



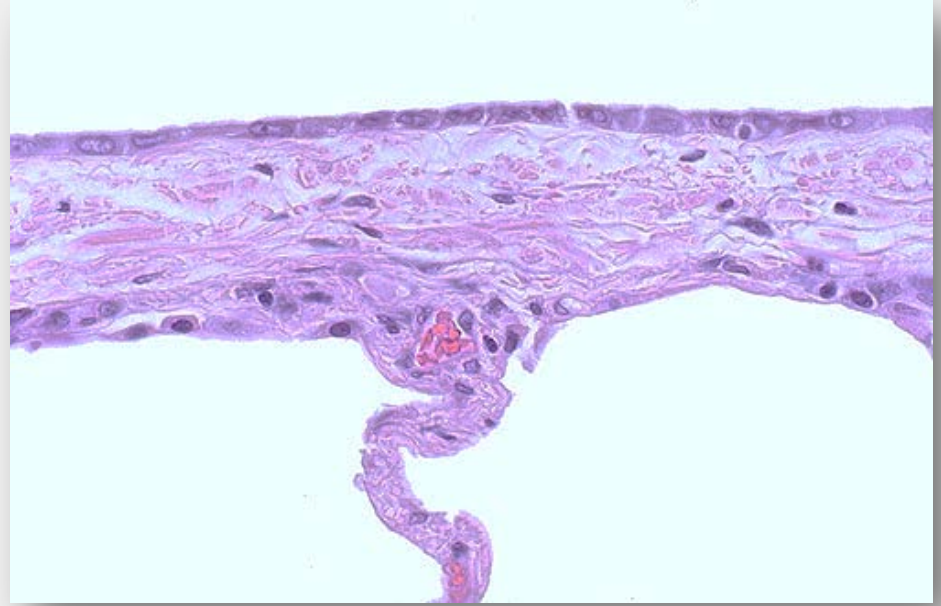
# PLEVRAL LEZYONLARDA AYIRICI TANIDA TUZAKLAR

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Patoloji AD

Plevra, kollajen, elastik lif, kan damarları ve lenfatiklerin bulunduğu matriks üzerinde tek sıralı mezotel hücreleri ile döşeli bir yapıdır

"Kampmeier" odağı olarak bilinen özel lenfoid doku bulunabilir

Bu hücresel elemanların herhangi birinden tümör gelişebilir



# Plevral efüzyon

- Enfeksiyöz, neoplastik, ilaçlara bağlı, travmatik, kollajen doku hastalığına sekonder, iatrojenik
- Malign plevral efüzyonların %75'i akciğer ve meme; **sekonder**

# Plevral neoplaziler

- **Primer** plevra tümörleri nadir (2.8/100000)
  - Malign mezotelyoma- **malign epitelyal**
  - Soliter fibröz tümör- **mezenkimal**
- Bunların %90'ı mezotelyoma, %5'i soliter fibröz tümör, %5'i diğer
- Tüm dünyada torasik tümörler içinde plevral tümör sıklığı %0,3-%3,5

**TUZAKLAR!**

# TUZAKLAR!

- Biyopsinin yeterli olmaması
- Kandırıkçı yağ
- Yalancı invazyon
- Sarkomatoid mezotelyoma
- Nadir görülen tip veya alt tip ile karşı karşıya olmak
- İmmünohistokimyasal nedenli tuzaklar

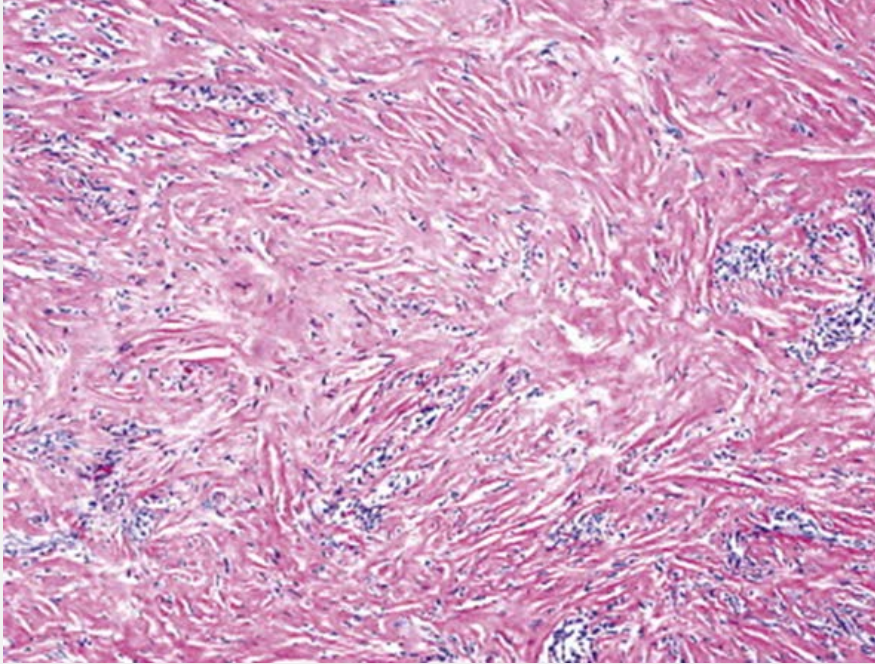
# TUZAKLAR!

- Biyopsinin yeterli olmaması
  - Dezplastik MM/Fibröz plörezi
- Kandırıkçı yağ
  - Organize plörit
- Yalancı invazyon
  - İnflamatuvar reaktif prosesler
- Sarkomatoid mezotelyoma
- Nadir görülen tip veya alt tip ile karşı karşıya olmak
  - Epiteloid hemanjoendotelioma/anjiosarkom/Mikrokistik adenomatoid MM, şeffaf hücreli MM vs
- İmmünohistokimyasal nedenli tuzaklar
  - Sensitivite-spesifite problemleri/standardizasyon
  - Fokal zayıf pozitifliğe çok fazla anlam yüklemek
  - Belirteçleri iyi tanımamak
  - .....

# Dezmoplastik tip

Biyopsi yetersizliğinden en çok etkilenen tip; potansiyel tuzak  
#1





- Desmoplastik mezotelyoma tanısı vermek için en önemli histopatolojik bulgular:
  - Göğüs duvarı ve akciğer invazyonu
  - "Sakin" nekroz odakları
  - Sarkomatöz odak
  - Uzak metastaz

