Linfoma B de células grandes hepatoesplénico: Un caso sin autopsia

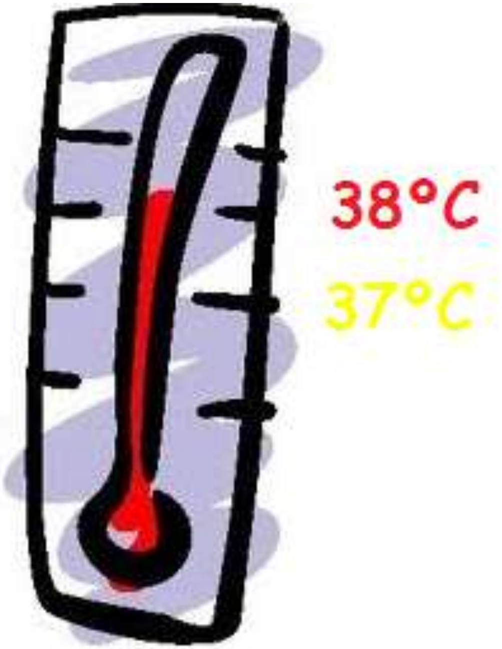
Ana Martínez López R3 Anatomía Patológica

HISTORIA CLÍNICA

- Varón 69 años, exfumador.

  Hábito enólico de larga evolución, abusivo en su juventud y ahora algo más moderado.

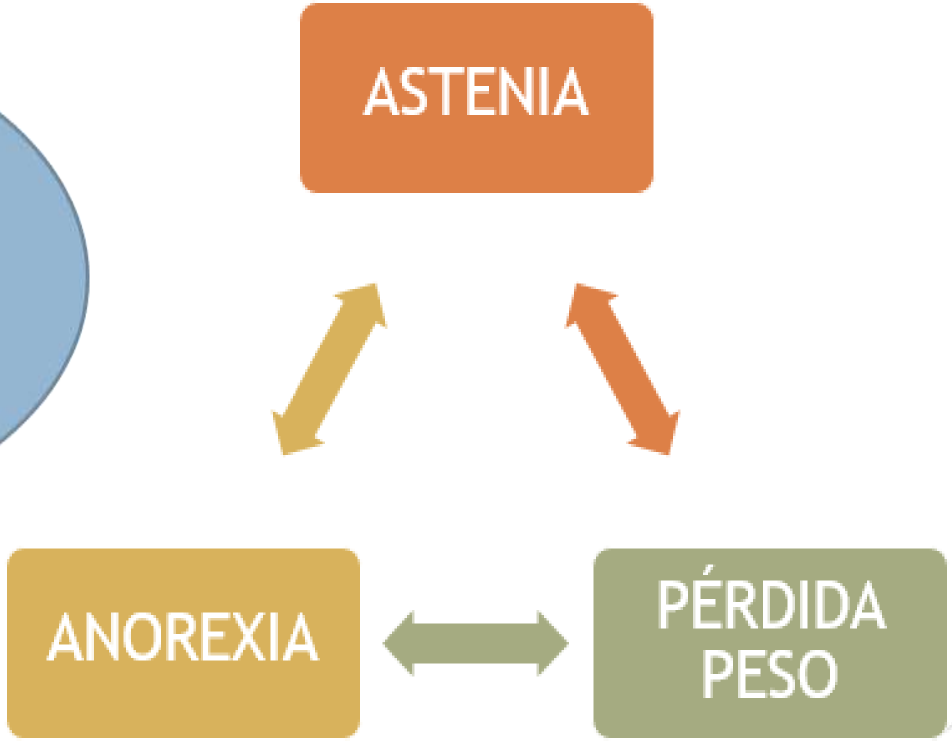
MOTIVO CONSULTA



FIEBRE DE > 15 DIAS

ENFERMEDAD ACTUAL

1 MES DE
EVOLUCIÓN
APROX.



ASTENIA

ANOREXIA

PÉRDIDA
PESO

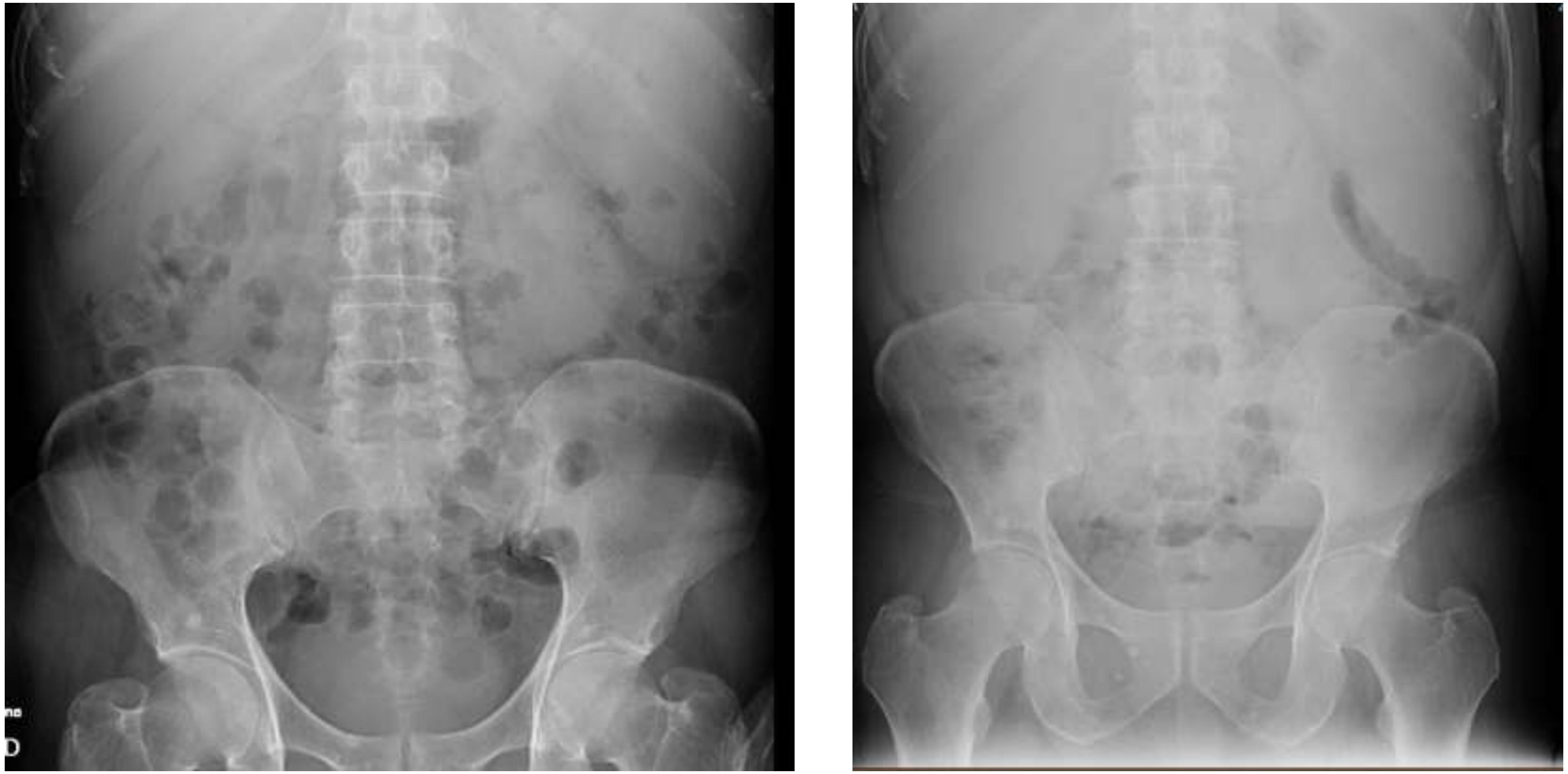
SÍNDROME
CONSTITUC.

ENFERMEDAD ACTUAL

- Fiebre de hasta 39ºC
- Sudoración profusa
- Tratamiento antibiótico sin respuesta (amoxicilina y levofloxacino)

- **Exploración física:**
- Dolor punzante en abdomen
- Ictericia escleral.
- Hepatomegalia dolorosa. Esplenomegalia.

PRUEBAS COMPLEMENTARIAS



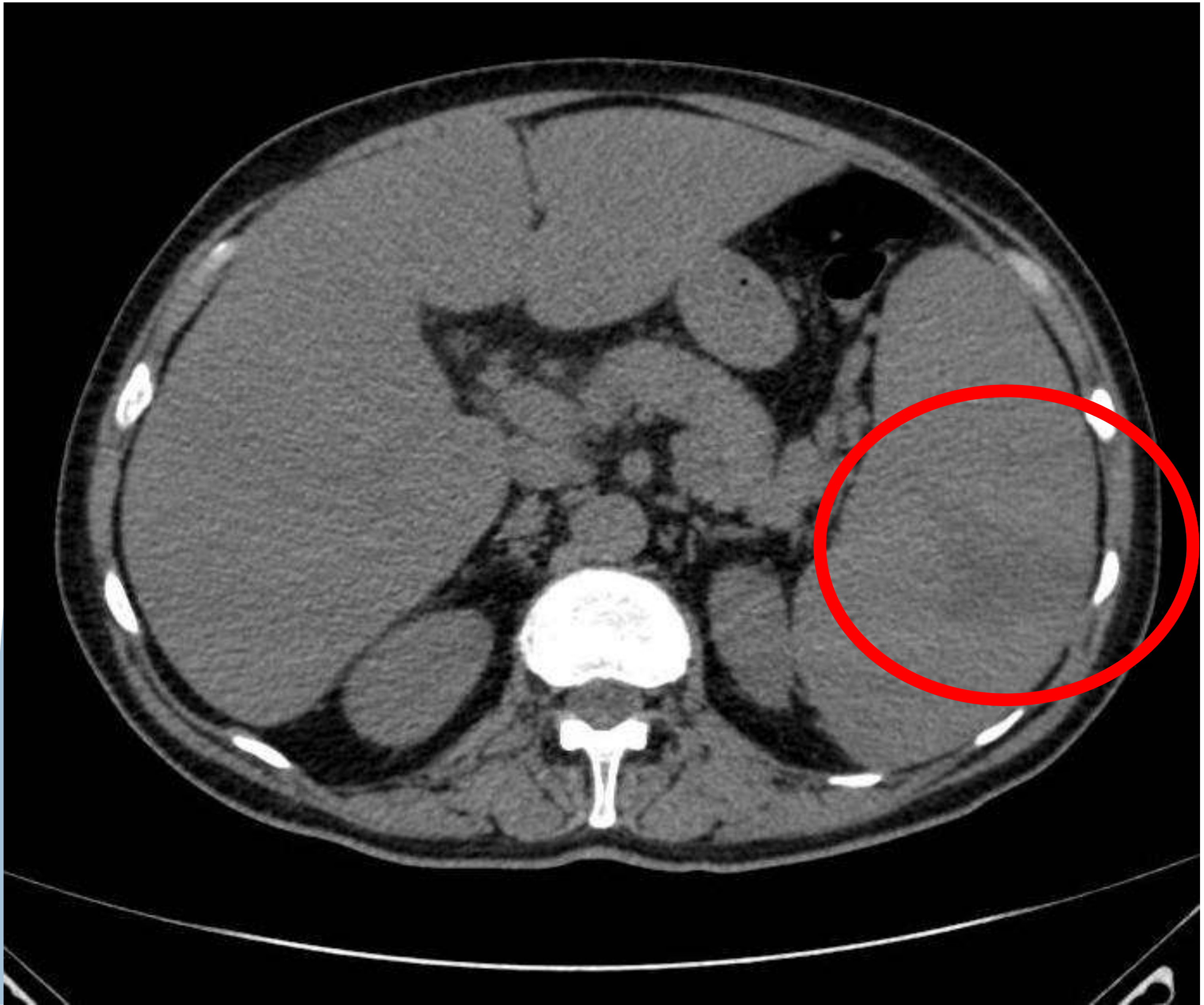
Hepato-esplenomegalias radiológicas

PRUEBAS COMPLEMENTARIAS

- **Hemograma**: ligera plaquetopenia.
- **Bioquímica**: creatinina 2.70, AST 95/ALT 94, GGT 1336, FA 817, TG 386, hipergammaglobulinemia. LDH 1020, TSH 5.56, FE 51, Ferritina 51309.1, transferrina 147, PCR 141,91.
- **Ecografía Abdominal**: Hepatomegalia con aumento de ecogenicidad sin lesiones focales. Esplenomegalia.

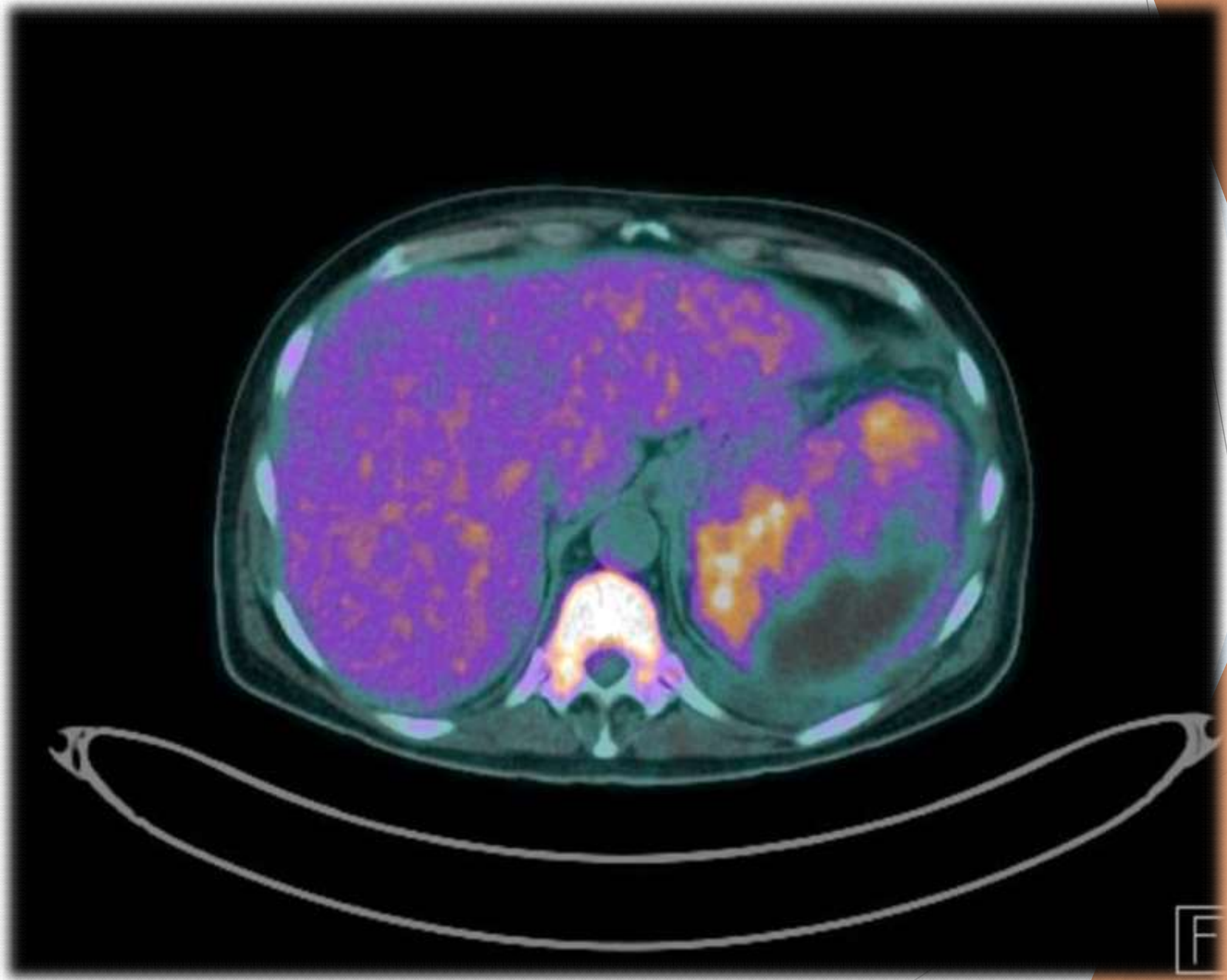
Diagnóstico: *Cirrosis hepática con datos de HTTP y esplenomegalia.*

