Mujer de 51 años con nódulo en CSE

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GENERALITAT VALENCIANA

La Fe
Hospital Universitari i Politècnic



Mujer de 51 años con antecedentes patológicos :
-No HTA,DM ni dislipemia.
-Discopatía L5-S1
-Cefalea migrañosa.

-Percibe nódulo en CSE, se remite a radiología para estudio.

-Ecografía: lesión nodular sospechosa.



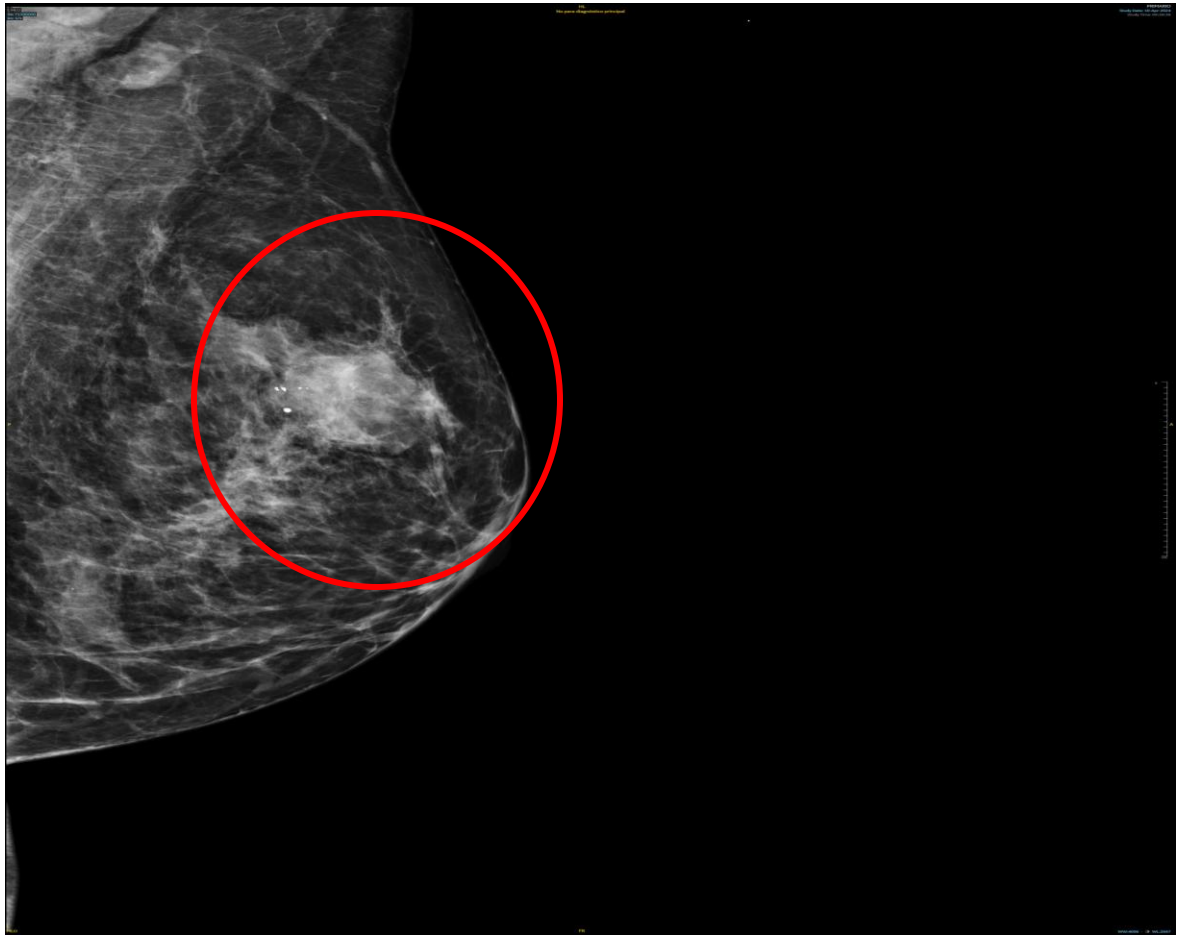




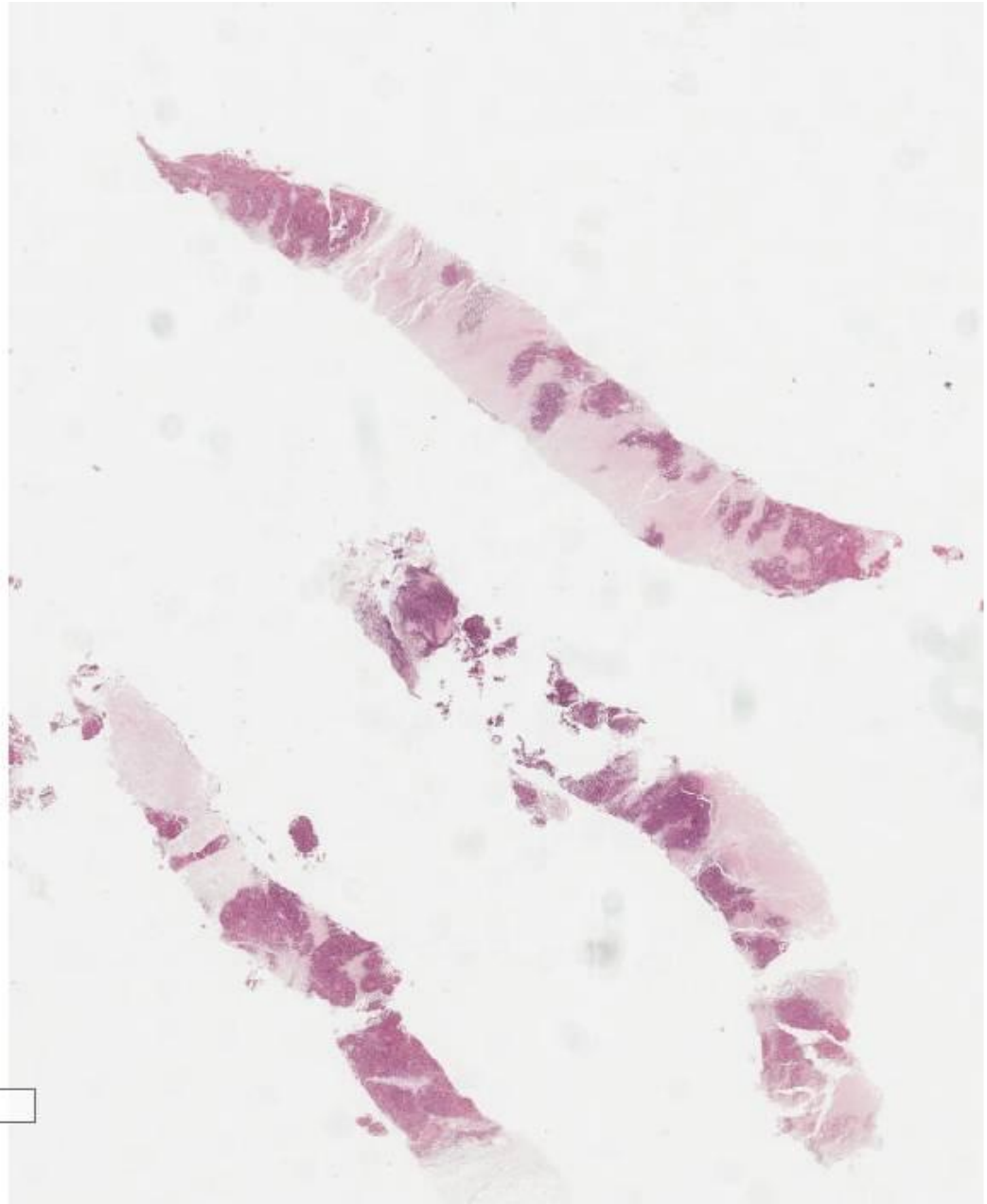
Mamografía

MAMOGRAFÍA

Nódulo sólido parcialmente circunscrito. Adyacente al mismo en su vertiente externa otro pequeño nódulo de similares características. Considero lesión conjunta, de tamaño aproximado 51x26x30 mm TVxAPxCC. Este nódulo no se visualiza en estudios previos, categoría BIRADS 4c.