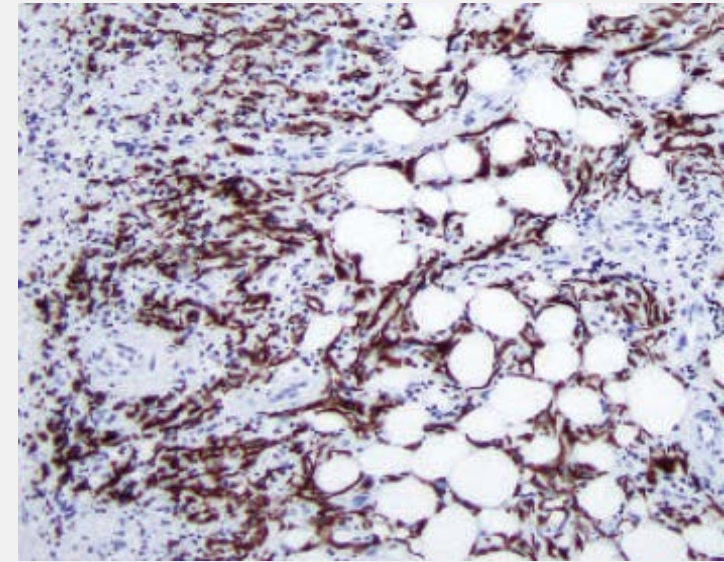
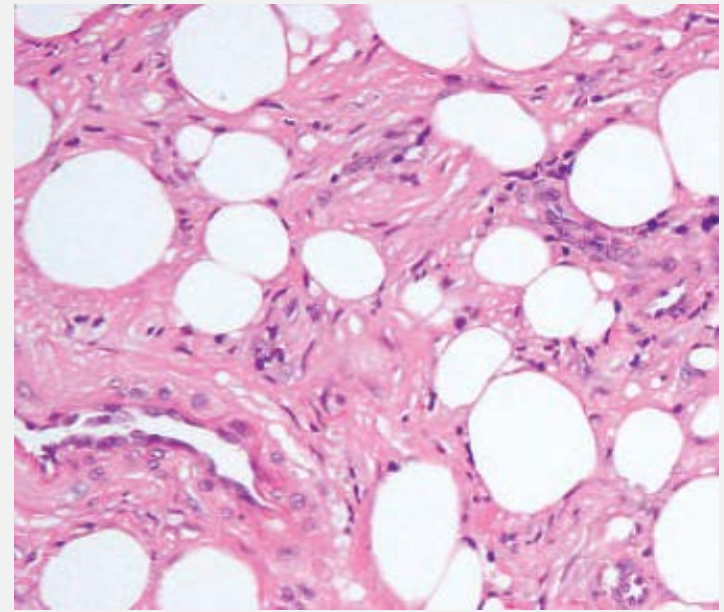
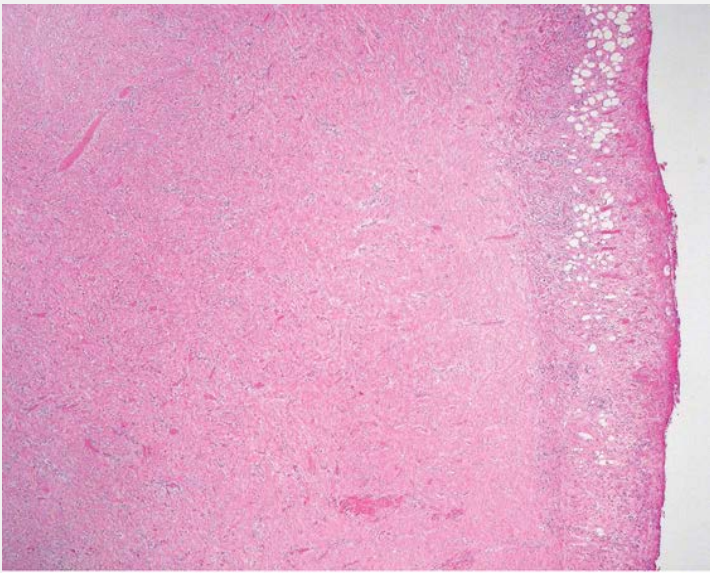
## Dezmoplastik Mezotelyoma/Organize Plörit Ayırıcı Tanısı

Organize plörit

Sellülarite efüzyonun hemen altında en fazla, giderek azalır (zonasyon)  
Stromal invazyon yok (ancak küçük damarlar boyunca yağ dokuya giren fibröz doku olabilir)  
Efüzyonun hemen altındaki hücreler atipiktir  
Kapillerler yüzeye diktir  
Nekroz yoktur  
Sarkomatöz odak yoktur  
Nodüler stromal genişleme yoktur

Dezmoplastik Mezotelyoma

Zonasyon yok  
Yağ doku, kas ve akciğer invazyonu  
Atipiyi ayırmak zordur  
Kapillerler belirsizdir  
Nekroz  
Sarkomatöz odak  
Nodüler stromal genişleme



Organize plörit

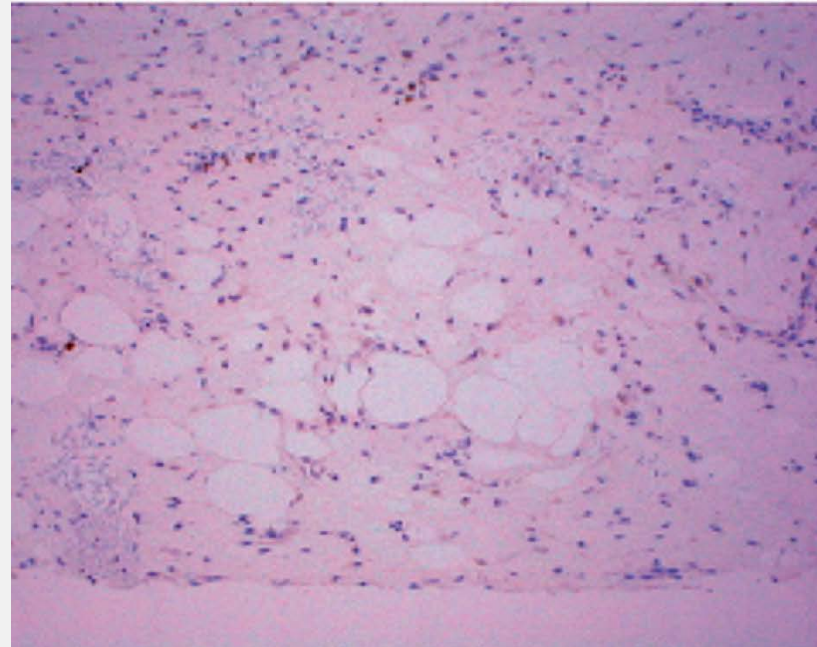
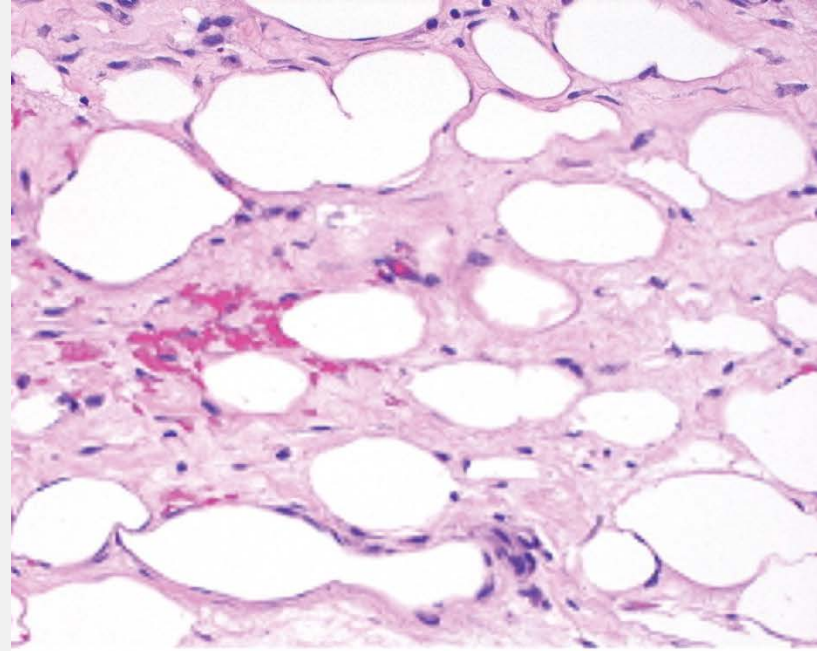
DMM