TAC ABDOMEN SIN CONTRASTE

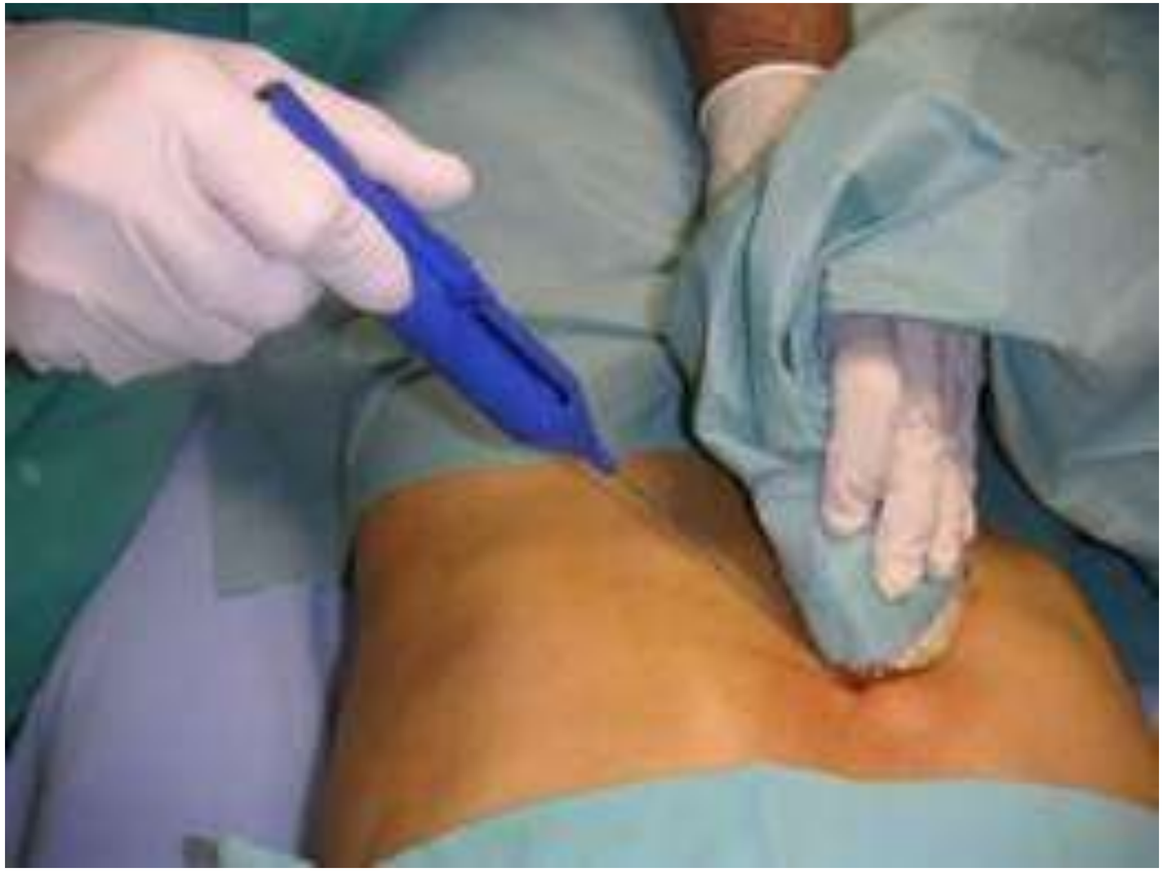


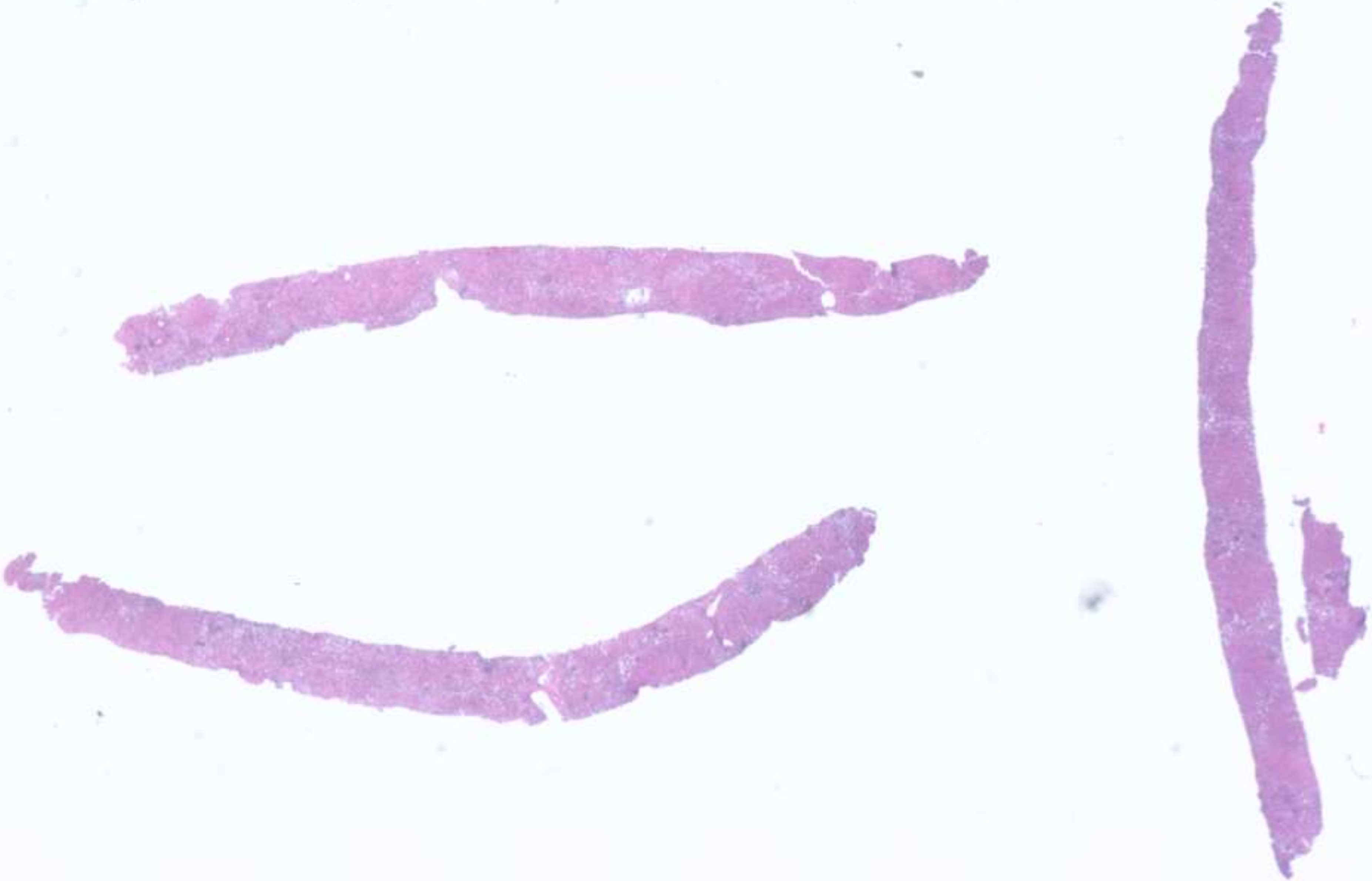
Aspecto de hepatopatía crónica.
No se pueden valorar LOEs, por falta de contraste.
Circulación colateral por HT portal.
Importante esplenomegalia, con áreas de hipodensidad.