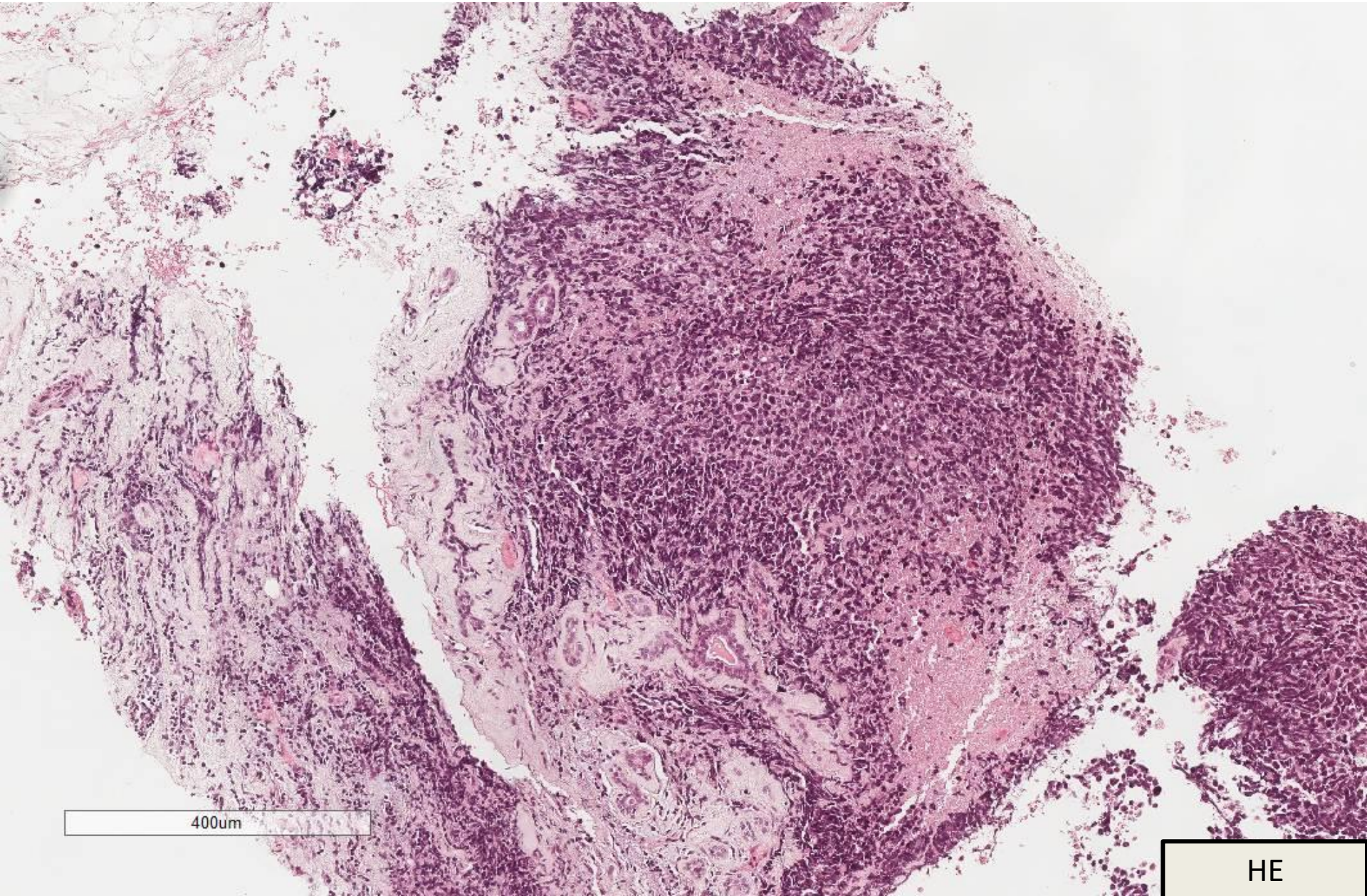


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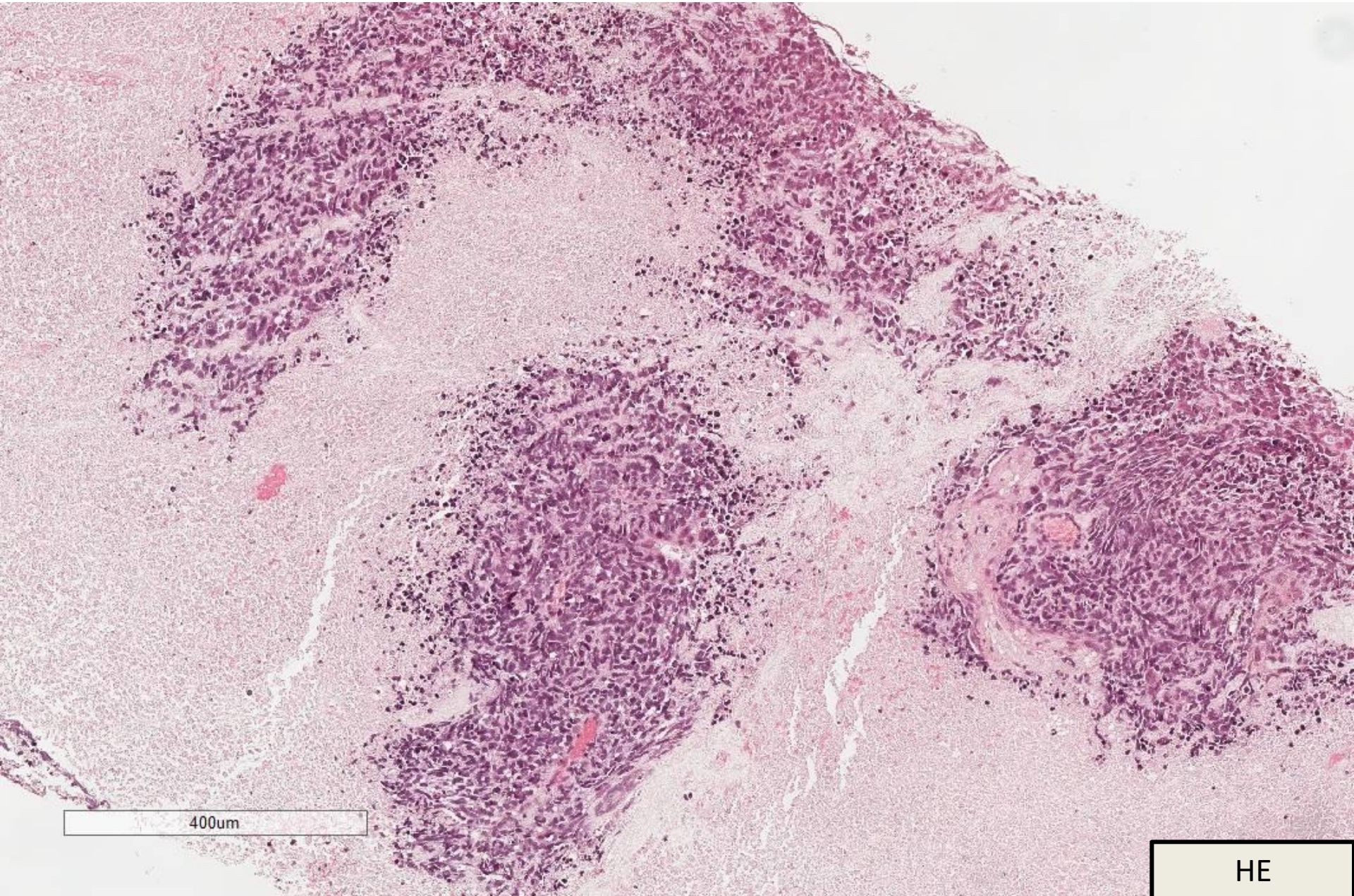
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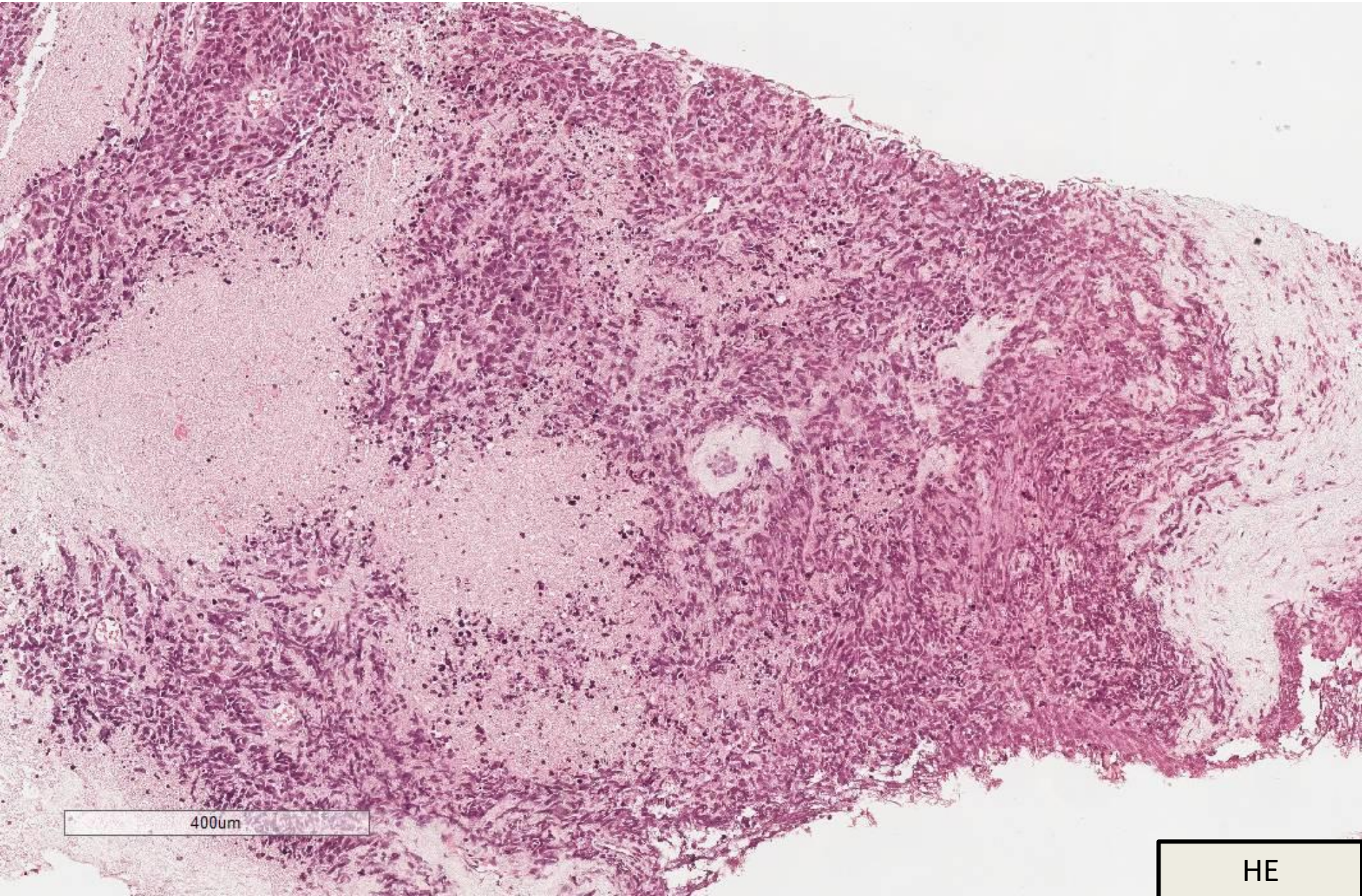
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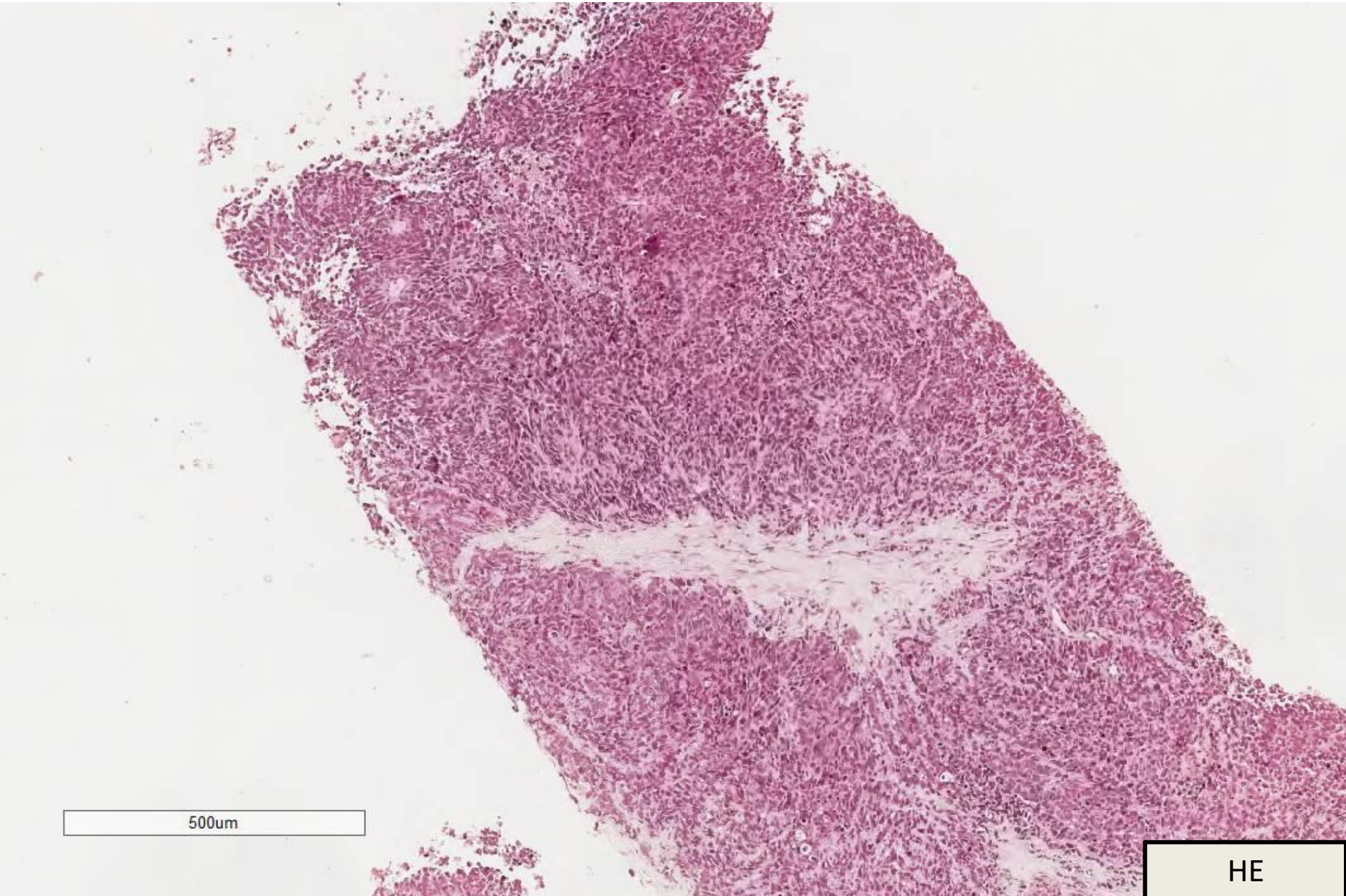
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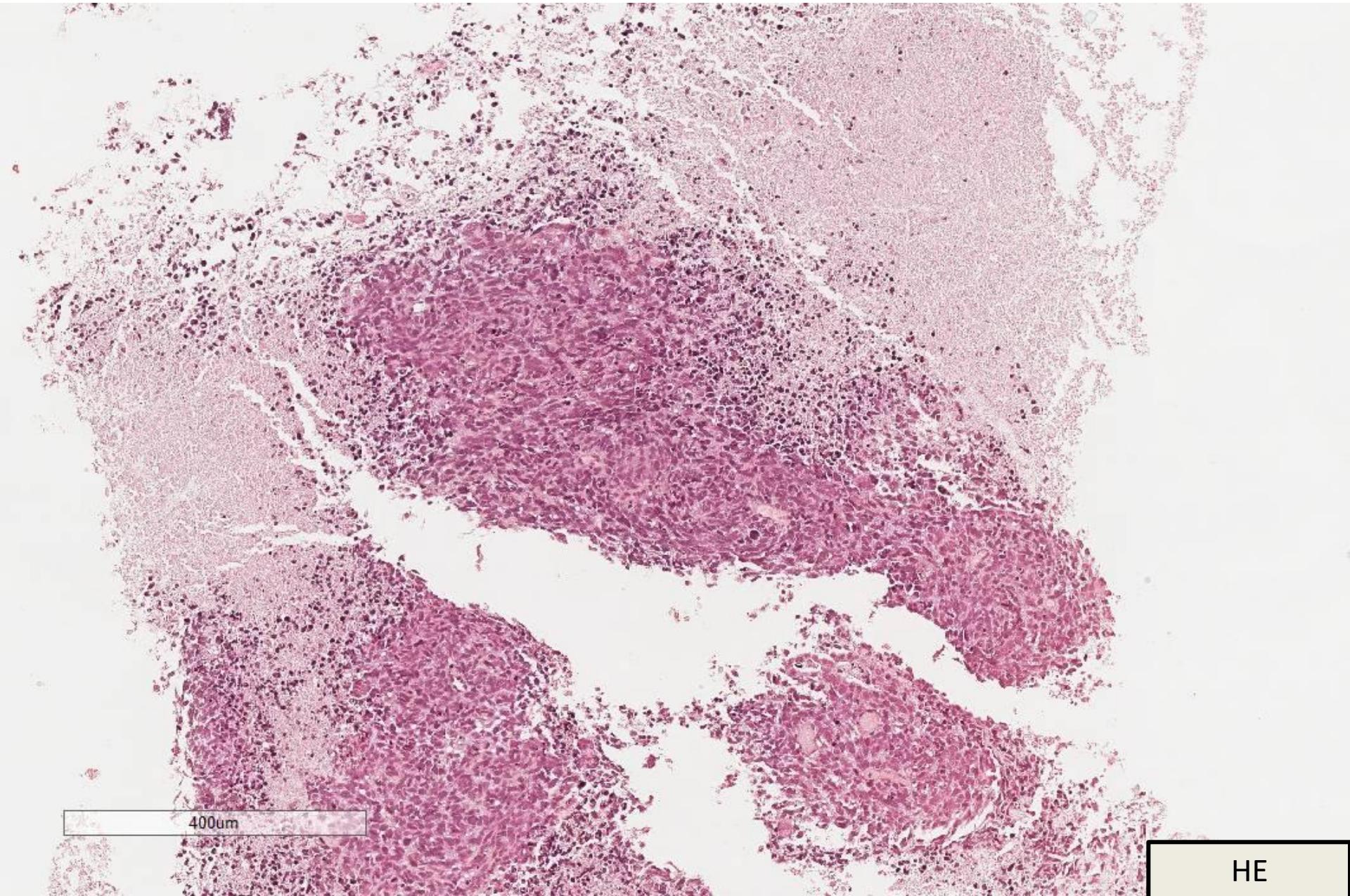
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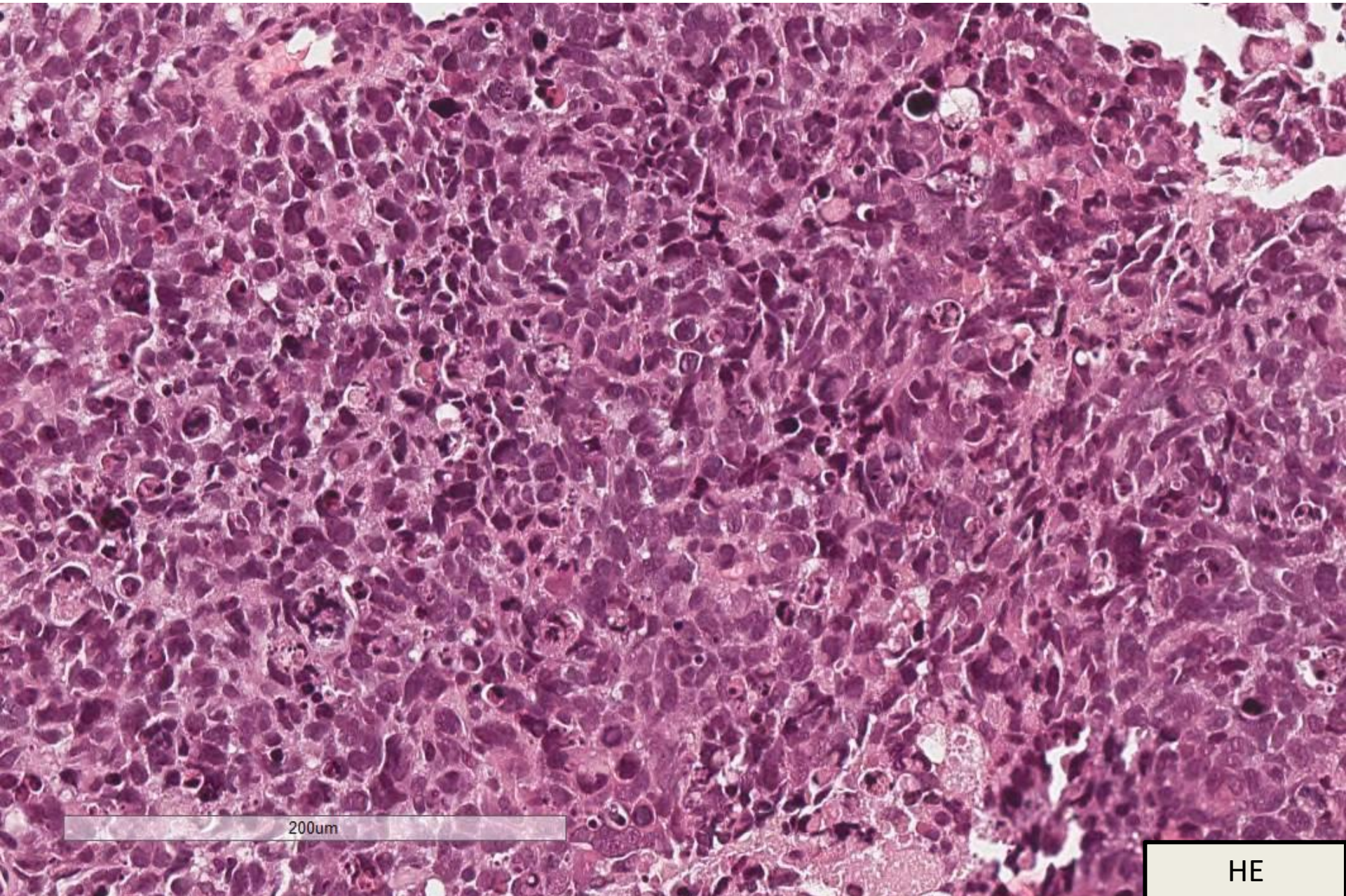


