

GASTROİNTESTİNAL SİSTEM LENFOMALARI

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DEÜTF Patoloji AD

- ▣ GIS → Ekstranodal lenfoma en sık
- ▣ DBBHL > MALT Lenfoma > Diğer
- ▣ Mide > ince barsak > kalın barsak* ve rektum*
- ▣ Ekstranodal Lenfoma X Lenfoid Hiperplazi
 - Özellikle "küçük lenfoid neoplazi"
 - Kriterler değişken!!!!
Monomorfik infiltrat, sitolojik atipi, GM*, yapısal yıkım.

Reaktif Lenfoid Hiperplazi

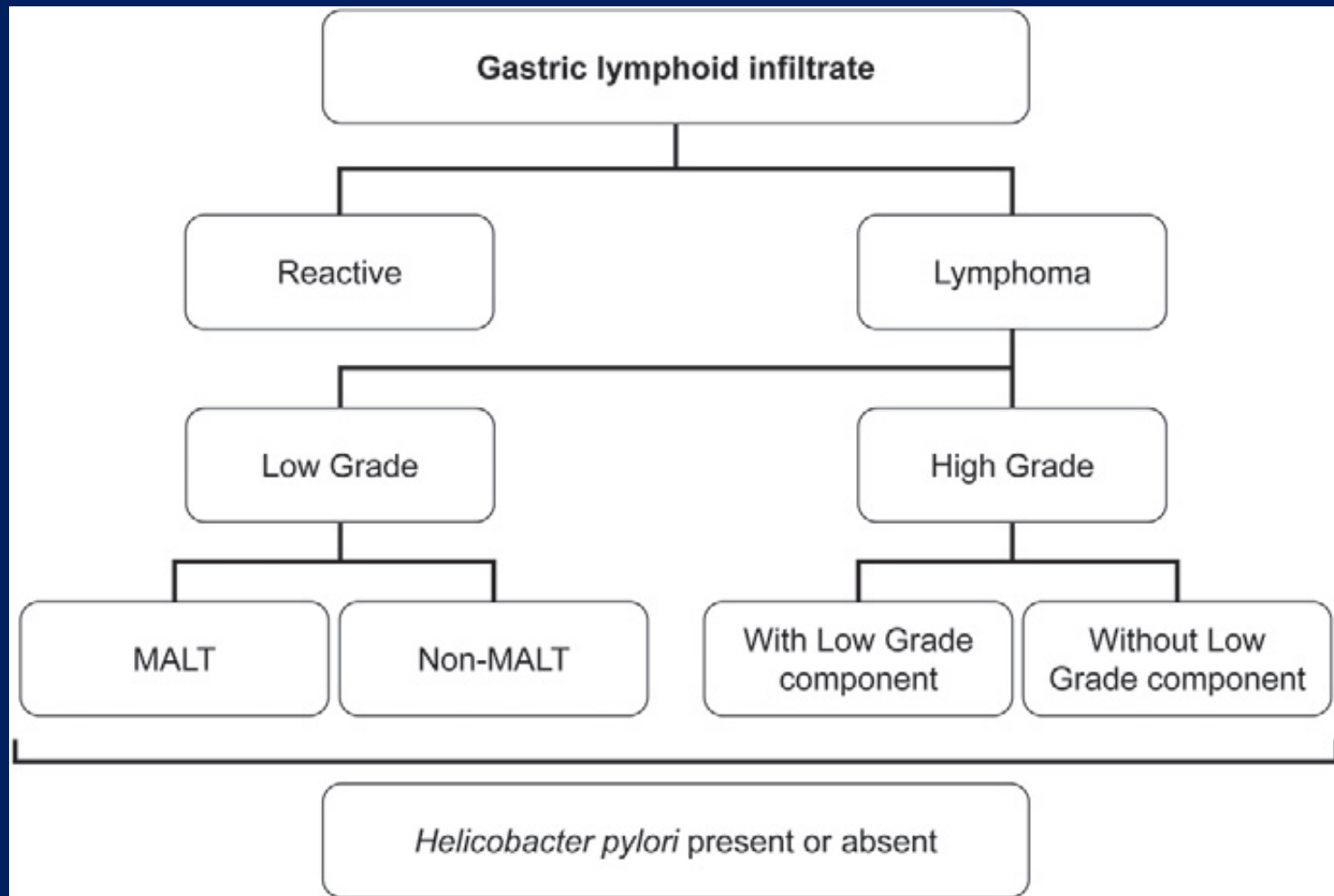


Küçük lenfositik neoplaziler
MALTL, (KLL, MHL, FL)



Büyük B Hücreli Lenfoma

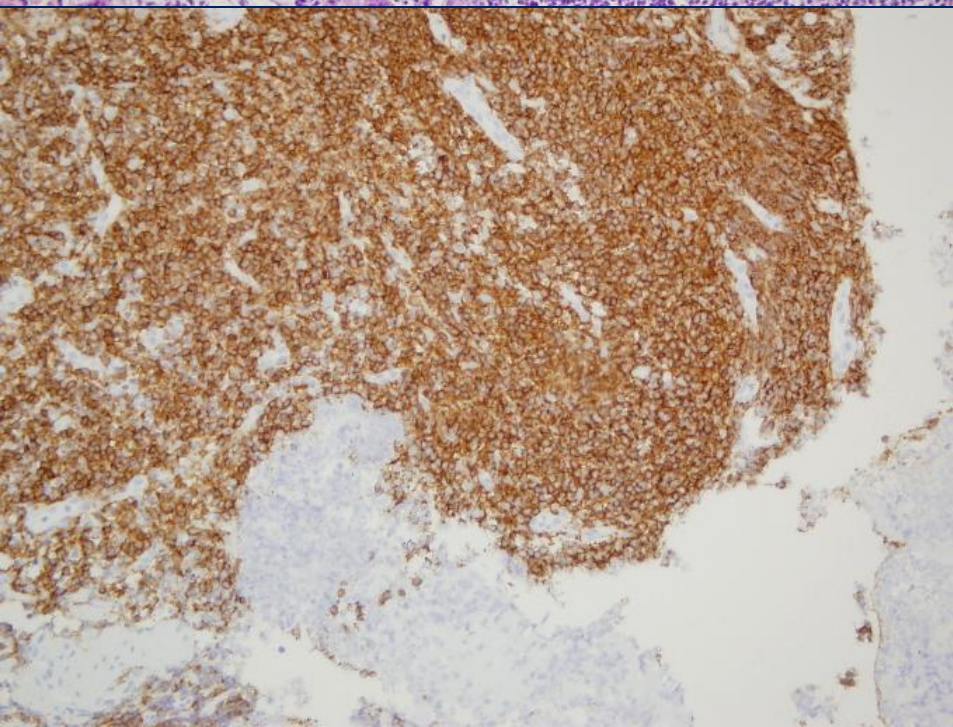
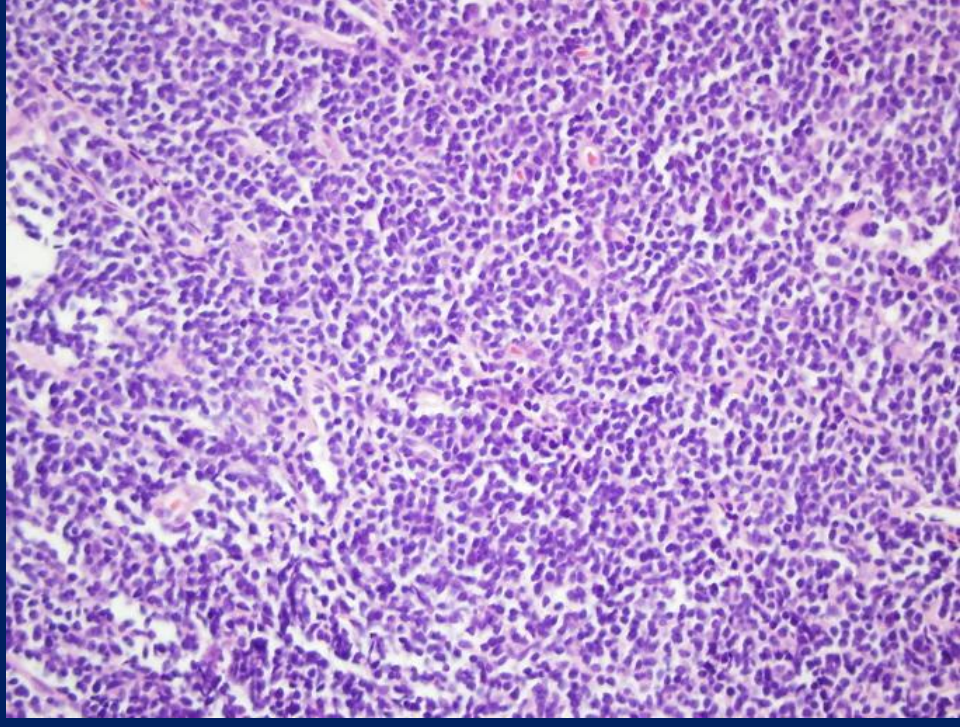
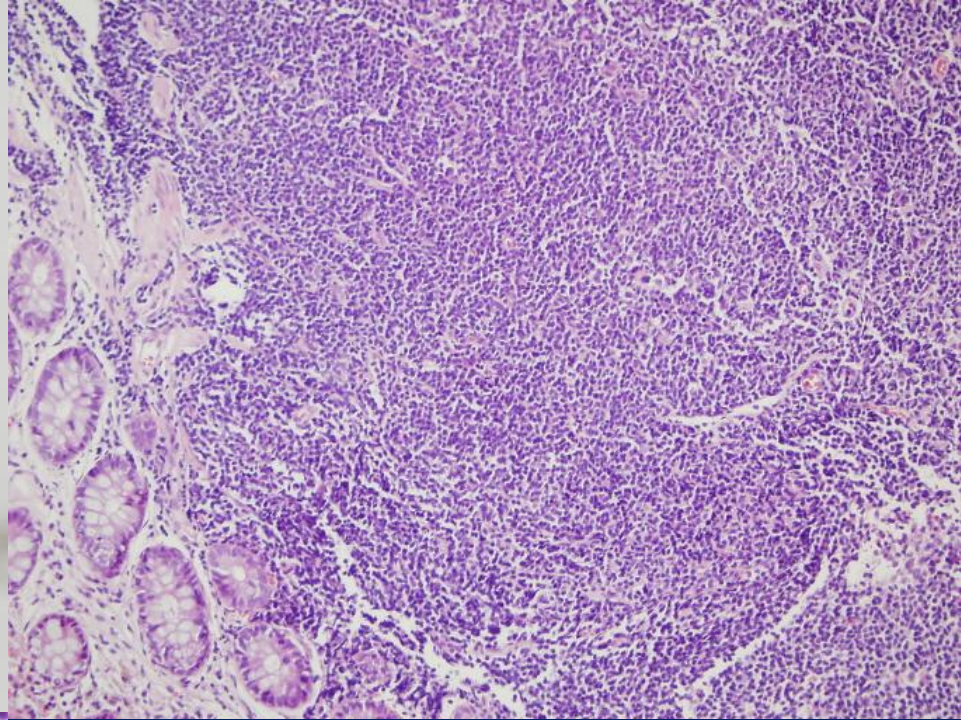
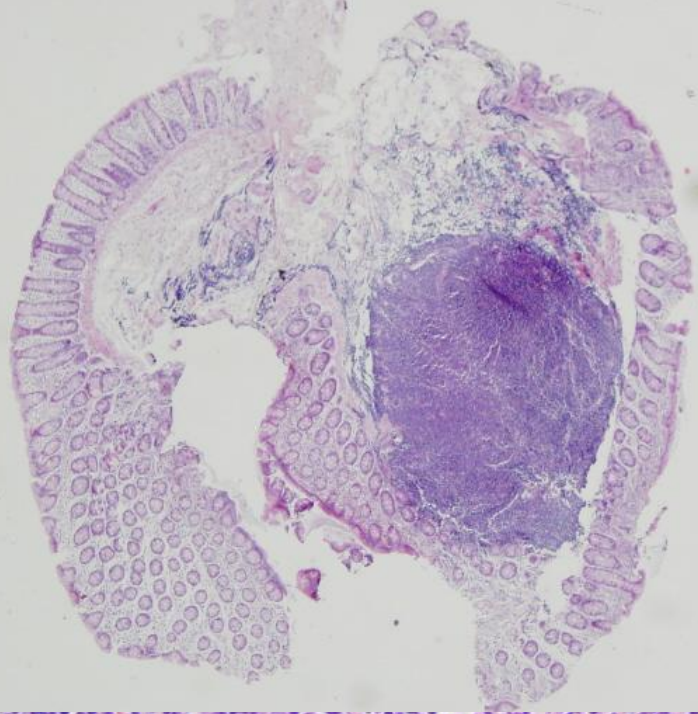
Gastrik Lenfoid lezyonlarda histopatolojik tanı;



Hücresel İnfiltrat,

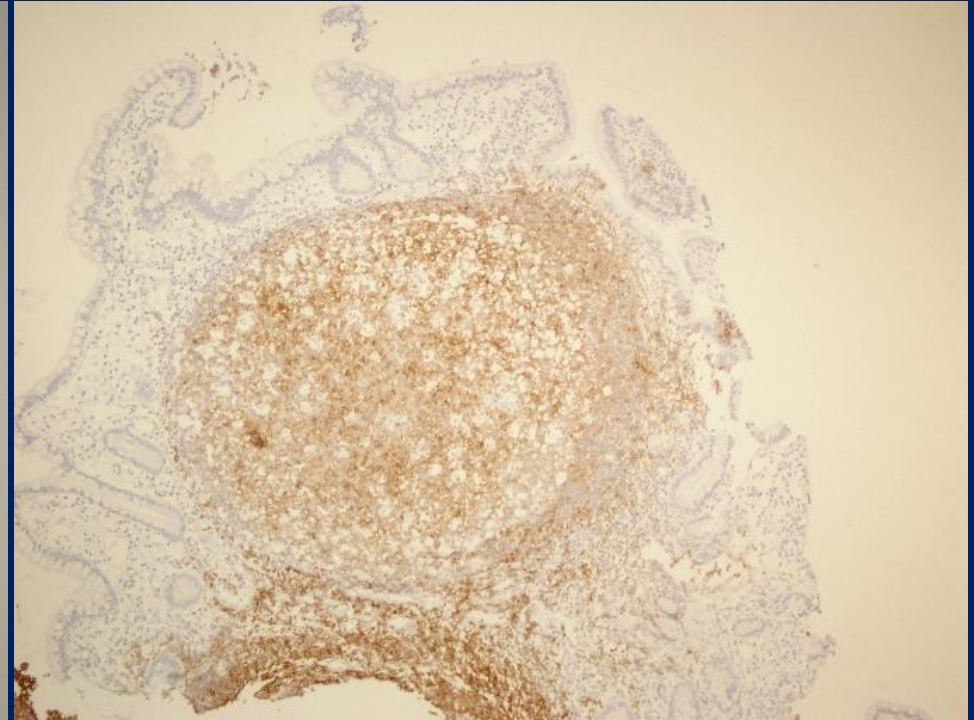
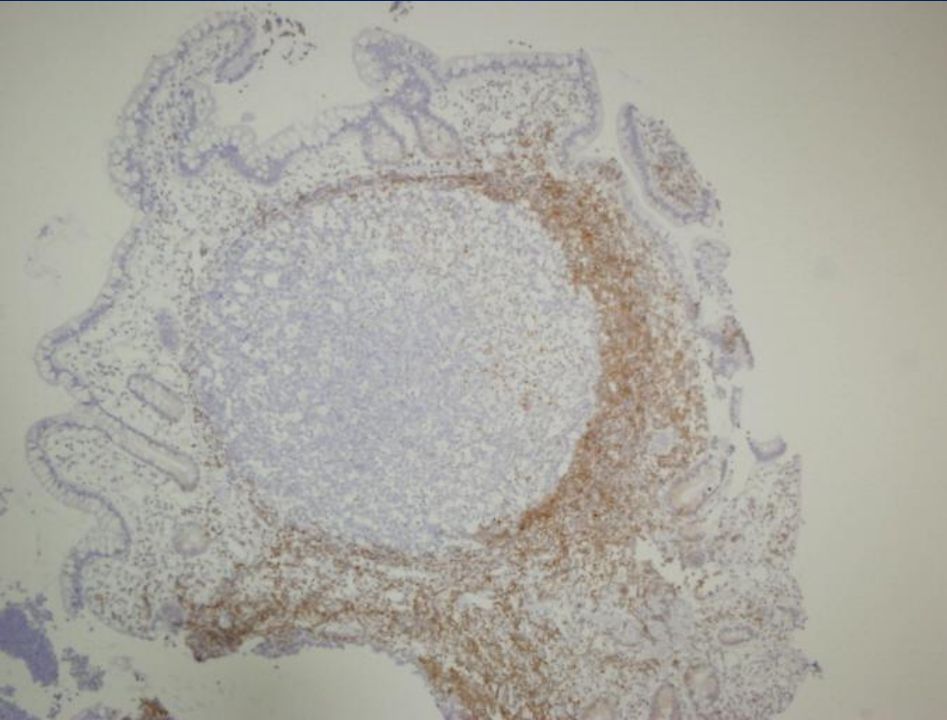
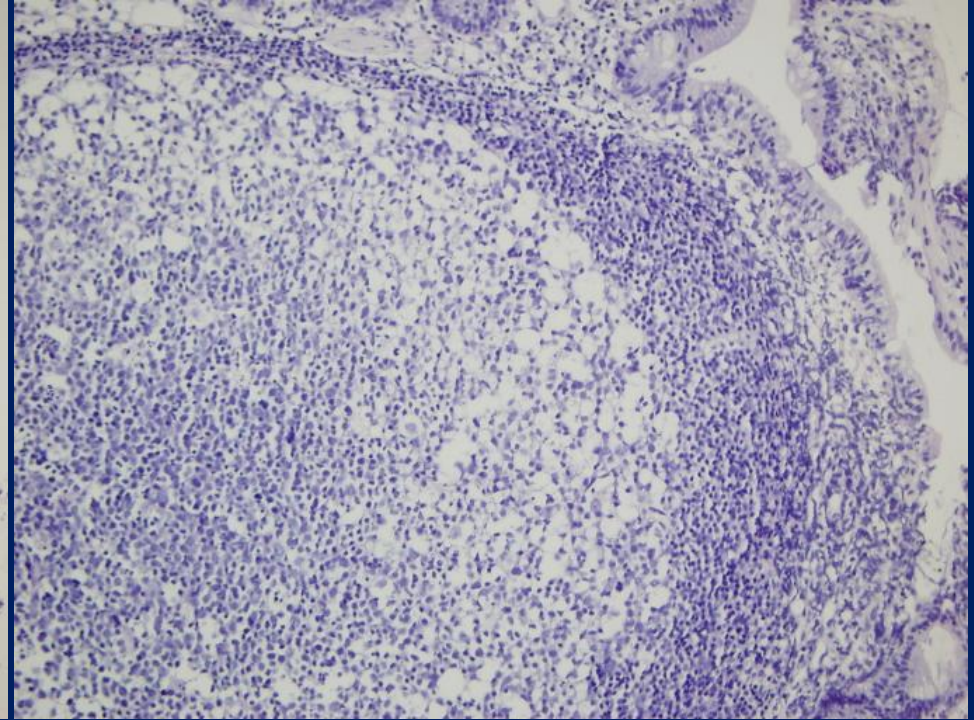
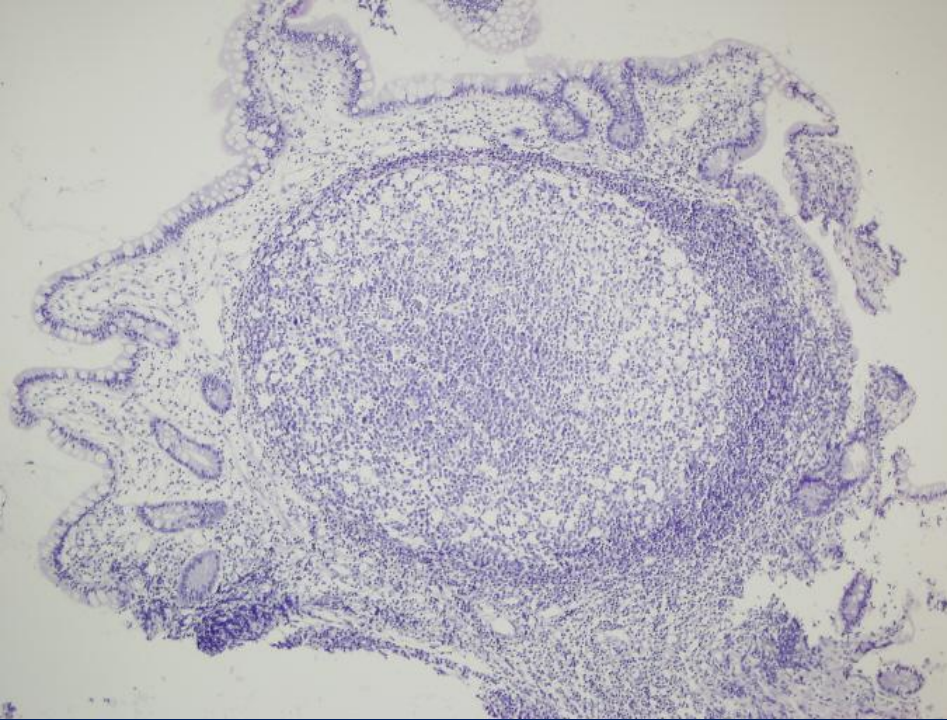
- ▣ Özellikle küçük biyopsilerde ve küçük lenfositik neoplazilerde ayırım zor olabilir!!!
- ▣ Bazen sadece histolojik bulgularla bu ayırım mümkün olmaz → Ekstranodal küçük lenfositik proliferasyon
- ▣ Monomorfik, yoğun, sitolojik atipi gösteren, "dutcher body" içeren, bezleri yıkıma uğratan, follikül yapısı +/-

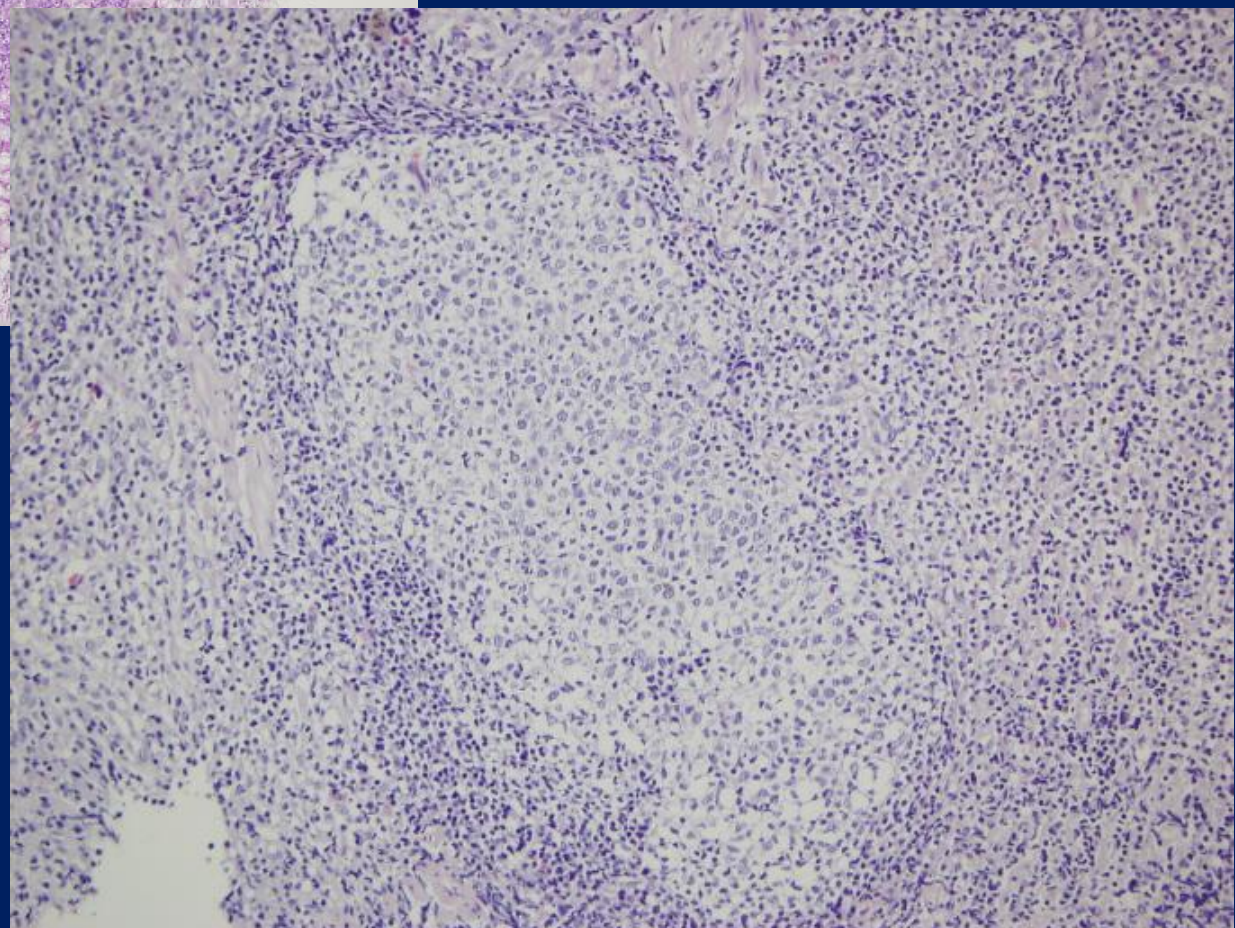
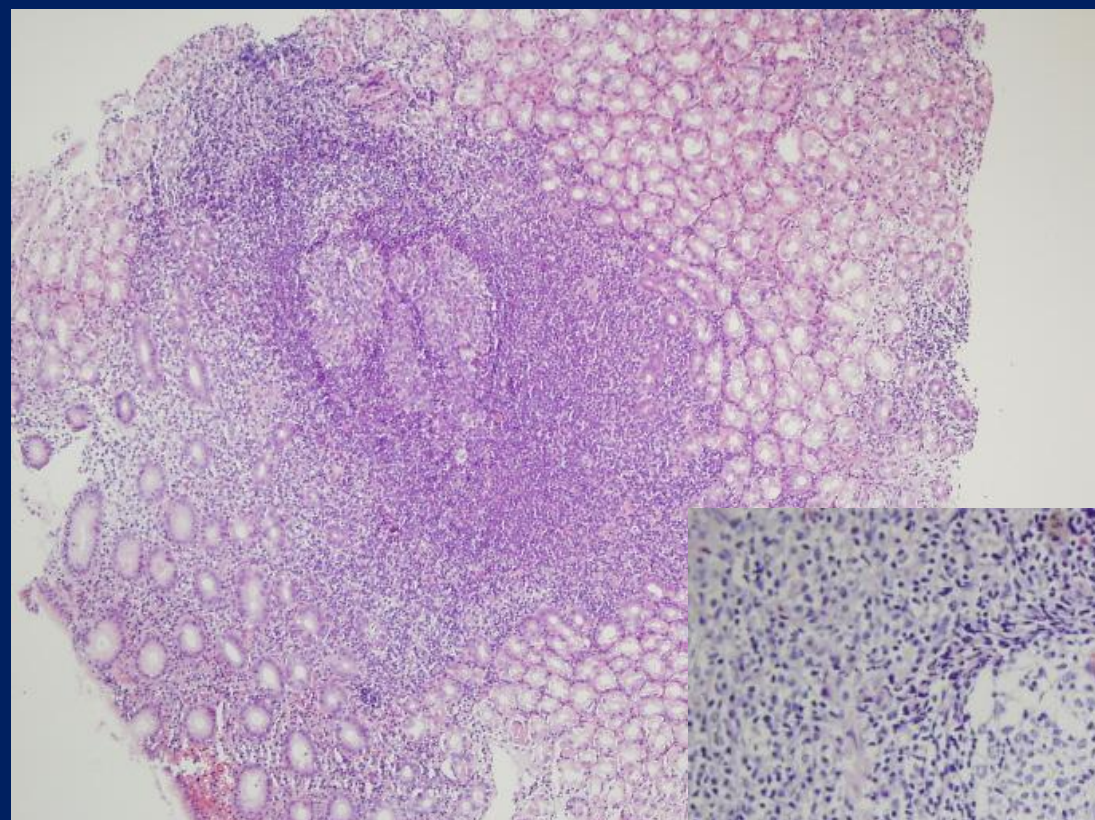
- ▣ Definitif tanı verilemeyen şüpheli infiltrat için yeni biyopsi önerilebilir.
- ▣ Ek incelemeler gerekebilir (İHK, klonalite*, ISH, flow, gen rearr., diğer moleküler teknikler)
- ▣ Aberan immunfenotip; B hücre (CD20) ve T hücre (CD43) antijen co-expresyonu

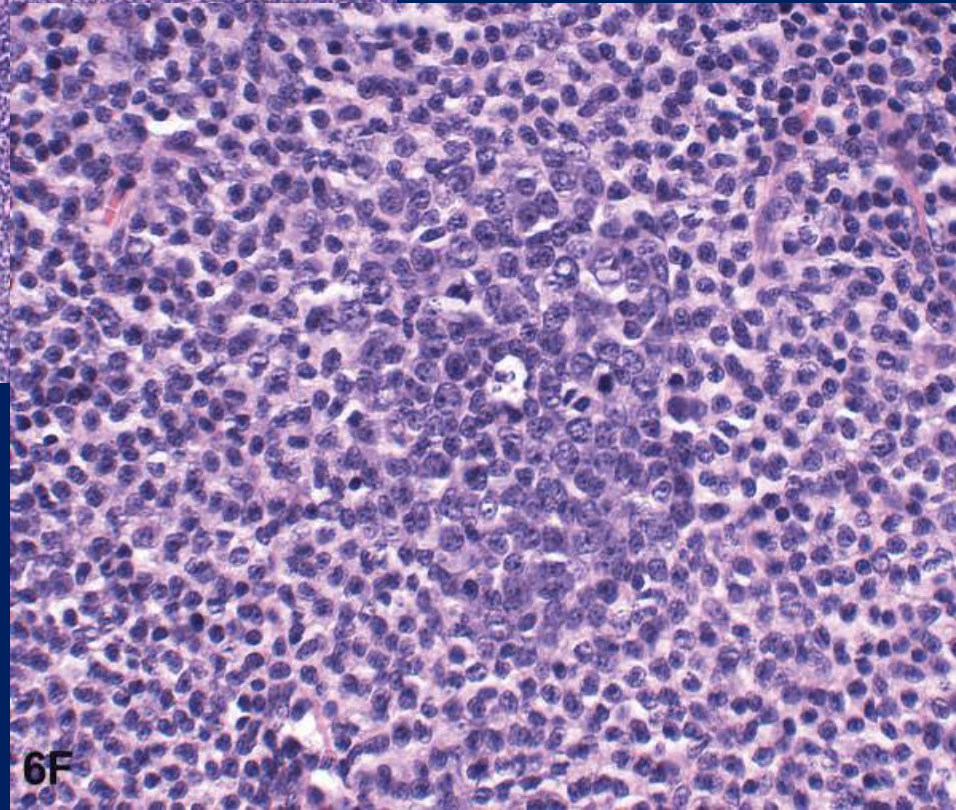
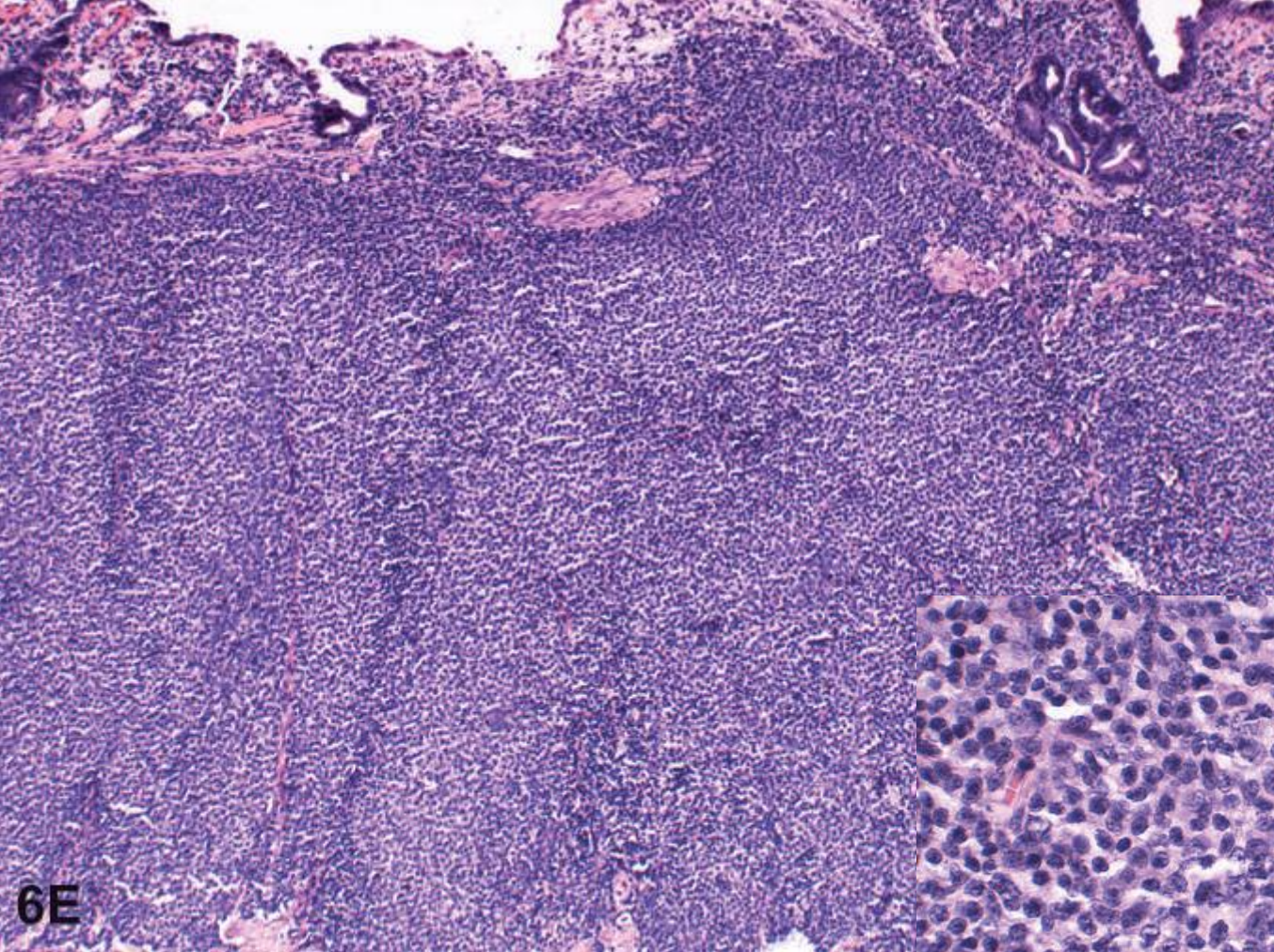


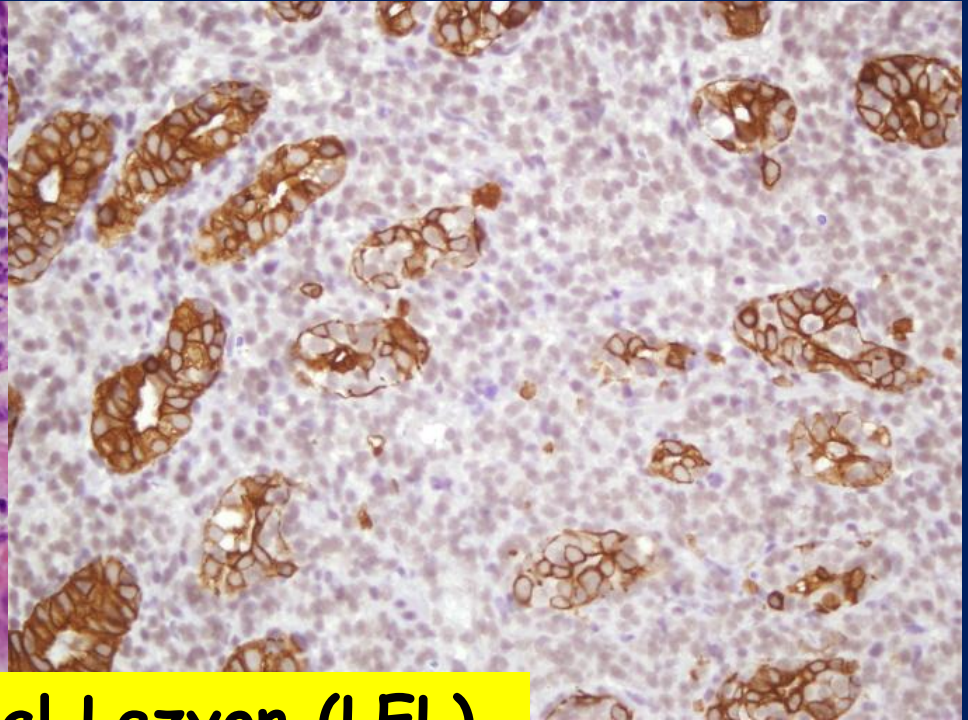
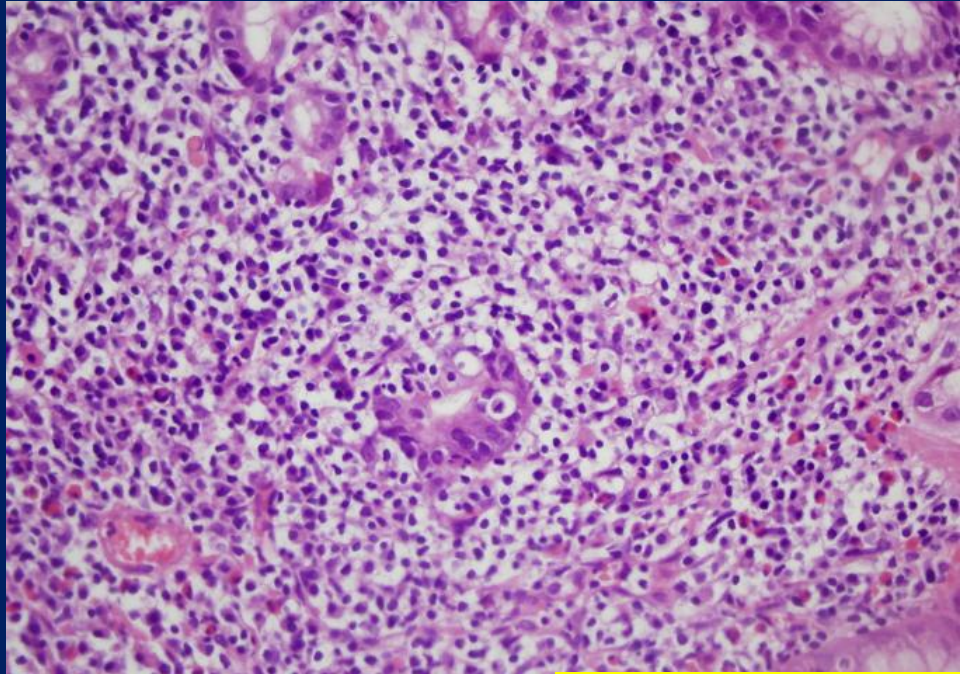
Germinal Merkez;

- ▣ MALT lenfomada GM içeren lenfoid follikül yapısı bulunabilir.
- ▣ GM'ler atrofik olabilir.
- ▣ Lenfoid follikül neoplastik hücrelerle çevrilidir.
- ▣ Ülser ile birlikte olduğunda LF ülser tabanında bulunur.
- ▣ Folliküler kolonizasyon olabilir. (X FL)

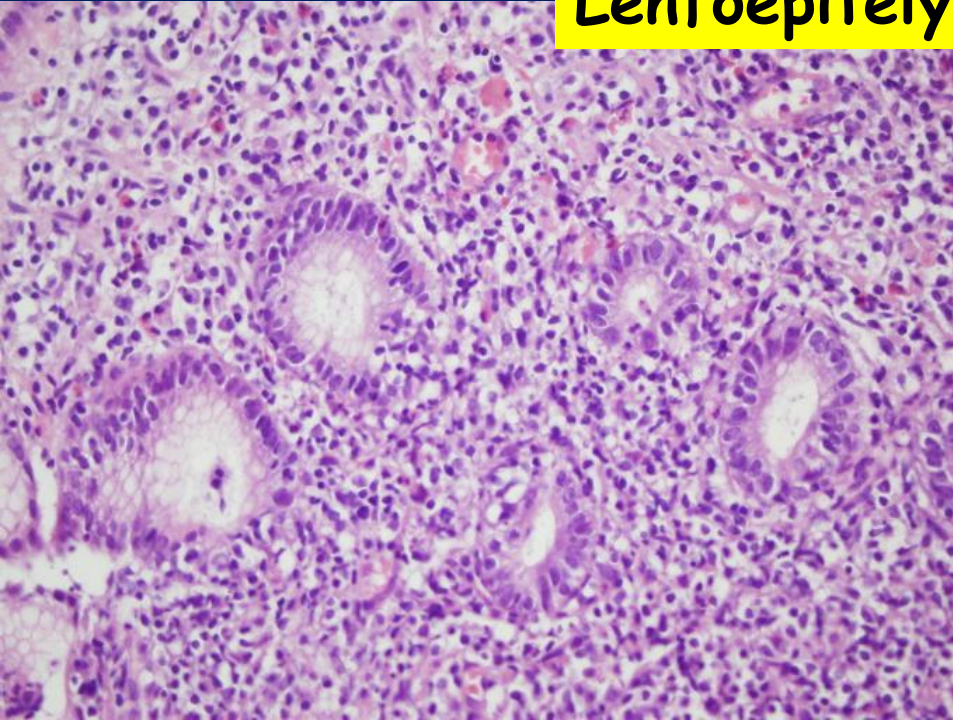








Lenfoepitelyal Lezyon (LEL)



Florid lenfoid Hiperplazi (psödolenfoma)

- ▣ GIS'de fokal veya nodüler olabilir.
- ▣ Mide yanısıra ileumda (peyer plakları) belirgin olabilir.
- ▣ Rektumda; **rektal tonsil**
- ▣ LF veya reaktif GM
- ▣ HP ilişkili kronik gastrit ve lenfoid hiperplazide monoklonalite saptanabilir.
- ▣ Multipl tekrar biyopsiler,

Grade 0
(normal)

LP'da seyrek plazma hücresi +
Lenfoid follikül θ

Grade 1
(kronik aktif gastrit)

LP'da lenfosit kümeleri +
Lenfoid follikül θ
LEL θ

Grade 2 (florid lenfoid follikül formasyonu gösteren kronik aktif gastrit)

Mantle zon ve plazma hücreleri ile çevrili lenfoid follikül +
LEL θ

Grade 3 (LP'da şüpheli lenfoid infiltrat, muhtemelen reaktif)

LP'da diffüz infiltrasyon gösteren küçük lenfositler ile çevrili lenfoid follikül +
Epitelde seyrek lenfosit +

Grade 4 (LP'da şüpheli lenfoid infiltrat, muhtemelen lenfoma)

LP'da diffüz infiltrasyon gösteren küçük lenfositler ile çevrili lenfoid follikül +
Epitel içinde gruplar oluşturan lenfositler +

Grade 5 (Düşük dereceli B-hücreli lenfoma, MALT)

LP'da diffüz lenfoid infiltrat +
Belirgin LEL +

- ▣ LP'da sentrosit benzeri/MZ hücrelerinin infiltrasyon paterni ve LEL
- ▣ İnterobserver uyum değişken
- ▣ Özellikle derece 3 ve 4 arasında????
 - Klinik bilgi,
 - Yaygın örnekleme,
 - LEL'un tanınması,
 - İmmunohistokimya,
 - Sitogenetik /klonalite**.

