



Epitelioid Sarkom: INI1, CD34, SALL4 ve CyclinD1 Ekspresyonu

Ece Özođul

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Gökhan Gedikođlu

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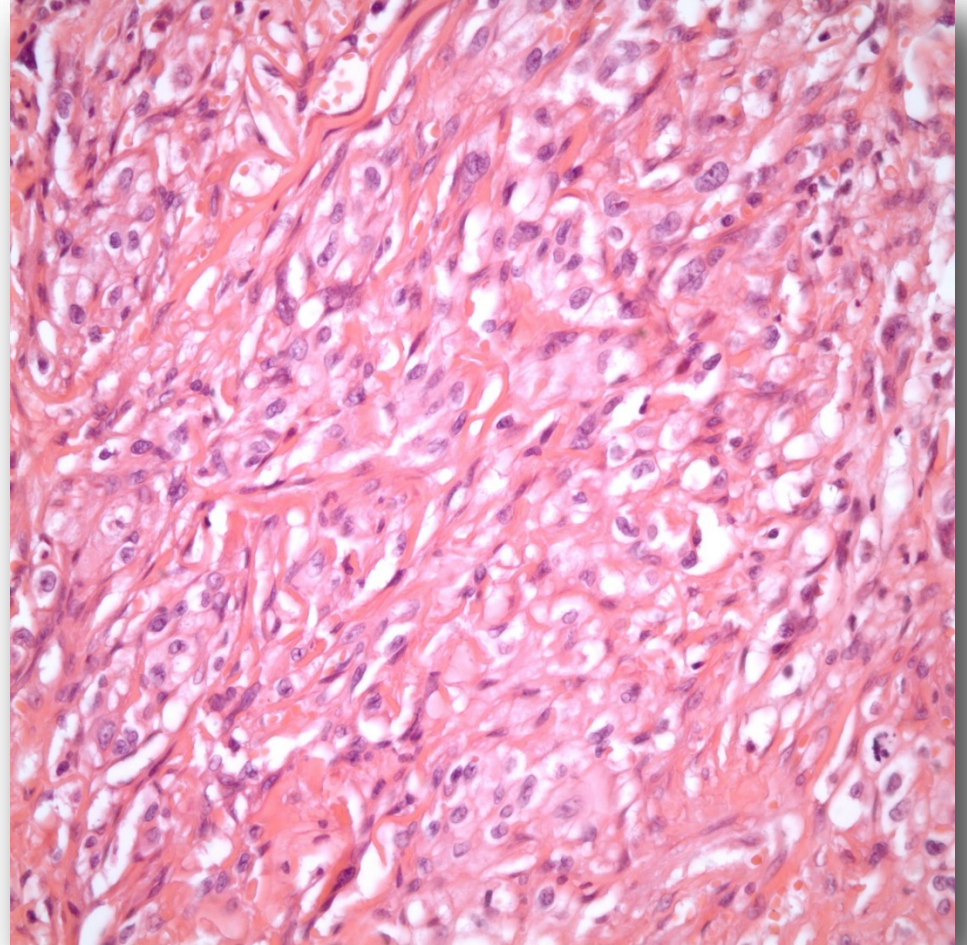
Giriş

Epitelioid sarkom klasik olarak **genç erişkin**lerin **distal ekstremitelerinde** görülen **epitelioid ve iğsi karakterde** kökeni belirlenemeyen **yüksek dereceli** mezenkimal bir tümördür.