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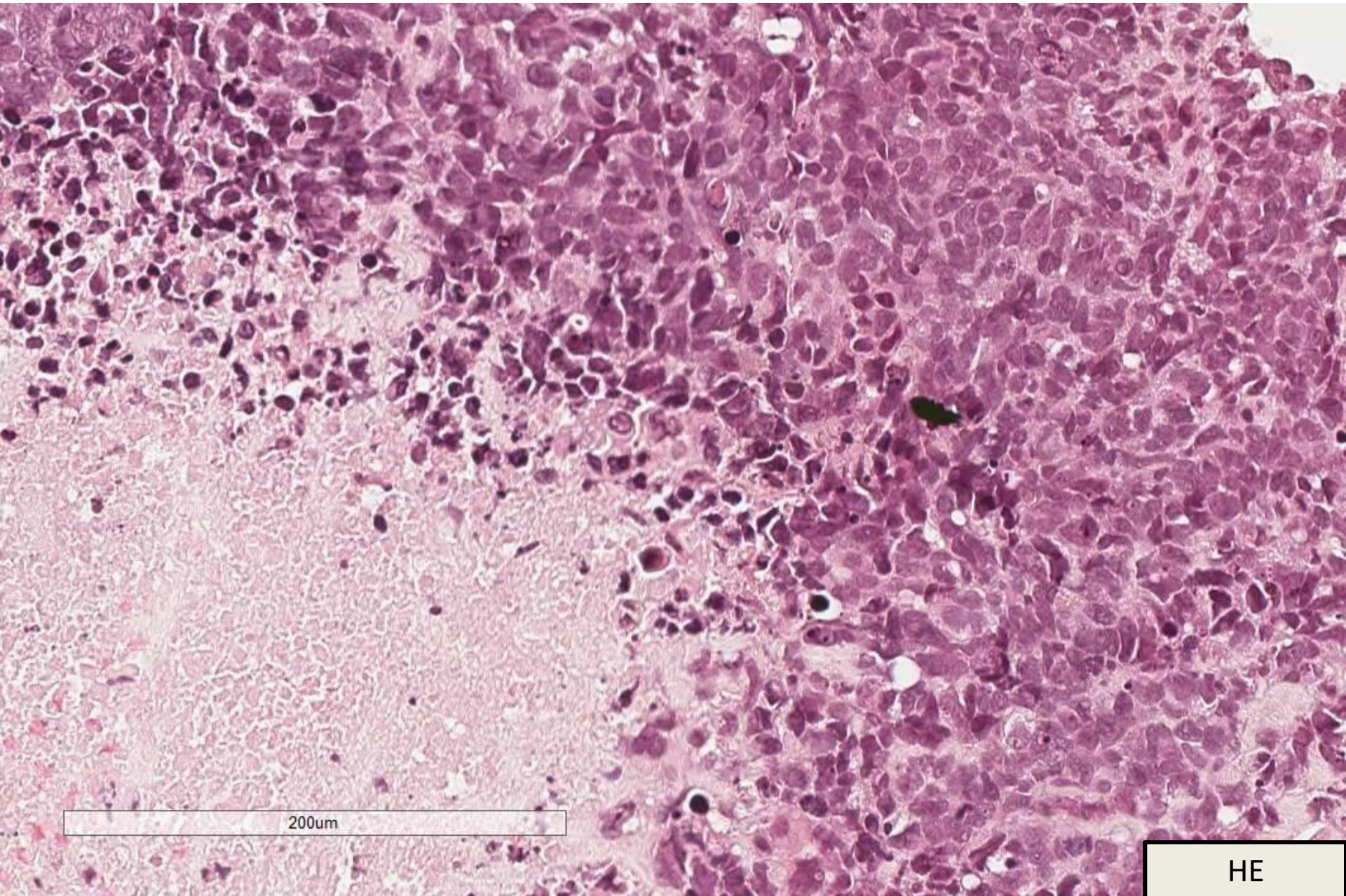
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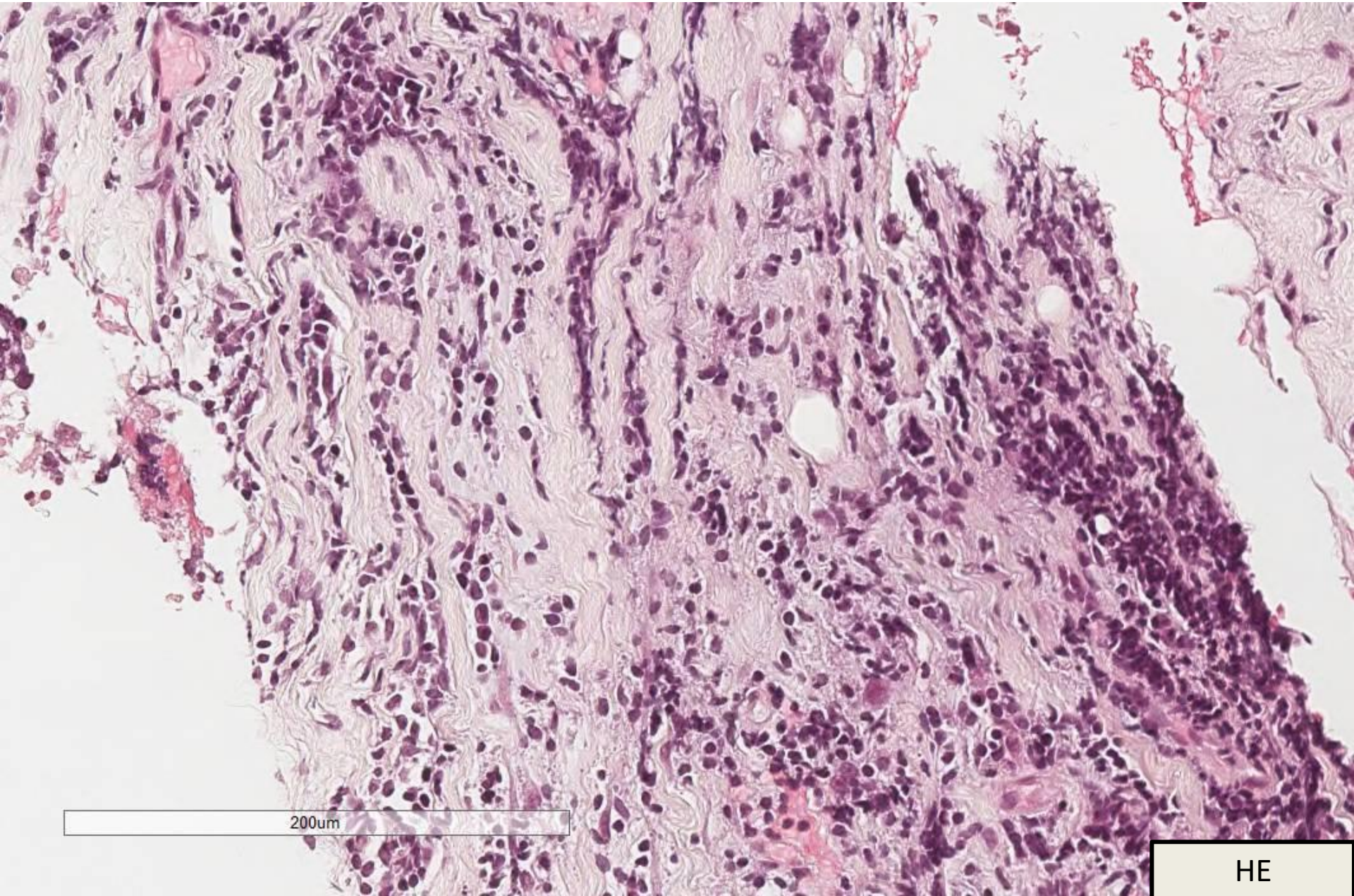
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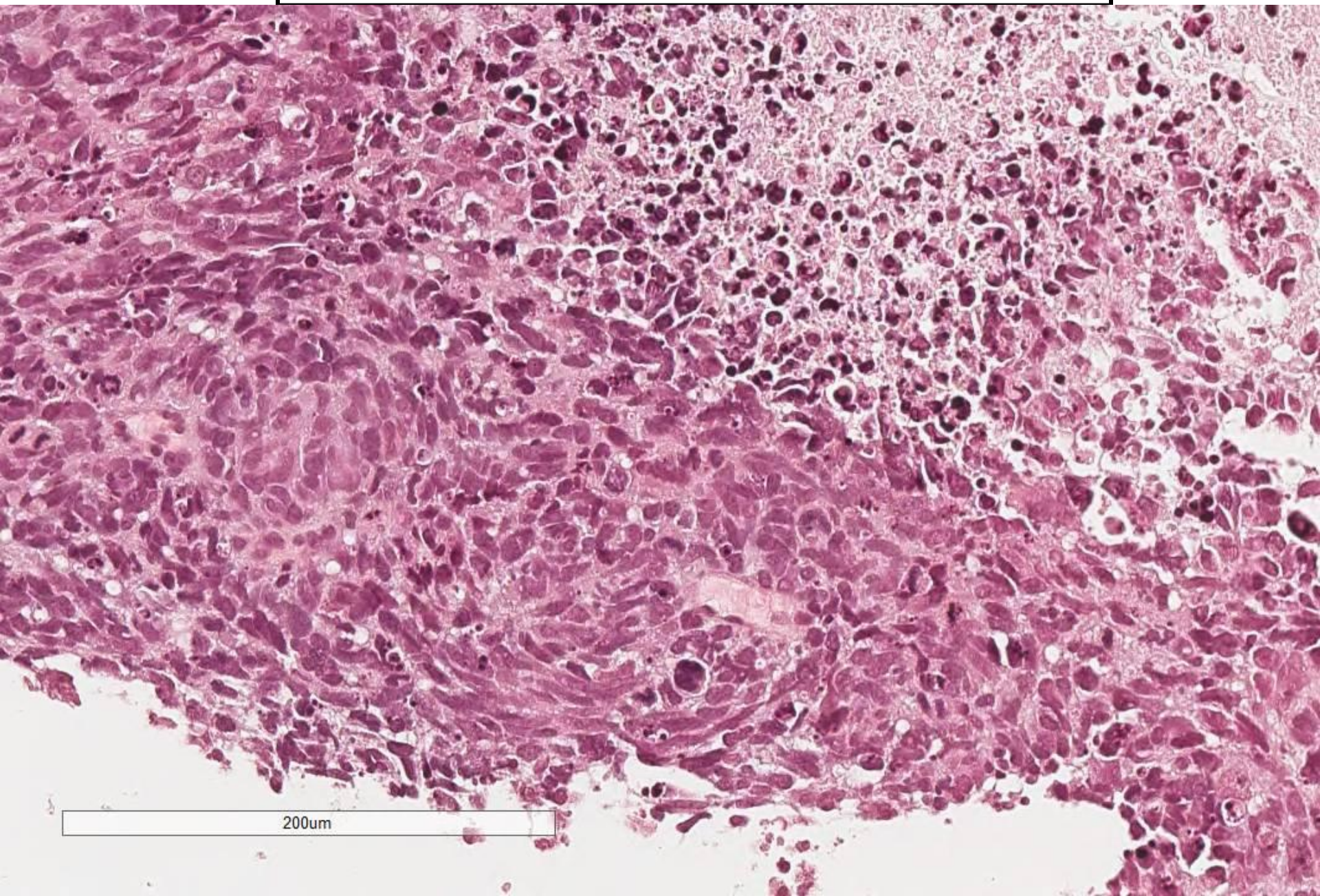
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DIAGNÓSTICO DIFERENCIAL

Punto de partida: confirmar linaje antes de asignar origen. La necrosis extensa y la elevada actividad mitótica no son específicas.