LENFOİD NEOPLAZİLER

NON-HODGKIN LENFOMA (who2008)

PREKÜRSÖR B HÜCRE NEOPLAZİSİ:

prekürsör B-lenfoblastik lösemi / lenfoma (prekürsör B hücreli akut lenfoblastik lösemi)

MATÜR (PERİFERAL) B HÜCRE NEOPLAZİLERİ

Kronik lenfositik lösemi / küçük lenfositik lenfoma

B hücreli prolenfositik lösemi

Hairy cell lösemi

Lenfoplazmasitik lenfoma

Ağır zincir hastalığı (gamma, mü, alfa)

Plazma hücreli neoplazileri

Nodal marjinal zon B hücreli lenfoma

Ekstranodal marjinal zon B hücre lenfoması (MALT lenfoma)

Splenik marjinal zon B hücreli lenfoma

Splenik B hücreli lenfoma/lösemi, sınıflanamayan

Foliküler lenfoma

Primer kutanöz follikül merkez hücreli lenfoma

Mantle cell lenfoma

Diffüz büyük B hücreli lenfoma, NOS

NON-HODGKIN LENFOMA

MATÜR (PERİFERAL) B HÜCRE NEOPLAZİLERİ

Kronik enflamasyonla ilişkili DBBHL

Lenfomatois granülomatozis

Primer Mediastinal (timik)büyük B hücreli lenfoma

İntravasküler büyük B hücreli lenfoma

ALK pozitif büyük B hücreli lenfoma

Plazmablastik lenfoma

HHV ilişkili multisentrik castlemann hastalığından gelişen BBHL

Primer effüzyon lenfoma

Burkitt lenfoma

BCLUWFIBDLBCLBL

BCLUWFIBDLBCLHL

NON-HODGKIN LENFOMA

PREKÜRSÖR T HÜCRE NEOPLAZİSİ:

Prekürsör T-lenfoblastik lenfoma / lösemi (prekürsör T hücreli akut lenfoblastik lösemi)

MATÜR (PERİFERİK) T HÜCRE ve NK HÜCRE NEOPLAZİLERİ:

T hücreli prolenfositik lösemi

T hücreli büyük granüler lenfositik lösemi

NK hücrelerinin kronik lenfoproliferatif hastalığı

Agresif NK hücre lösemisi

Çocukların EBV+T hücreli lenfoproliferatif hastalığı

Erişkin T hücreli lösemi/ lenfoma

Ekstranodal NK / T hücreli lenfoma, nazal tip

Enteropati tipi T hücreli lenfoma

Hepatosplenik T hücreli lenfoma

Subkutan pannikülit benzeri T hücreli lenfoma

Mikozis fungoides

Sezary sendromu

Primer kutanöz CD30+ T hücreli lenfoproliferatif hastalık

NON-HODGKIN LENFOMA

MATÜR (PERİFERİK) T HÜCRE ve NK HÜCRE NEOPLAZİLERİ:

Primer kutanöz periferal T hücreli lenfoma

Periferal T hücreli lenfoma, spesifiye edilemeyen

Anjioimmünoblastik T hücreli lenfoma

Anaplastik büyük hücreli lenfoma, ALK pozitif

Anaplastik büyük hücreli lenfoma, ALK negatif

GIS LENFOMALARI

B HÜCRELİ

Ekstranodal Marjinal Zon Lenfoma, MALT Lenfoma

IPSID (Ağır zincir hastalığı)

Diğer (LN'ler ile benzer)

MHL (Lenfomatöz polipozis)

FL

DBBHL, NOS

Burkitt Lenfoma

T HÜCRELİ

Enteropati İlişkili (EATL)

Klasik ve Tip II

Diğer (Enteropati ilişkili olmayan)

NK/T, nasal tip

$\gamma\delta$

ABHL

Ekstranodal Marjinal Zon Lenfoma (MALT Lenfoma)

MALT Lenfoma;

- ▣ İlk 1983'te,
- ▣ Primer gastrik lenfomaların yaklaşık %50'si
- ▣ Ortalama yaş; 60
- ▣ Önceden "**a ağır zincir hastalığı**" olarak bilinen **IPSID** bu hastalığın özel bir tipidir.
- ▣ Klinik ve endoskopik bulgular spesifik değil.

- ▣ OI hastalık veya enfeksiyona sekonder

MALT



LENFOMA

- ▣ Multifokal olabilir.
- ▣ Post germinal merkez marjinal zon hücreleri

HP İLE ENFEKSİYON

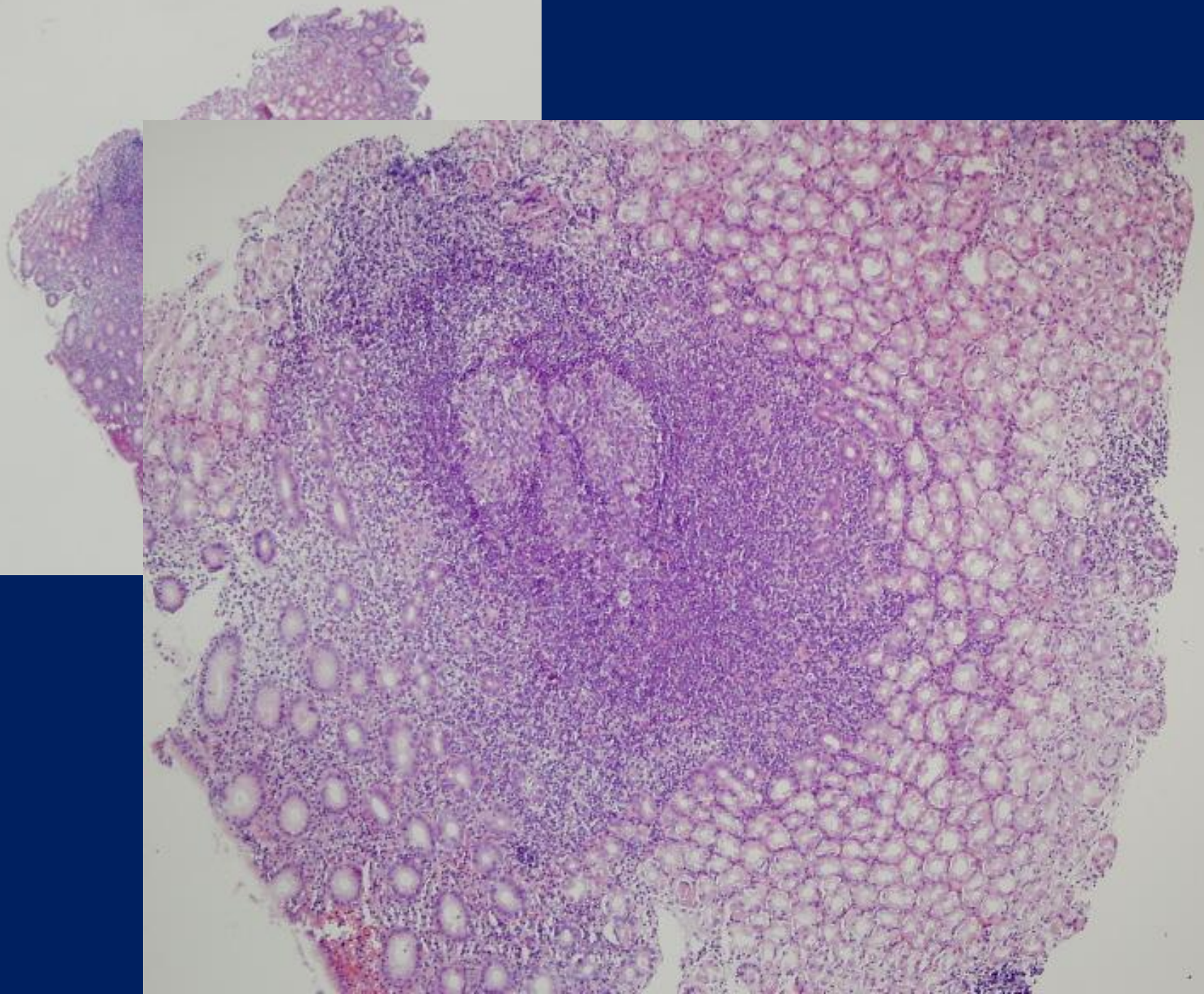
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graph TD; A[HP İLE ENFEKSİYON] --> B[HP antijeni ile aktive olan T hücreleri]; B --> C[Gastrik MALT lenfoma hücre proliferasyonu];
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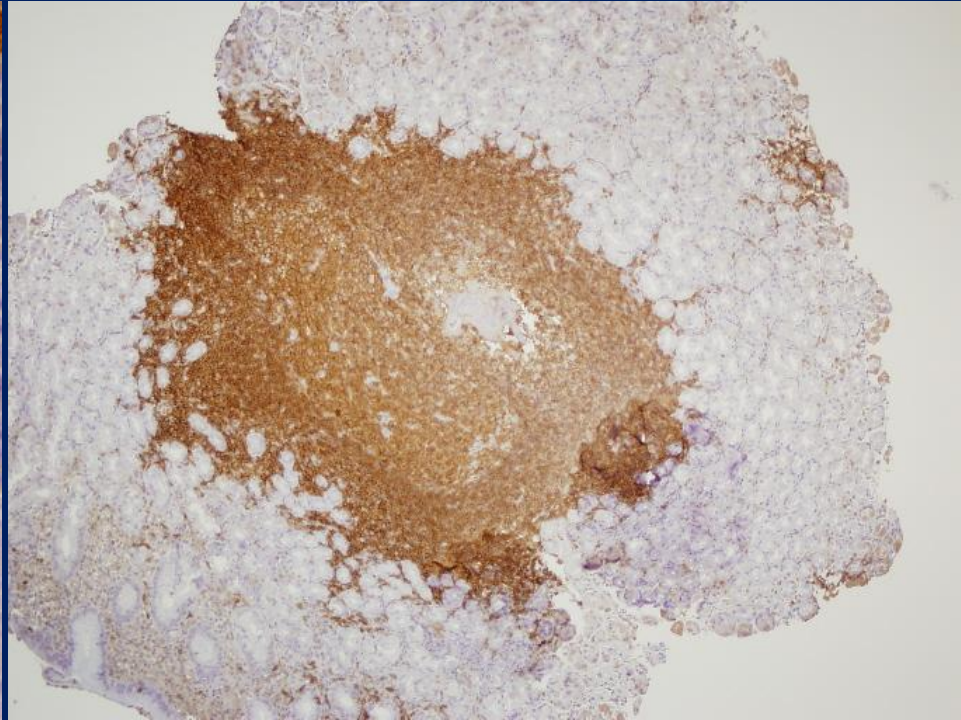
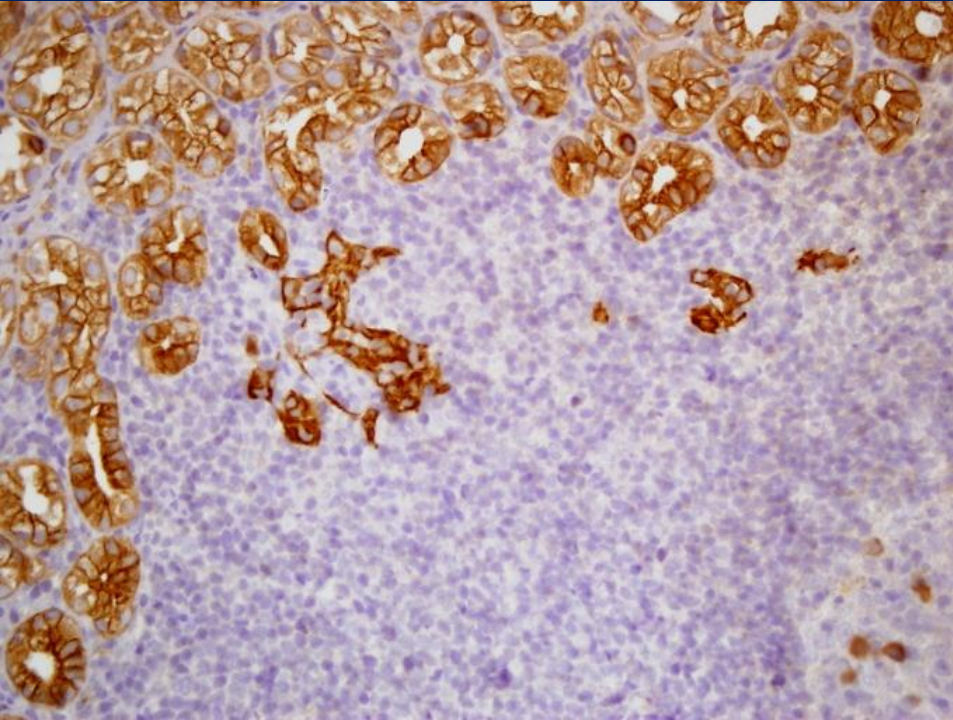
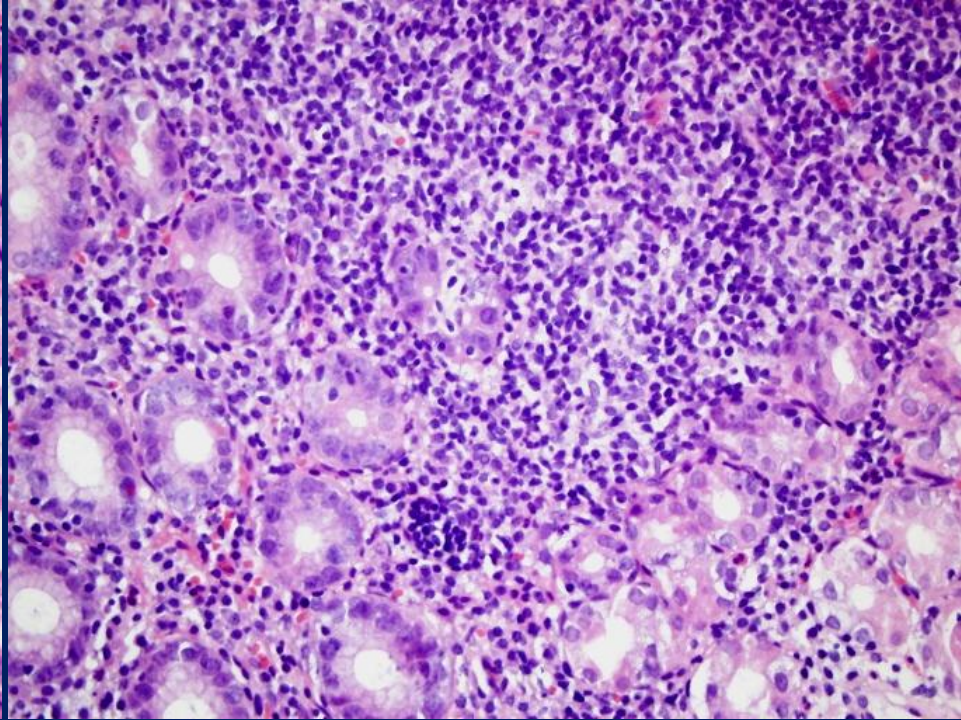
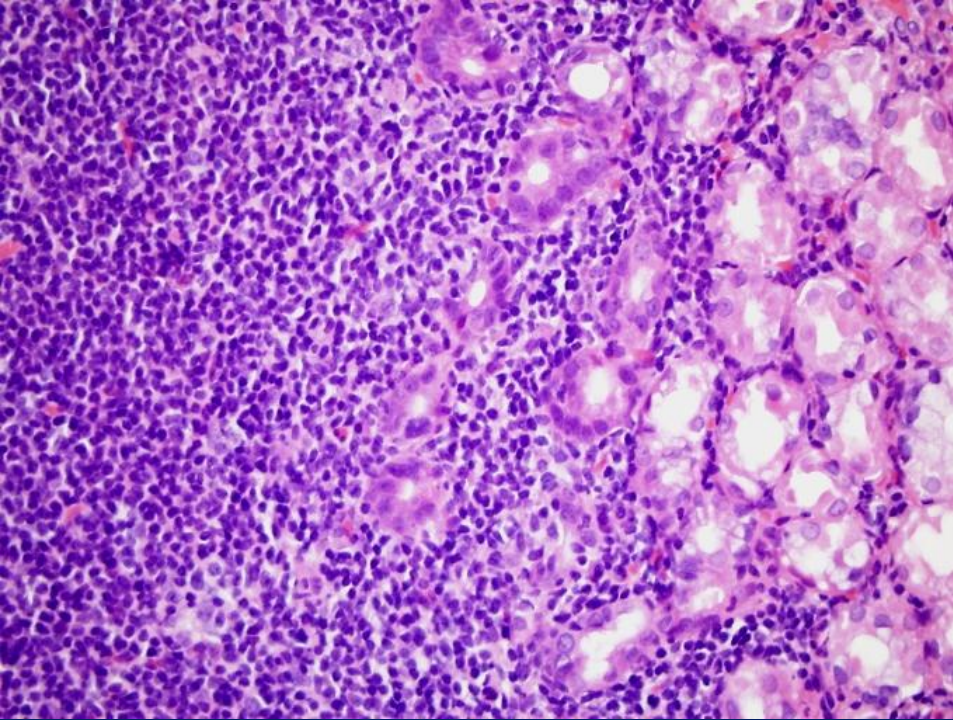
**HP antijeni ile aktive
olan T hücreleri**

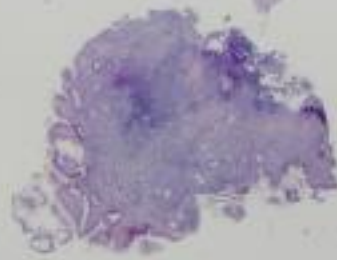
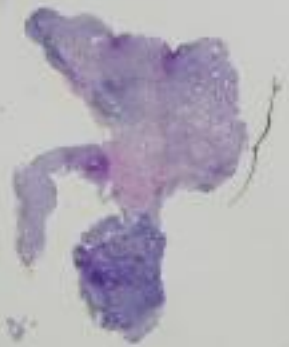
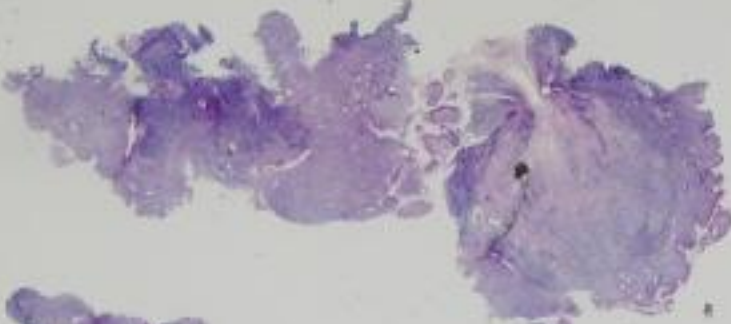
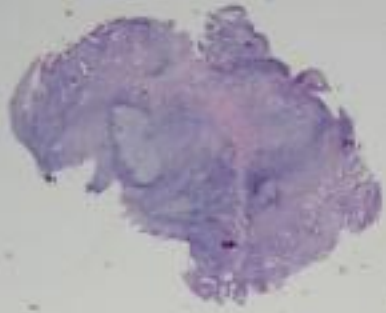
**Gastrik MALT lenfoma
hücre proliferasyonu**

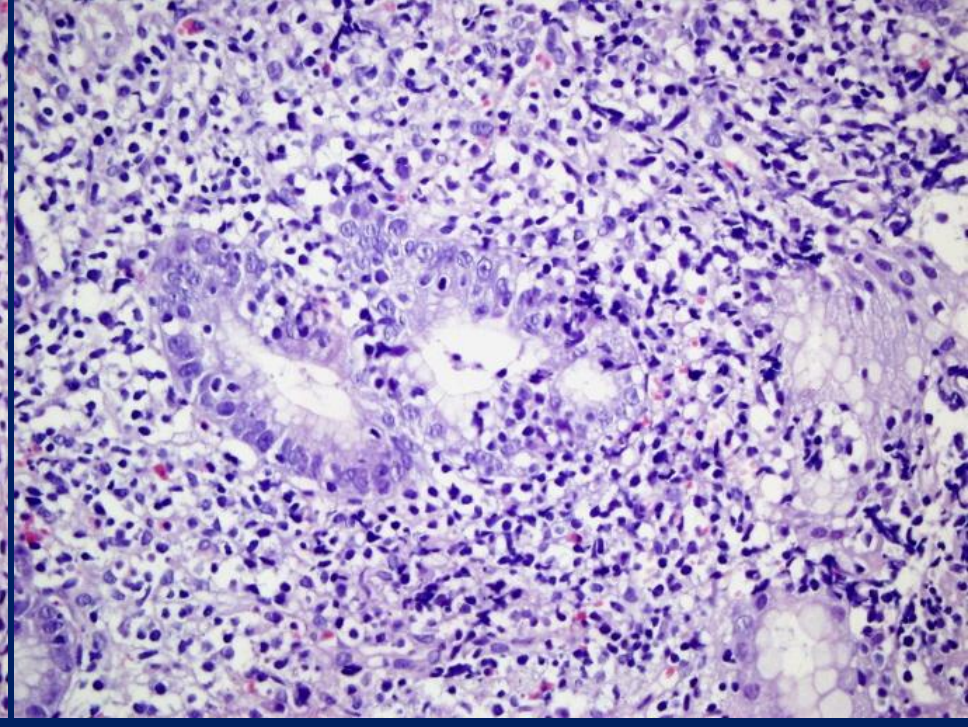
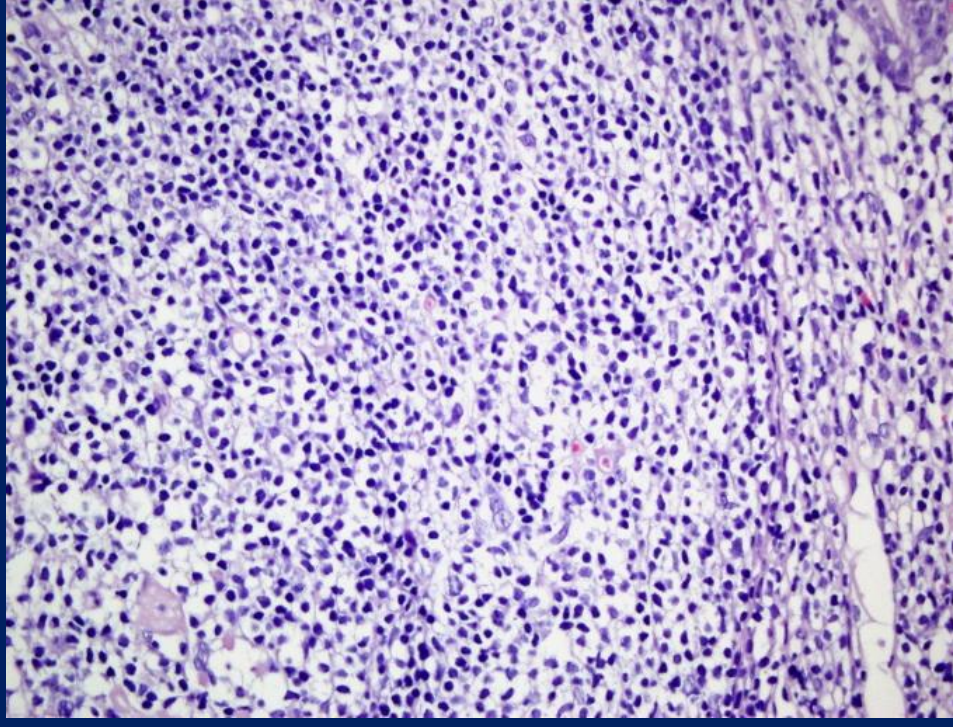
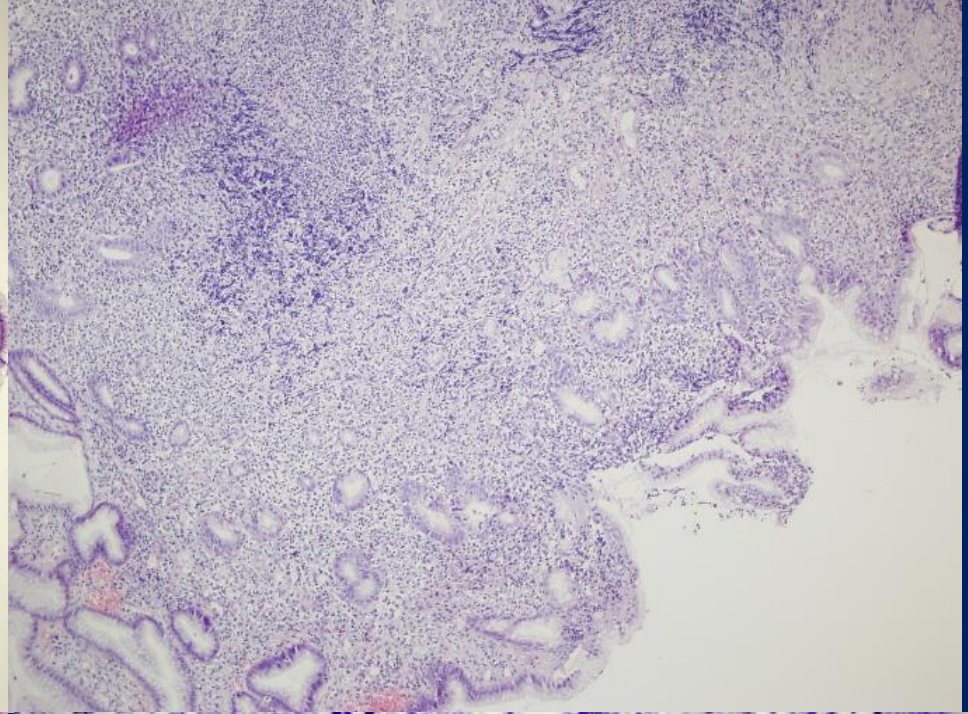
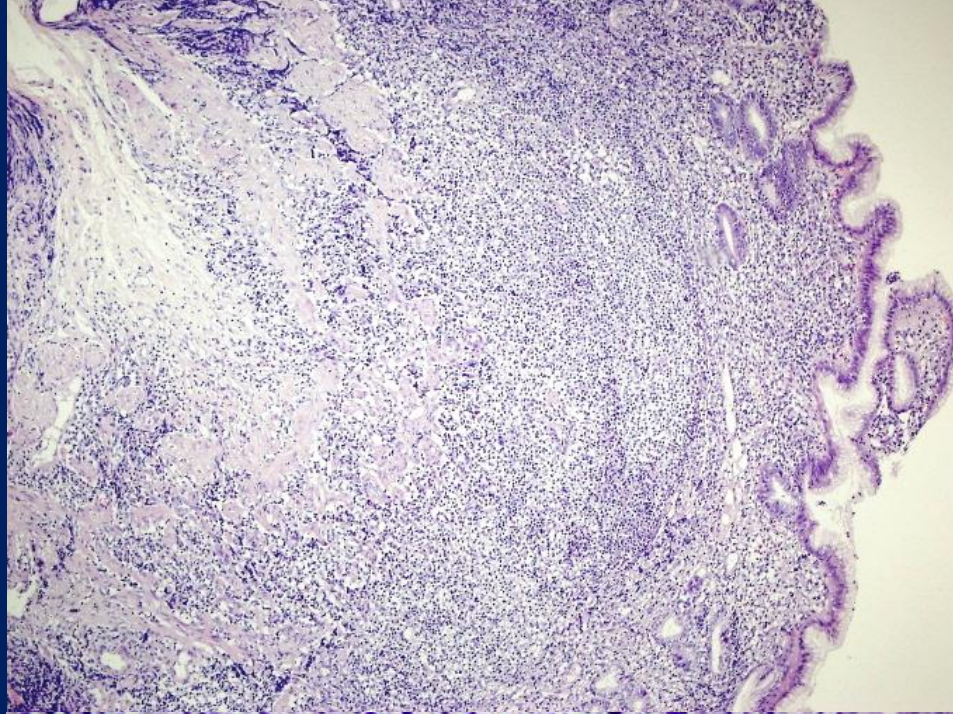
- ▣ Reaktif follikülde korunmuş mantle zon çevresinde marjinal zonda ve bunun dışındaki alanlarda neoplastik infiltrasyon,
- ▣ Küçük-orta boyutta, nükleolü belirsiz sentrosit benzeri hücreler,
- ▣ Abondan soluk sitoplazma olabilir... monositoid
- ▣ Küçük lenfositler,
- ▣ İmmunoblast yada sentroblast benzeri iri hücre,
- ▣ Sentroblast benzeri hücreler,
- ▣ Plazma hücre diferansiyasyonu.