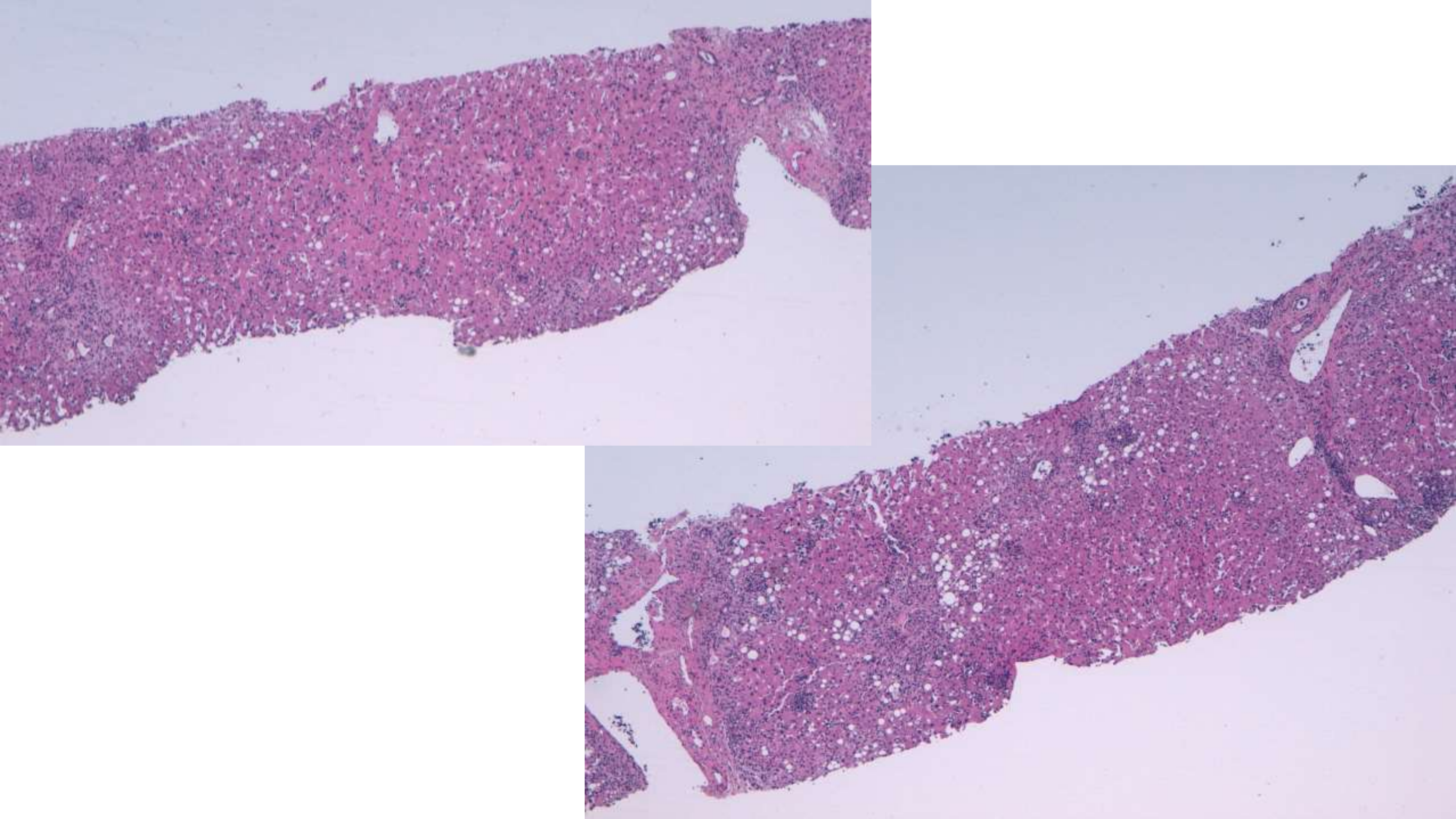
PET

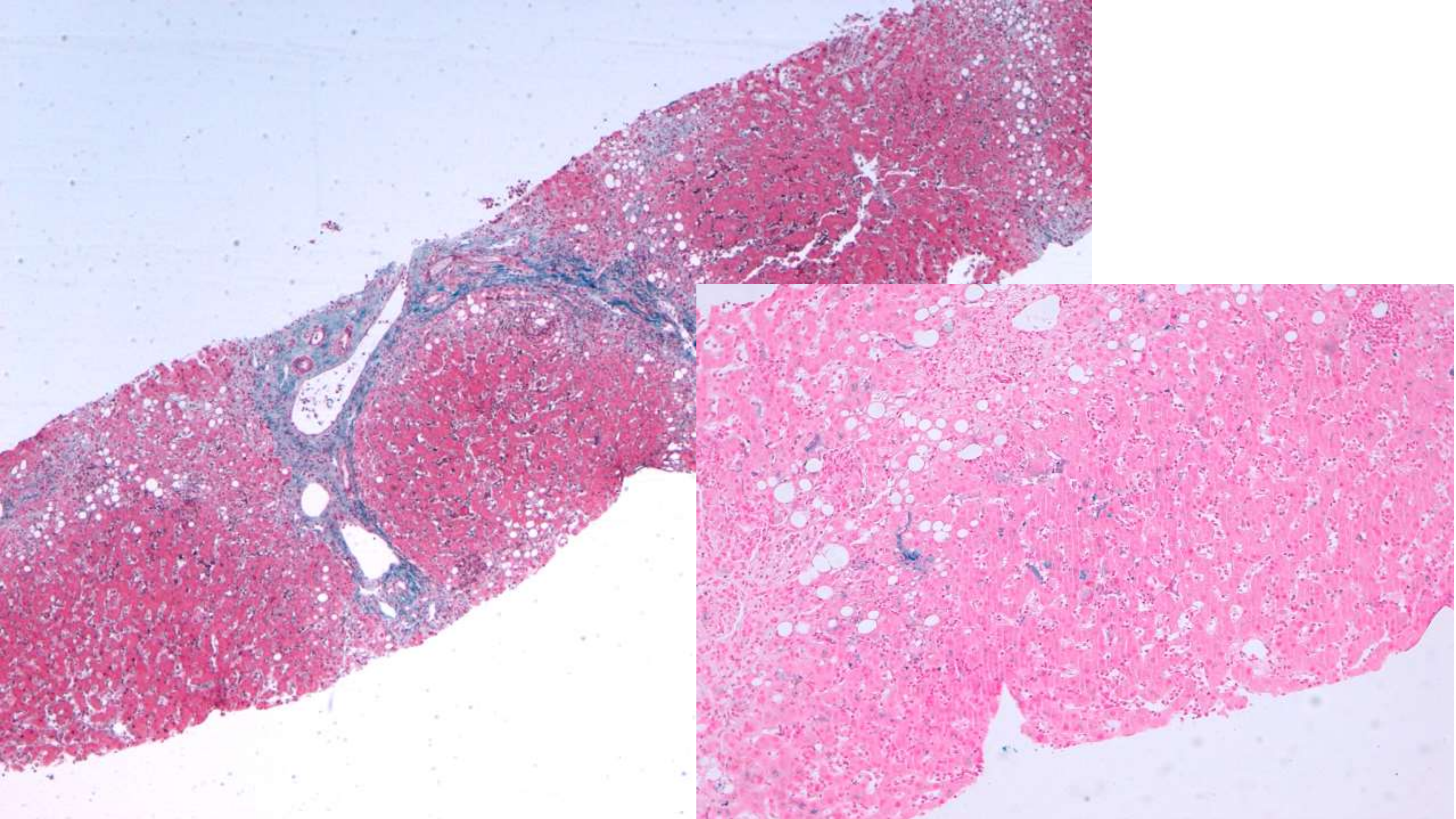


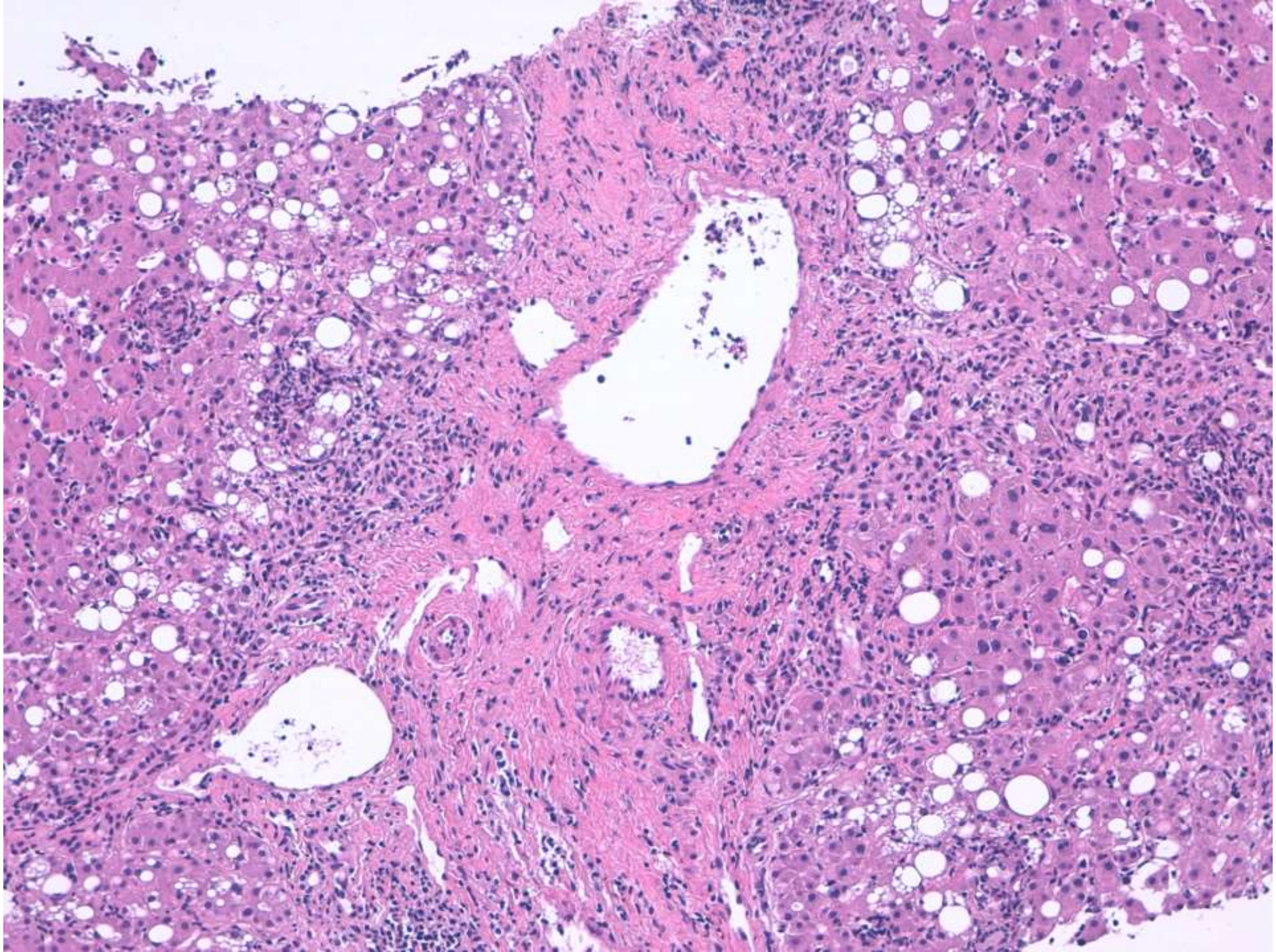
BIOPSIA HÍGADO

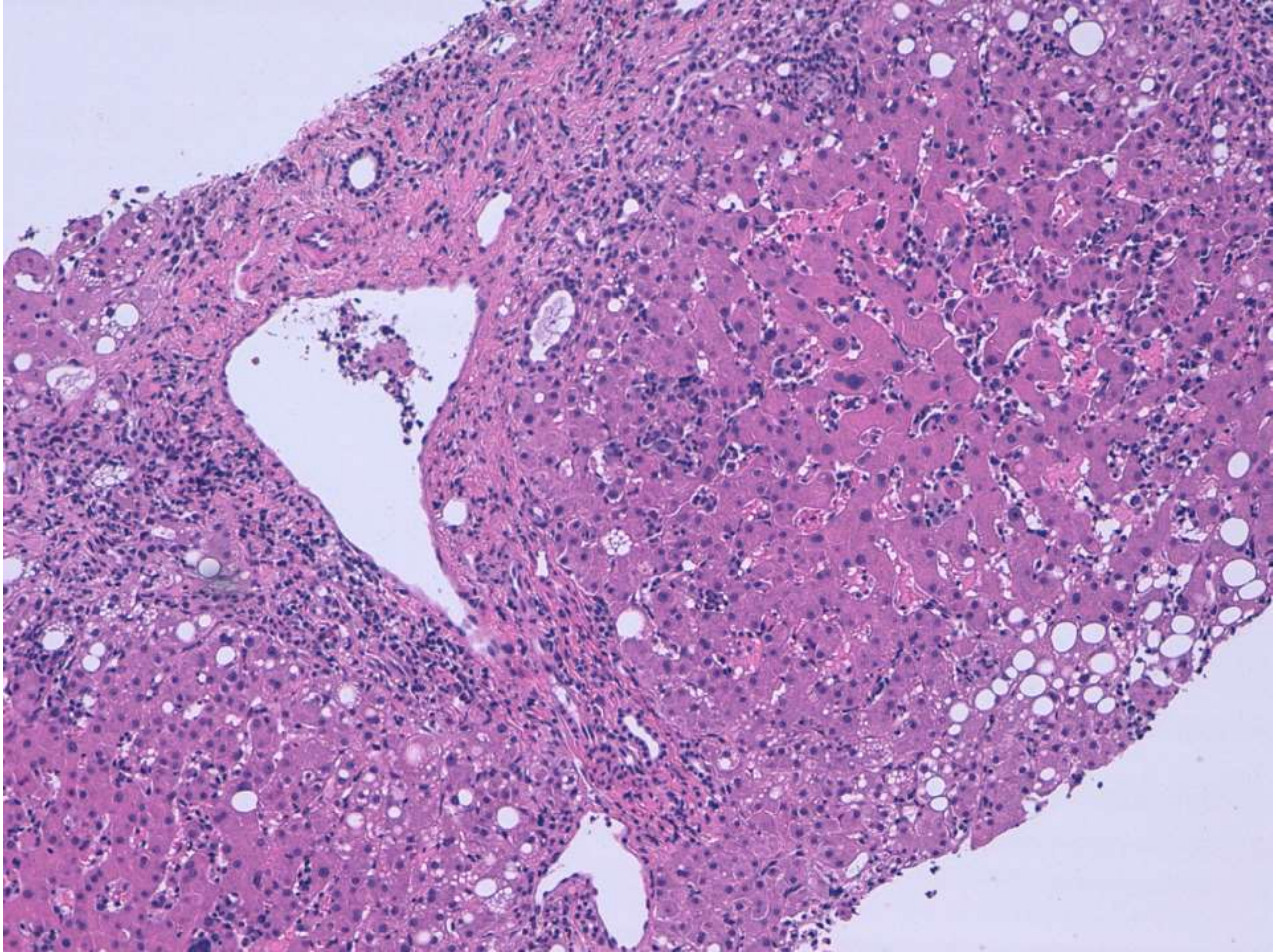


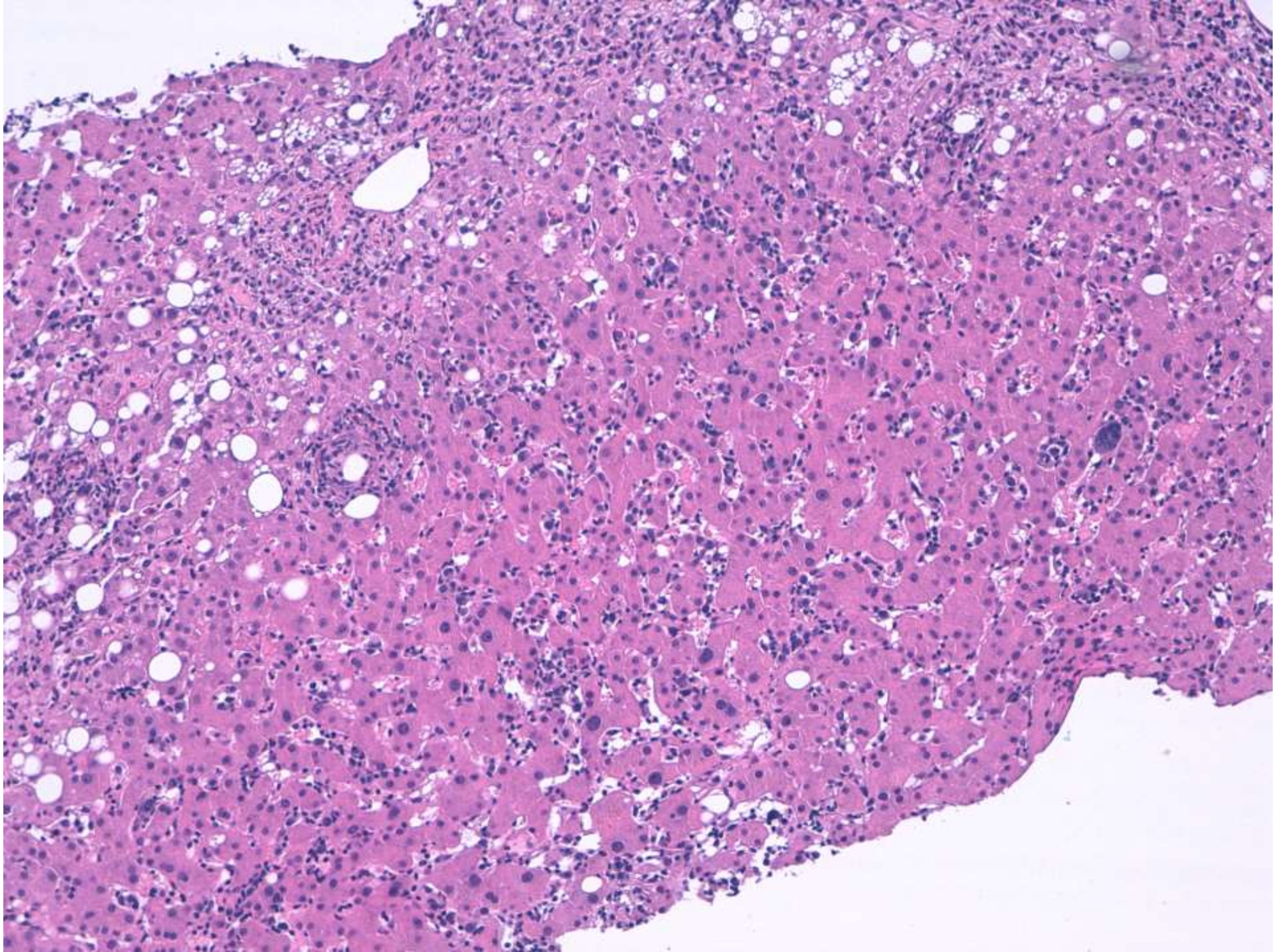


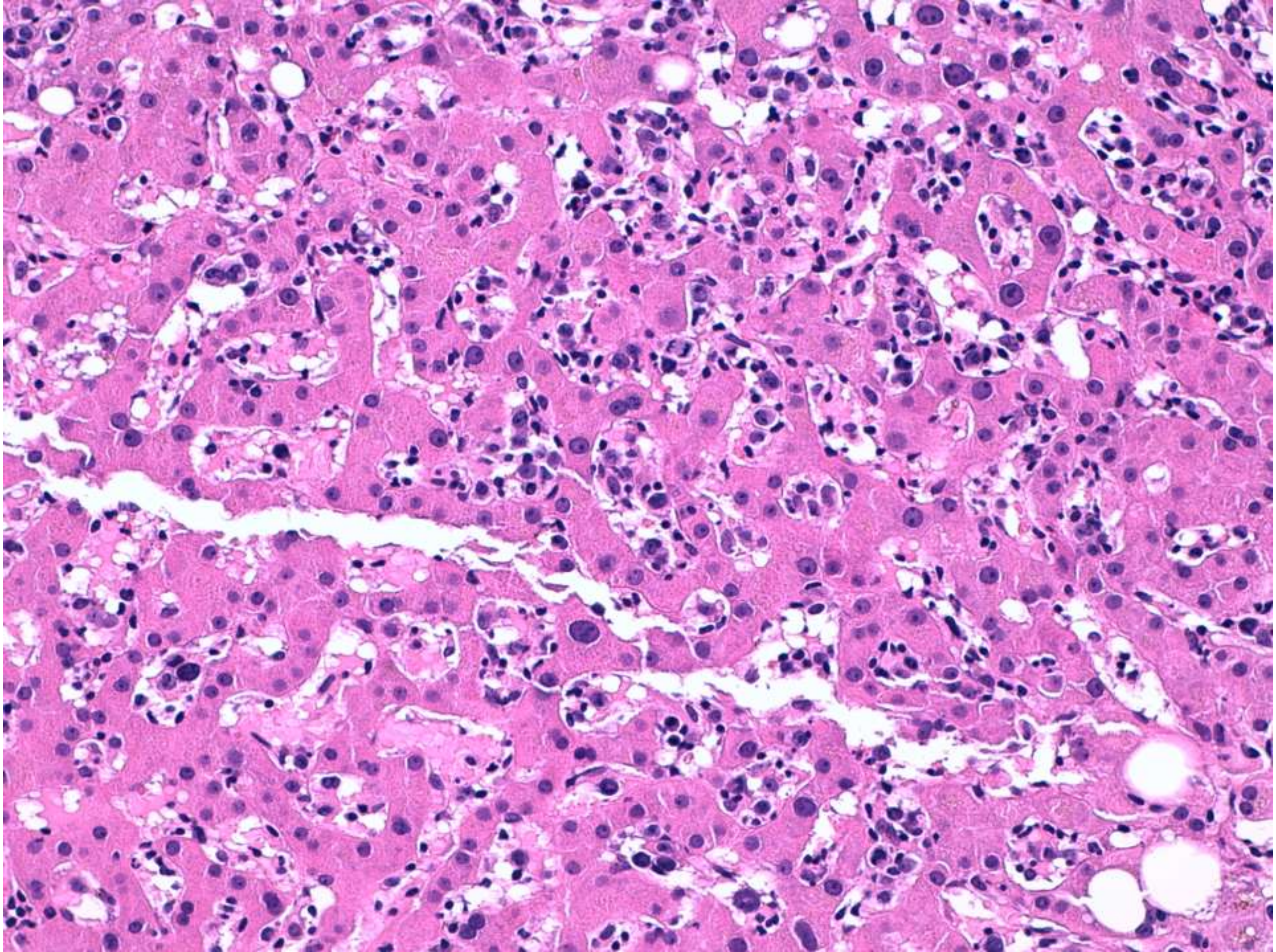


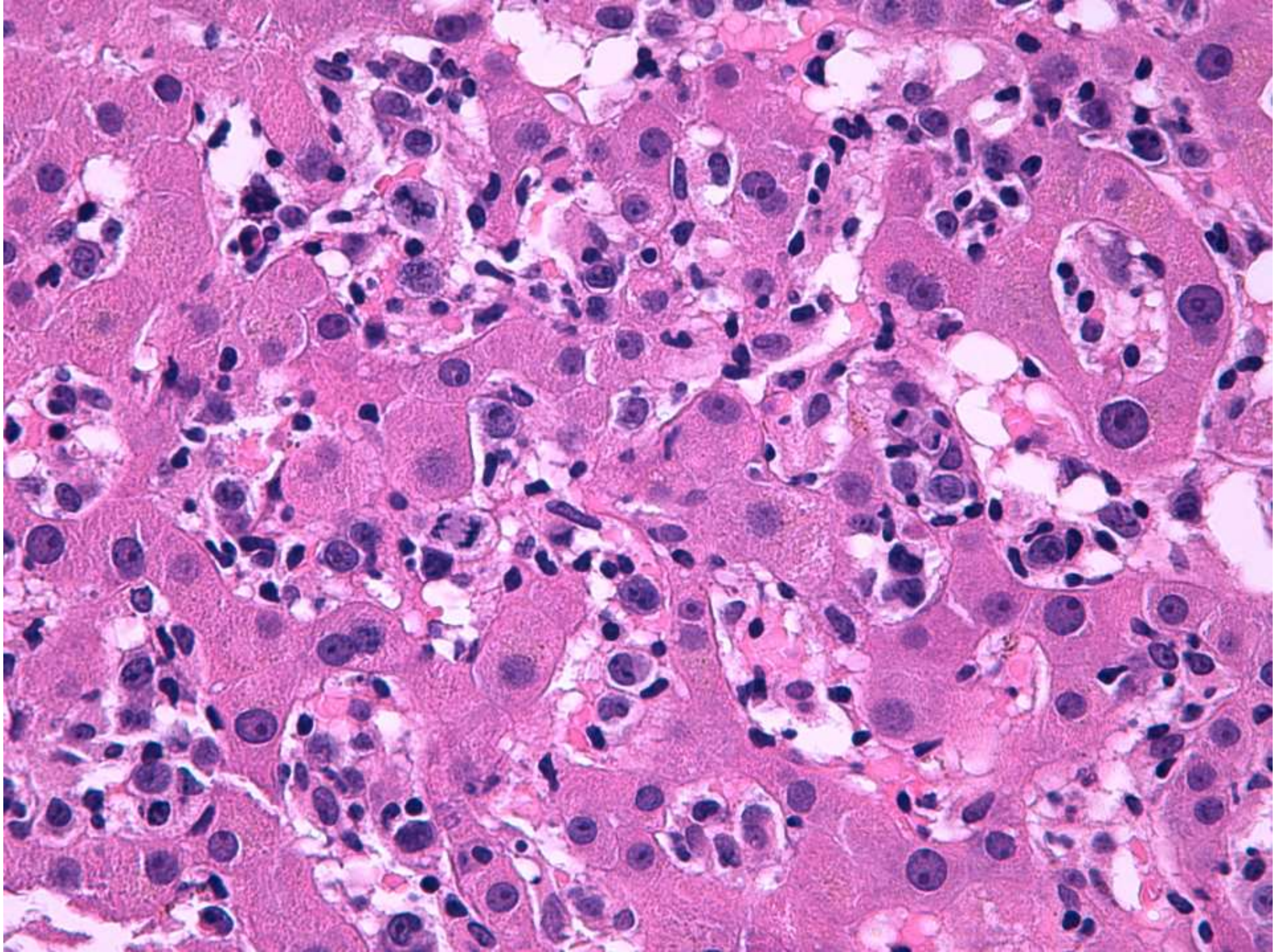


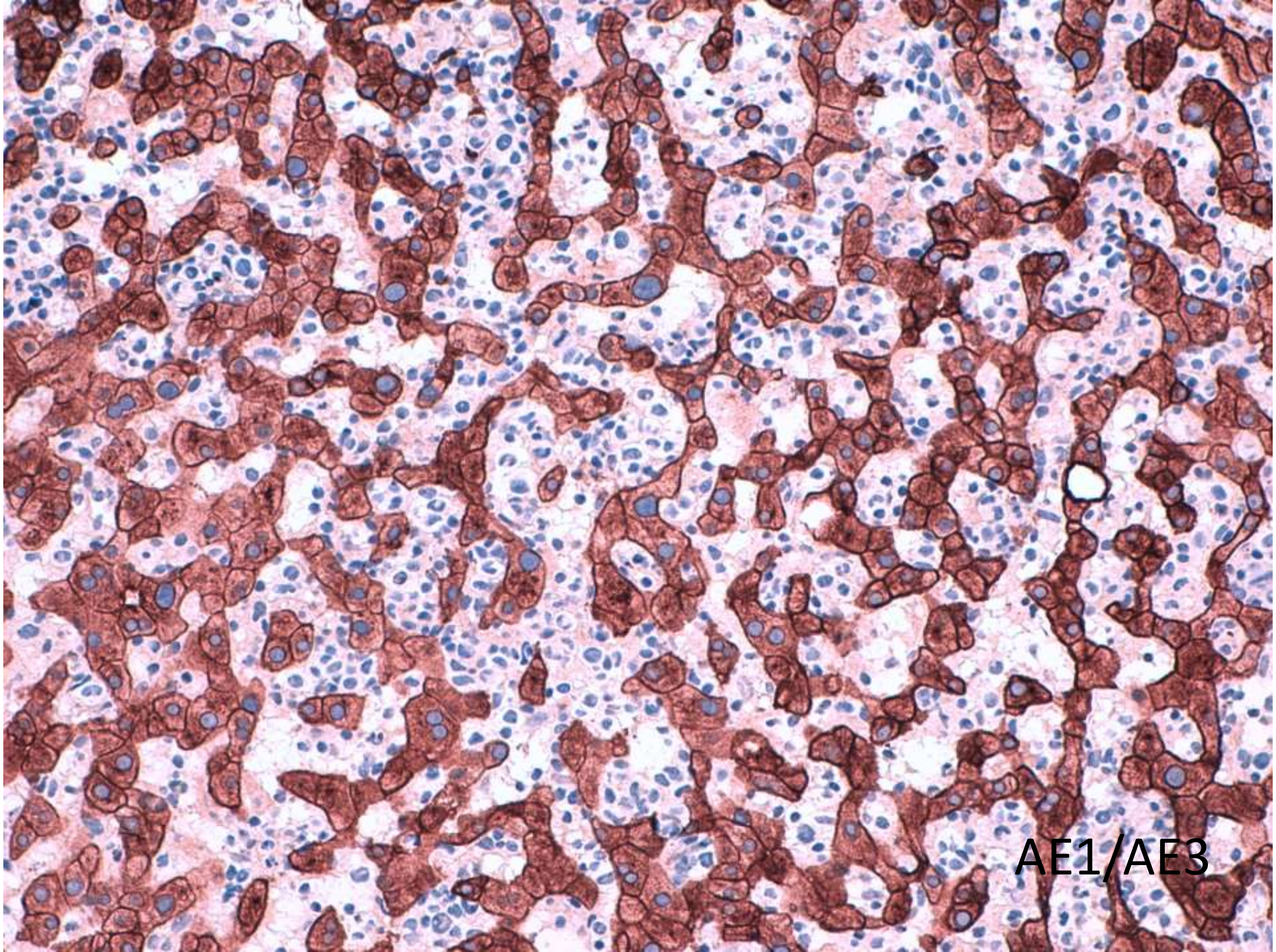




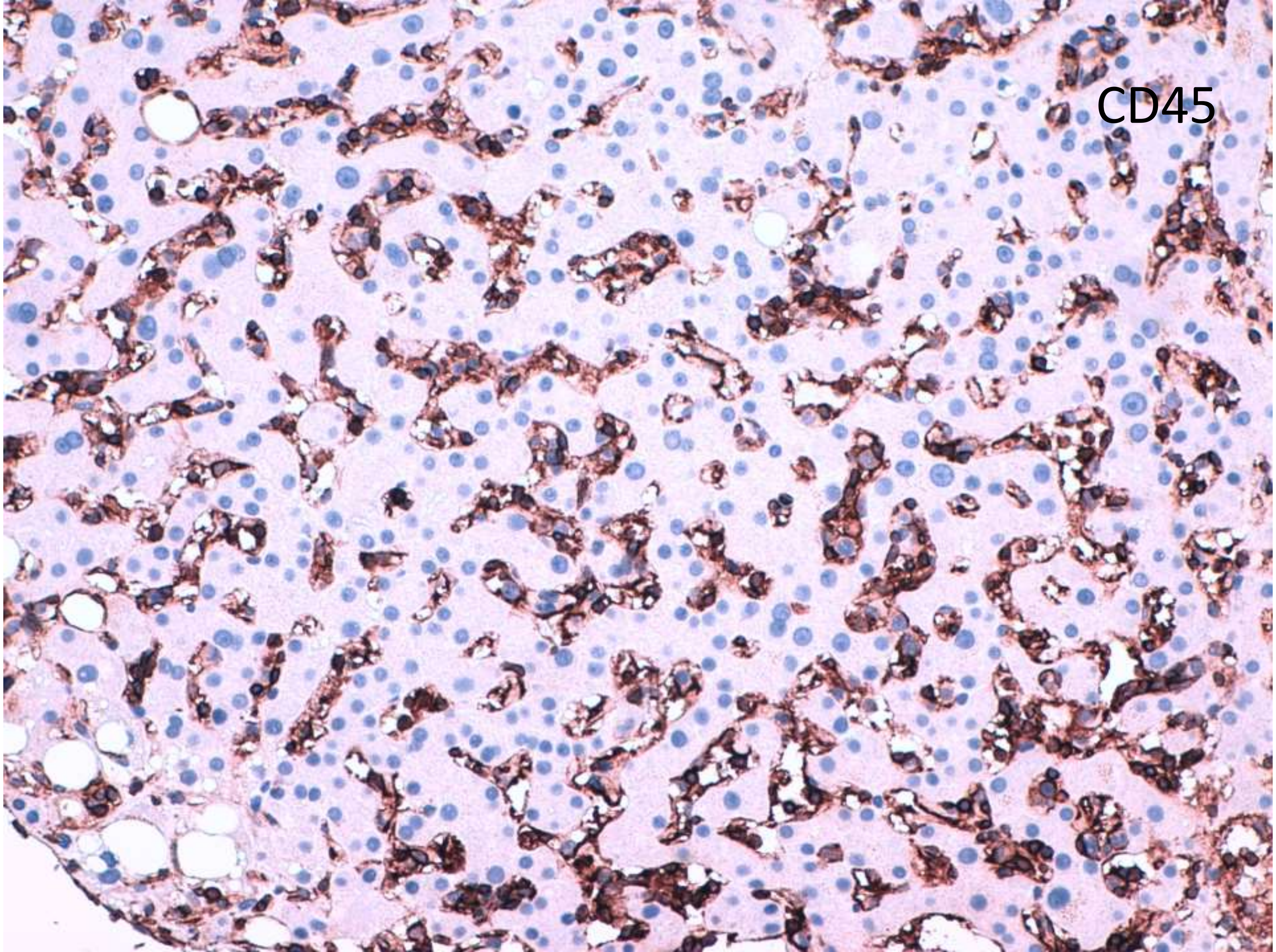


