



OLGU 5

Dr.Gülşah KAYGUSUZ
Ankara Üniversitesi Tıp Fakültesi
Patoloji AD

- 64 yaş, erkek hasta, halsizlik
- Fizik Muayene: Splenomegali
- Özgeçmiş/soygeçmiş: özellik yok

TAM KAN:

Test Adı	Sonuç	Birim	Referans Değer
WBC	5.1	$10^3/uL$	4.1-10.9
RBC	2.61	$10^6/uL$	4.4-5.5
HGB	7.6	g/dL	12.9-16.6
HCT	23.5	%	38.6-48.0
MCV	90.0	fL	81.2-95.1
MCH	29.0	pg	27.4-33.0
MCHC	32.2	g/dL	33.3-35.2
RDW	20.7	%	11.8-15.6
NE%	63.6	%	44-77
LY%	20.4	%	20-47
MO%	15.3	%	2-10
EO%	0.3	%	1-6
BA%	0.4	%	0-2
NE#	3.2	$10^3/uL$	1.7-7.0
LY#	1.0	$10^3/uL$	1.3-2.9
MO#	0.8	$10^3/uL$	0.3-0.9
EO#	0.0	$10^3/uL$	0.05-0.50
BA#	0.0	$10^3/uL$	0-0.3
PLT	69	$10^3/uL$	184-370
MPV	7.6	fL	7.6-10.8

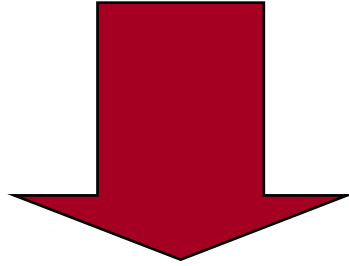
Test Adı	Sonuç	Birim	Referans Değer
Sedimantasyon	60	mm/Saat	0-20

Test Adı	Sonuç	Birim	Referans Değer
Vitamin B12	154.9	pg/mL	191-663

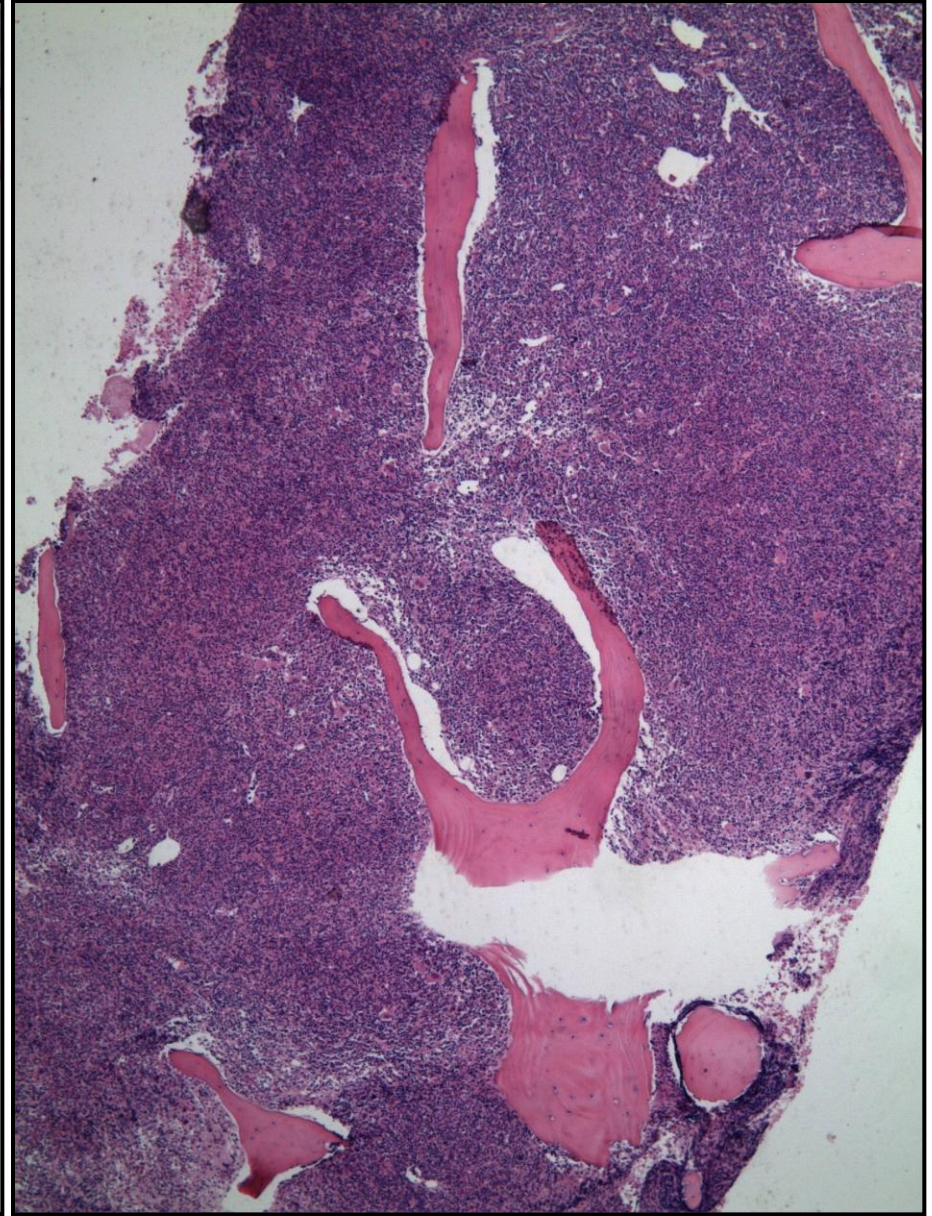
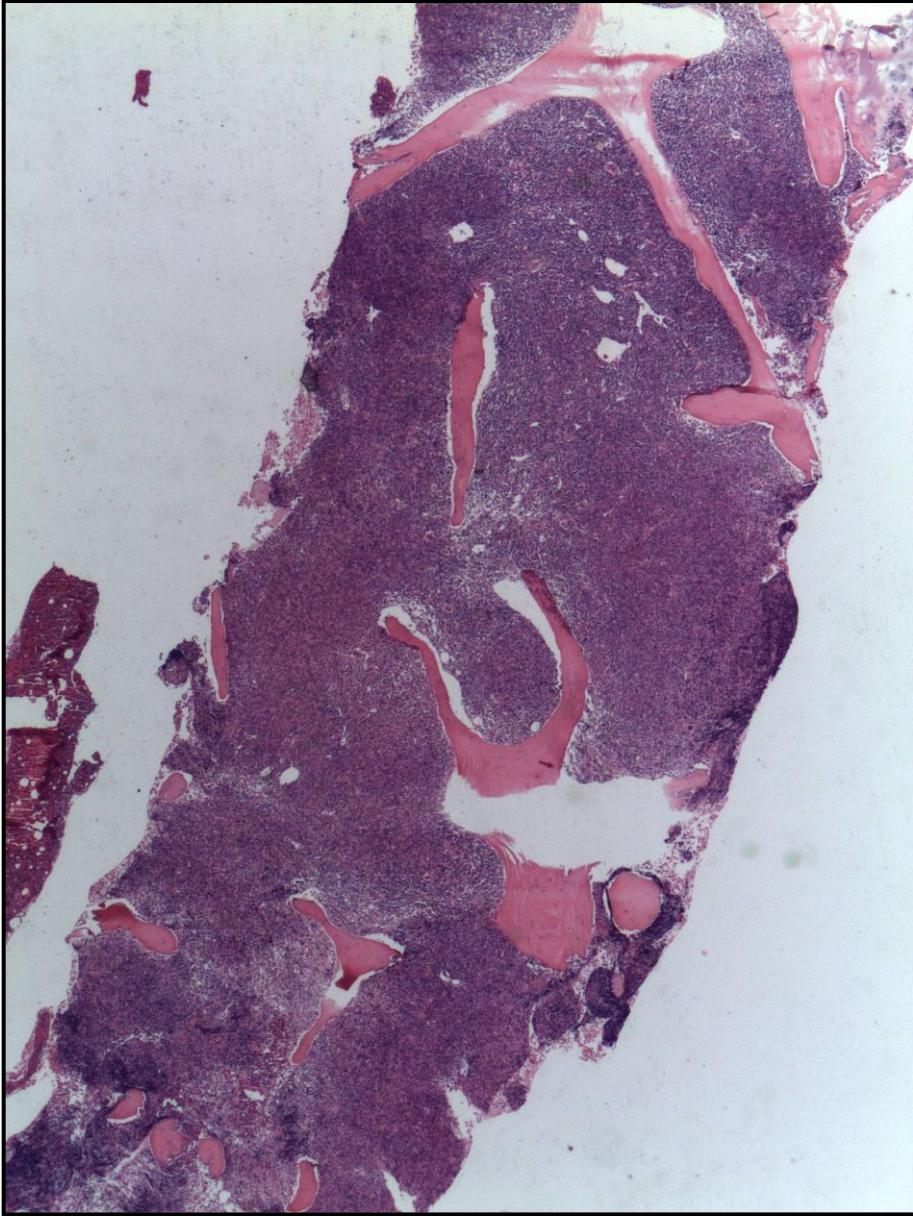
BİYOKİMYASAL TESTLER:

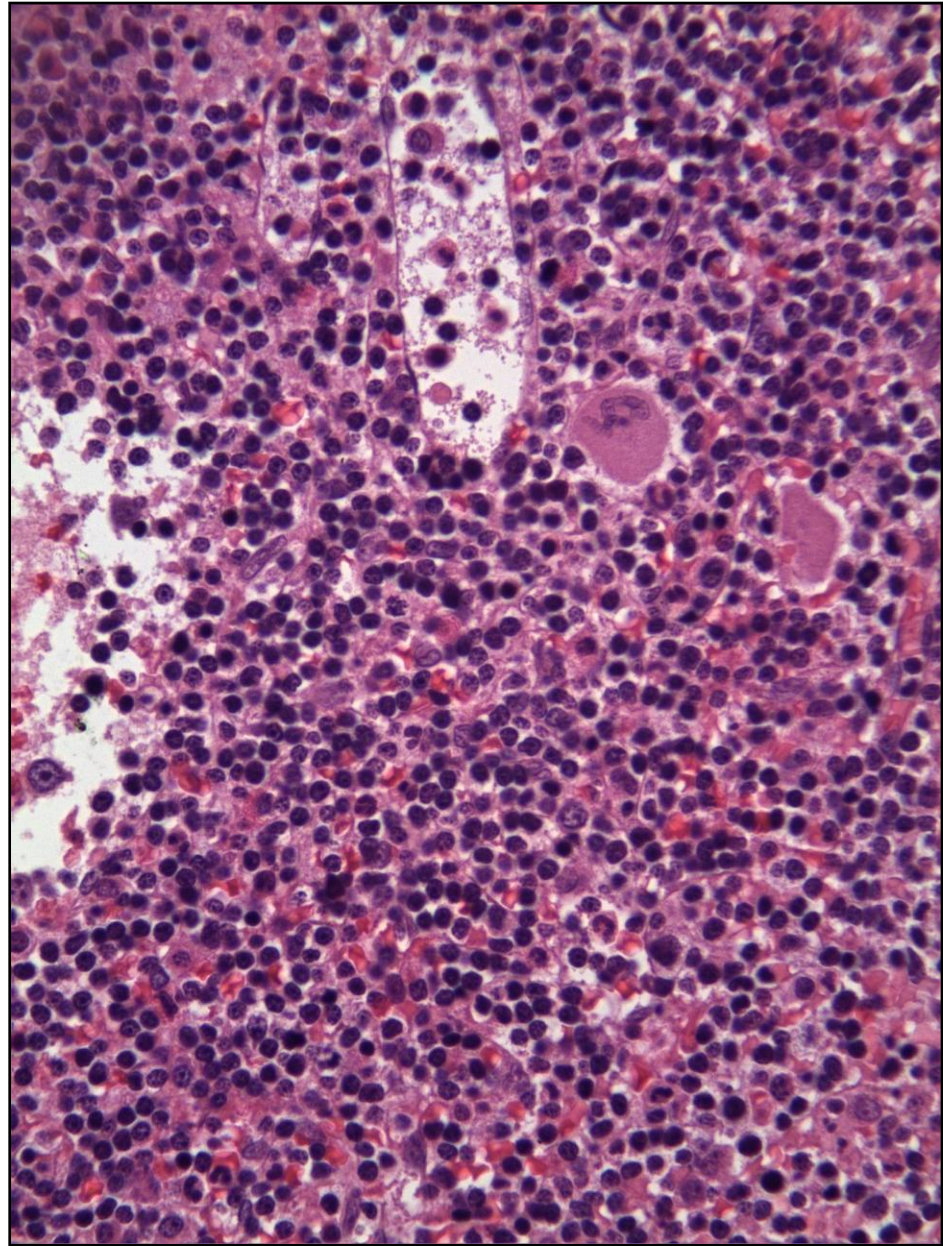
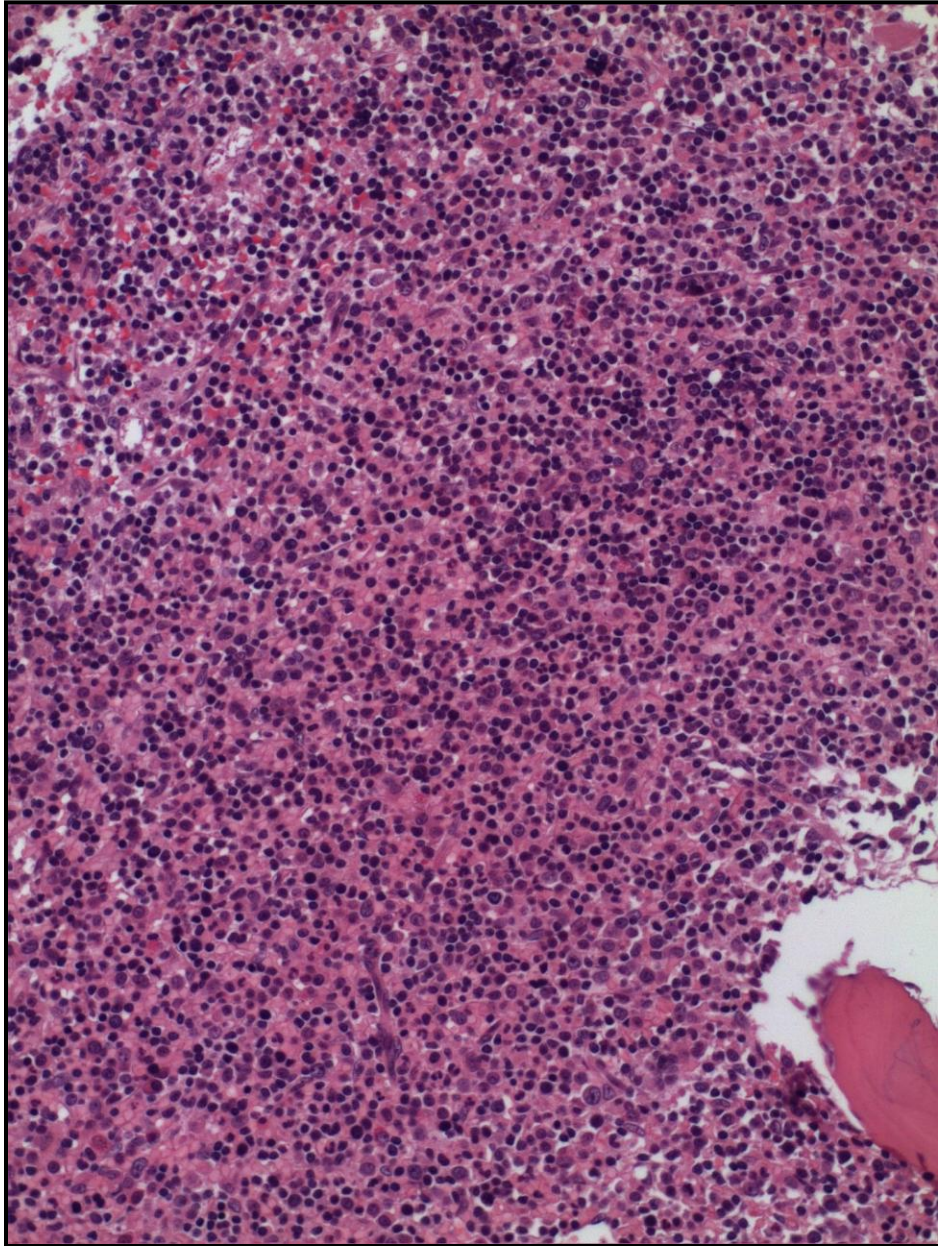
Test Adı	Sonuç	Birim	Referans Değer
AÇLIK KAN ŞEKERİ	94	mg/dL	74-106
	5.2	mmol/L	4.1-5.9
BUN (KAN ÜRE AZOTU)	20.56	mg/dL	8-23
	7.3	mmol/L	2.9-8.2
KREATİNİN	0.75	mg/dL	0.7-1.2
	66	umol/L	62-106
ÜRİK ASİT	5.1	mg/dL	3.4-7
	303	umol/L	202-416
KALSİYUM	8.74	mg/dL	8.6-10.2
	2.2	mmol/L	2.1-2.5
TOTAL PROTEİN	7.2	g/dL	6.6-8.7
	72	g/L	66-87
ALBÜMİN	4.3	g/dL	3.5-5.2
	43	g/L	35-52
TOTAL BİLİRUBİN	0.62	mg/dL	<1.1-
	10.6	umol/L	0.0-0.0
DİREKT BİLİRUBİN	0.21	mg/dL	<0.3-
	3.6	umol/L	0.0-0.0
ASPARTAT TRANSAMİNAZ (AST)	8	UI/L	<37-
	0.14	uKat/L	0.00-0.00
ALANİN TRANSAMİNAZ (ALT)	7	UI/L	<41-
	0.12	uKat/L	0.00-0.00
LAKTAT DEHİDROGENAZ (LDH)	251	UI/L	240-480
	4.27	uKat/L	4.08-8.16