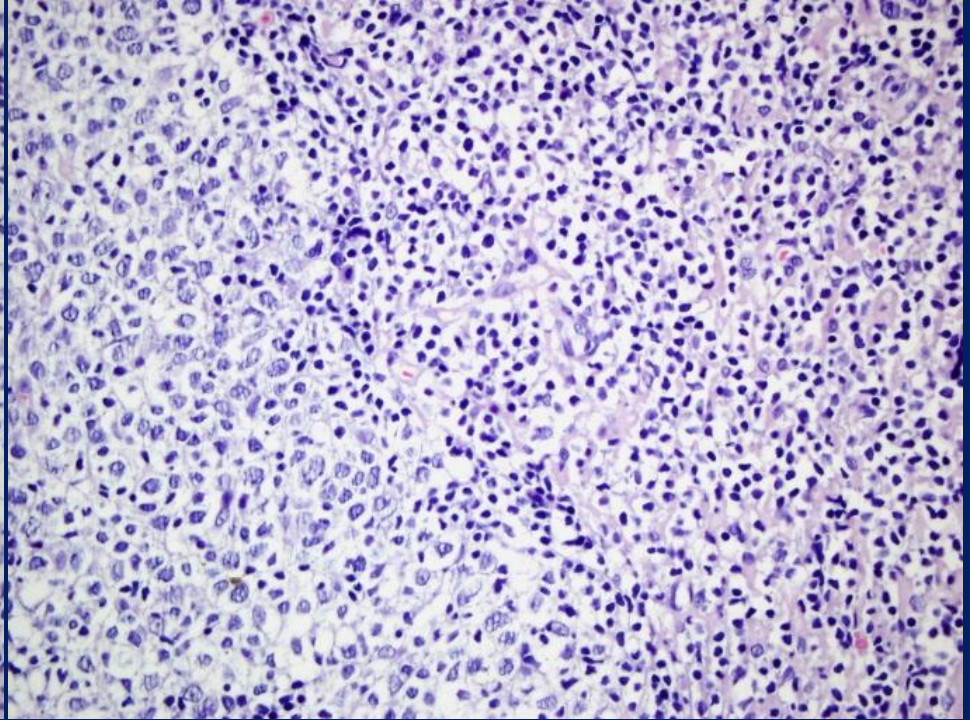
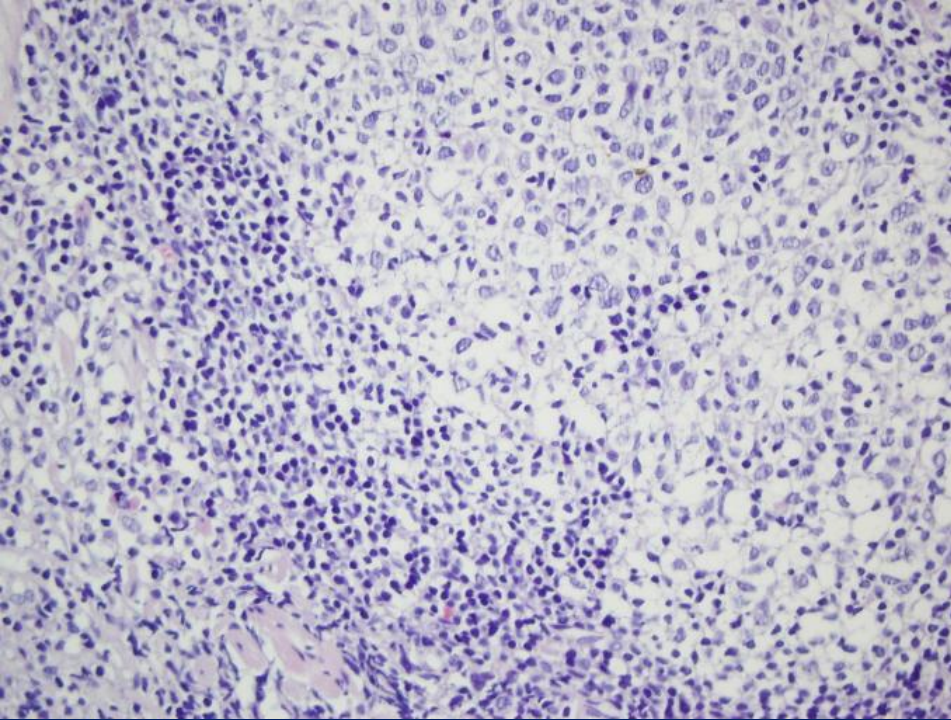
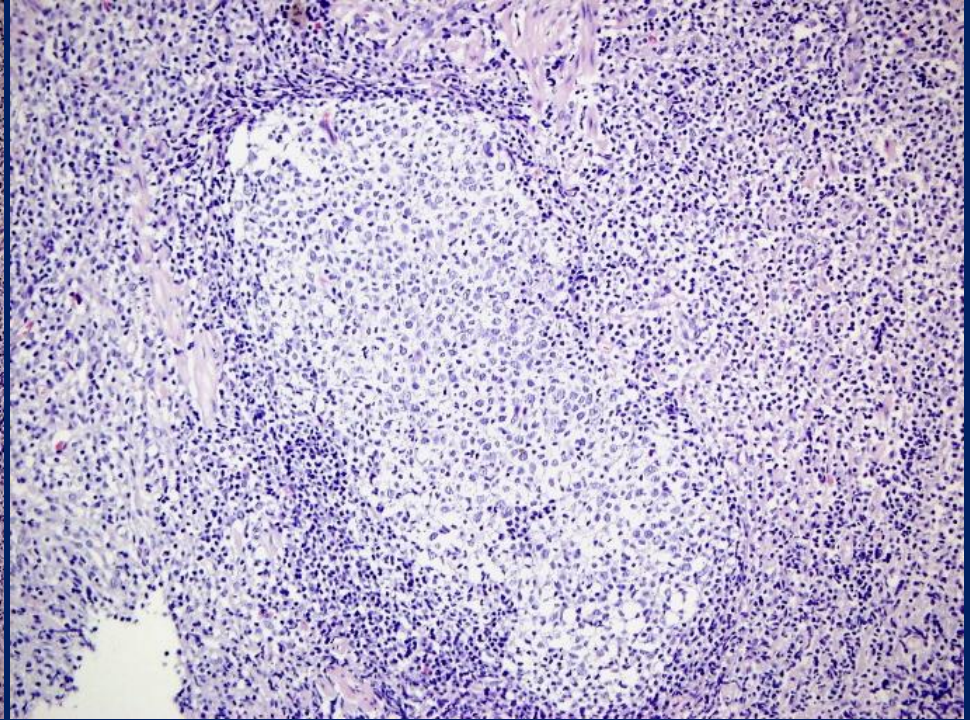
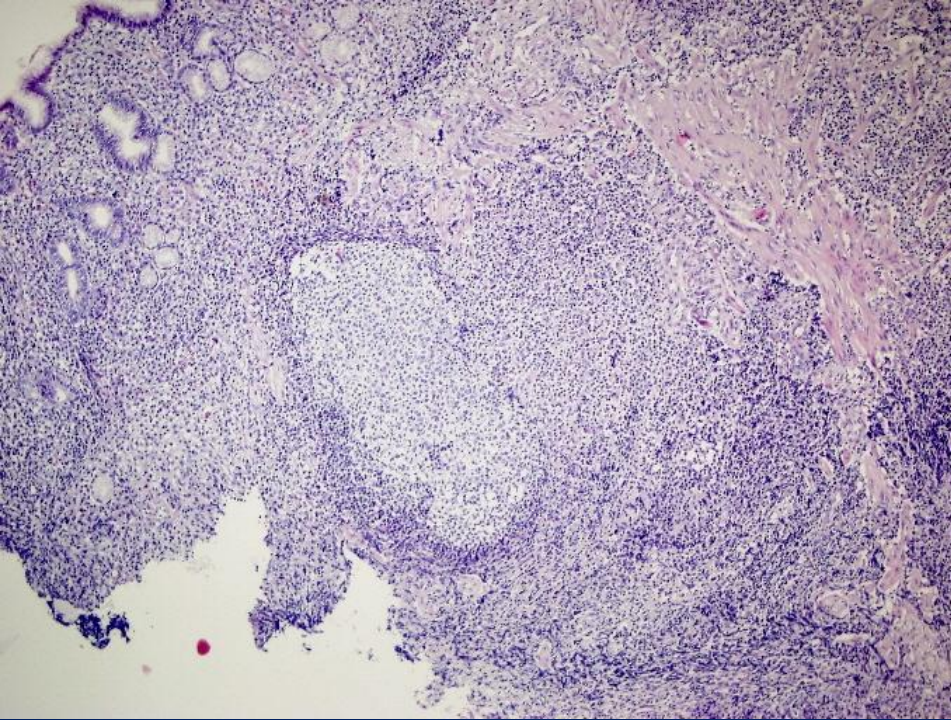
- Epitel; lenfoma hücreleri ile infiltre olur ve yıkıma uğrar.....**Lenfoepitelyal lezyon (LEL) (özellikle mide)**
- LEL'da; bez yapısında şekil bozukluğu yada yıkıma neden olan 3 (4) yada daha fazla lenfosit infiltrasyonu vardır.
- Epitel hücrelerinde; eozinofilik dejenerasyon.

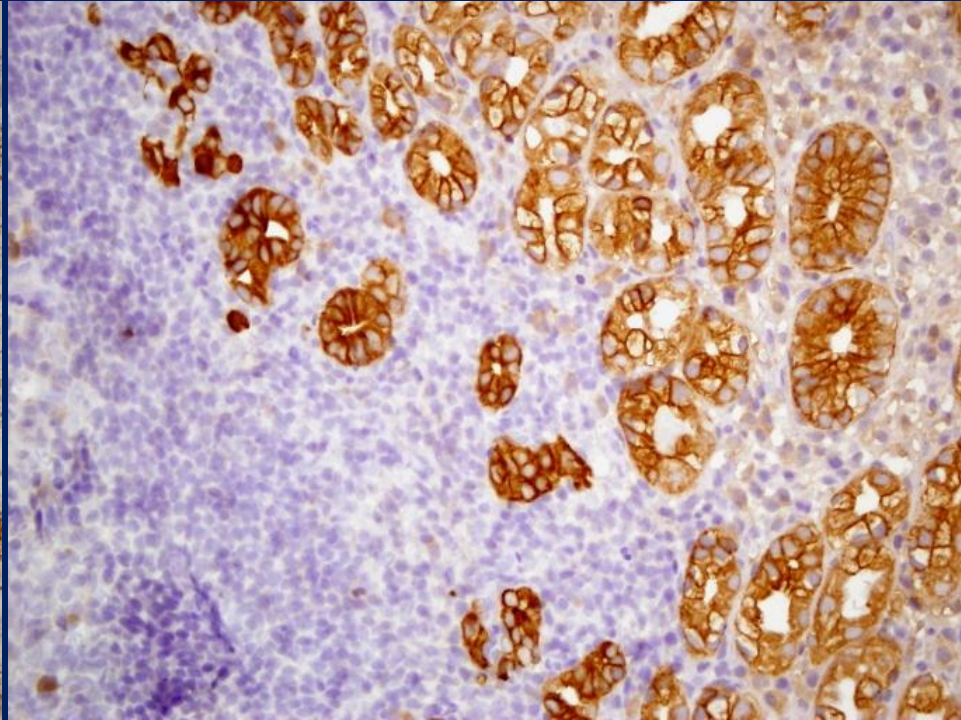
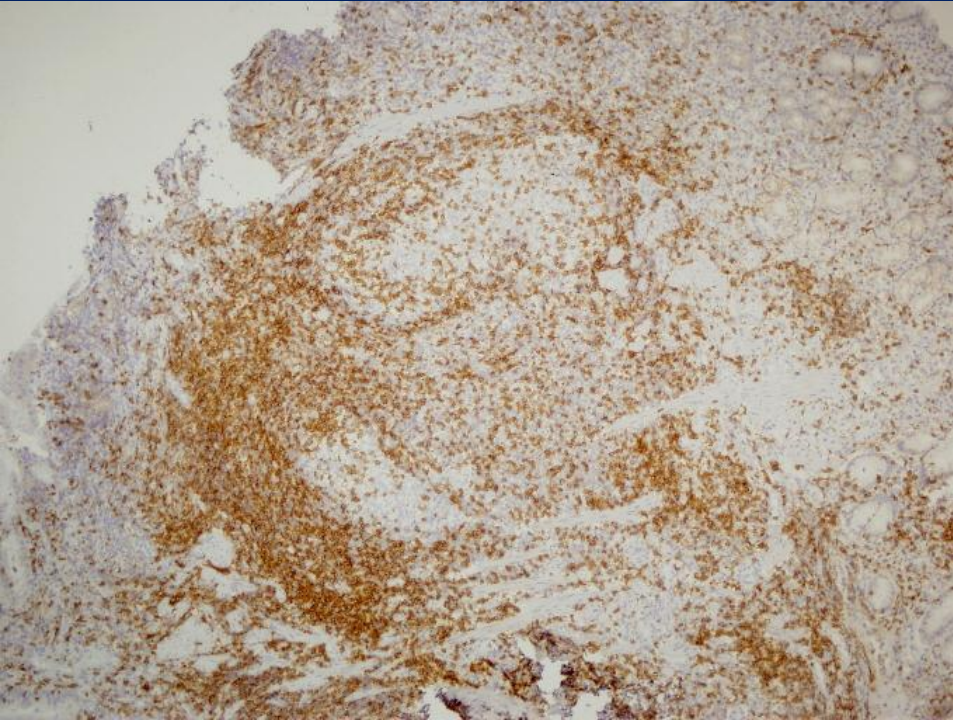
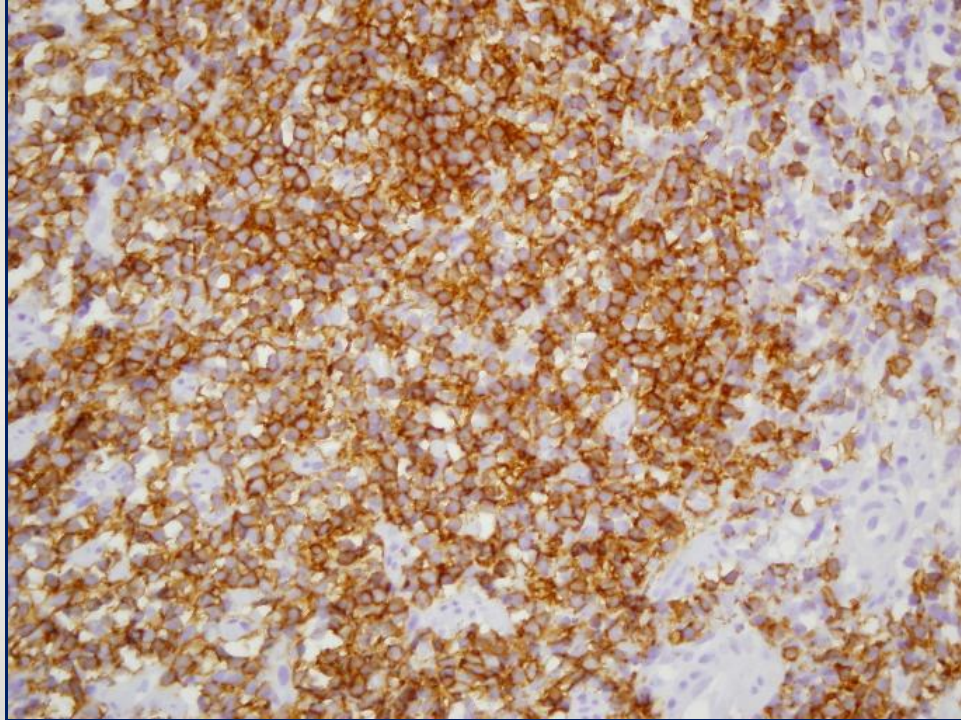
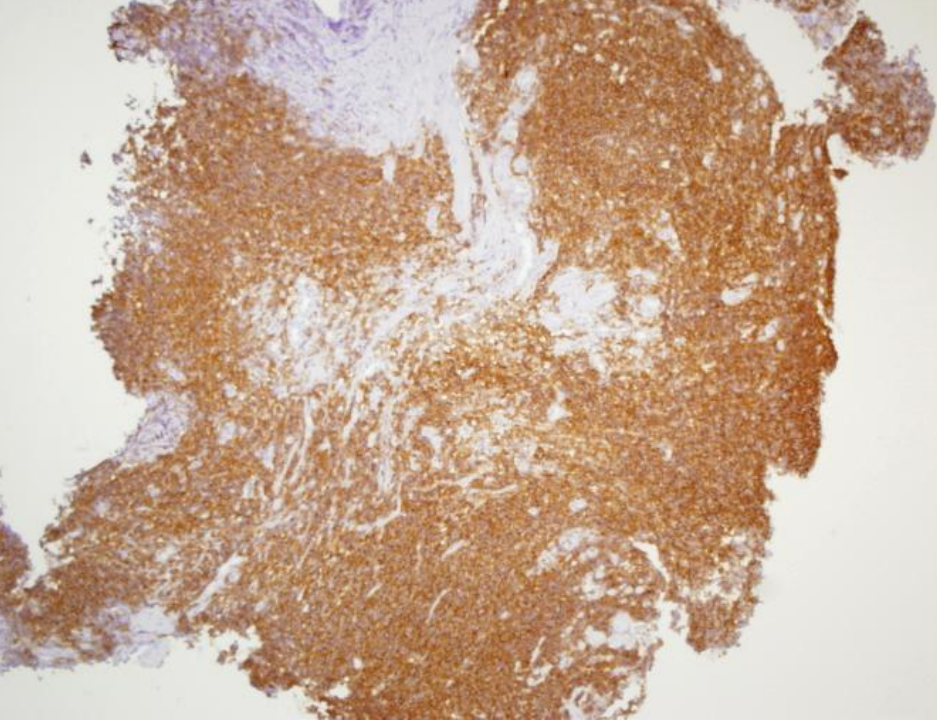


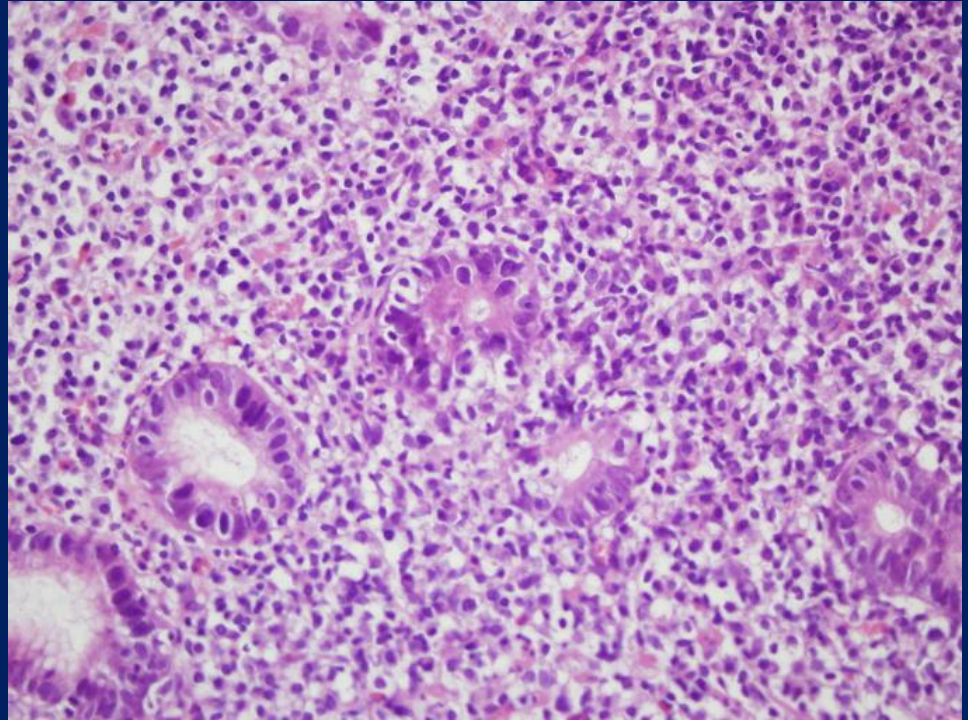
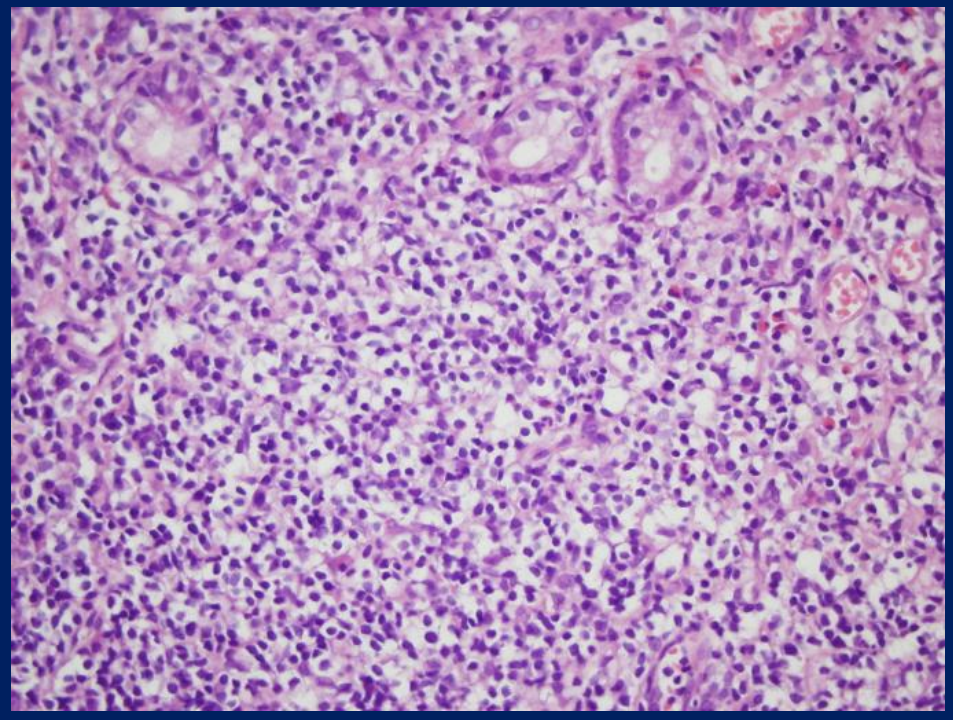
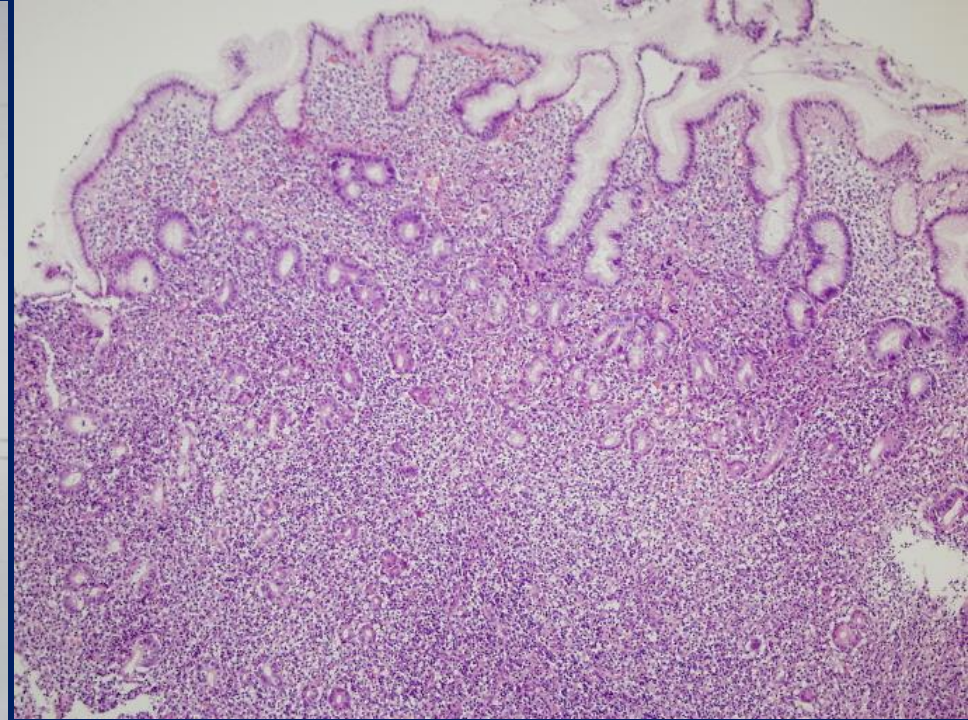
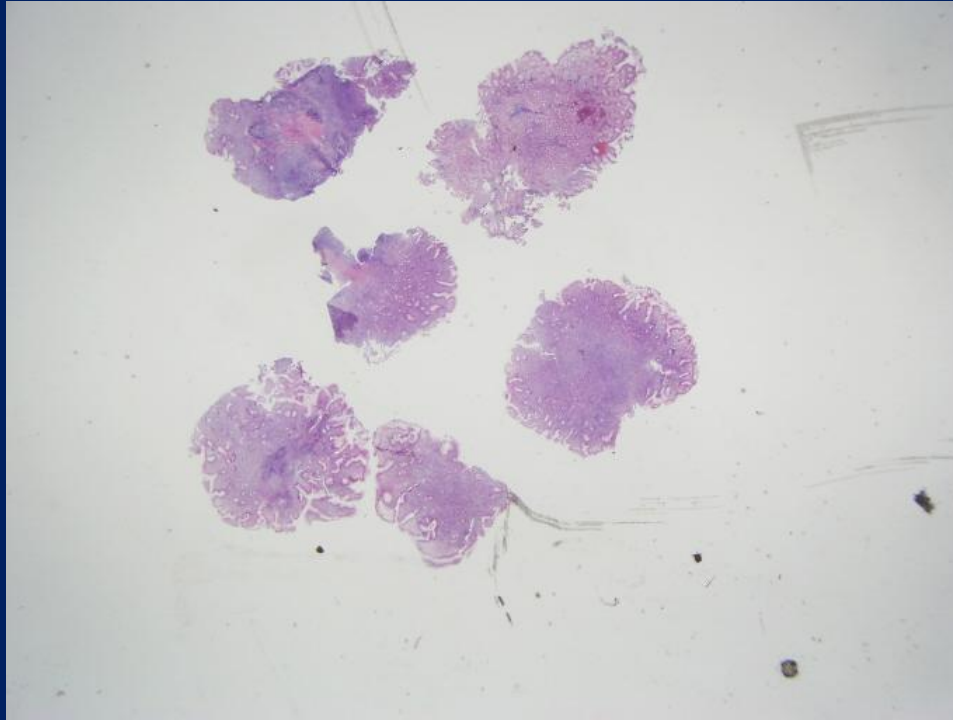


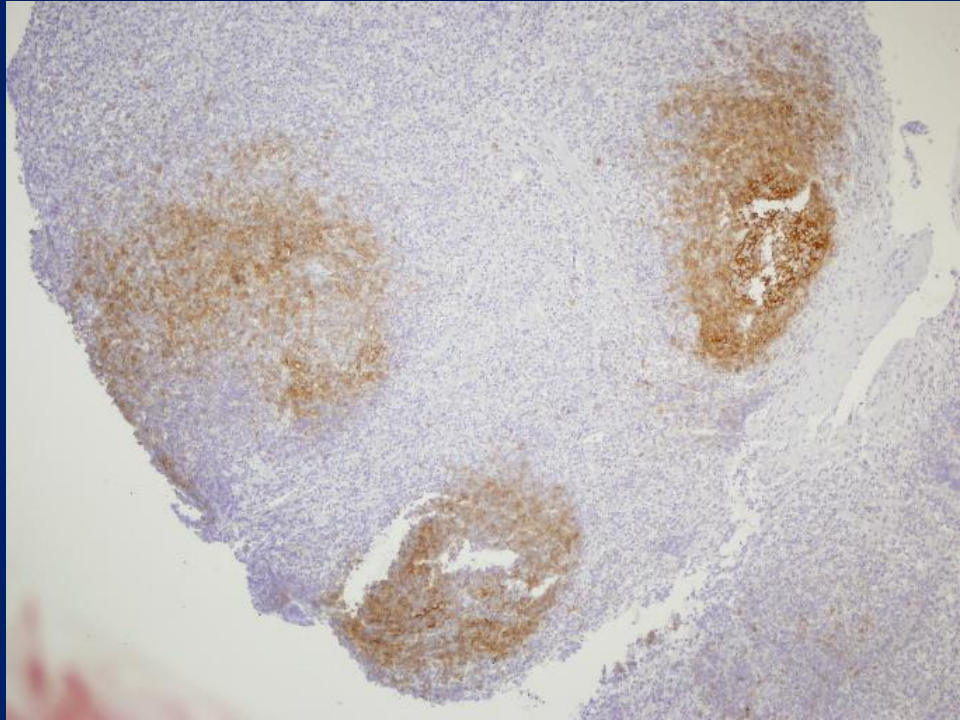
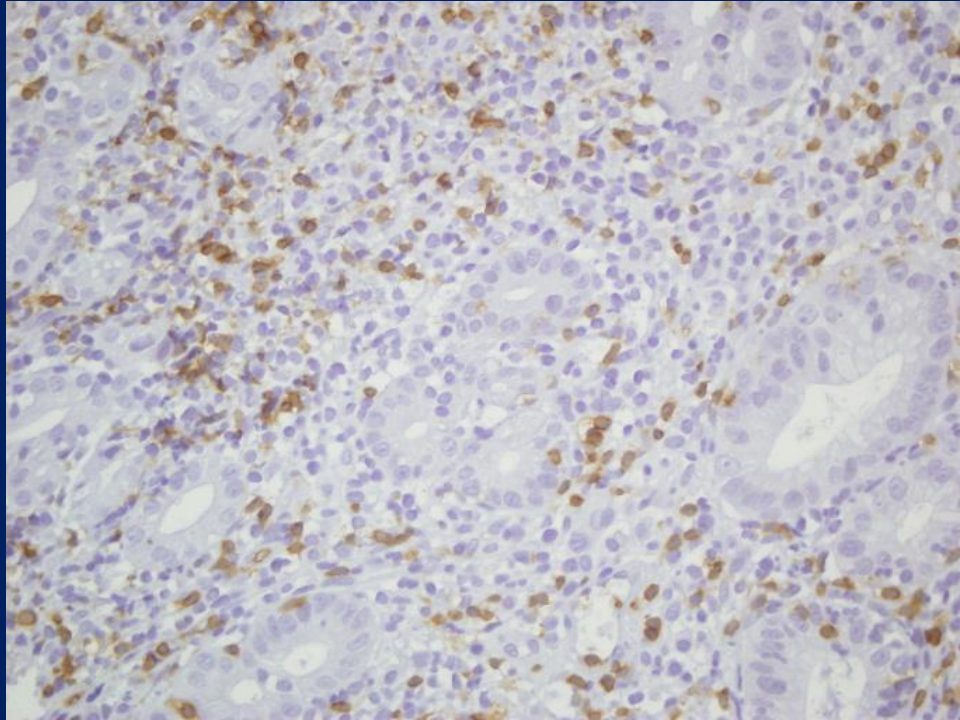
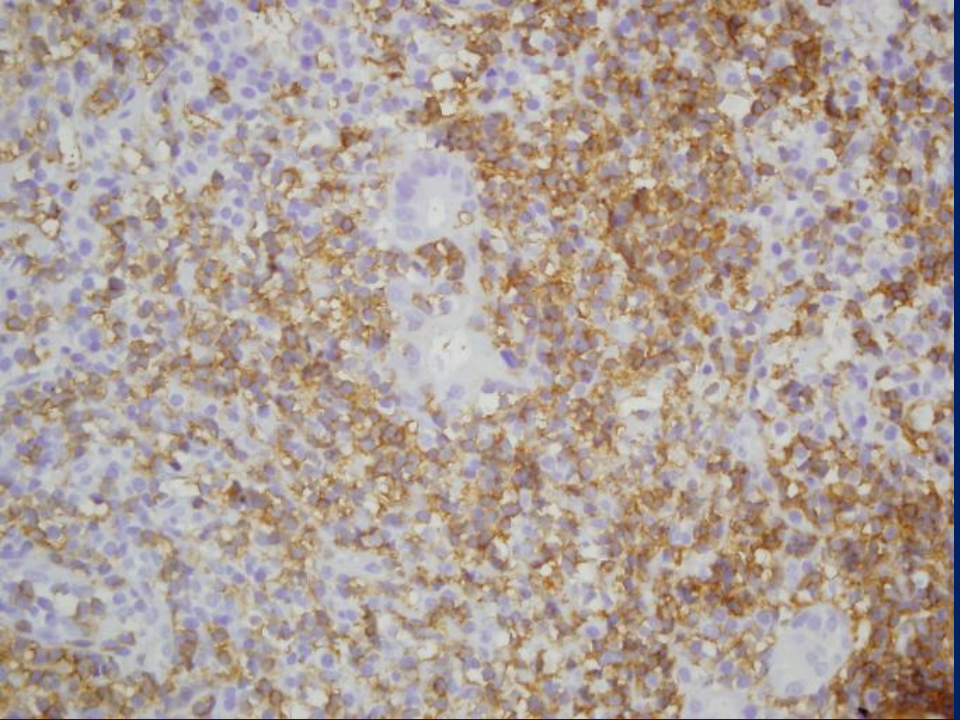
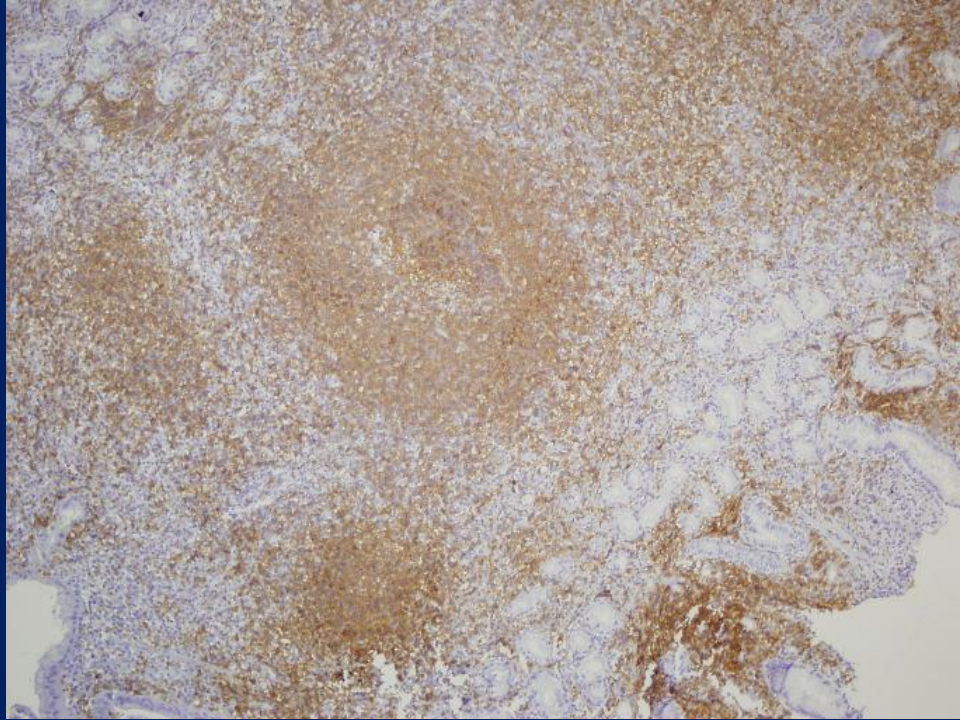




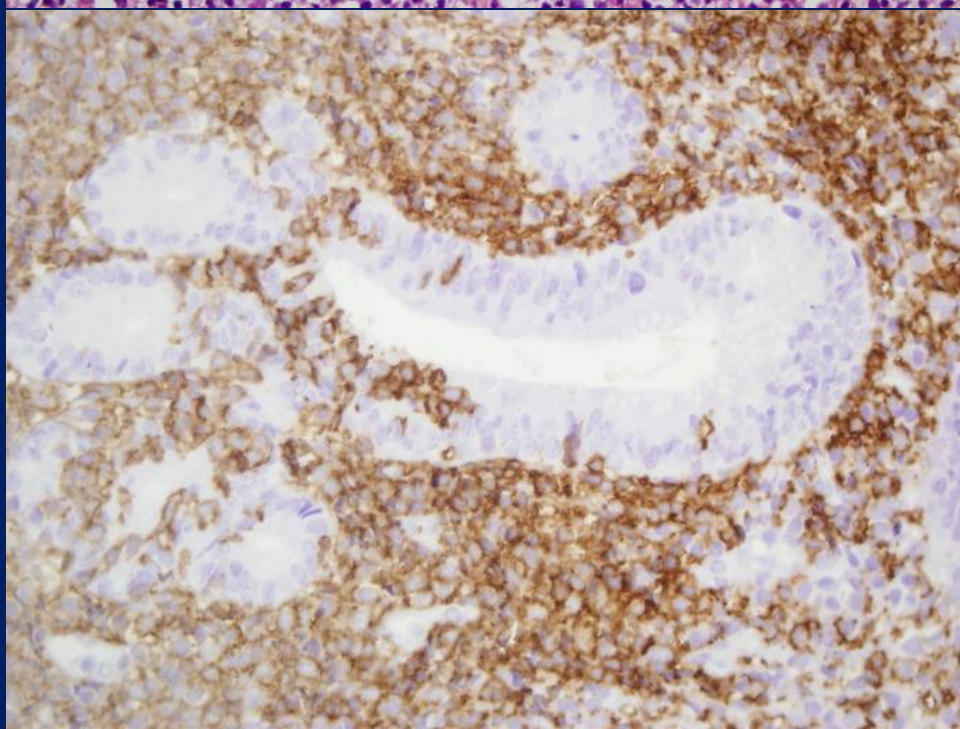
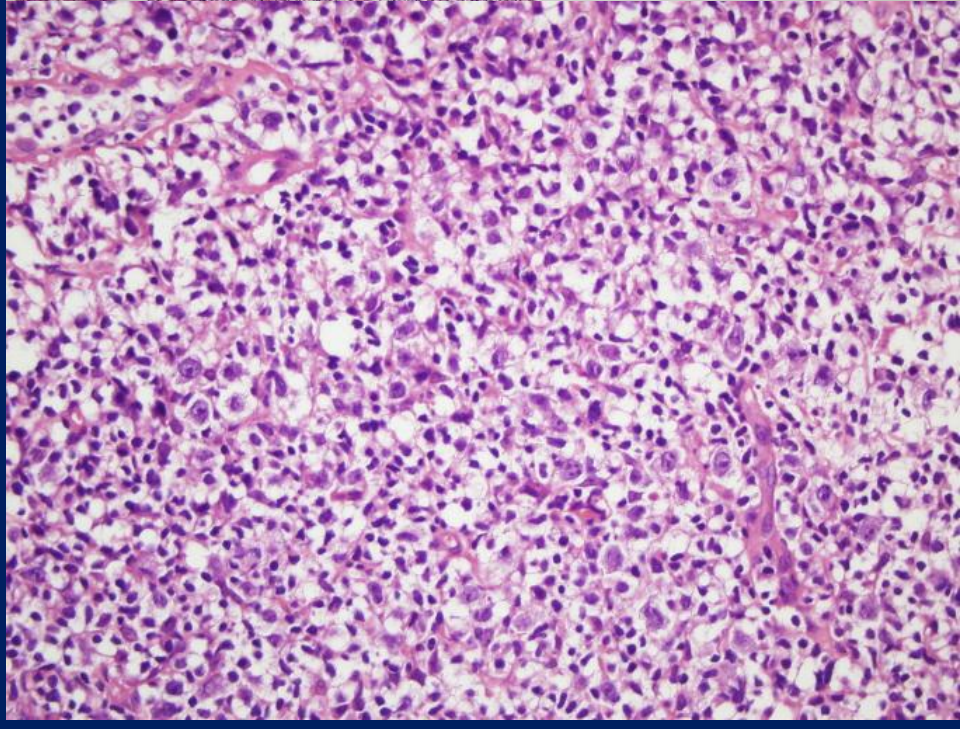
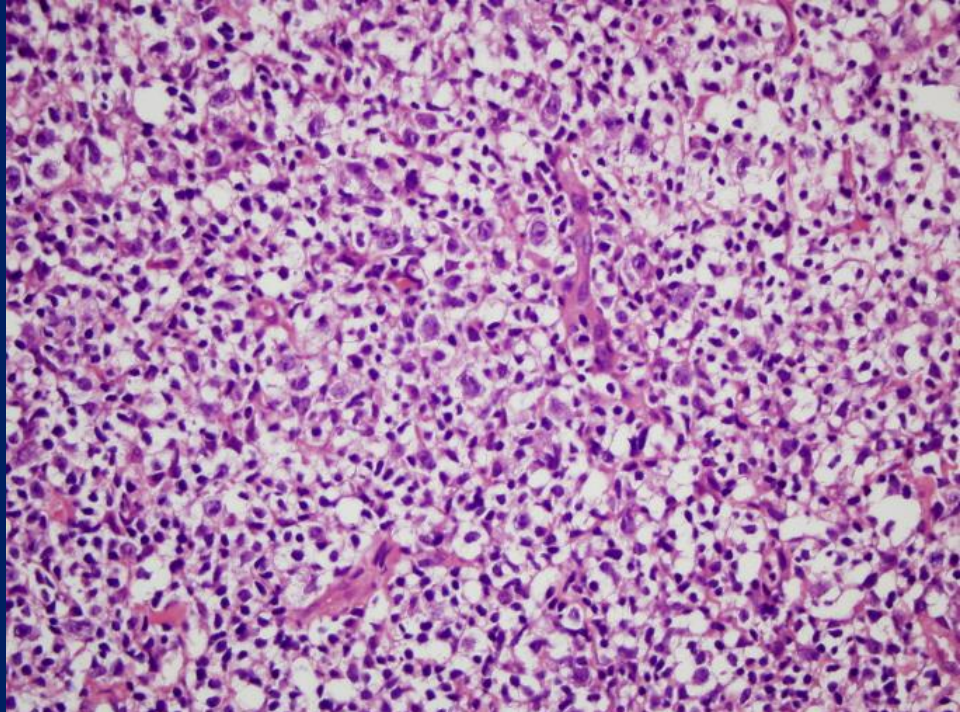
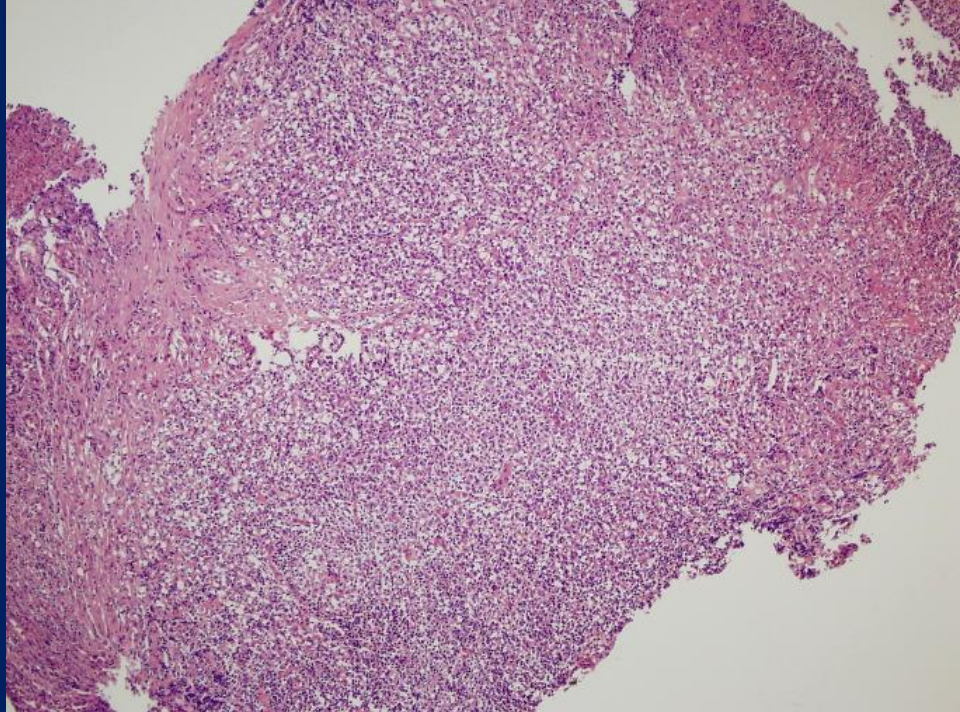