CARCINOMA INVASIVO NST DE ALTO GRADO

CARCINOMA NEUROENDOCRINO DE ALTO GRADO

LINFOMA DE ALTO GRADO

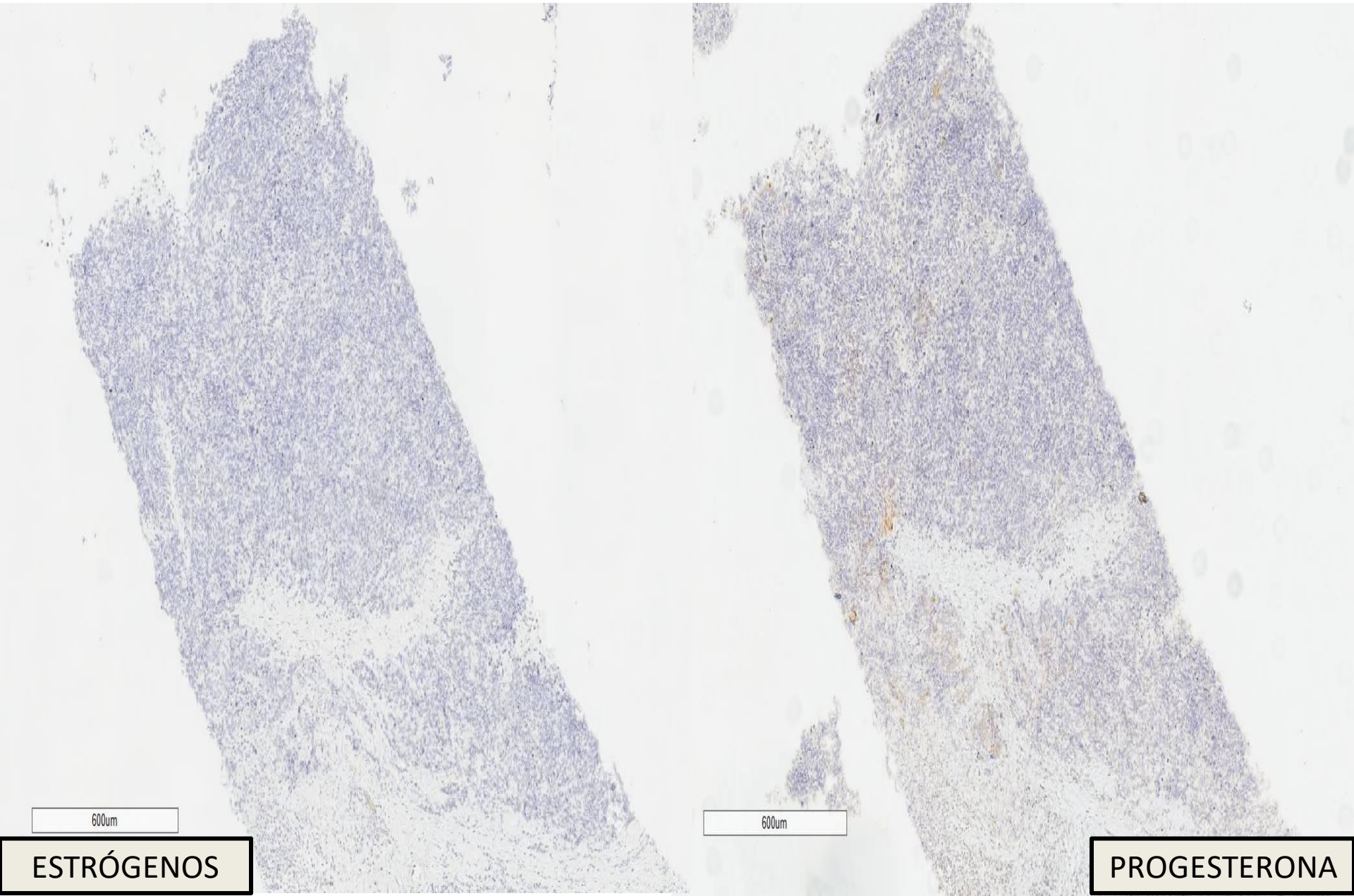
METÁSTASIS INDIFERENCIADA

SECUENCIA PRÁCTICA

1. **Pancitoqueratina AE1/AE3**
2. **CD45 ± CD20/PAX5**
3. **INSM1 / sinaptofisina si morfología sugestiva**
4. **Panel de origen según clínica y morfología**

Nota: panel inicial escalonado y adaptado a la morfología; los marcadores deben interpretarse por patrón y localización celular, no de forma aislada.

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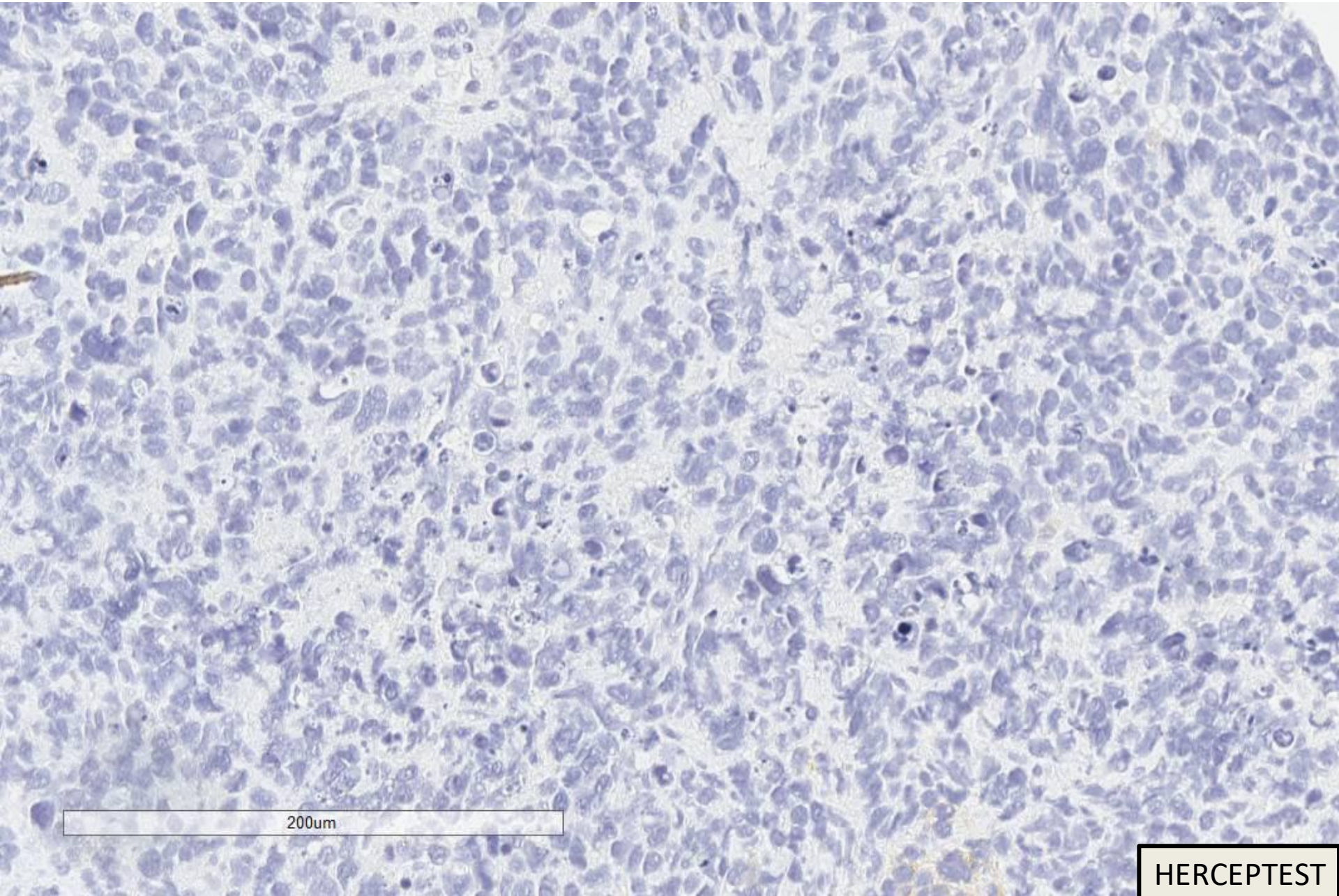


ESTRÓGENOS

PROGESTERONA

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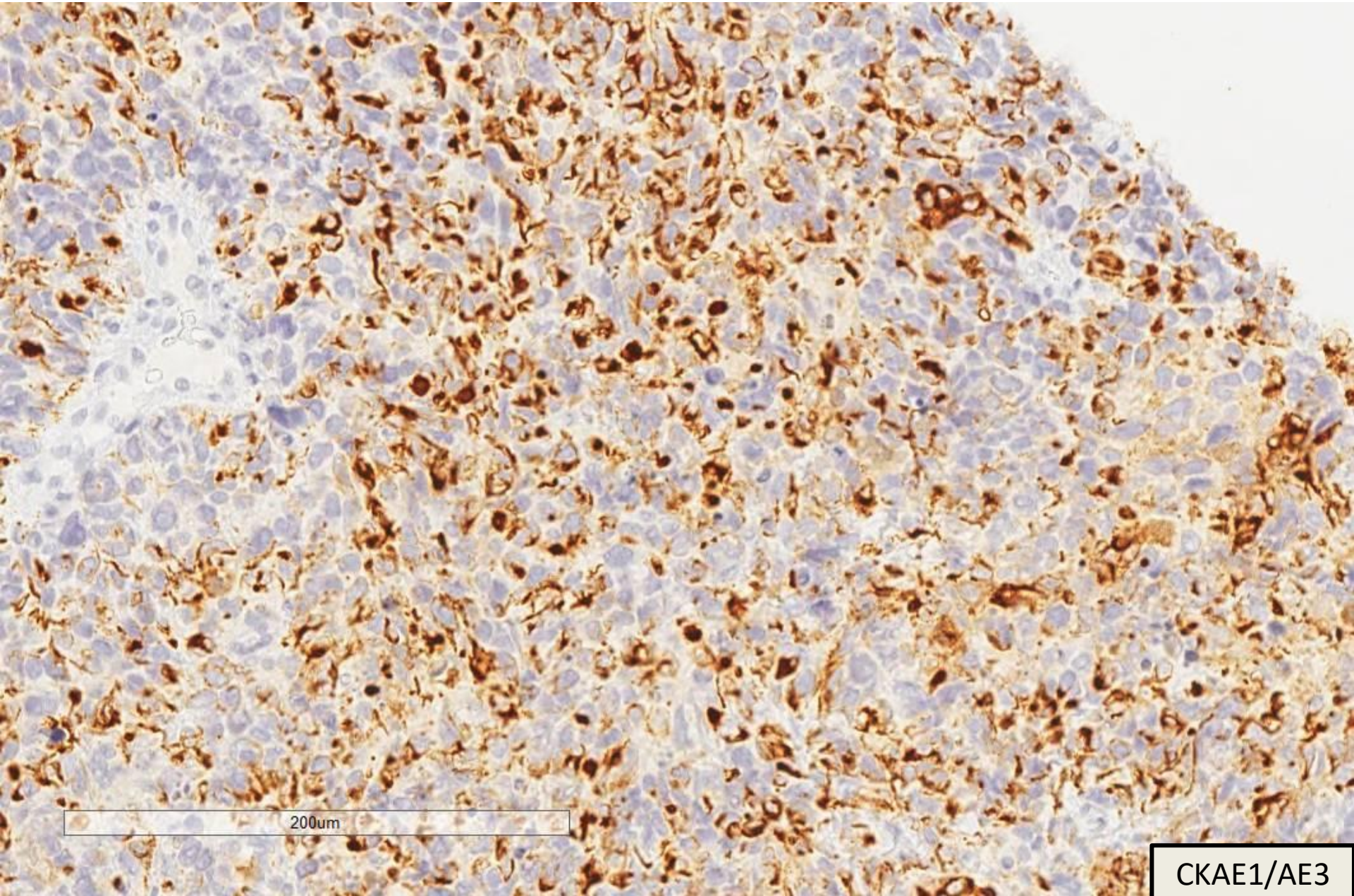
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HERCEPTEST