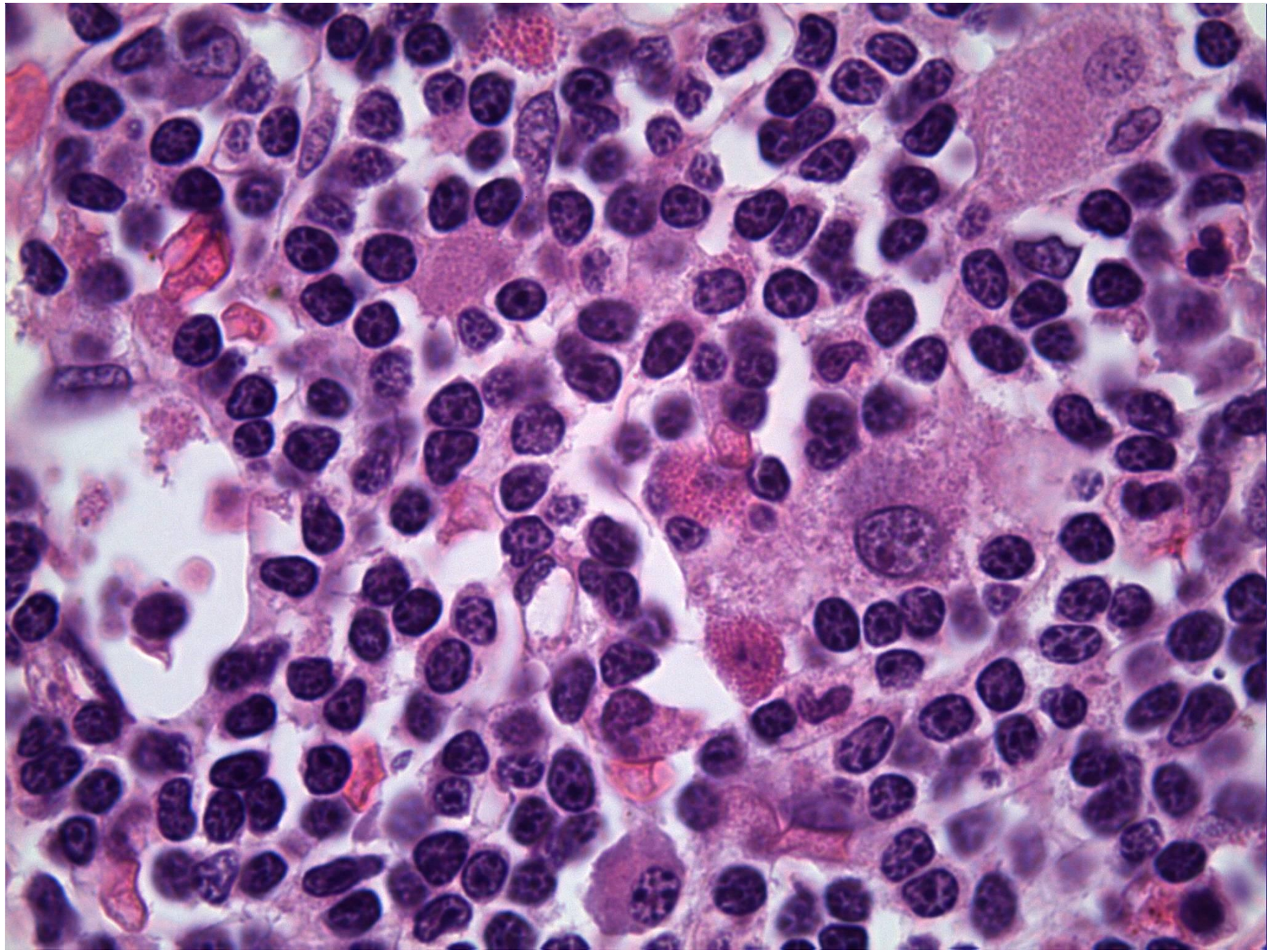
- 64 yař, erkek hasta, halsizlik, splenomegali
- Anemi, trombositopeni, monositoz
- Sedimentasyon ↑, VitB12 ↓