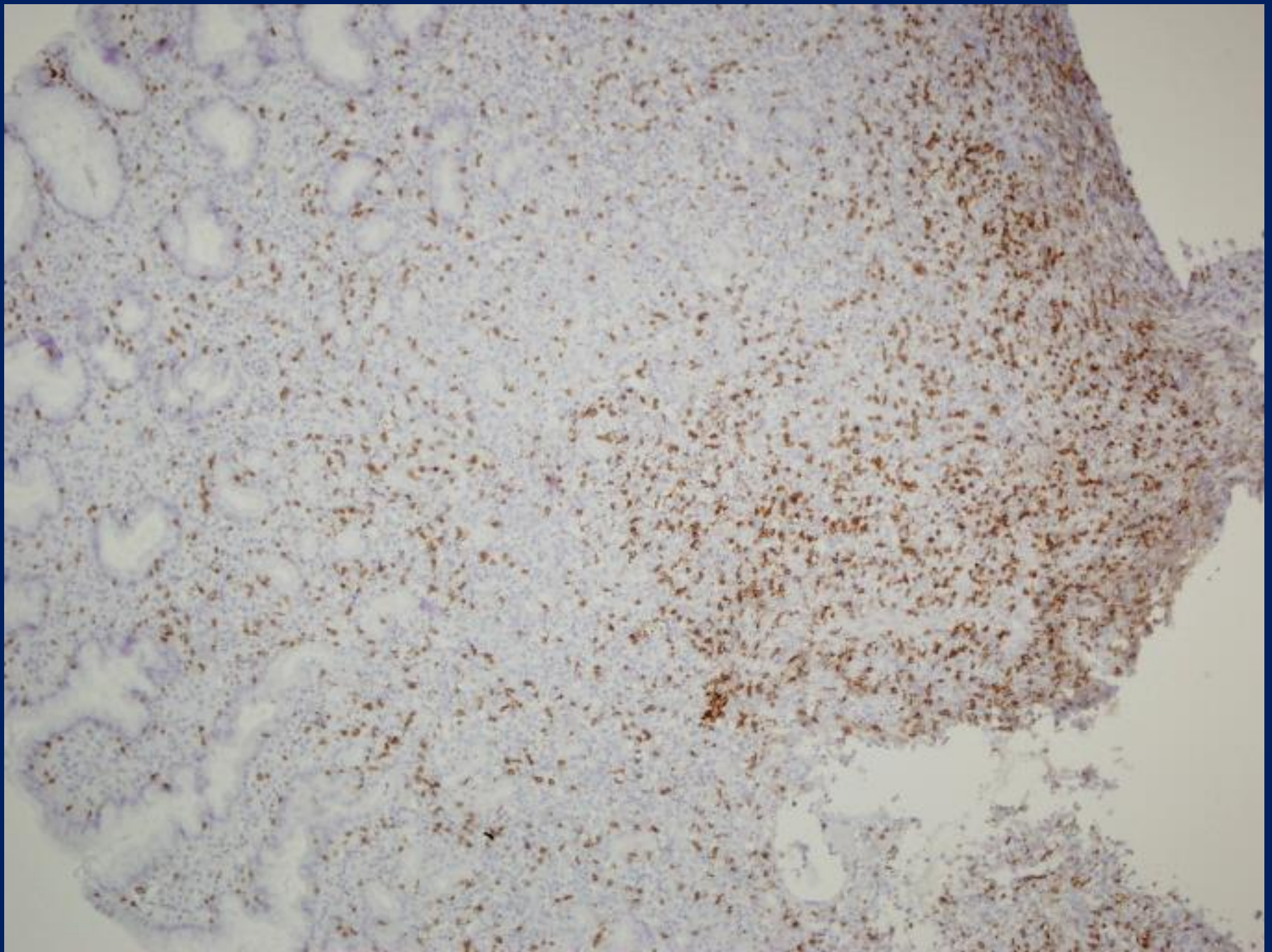






- ▣ Sentroblast- yada immunoblast-benzeri hücreler çok fazla* (%10, 20 hcr) olduğunda yada solid tabakalar oluşturduğunda tanı:
MALT lenfomanın eşlik ettiği DBBHL
(multipl biyopsi!)
- ▣ "Yüksek dereceli MALT lenfoma" tanısı kullanılmamalıdır.
- ▣ GM fragmanlarına dikkat.....





İmmunohistokimya:

- ▣ Ig M > Ig A veya Ig G
- ▣ IPSID'de plazma hücreleri ve marjinal zon hücreleri α ağır zincir
- ▣ CD20 +, CD79a +,
- ▣ CD5 -, CD23 -, CD10 -, cyclin D1-
- ▣ CD43* +/- (%50),
- ▣ Ki 67
- ▣ CD21 ve CD35 ile genişlemiş FDH ağı

Genetik:

- ▣ Ig ağır ve hafif zincir genlerinde yeniden düzenlenme, somatik hipermutasyon
- ▣ t (11;18) (q21;q21)..... **API2-MALT1**
- ▣ t (1;14) (p22;q32)..... **IGH-BCL10**
- ▣ t (14;18) (q32;q21)..... **IGH-MALT1**
- ▣ t (3;14) (p14;q32)

- ▣ Trisomi 3, Trisomi 12, Trisomi 18

Prognoz:

- ▣ Sessiz gidiş, yavaş yayılım, uzun süre lokalize.
- ▣ Gastrik duvarda yayılım derinliği, perigastrik LN
- ▣ Diğer ektranodal alanlara yayılım.
- ▣ Uzak LN ve Kİ tutulumu seyrek, geç dönemde.
- ▣ Diğer ektranodal alan ve Kİ tutulumu prognozu kötüleştirmez.
- ▣ Yıllar sonra rekürrens,
- ▣ **DBBHL'ya transformasyon**

"Paris Staging System"

- ▣ "European Gastrointestinal Lymphoma" grubu tarafından, TNM modifikasyonu:
 - İntestinal duvarda tümör infiltrasyonu derinliği,
 - LN tutulumu yaygınlığı,
 - Lokal doku infiltrasyonu yayılımı.

Antibakteriyal tedavi;

- ▣ HP için antibiyotik tedavisi ilk seçim* (HP-, HP+, DBBHL)
- ▣ t(11;18); HP eradikasyonuna dirençli, yayılım fazla
- ▣ Tedaviye cevap; "Groupe d'Etude des Lymphomes de l'Adulte" (GELA)
 - Sellüler infiltrat
 - LEL
 - Stromal değişiklik.

skor	Lenfoid infiltrat	LEL	Stromal deęişiklik
* Tam histolojik remisyon	LP'da küçük lenfoid hücreler ve plazma hücreleri yok yada çok az	yok	Normal veya boş LP ve/veya fibrozis
* Olası Minimal rezidüel hastalık	LP/MM ve/veya SM'da lenfoid nodül veya lenfoid hücre topluluęu	yok	LP boş ve/veya fibrozis
Cevap +, Rezidüel hastalık	LP'da bezleri çevreleyen yoğun, diffüz yada nodüler infiltrat	+/-	Fokal boş LP ve/veya fibrozis
Deęişiklik yok	Yoęun diffüz veya nodüler infiltrat	+/-	Deęişiklik yok

Raporlama;

- ▣ İlk tanıda;
 - WHO'ya göre lenfoma tipi,
 - Mukozal tutulum alanı,
 - HP durumu,
 - İmmunfenotipik profil yer almalıdır.
Eğer uygulandıysa; IgH gen rearr. , FISH sonuçları eklenmelidir.
 - Şüpheli olgularda (Wotherspoon 3-4) daha ayrıntılı rapor yazılmalıdır.

- ▣ Tedavi sonrası raporda;
 - GELA kriterleri,
 - HP durumu,
 - İmmunfenotipik sonuçlar,
 - İlk tanı aldığı biyopsi ile karşılaştırma

Ayırıcı tanı;

- ▣ HP gastriti dahil olmak üzere reaktif inflamatuvar olaylar,
- ▣ Diğer küçük B hücreli lenfomalar (FL, MHL, KLL)

Ayırıcı tanı;

- ▣ HP gastriti dahil olmak üzere reaktif inflamatuvar olaylar,

İnfiltrat paterni

Hücre morfolojisi

İmmunfenotip

Moleküler inceleme

- ▣ Diğer küçük B hücreli lenfomalar (FL, MHL, KLL)

Ayırıcı tanı;

- ▣ HP gastriti dahil olmak üzere reaktif inflamatuvar olaylar,
- ▣ Diğer küçük B hücreli lenfomalar (FL, MHL, KLL)

	CD20	CD3	CD5	CD43	CYCD1	CD10
MALT Lenfoma	+	-	-	+/-	-	-
MHL	+	-	+	+/-	+	-
KLL	+	-	+	+/-	-	-
FL	+	-	-	-	-	+

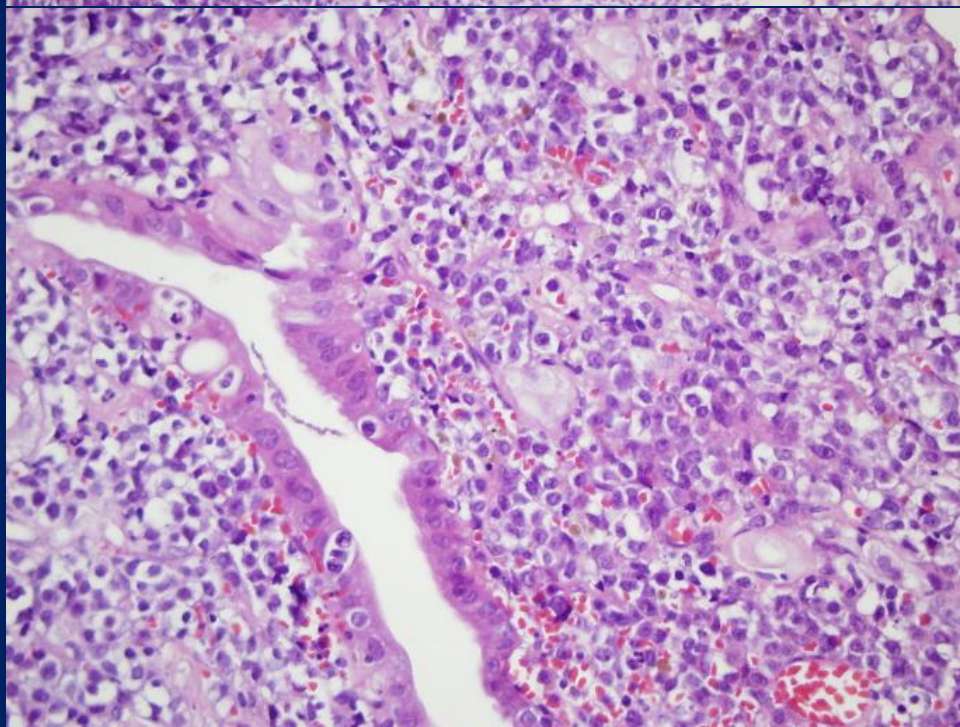
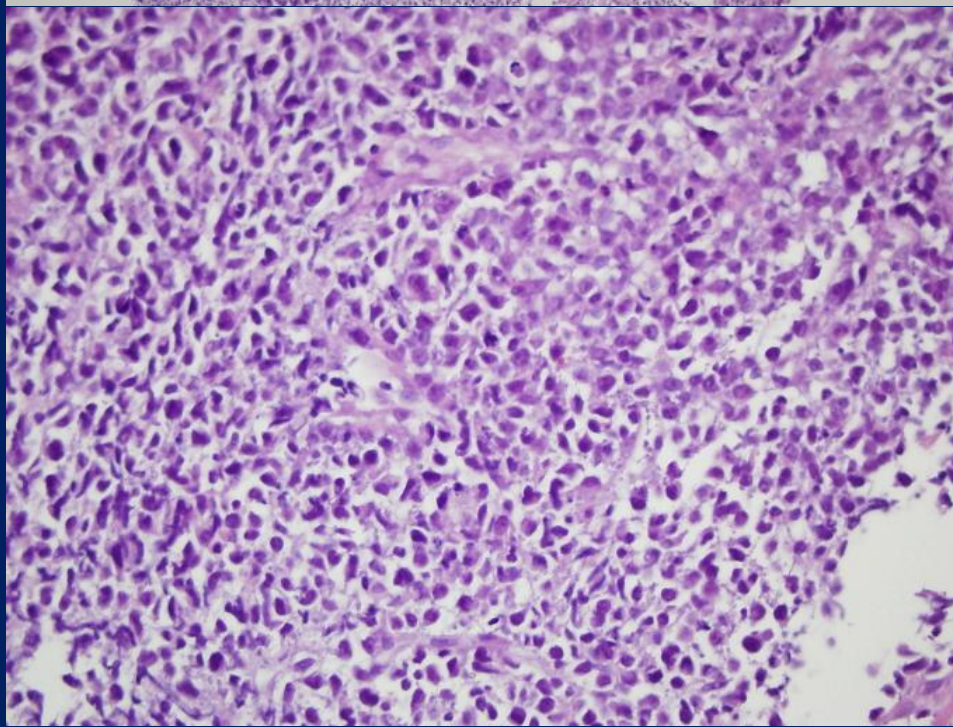
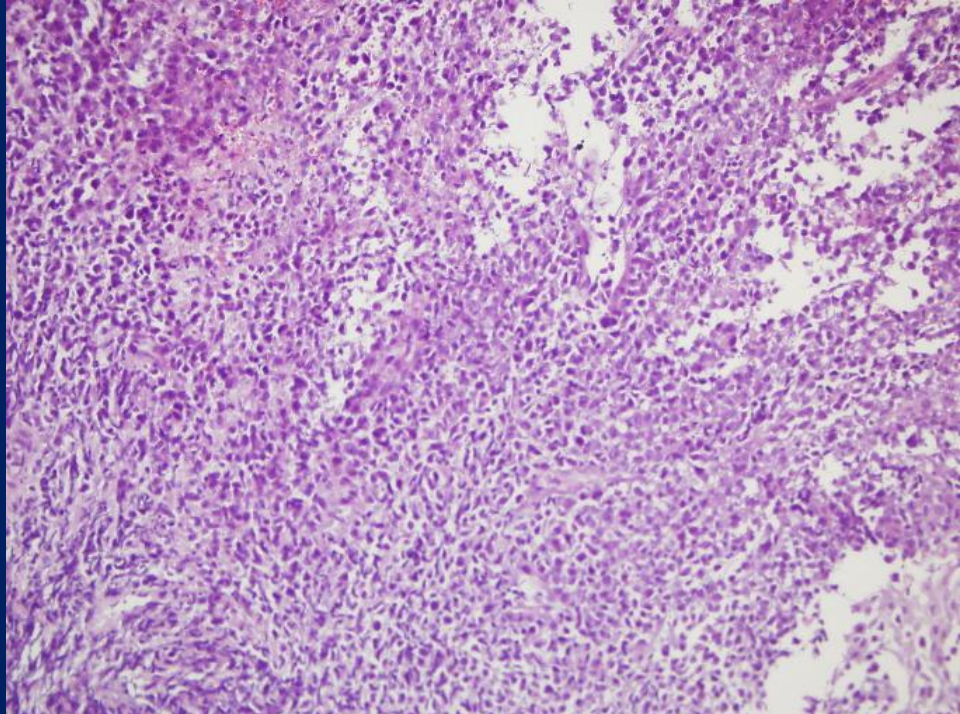
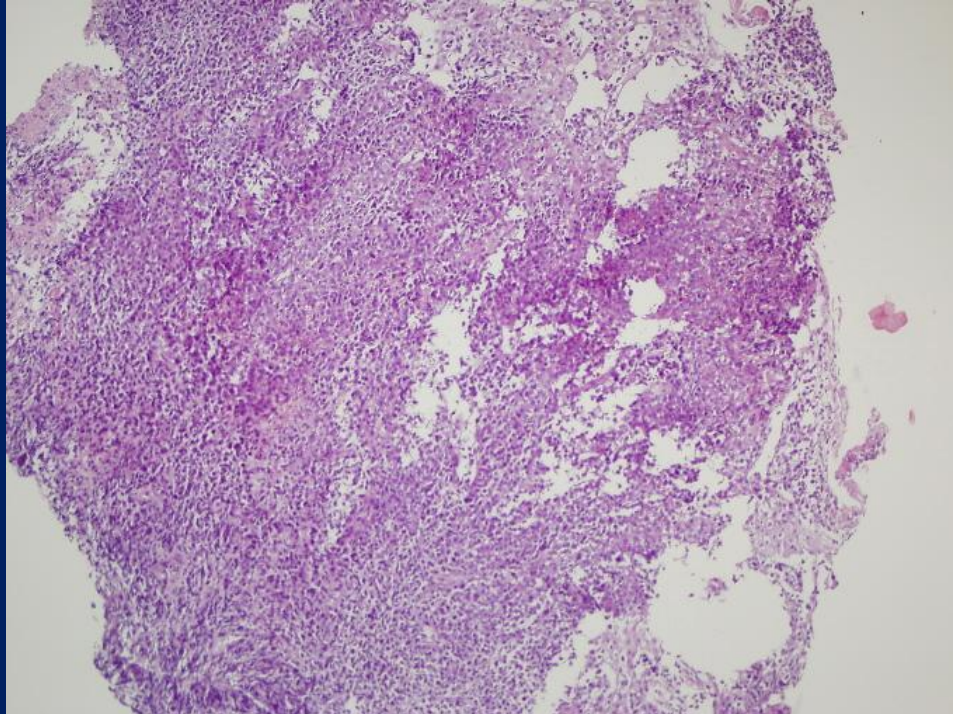
"Immunoproliferative small intestinal disease" IPSID;

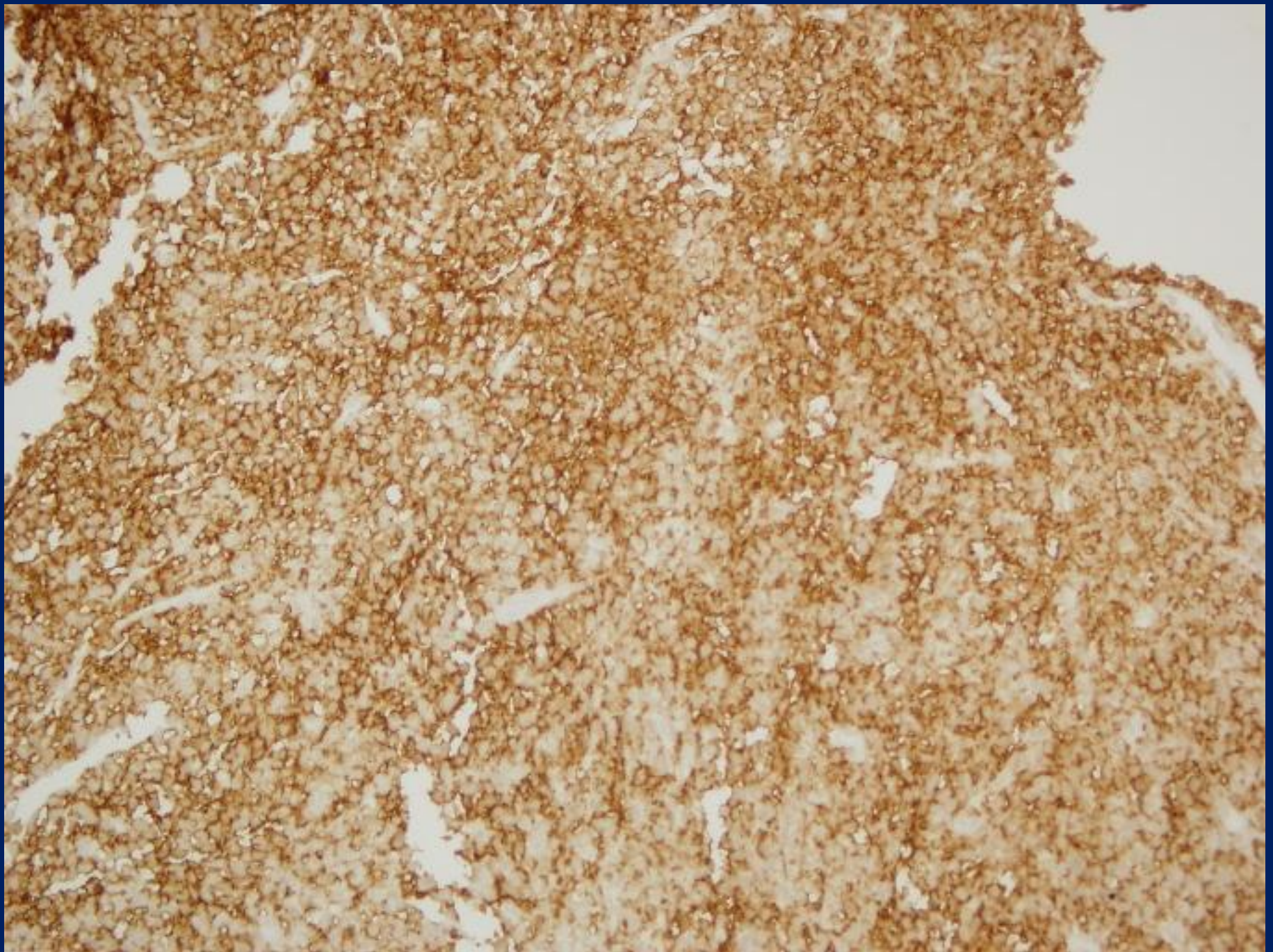
- ▣ Seyrek görülür. Daha önceden "a ağır zincir hastalığı" olarak biliniyordu.
- ▣ Genç adultlarda, malabsorbsiyonla birlikte,
- ▣ GIS diffüz olarak etkilenebilir. Duodenum ve jejunumda daha sık.
- ▣ Villöz atrofi,
- ▣ *Campylobacter jejuni* ???

- ▣ Histolojik olarak; belirgin plazmasitik diferansiyasyon gösteren MALTL özelliğindedir.
- ▣ Büyük hücreli lenfomaya transforme olabilir.

Diffüz Büyük B Hücreli Lenfoma

- ▣ *Gastrik lenfomaların %50'den fazlası*
- ▣ *Küçük biyopsilerde genelde tanı zorluğu olmaz.*
- ▣ *MALTL ile birlikteliği ????*





Ayırıcı tanı;

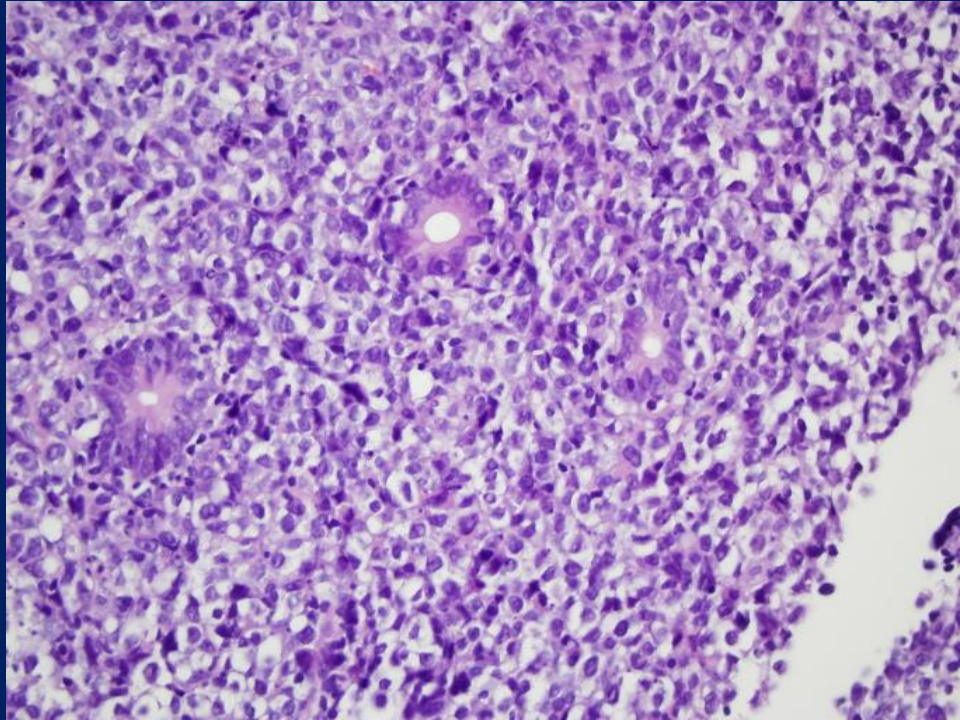
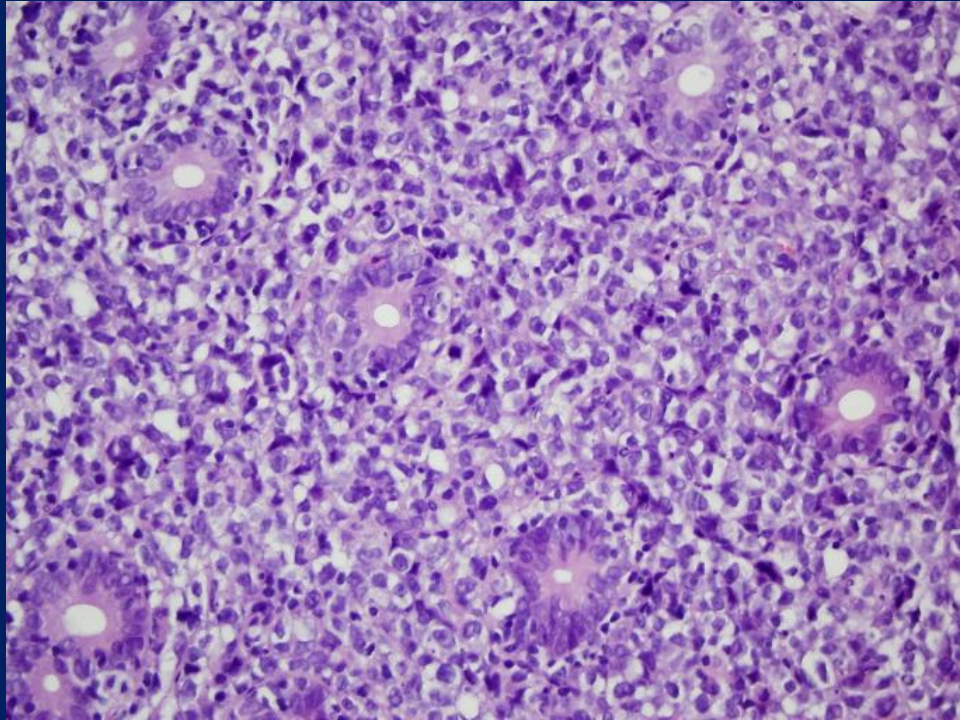
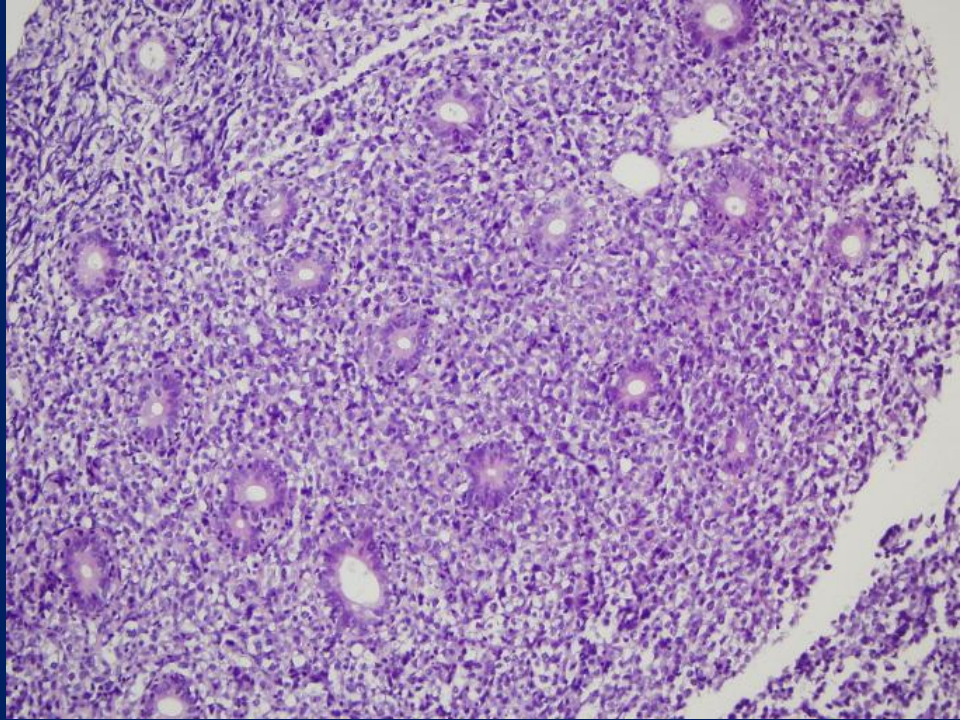
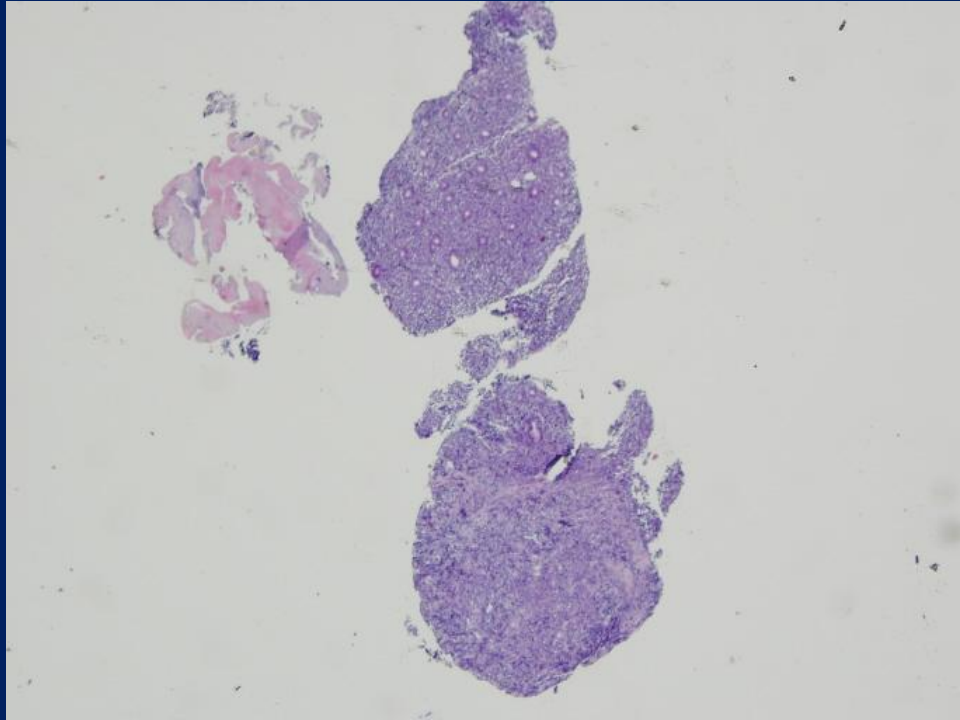
▣ Karsinomdan ayırımında İHK faydalı

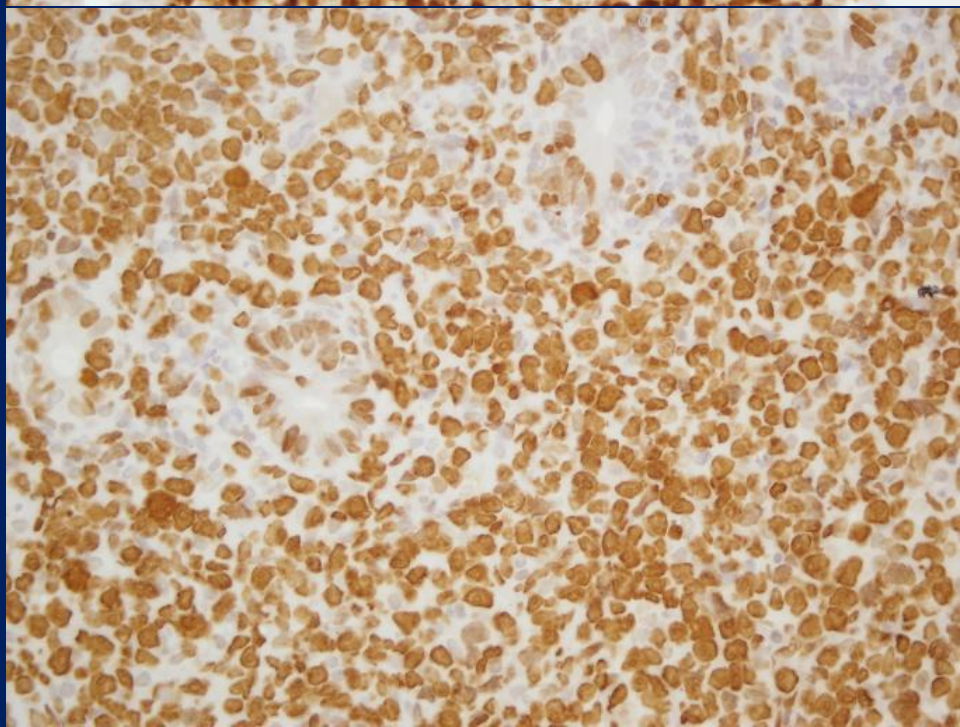
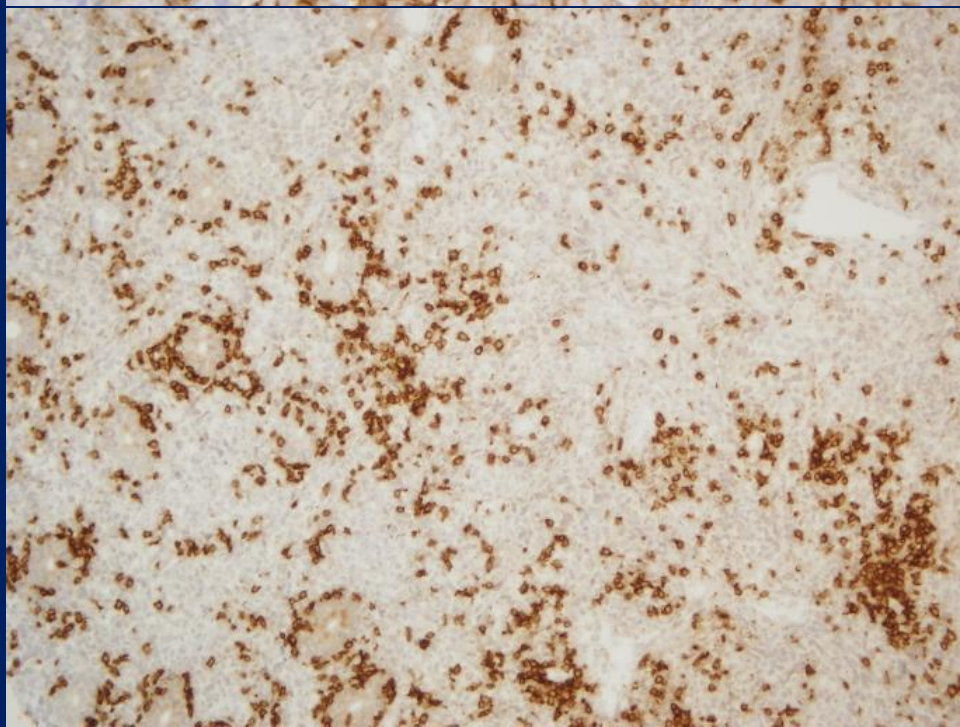
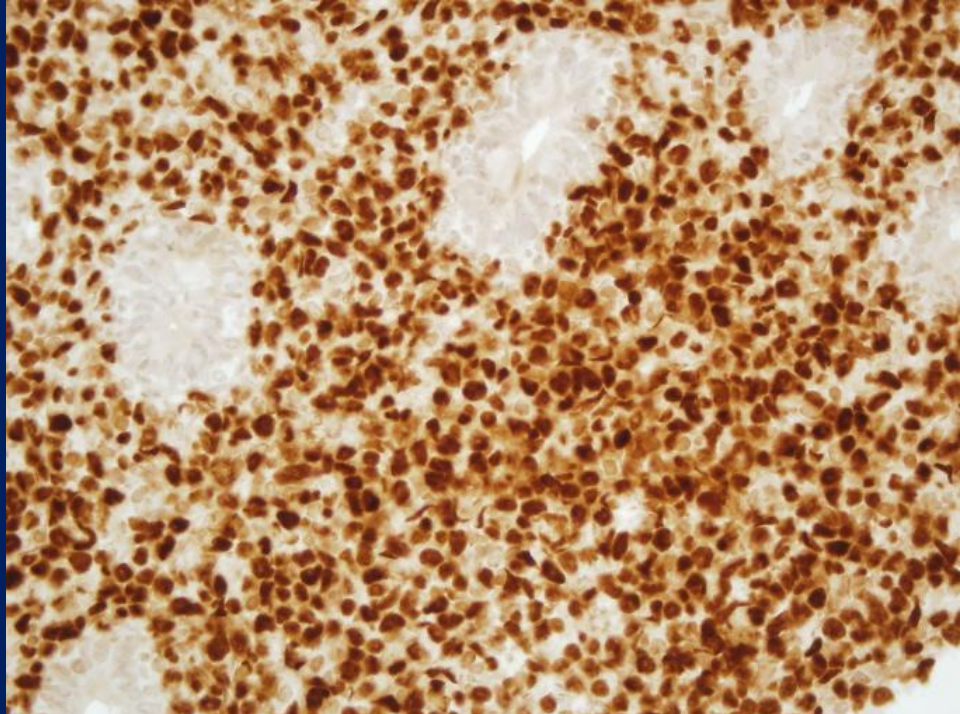
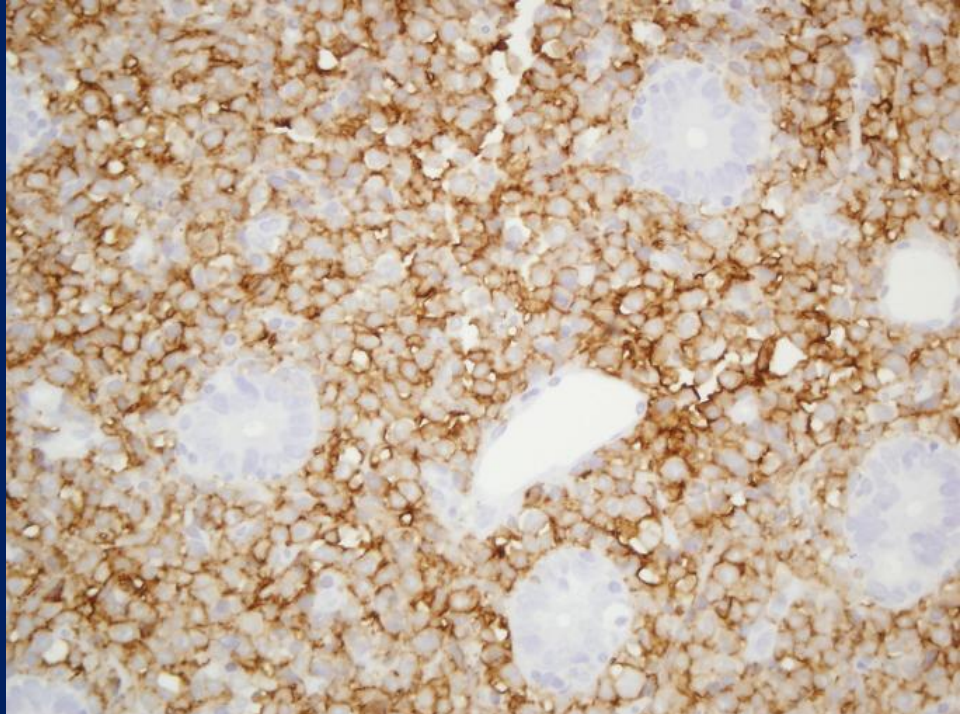
Müsin ve keratin negatif