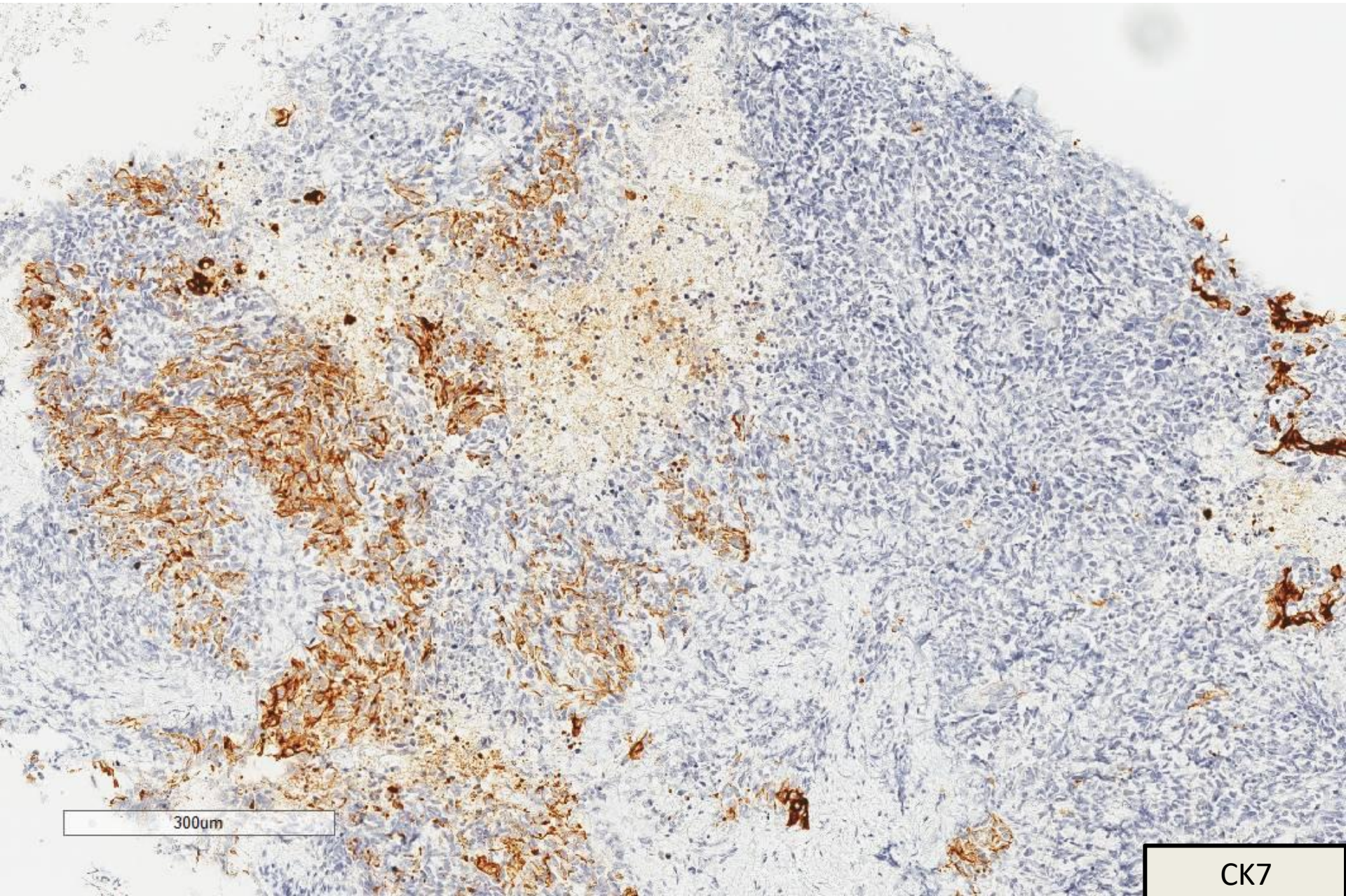
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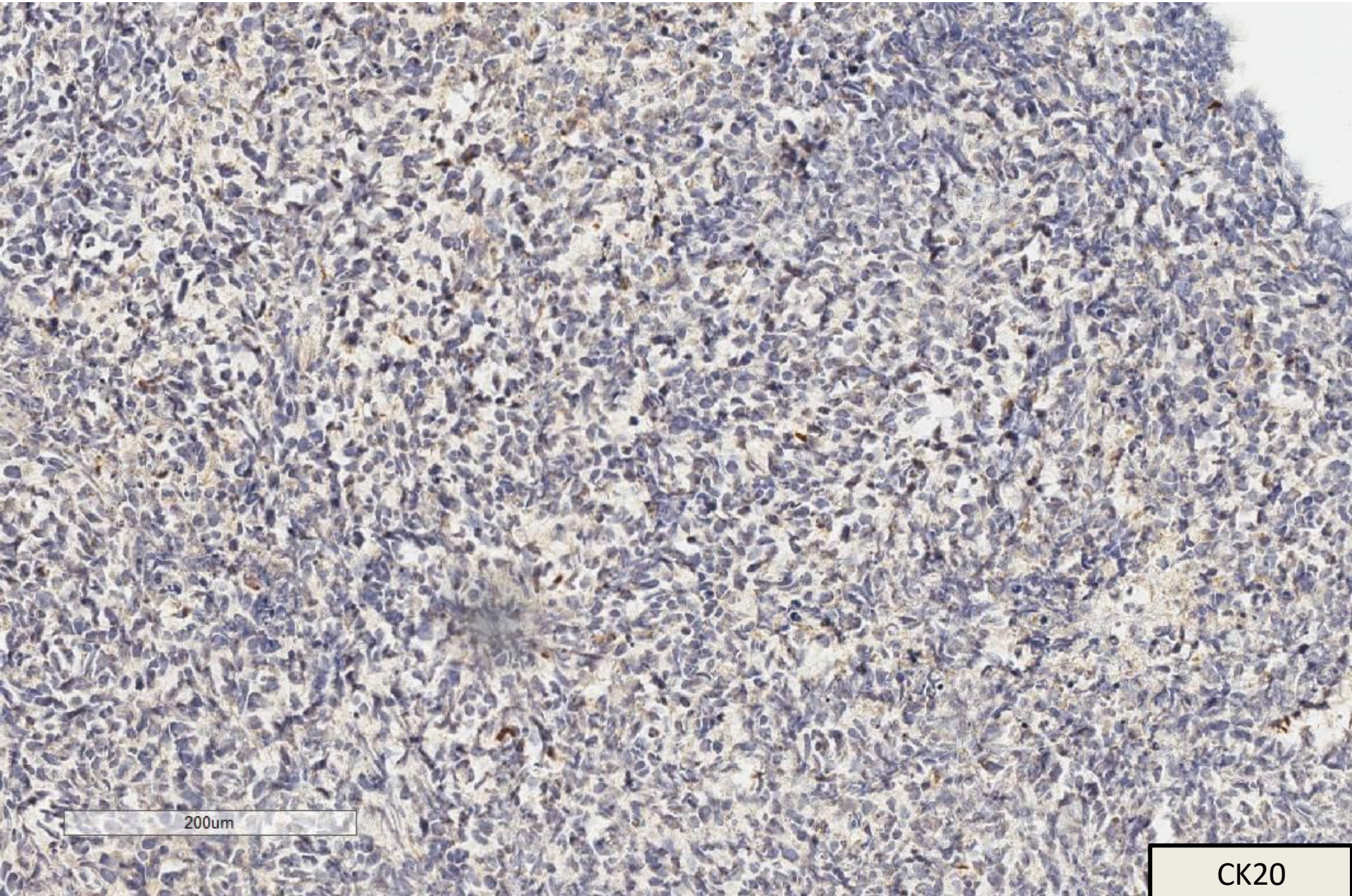
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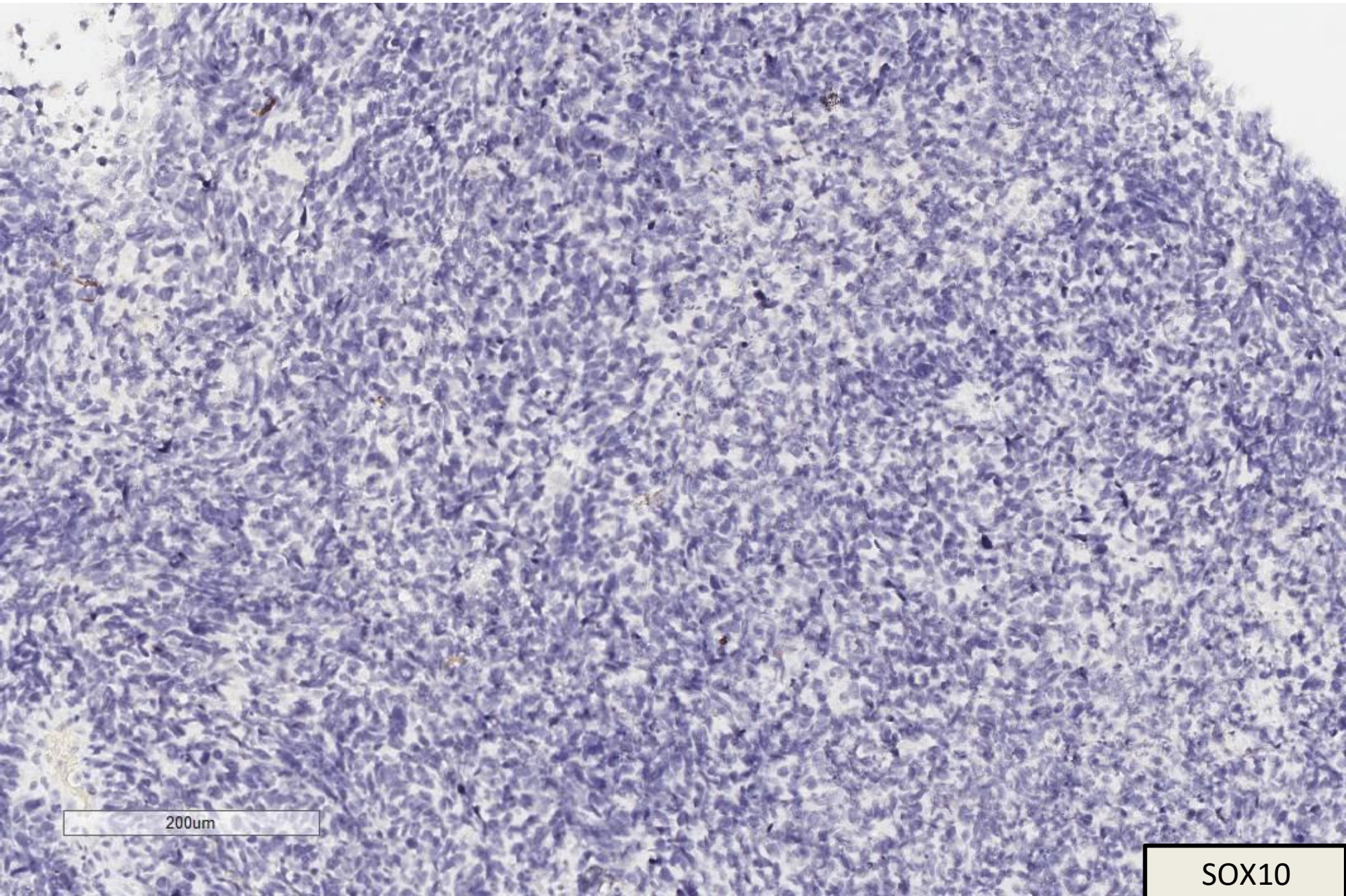
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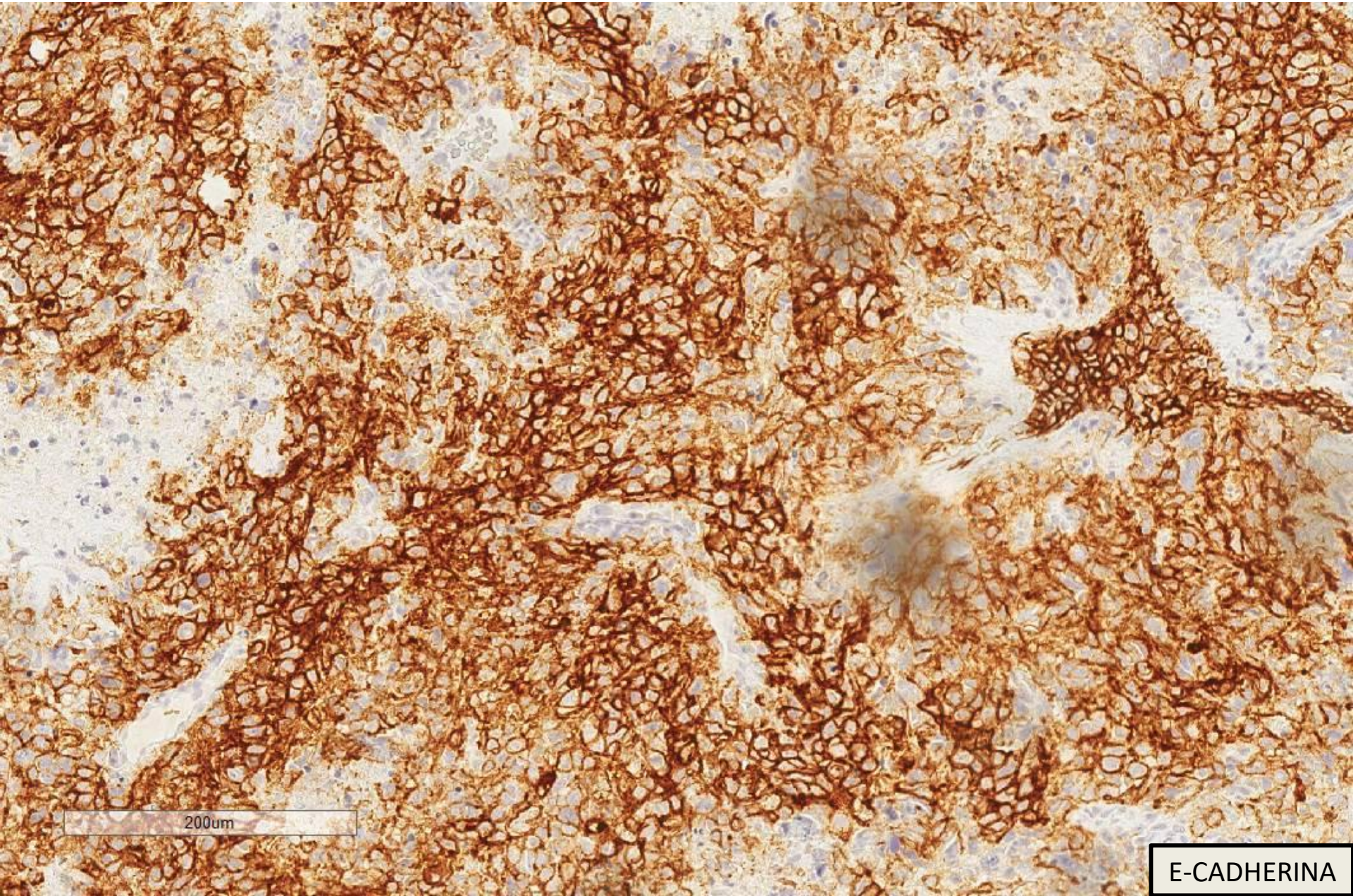
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SOX10