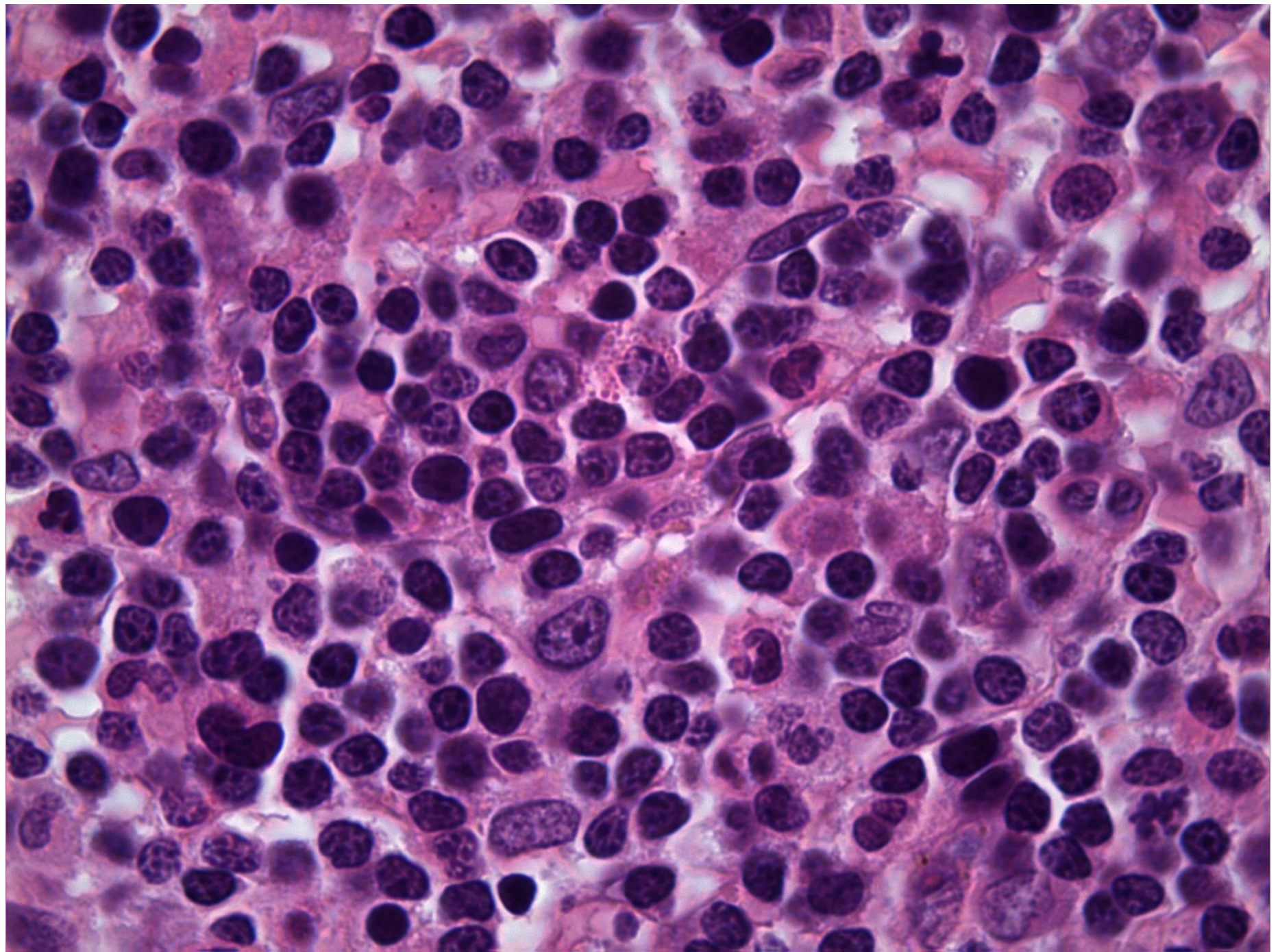


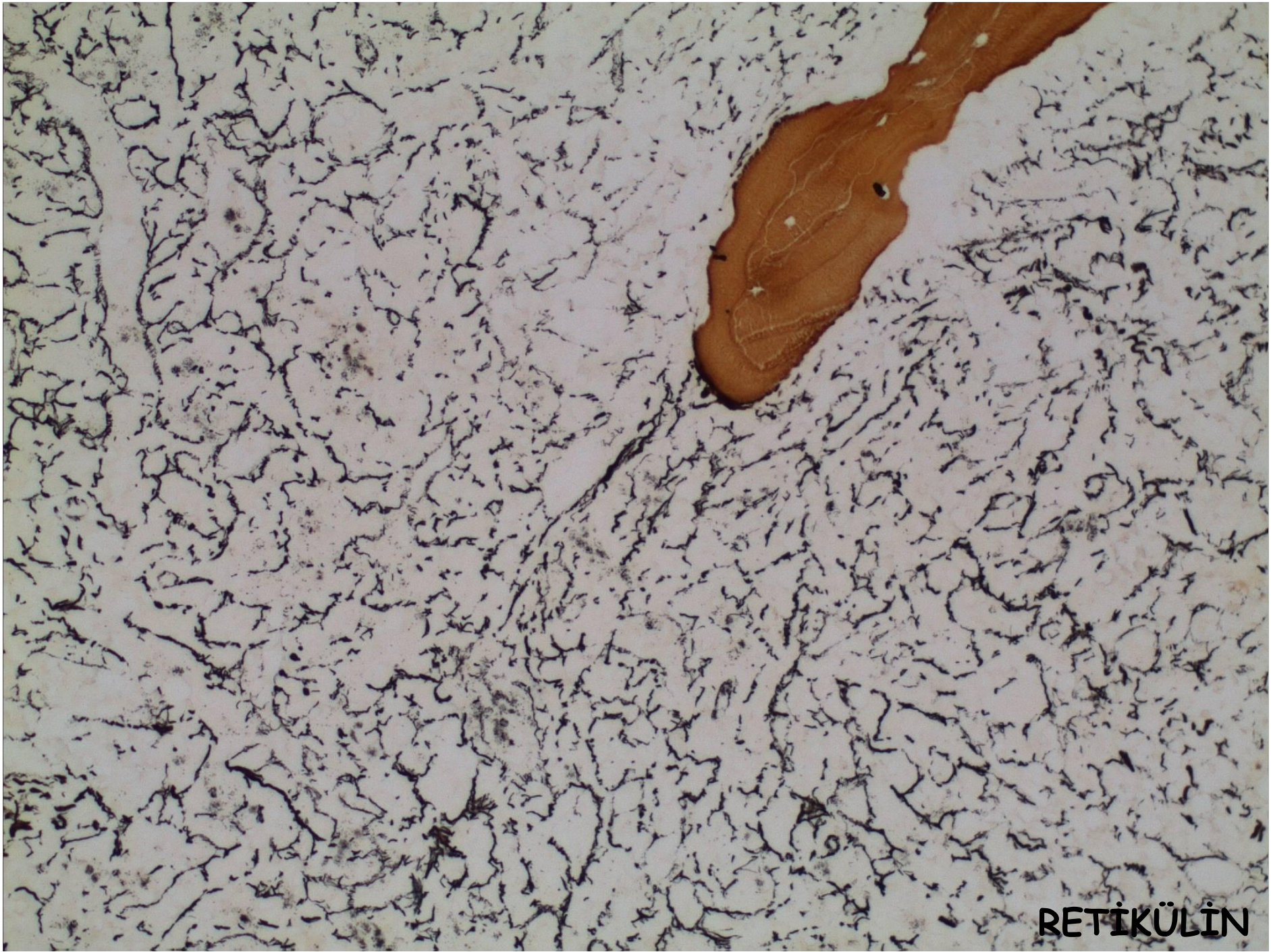
KEMİK İLİĞİ BİYOPSİSİ



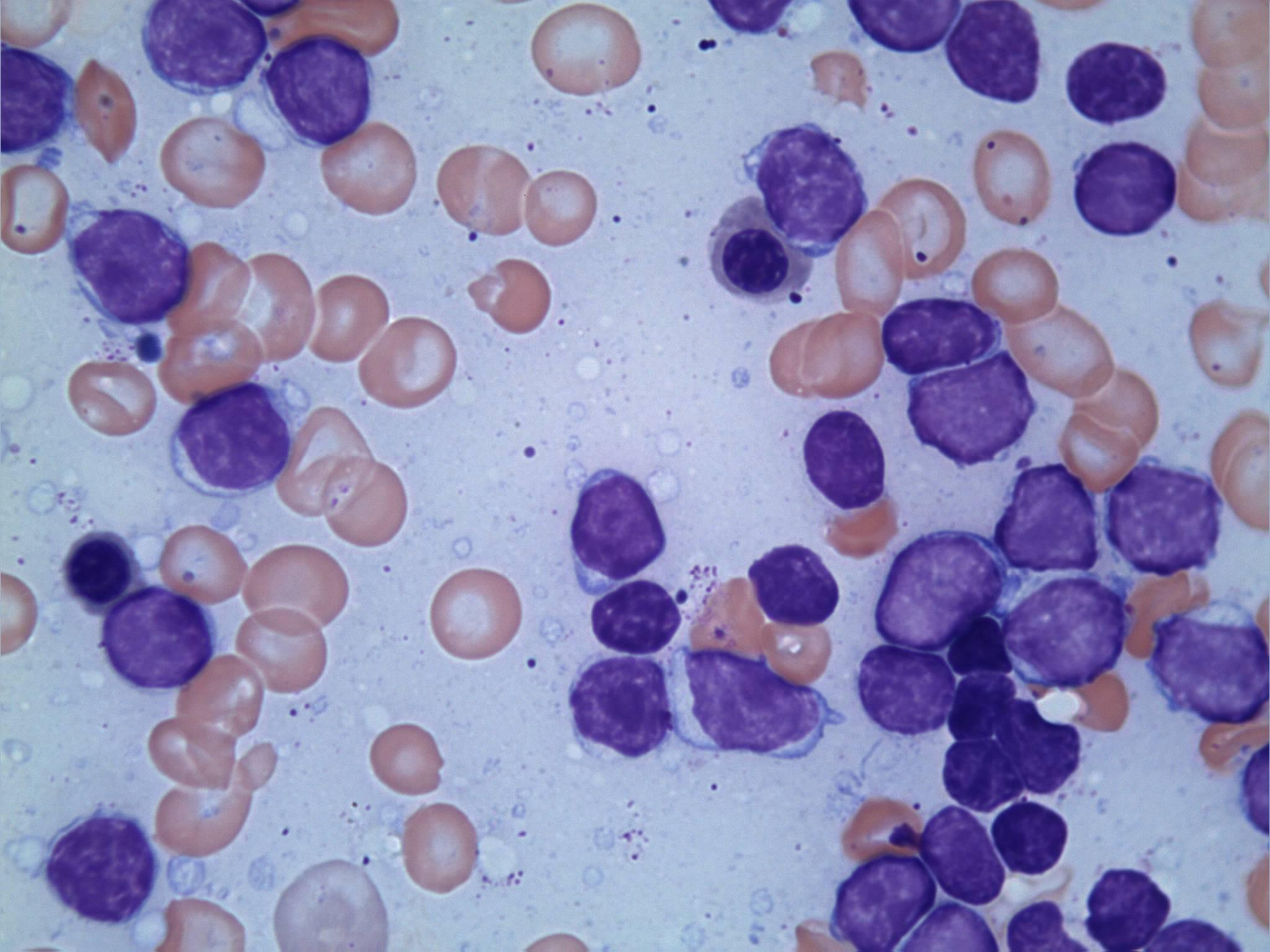


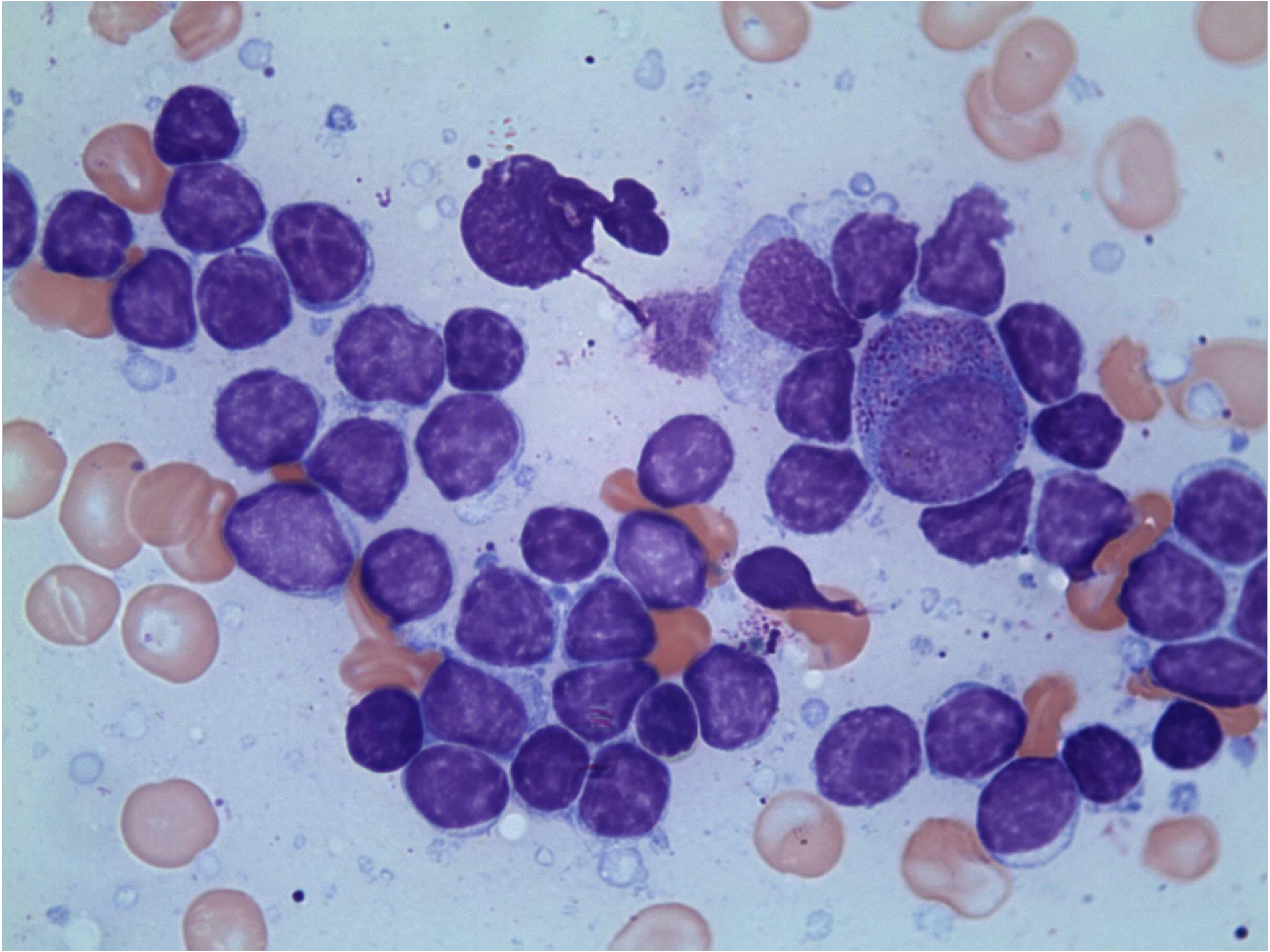


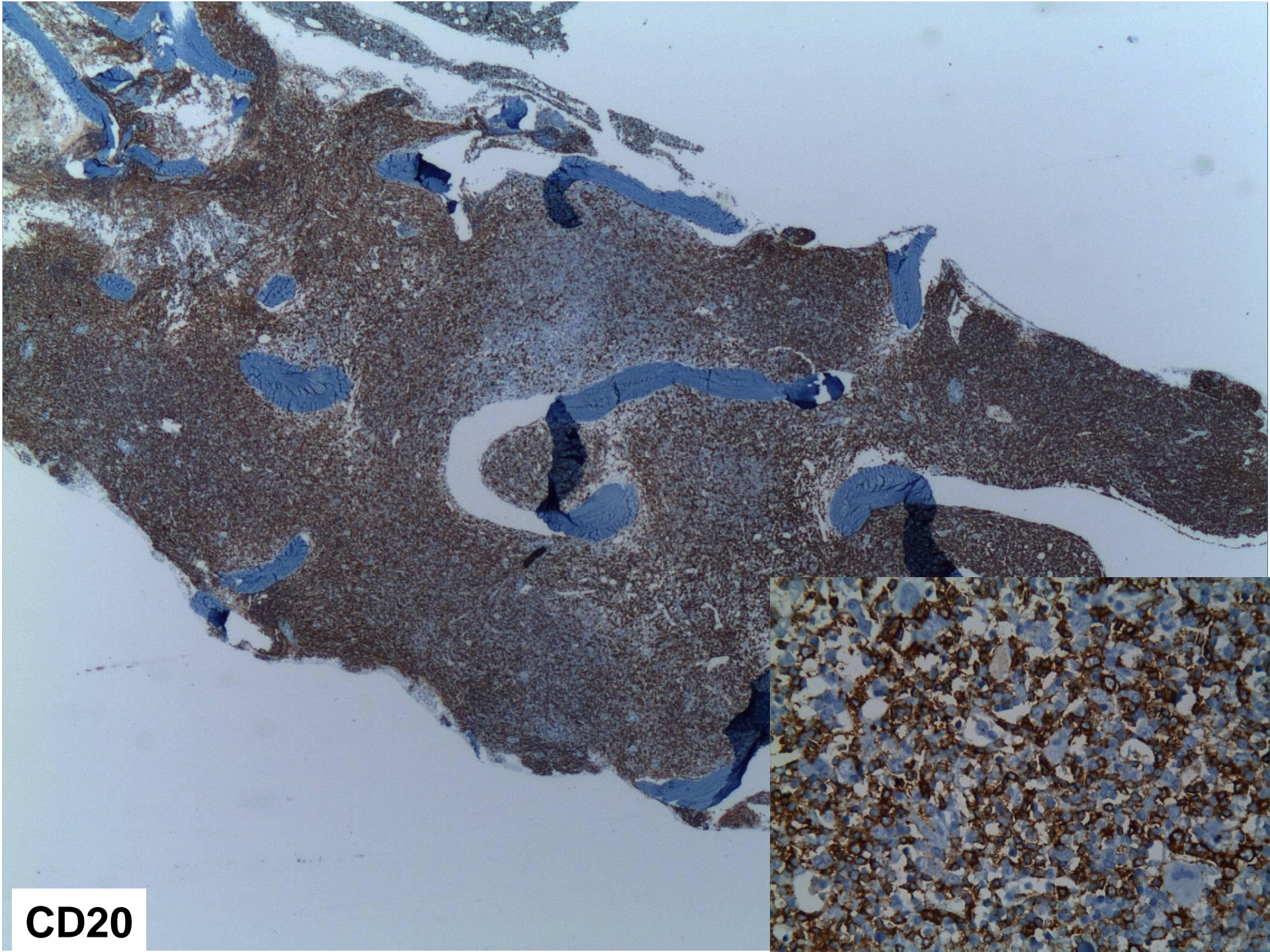




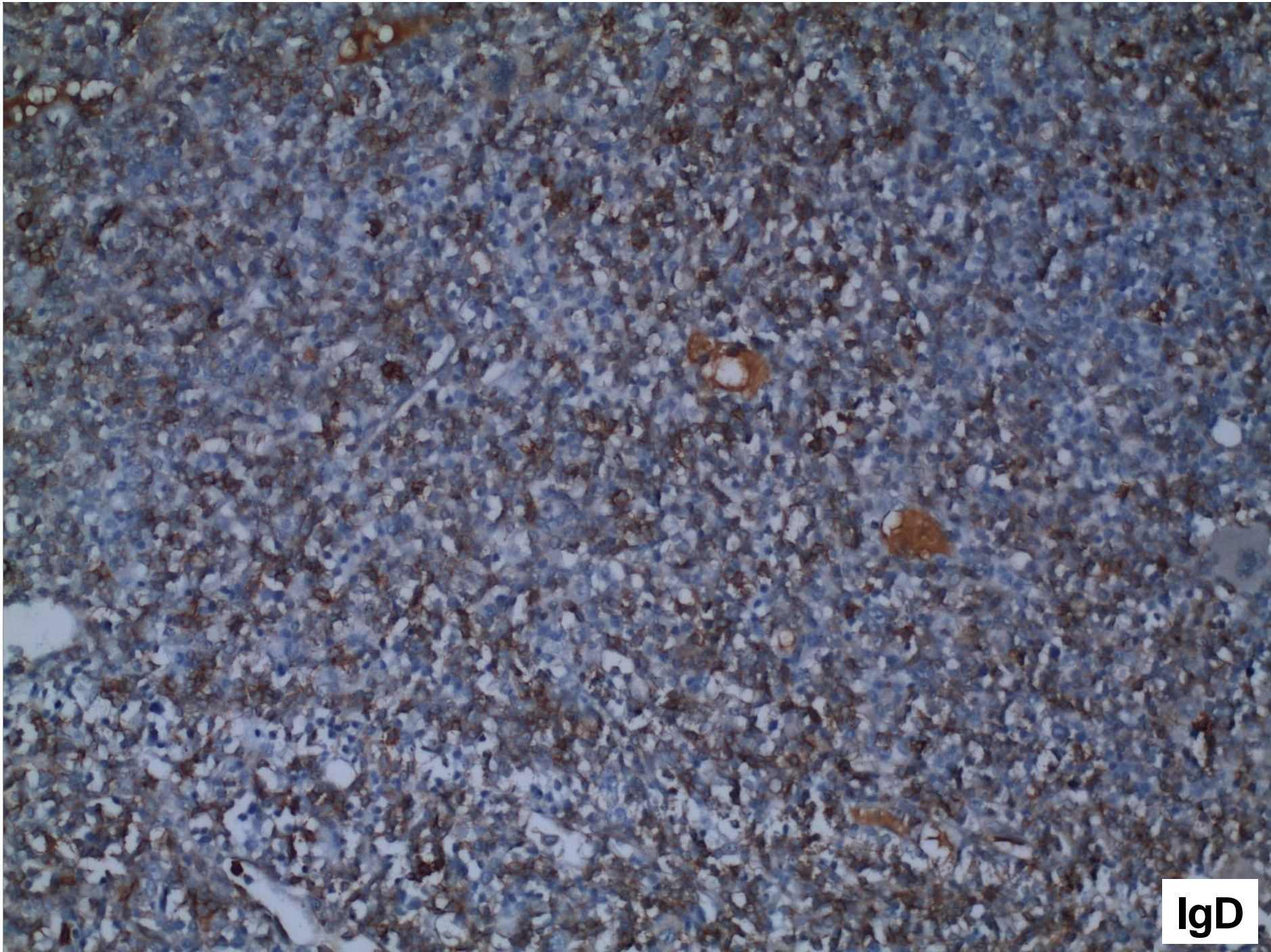
RETİKÜLİN





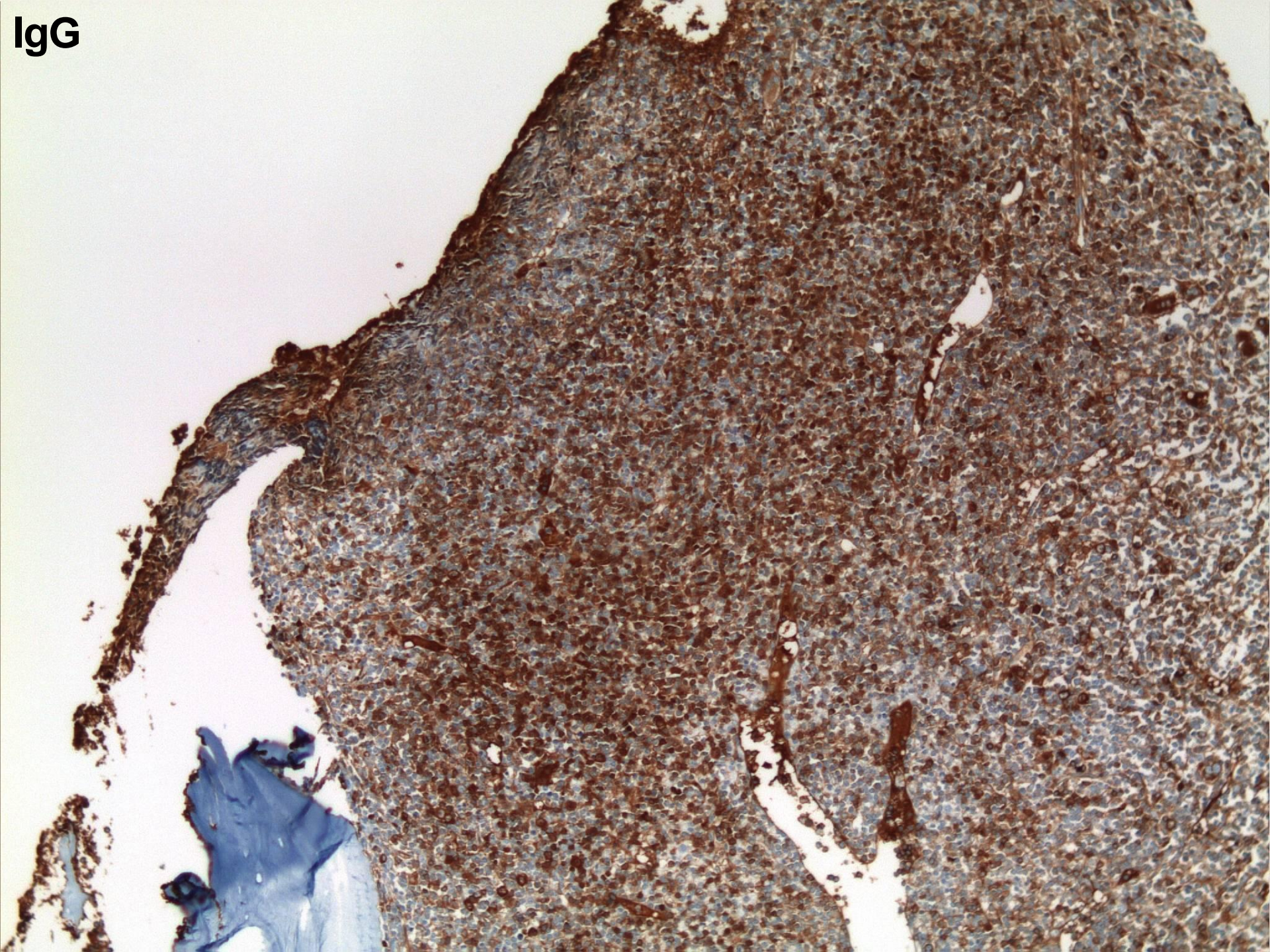


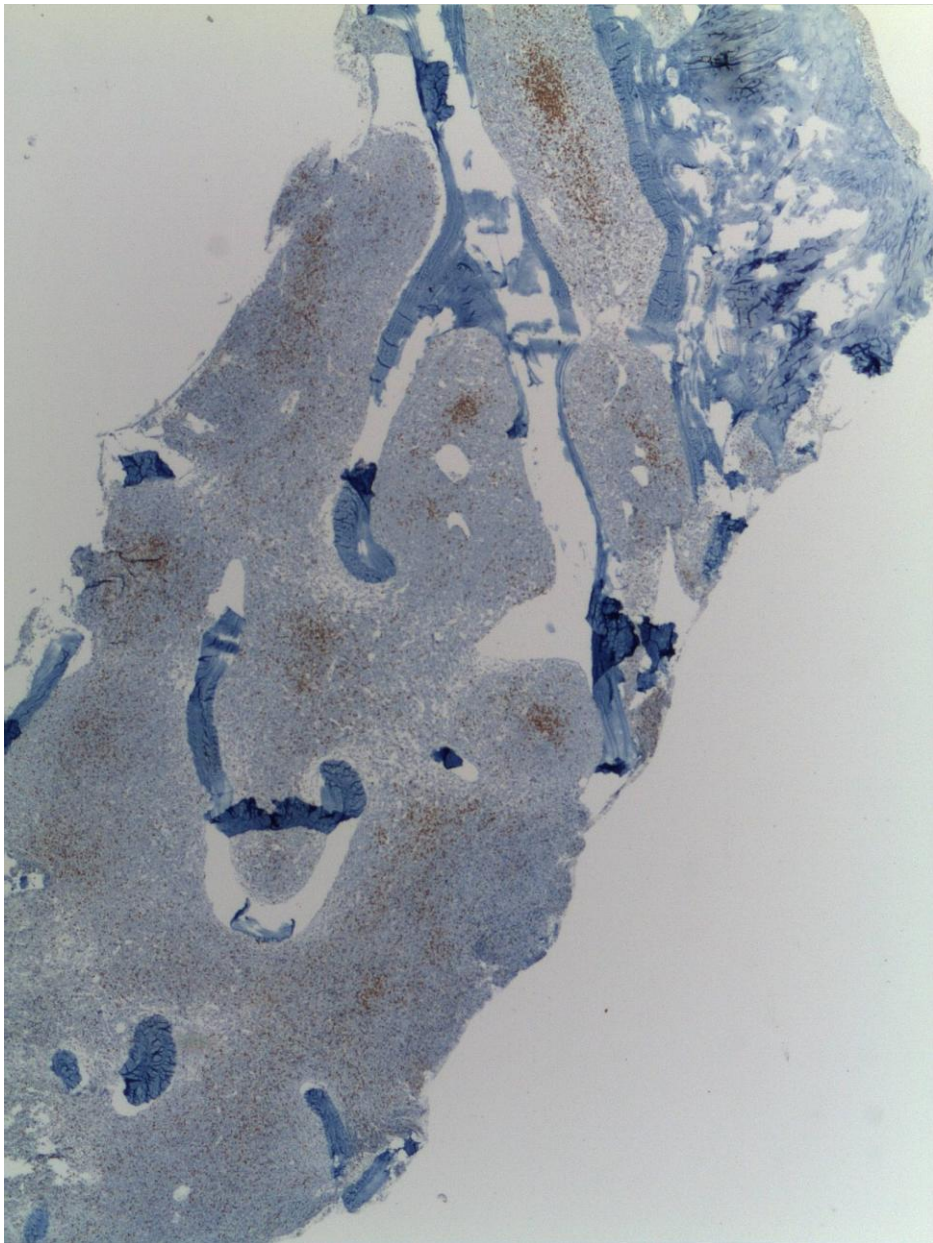
CD20



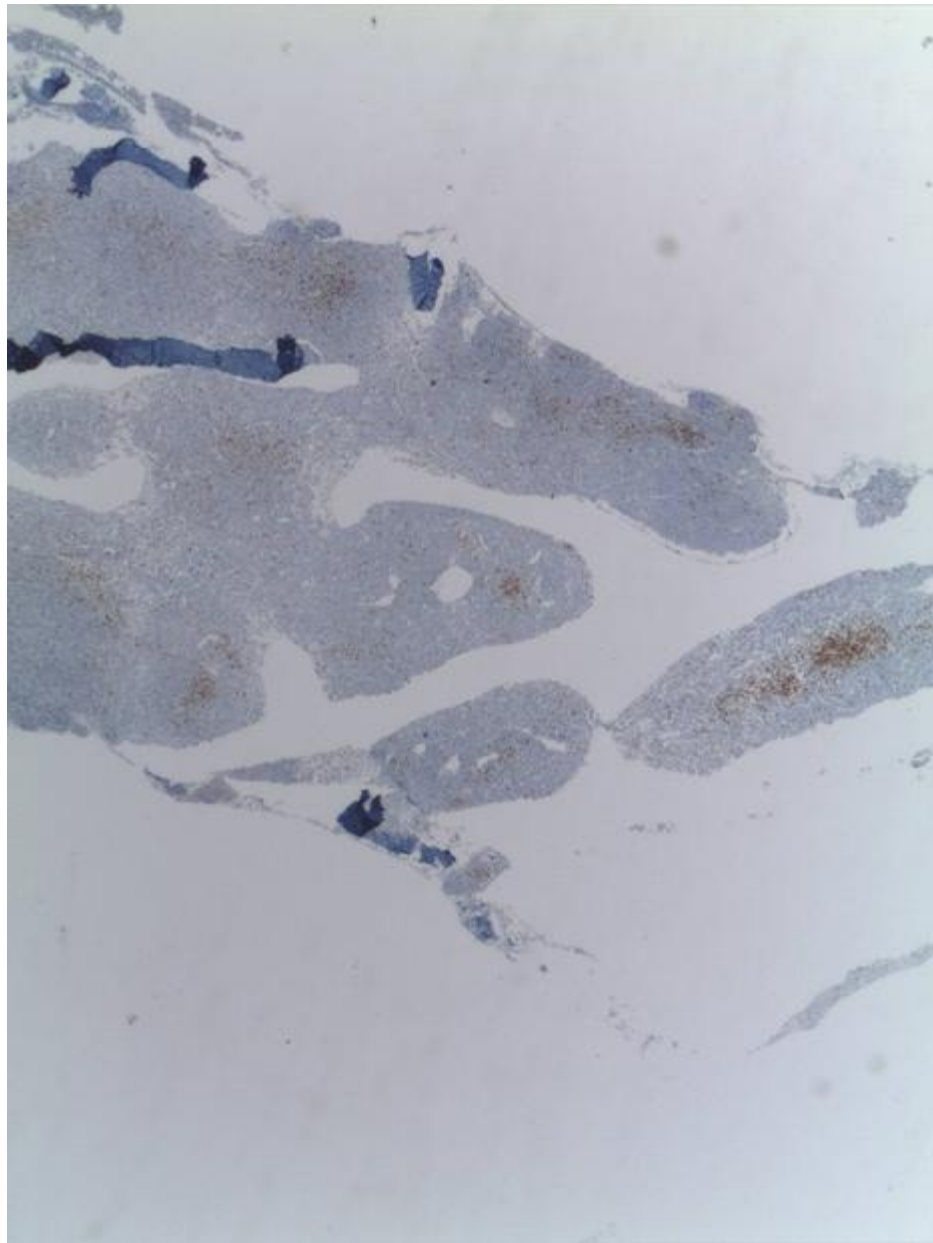
IgD

IgG





CD3



CD5

IHK:

Pozitif:

- CD20
- IgD
- IgG

Negatif:

- CD3
- CD5
- Kappa
- Lambda
- CD38
- CD23
- BCL-1
- BCL-6
- CD10
- Annexin A1
- TRAP

FLOW SİTOMETRİ:

CD 45	93	%
Pan Lökosit		
CD 14	0	%
Monosit		
HLA-DR	52	
CD 19	47	%
B Hücre		
CD 5	40	%
T Lenfosit		
CD 2	43	%
CD 10	0	%
CD 103	0,2	%
CD 11c	36	%
CD 25	19	%
CD 79b	48	%
CD 27	14	%
CD 38	3	%
CD 23	16	%
CD 20	46	%
FMC 7	1	%
CD 22	24	%
Kappa.	0	%
Lambda.	0	%

Çevre kan örneğindeki lökositlerin %61'i lenfosit, %9'u monosit, %30'u granülosittir. Lenfositlerin %53'ü B, %44'ü T, %3'ü NK hücredir. Örnekteki B hücrelerin ~ tümünde CD19+, HLA DR+, CD5-, CD23+/-, CD20+, CD10-, FMC7-, CD22+, CD79b+, kappa-, lambda-, CD25-, CD11c-, CD27-, CD49d+ izlenmektedir.

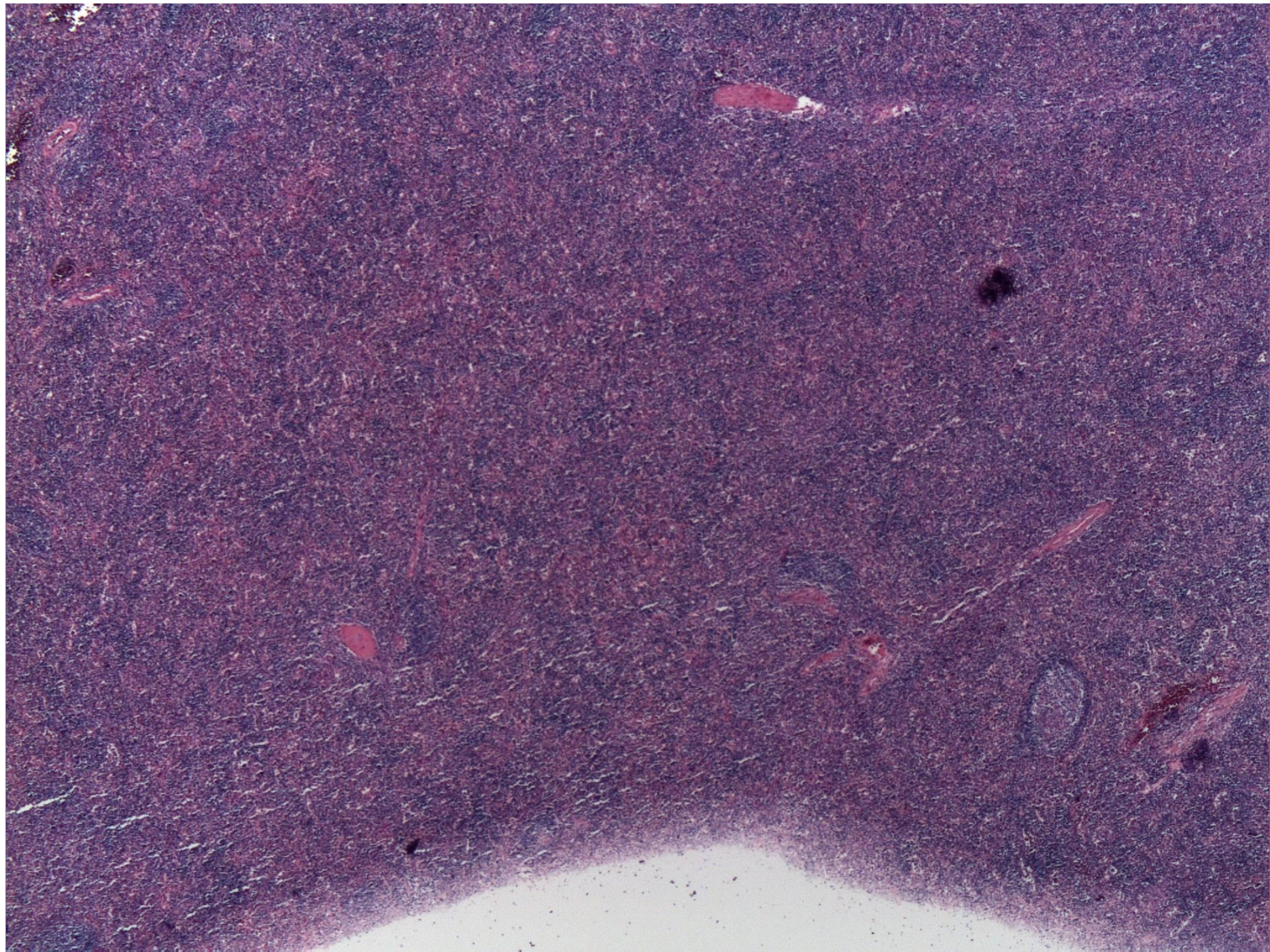
Sitogenetik inceleme ?

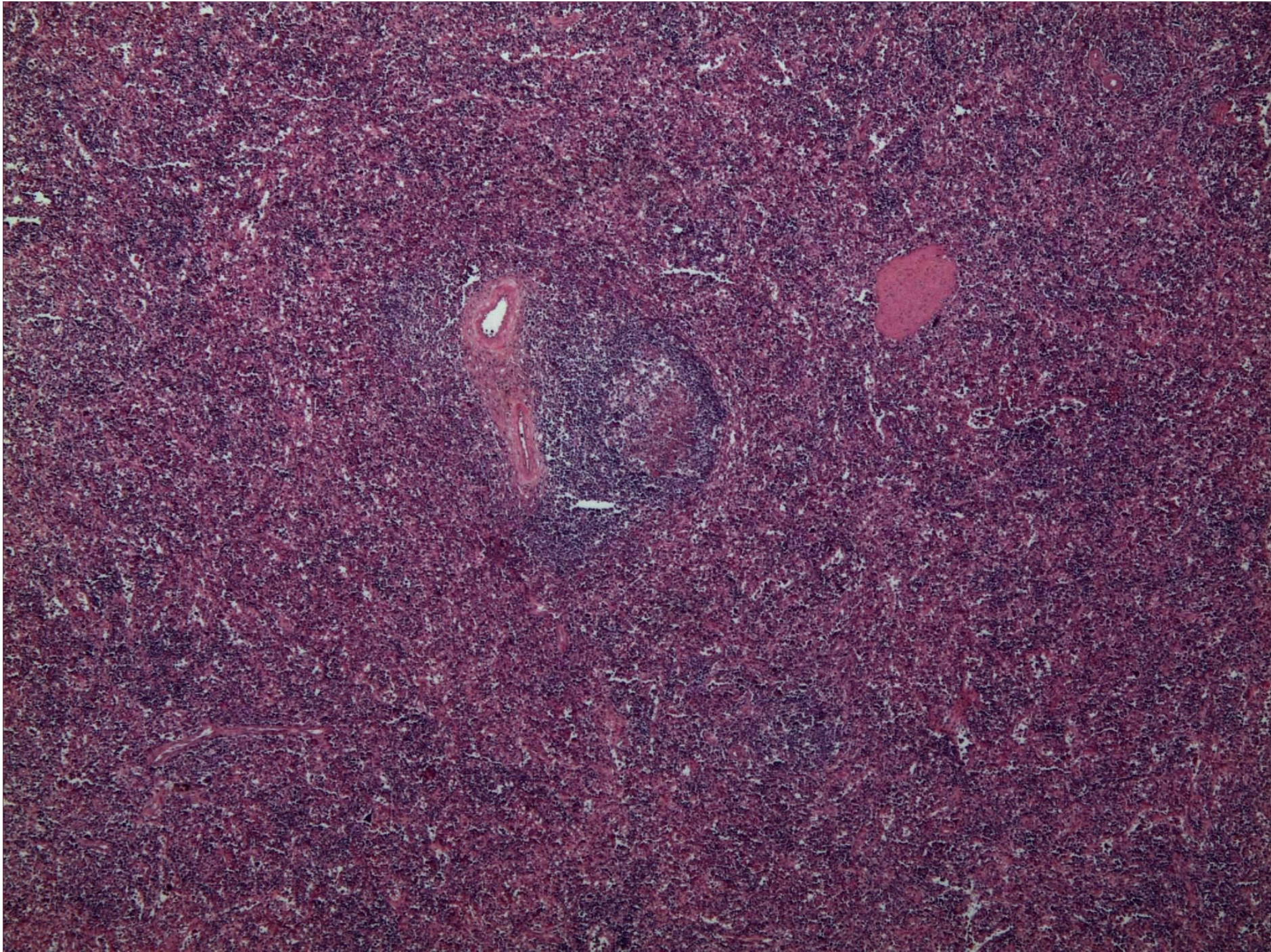
TANI:

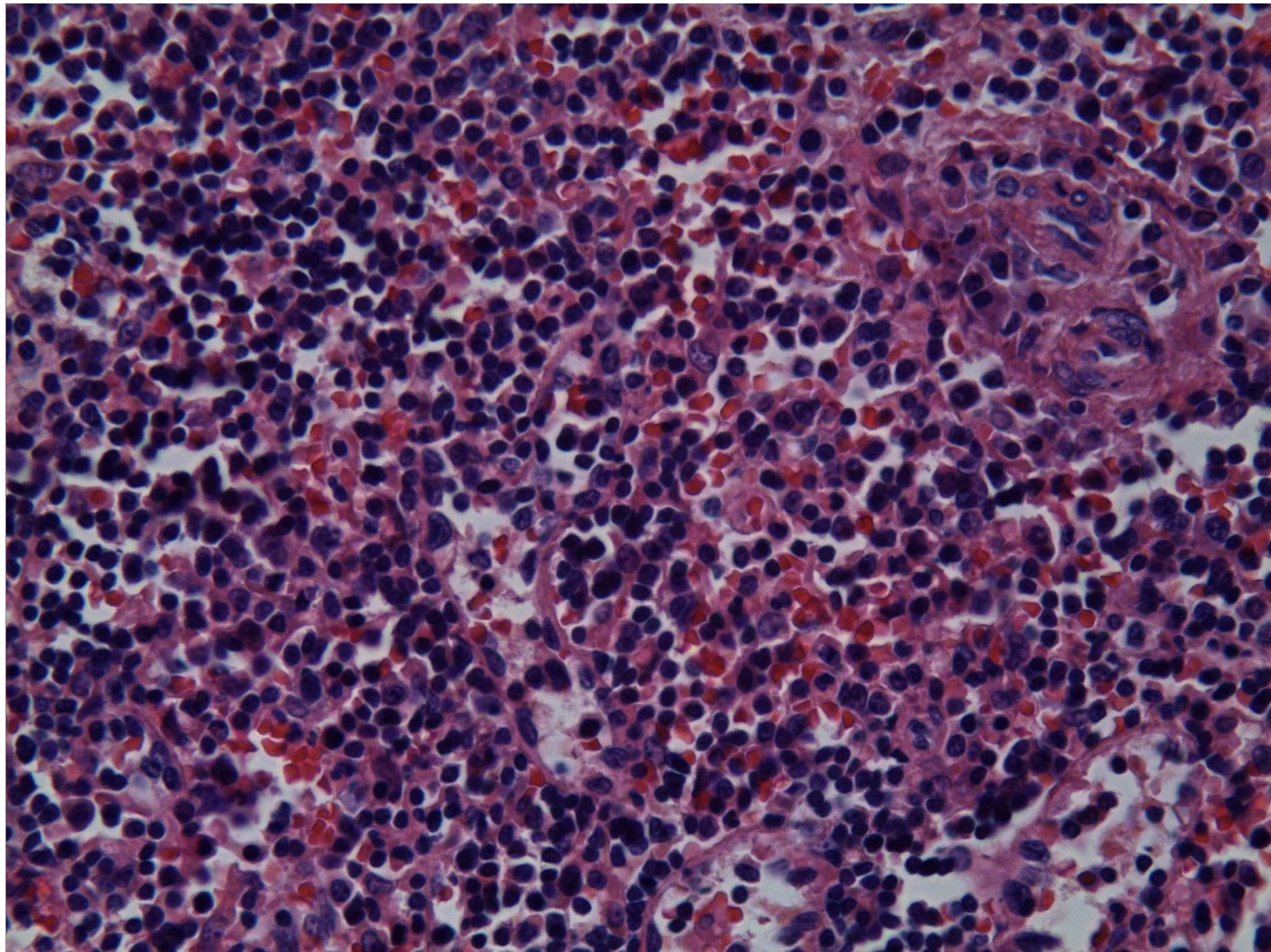
- Diffüz interstisyel B lenfoproliferatif hastalık infiltrasyonu gösteren hipersellüler kemik iliği biyopsisi
- Olgunun klinik olarak ön planda marjinal zon lenfoma açısından araştırılması önerilir

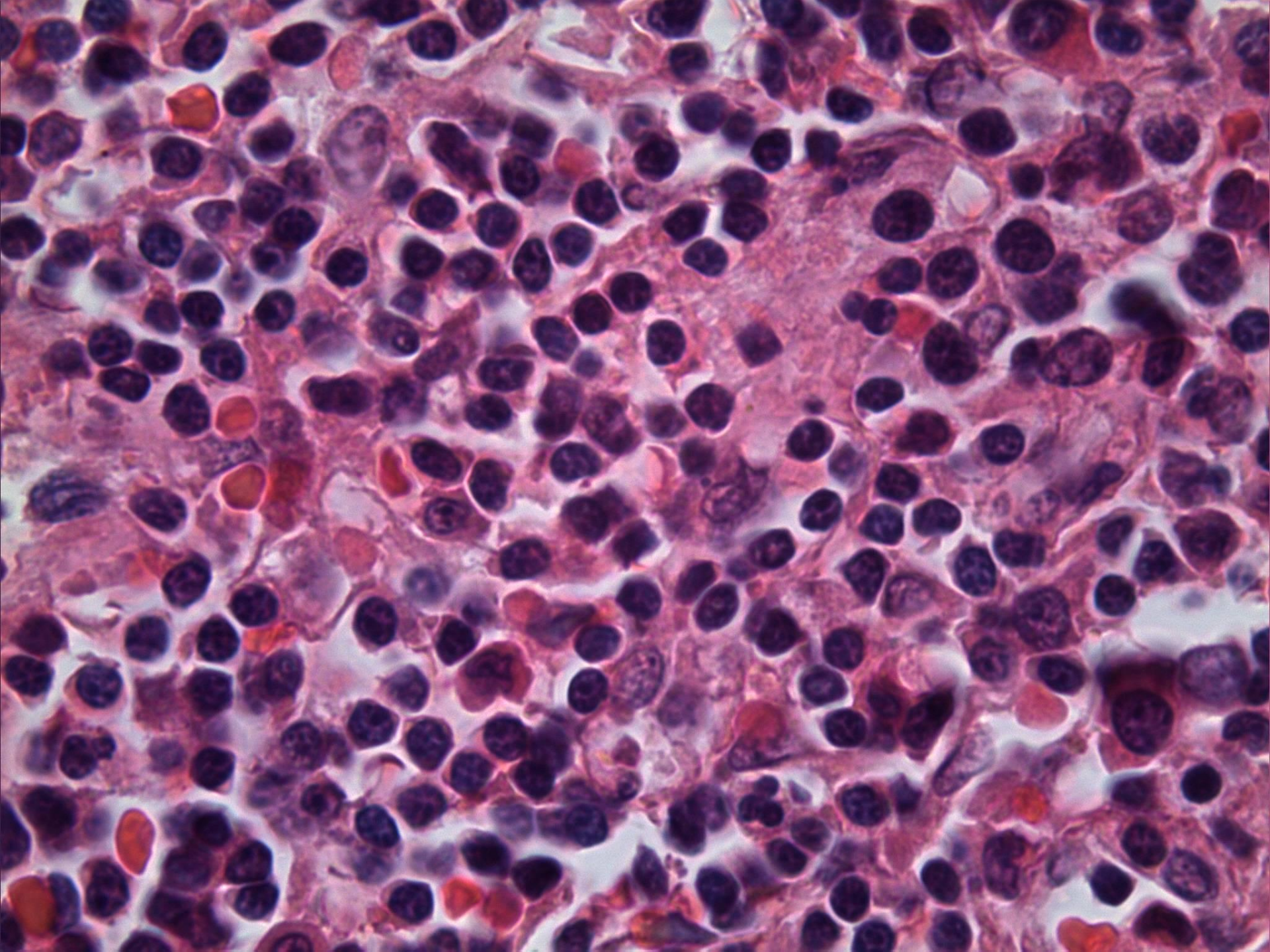
Tanıdan 3 ay sonra.....