CD20 pozitif

▣ Malign melanom

▣ Myeloid sarkom

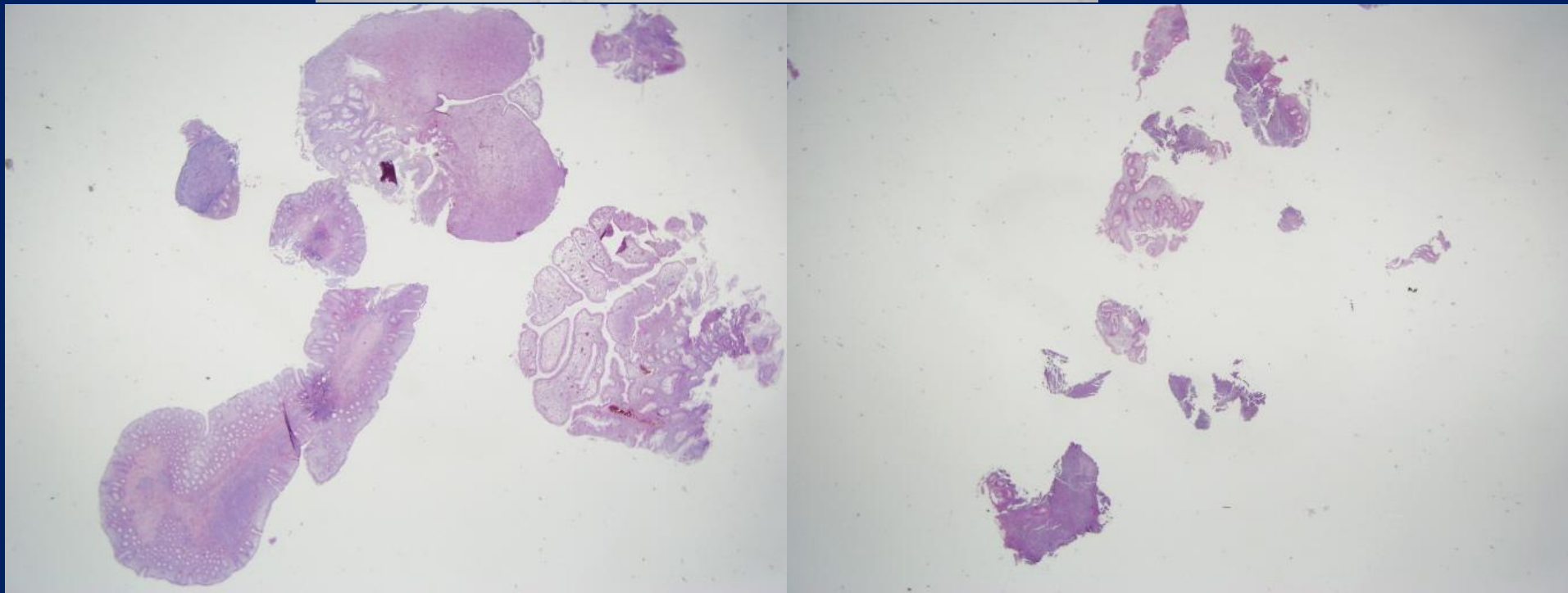
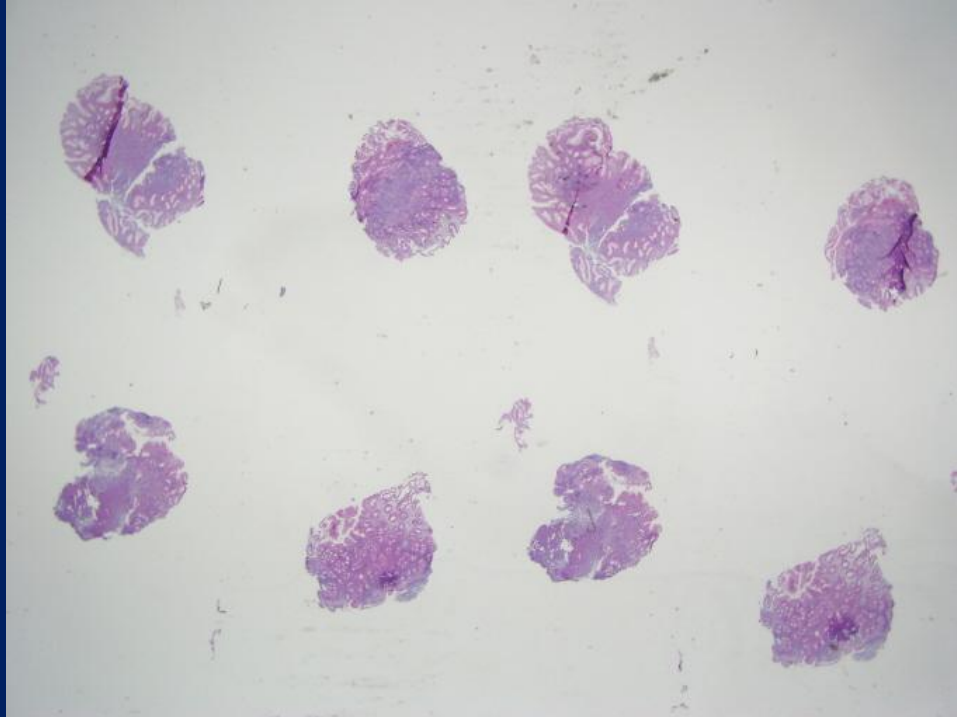


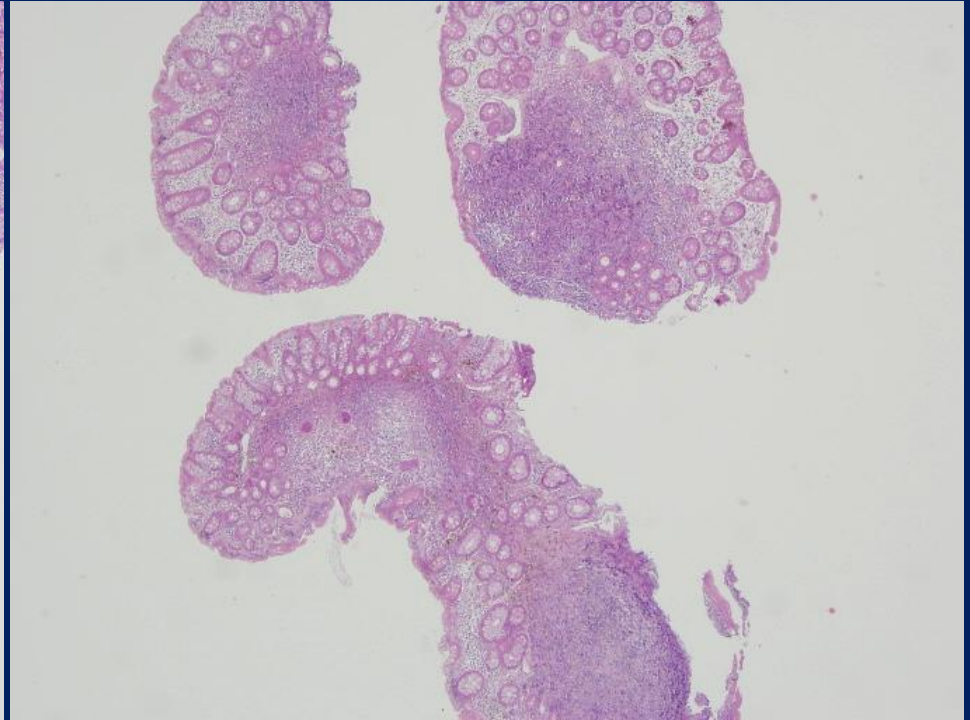
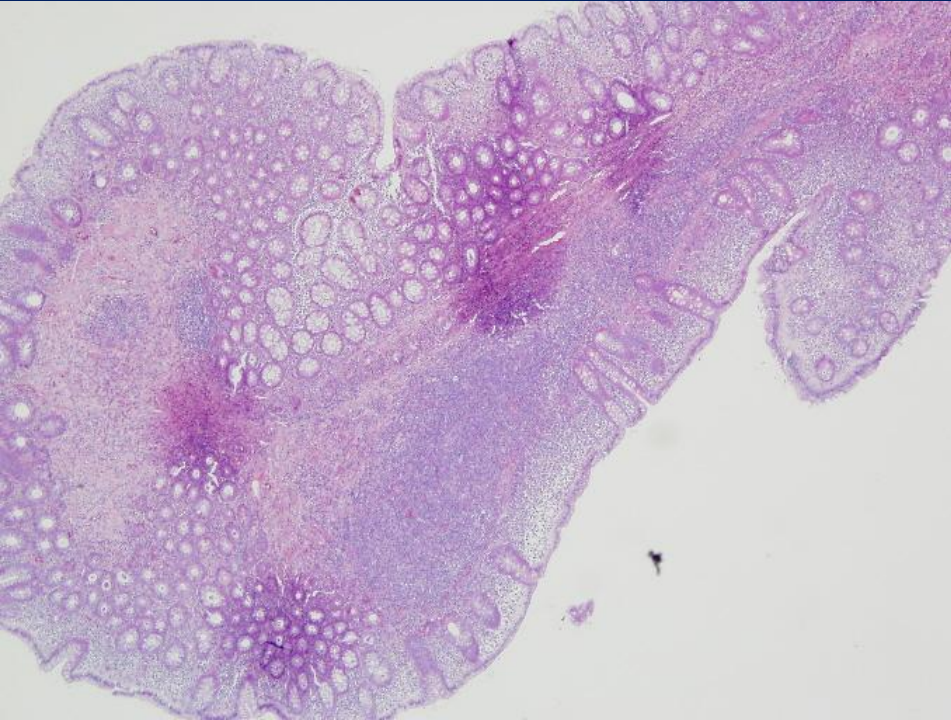
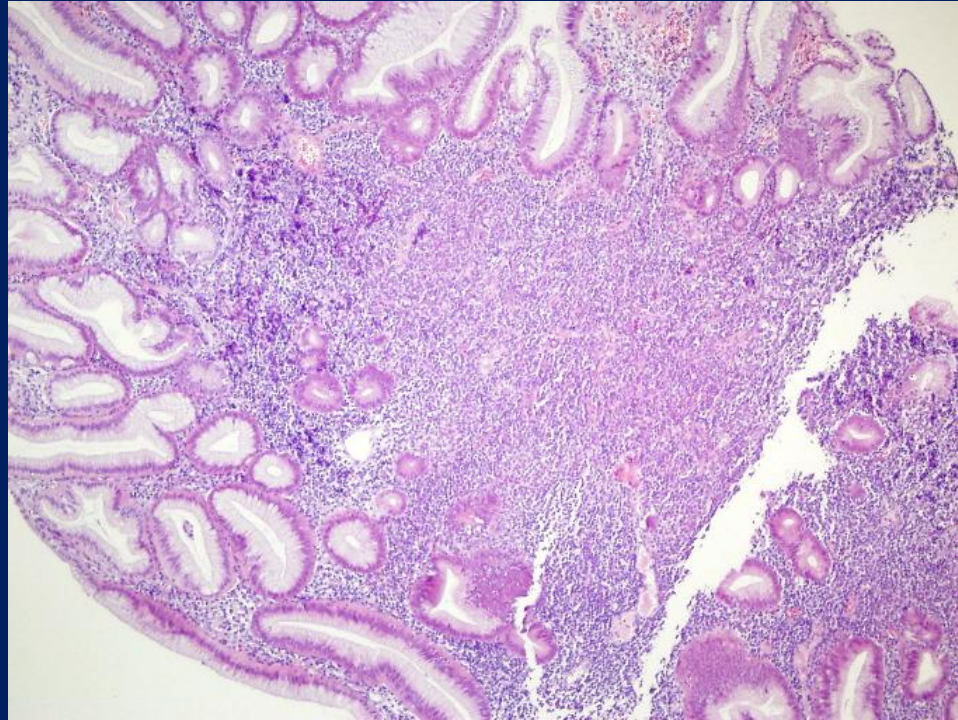


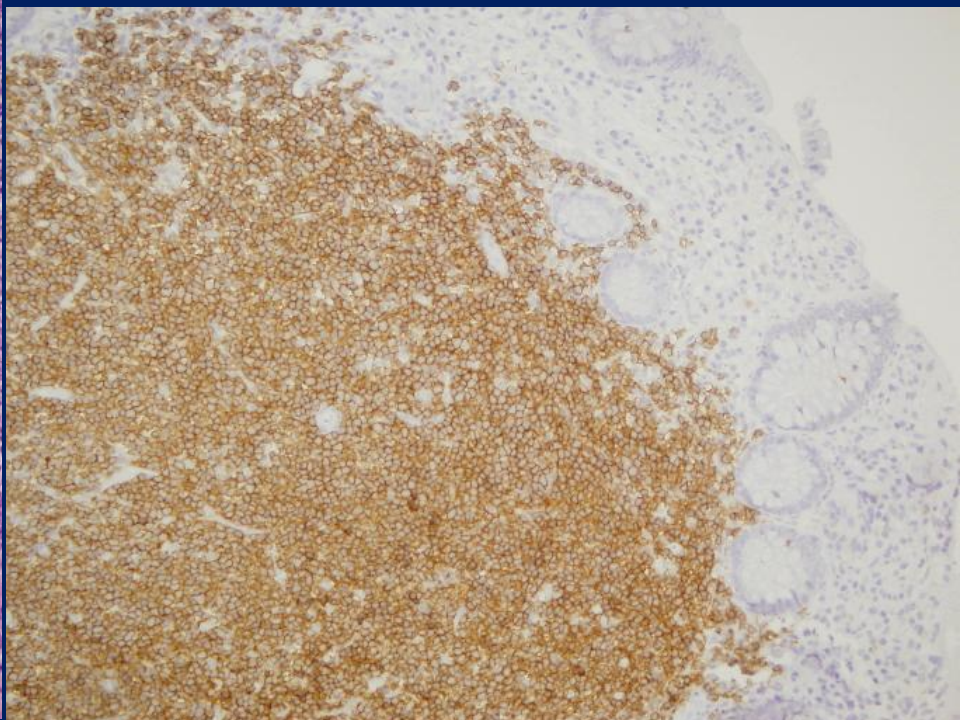
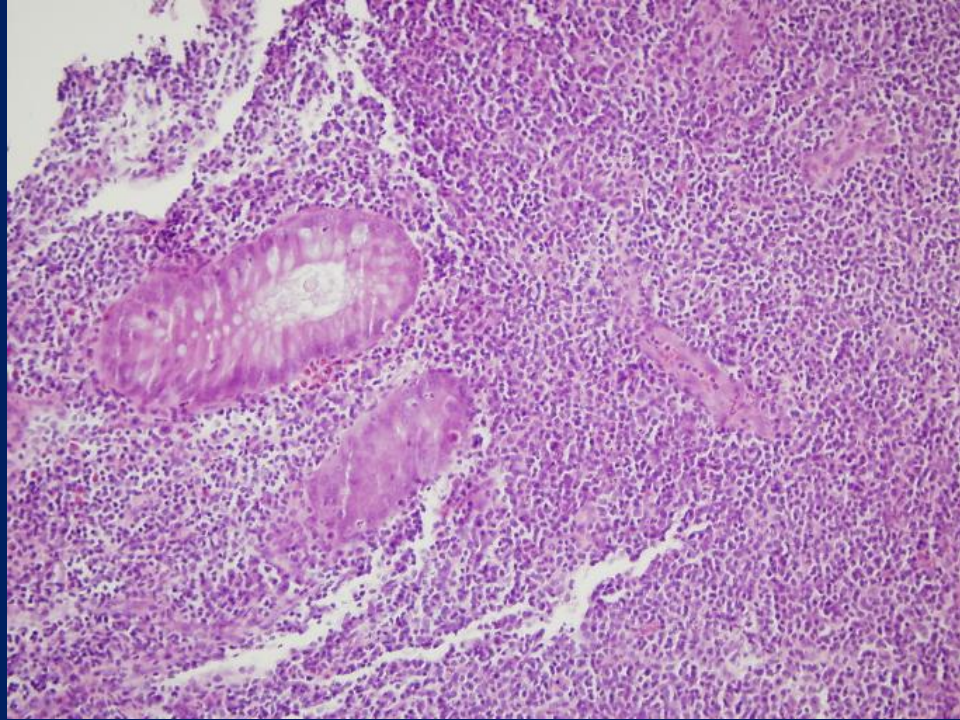
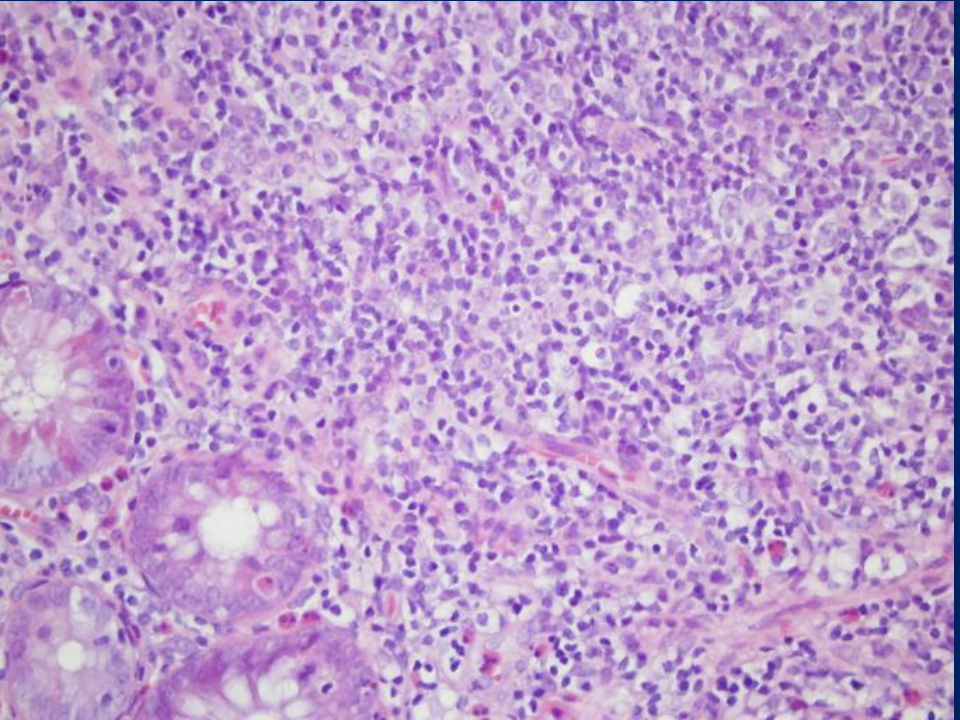
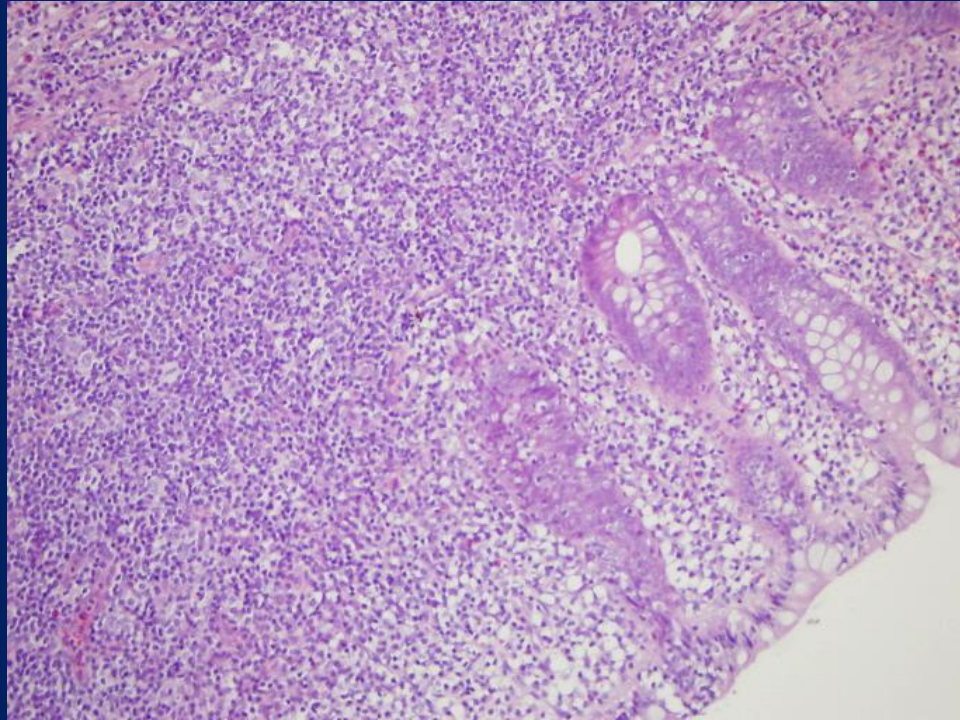
Mantle Hücreli Lenfoma

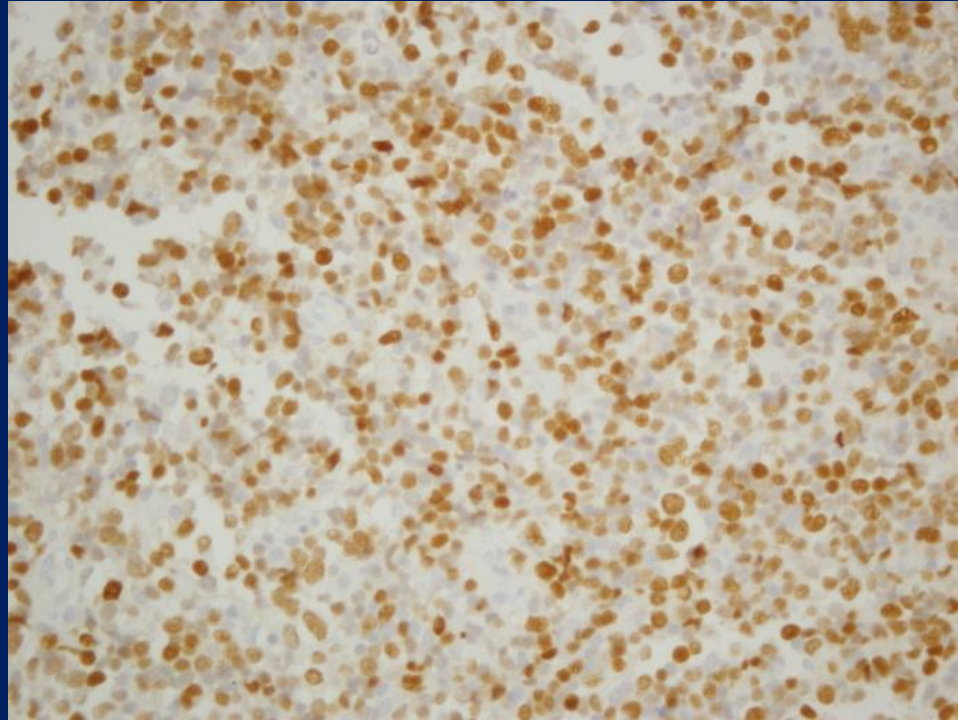
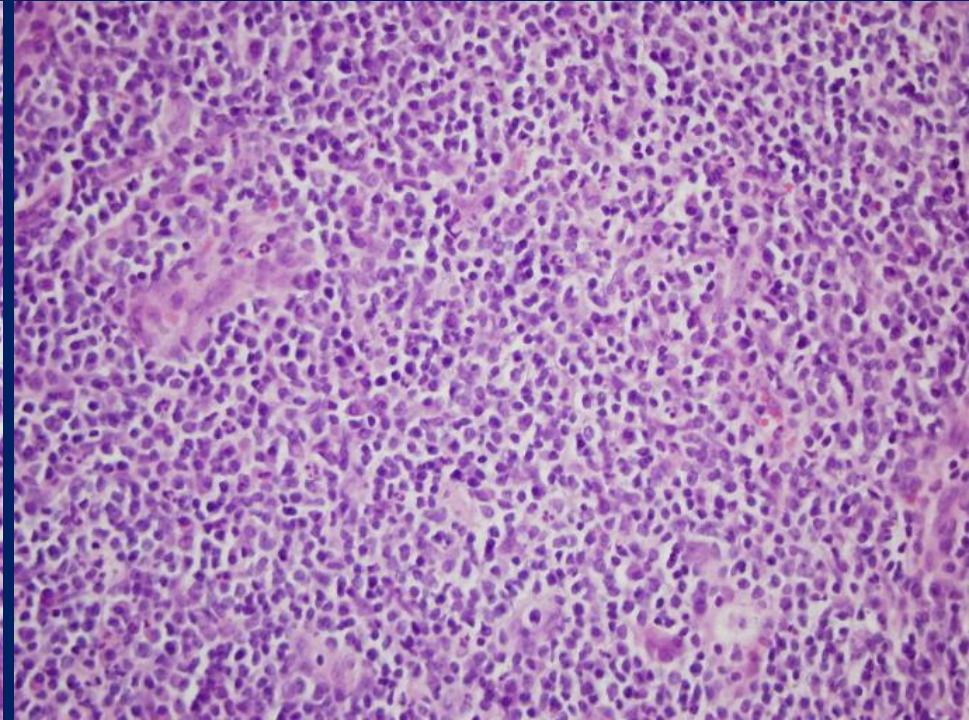
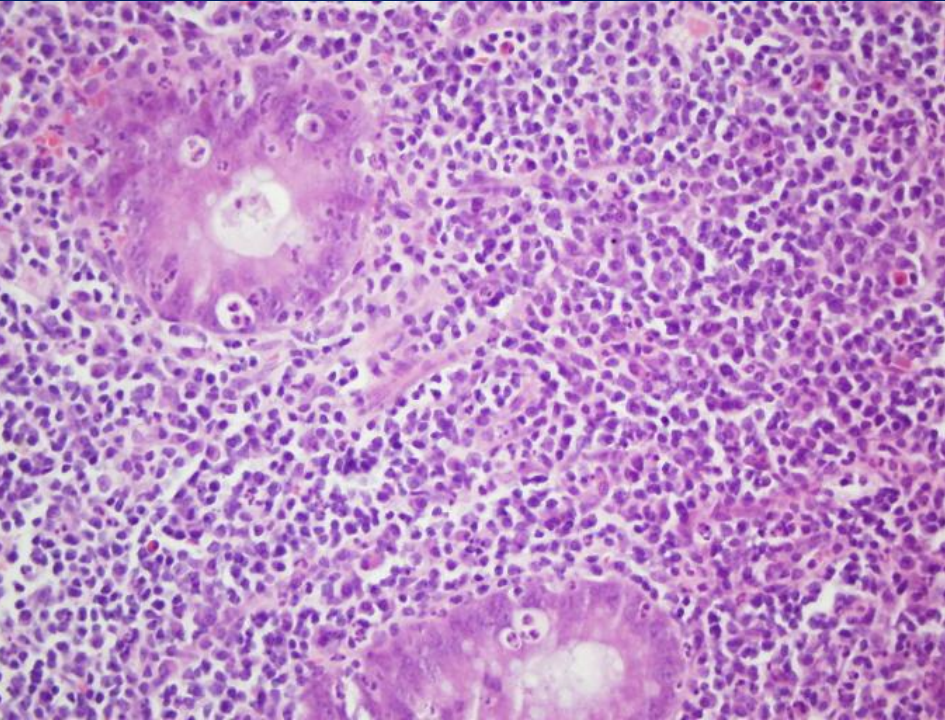
- ▣ GIS B-hücreli NHL'in %4-9'u,
- ▣ Multipl lenfomatöz polipozis olarak görülür.
- ▣ Özellikle ince ve kalın barsakta uzun segmentler halinde, polipoid tutulum olur.
- ▣ Lenfomatöz polipozis; MHL, FL, MALTL

- ▣ Mukoza ve/veya submukozada; atipik sentrosit tipi hücre toplulukları,
- ▣ Nodüler lenfoid infiltrat içinde reaktif GM'ler olabilir.
- ▣ CD20 +, CD5 +, CYCLIN D1+
- ▣ CD23 -
- ▣ Primer MHL; agresif gidişli; (ort 3-4yıl)
- ▣ Sekonder tutulum olabilir.









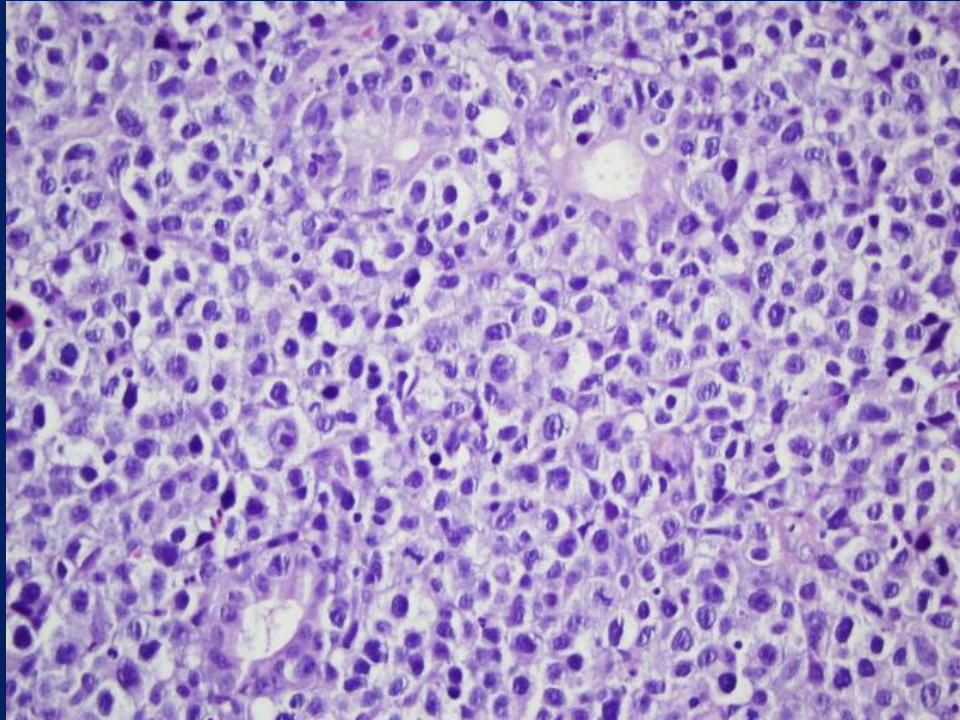
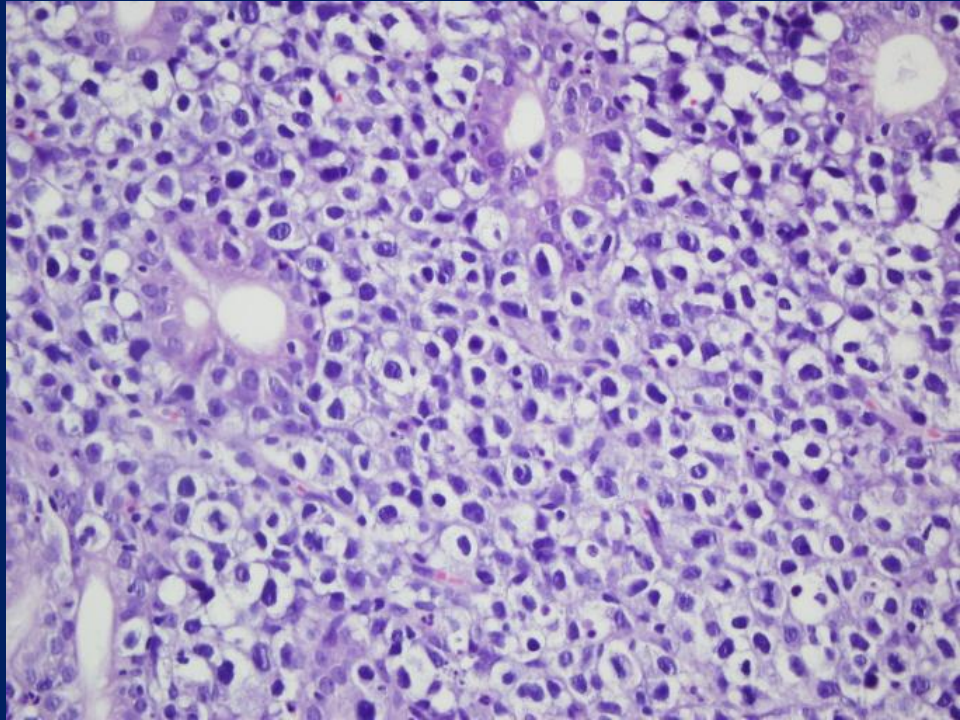
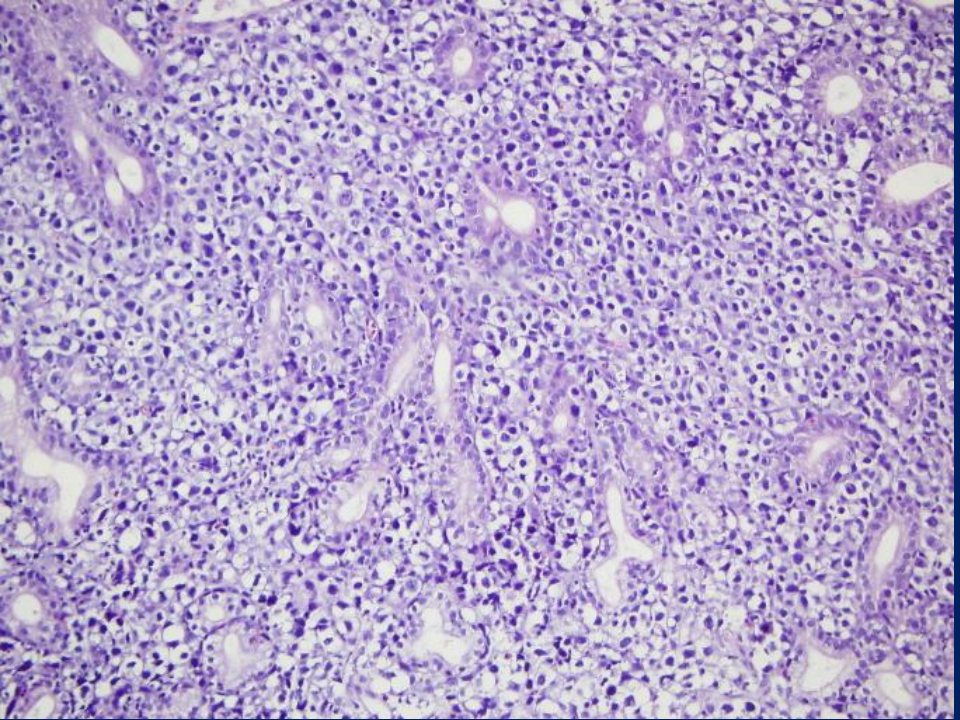
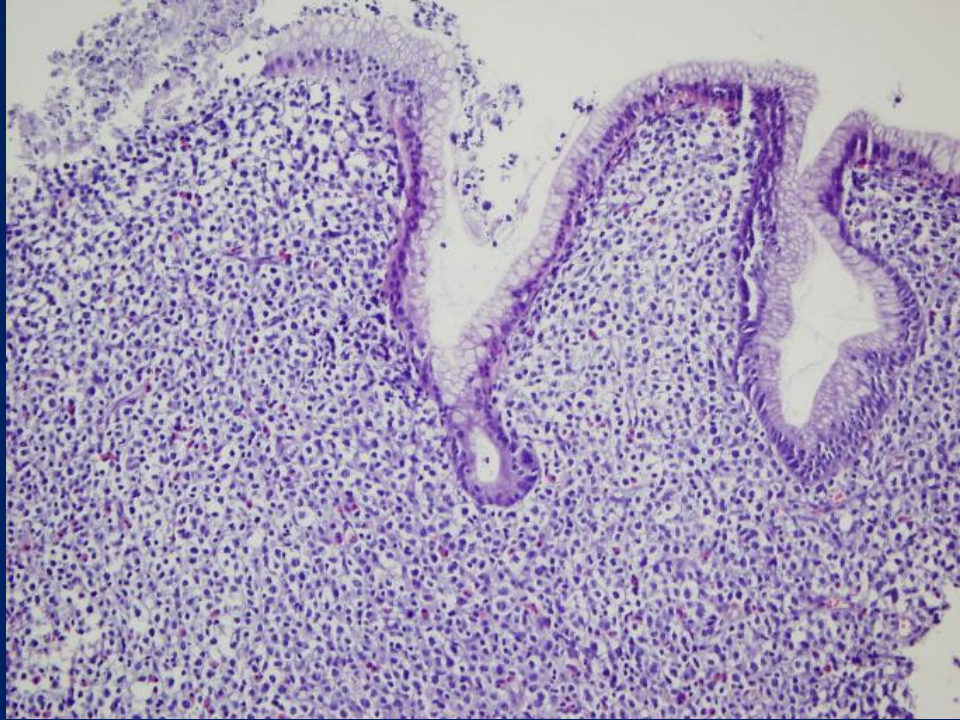
Morfolojik varyantlar;