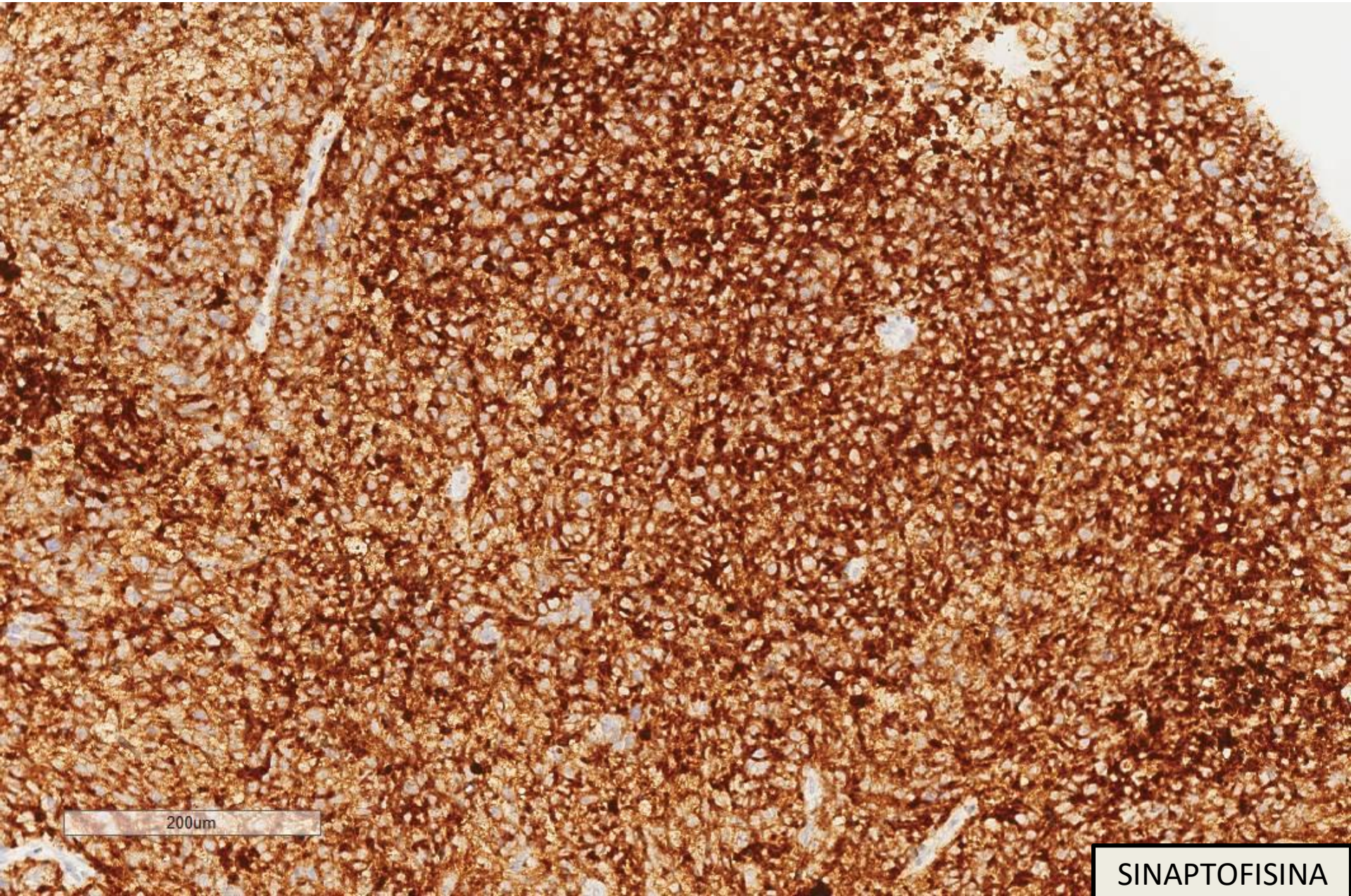
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E-CADHERINA

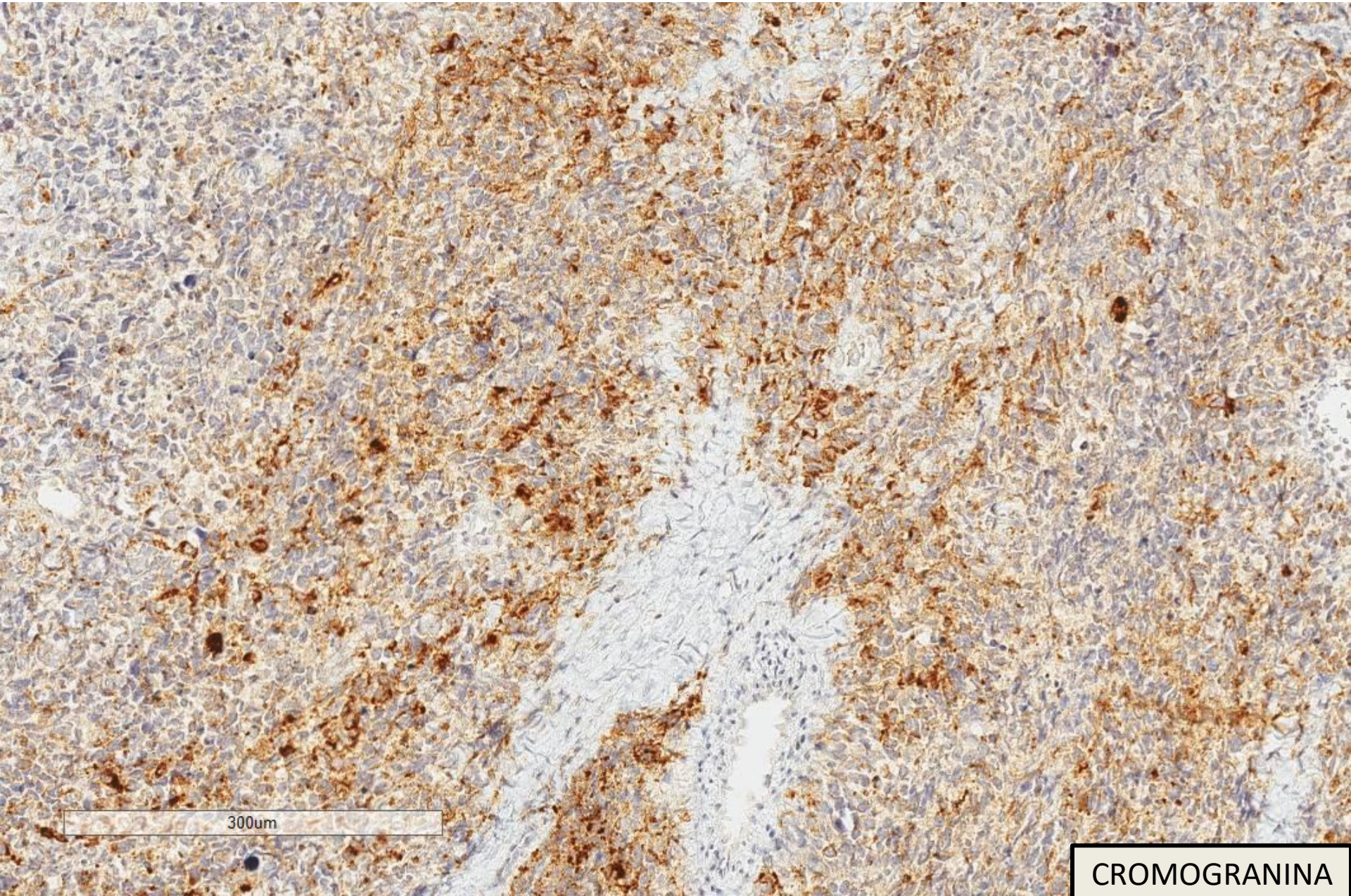
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SINAPTOFISINA

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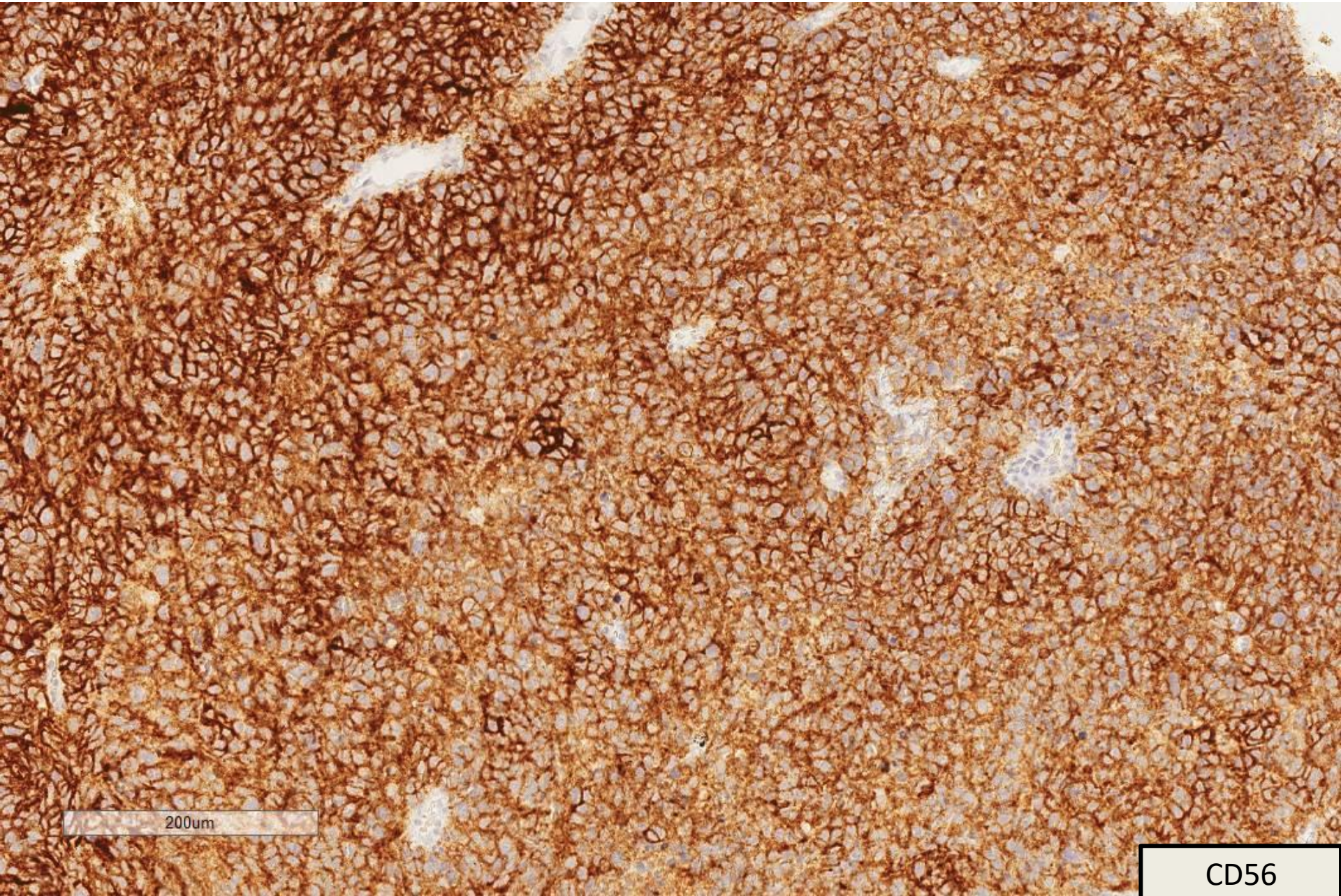
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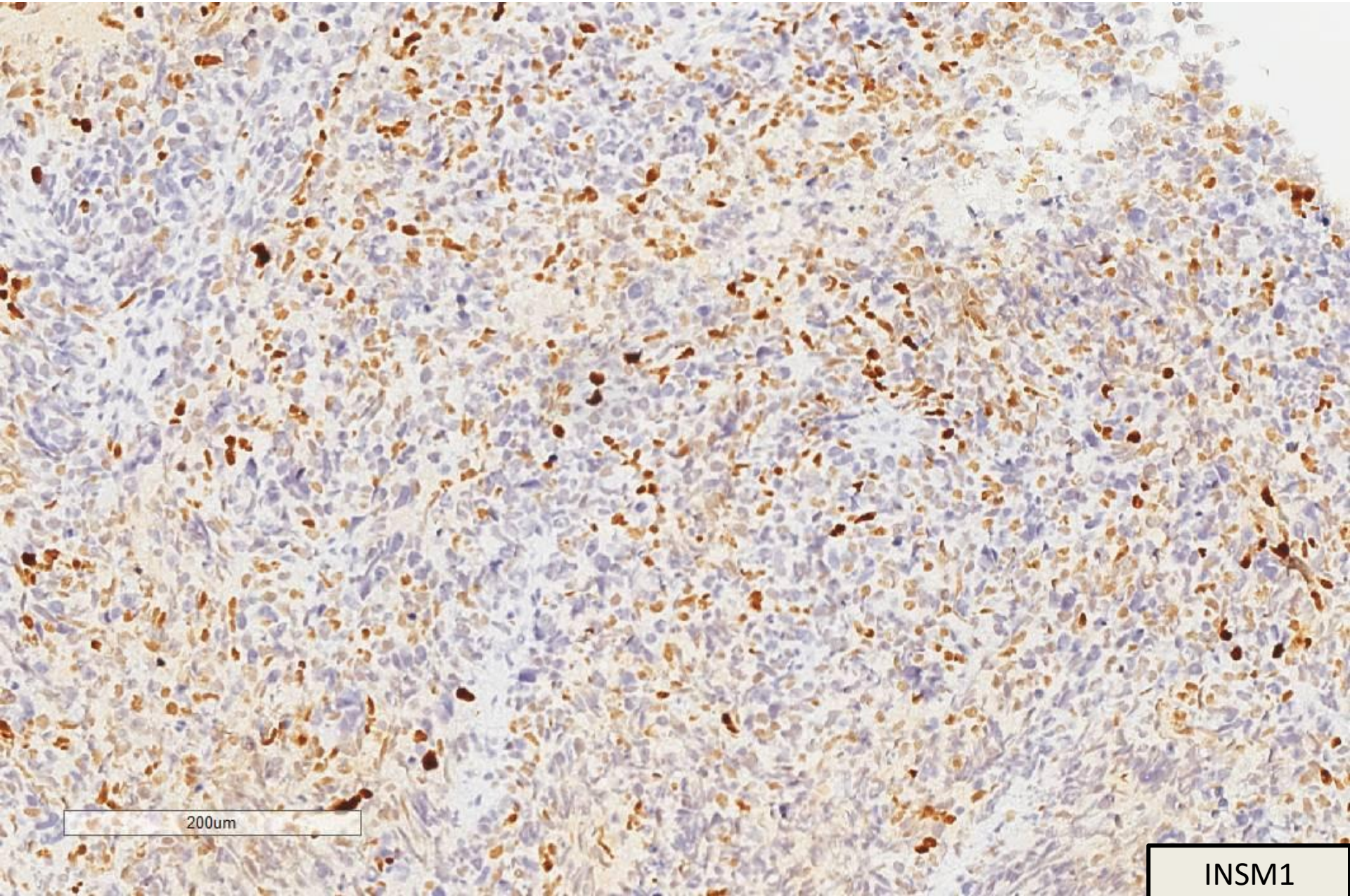
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CD56