# “Kandırıkçı” yağ invazyonu

Potansiyel Tuzak #2

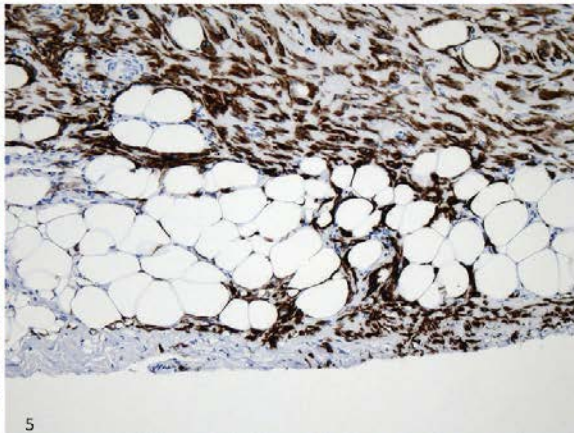
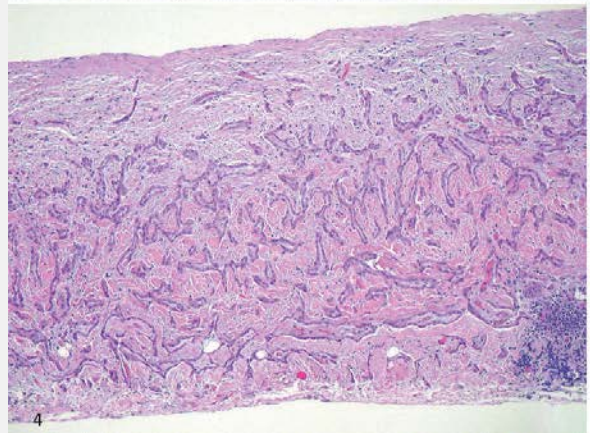
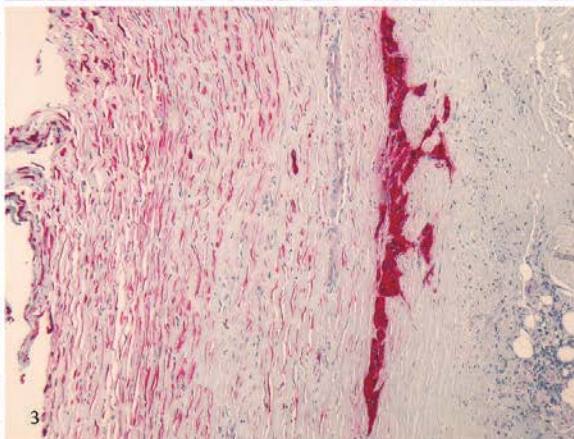
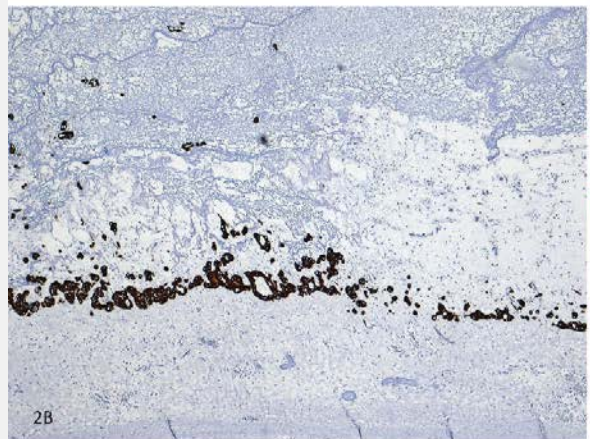
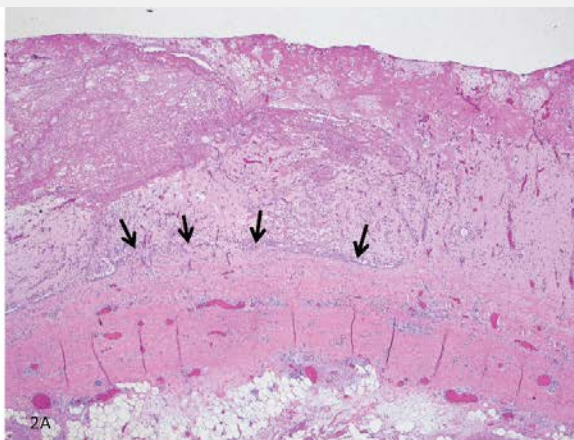
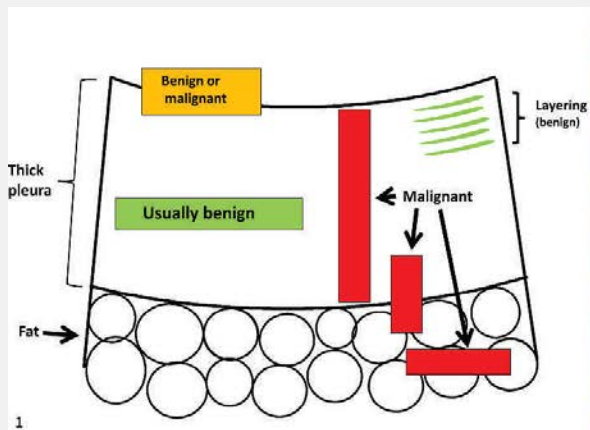
## **“Kandırıkçı” yağ invazyonu**

Yuvarlak olmaktan çok,  
düzensiz köşeli formda,  
Yüzeye paralel,  
S-100 ve vimentin negatif



# Reaktif mezotelyal “aşırı” proliferasyon

Potansiyel Tuzak #3



Churg A, et al.  
Arch Pathol Lab Med—Vol 136, October 2012

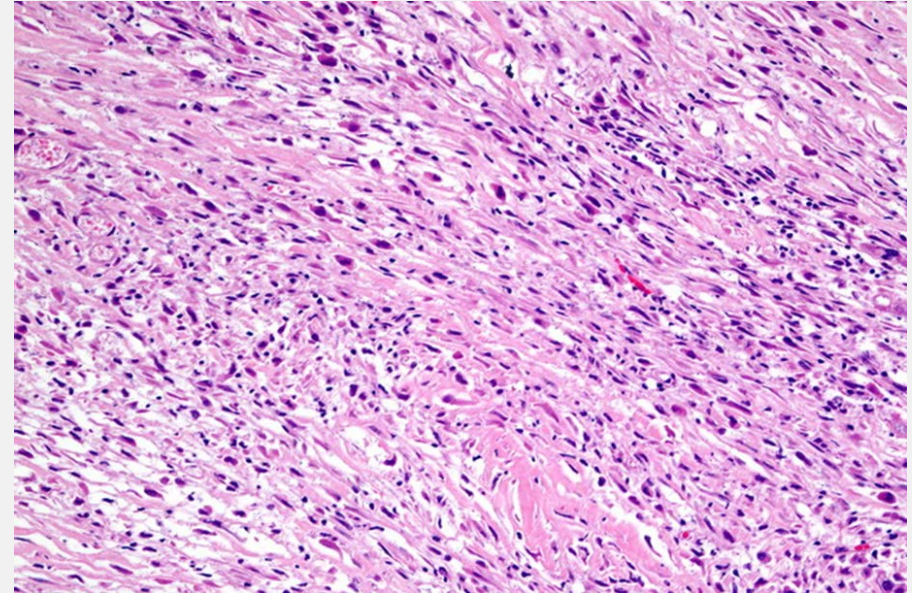
# Sarkomatoid mezotelyoma

Potansiyel Tuzak #4



# Sarkomatoid mezotelyomada mezotelyoma belirteçleri:

AE1/AE3	%75 (18/24)
CAM5.2	%96 (23/24)
MNF116	%100 (21/21)
Calretinin	%25 (6/24)
WT1	%33 (8/24)
<b>D2-40</b>	<b>%100 (24/24)</b>



# Pleomorfik iğsi hücreli bir tümörde

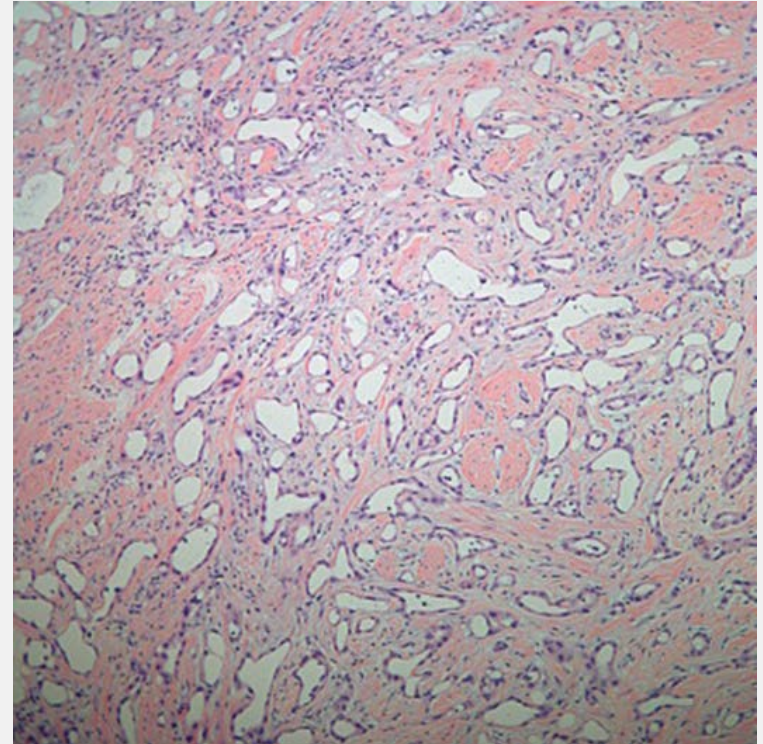
- Diffüz keratin ekspresyonu varsa AT;
  - Sarkomatoid MM,
  - Sarkomatoid karsinom
  - Sinoviyal sarkom
  - Sarkomatoid RCC