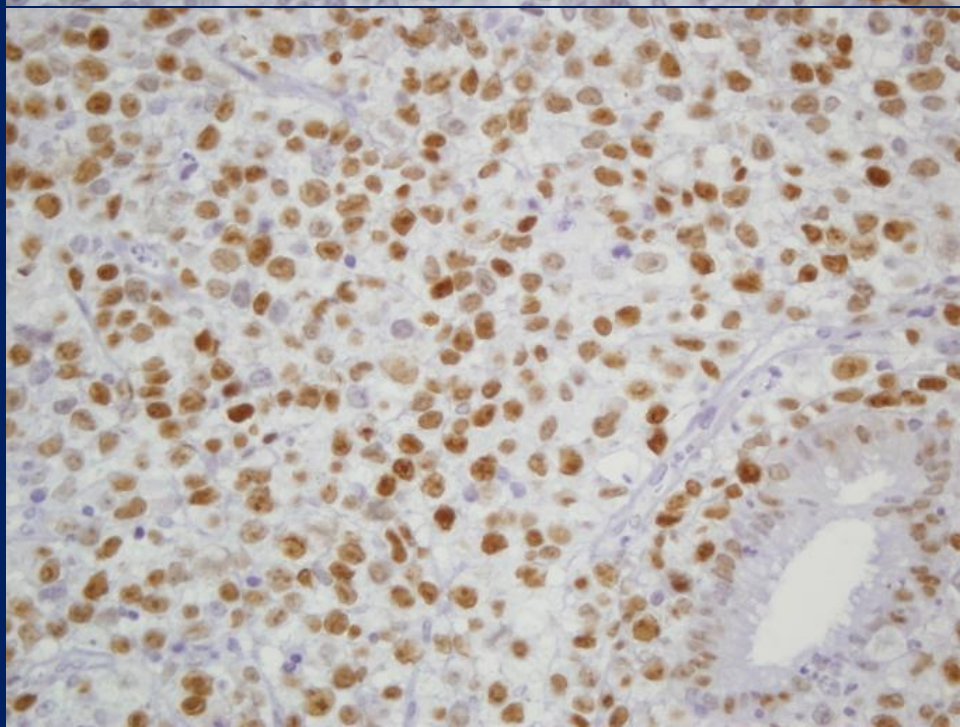
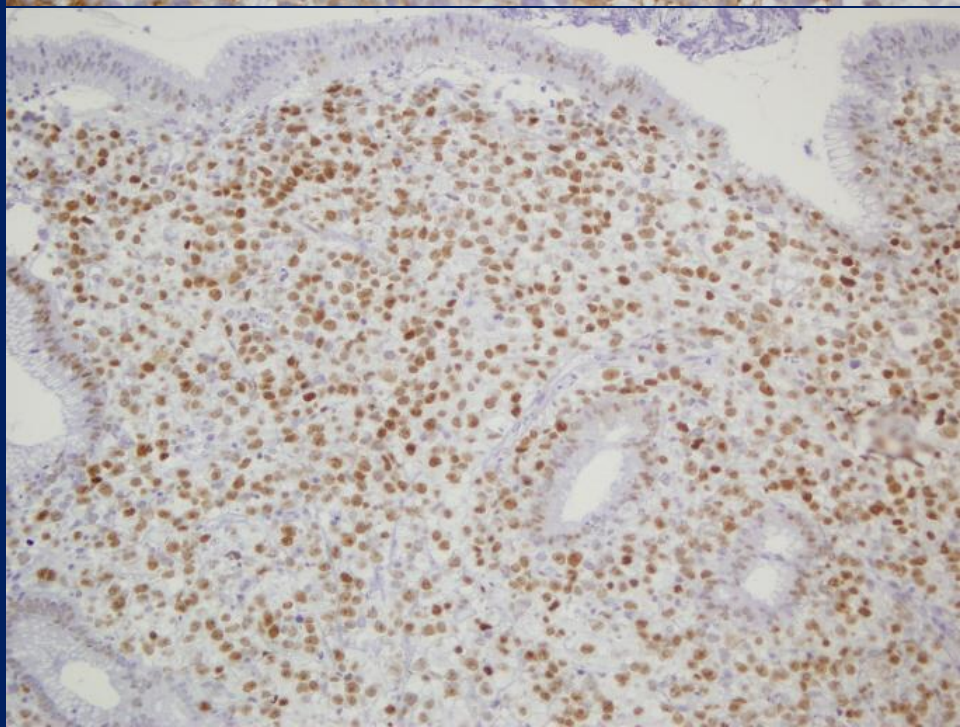
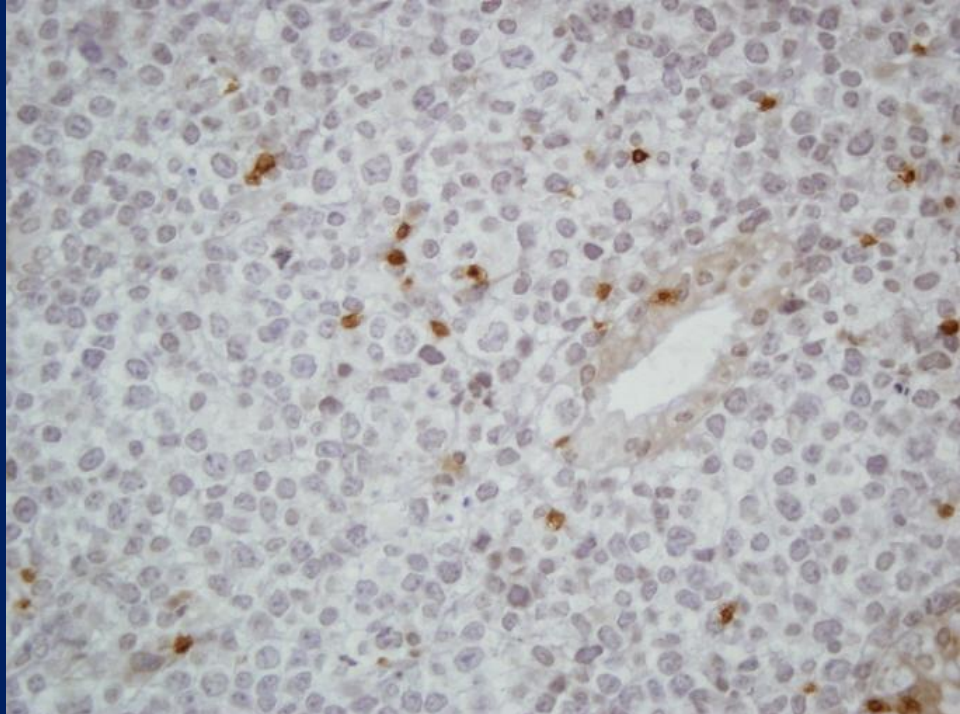
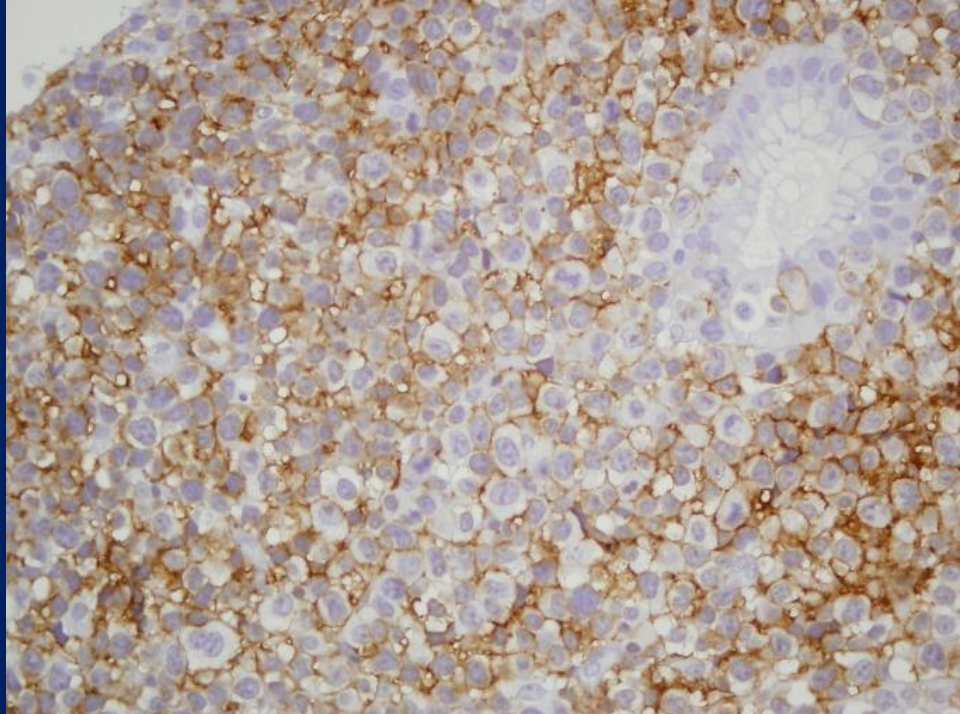
▣ AGRESİF VARYANTLAR

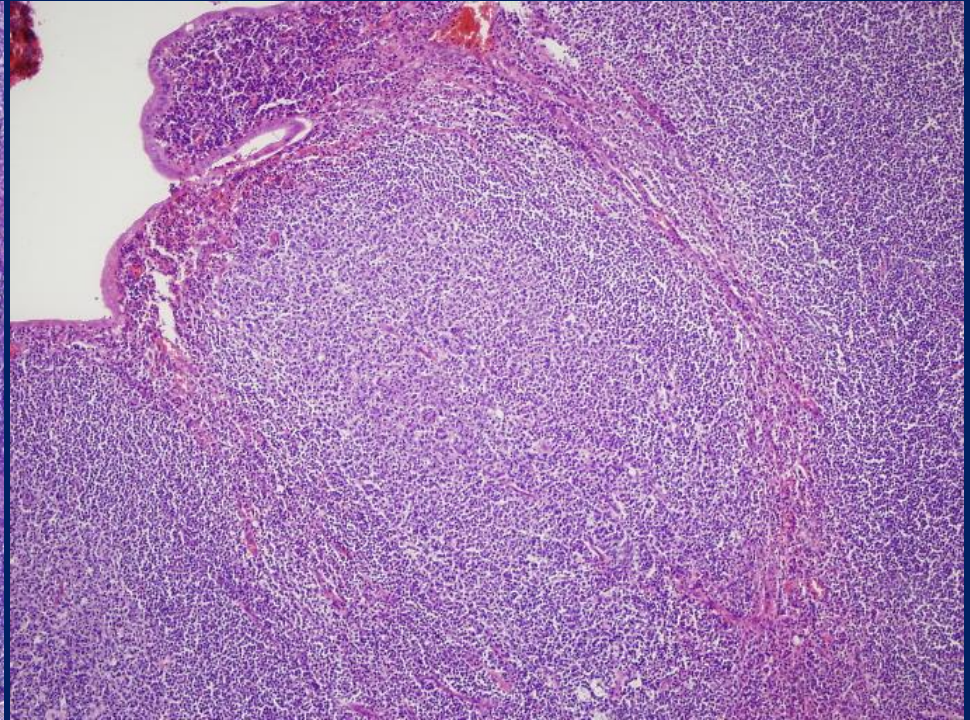
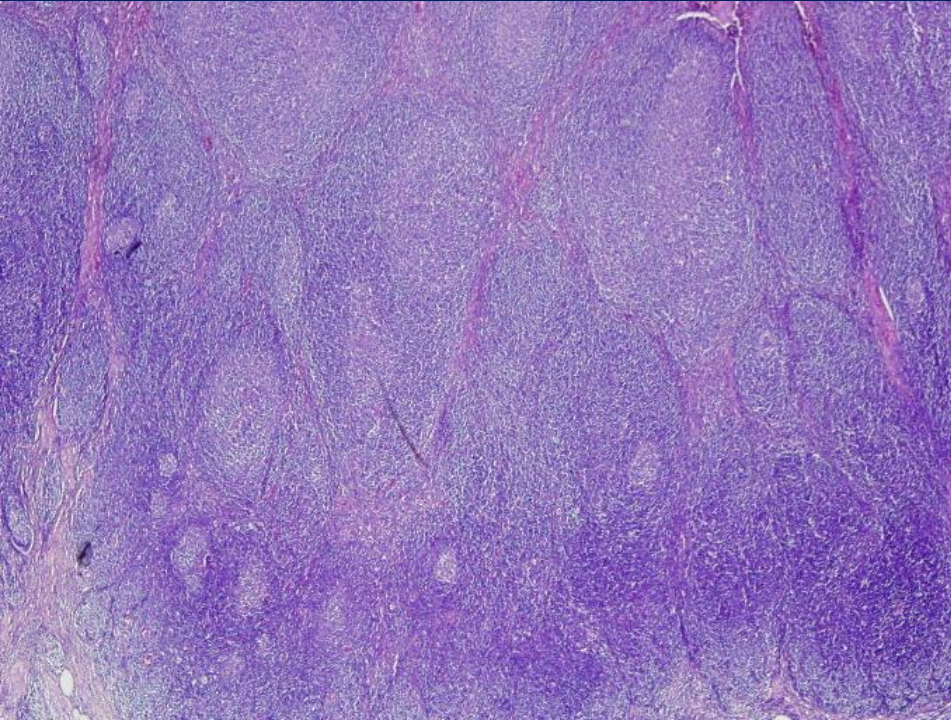
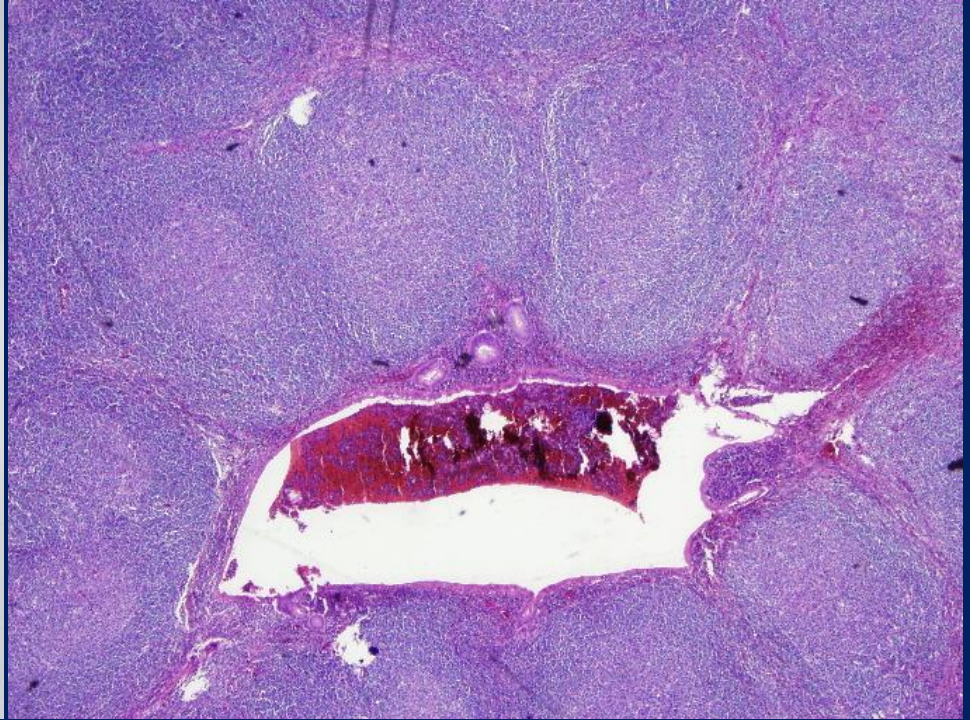
- Blastoid
- Pleomorfik

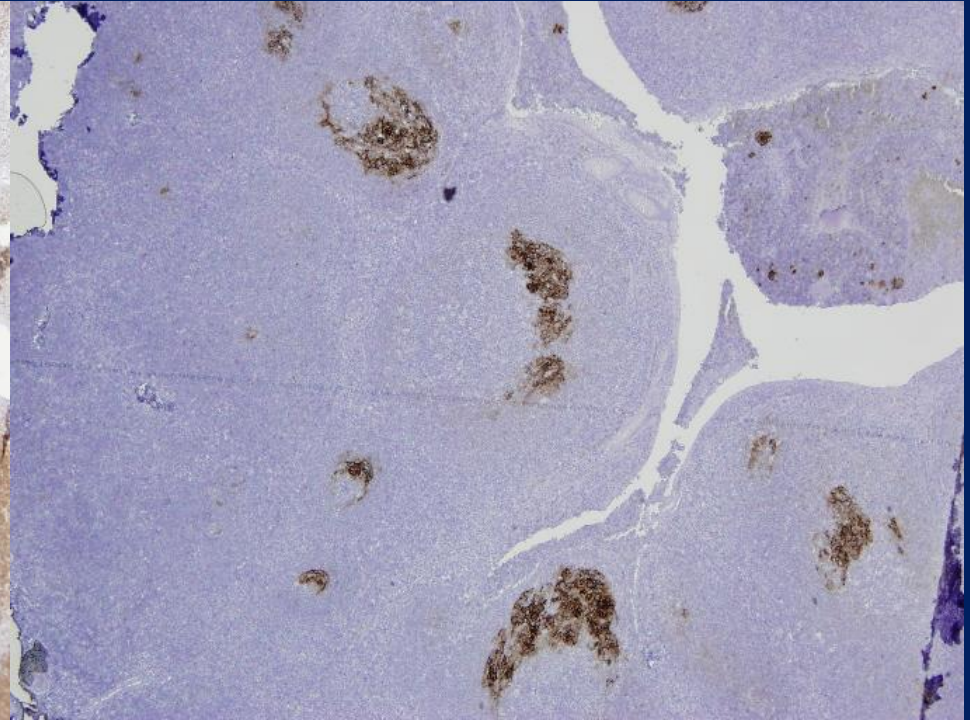
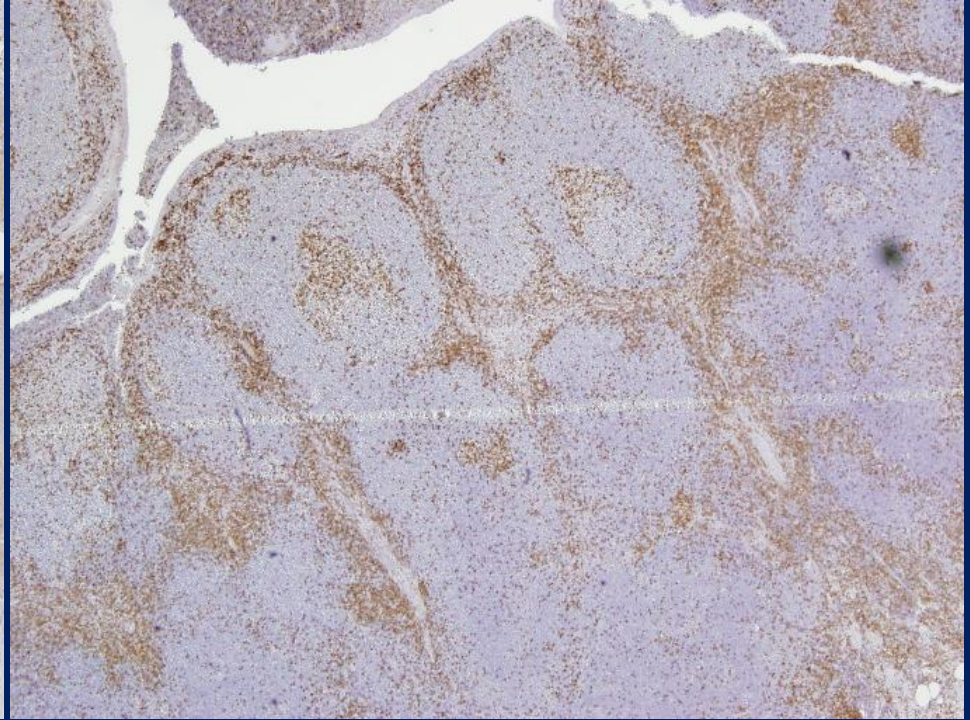
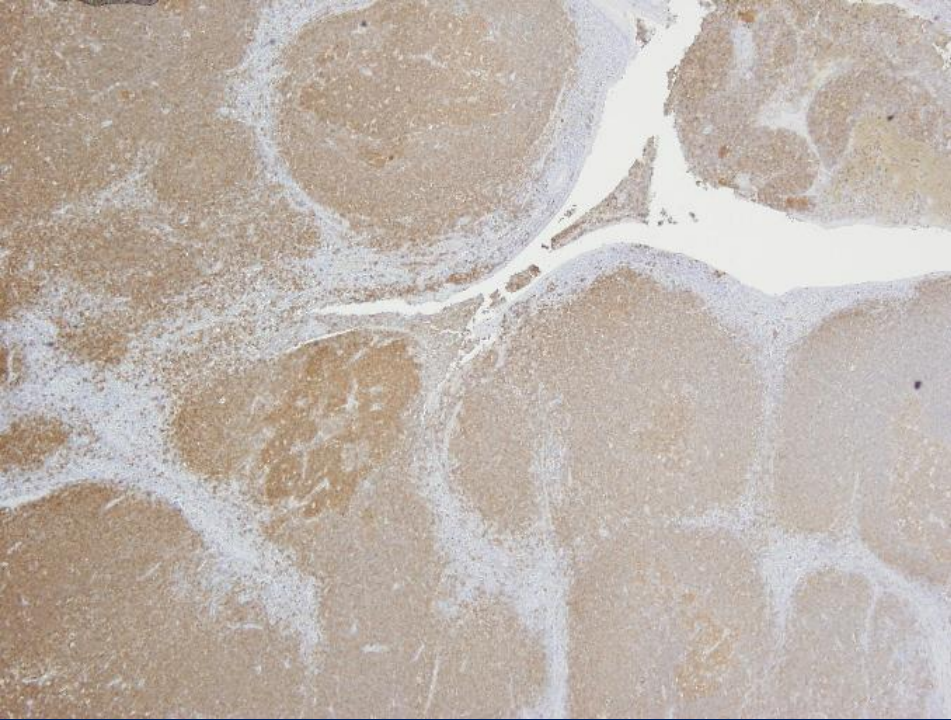
▣ DİĞER VARYANTLAR

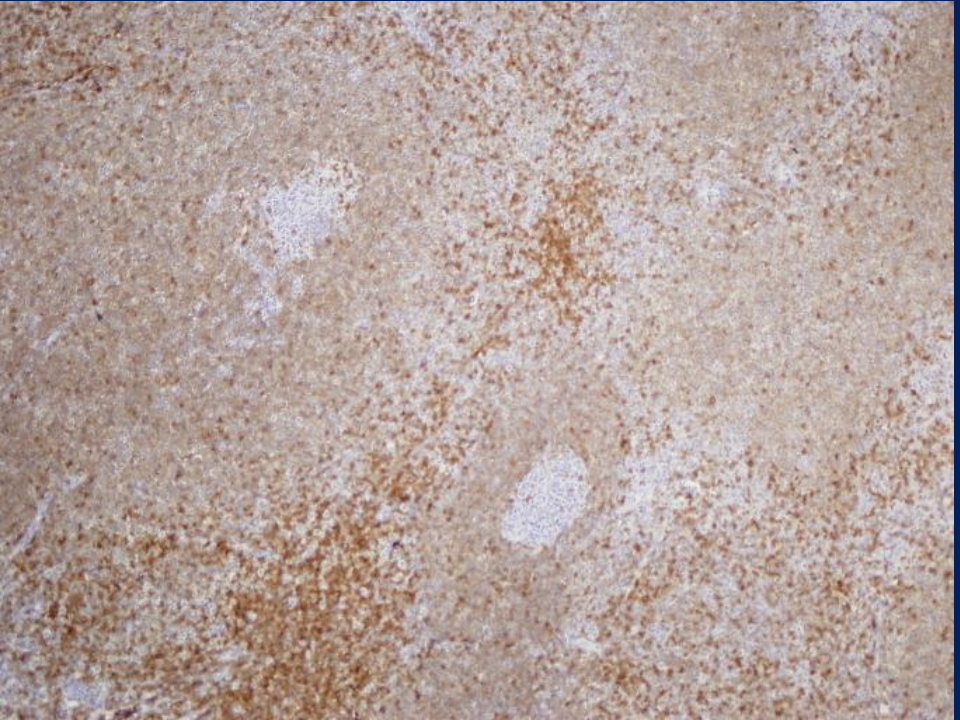
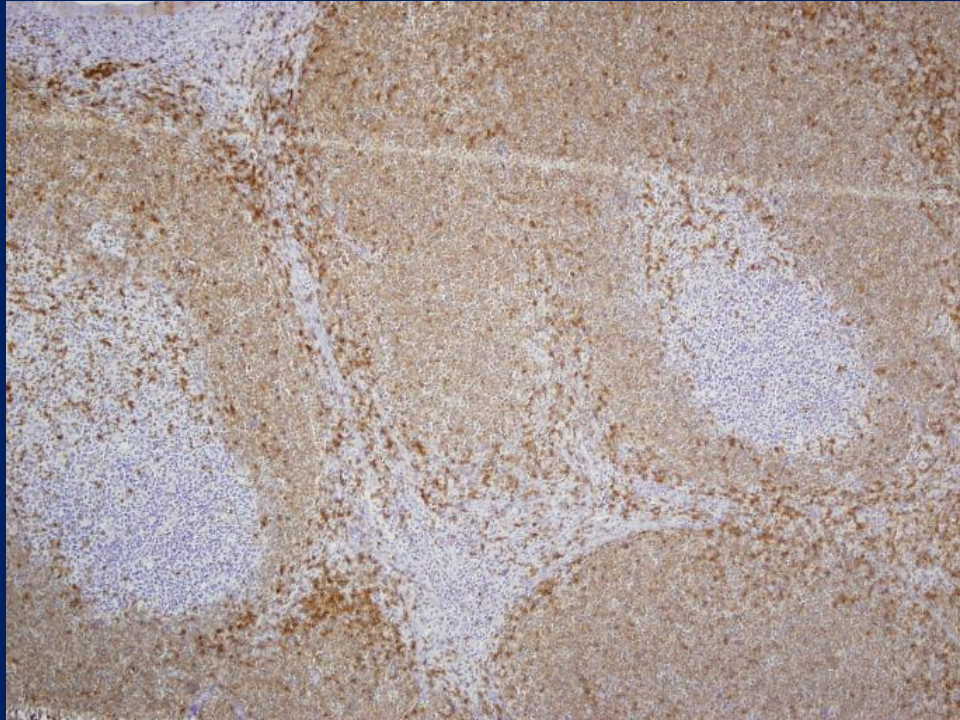
- Küçük hücreli
- Marjinal zon benzeri

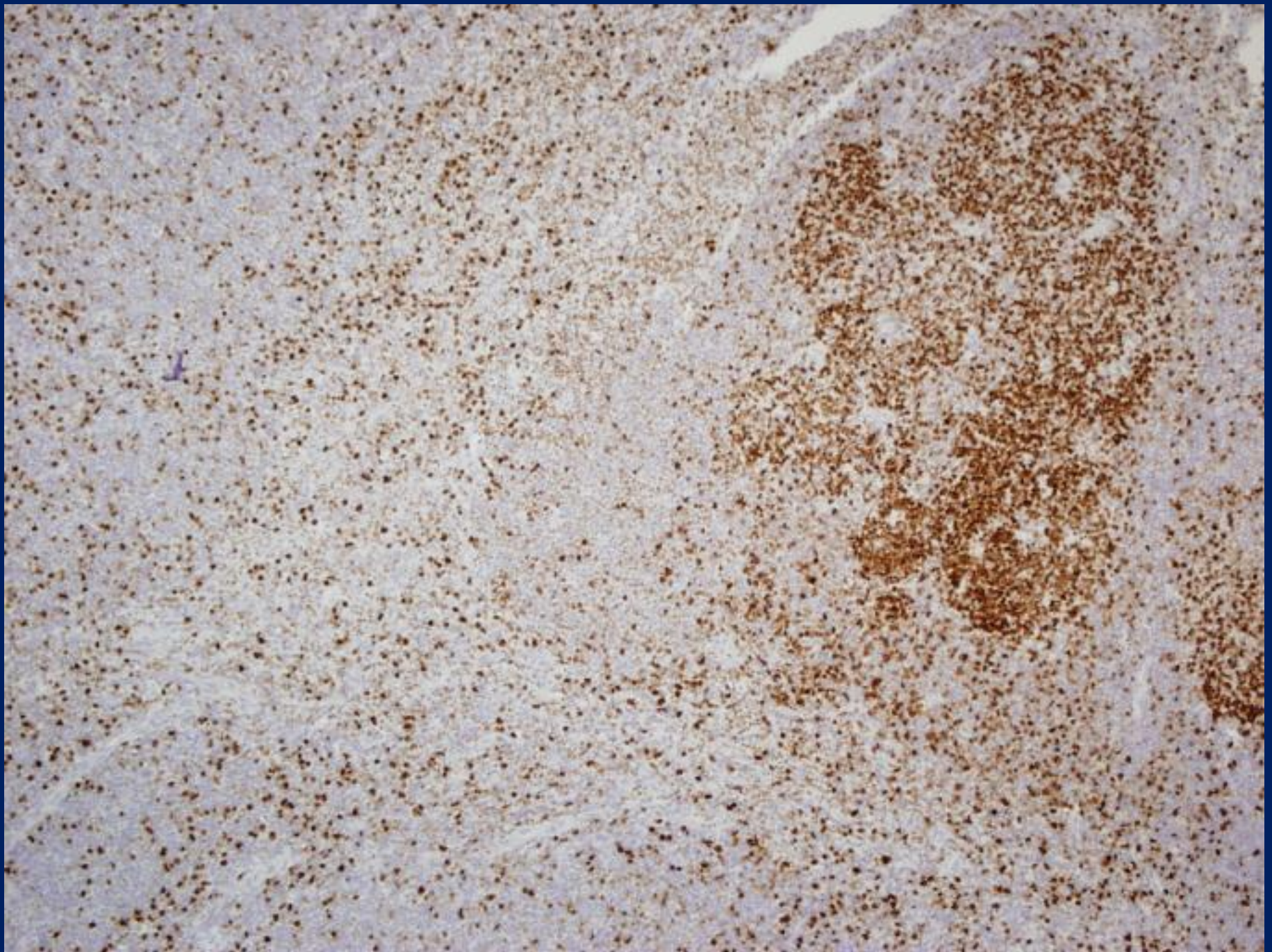










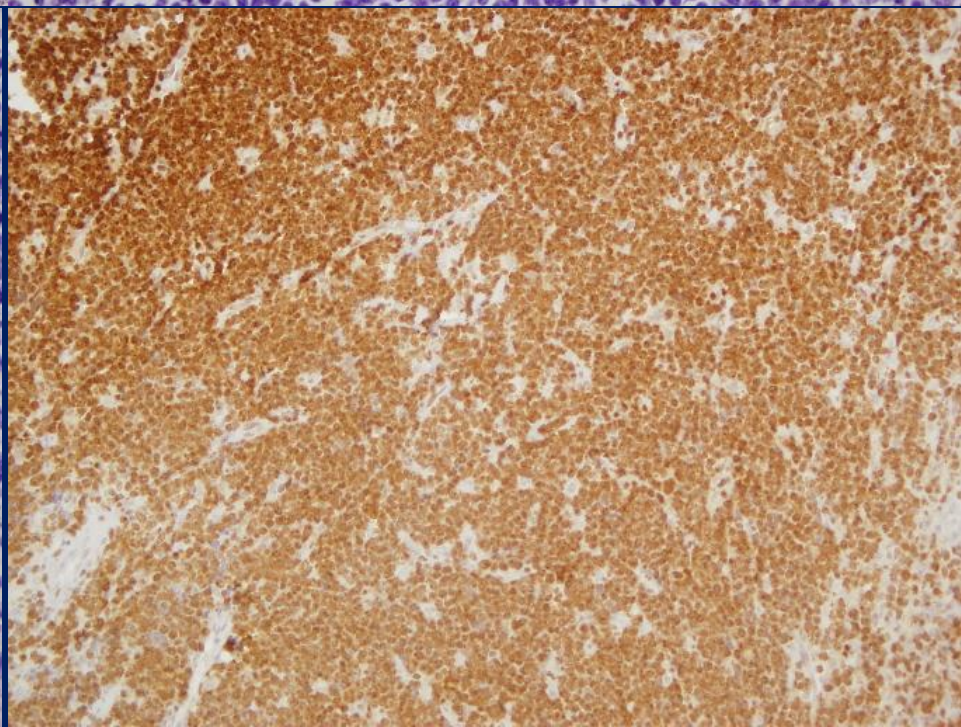
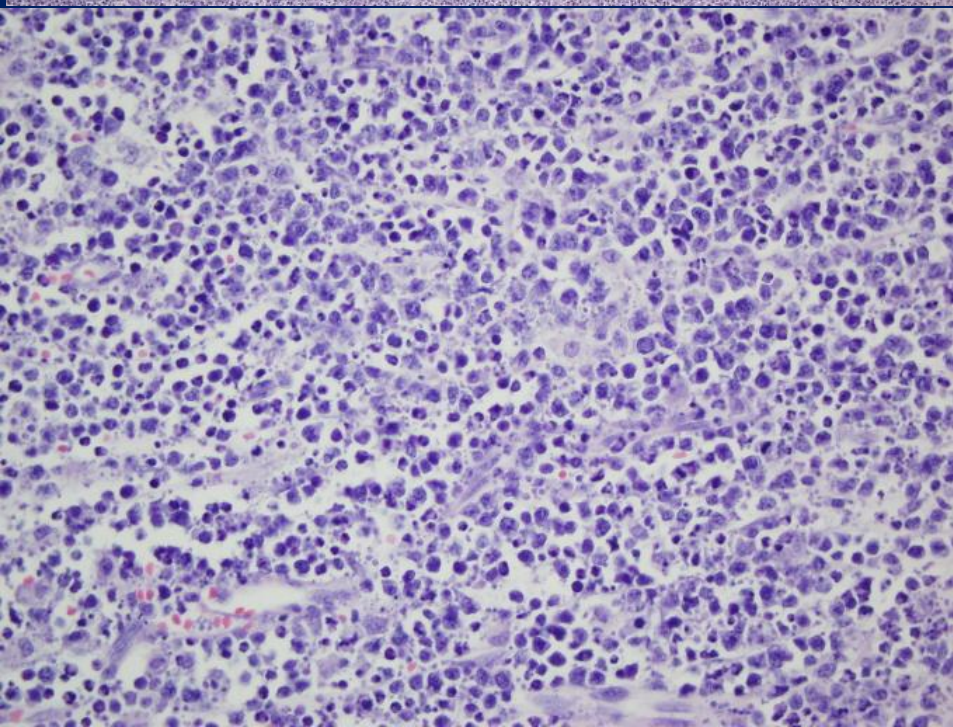
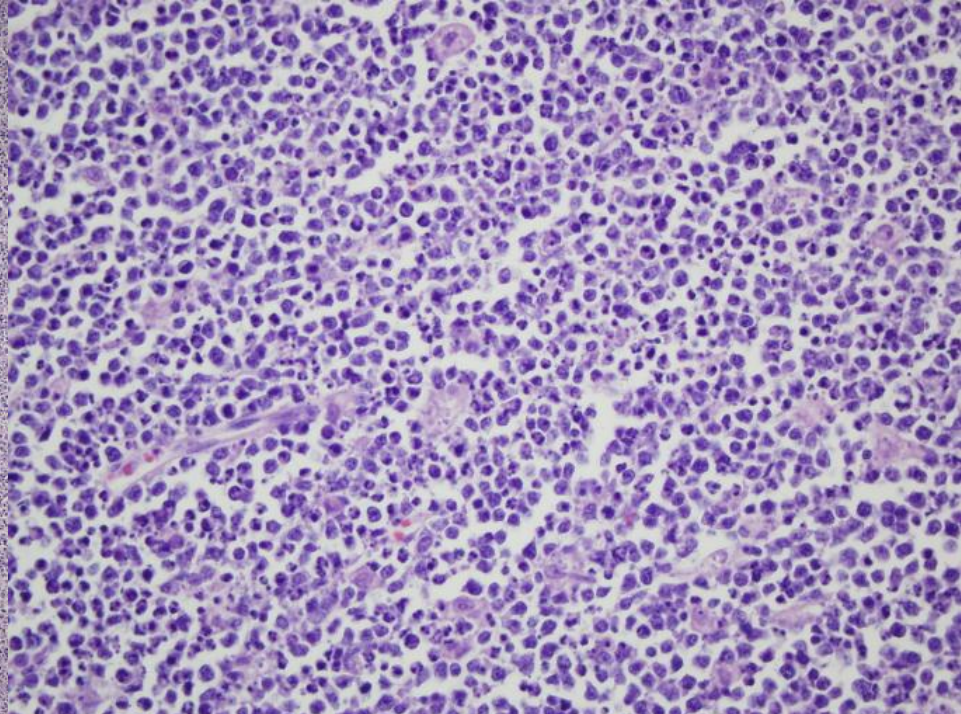
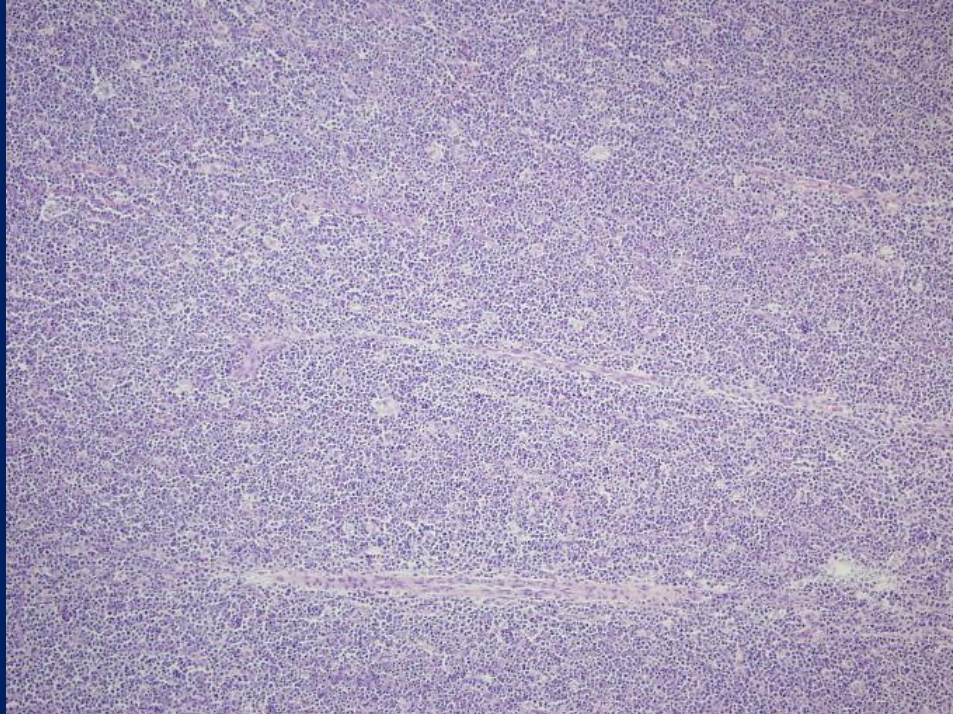