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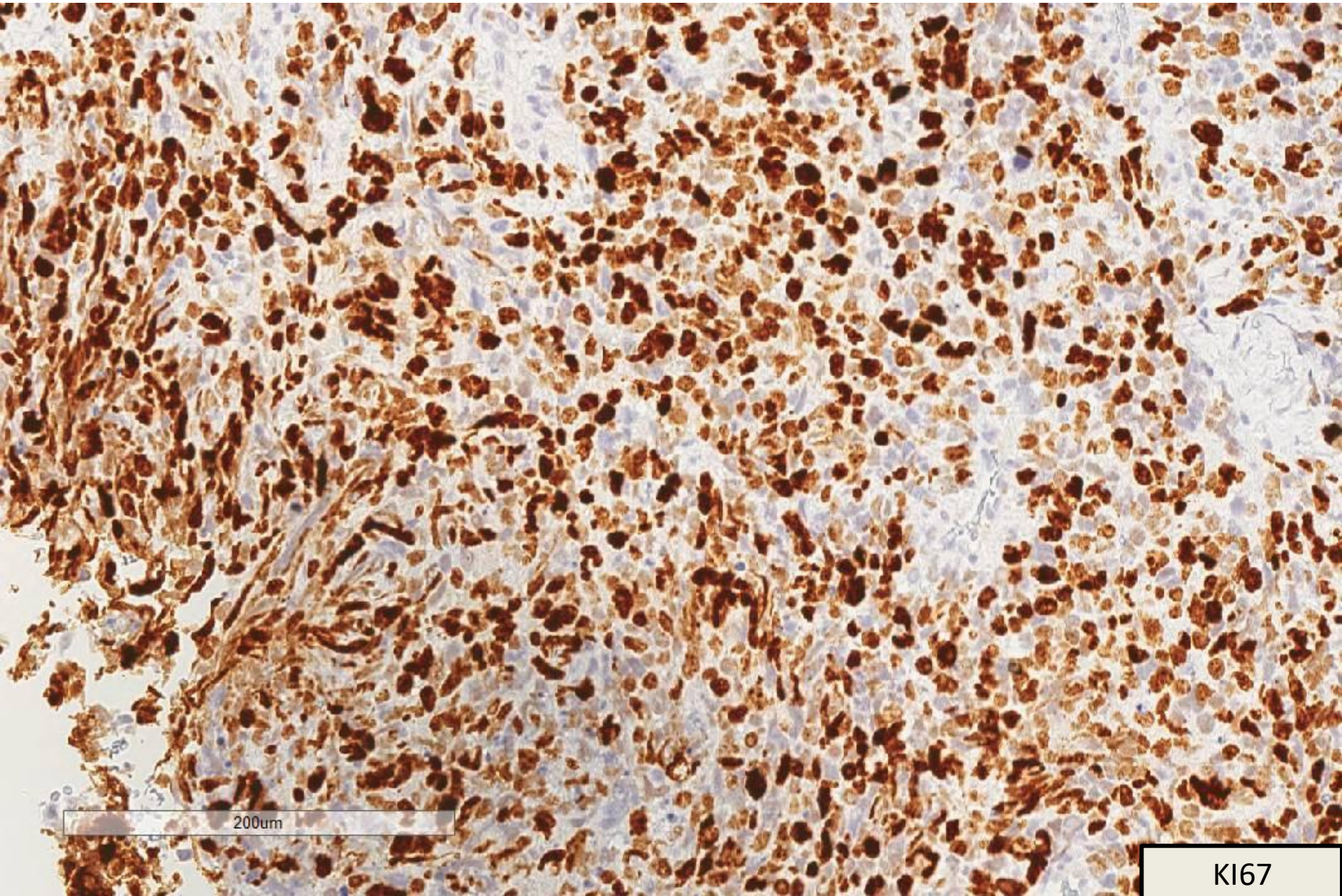
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INSM1

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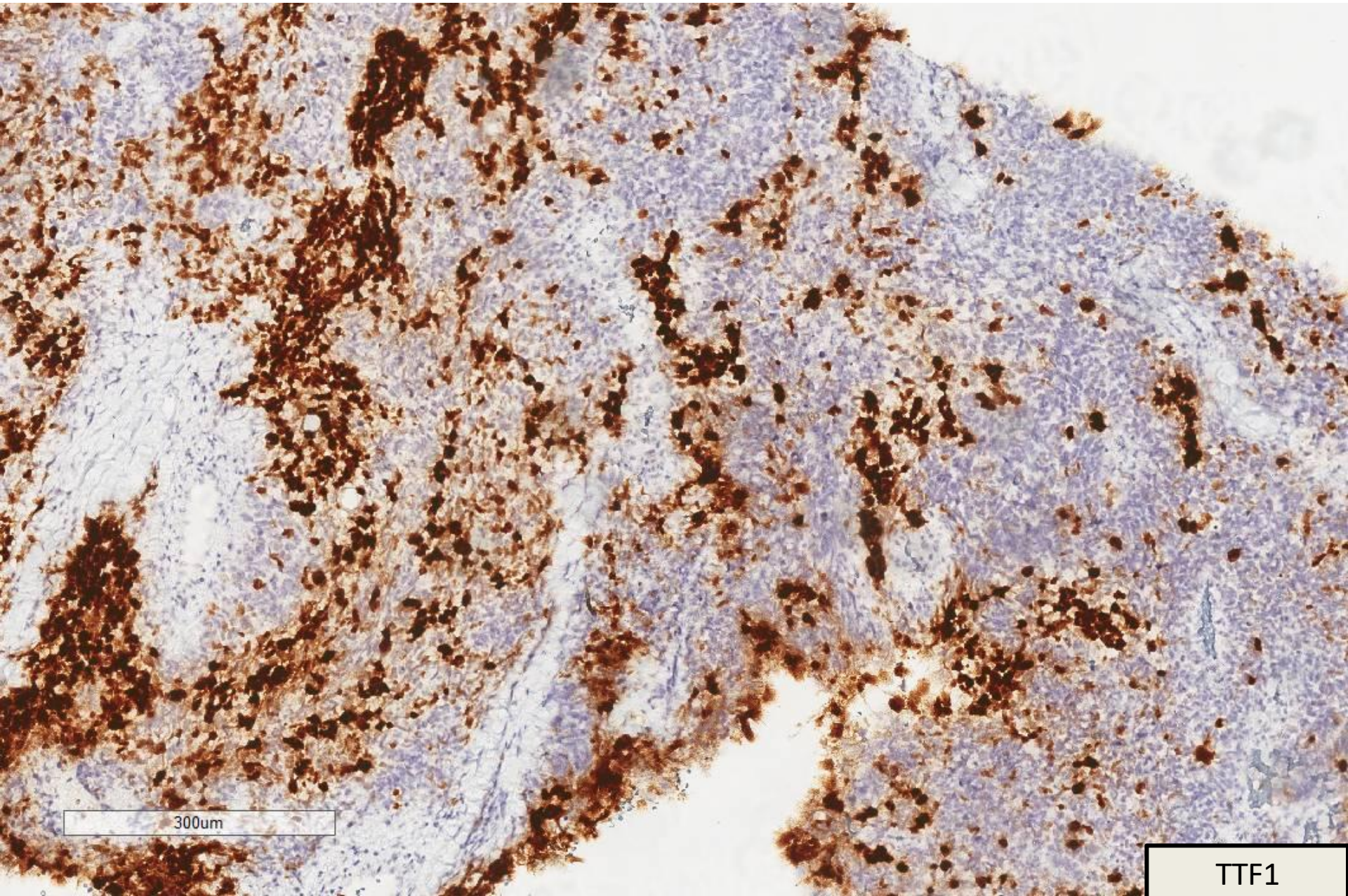
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KI67

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TTF1

DIAGNÓSTICO DIFERENCIAL

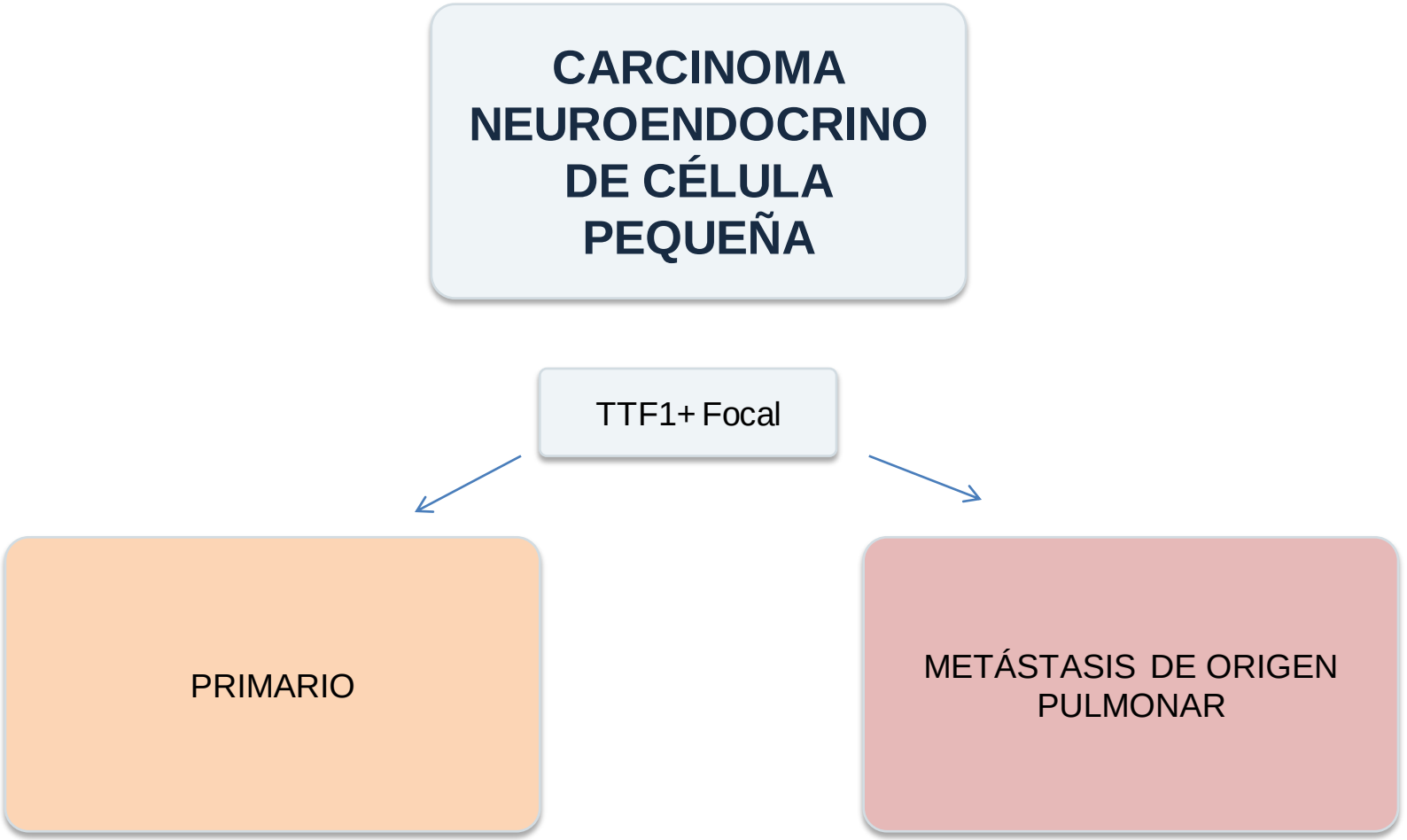
CA[illegible]OMA INVASIVO NST DE ALTO GRADO

LINF[illegible]E ALTO GRADO

CARCINOMA NEUROENDOCRINO DE CÉLULA PEQUEÑA

MET[illegible]ASIS INDI[illegible]ADA

DIAGNÓSTICO DIFERENCIAL



Localization
Clinical features
Epidemiology
Etiology
Pathogenesis
Macroscopic appearance
Histopathology
Cytology
Diagnostic molecular pathology
Essential and desirable diagnostic criteria
Staging
Prognosis and prediction

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Histopathology

Histologically and immunohistochemically, NECs are morphologically indistinguishable from their counterparts in the lung { 29661717 ; 26960398 }. SCNECs display an infiltrative growth pattern and are composed of densely packed, fairly uniform, small, dark hyperchromatic cells that have a high N:C ratio, scant cytoplasm, inconspicuous nucleoli, and poorly defined cytoplasmic borders. In LCNEC, the cells show evident cytoplasm and highly pleomorphic nuclei with variably coarse chromatin. Common features of both SCNEC and LCNEC are high numbers of mitotic figures and focal areas of necrosis. An in situ component with the same cytological features may be detected. Lymphatic tumour emboli are frequently encountered { 15976350 ; 10976697 }.