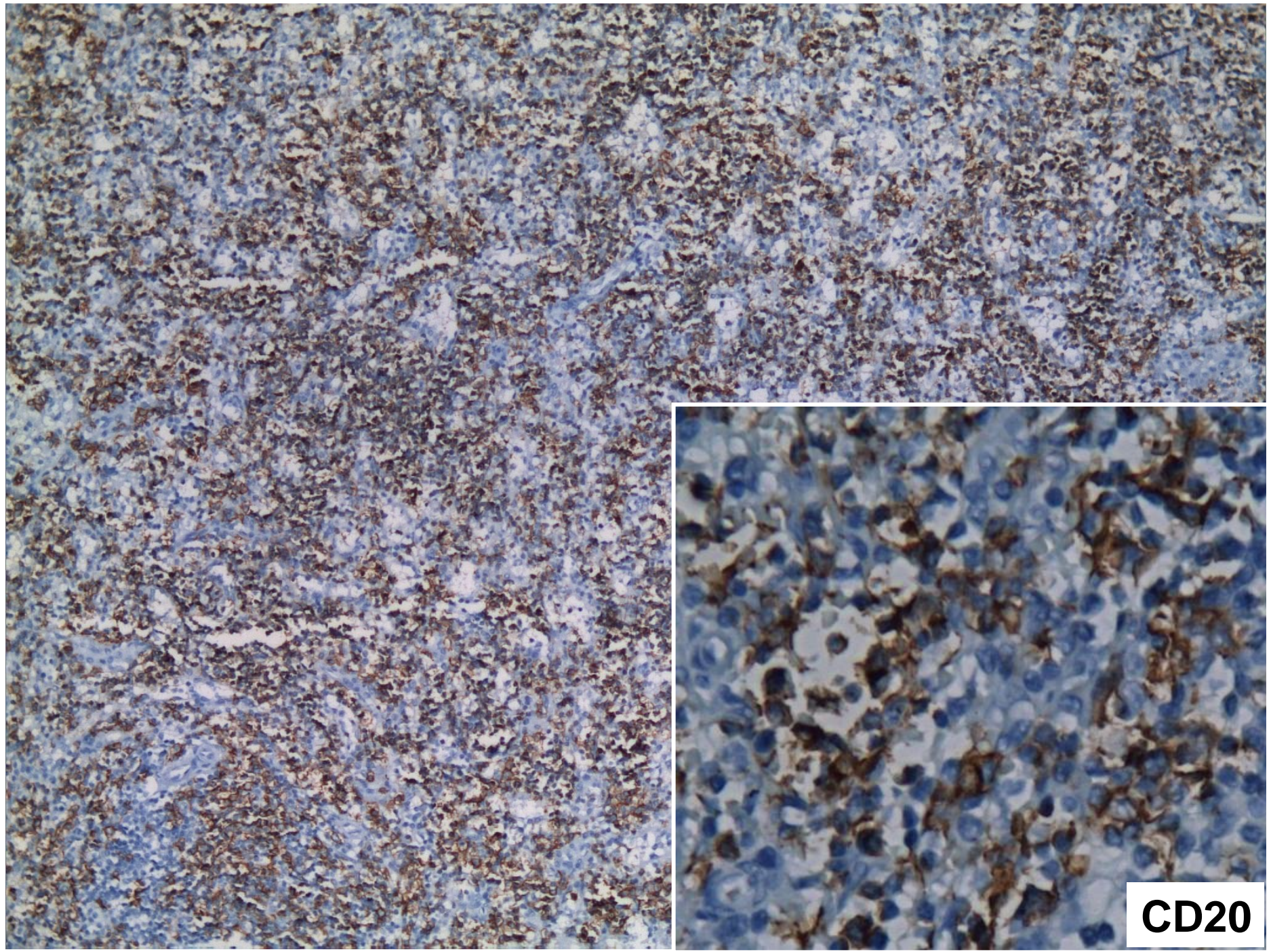
1050 gr ağırlığında, 25x20x7cm boyutlarında splenektomi materyali. Kesitlerde homojen kırmızı-kahverenkte ve kitlesel lezyon izlenmedi.











CD20

Splenektomi:

- Diffüz kırmızı pulpa infiltrasyonu gösteren küçük lenfoid hücreler

- IHK:

CD20+

IgD+

Annexin A1-

Kappa-

Lambda-

CD5-

CD10-

TRAP-

Bcl1-

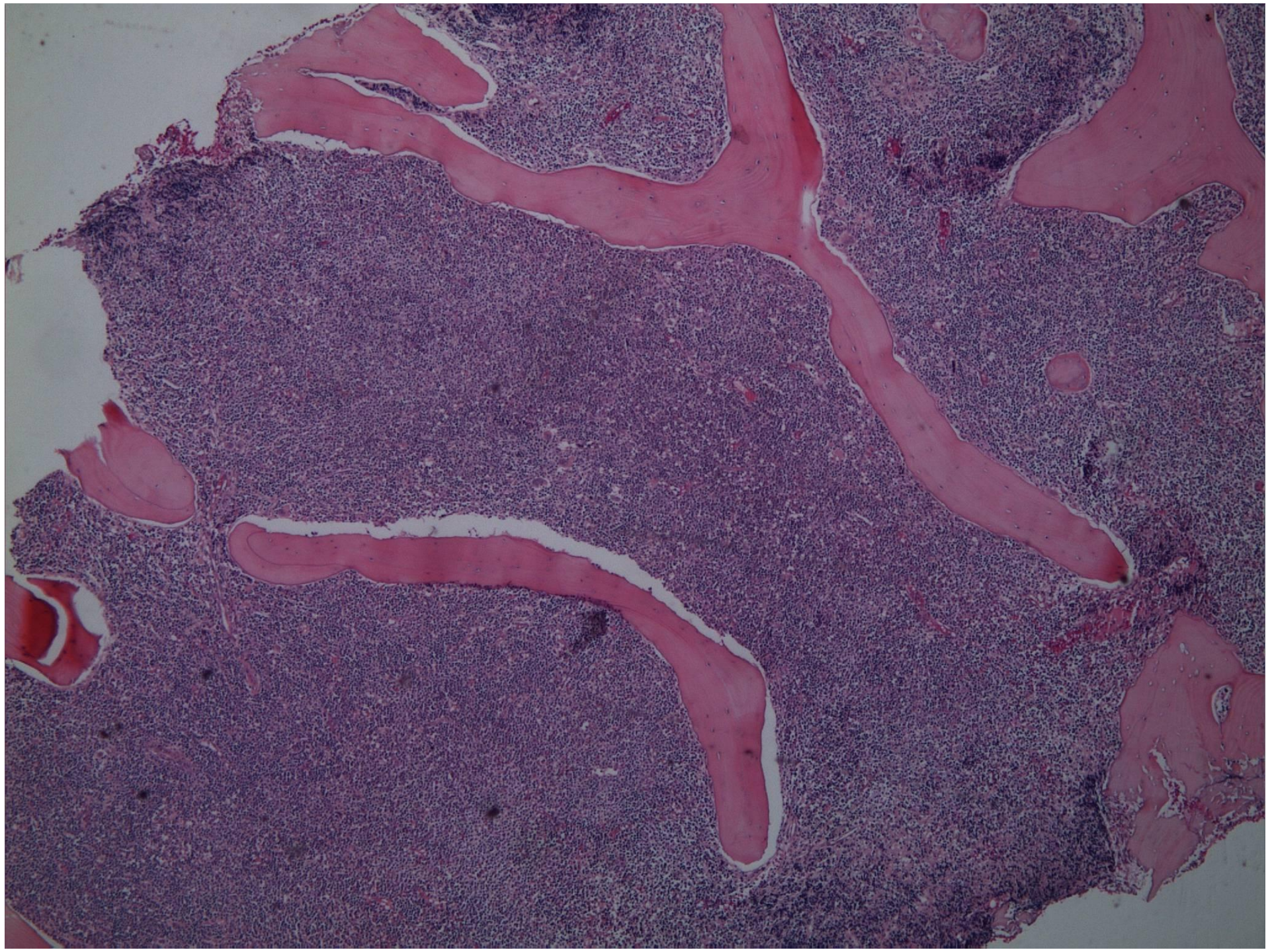
CD23-

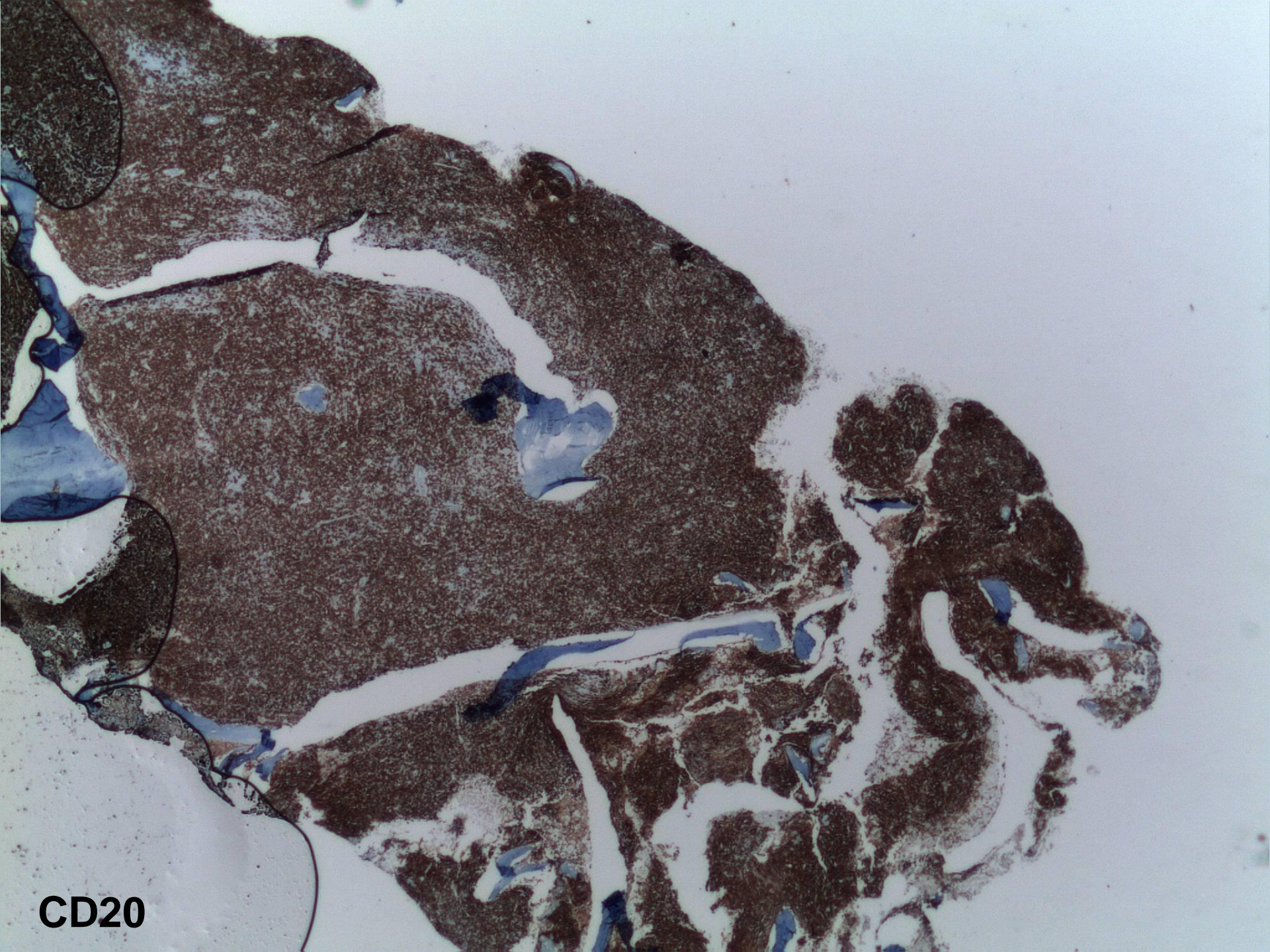
TANI:

- DİFFÜZ KIRMIZI PULPA İNFİLTRASYONU GÖSTEREN B LENFOPROLİFERATİF HASTALIK
- SINIFLANDIRILAMAYAN SPLENİK B HÜCRELİ LENFOMA/LÖSEMİ (KIRMIZI PULPANIN DİFFÜZ KÜÇÜK B HÜCRELİ LENFOMASI ?)

21 ay tedavisiz takip sonucu...

Sedimentasyon	* 58	mm/saat	0 - 20
Tam Kan Sayımı			
Lökosit (WBC)	* 15	x10 ⁹ /L	4,5 - 11
Eritrosit (RBC)	* 2,55	x10 ¹² /L	4,2 - 5,6
Trombosit (PLT)	* 71	x10 ⁹ /L	150 - 400
Hemoglobin (Hb)	* 8,9	g/dL	13,1 - 17,2
Hematokrit	* 27,7	%	39 - 50
Ortalama Eritrosit Hacmi (MCV)	* 108,6	fL	81 - 103
Ortalama Eritrosit Hemoglobini (MCH)	34,9	pg/cell	27 - 35
Ortalama Eritrosit Hemoglobin Kons.(MCHC)	32,1	gHb/dLErCS	32 - 36
Eritrosit Dağılım Genişliği (RDW)	* 23,5	%	11,5 - 14,5
Nötrofil %	40,5	%	40 - 70
Lenfosit %	* 46,9	%	30 - 36
Monosit %	* 12,6	%	0 - 7
Eozinofil %	0	%	0 - 6
Bazofil %	0	%	0 - 1
Nötrofil Sayısı	6,1	x10 ⁹ /L	1,8 - 7,7
Lenfosit Sayısı	* 7,1	x10 ⁹ /L	1,5 - 4
Monosit Sayısı	* 1,9	x10 ⁹ /L	0,2 - 0,95
Eozinofil Sayısı	0	x10 ⁹ /L	0 - 0,7





CD20

Splenomegali ve kemik iliđi tutulumu ile karakterli matür B hücreli lenfomalar:

Splenomegali ve kemik iliđi tutulumu ile karakterli matür B hücreli lenfomalar:

- SMZL
- KLL/SLL
- B-PLL
- HCL
- LPL
- MCL
- Sınıflandırılmayan splenik B hücreli lenfoma/lösemi kategorisi (splenic diffuse red pulp small B-cell lymphoma, HCL-v)

Table 1
Differential diagnosis of small B-cell lymphomas: morphology

Disease	Lymph Node	Spleen	Bone Marrow	Cytology
B-cell small lymphocytic/CLL	Diffuse pattern, proliferation centers	Red pulp; cords, sinuses; white pulp	Intertrabecular nodules, interstitial; not paratrabecular	Small lymphocytes, prolymphocytes & paraimmunoblasts
Mantle cell	Diffuse or nodular	White pulp; atrophic germinal centers, obliterated marginal zones	Intertrabecular nodules, paratrabecular aggregates	Small lymphocytes with nuclear irregularity; No large cells
MALT lymphoma	Paracortical infiltrates; surrounding germinal centers	White pulp marginal zones	Intertrabecular nodules, paratrabecular; intrasinusoidal	Centrocyte-like cells, plasma cells, large transformed lymphocytes; non-neoplastic germinal centers
Splenic marginal zone lymphoma	Surrounds primary and secondary follicles, interfollicular	White pulp expanded with neoplastic cells spilling into red pulp	Intertrabecular nodules, paratrabecular; intrasinusoidal	Medium-size cells; irregular nuclei, abundant pale cytoplasm; occasional large transformed cells
Nodal marginal zone lymphoma	Perisinusoidal or surrounding benign germinal centers and mantle zones	White pulp; small germinal centers, residual non-neoplastic mantle cells	Intertrabecular nodules, paratrabecular; intrasinusoidal	Medium-size cells; irregular nuclei, abundant pale cytoplasm; occasional large transformed cells
Follicular lymphoma	True follicular nodularity	White pulp; neoplastic germinal centers, benign mantle and marginal zones	Intertrabecular nodules, paratrabecular	Small centrocytes and large centroblasts in varying proportions
Lymphoplasmacytic lymphoma	Paracortical and hilar infiltrates, open sinuses	Red pulp and occasionally white pulp	Intertrabecular nodules, paratrabecular, interstitial	Small lymphocyte-plasma cell spectrum; varying large cells