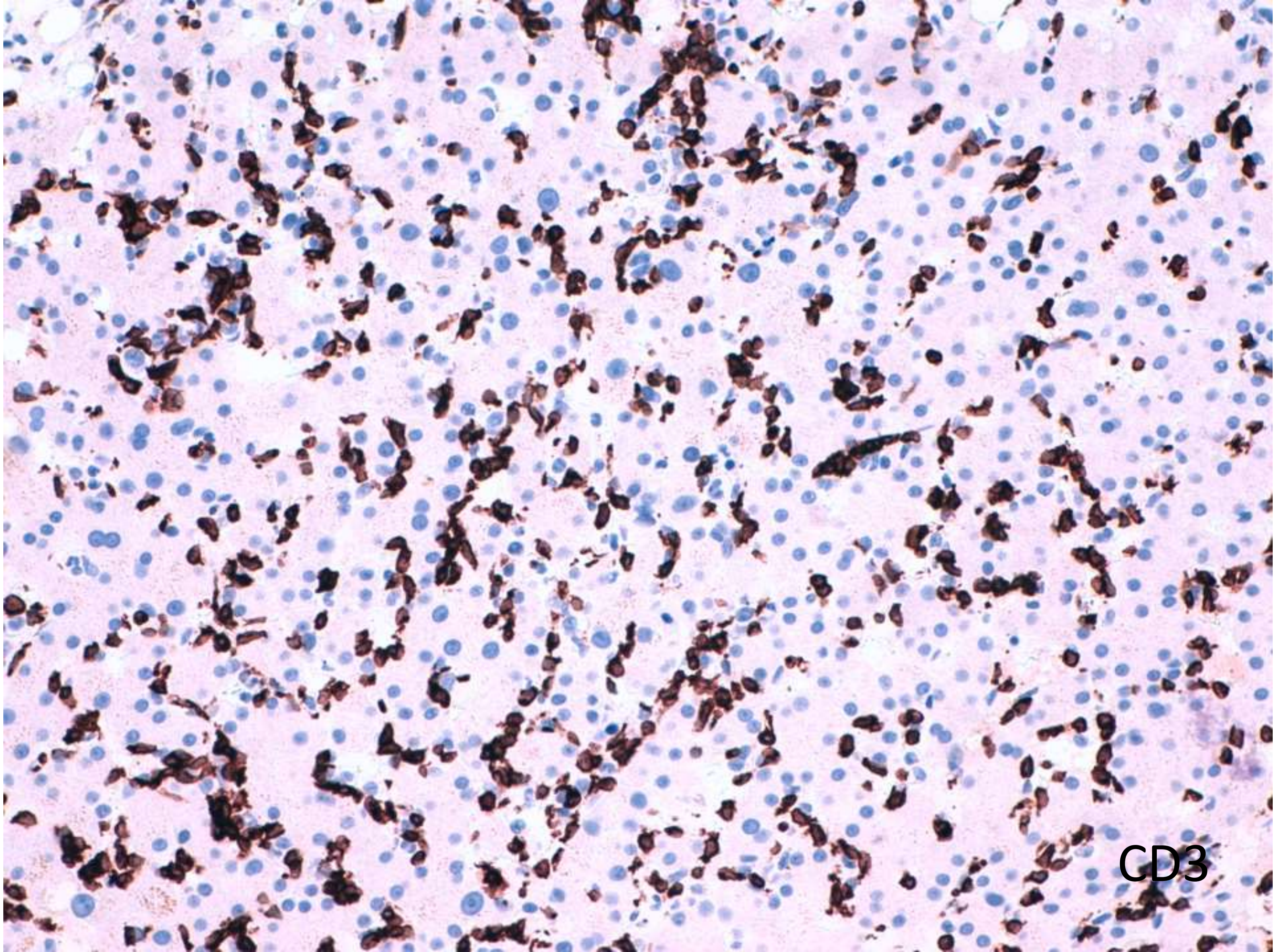




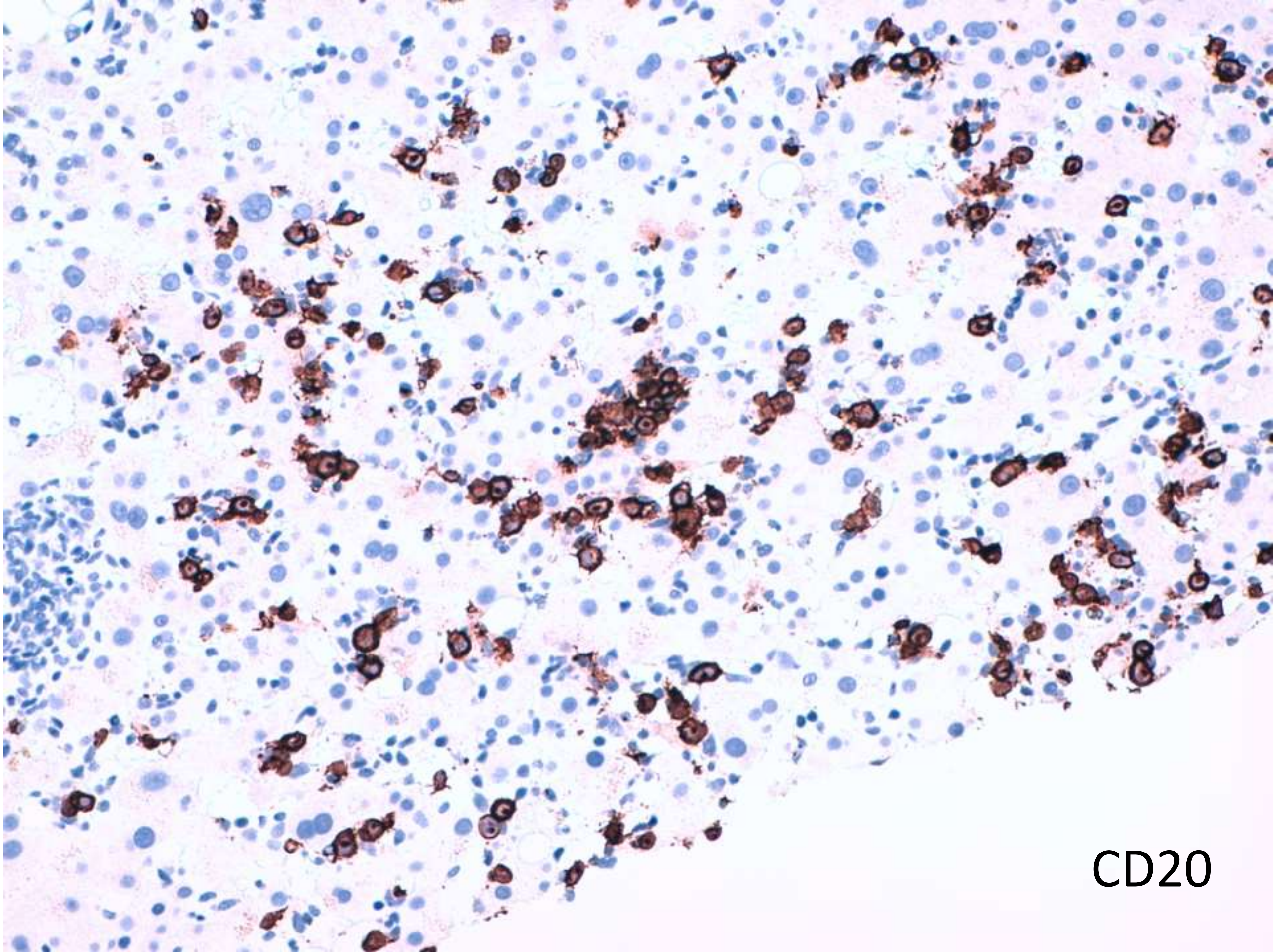


AE1/AE3

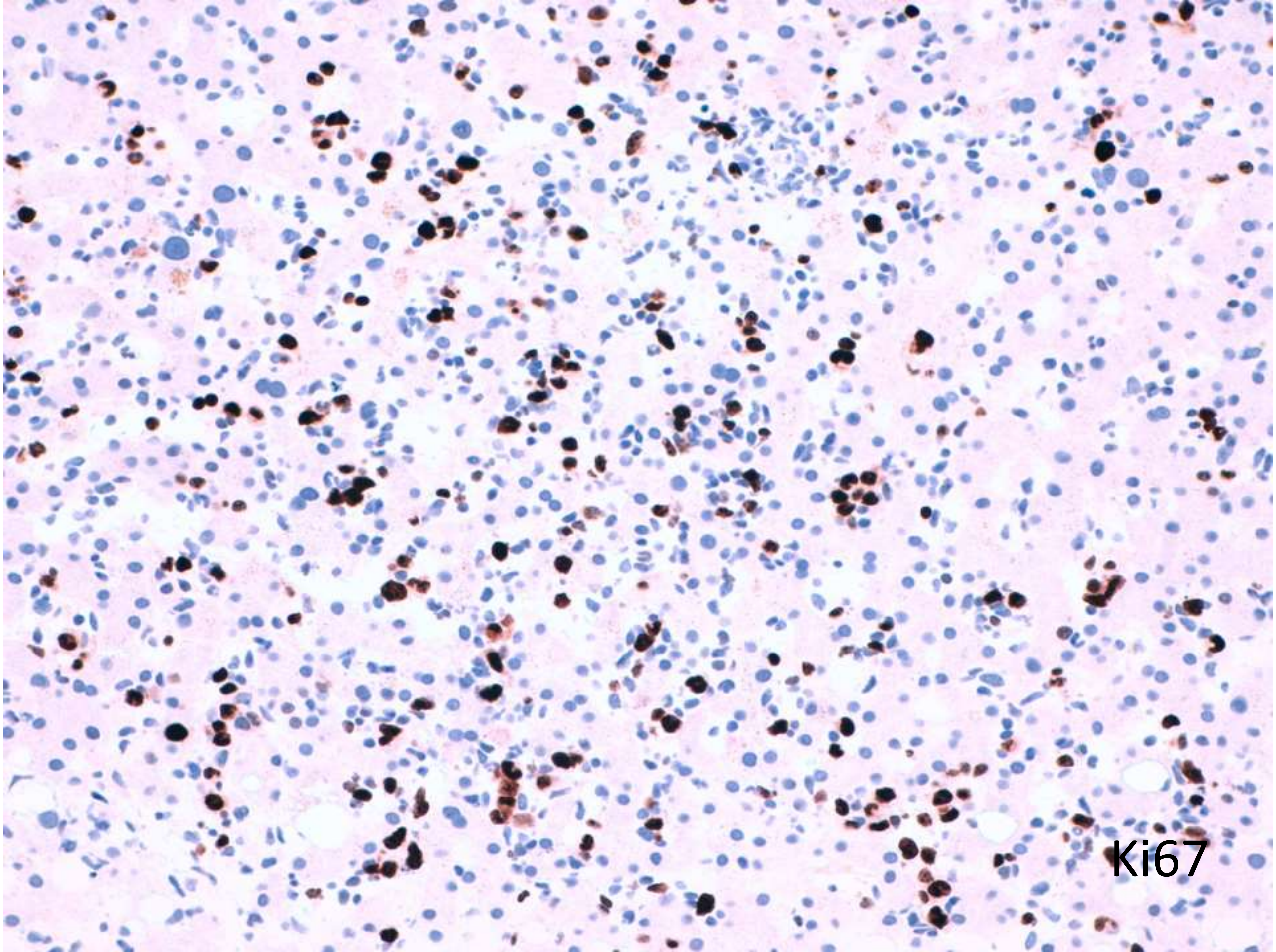

CD45



CD3



CD20



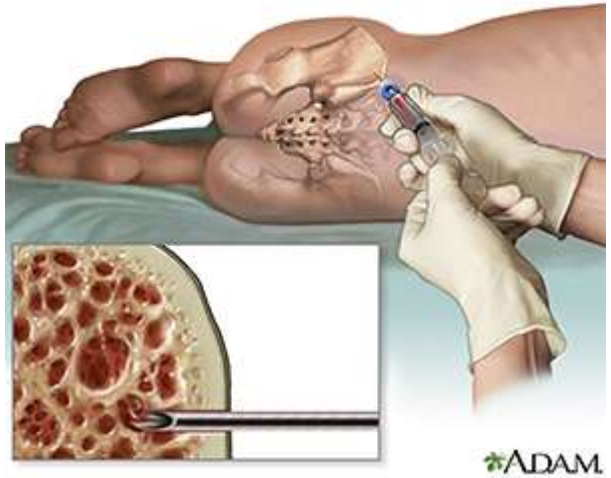
Ki67

ANATOMÍA PATOLÓGICA

- HÍGADO: INFILTRACIÓN SINUSOIDAL POR **LINFOMA B DIFUSO DE CÉLULAS GRANDES.**
- INMUNOFENOTIPO: CD20+, CD3-, CD43-, BCL2+, BCL6+, CD10-, MUM1+, EBER- Y ALTO ÍNDICE PROLIFERATIVO.