# Nadir görülen plevral tümörler ve mezotelyoma alt tipleri

Potansiyel Tuzak #5

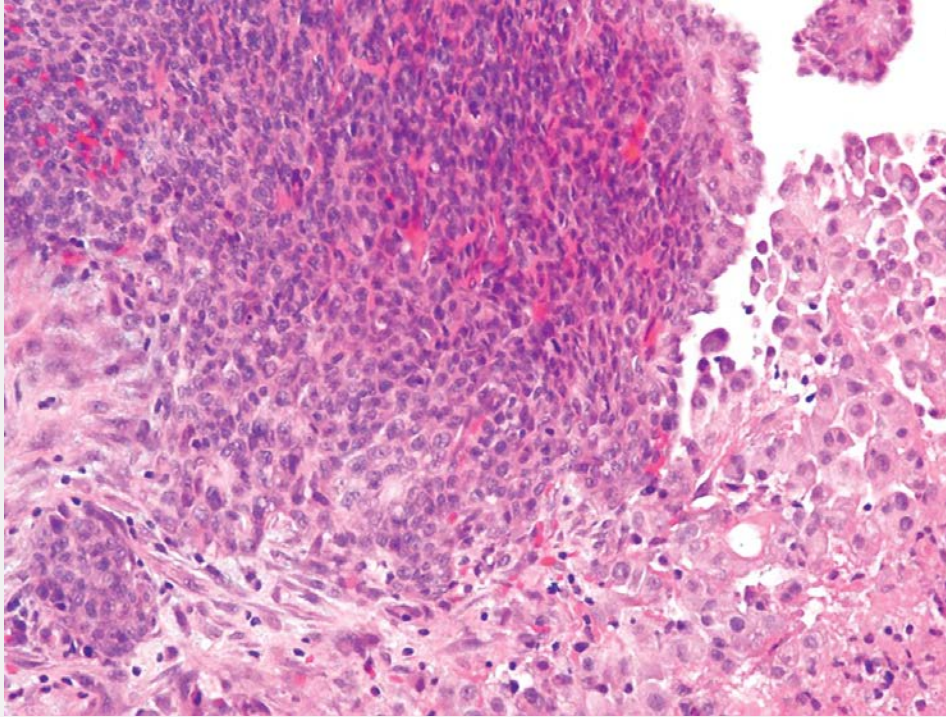
# Adenomatoid mezotelyoma

- AT;
- Benign adenomatoid  
tumor
- Metastatic  
adenocarcinoma
- Epithelioid  
hemangioendothelioma

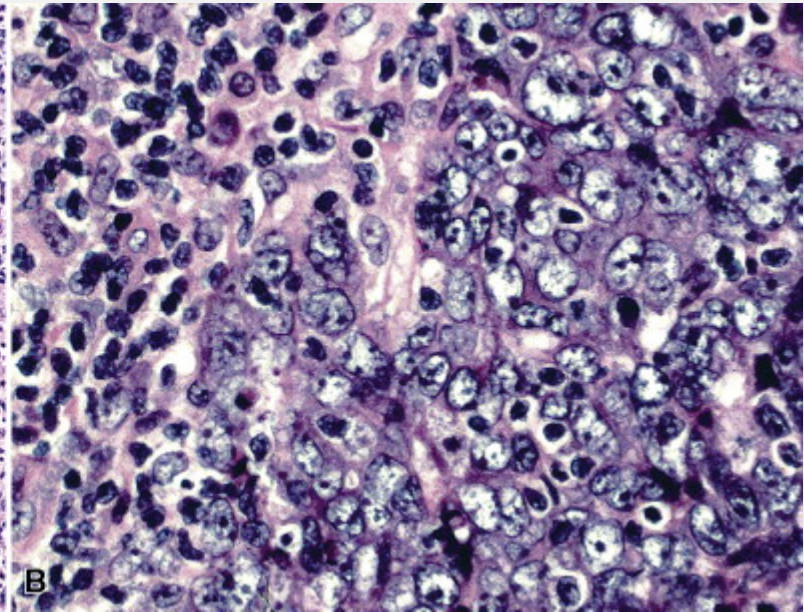
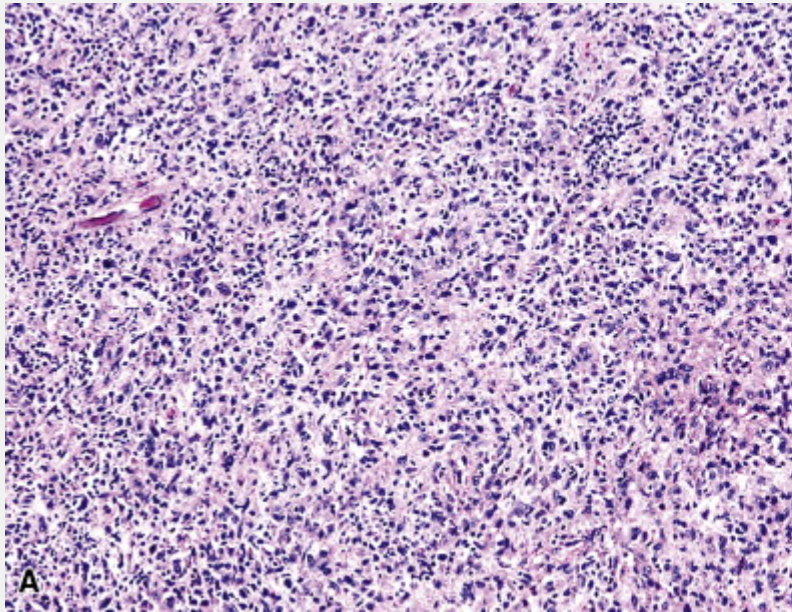


*Weissferdt A, et al. Ann Diagn Pathol. 2011*

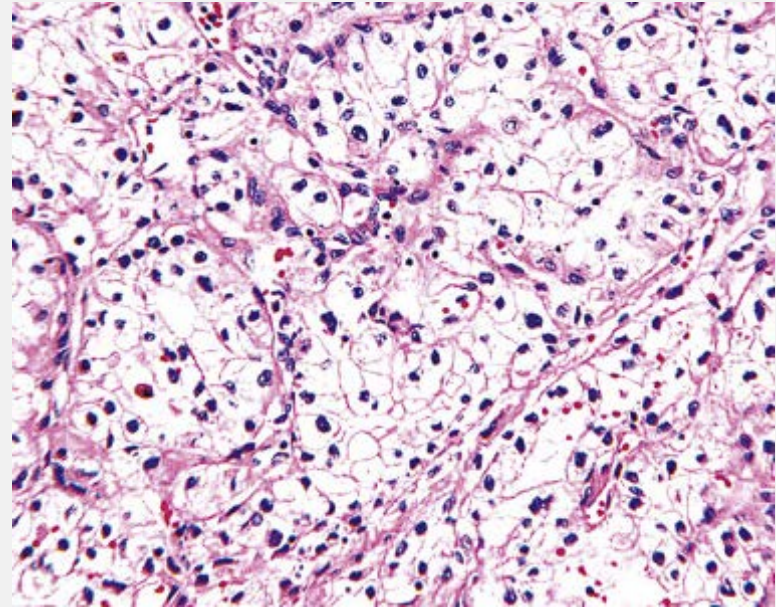
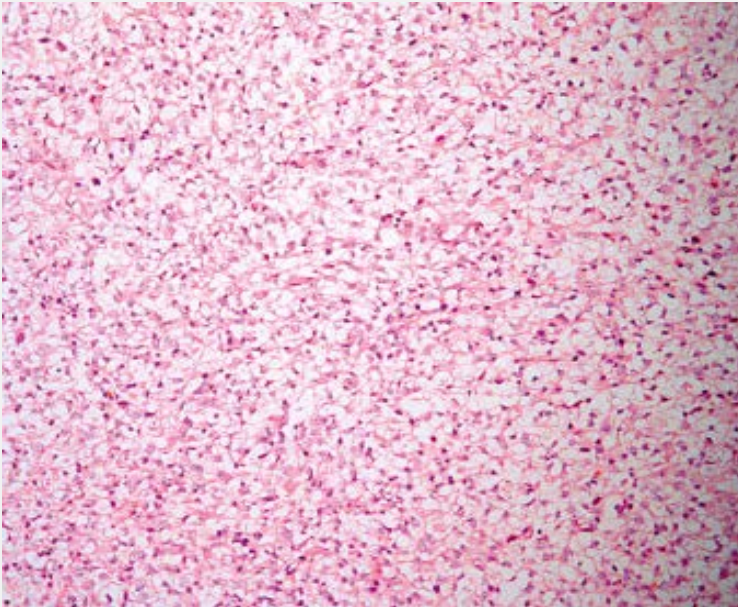
- Küçük hücreli mezotelyoma