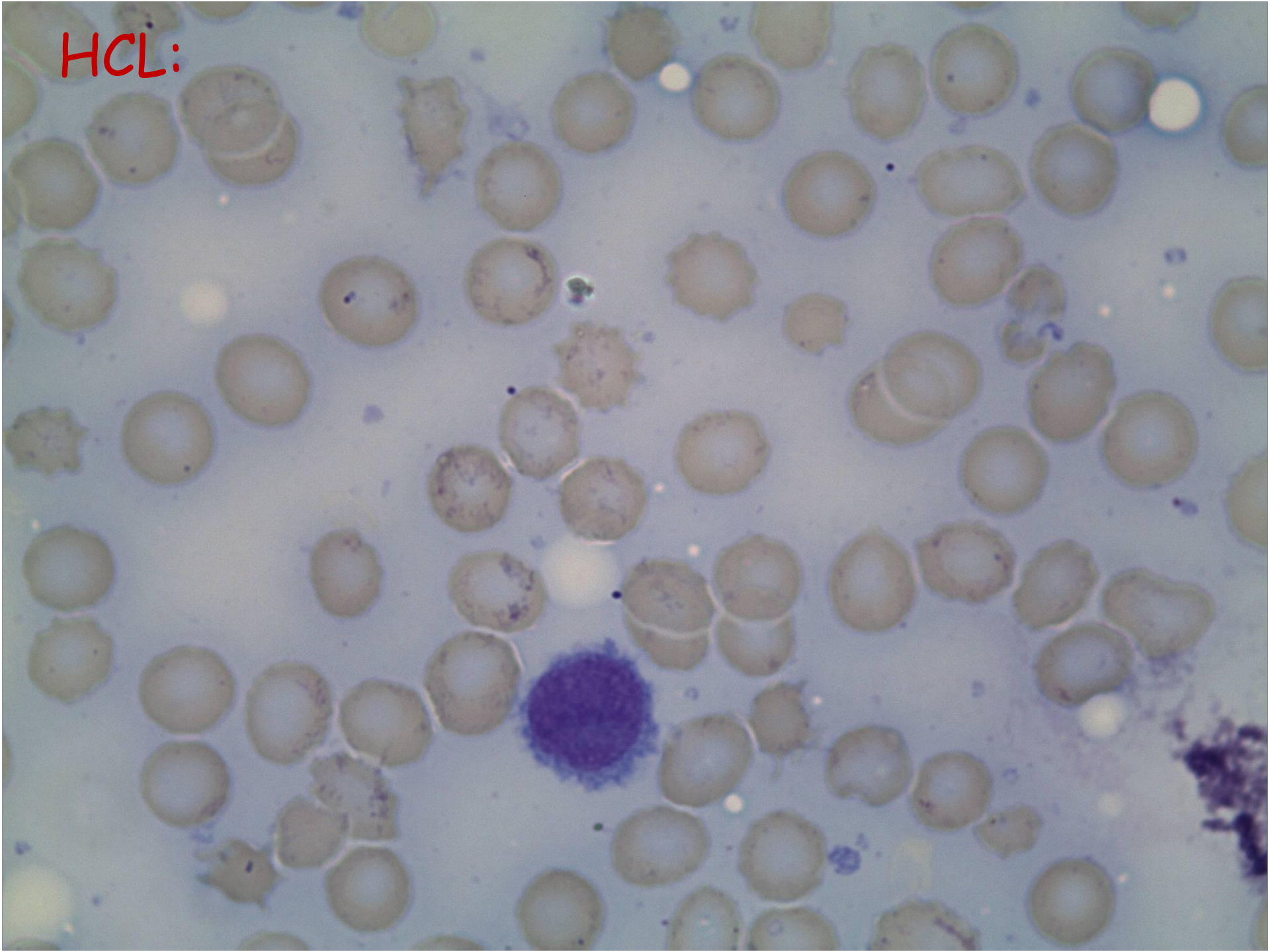
Dalakta kırmızı pulpa ve kemik iliği tutulumu ile karakterli B hücreli lenfoproliferatif hastalıklar:

- HCL
- Sınıflandırılmayan splenik B hücreli lenfoma/lösemi kategorisi
 - HCL-v
 - SDRPSBCL (splenic diffuse red pulp small B-cell lymphoma)

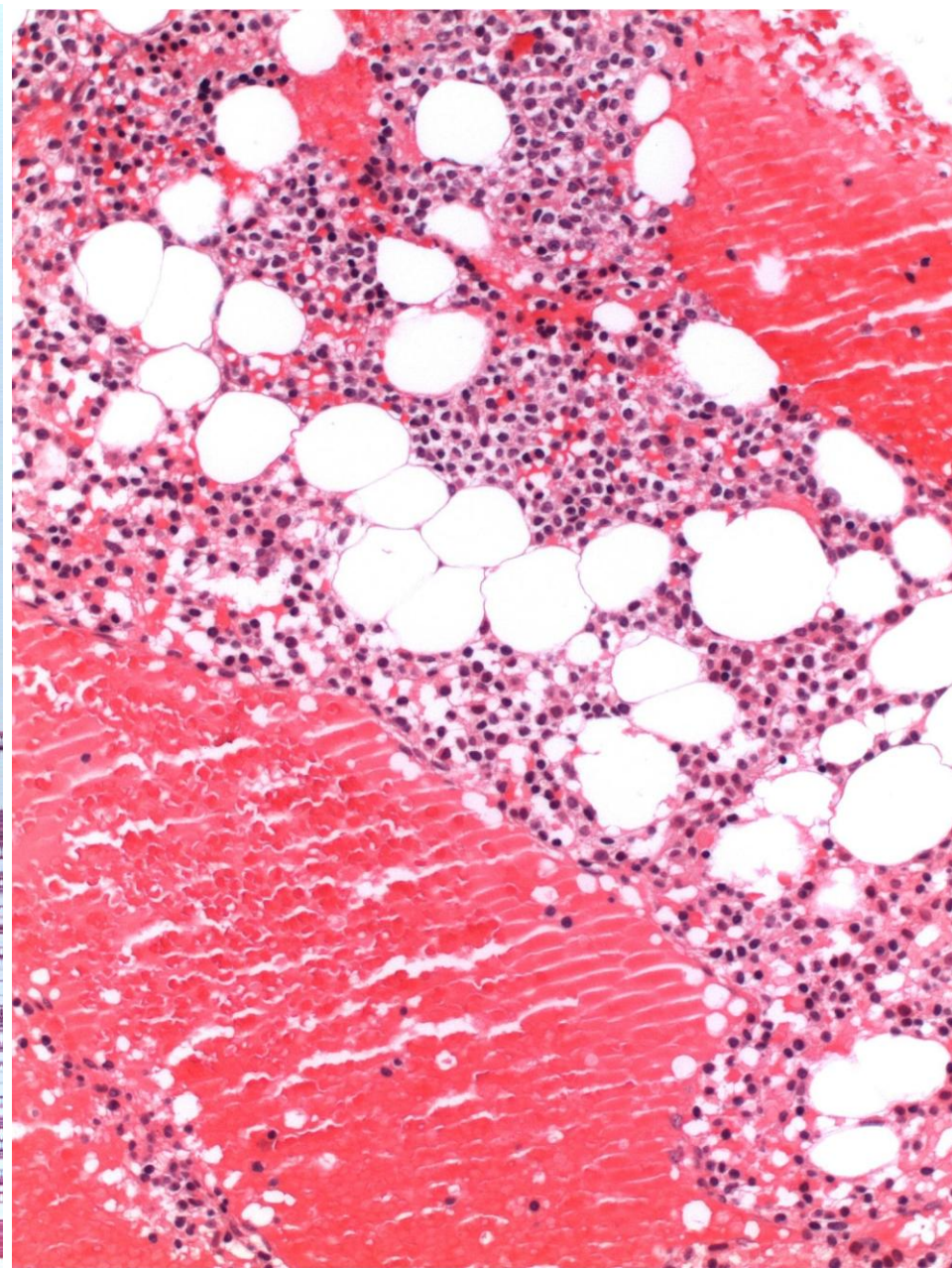
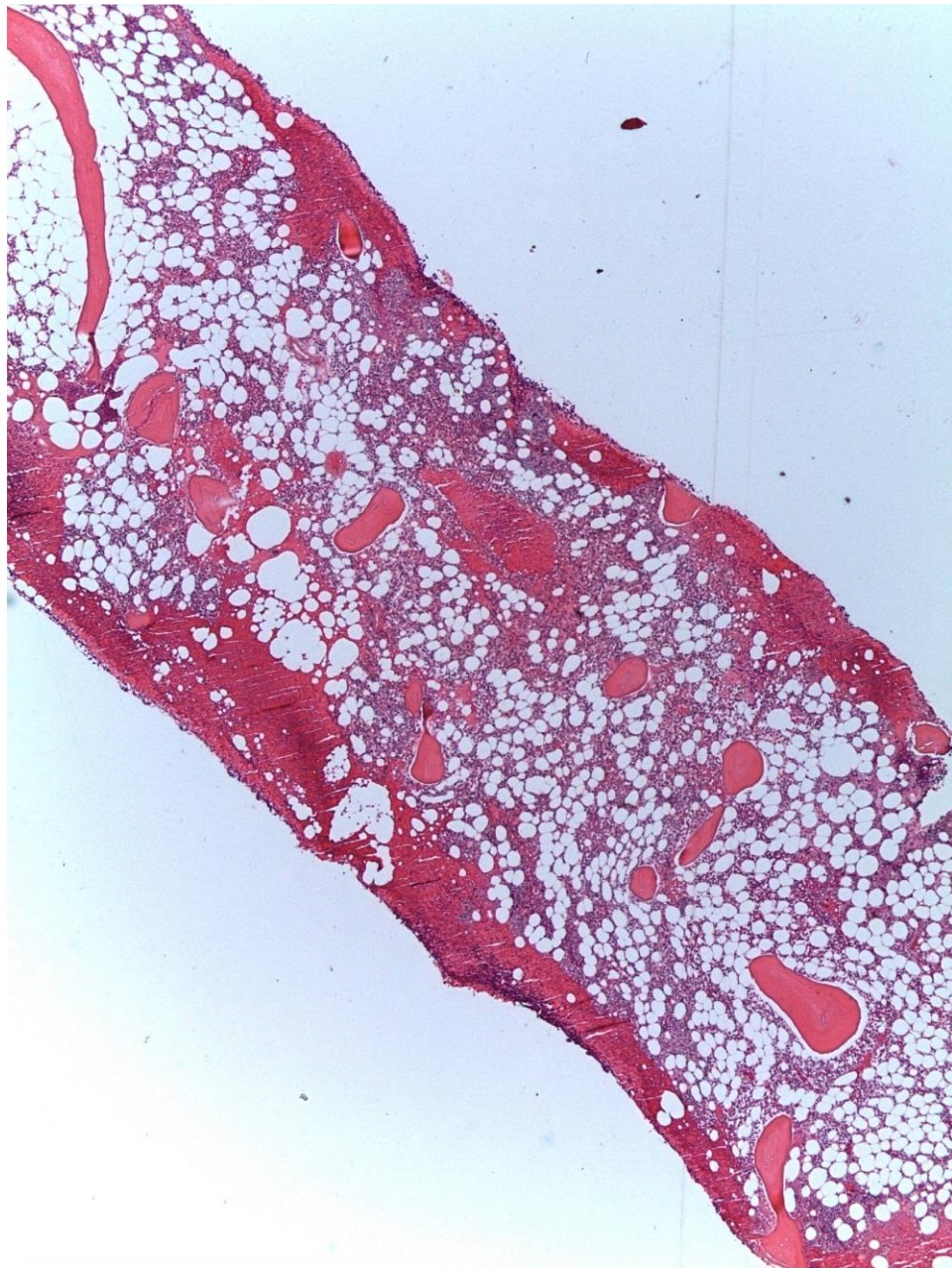
HCL:

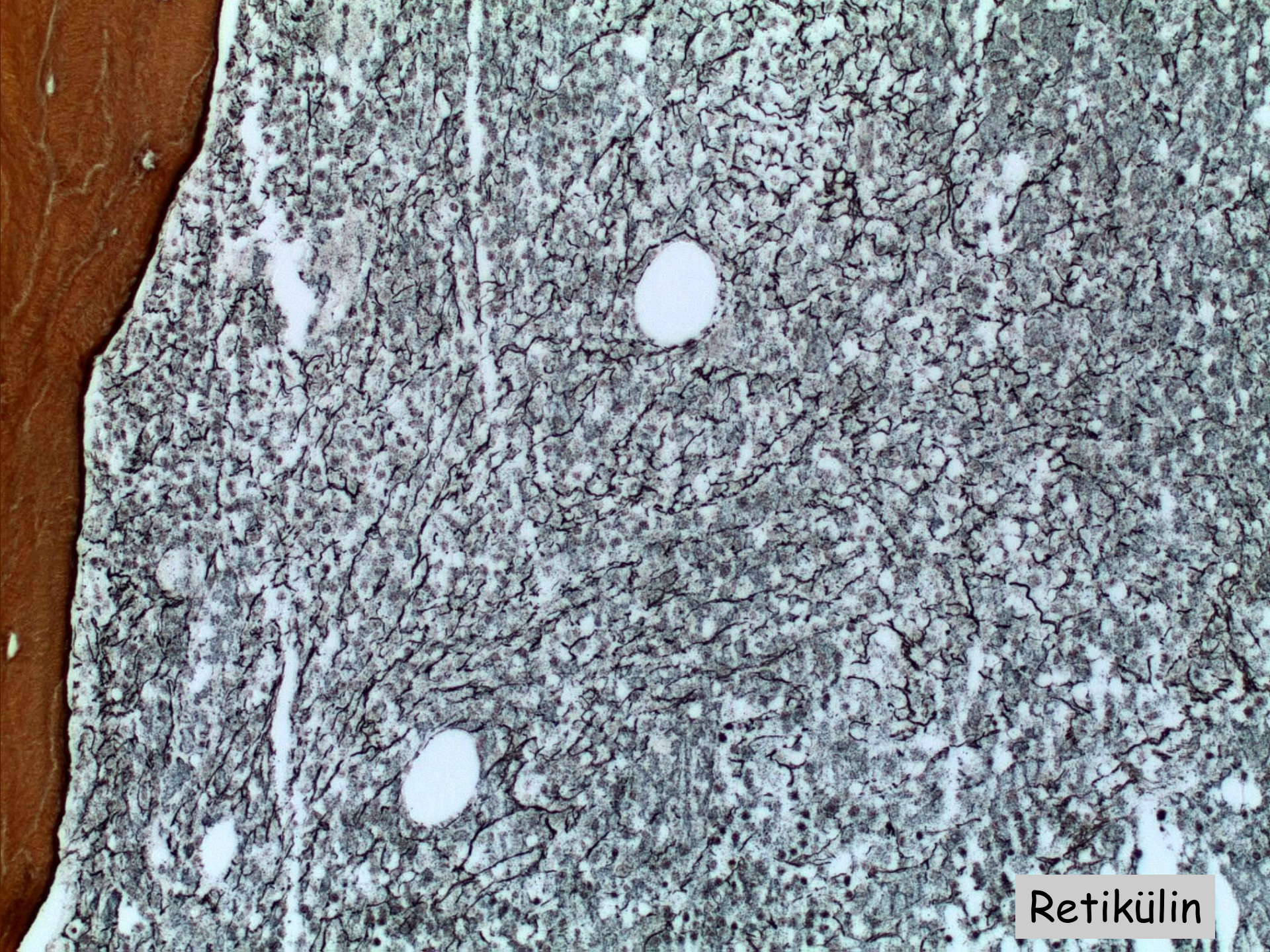
- Lenfoid lösemilerin %2'ni oluşturan nadir bir hastalık
- 50 yaş ve üstü
- Pansitopeni, splenomegali ve kanda az oranda sirküle eden neoplastik lenfositler

HCL:

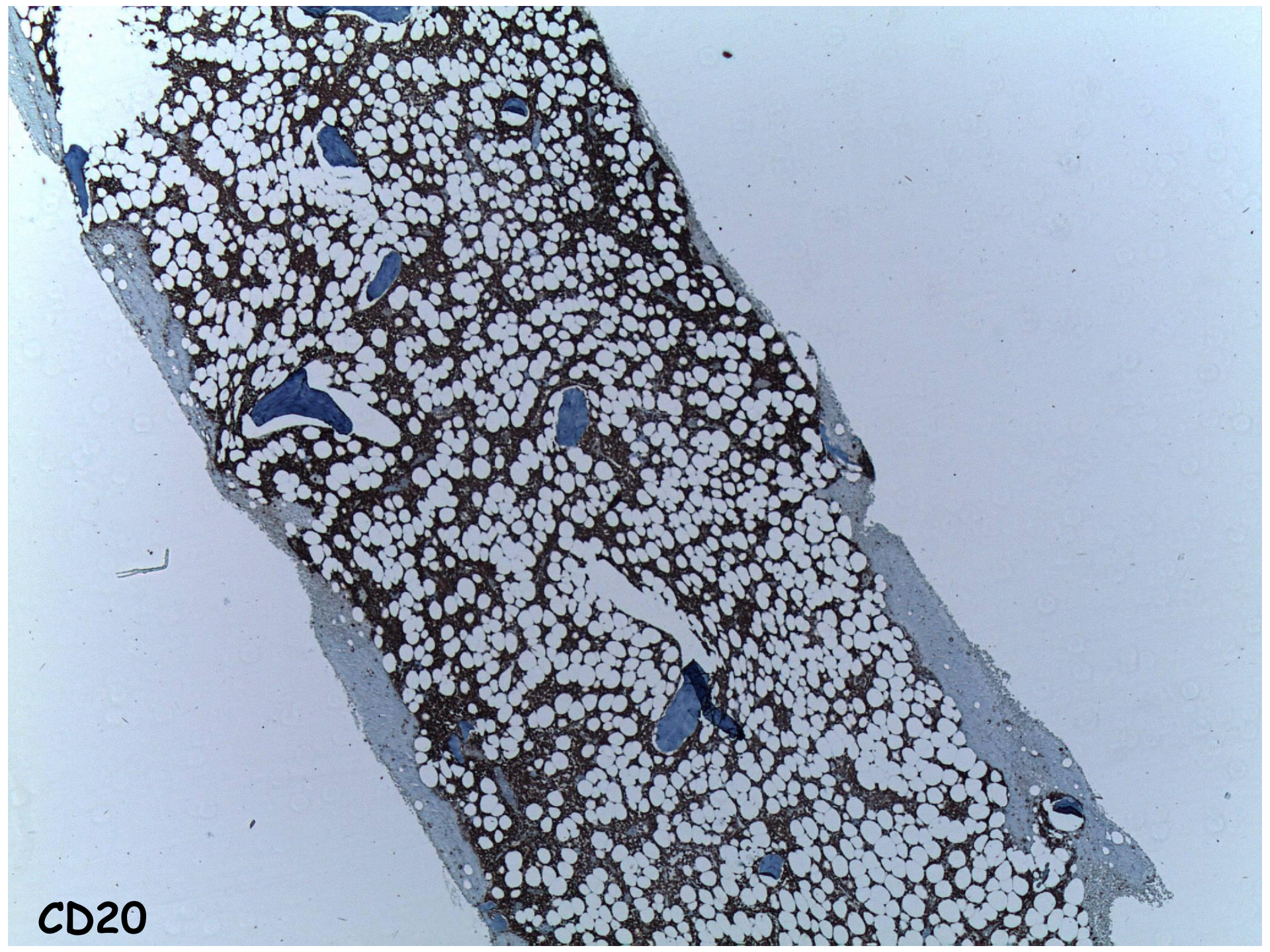


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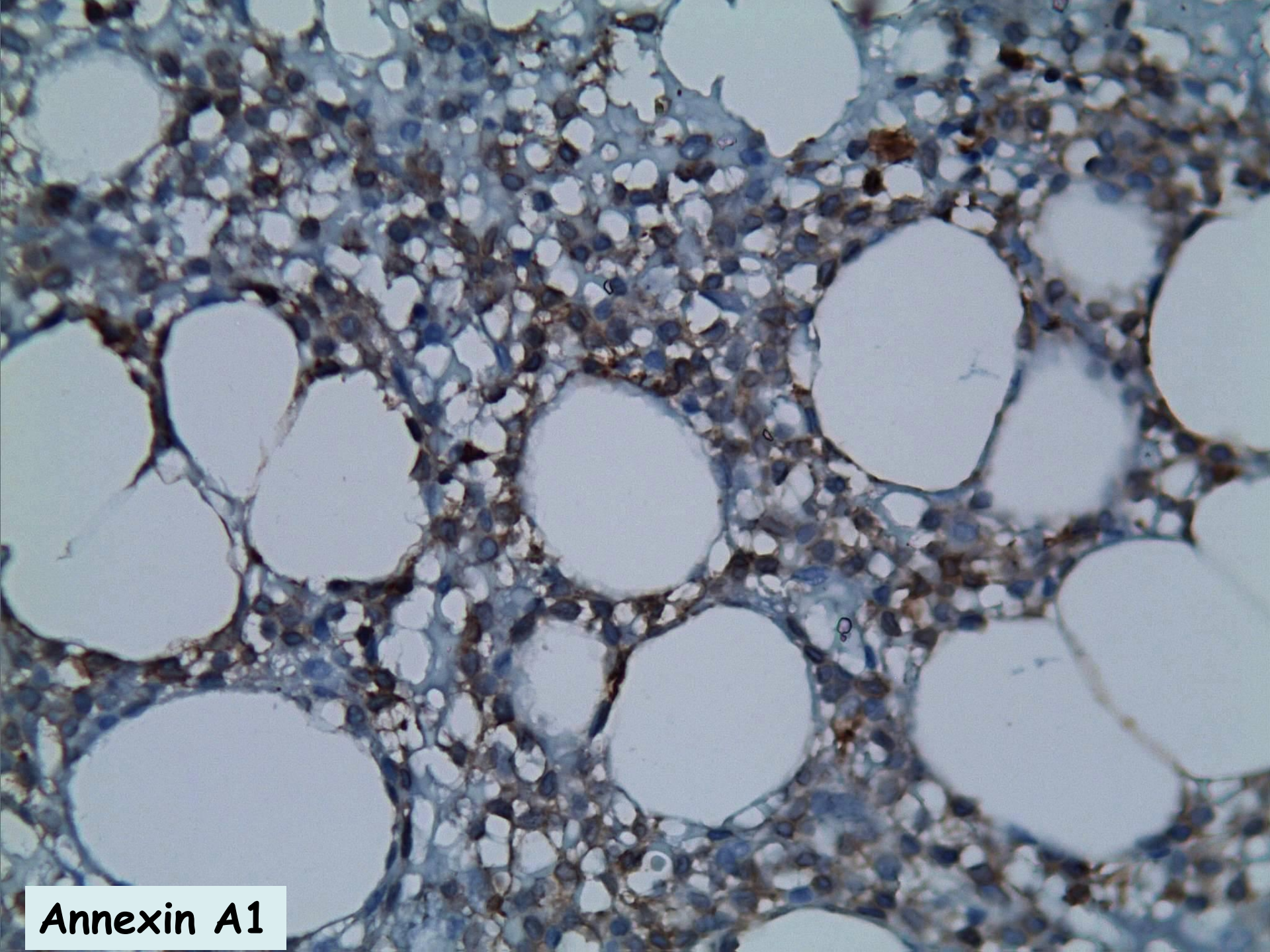