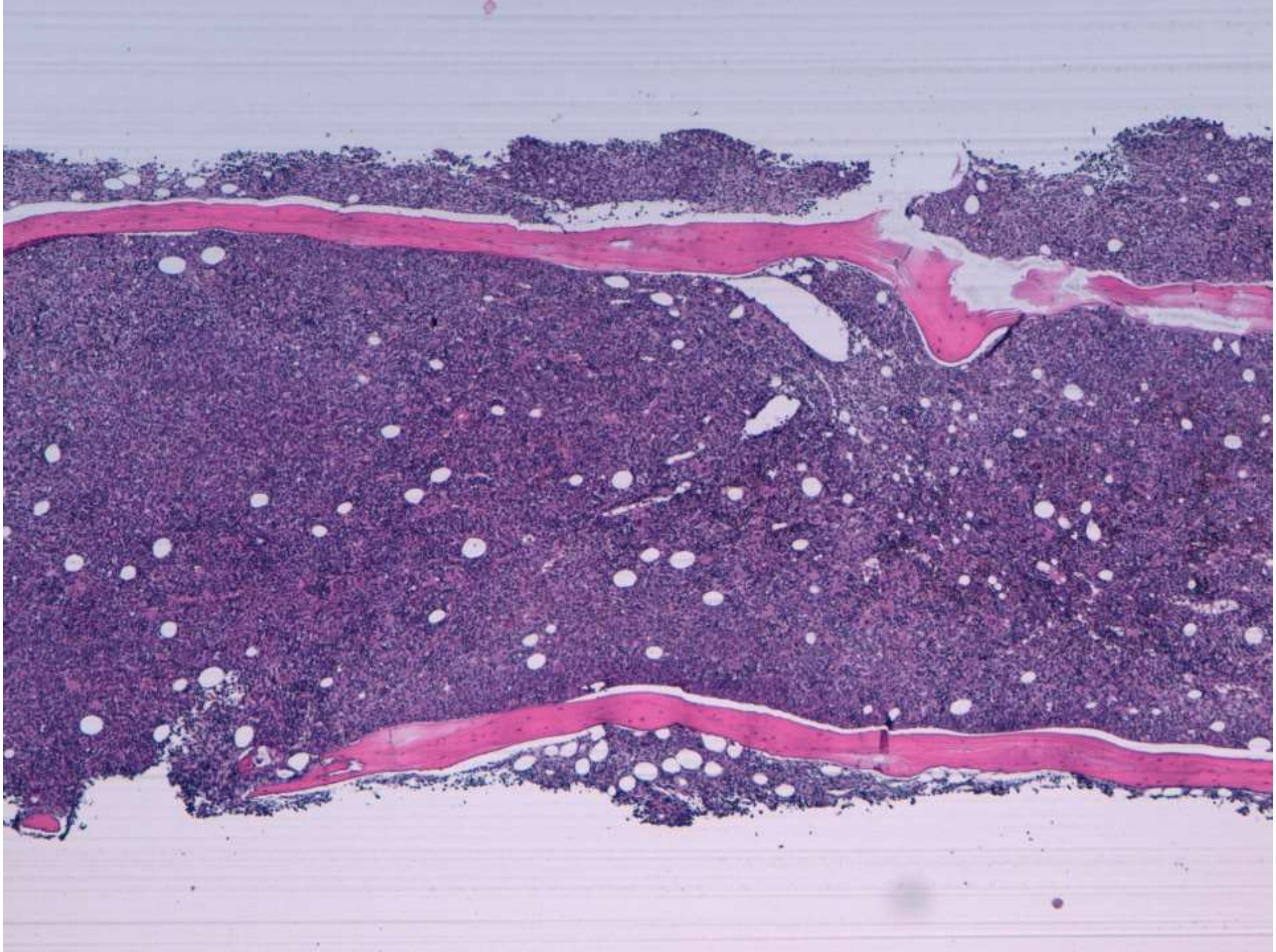
- ESTEATOHEPATITIS CON AMPLIACIÓN Y FIBROSIS PORTAL CON FORMACIÓN DE PUENTES INCOMPLETOS PORTOPORTALES, INFLAMACIÓN Y GRANULOMAS PORTALES CON PROLIFERACIÓN DE DUCTOS BILIARES, CONGRUENTES CON ETIOLOGÍA ENÓLICA

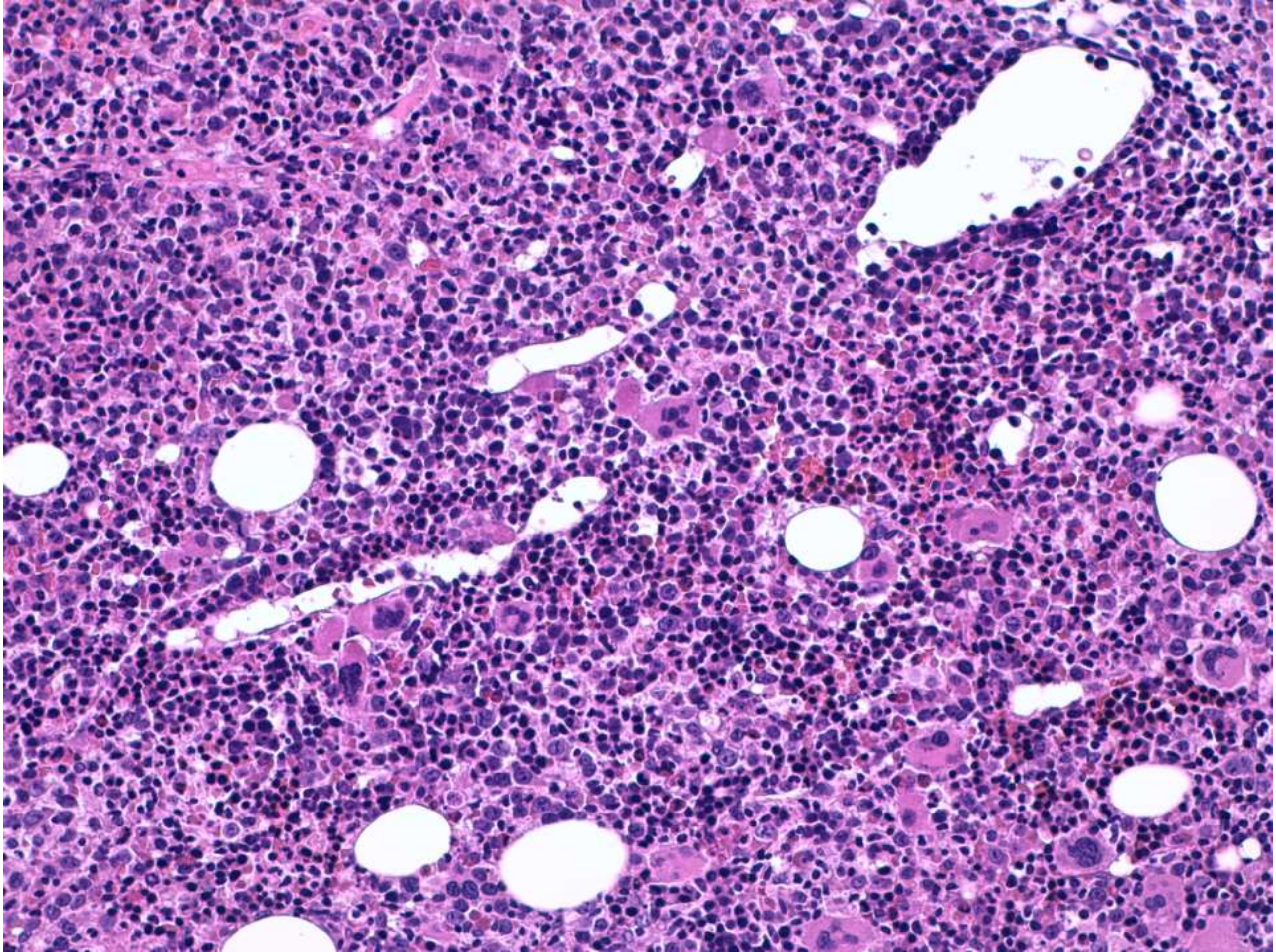
BIOPSIA MÉDULA ÓSEA

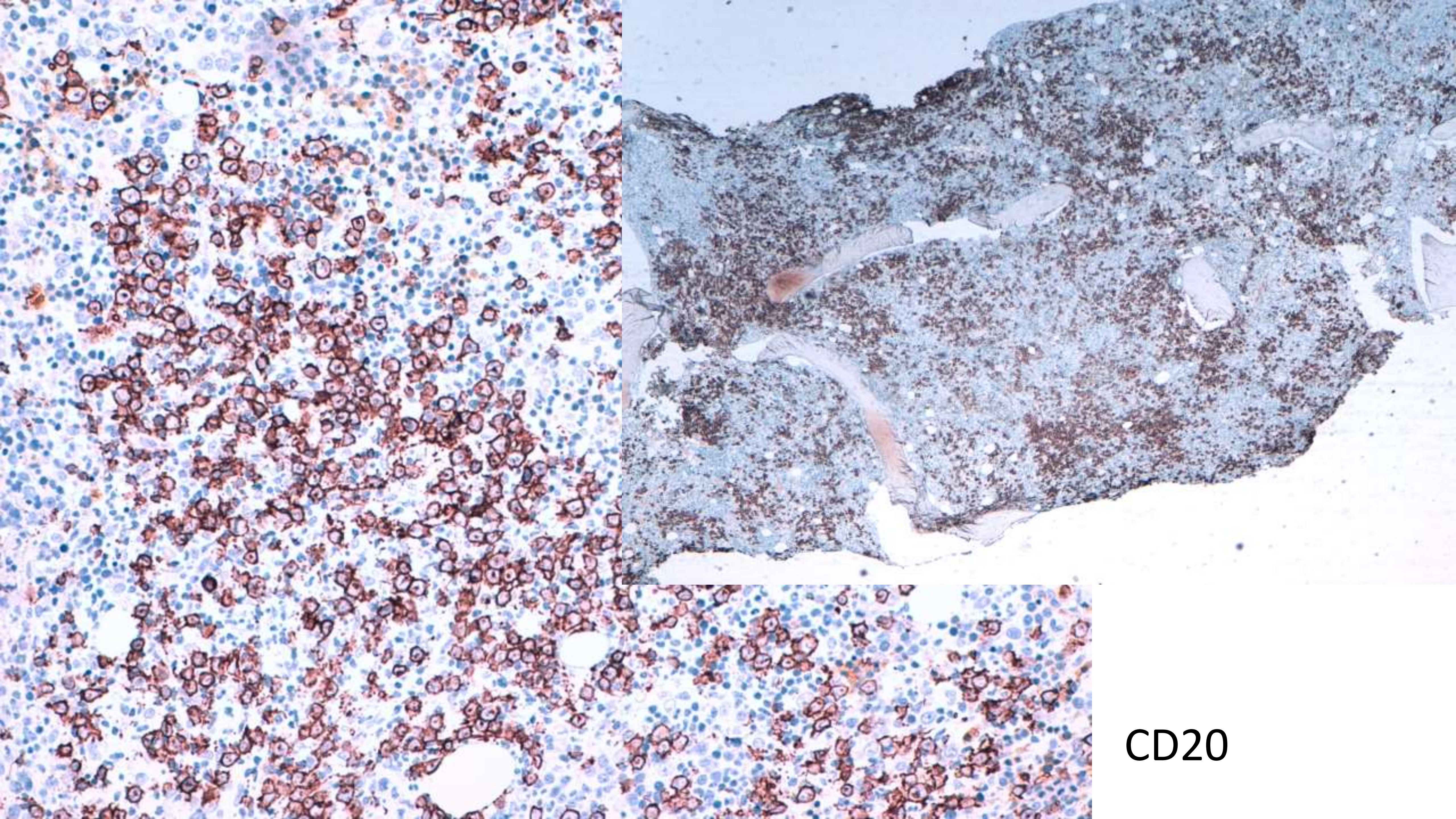


ESTADIAJE

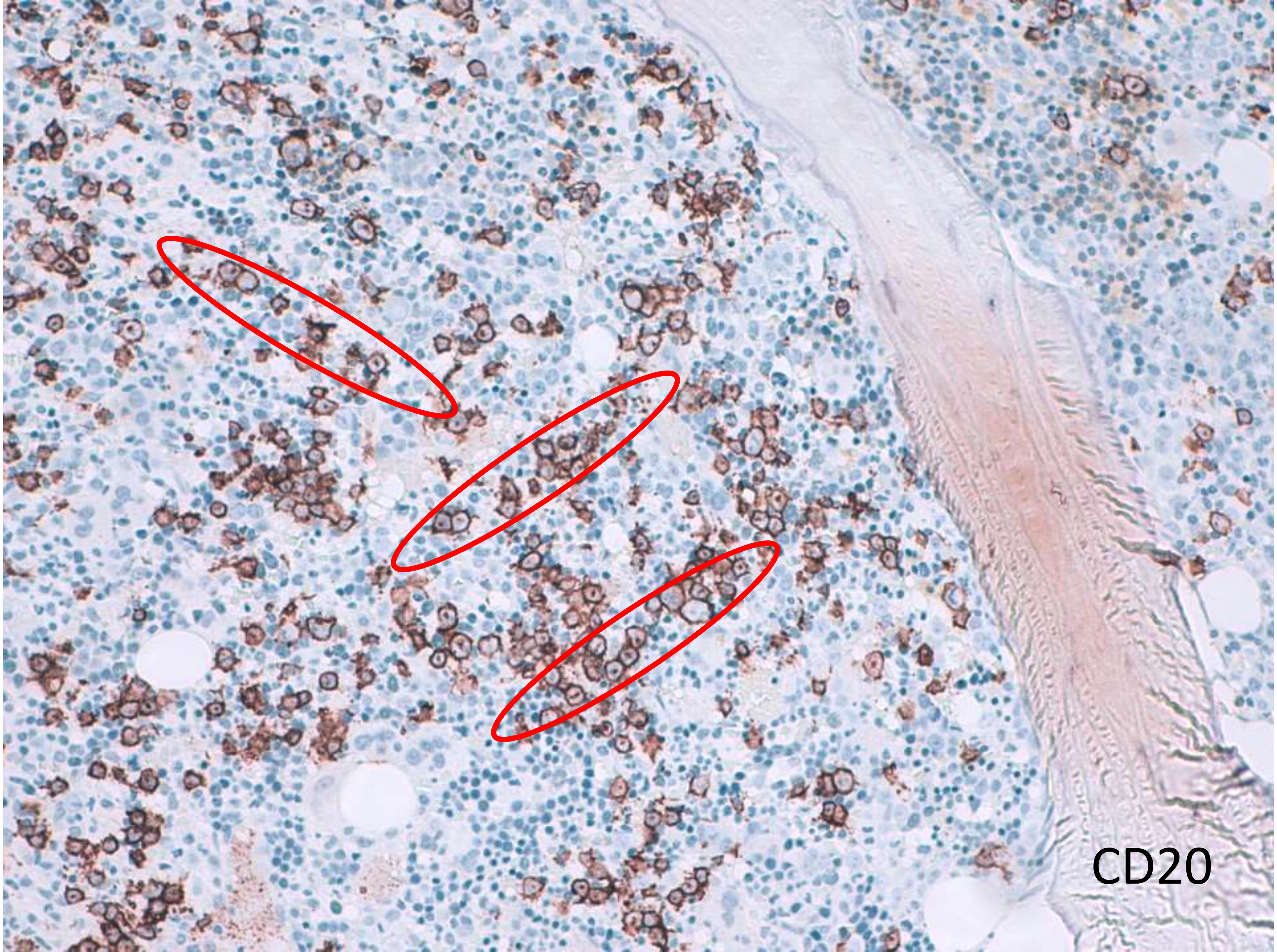
PLAQUETOPENIA







CD20


CD20

ANATOMÍA PATOLÓGICA

- MÉDULA ÓSEA: INFILTRACIÓN POR **LINFOMA B DIFUSO DE CÉLULAS GRANDES.**
- PATRÓN DE INFILTRACIÓN: DIFUSO, INTERSTICIAL E INTRASINUSOIDAL, **CONCORDANTE** EN MÉDULA E HÍGADO.
- INMUNOFENOTIPO: CD20+, CD3-, CD43-, BCL2+, BCL6+, CD10-, MUM1+, EBER- Y ALTO ÍNDICE PROLIFERATIVO.