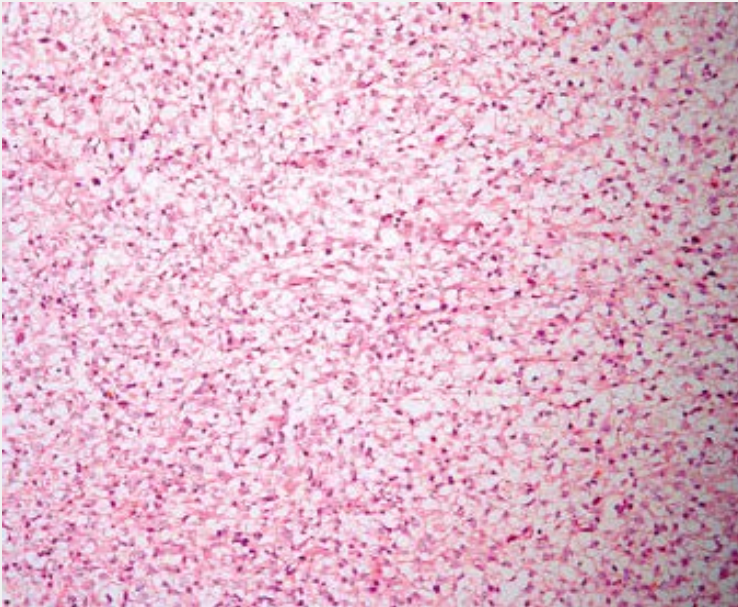
- Lenfohistiositoid mezotelyoma



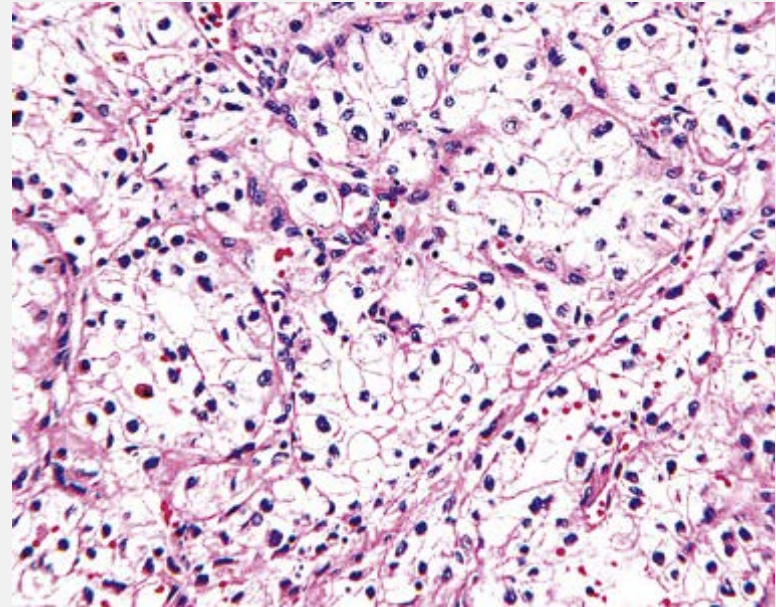
- Berrak hücreli mezotelioma



- Berrak hücreli mezotelioma



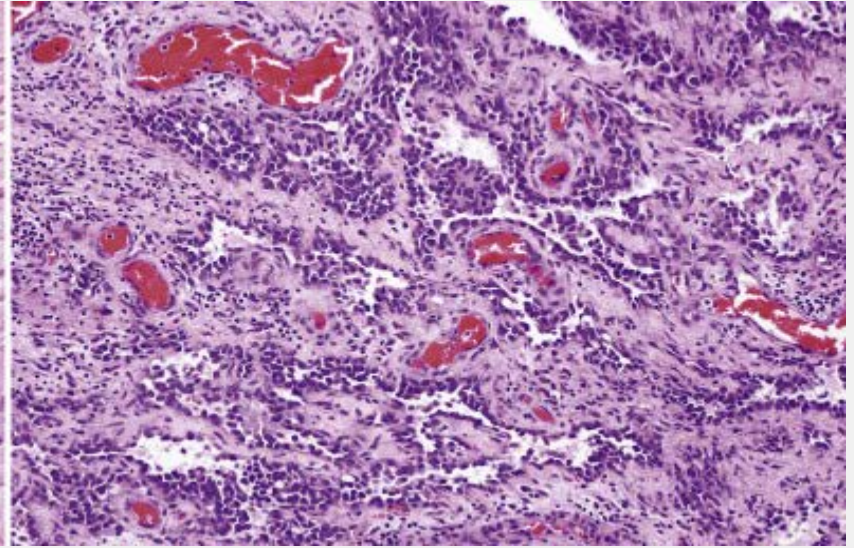
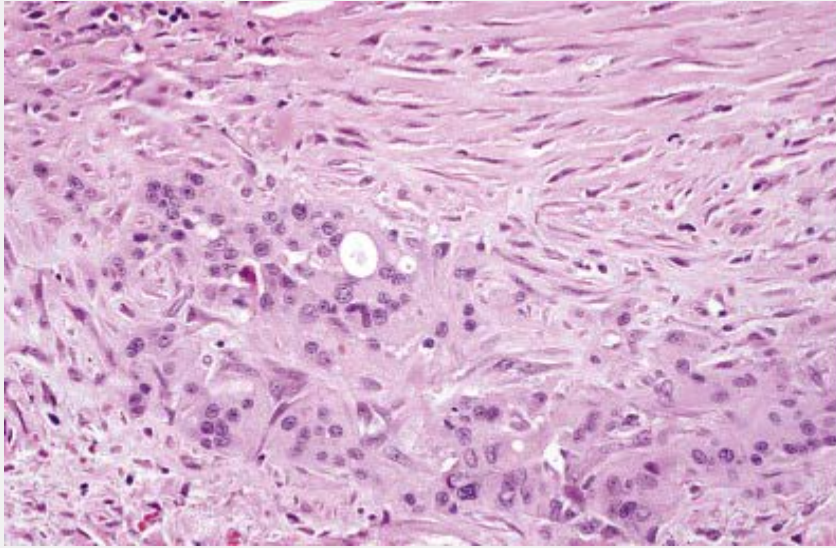
mezotelyoma