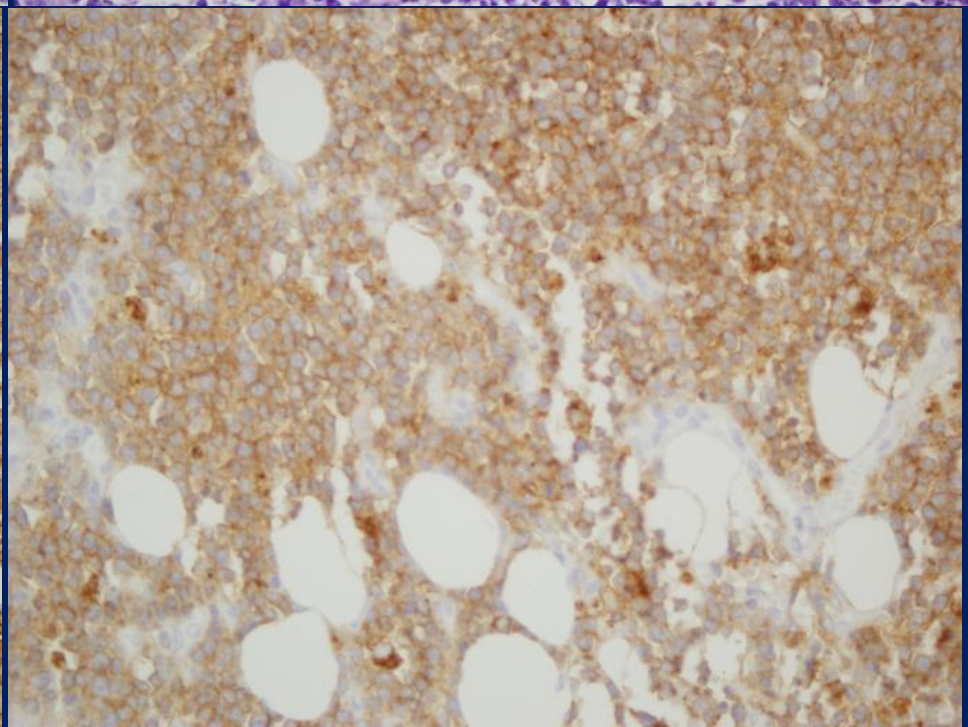
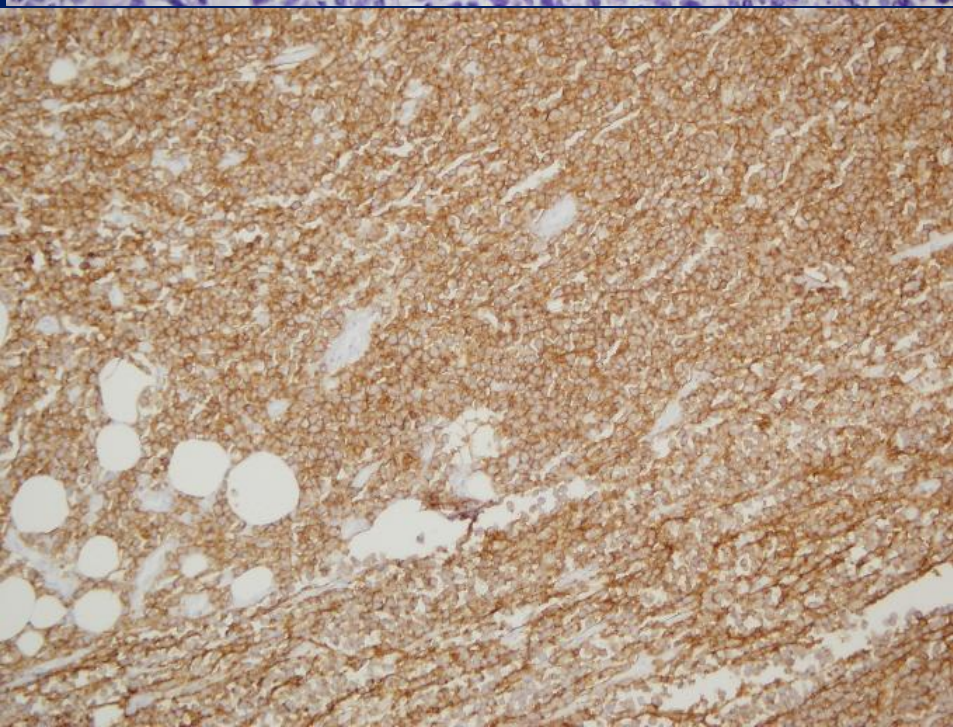
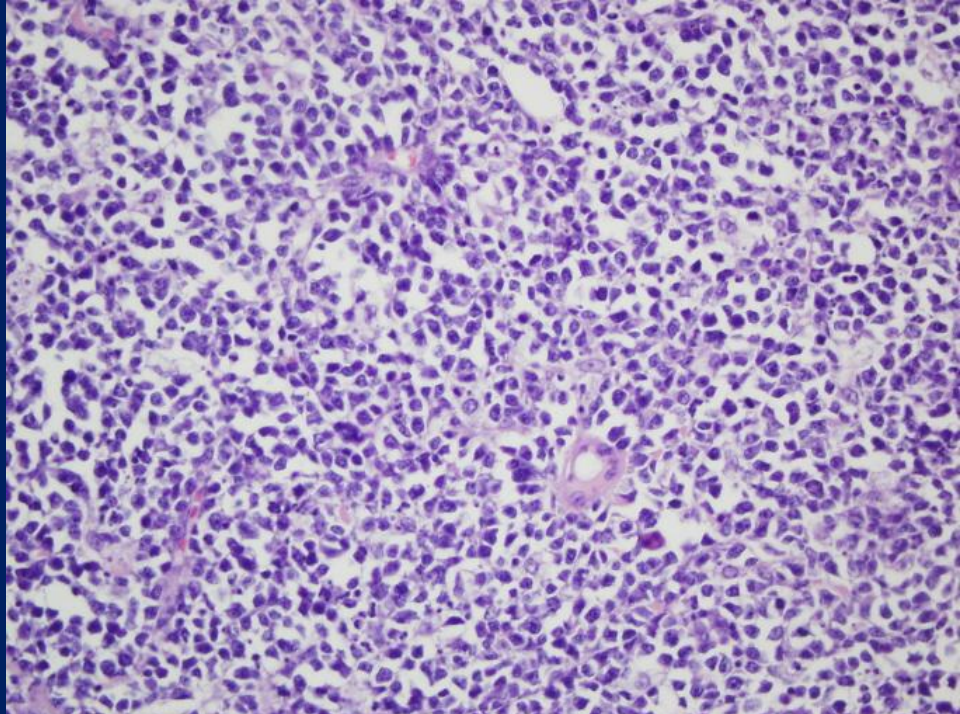
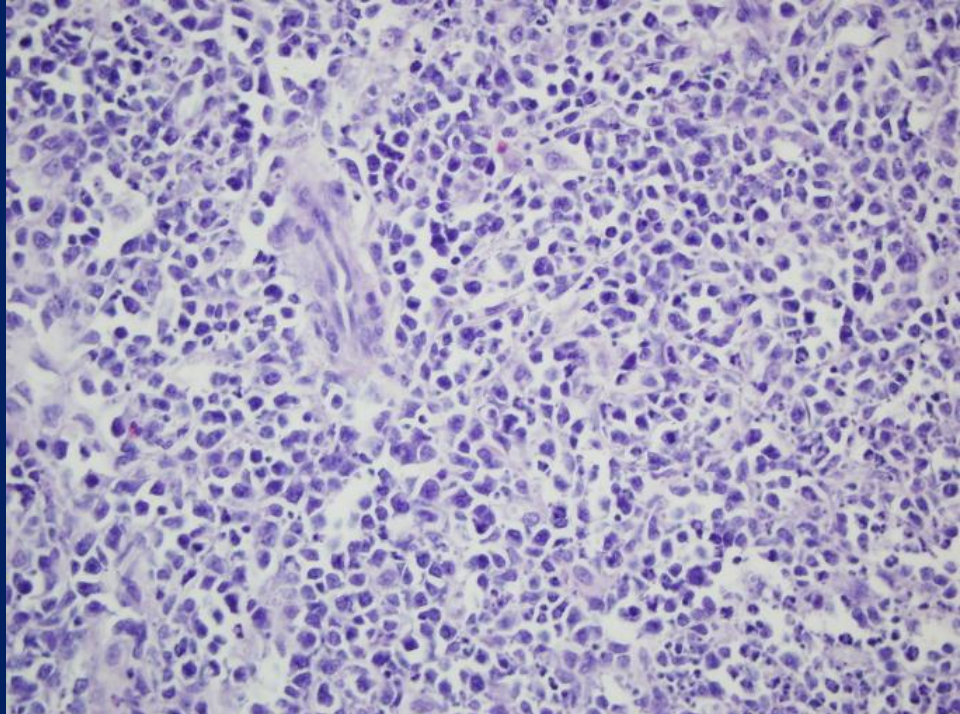
Foliküler Lenfoma

- ▣ GIS'de seyrek.
- ▣ Özellikle ince barsak ve duodenumda,
- ▣ Multipl küçük polipler şeklinde (lenfomatoz polipozis)
- ▣ LN'daki ile benzer özellikler,
- ▣ CD20 +, CD10 +, BCL-2 +, BCL-6 +
- ▣ t (14; 18)
- ▣ MHL'ya göre daha iyi gidişli

Dereceleme;

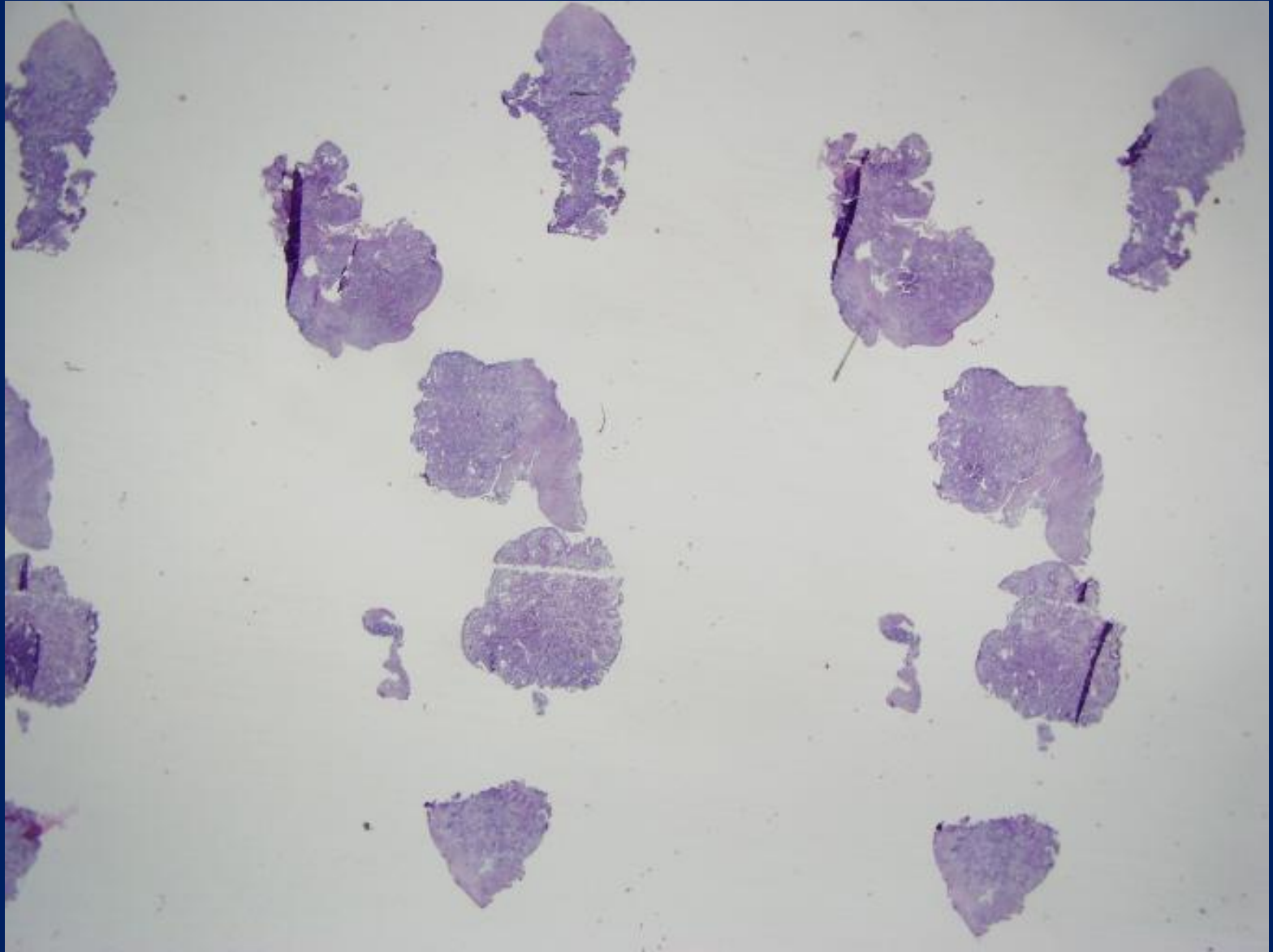
- ▣ **Düşük Dereceli (Derece 1-Derece 2)**
 - Derece 1: 1 BBA'da 0-5 sentroblast
 - Derece 2: 1 BBA'da 6-15 sentroblast
- ▣ **Yüksek Dereceli- Derece 3**
 - Derece 3: 1 BBA'da >15 sentroblast
 - 3A: sentrosit var
 - 3B: sentroblast tabakaları

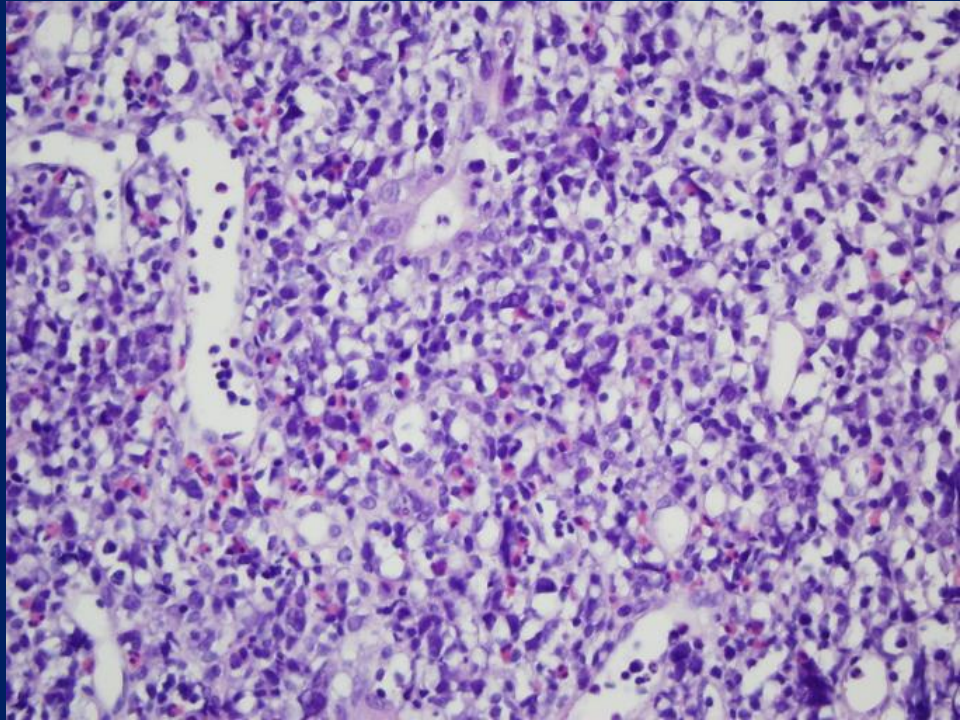
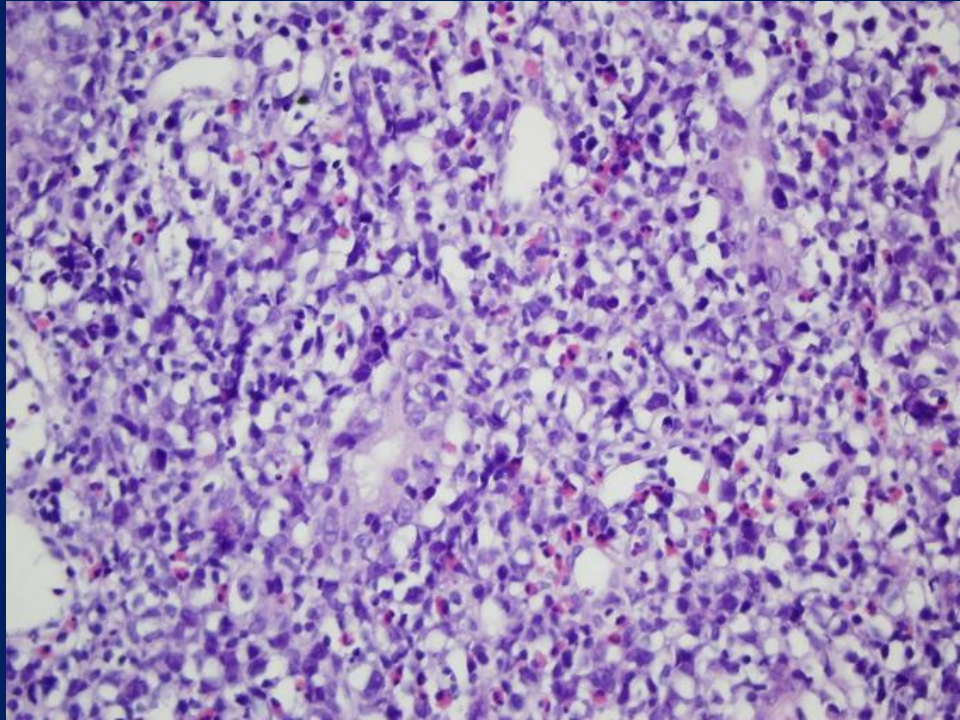
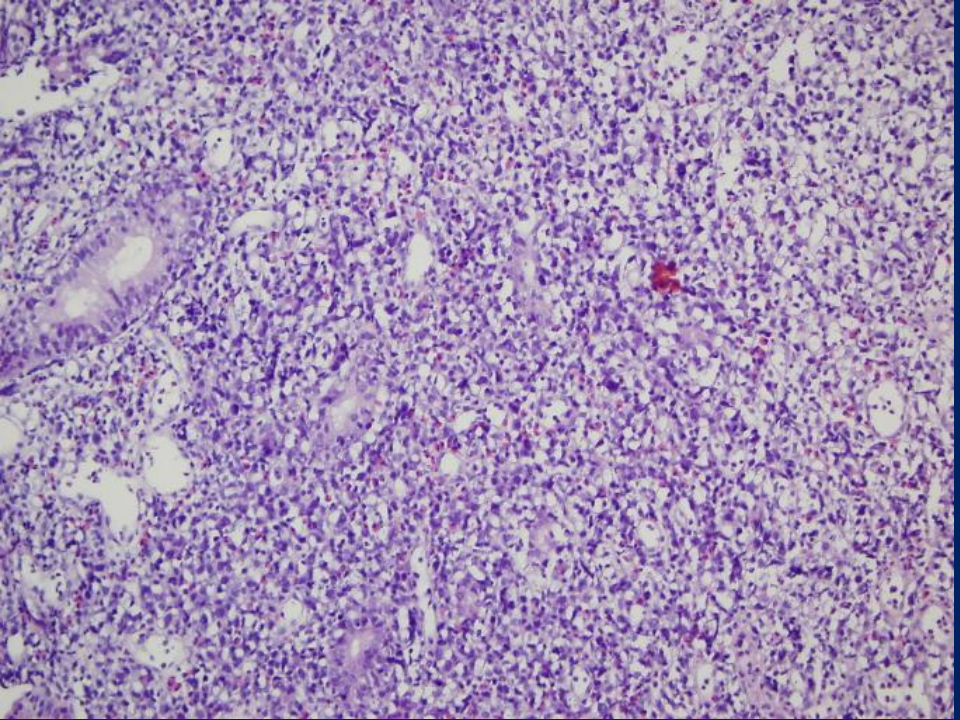
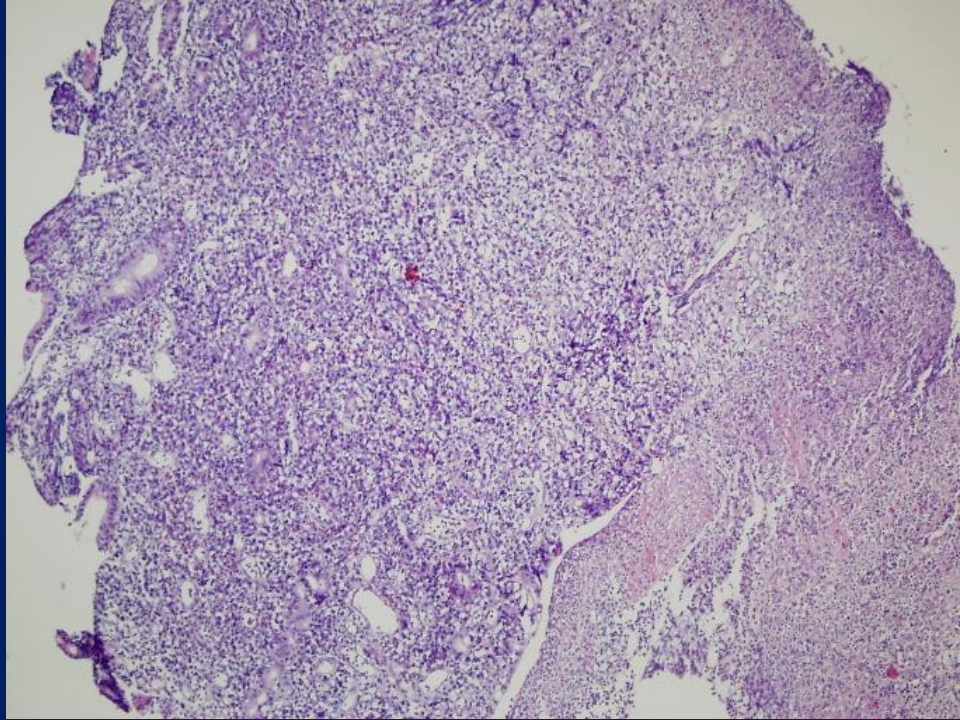


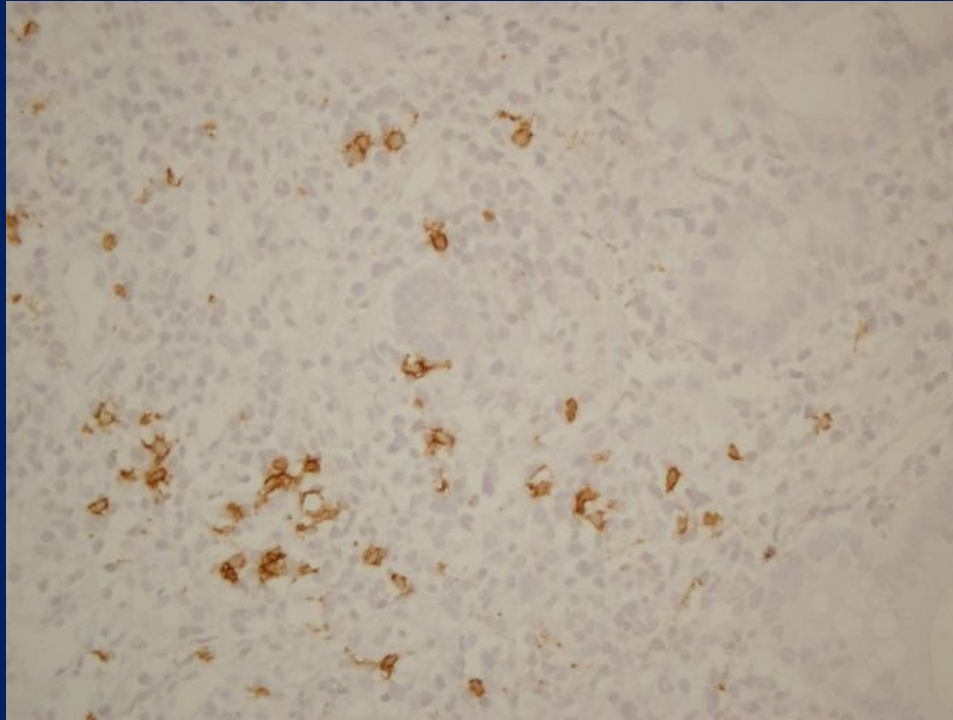
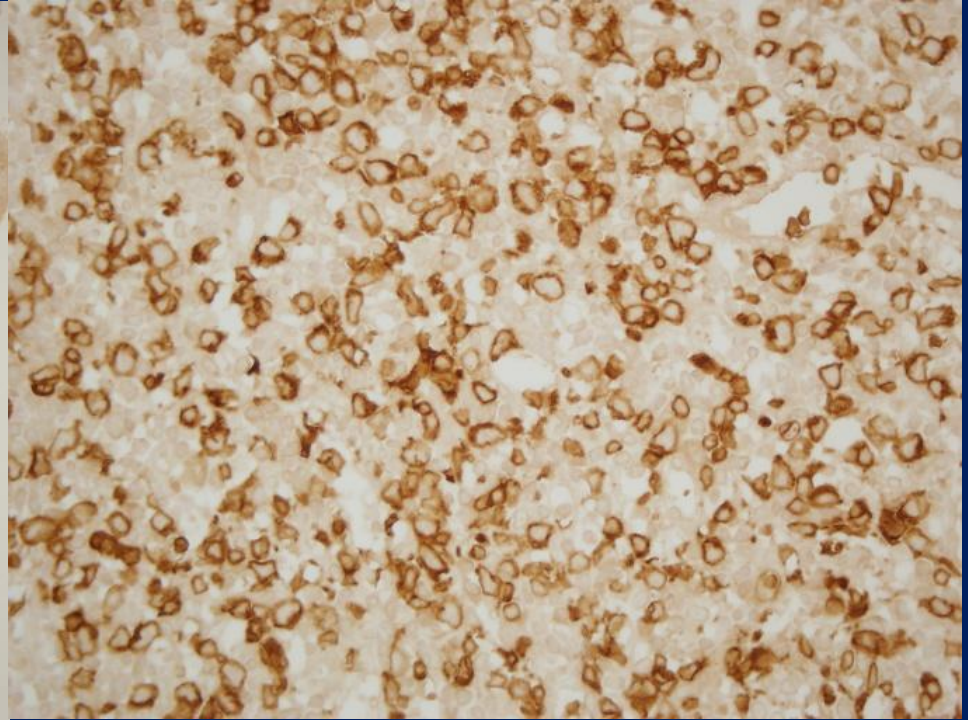
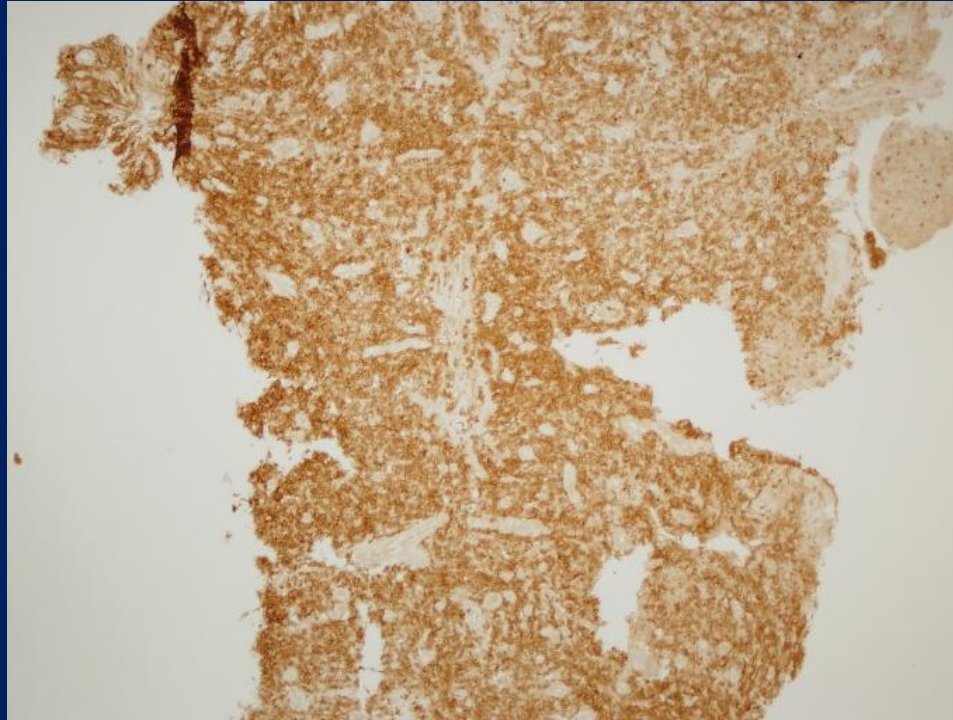