EVOLUCIÓN

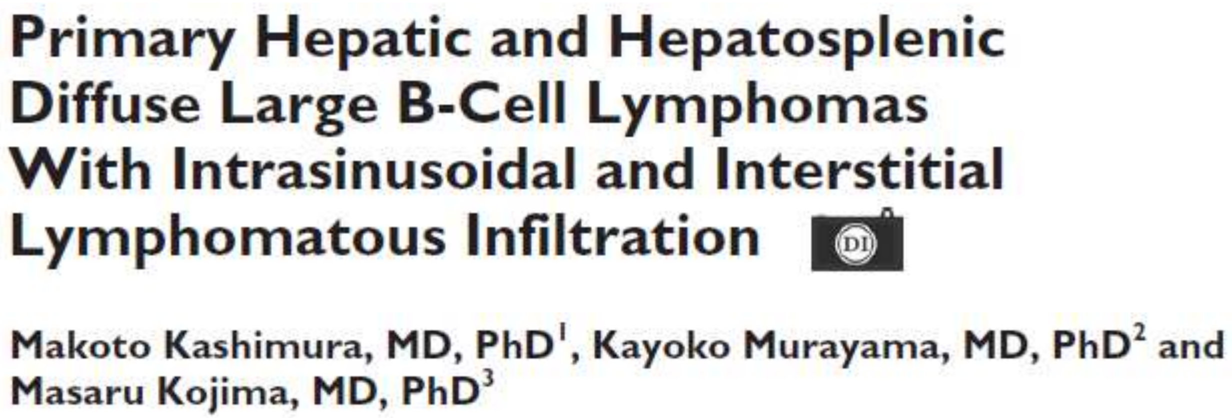
- ESTABILIZACIÓN Y ALTA DOMICILIARIA
- INICIO **TERAPIA R-CHOP** AL 5º DÍA DEL ALTA
- TAC ABDOMEN (ENERO 2018):

  Hígado de tamaño normal y Bazo de 13 cm

  (han disminuido de tamaño)

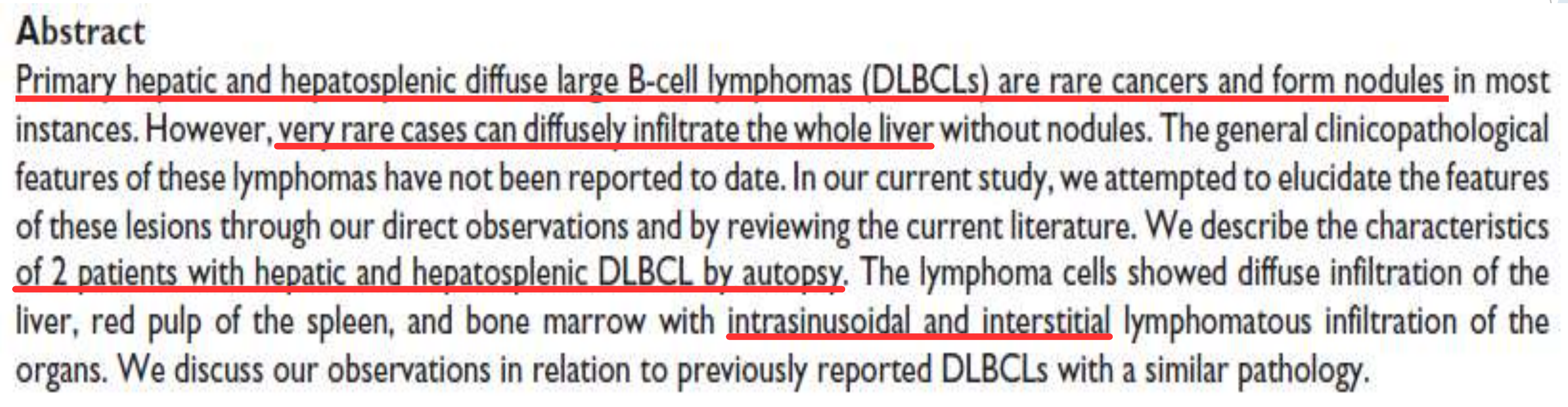
- ANALÍTICA (ENERO 2018): leucocitos 6460 (3240 neutrófilos abs), Hb 11.2, Plaquetas 424.000. Bioquímica: ALT/AST 44/27, GGT/FA 62/83, LDH NORMAL.

DISCUSIÓN



Primary Hepatic and Hepatosplenic Diffuse Large B-Cell Lymphomas With Intrasinusoidal and Interstitial Lymphomatous Infiltration

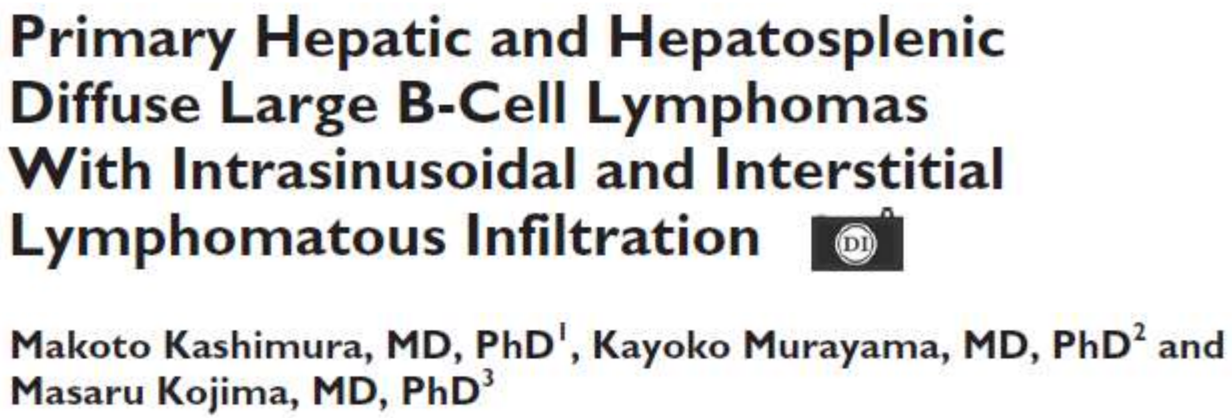
Makoto Kashimura, MD, PhD[1], Kayoko Murayama, MD, PhD[2] and Masaru Kojima, MD, PhD[3]



Abstract

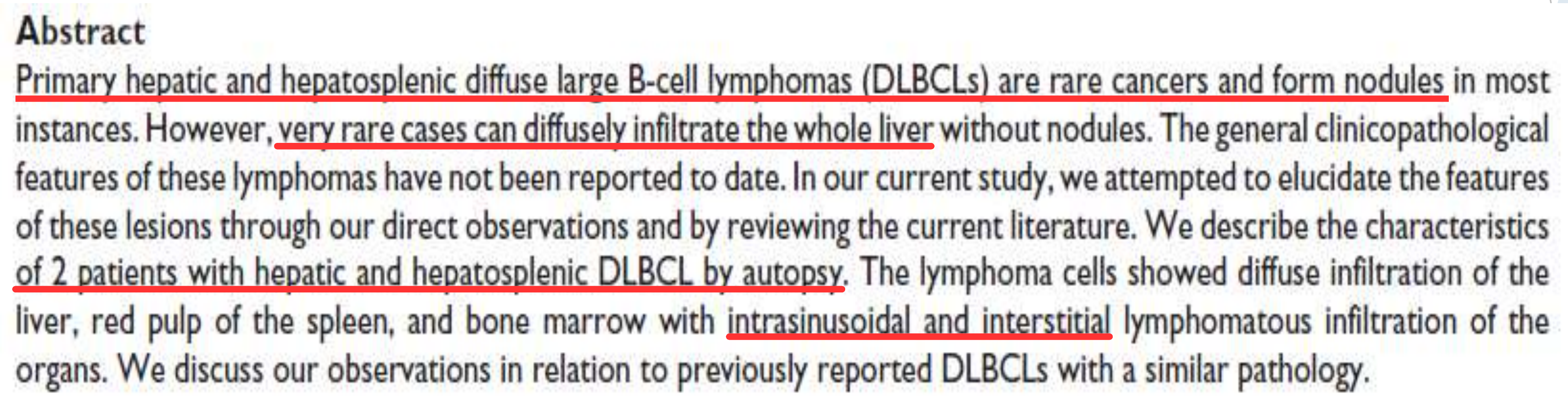
Primary hepatic and hepatosplenic diffuse large B-cell lymphomas (DLBCLs) are rare cancers and form nodules in most instances. However, very rare cases can diffusely infiltrate the whole liver without nodules. The general clinicopathological features of these lymphomas have not been reported to date. In our current study, we attempted to elucidate the features of these lesions through our direct observations and by reviewing the current literature. We describe the characteristics of 2 patients with hepatic and hepatosplenic DLBCL by autopsy. The lymphoma cells showed diffuse infiltration of the liver, red pulp of the spleen, and bone marrow with intrasinusoidal and interstitial lymphomatous infiltration of the organs. We discuss our observations in relation to previously reported DLBCLs with a similar pathology.

DISCUSIÓN



Primary Hepatic and Hepatosplenic Diffuse Large B-Cell Lymphomas With Intrasinusoidal and Interstitial Lymphomatous Infiltration

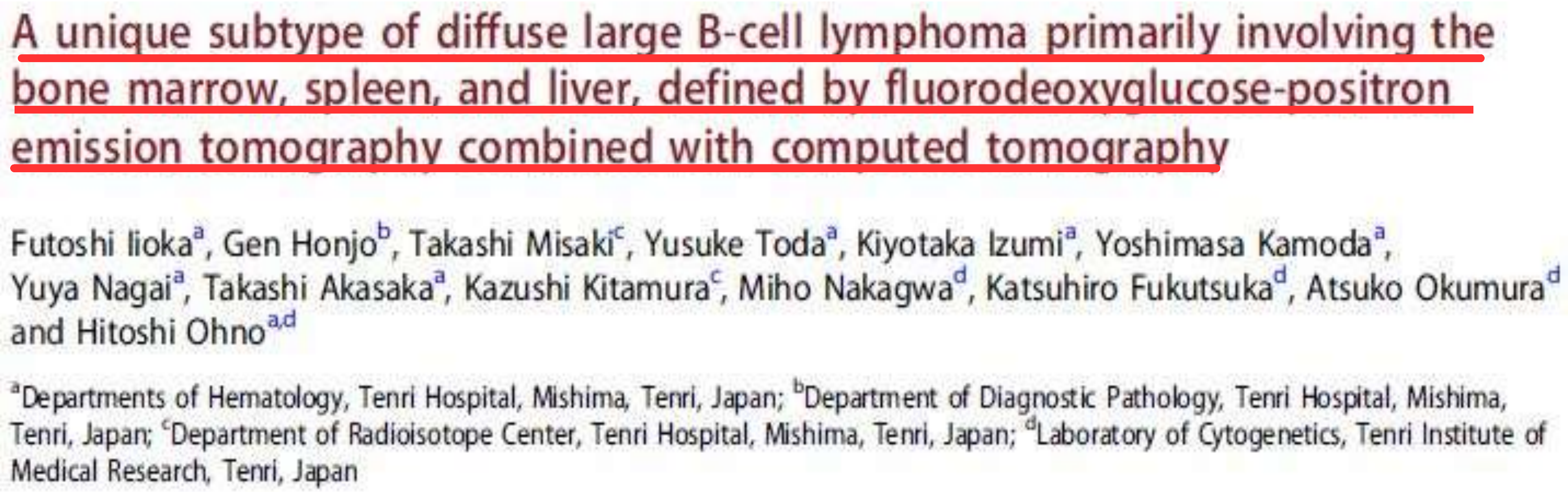
Makoto Kashimura, MD, PhD[1], Kayoko Murayama, MD, PhD[2] and Masaru Kojima, MD, PhD[3]



Abstract

Primary hepatic and hepatosplenic diffuse large B-cell lymphomas (DLBCLs) are rare cancers and form nodules in most instances. However, very rare cases can diffusely infiltrate the whole liver without nodules. The general clinicopathological features of these lymphomas have not been reported to date. In our current study, we attempted to elucidate the features of these lesions through our direct observations and by reviewing the current literature. We describe the characteristics of 2 patients with hepatic and hepatosplenic DLBCL by autopsy. The lymphoma cells showed diffuse infiltration of the liver, red pulp of the spleen, and bone marrow with intrasinusoidal and interstitial lymphomatous infiltration of the organs. We discuss our observations in relation to previously reported DLBCLs with a similar pathology.

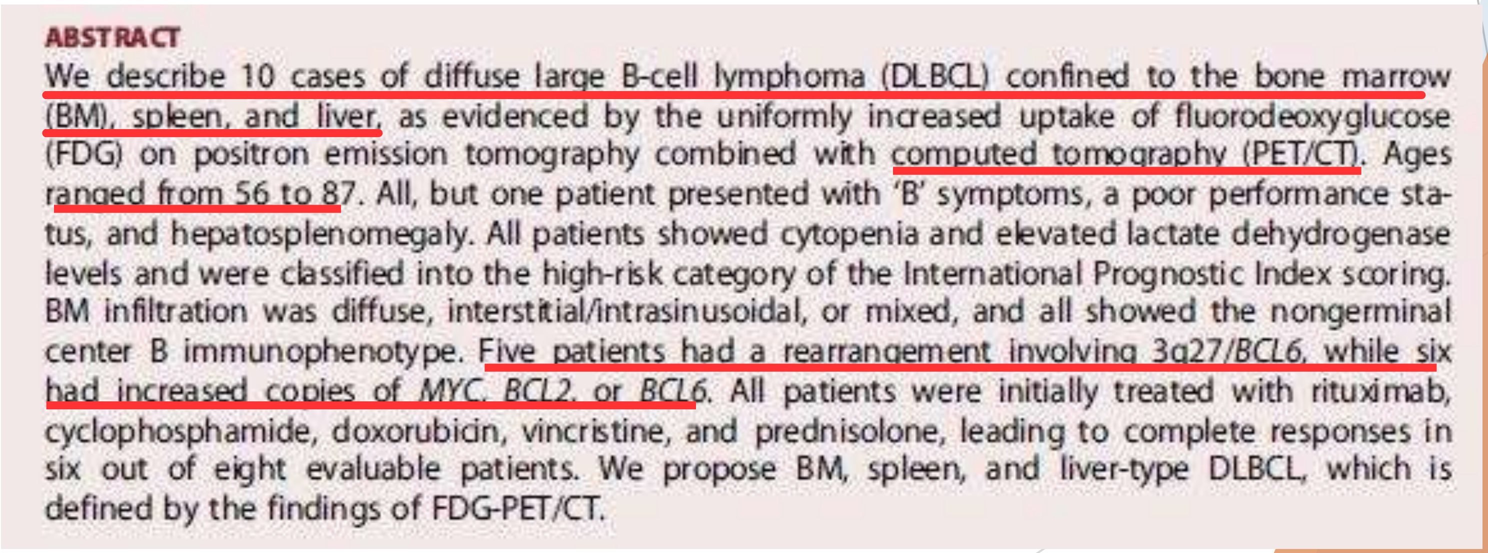
DISCUSIÓN



A unique subtype of diffuse large B-cell lymphoma primarily involving the bone marrow, spleen, and liver, defined by fluorodeoxyglucose-positron emission tomography combined with computed tomography

Futoshi Iioka[a], Gen Honjo[b], Takashi Misaki[c], Yusuke Toda[a], Kiyotaka Izumi[a], Yoshimasa Kamoda[a], Yuya Nagai[a], Takashi Akasaka[a], Kazushi Kitamura[c], Miho Nakagwa[d], Katsuhiro Fukutsuka[d], Atsuko Okumura[d] and Hitoshi Ohno[a,d]

[a]Departments of Hematology, Tenri Hospital, Mishima, Tenri, Japan; [b]Department of Diagnostic Pathology, Tenri Hospital, Mishima, Tenri, Japan; [c]Department of Radioisotope Center, Tenri Hospital, Mishima, Tenri, Japan; [d]Laboratory of Cytogenetics, Tenri Institute of Medical Research, Tenri, Japan



ABSTRACT

We describe 10 cases of diffuse large B-cell lymphoma (DLBCL) confined to the bone marrow (BM), spleen, and liver, as evidenced by the uniformly increased uptake of fluorodeoxyglucose (FDG) on positron emission tomography combined with computed tomography (PET/CT). Ages ranged from 56 to 87. All, but one patient presented with 'B' symptoms, a poor performance status, and hepatosplenomegaly. All patients showed cytopenia and elevated lactate dehydrogenase levels and were classified into the high-risk category of the International Prognostic Index scoring. BM infiltration was diffuse, interstitial/intrasinusoidal, or mixed, and all showed the nongerminal center B immunophenotype. Five patients had a rearrangement involving 3q27/*BCL6*, while six had increased copies of *MYC*, *BCL2*, or *BCL6*. All patients were initially treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone, leading to complete responses in six out of eight evaluable patients. We propose BM, spleen, and liver-type DLBCL, which is defined by the findings of FDG-PET/CT.

DISCUSIÓN

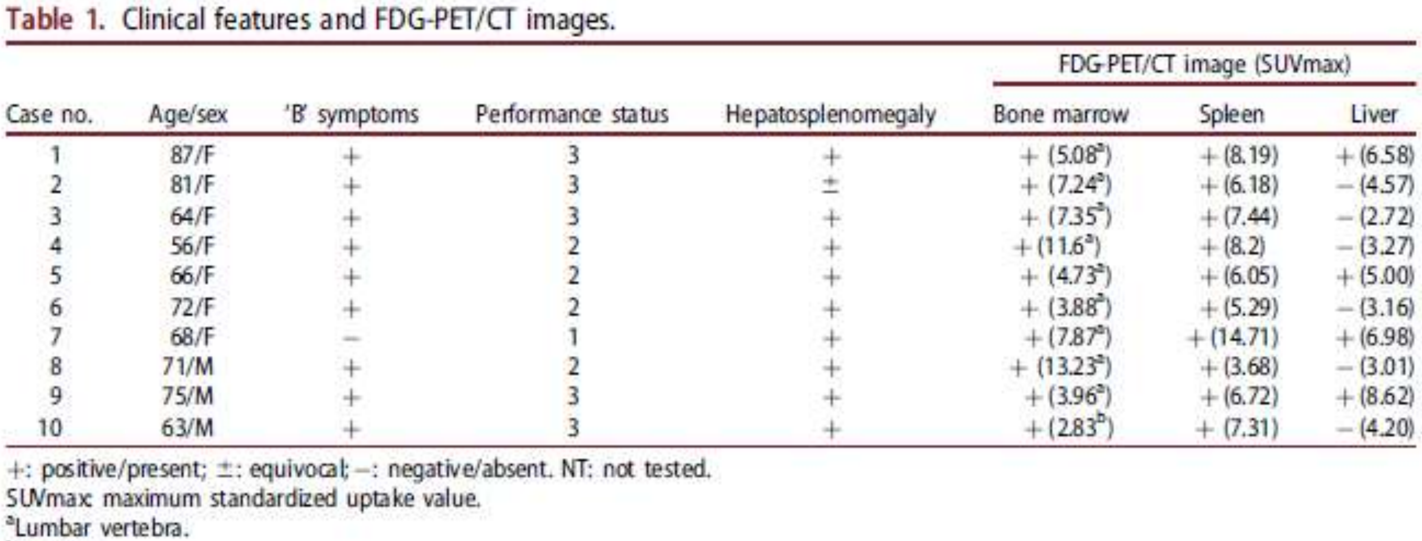


Table 1. Clinical features and FDG-PET/CT images.