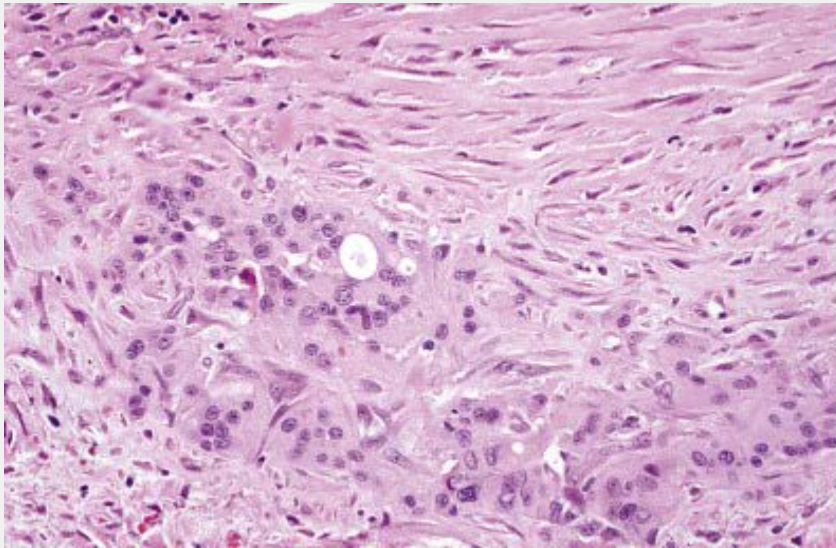
RCC metastazı



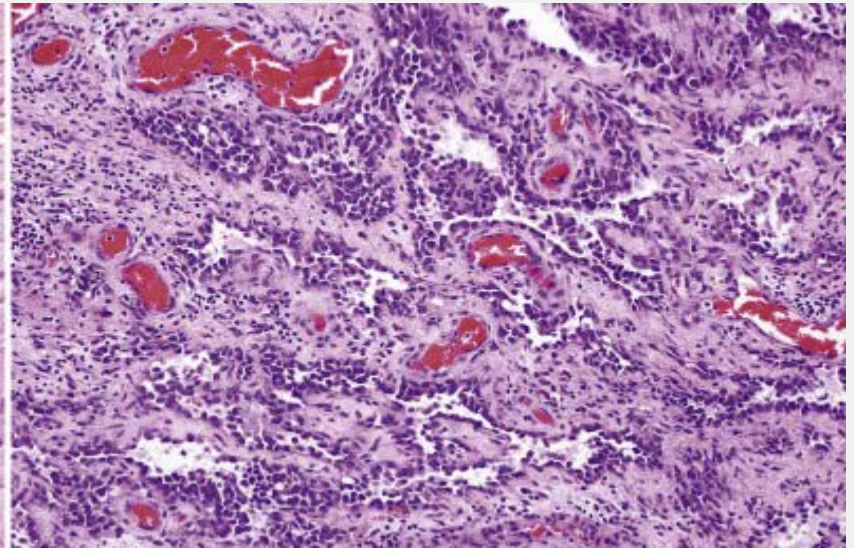
- Ordonez ve ark.;
- RCC-ma RCC %50/MM%8
- CD10 MM %48 pozitif
- En güvenilir kombinasyon D2-40 ve CK5/6, en güvenilir negatif belirteç pax 2 ve 8



## MEZOTELYOMA



## ANJIOSARKOM



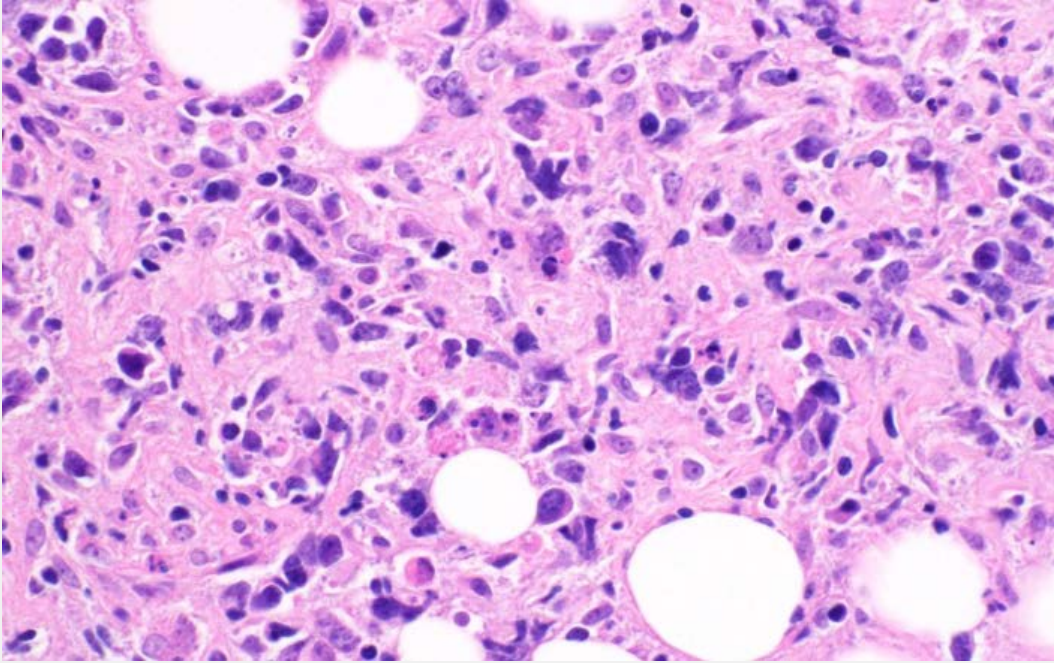
Tek bir immünohistokimyasal belirteçe "bel bağlamak"

Potansiyel tuzak #6

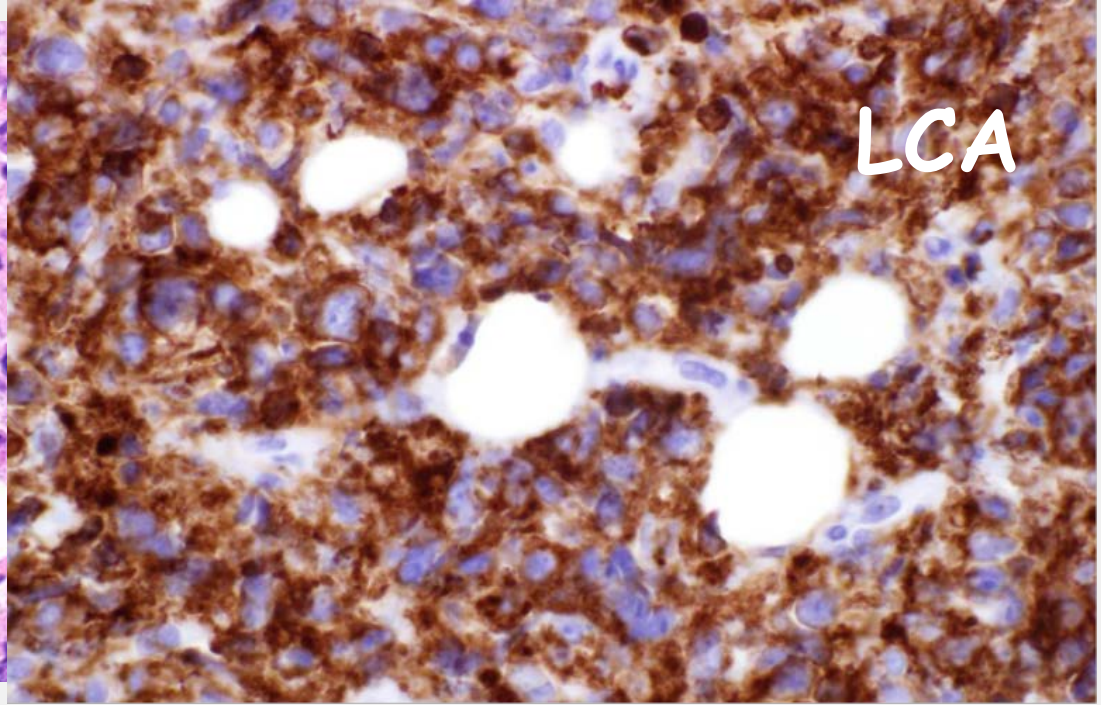
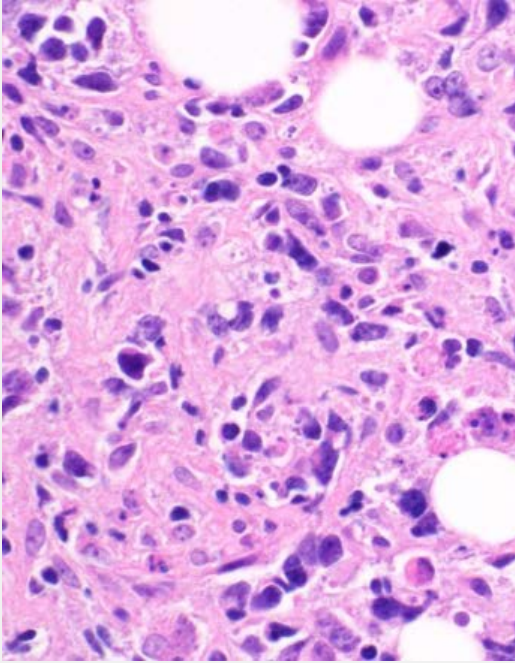
- Naito Y, et al. D2-40-positive solitary fibrous tumors of the pleura: diagnostic pitfall of biopsy specimen.