Periferal T Hücreli Lenfoma

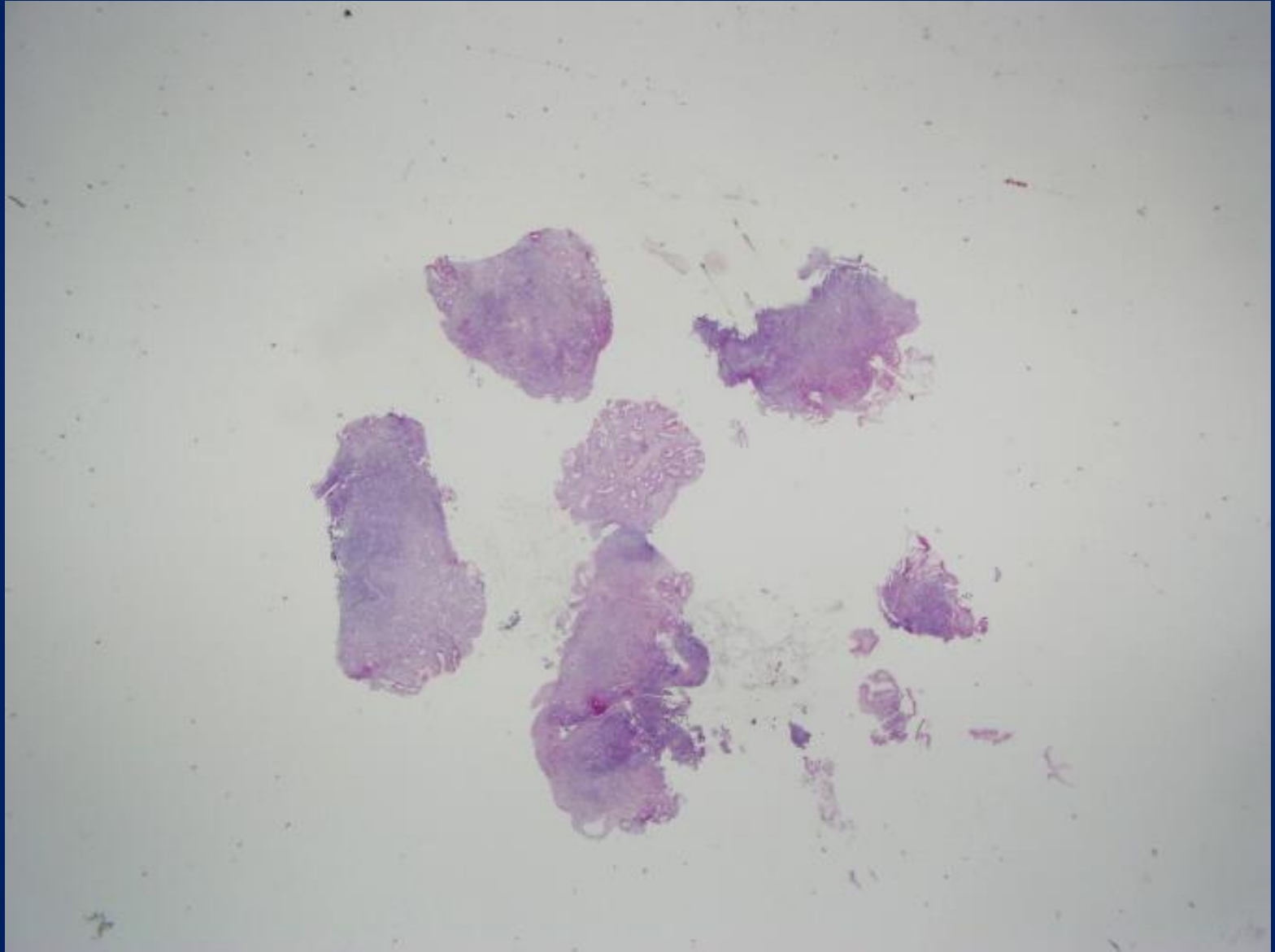
Periferal T Hücreli Lenfoma, NOS

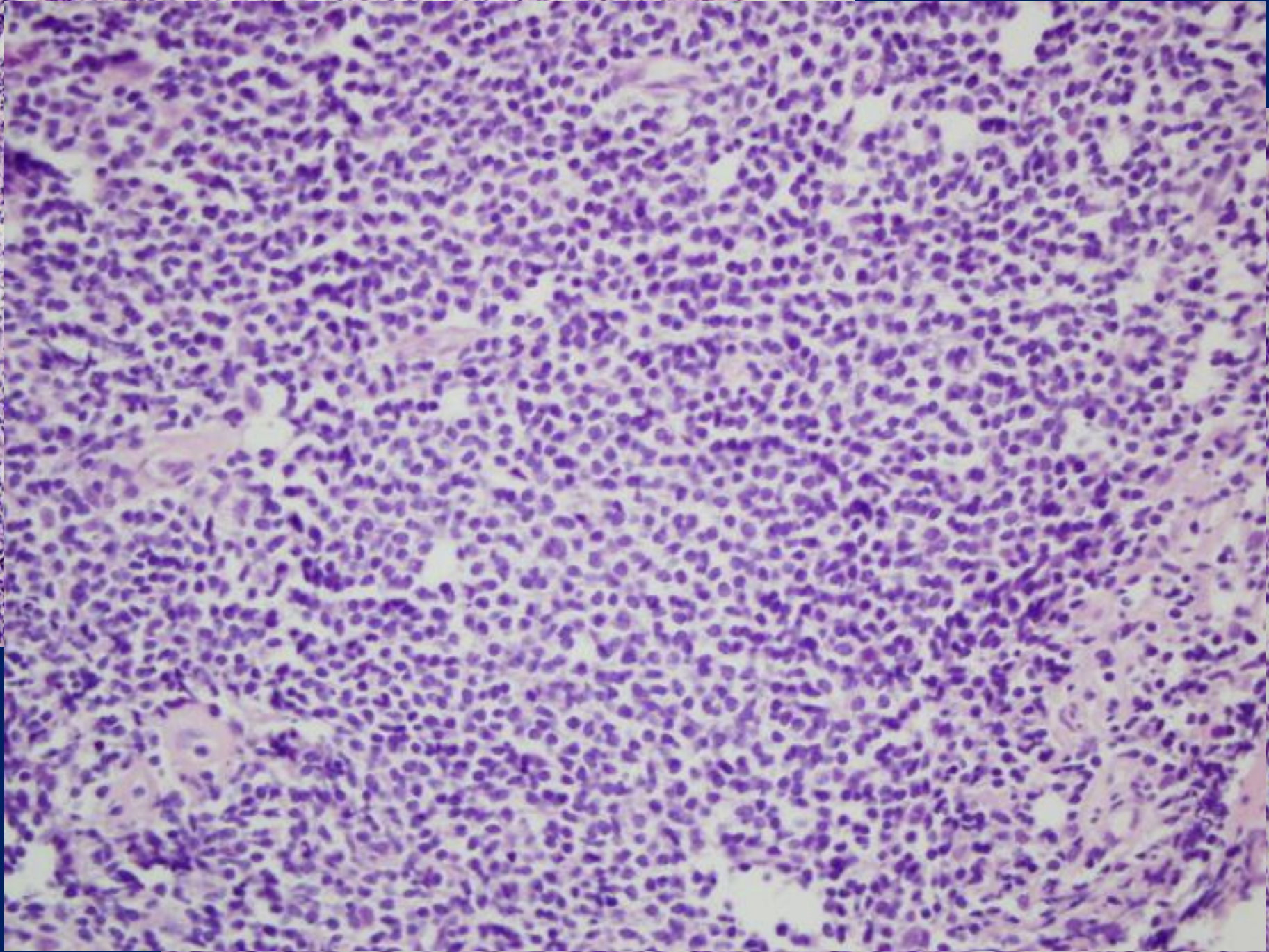


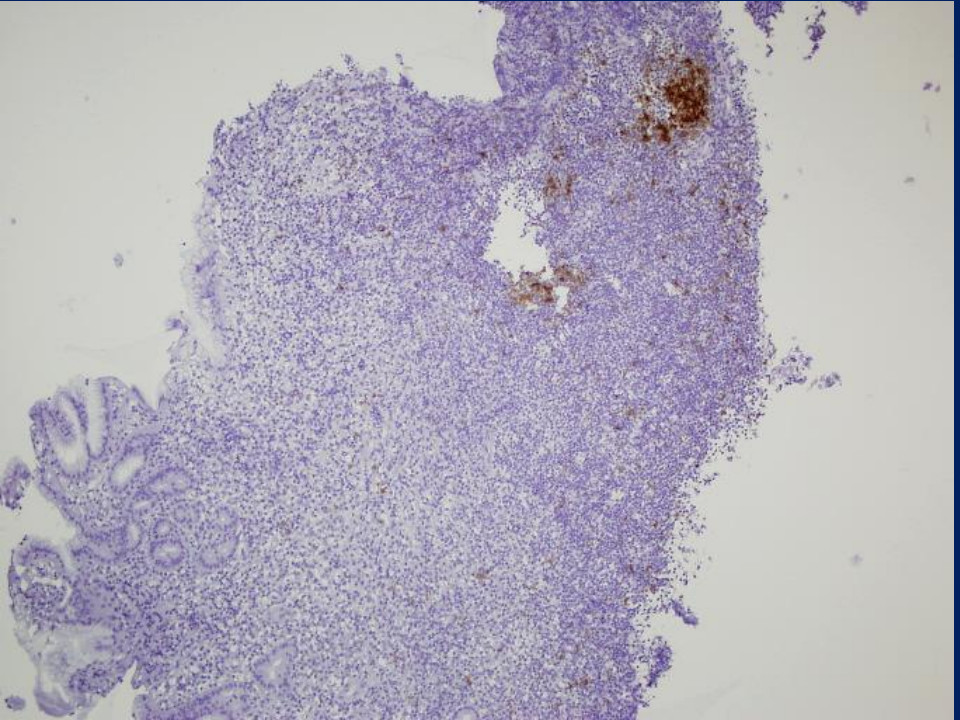
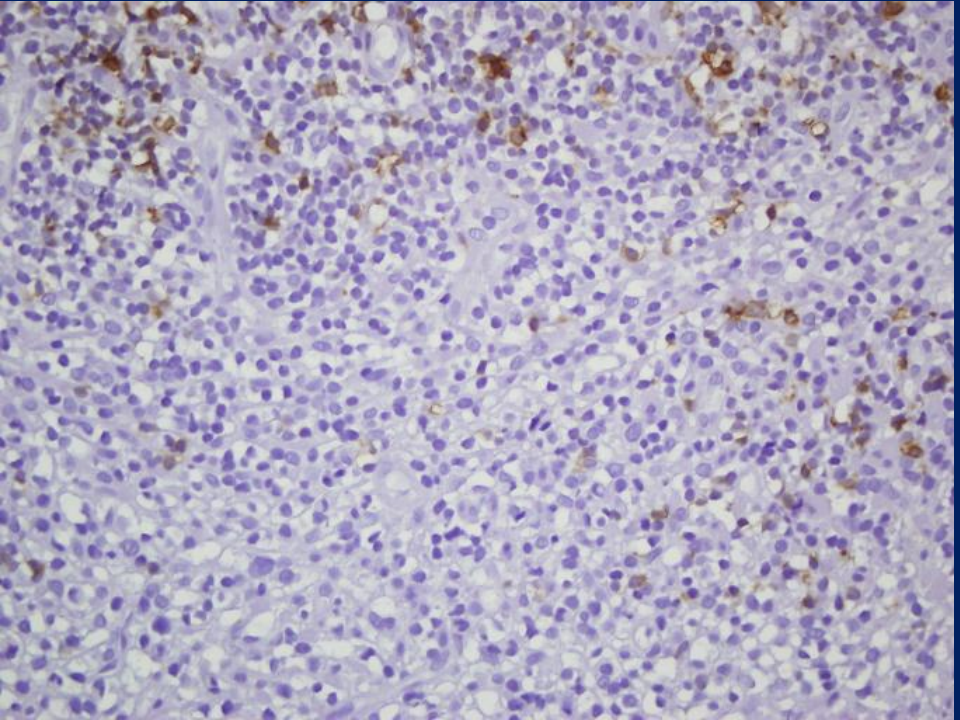
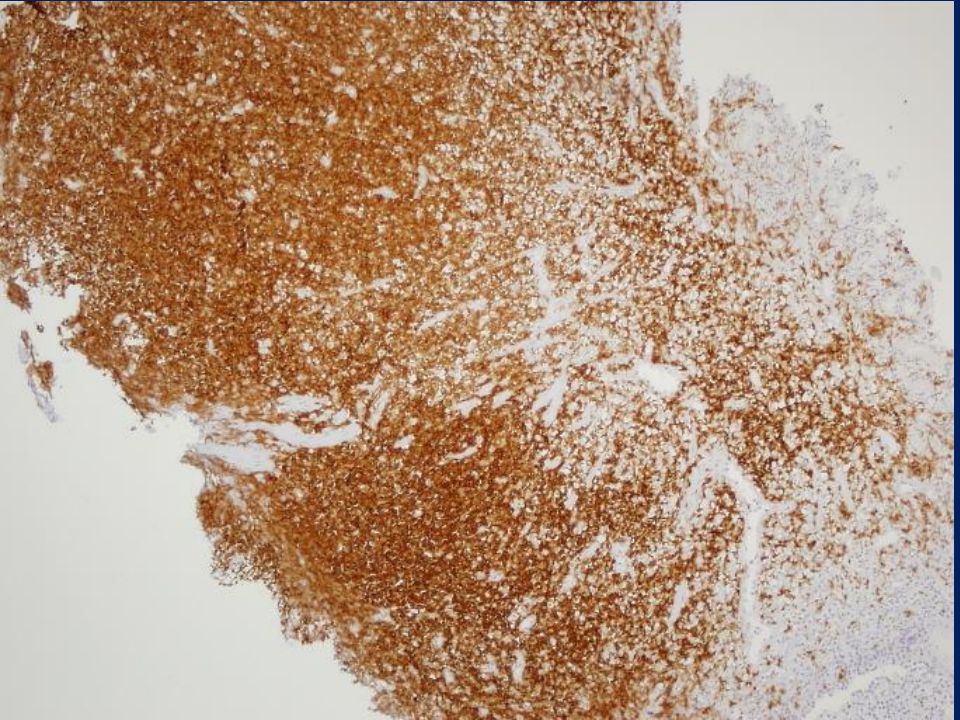
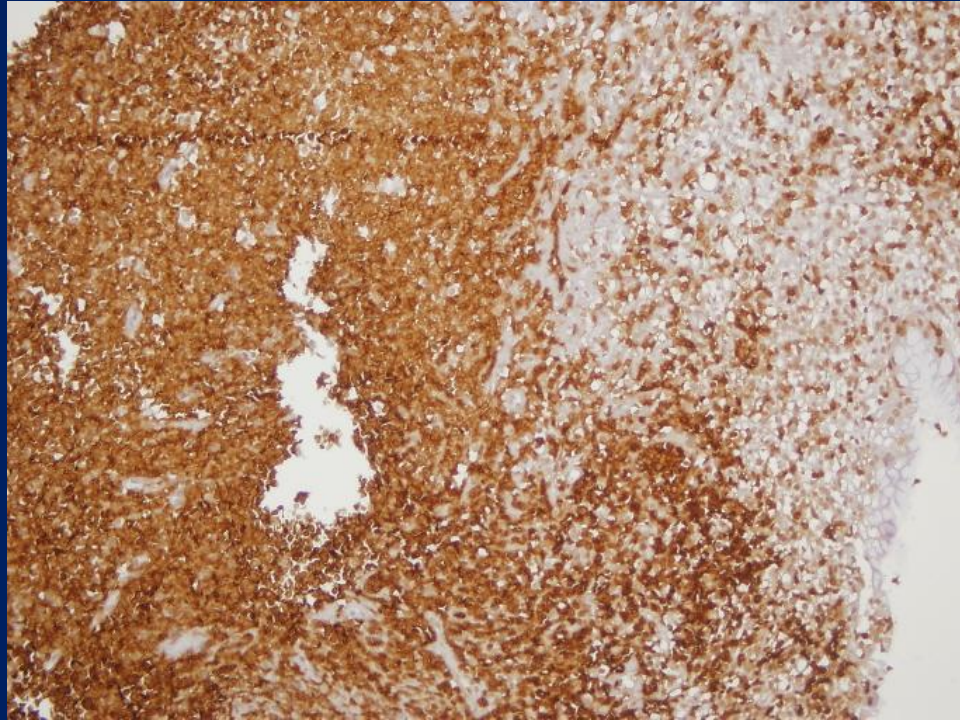




OLGU







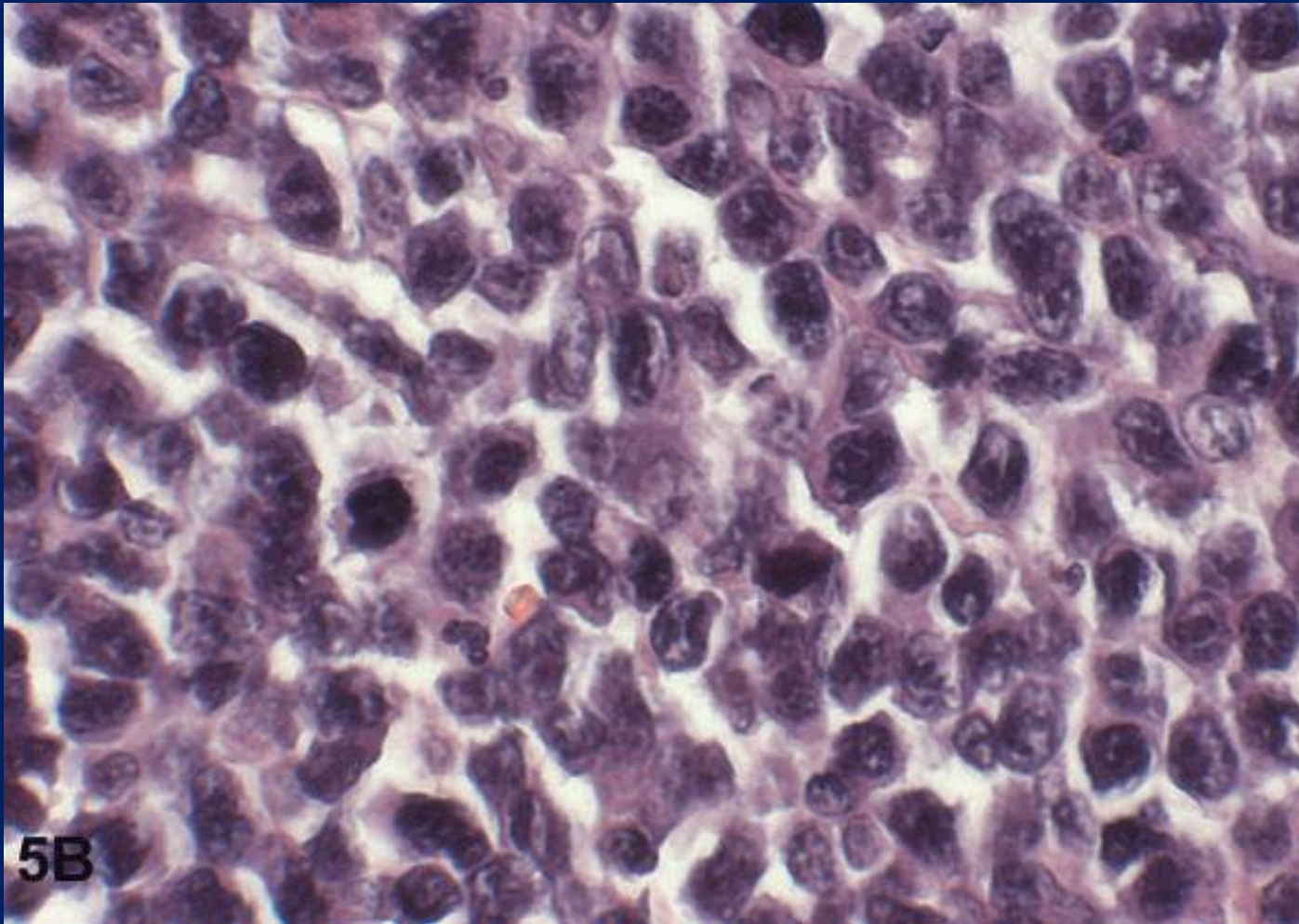
Enteropati İlişkili T Hücreli Lenfoma (EATL)

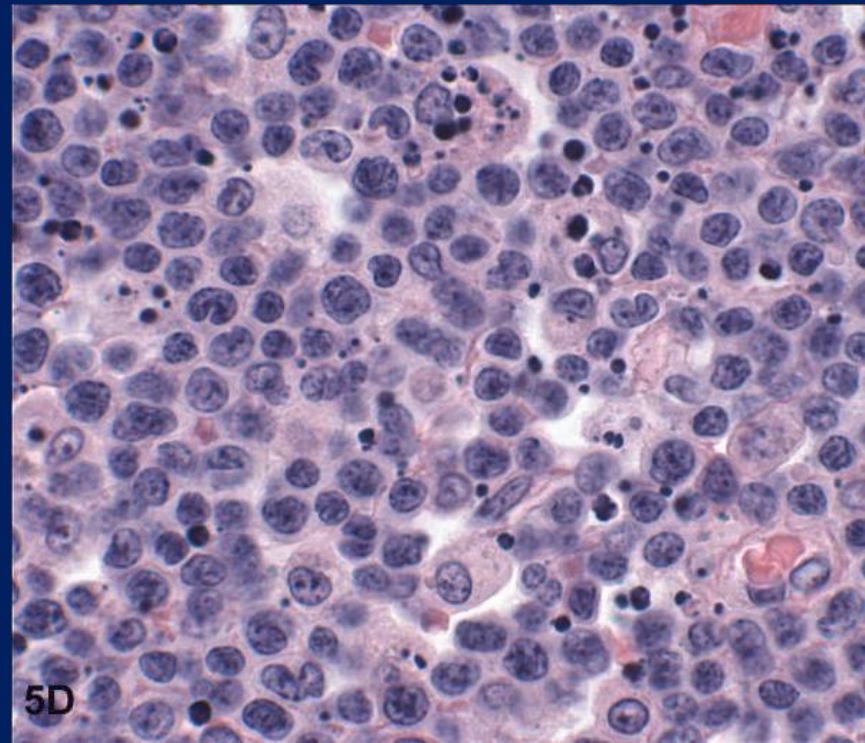
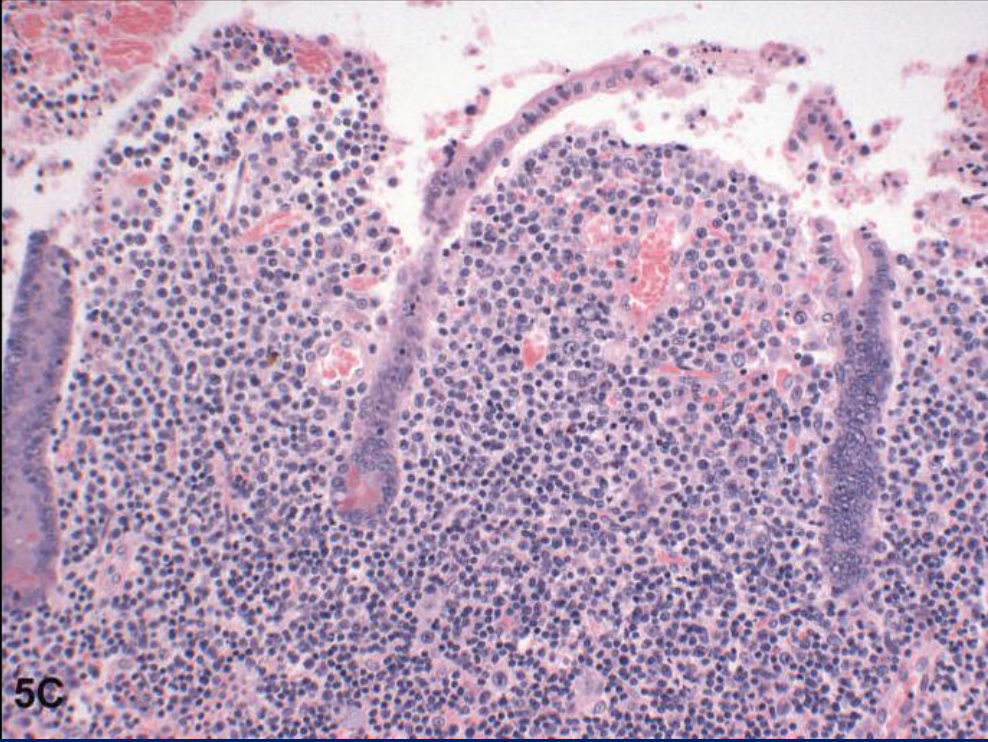
- ▣ Çölyak hastalığı ile ilişkili,
- ▣ Jejunum ve ileumda sık.

- ▣ İntraepitelyal T lenfositleri
- ▣ Değişik şekil ve boyutlarda, genelde iri hücreler,
- ▣ Zeminde inflamatuvar hücreler.

2 formu var;

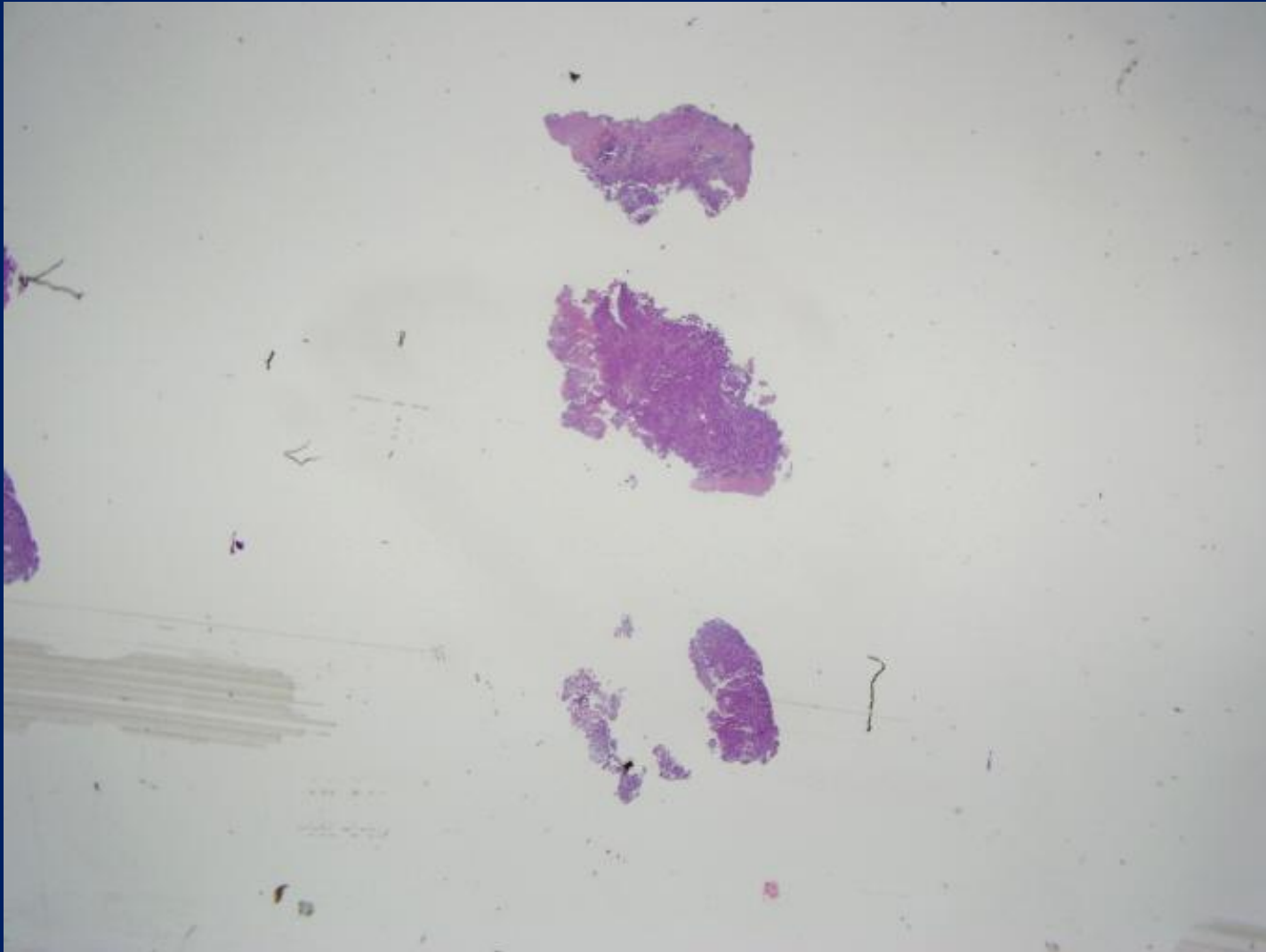
- ▣ Orta-iri boyutta, pleomorfik belirgin nükleollü hücrelerden oluşur. ALCL'ya benzer.
- ▣ Tip II EATL: Monomorfik formdur. Orta boyutta, yuvarlak, soluk sitoplazmalı hücrelerden oluşur.
- ▣ CD3 +, CD7 +, CD103 +, CD8 +/-, CD30*
- ▣ CD5 -, CD4-
- ▣ Tip II'de; CD56 +

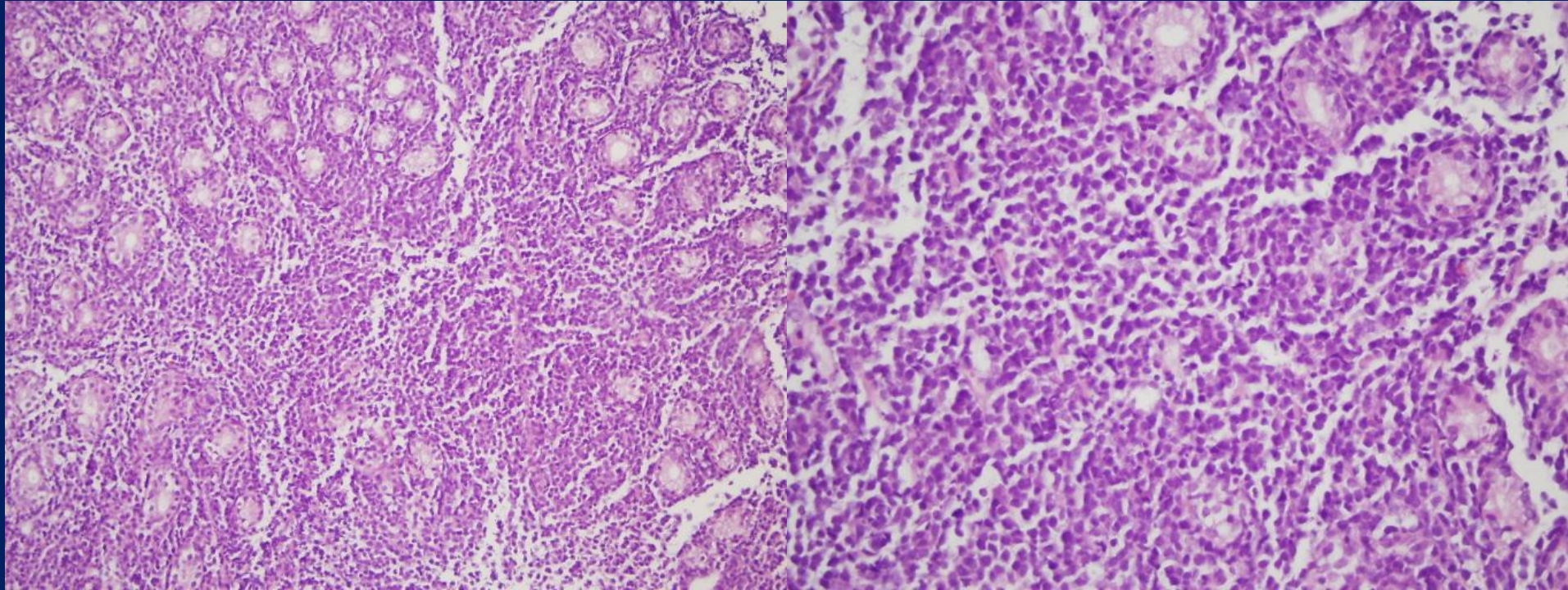
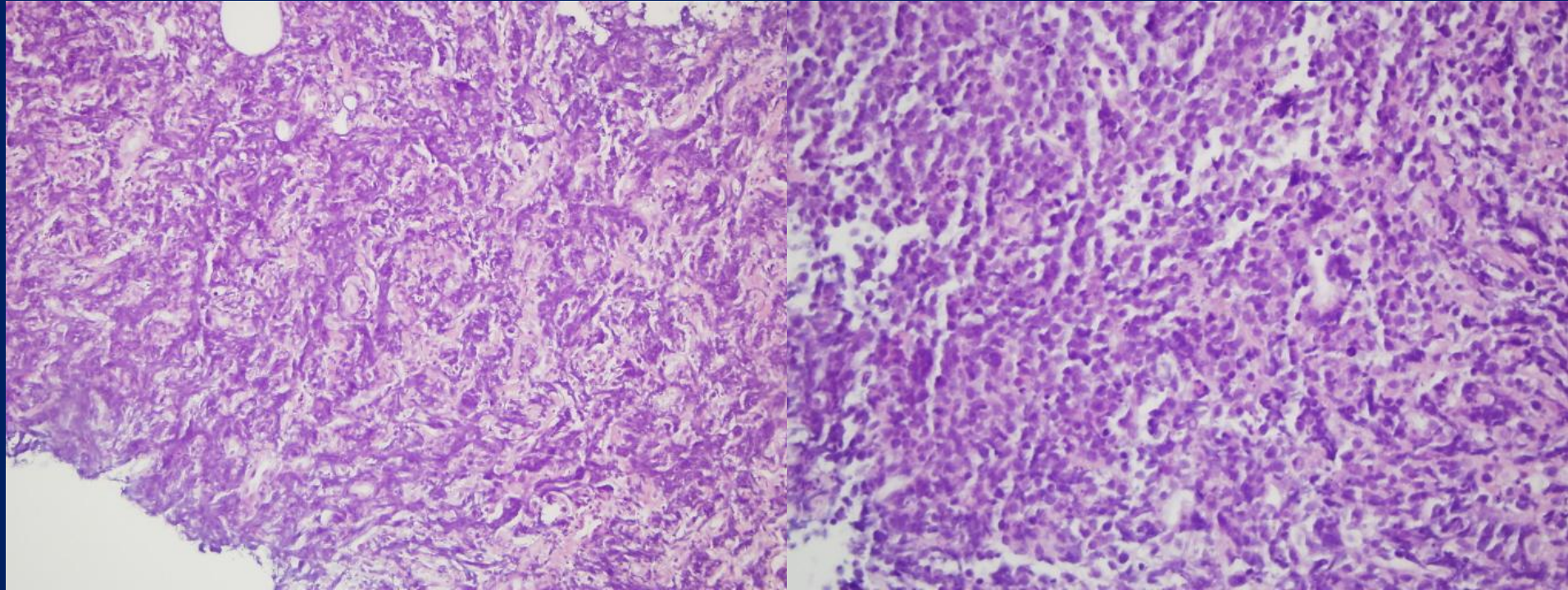




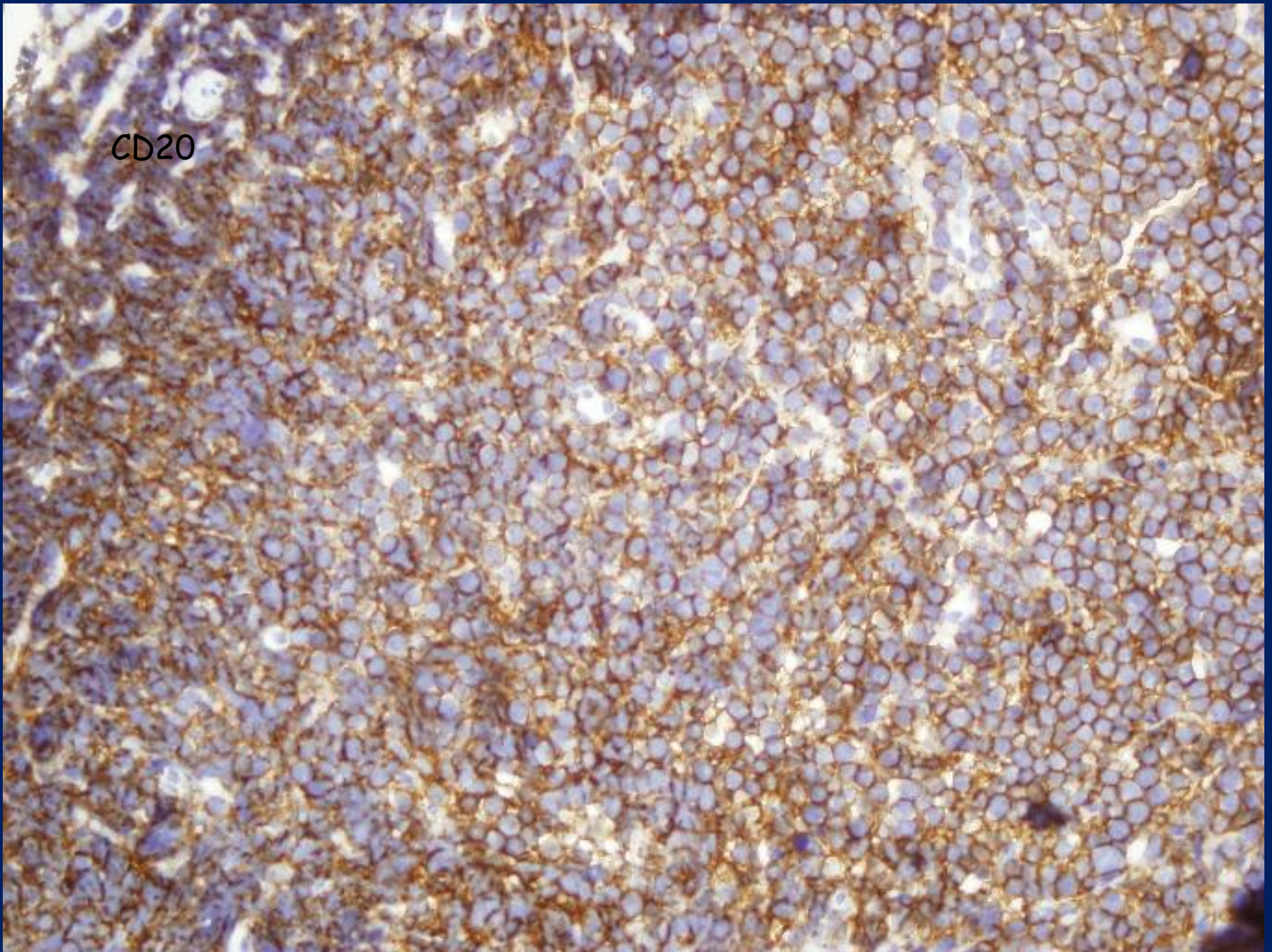
- ▣ Anaplastik Büyük Hücreli lenfoma
- ▣ Ekstranodal NK/T Hücreli Lenfoma
- ▣ NK Hücreli enteropati
(lenfomatoid gastropati)

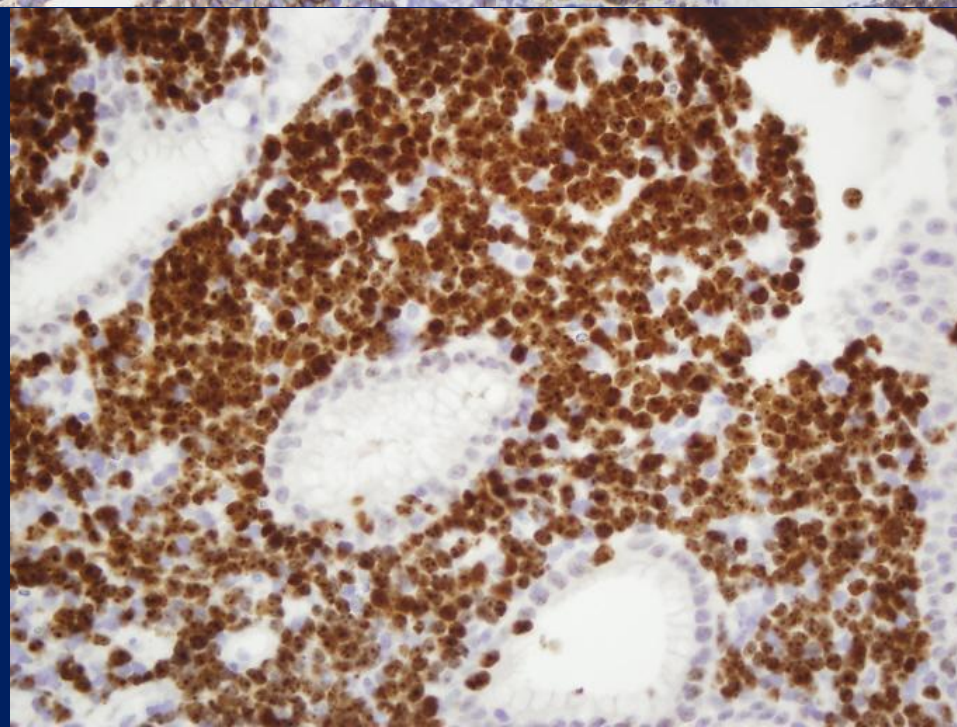
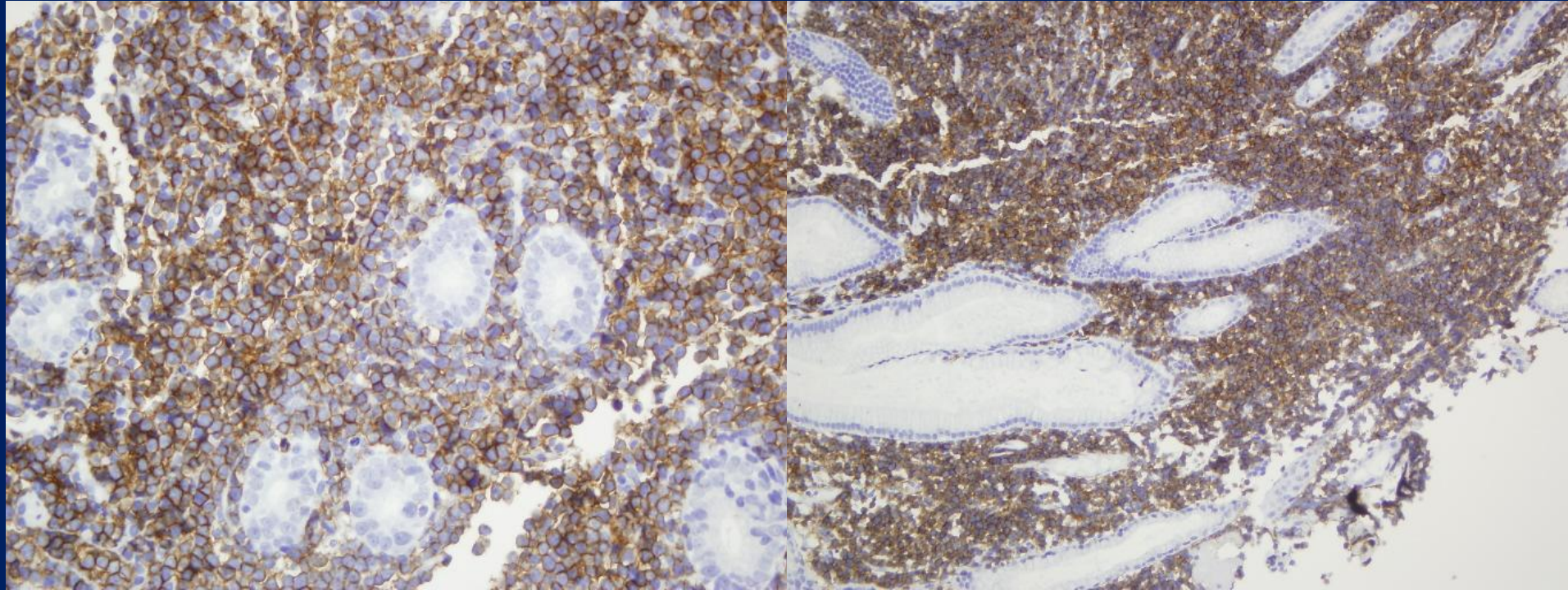
LENFOBLASTİK LENFOMA





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