Case no.	Age/sex	'B' symptoms	Performance status	Hepatosplenomegaly	FDG-PET/CT image (SUVmax) Bone marrow	Spleen	Liver
1	87/F	+	3	+	+ (5.08[a])	+ (8.19)	+ (6.58)
2	81/F	+	3	±	+ (7.24[a])	+ (6.18)	− (4.57)
3	64/F	+	3	+	+ (7.35[a])	+ (7.44)	− (2.72)
4	56/F	+	2	+	+ (11.6[a])	+ (8.2)	− (3.27)
5	66/F	+	2	+	+ (4.73[a])	+ (6.05)	+ (5.00)
6	72/F	+	2	+	+ (3.88[a])	+ (5.29)	− (3.16)
7	68/F	−	1	+	+ (7.87[a])	+ (14.71)	+ (6.98)
8	71/M	+	2	+	+ (13.23[a])	+ (3.68)	− (3.01)
9	75/M	+	3	+	+ (3.96[a])	+ (6.72)	+ (8.62)
10	63/M	+	3	+	+ (2.83[b])	+ (7.31)	− (4.20)

+: positive/present; ±: equivocal; −: negative/absent. NT: not tested.
SUVmax: maximum standardized uptake value.
[a]Lumbar vertebra.
[b]Sternum.

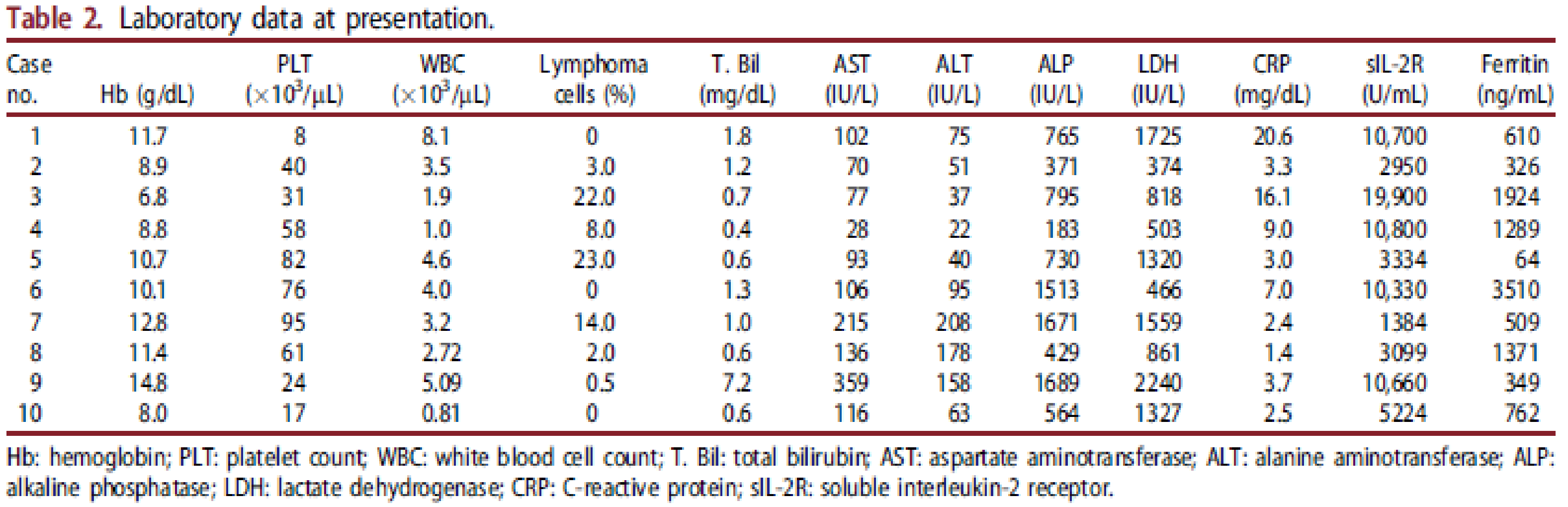


Table 2. Laboratory data at presentation.

Case no.	Hb (g/dL)	PLT ($\times 10^3/\mu L$)	WBC ($\times 10^3/\mu L$)	Lymphoma cells (%)	T. Bil (mg/dL)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	LDH (IU/L)	CRP (mg/dL)	sIL-2R (U/mL)	Ferritin (ng/mL)
1	11.7	8	8.1	0	1.8	102	75	765	1725	20.6	10,700	610
2	8.9	40	3.5	3.0	1.2	70	51	371	374	3.3	2950	326
3	6.8	31	1.9	22.0	0.7	77	37	795	818	16.1	19,900	1924
4	8.8	58	1.0	8.0	0.4	28	22	183	503	9.0	10,800	1289
5	10.7	82	4.6	23.0	0.6	93	40	730	1320	3.0	3334	64
6	10.1	76	4.0	0	1.3	106	95	1513	466	7.0	10,330	3510
7	12.8	95	3.2	14.0	1.0	215	208	1671	1559	2.4	1384	509
8	11.4	61	2.72	2.0	0.6	136	178	429	861	1.4	3099	1371
9	14.8	24	5.09	0.5	7.2	359	158	1689	2240	3.7	10,660	349
10	8.0	17	0.81	0	0.6	116	63	564	1327	2.5	5224	762

Hb: hemoglobin; PLT: platelet count; WBC: white blood cell count; T. Bil: total bilirubin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; LDH: lactate dehydrogenase; CRP: C-reactive protein; sIL-2R: soluble interleukin-2 receptor.

DISCUSIÓN

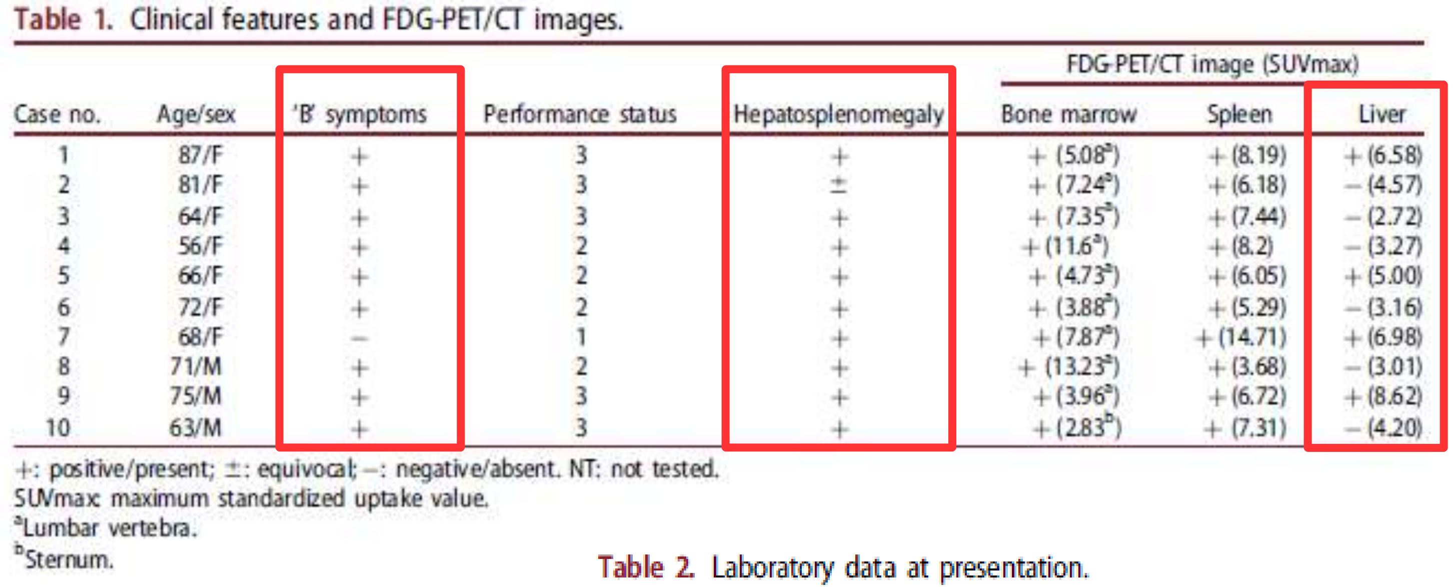


Table 1. Clinical features and FDG-PET/CT images.

Case no.	Age/sex	'B' symptoms	Performance status	Hepatosplenomegaly	FDG-PET/CT image (SUVmax) Bone marrow	Spleen	Liver
1	87/F	+	3	+	+ (5.08[a])	+ (8.19)	+ (6.58)
2	81/F	+	3	±	+ (7.24[a])	+ (6.18)	− (4.57)
3	64/F	+	3	+	+ (7.35[a])	+ (7.44)	− (2.72)
4	56/F	+	2	+	+ (11.6[a])	+ (8.2)	− (3.27)
5	66/F	+	2	+	+ (4.73[a])	+ (6.05)	+ (5.00)
6	72/F	+	2	+	+ (3.88[a])	+ (5.29)	− (3.16)
7	68/F	−	1	+	+ (7.87[a])	+ (14.71)	+ (6.98)
8	71/M	+	2	+	+ (13.23[a])	+ (3.68)	− (3.01)
9	75/M	+	3	+	+ (3.96[a])	+ (6.72)	+ (8.62)
10	63/M	+	3	+	+ (2.83[b])	+ (7.31)	− (4.20)

+: positive/present; ±: equivocal; −: negative/absent. NT: not tested.
SUVmax: maximum standardized uptake value.
[a] Lumbar vertebra.
[b] Sternum.

Sin linfadenopatías

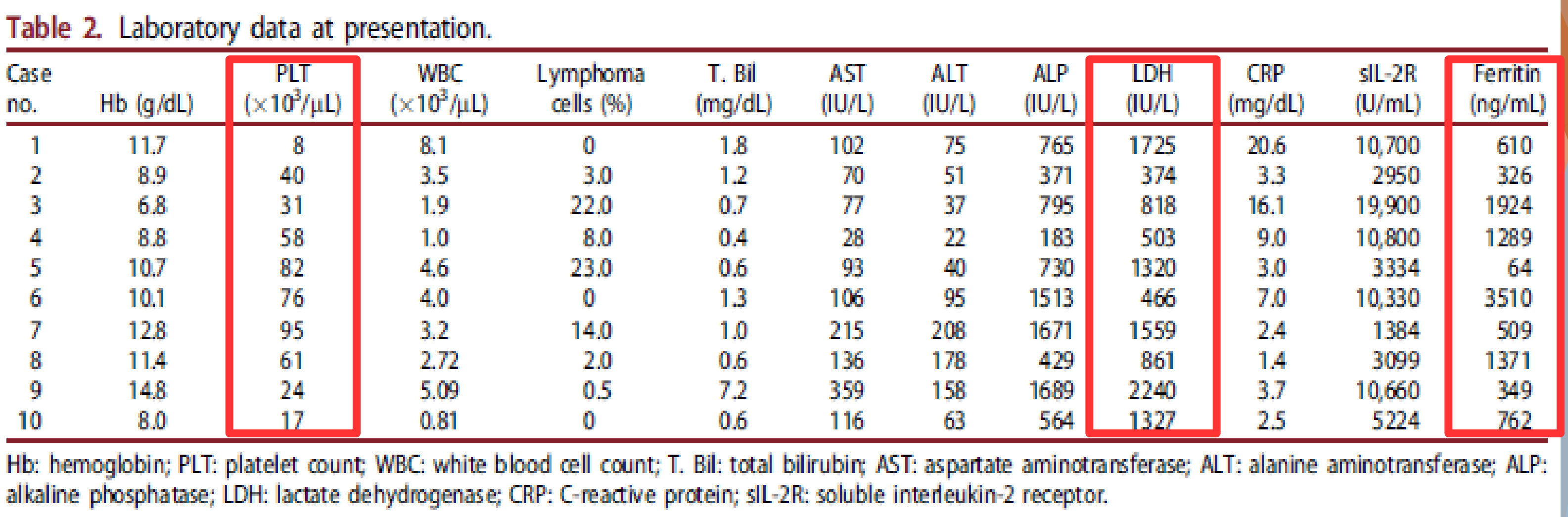


Table 2. Laboratory data at presentation.

Case no.	Hb (g/dL)	PLT (×10³/μL)	WBC (×10³/μL)	Lymphoma cells (%)	T. Bil (mg/dL)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	LDH (IU/L)	CRP (mg/dL)	sIL-2R (U/mL)	Ferritin (ng/mL)
1	11.7	8	8.1	0	1.8	102	75	765	1725	20.6	10,700	610
2	8.9	40	3.5	3.0	1.2	70	51	371	374	3.3	2950	326
3	6.8	31	1.9	22.0	0.7	77	37	795	818	16.1	19,900	1924
4	8.8	58	1.0	8.0	0.4	28	22	183	503	9.0	10,800	1289
5	10.7	82	4.6	23.0	0.6	93	40	730	1320	3.0	3334	64
6	10.1	76	4.0	0	1.3	106	95	1513	466	7.0	10,330	3510
7	12.8	95	3.2	14.0	1.0	215	208	1671	1559	2.4	1384	509
8	11.4	61	2.72	2.0	0.6	136	178	429	861	1.4	3099	1371
9	14.8	24	5.09	0.5	7.2	359	158	1689	2240	3.7	10,660	349
10	8.0	17	0.81	0	0.6	116	63	564	1327	2.5	5224	762

Hb: hemoglobin; PLT: platelet count; WBC: white blood cell count; T. Bil: total bilirubin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; LDH: lactate dehydrogenase; CRP: C-reactive protein; sIL-2R: soluble interleukin-2 receptor.

DISCUSIÓN

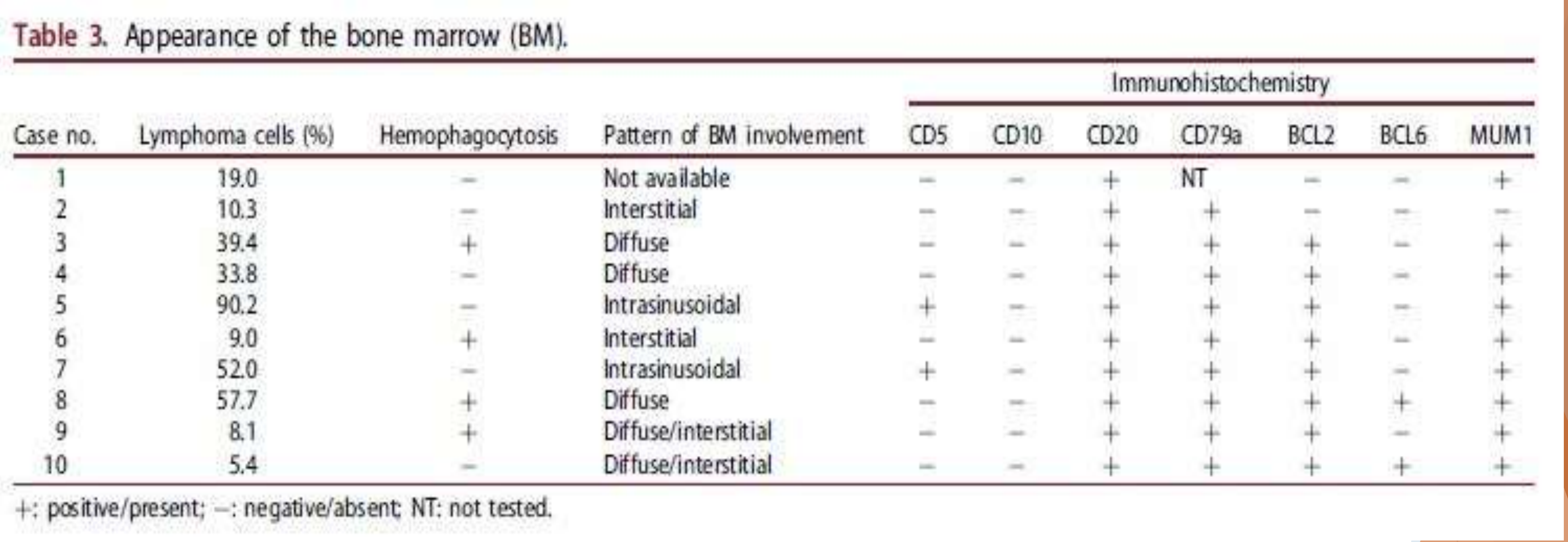
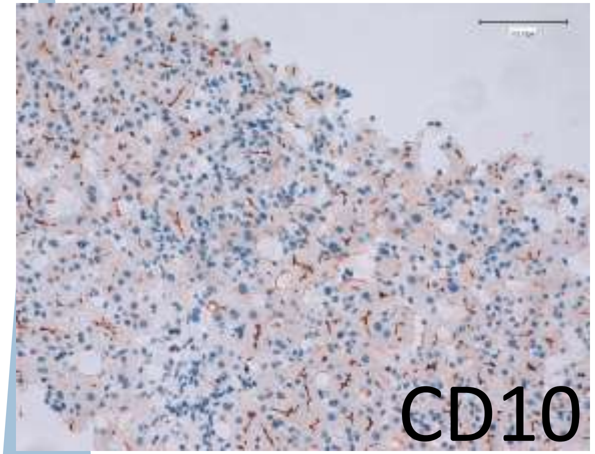


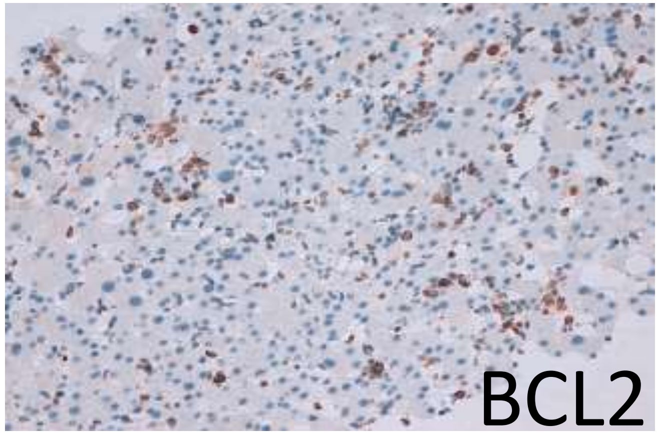
Table 3. Appearance of the bone marrow (BM).