**İçine sinmiyorsa, zorlama!**

Potansiyel tuzak #7



64 yaşında kadın hasta, göğüs duvarına invaze kitle, akciğer? Plevra?  
Vim+, PK-, p63+, Kalretinin-, WT1-



64 yaşında kadın hasta, göğüs duvarına invaze kitle, akciğer? Plevra?  
Vim+, PK-, p63+, Kalretinin-, WT1-



# Lenfomalarda p63

ABHL, n=2	%50
KLL/SLL, n=13	%23
DBBHL, n=27	%33
FL, grade 1 (n=12)	%0
FL, grade 2 (n=13)	%31
FL, grade 3 (n=11)	%36
MHL (n=5)	%0
MZL (n=4)	%25
KHL (n=28)	%0
NLPHL (n=6)	%17

Di Como CJ, et al. Clin Cancer Res. 2002 Feb;8(2):494-501.

# LCA negatif hematolenfoid tümörler

Potansiyel tuzak #7

- Akut megakaryoblastik lösemi
- B hücreli ALL
- ALK pozitif büyük B hücreli lenfoma
- Anaplastik büyük T hücreli lenfoma, ALK+ (bazan)
- Klasik Hodgkin lenfoma
- Folliküler dentritik hücreli sarkom

# İMMÜNHİSTOKİMYA NEDENLİ TUZAKLAR

# İMMÜNİSTOKİMYA NEDENLİ TUZAKLAR

Histolojik kategori ve patern tanımlamadan panel istemek

Potansiyel tuzak #8

- Histolojik kategori; (1) iğsi hücreli, (2) epithelioid hücreli, (3) Bifazik, ve (4) küçük mavi hücreler.
- Histolojik patern; (1) papiller, (2) diskoheziv, (3) anjiomatoid, (4) lipomatöz/berrak hücreli

Antibodies	Epithelioid MM	Lung ADC	Other Carcinomas
Calretinin	+ <sup>a</sup>	-/+	Breast CA -/+; SCC -/+; RCC -/+; SCLC -/+
D2-40	+ <sup>b</sup>	-	SCC -/+; RCC -
CK5/6	+	-	SCC +; RCC -; UC +
WT1	+ <sup>c</sup>	-	Breast CA +/-; SCC -; RCC -
Mesothelin	+	+/-	SCC -/+; pancreatic ADC +; UC +; RCC -
Thrombomodulin	+	+/-	SCC +/-; RCC -; UC +
MOC31	-/+ (small area or sparse)	+	Breast +; SCC +; UC -/+; RCC -/+
Ber-EP4	-/+ (small area or a few)	+	SCC +; RCC +/-
pCEA and mCEA	-	+	Breast CA +; SCC -/+; RCC -; colon ADC +
B72.3	-	+	breast CA +; SCC +/-
BG8	-/+ (small area or sparse)	+	breast CA +; SCC +/-
CD15	-	+/-	RCC +; SCC -/+
Claudin-4	-	+	Breast CA +; SCC +; RCC +/-; UC +/-

Abbreviations: ADC, adenocarcinoma; Ber-EP4, epithelial cell adhesion molecule antibody; BG8, anti-blood group Lewis Y; CA, carcinoma; CD15, cluster of differentiation 15; CK5/6, cytokeratin 5/6; D2-40, podoplanin; mCEA, monoclonal carcinoembryonic antigen; MM, malignant mesothelioma; pCEA, polyclonal carcinoembryonic antigen; RCC, renal cell carcinoma; SCLC, small cell lung carcinoma; SCC, squamous cell carcinoma; UC, urothelial carcinoma; WT1, Wilms tumor 1; +, greater than 75% of cases are positive; +/-, 50%-75% of cases are positive; -/+, 5%-50% of cases are positive; -, less than 5% of cases are positive.

<sup>a</sup> Both nuclear and cytoplasmic stains.

<sup>b</sup> Membranous stain, usually along the apical surface of the cells.

<sup>c</sup> Nuclear stain.

Antibody	Mesothelioma	Sarcomatoid Carcinoma	Synovial Sarcoma	Solitary Fibrous Tumor	Desmoplastic Small Round Cell Tumor	Desmoid Tumor
Pan-CK	+	+/-	+/- <sup>a</sup>	-	+ (focal patchy positivity)	-
CKAE1/3	+	+/-	+/- <sup>a</sup>	-	+ (focal patchy positivity)	-
CK5/6	+/-	Rare +	+/- <sup>a</sup>	-	-	-
Calretinin	+	-/+	+/- <sup>a</sup>	-	-	-
WT1	+	-	-	-	+	-
D2-40	+	-	+	-	-	-
CD34	-	-	-	+	-	-
Bcl2	-/+	-	+	+	-/+	-/+
CD99	-	-/+	+/-	+	-/+	-
Desmin	-	-	-	-	+ (dotlike pattern)	-
Vimentin	+	+/-	+	+	+	+
β-Catenin	-	-	-	-	-	+ (nuclear and cytoplasmic pattern)

Abbreviations: Bcl2, B-cell CLL lymphoma 2; CD, cluster of differentiation; CK, cytokeratin; D2-40, podoplanin; Pan-CK, pancytokeratin; WT1, Wilms tumor 1; +, greater than 75% of cases are positive; +/-, usually more than 50% of cases are positive; -, less than 5% of cases are positive; -/+, less than 50% of cases are positive.

<sup>a</sup> More often positive in biphasic synovial sarcoma.



## Primer plevral sarkomların immünohistokimyasal analizi

*Erb CT, Johnson KM, Kim AW. Rare pleural tumors. Clin Chest Med. 2013*

Tumor Type	Vimentin	Cytokeratin	Desmin	Actin	EMA	S-100	C99	Factor 8	Calretinin	SMA
SFTP	+	-	-	-	-	-	+	-	-	-
Carcinoma	-	+	-	-	-	-	-	-	-	-
Primary smooth muscle tumor	+	-	+	-	-	-	-	-	-	+
Vascular sarcoma	+	-	-	-	-	-	-	-	-	-
Rhabdomyosarcoma	+	-	+	-	-	-	-	-	-	-
Malignant fibrous histiocytoma	+	-	-	-	-	-	-	-	+	-
Synovial sarcoma	+	+/-	-	-	+	-	+	-	-	-
Liposarcoma	+	-	-	-	-	-	-	-	-	-
Fibrosarcoma	+	-	-	-	-	+	-	-	-	-
Epithelioid hemangioendothelioma	+	-	-	-	-	-	-	+	-	-
Chondrosarcoma	+	-	-	+	-	+	+	-	-	-

(+) indicates the marker is typically positive in the tumor type indicated; (-) indicates the marker is typically negative in the tumor type indicated; (-) indicates the marker is not routinely tested for in the work up or a particular tumor type, but would presumably be negative if it were to be tested for.

*Abbreviations:* CEA, carcinoembryonic antigen; EMA, epithelial membrane antigen; SFTP, solitary fibrous tumor of the pleura; SMA, smooth muscle actin; TTF-1, thyroid transcription factor-1.

# İMMÜNİSTOKİMYA NEDENLİ TUZAKLAR

## Belirteçleri tanımamak

Potansiyel tuzak #9

# İMMÜNHİSTOKİMYA NEDENLİ TUZAKLAR

## Calretinin

- Calretinin

- Yüksek dereceli, çoğunlukla BRCA-1 ilişkili meme karsinomlarınınin %15'i pozitif (ER-, CK5/6 pozitif olabilir!)
- Sinovial sarkom ve bazı germ hücre tümörleri

Powel G, et al. Histopathology 2011.