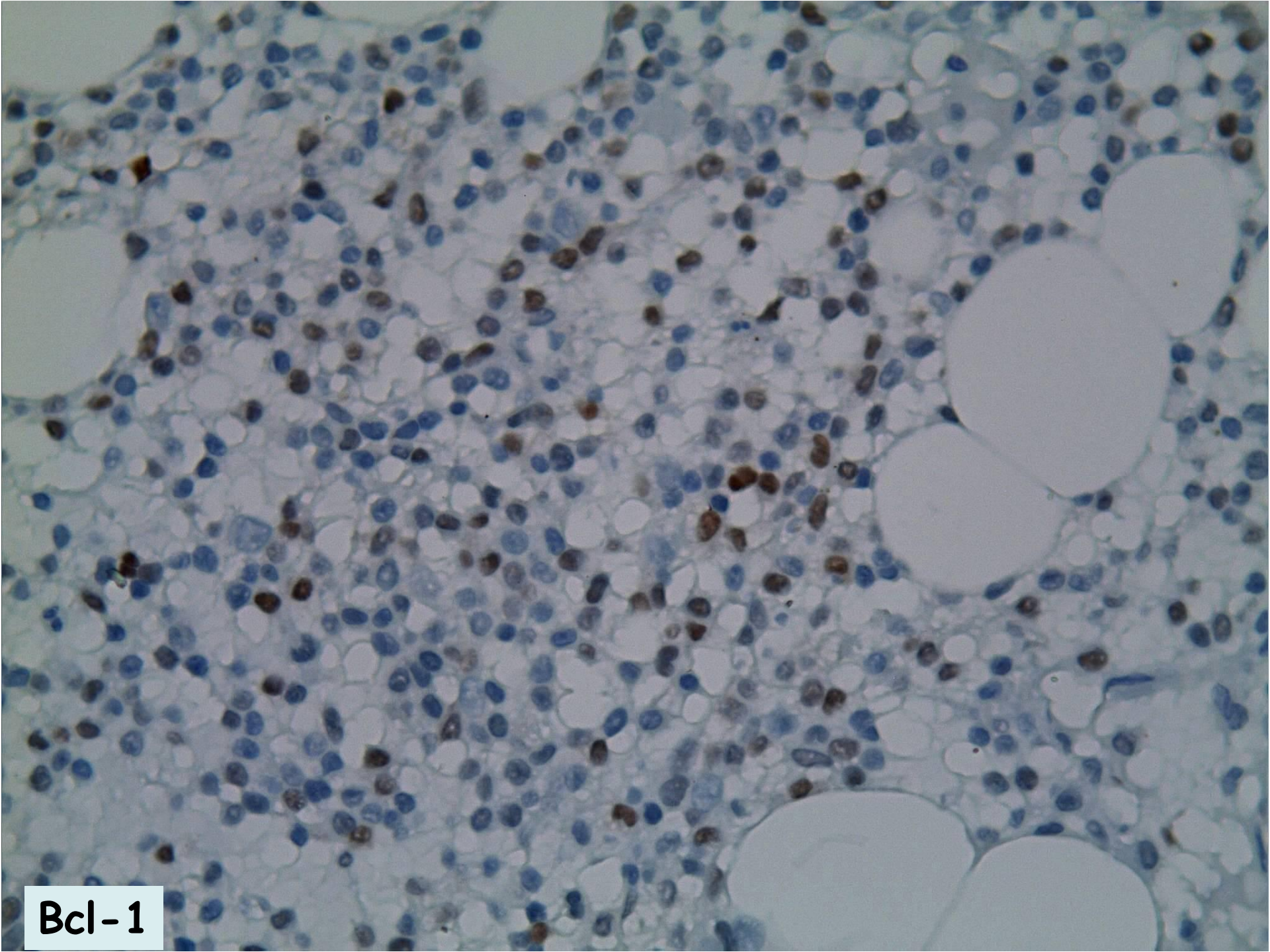
Retikülin



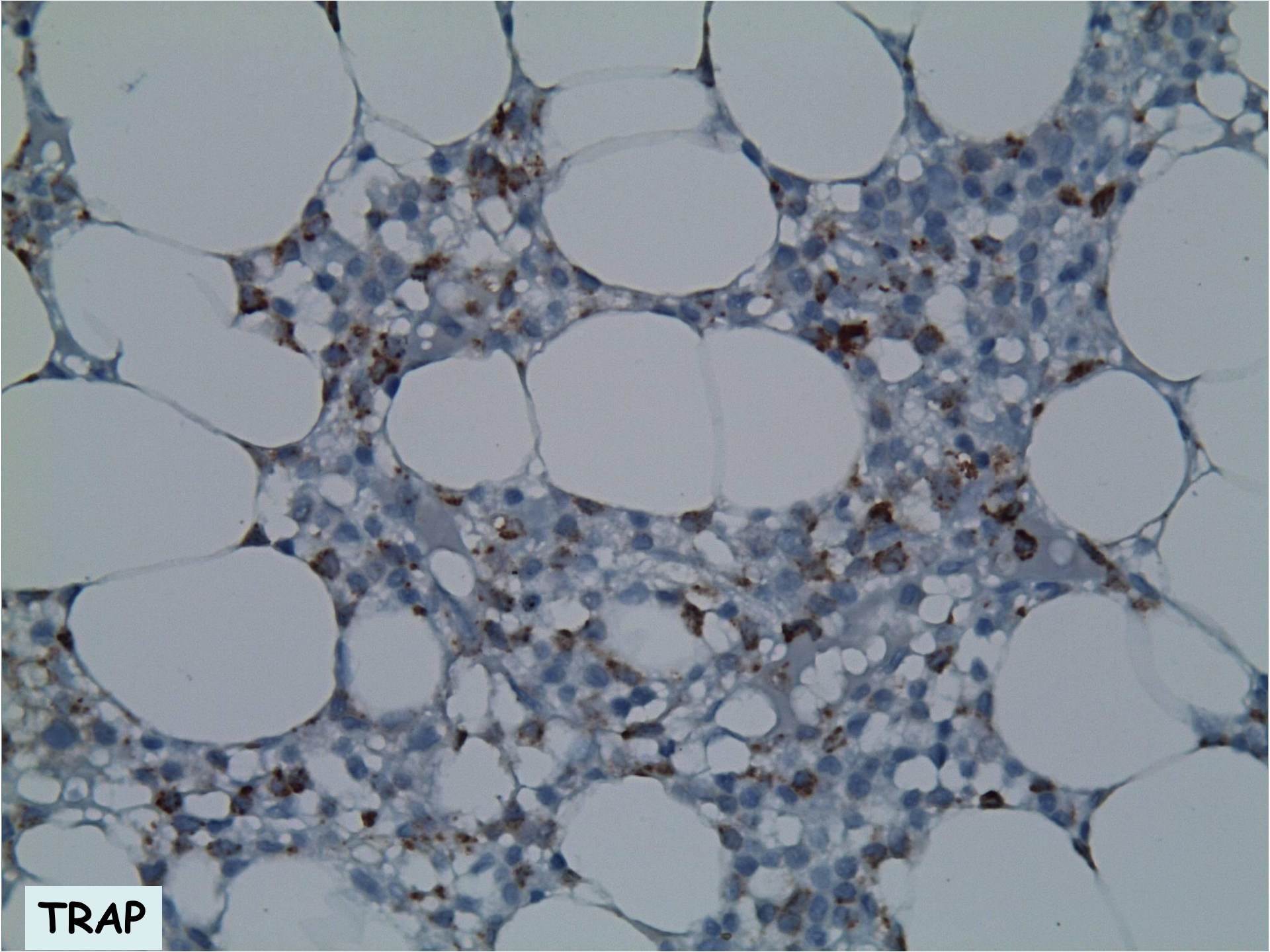
CD20



Annexin A1

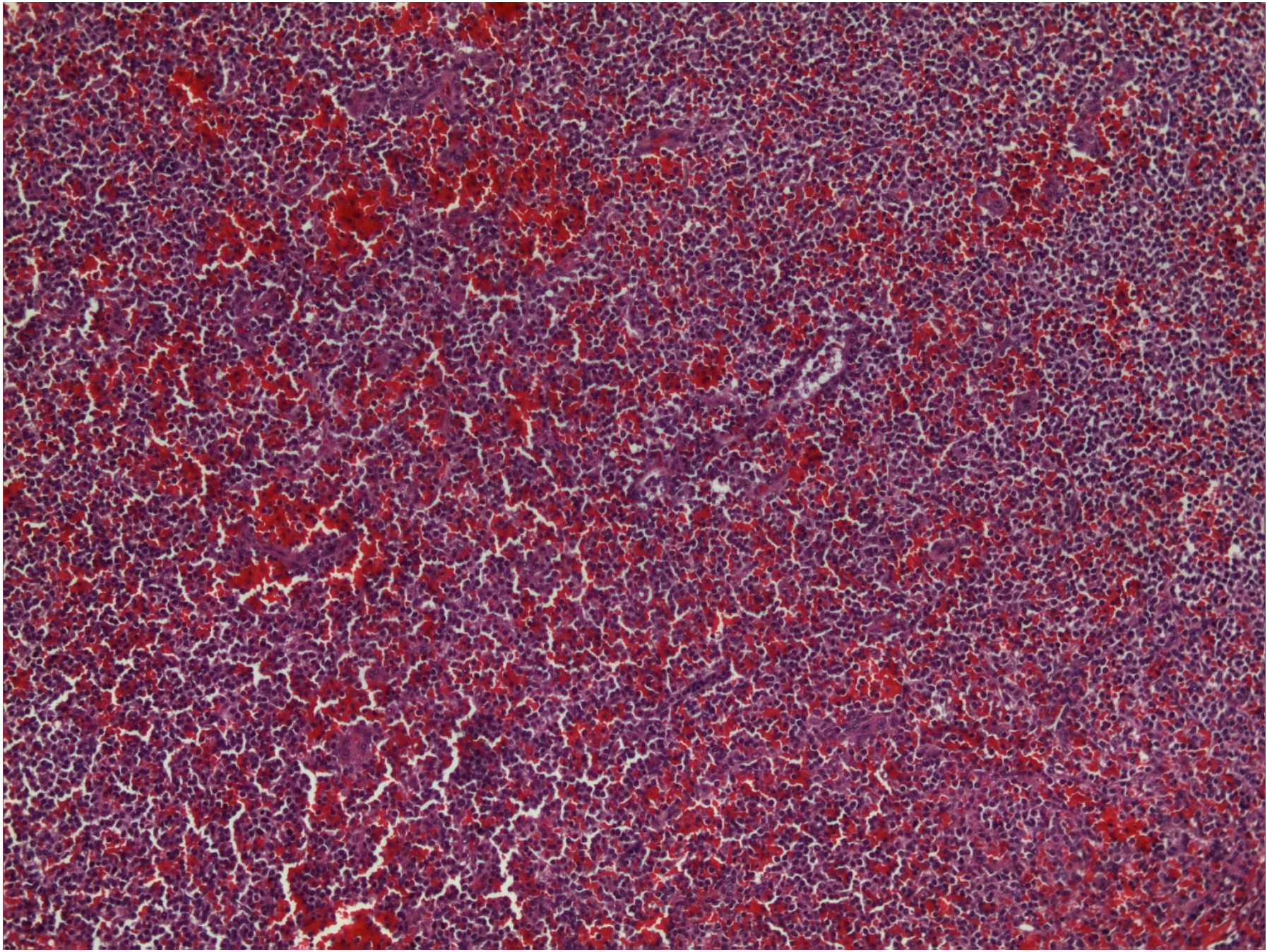


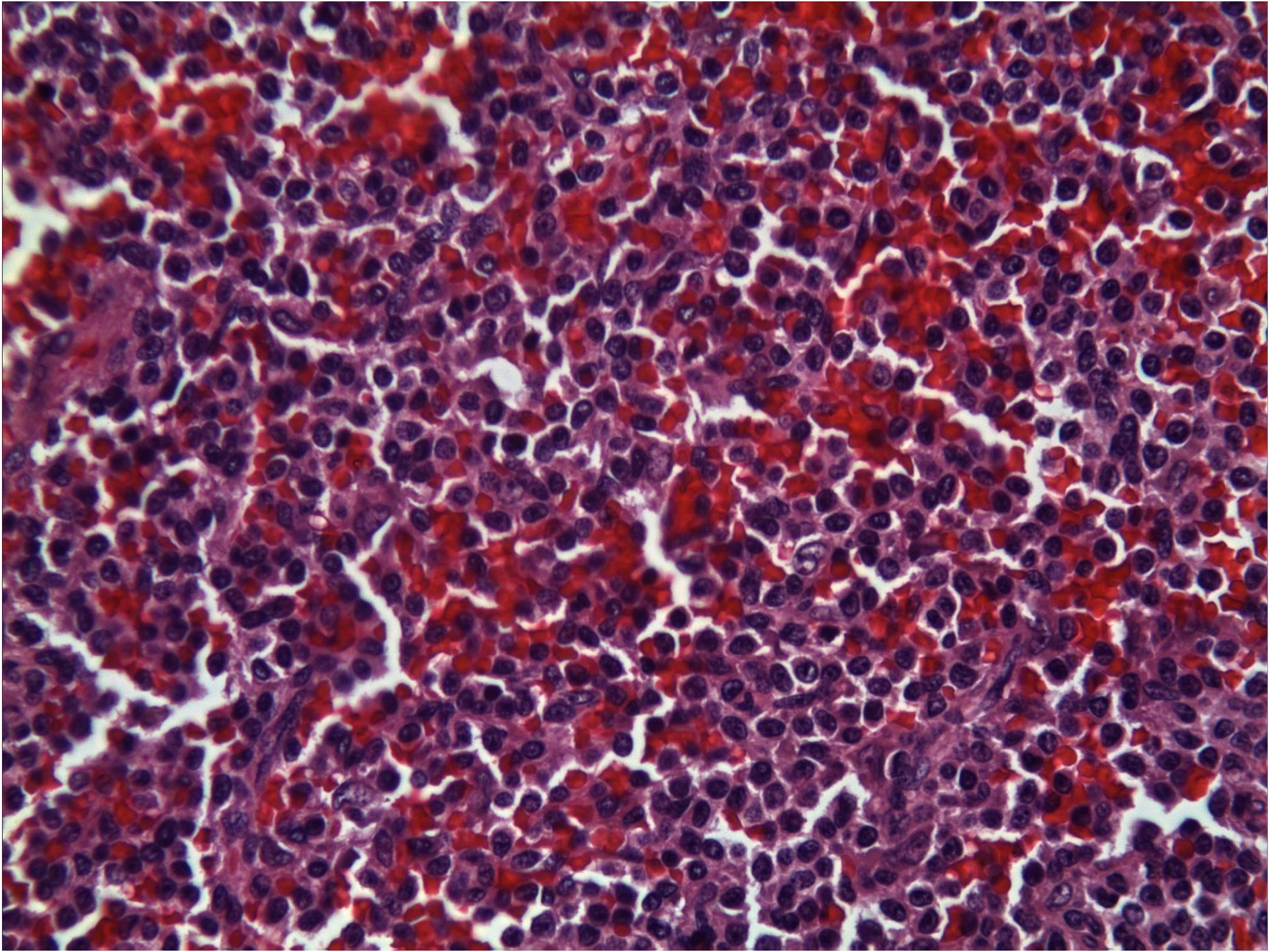
Bcl-1

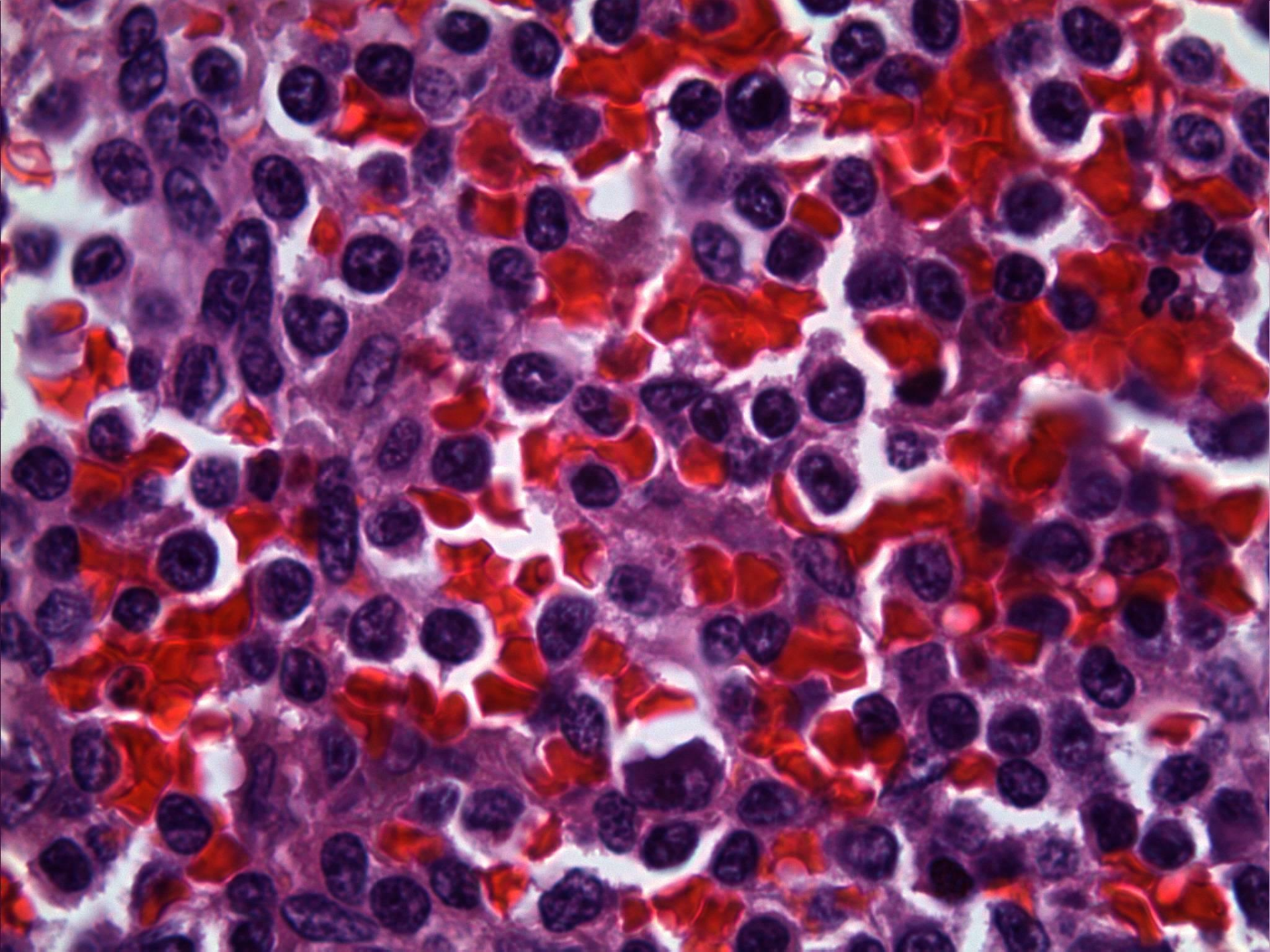


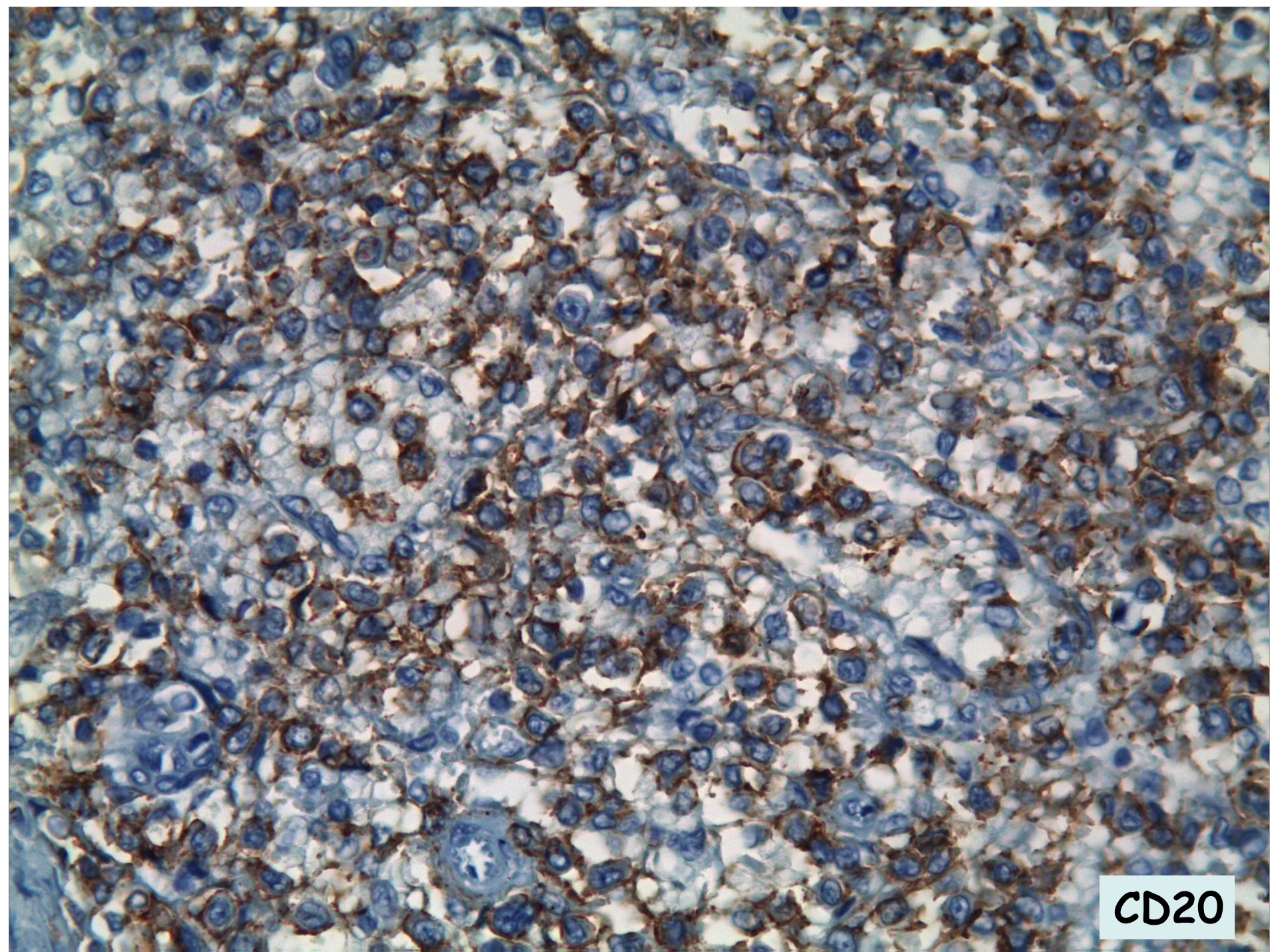
TRAP

HCL









CD20

HCL:

- **IHK:**

CD20, DBA44, annexin A1, T-bet, CD25, TRAP, soluk
bcl1 pozitif (CD5, CD10, CD23 -)

- **Flow sitometri:**

Yüzey immunoglobulin, CD20, CD22, CD11c, CD103,
CD25, CD123 pozitif

Dalakta kırmızı pulpa ve kemik iliği tutulumu ile karakterli B hücreli lenfoproliferatif hastalıklar:

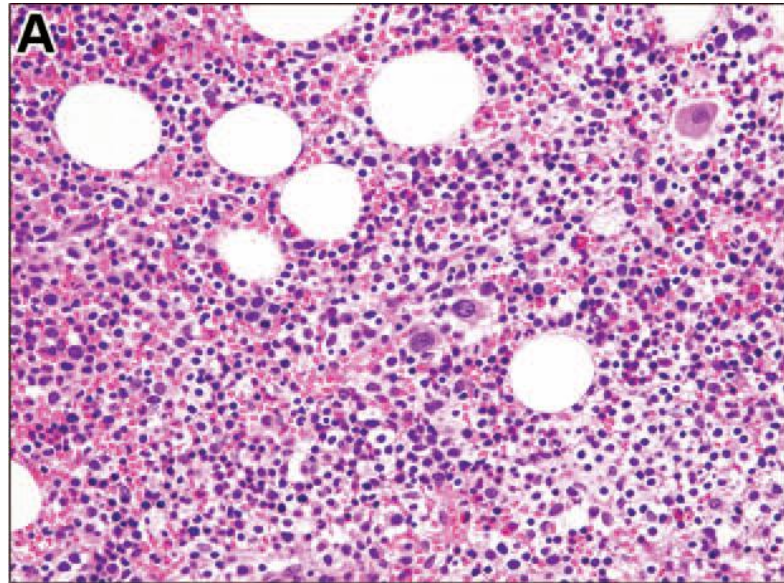
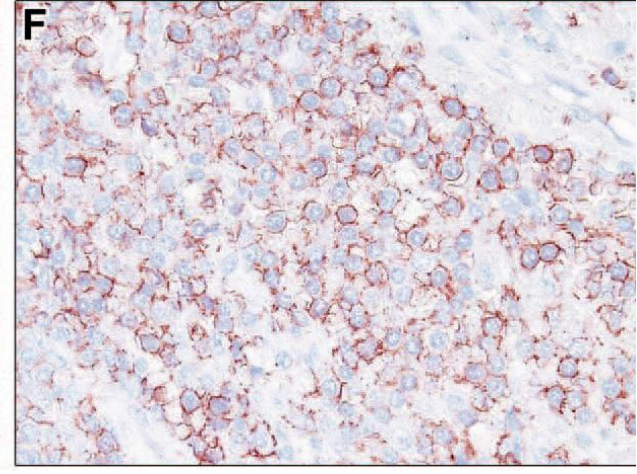
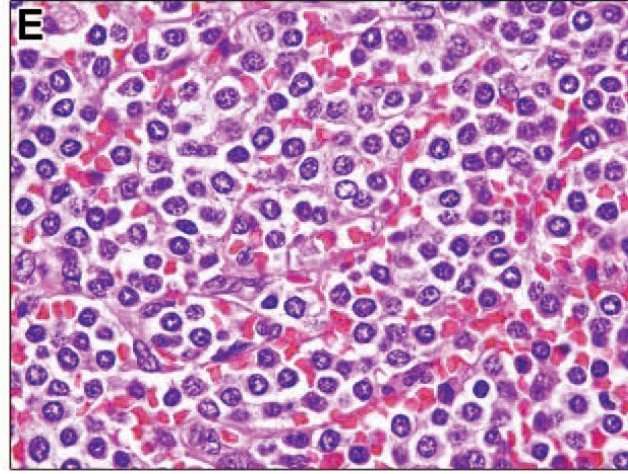
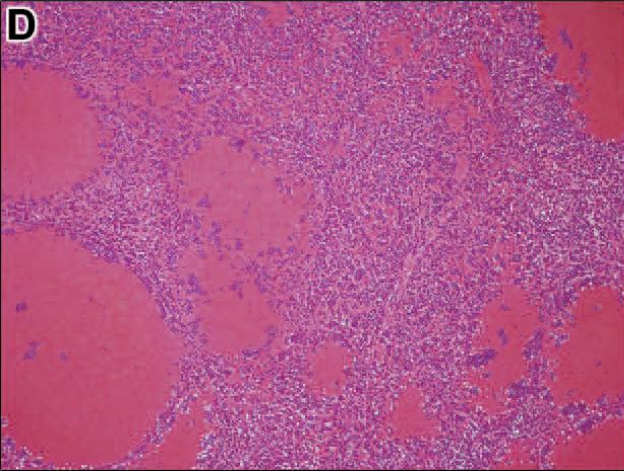
- HCL
- Sınıflandırılmayan splenik B hücreli lenfoma/lösemi kategorisi
 - HCL-v
 - SDRPSBCL (splenic diffuse red pulp small B-cell lymphoma)

HCL-v:

- Orta- ileri yaş, erkek cinsiyet hakim
- Klasik HCL bulgularının bir kısmı yanında farklı sitohematolojik ve immünofenotipik bulgular ve klasik HCL tedavisine yanıtızsızlıkla karakterlidir
- Lökositoz, monositoz, splenomegali ve kanda sirküle eden neoplastik hücreler
- Neoplastik hücreler prolenfosit benzeyen küçük nükleol bulundurur

HCL-v

Dalak tutulumu: Kırmızı pulpa infiltrasyonu, pseudosinüs formasyonu ve kan gölcükleri izlenir, beyaz pulpa atrofiktir



B Kemik iliği tutulumu genellikle interstisyel retikülin lif artışı görülmez

HCL-v:

- **IHK:**

CD20, DBA44, yüzey immunoglobulin-genellikle IgG pozitif. (Annexin A1, CD25, TRAP, bcl1, CD5, CD10, CD23 negatif)

- **Flow sitometri:**

Parlak CD20, CD22, CD11c, CD103 pozitif
(CD25, CD123-)

Dalakta kırmızı pulpa ve kemik iliği tutulumu ile karakterli B hücreli lenfoproliferatif hastalıklar:

- HCL
- Sınıflandırılmayan splenik B hücreli lenfoma/lösemi kategorisi
 - HCL-v
 - SDRPSBCL (splenic diffuse red pulp small B-cell lymphoma)

SDRPSBCL (splenic diffuse red pulp small B-cell lymphoma):

- Sinonim: SMZL-diffüz varyant, 'splenic red pulp lymphoma with numerous basophilic villous lymphocytes'
- Trombositopeni, hafif-orta derecede lenfositoz, masif splenomegali
- Kemik iliği tutulumu: intrasinüzoidal infiltrasyon kural, interstisyel ve nodüler infiltrasyon eşlik edebilir

A

Kırmızı pulpa infiltrasyonu, beyaz pulpa atrofik

B**C****D****E**

SDRPSBCL:

- **IHK:**

CD20, CD22, DBA-44, IgM + D, IgM + G, IgM veya IgG pozitif

(Annexin A1, CD5, CD25, CD10, CD23 negatif)

- **Flow sitometri:**

Parlak CD20, CD22; CD103 ve CD11c ±.

Table 2 Clinicopathological comparison between SMZL, SDRPL, HCL-V and HCL

	SMZL	SRPL	HCL-V	HCL
Frequency (% of chronic lymphoid malignancies)	25	0.5	0.4	2
Clinical presentation				
Sex ratio	0.48	1.64	1.6	5
Median age	62	77	71	55
Splenomegaly	Yes	Yes	Yes	Yes
Lymphocytosis	Moderate	Moderate (median $15.8 \times 10^9/l$)	High (median $34 \times 10^9/l$)	Pancytopenia
Neutropenia	No	No	No	Yes
Monocytopenia	No	No	No	Yes
Survival	10 years	10 years	9	12 years
Cytology	Heterogeneous	Homogeneous	Homogeneous	Homogeneous
Cytoplasm	Variable	Abundant basophilic	Abundant basophilic	Abundant clear or pale blue
Cytoplasm projection	Short, thin	Long, broad based, polar	Fine, or poorly defined	Fine, circumferential
Nucleolus	Small	Occasional large nucleolus	Large nucleolus similar to polymorphocytes	Occasional small nucleolus
Chromatin	Condensed	Clumped	Condensed	Granular
Immunophenotype				
CD20	Bright	Bright +	Bright ++	Bright
CD22	Moderate	Bright +	Bright ++	Bright
CD11c	33% faint	97% moderate	87% bright	100% bright
CD76	27%, partial	86%, all cells	Bright	Bright
CD103	Negative	38% variable	60% faint to moderate	100% bright
CD123	Negative	16% faint	9%	95% bright
CD25	Rare	Negative	Dim or negative	Bright
CD27	Usual	Negative	Negative	Negative
ANX1	Negative	Negative	Negative	Positive
IgS	M ± D ± G kappa > lambda	M ± D ± G or IgG ± D kappa = lambda	IgG alone or in combination with other heavy chain kappa = lambda	IgG or multiple heavy chain isotype (all classes expressed except IgE; IgG3 most frequent) kappa = lambda
Spleen morphology	Marginal zone expansion with biphasic or monophasic pattern	Diffuse monomorphic in congested red pulp, blood lakes possible	Diffuse monomorphic in congested red pulp	Diffuse red pulp infiltration, atrophic white pulp; characteristic blood lakes
Bone marrow morphology	Intrasinusoidal and nodular, rarely interstitial	Mild fibrosis, interstitial or intrasinusoidal	Mild fibrosis interstitial or intrasinusoidal	Reticulin fibrosis interstitial spacing diffuse
Abnormal karyotype	80%	32%	Rare	Rare
Recurrent chromosomal abnormalities	+3,+18,del7q	+3, del7q	del17p, +12,	del17p, +12, D31cyclin D1 expression not associated with bcl-1

Teşekkürler...