Case no.	Lymphoma cells (%)	Hemophagocytosis	Pattern of BM involvement	Immunohistochemistry						
				CD5	CD10	CD20	CD79a	BCL2	BCL6	MUM1
1	19.0	–	Not available	–	–	+	NT	–	–	+
2	10.3	–	Interstitial	–	–	+	+	–	–	–
3	39.4	+	Diffuse	–	–	+	+	+	–	+
4	33.8	–	Diffuse	–	–	+	+	+	–	+
5	90.2	–	Intrasinusoidal	+	–	+	+	+	–	+
6	9.0	+	Interstitial	–	–	+	+	+	–	+
7	52.0	–	Intrasinusoidal	+	–	+	+	+	–	+
8	57.7	+	Diffuse	–	–	+	+	+	+	+
9	8.1	+	Diffuse/interstitial	–	–	+	+	+	–	+
10	5.4	–	Diffuse/interstitial	–	–	+	+	+	+	+

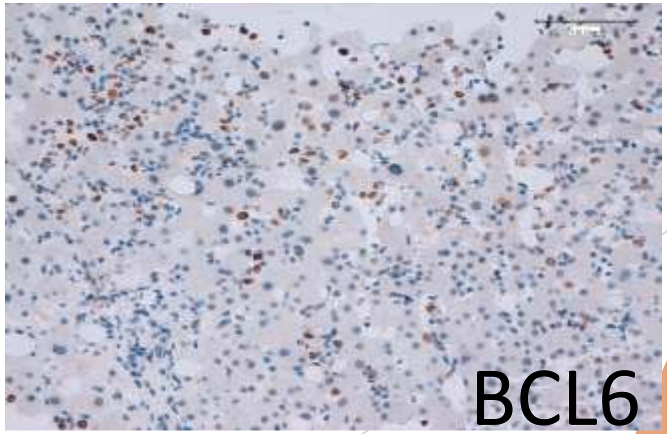
+: positive/present; –: negative/absent; NT: not tested.



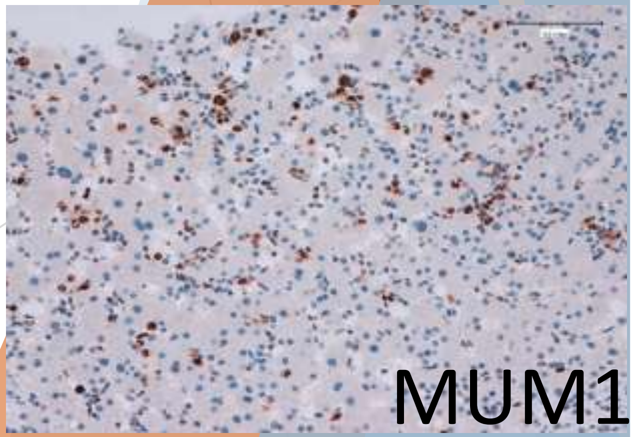
CD10



BCL2



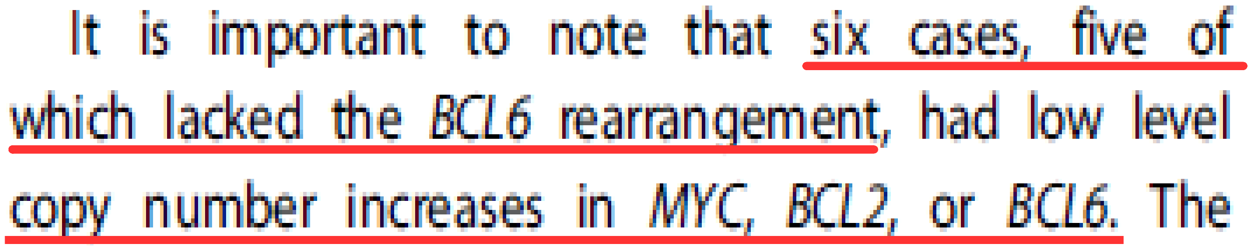
BCL6



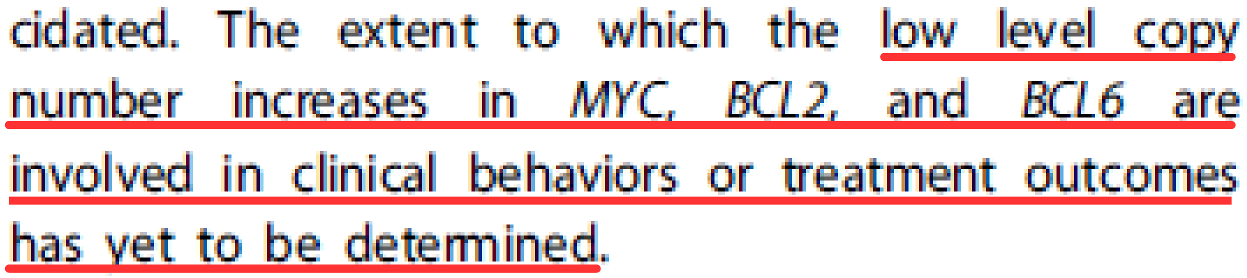
MUM1

DISCUSIÓN

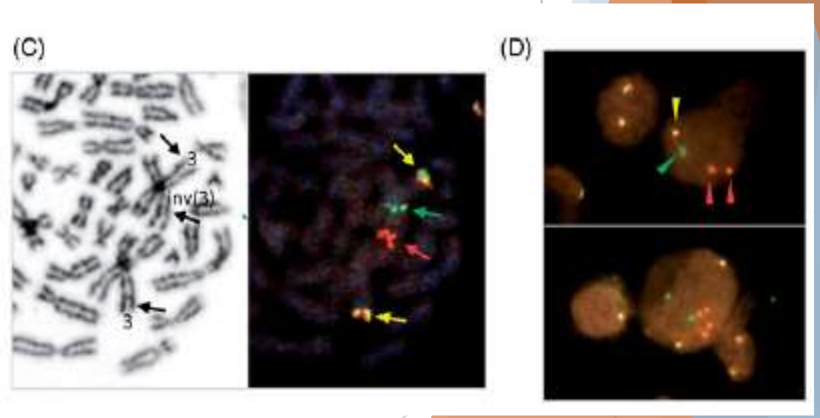
FISH



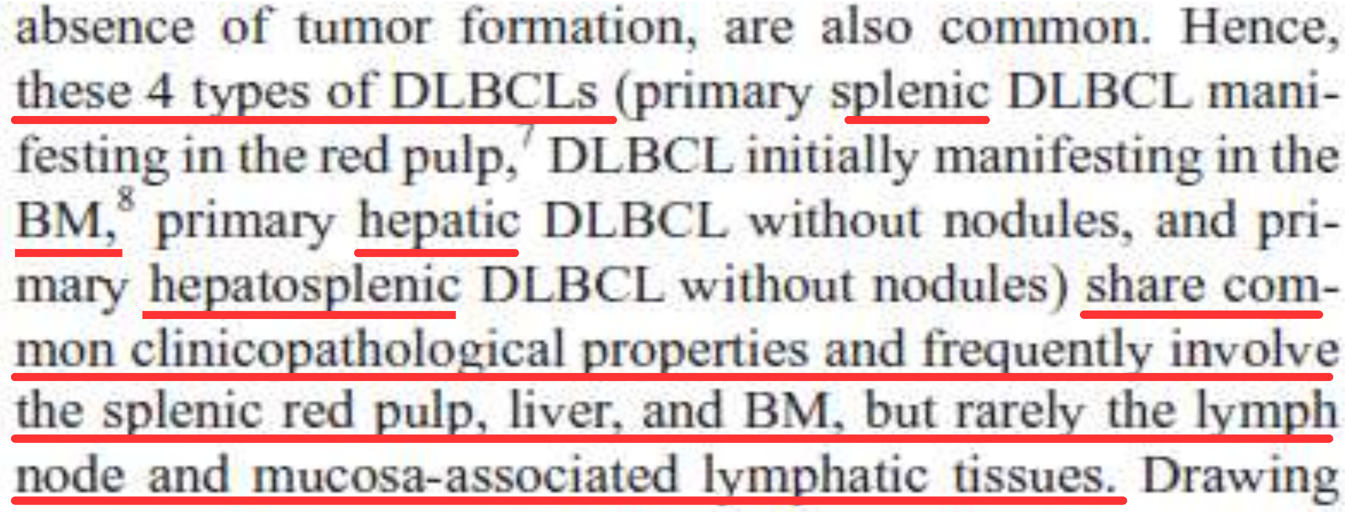
It is important to note that six cases, five of which lacked the *BCL6* rearrangement, had low level copy number increases in *MYC*, *BCL2*, or *BCL6*. The

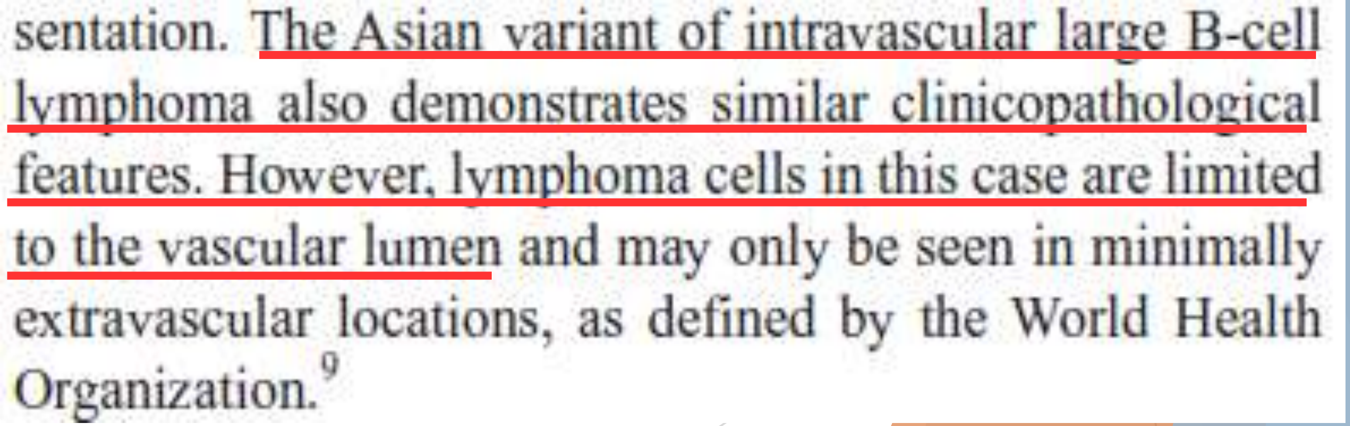


cidated. The extent to which the low level copy number increases in *MYC*, *BCL2*, and *BCL6* are involved in clinical behaviors or treatment outcomes has yet to be determined.

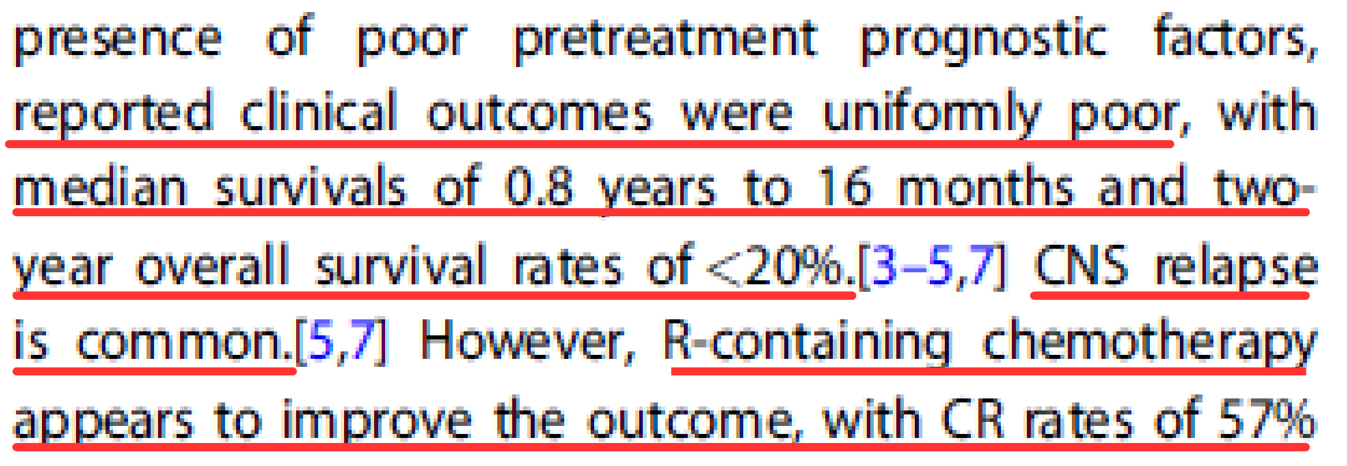


DISCUSIÓN

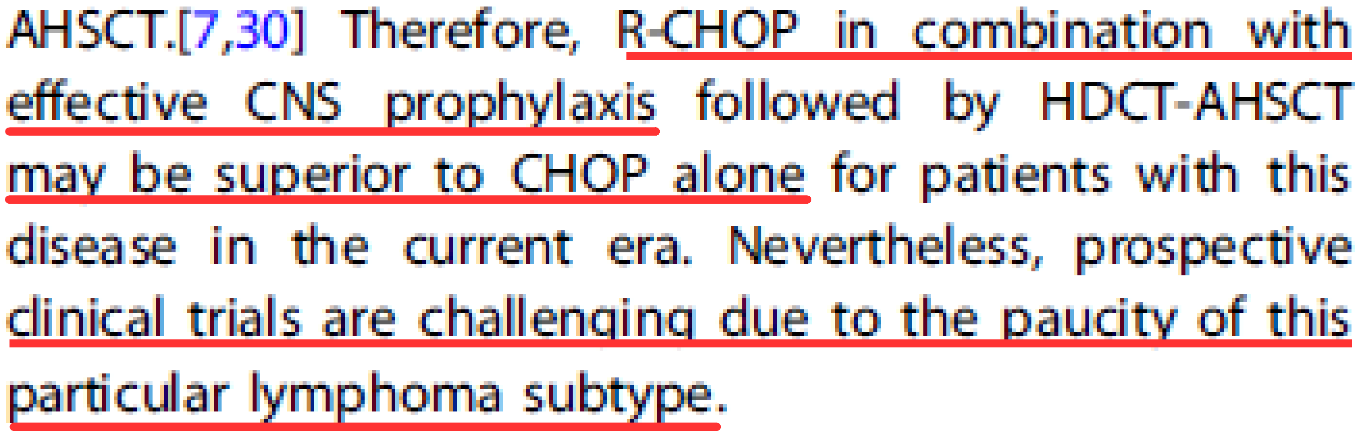

absence of tumor formation, are also common. Hence, these 4 types of DLBCLs (primary splenic DLBCL manifesting in the red pulp,[7] DLBCL initially manifesting in the BM,[8] primary hepatic DLBCL without nodules, and primary hepatosplenic DLBCL without nodules) share common clinicopathological properties and frequently involve the splenic red pulp, liver, and BM, but rarely the lymph node and mucosa-associated lymphatic tissues. Drawing


sentation. The Asian variant of intravascular large B-cell lymphoma also demonstrates similar clinicopathological features. However, lymphoma cells in this case are limited to the vascular lumen and may only be seen in minimally extravascular locations, as defined by the World Health Organization.[9]

DISCUSIÓN



presence of poor pretreatment prognostic factors, reported clinical outcomes were uniformly poor, with median survivals of 0.8 years to 16 months and two-year overall survival rates of <20%.[3–5,7] CNS relapse is common.[5,7] However, R-containing chemotherapy appears to improve the outcome, with CR rates of 57%



AHSCT.[7,30] Therefore, R-CHOP in combination with effective CNS prophylaxis followed by HDCT-AHSCT may be superior to CHOP alone for patients with this disease in the current era. Nevertheless, prospective clinical trials are challenging due to the paucity of this particular lymphoma subtype.

EN ACTUALIDAD

- YA FINALIZADO 6º CICLO DE TERAPIA R-CHOP
- PENDIENTE DE PET CONTROL (VALORAR FIN DE TRATAMIENTO)
- EL PACIENTE SE ENCUENTRA ASINTOMÁTICO, BUEN ESTADO GENERAL.

GRACIAS

Amanecer sobre la Bahía