# İMMÜNİSTOKİMYA NEDENLİ TUZAKLAR

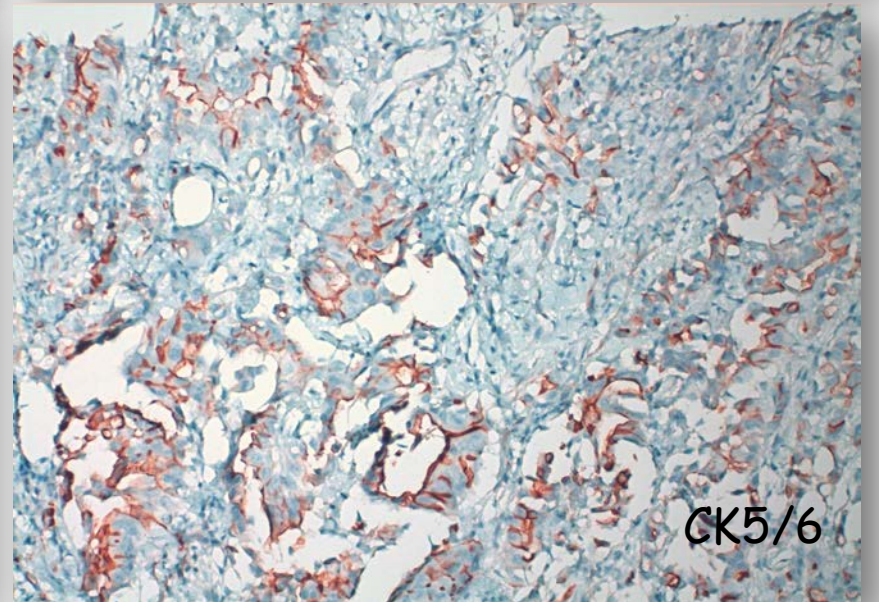
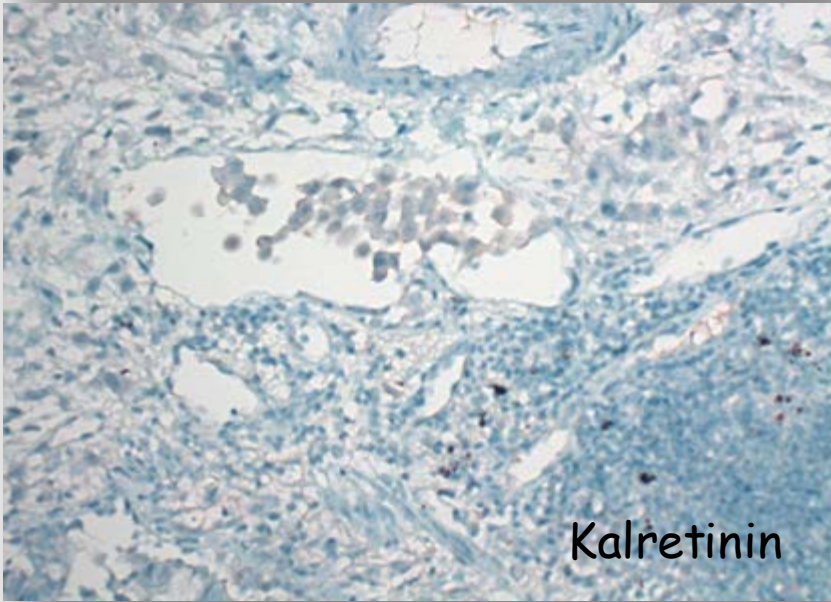
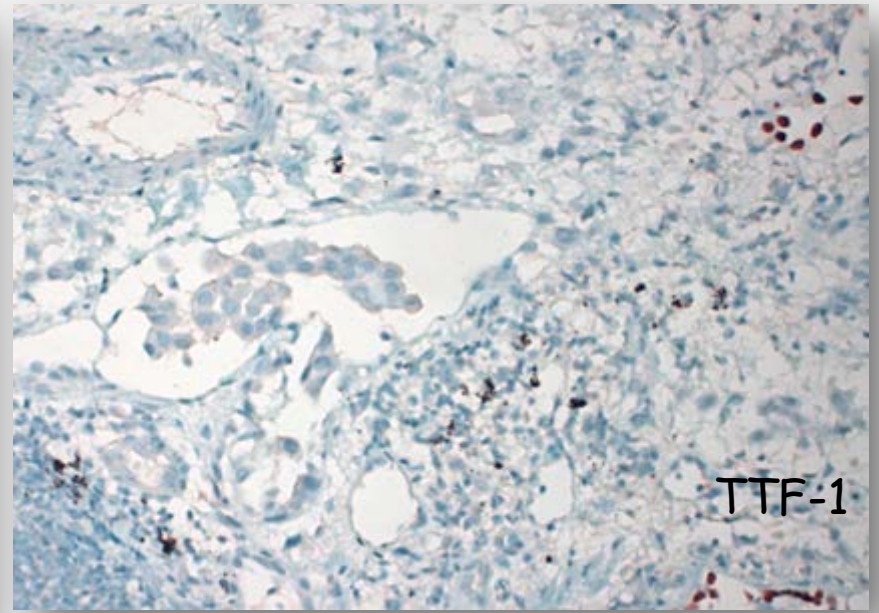
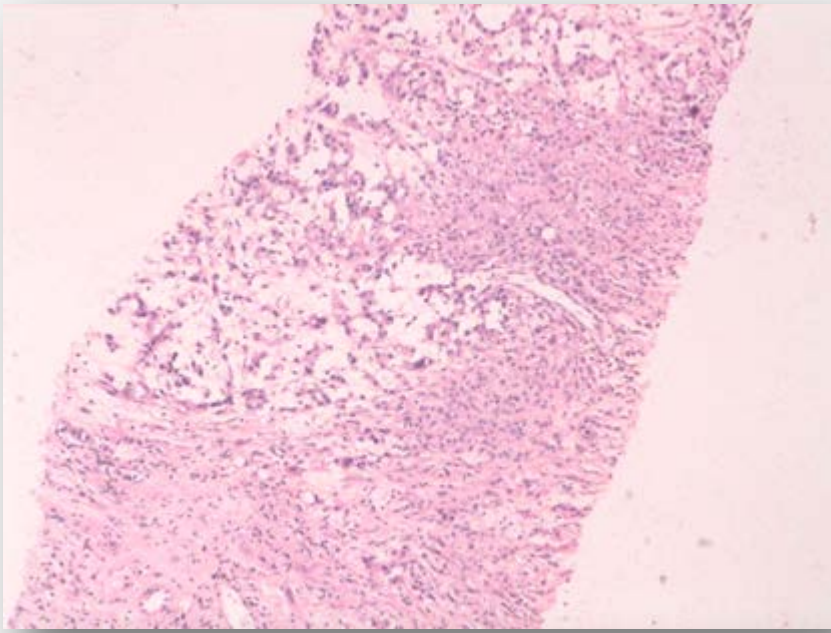
WT1

- WT1
  - Over seröz karsinomlarında ve melanomda pozitif olabilir

# İMMÜNİSTOKİMYA NEDENLİ TUZAKLAR

Zayıf ve fokal pozitifliğe çok fazla anlam yüklemek

Potansiyel tuzak #10



B-8597-2015 77 k, Sol akciğer, plevral kalınlaşma, trucut iğne biyopsi materyali  
P63 negatif



- **Eve gidecek mesajlar;**
- En çok bilinen üç tip dışındaki «tuzak» nadir tipleri bilmek ve akılda tutmak
- Kandırıçı yağ doku ve yalancı invazyon ile mücadeleyi bilmek
- Yetersiz biyopsilerde immünohistokimya paneli seçmek ve değerlendirmeye dikkat etmek
- İmmünohistokimyanın standadizasyonu ve belirteçlerin tanınması
  - Tuzakları azaltacaktır



Teşekkürler....