The differential diagnoses of primary SCNEC include metastatic small cell carcinoma of non-mammary origin (most commonly from the lung), Merkel cell carcinoma, lymphoma, and melanoma. The presence of an associated ductal carcinoma in situ or conventional-type mammary carcinoma component confirms the primary nature of the tumour. SCNEC should also be differentiated from some forms of the high-grade solid subtype of adenoid cystic carcinoma, metaplastic carcinomas or ductal of no special type (NST) with basaloid cells and an increased N:C ratio. LCNEC should be differentiated from high-grade invasive breast carcinoma NST, by the presence of extensive neuroendocrine differentiation, and from metastatic LCNEC of non-mammary origin (i.e. from the lung).

Cytology

FNA of SCNEC shows the presence of malignant cells with small cell phenotypes, which may display nuclear moulding, finely granular or salt-and-pepper chromatin, and scant delicate cytoplasm. Necrosis is frequently present in cytological samples of NEC.

Diagnostic molecular pathology

Immunohistochemical analysis shows consistent staining for cytokeratin markers but variable staining for neuroendocrine markers, with more than two thirds of cases staining positively for chromogranin and synaptophysin. PGP9.5, CD56 (NCAM), and NSE are positive in the majority of cases. SCNECs are positive for BCL2 and negative for ERBB2 (HER2) { 10976697 }. ER positivity has been reported in 30–50% of cases { 10976697 ; 27329168 } and PR positivity in a smaller proportion, but other authors did not identify receptor expression in SCNEC { 18357385 }. TTF1 expression in SCNEC of the breast has been reported, but not diffuse strong nuclear staining as seen in small cell carcinoma of the lung { 20661411 ; 19578049 }. GATA3 expression has been reported in NEC of the breast but not in metastatic NECs, including those from the lung { 27125358 }.

Essential and desirable diagnostic criteria

Essential: histological features similar to those of SCNEC and LCNEC of the lung; high-grade tumour.

Desirable: coexisting ductal carcinoma in situ.

Staging

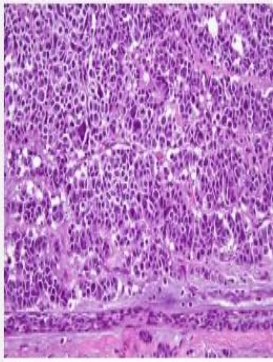
NECs are staged similarly to other types of invasive breast carcinoma.

Prognosis and prediction

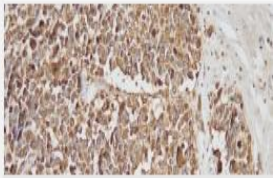
SCNEC is significantly associated with a worse prognosis than other neuroendocrine tumours (NETs) of the breast { 25399232 }. The outcomes of patients with breast SCNEC were superior to those of patients with stage-matched small cell lung carcinoma, except in patients with distant disease { 25853028 }. It was reported that radiation therapy is not associated with a significant difference in survival for patients with either localized or regional disease { 25853028 }. Localized SCNEC is usually managed similarly to usual ductal breast cancer. In the metastatic SCNEC setting, regimens that are implemented in small cell lung cancer are usually attempted. There is some evidence that ER-positive SCNEC may respond to hormone therapy { 22424945 }. LCNECs of the breast are rare, and no clinical data on prognosis are available.



#2068
Small cell neuroendocrine carcinoma (SCNEC) of the breast

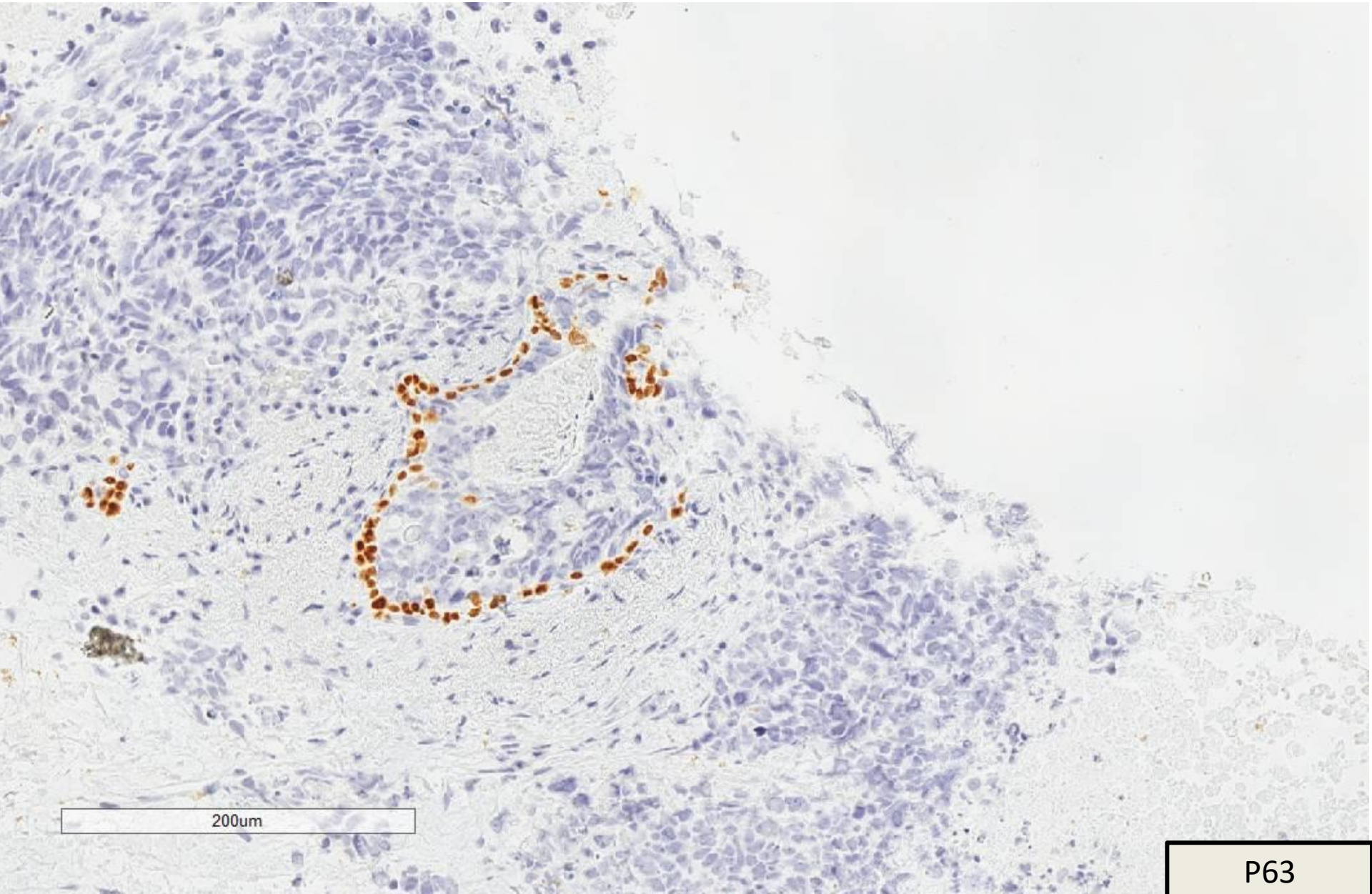


#2488
Large cell neuroendocrine carcinoma (LCNEC) of the breast



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P63

Case Reports > Int J Clin Exp Pathol. 2010 Jun 30;3(6):629-33.

Primary small cell carcinoma of the breast with TTF-1 and neuroendocrine marker expressing carcinoma in situ

Michael Christie [1], Laura Chin-Lenn, Monique M Watts, Alpha E Tsui, Malcolm R Buchanan

Affiliations + expand

PMID: 20661411 PMCID: PMC2907125

Abstract

Primary small cell carcinoma (SmCC) of the breast is very rare and may be difficult to distinguish from metastatic small cell carcinoma. Confident histopathological diagnosis of a primary breast SmCC requires the demonstration of an in situ component. We report a case of primary small cell carcinoma of the breast with coexisting carcinoma in situ in which the invasive carcinoma and in situ component both expressed neuroendocrine markers and Thyroid transcription factor-1 (TTF-1) by immunohistochemistry. Expression of neuroendocrine markers and TTF-1 in the in situ component allowed a highly confident diagnosis of primary small cell carcinoma of the breast. To our knowledge there is only one previous report of TTF-1 expressing in situ carcinoma associated with a primary SmCC of the breast.

Keywords: Breast; Carcinoma in situ; Neuroendocrine; Small cell carcinoma; Thyroid transcription factor-1.

PubMed Disclaimer

> Am J Surg Pathol. 2010 Dec;34(12):1881-5. doi: 10.1097/PAS.0b013e3181f884e8.

Thyroid transcription factor-1 expression in breast carcinomas

Judith Robens [1], Lynn Goldstein, Allen M Gown, Stuart J Schnitt

Affiliations + expand

PMID: 21107096 DOI: 10.1097/PAS.0b013e3181f884e8

Abstract

Immunostaining for thyroid transcription factor-1 (TTF-1) is frequently used to help assess the site of origin of metastatic carcinomas. TTF-1 expression is most frequently seen in carcinomas of thyroid and lung origin. Furthermore, it has been assumed that the expression of TTF-1 in a carcinoma excludes the possibility of a breast origin. We have recently encountered in our consultation practice 4 cases of invasive breast carcinoma (confirmed by clinical findings and other immunophenotypic features) that showed unequivocal tumor cell expression of TTF-1. However, the frequency with which TTF-1 expression is observed in breast carcinomas is unknown. To address this, we carried out immunostaining for TTF-1 on 546 primary breast carcinomas submitted for routine estrogen receptor, progesterone receptor, and/or HER2 testing. Cases were considered TTF-1 positive if they showed any nuclear staining for this marker. TTF-1 expression was identified in 13 cases (2.4%). Expression varied from focal and weak to diffuse and strong and was seen in both invasive and in situ components. We conclude that a small proportion of breast carcinomas show TTF-1 expression. Therefore, the presence of TTF-1 immunoreactivity in a carcinoma cannot by itself be used to exclude the possibility of a breast origin.

CARCINOMA NEUROENDOCRINO DE CÉLULA PEQUEÑA PRIMARIO DE MAMA

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≈ 0,1 %
de los carcinomas mamarios

PERFIL CLÍNICO-DEMOGRÁFICO

- Predominio femenino muy marcado; también descrito en varones.
- Presentación habitual en mujeres de edad avanzada: 6.ª–7.ª década (≈60–70 años).
- Clínica inespecífica: masa mamaria palpable; sin síndrome hormonal característico.
- Puede debutar en estadios avanzados y con afectación ganglionar.

HISTOLOGÍA

- **Patrón infiltrativo neuroendocrino de alto grado,frecuentenecrosis**.
- Células pequeñas y relativamente monomorfas; escaso citoplasma y alta relación N/C.
- Cromatina hipercromática, moldeamiento nuclear y nucléolos poco evidentes.
- Actividad mitótica elevada y apoptosis; aspecto análogo al carcinoma microcítico pulmonar.

INMUNOFENOTIPO Y PERFIL MOLECULAR

- **Sinaptofisina y cromogranina A positivas; INSM1 puede ser útil**.
- RE/RP positivos en una proporción variable (≈30–50 % en series/revisiones); HER2 suele ser negativo.
- **TTF-1 habitualmente negativo; su positividad no excluye por sí sola origen mamario.**
- **GATA3 / mammaglobina / GCDFP-15 y componente in situ pueden apoyar origen mamario.**

DIAGNÓSTICO Y COMPORTAMIENTO

- Clave: excluir metástasis de carcinoma microcítico pulmonar u otro primario neuroendocrino.
- Buscar CDIS asociado y correlacionar con imagen/estudio sistémico.
- Suele ser de alto grado; mayor proporción de enfermedad avanzada y triple negatividad que el carcinoma ductal convencional.
- Pronóstico generalmente desfavorable; evidencia limitada por la rareza y heterogeneidad de las series.

MENSAJE CLAVE: el diagnóstico de primario mamario es clinicopatológico: morfología microcítica + diferenciación neuroendocrina + exclusión de un primario extramamario.

Referencias: WHO Classification of Tumours Editorial Board. Breast Tumours, 5.ª ed. (2019); Quinn et al. Histopathology (2026), WHO 6.ª ed.; Bogina et al. Mod Pathol. 2022;35:904–914. doi:10.1038/s41379-021-00736-7; Zhang et al. (2023), estudio poblacional SEER de carcinoma microcítico primario de mama. doi/PMID: 38097248.

1.WHO Classification of Tumours Editorial Board Breast tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2024 [cited 2026]. (WHO classification of tumours series6th ed.; vol. 11). Available from: https://tumourclassification.iarc.who.int/chapters/63.

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4.Ordóñez NG. Value of thyroid transcription factor-1 immunostaining in distinguishing small cell lung carcinomas from other small cell carcinomas. Am J Surg Pathol. 2000 Sep;24(9):1217-23. doi: 10.1097/00000478-200009000-00004. PMID: 10976695.

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