several reasons. Determination of cellular lineage, an interesting but often diagnostically irrelevant task in the study of primary neoplasms, becomes critical for metastatic tumors, especially for those of unknown primary tumors or for those identified against the background of multiple primary tumors. Furthermore, the antigenic profiles of metastases may be different from those of their corresponding primary tumors. For example, the renal cell carcinoma marker, a sensitive marker for renal cell carcinoma, was noted in 80% of primary renal cell carcinomas but was expressed only in less than half of metastatic renal cell carcinomas with a marked decrease in the percentage of positive cells.[30] The current study showed that the sensitivity of PAX 8 as a tumor marker is comparable for metastatic and primary tumors. The overall PAX 8 expression for metastatic renal cell carcinomas compared with that of their primary tumors was 88 *vs* 89%, with a similar staining extent (>50% of tumor cells in >50% of cases). For collecting duct renal cell carcinoma, a type of renal cell carcinoma well known for a lack of expression for many other 'renal-specific' markers,

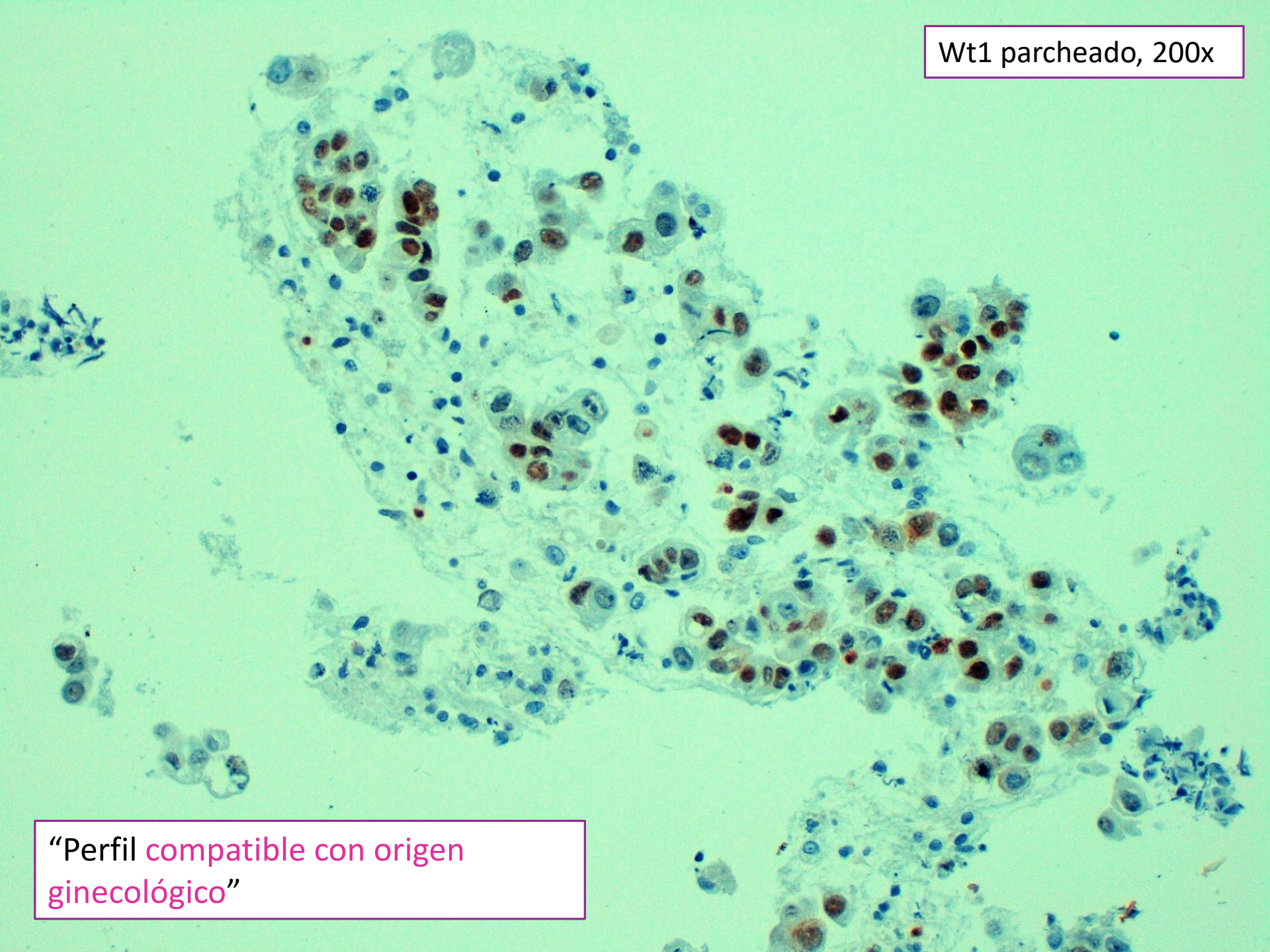
La importancia del PAX8

El perfil antigénico de las metástasis puede diferir del primario. Sin embargo en PAX8 la alta sensibilidad/especificidad se mantiene ¡tanto para los tumores primarios como para las metástasis!

Primarios müllerianos PAX8+ : 96%
Metástasis " PAX8+ : 90%

PAX8, 100x




Wt1 parcheado, 200x
“Perfil compatible con origen ginecológico”

Evolución

- Actualmente en tratamiento con quimioterapia (Carboplatino-paclitaxel, 3r ciclo)
- En seguimiento. Pendiente de valoración.
- Biopsia gástrica negativa

Conclusiones

Destacar la importancia de:

- Mirar bien los datos clínicos.
- La IQH en el diagnóstico de metástasis de origen desconocido. ¡Bloque celular!
- Aproximar el diagnóstico a fin de permitir un tratamiento específico (aumento de la supervivencia). Con clínica+histología+IQH se alcanza el diagnóstico en la mayor parte de los casos.
- El PAX8 como marcador de tumores de origen ginecológico. **Sensibilidad y especificidad muy altas, ¡también para las metástasis!**