Giriş

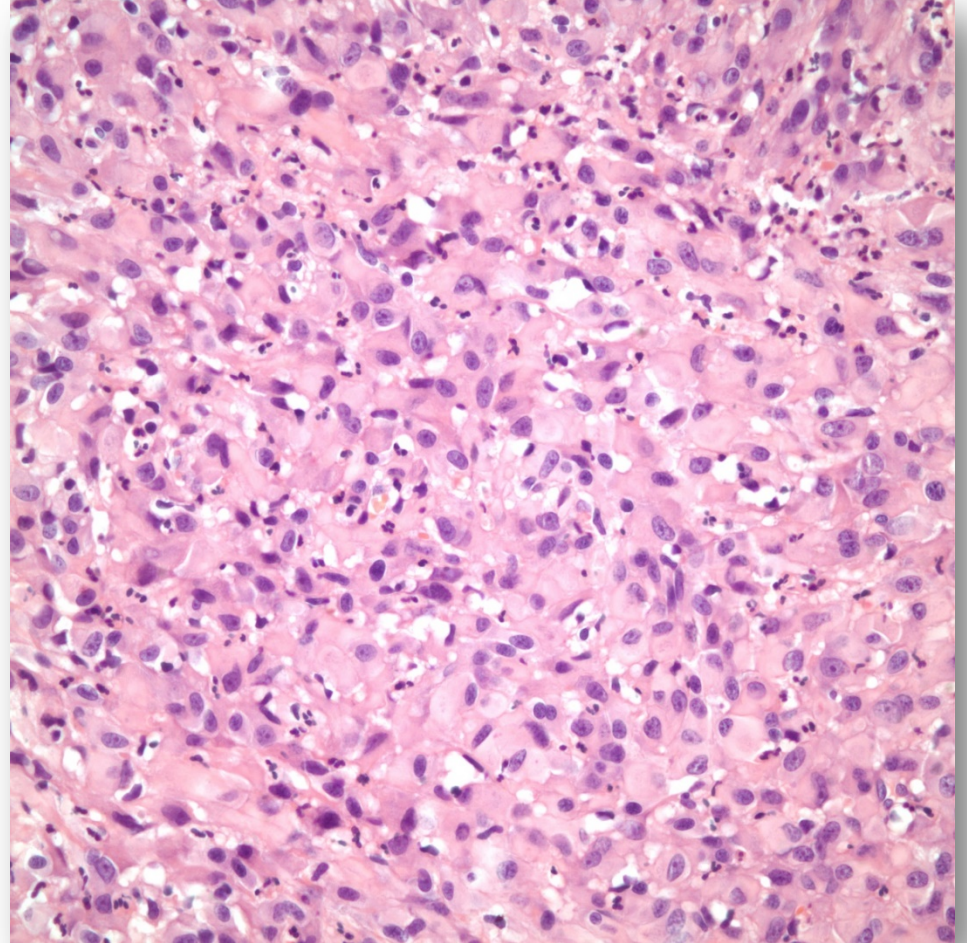
Klasik Varyant

- Psödogranülom
- Şişkin içsi/poligonal eozinofilik hücreler



Proksimal Varyant

- Belirgin atipiyeye sahip geniş epitelioid hücreler
- İntrasitoplazmik hyalen inklüzyonlar (rabdoid)
- Psödogranulomatöz görünüm Ø





Epitelioid Sarkom ve İHK

■ INI1 kaybı %90

* *Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma.* Hornick JL, et al. Am J Surg Pathol. 2009 Apr;33(4):542-50.

■ CD34 %50 olguda pozitif

* *Epithelioid sarcoma: an immunohistochemical analysis of 112 classical and variant cases and a discussion of the differential diagnosis.* Miettinen M et al. Hum Pathol. 1999 Aug;30(8):934-42.

* *Epithelioid sarcoma of Enzinger.* Fisher C. Adv Anat Pathol. 2006 May;13(3):114-21

■ CyclinD1 olguların %96'sında pozitif

* *Expression profile and molecular genetic regulation of cyclin D1 expression in epithelioid sarcoma.* Lin L et al. Mod Pathol. 2005 May;18(5):705-9.

■ SALL4, epitelioid sarkom – MERT ayrımında kullanılabilir

* *Differential SALL4 immunoexpression in malignant rhabdoid tumours and epithelioid sarcomas.* Akihiko Yoshida et al. (2015) Histopathology 66, 252–261. DOI: 10.1111/his.12460

* *ERG and SALL4 expressions in SMARCB1/INI1-deficient tumors: a useful tool for distinguishing epithelioid sarcoma from malignant rhabdoid tumor.* Kenichi Kohashi et al. Human Pathology (2015) 46, 225–230



Amaç

*Epitelioid sarkomların
morfolojik spektrumunu
ortaya koymak*

*Yeni tanımlanan bazı
immünohistokimyasal
belirteçlerin serimizdeki
durumunu belirlemek*

Materyal-Metod

- 2000 - 2015
- 26 hastaya ait 43 biyopsi örneği
 - 15 olgu
 - parafin bloktan 2-3'er adet 1 mm çaplı doku kullanılarak doku "mikroarray"i
 - 11 olgu
 - tam yüzey kesitler



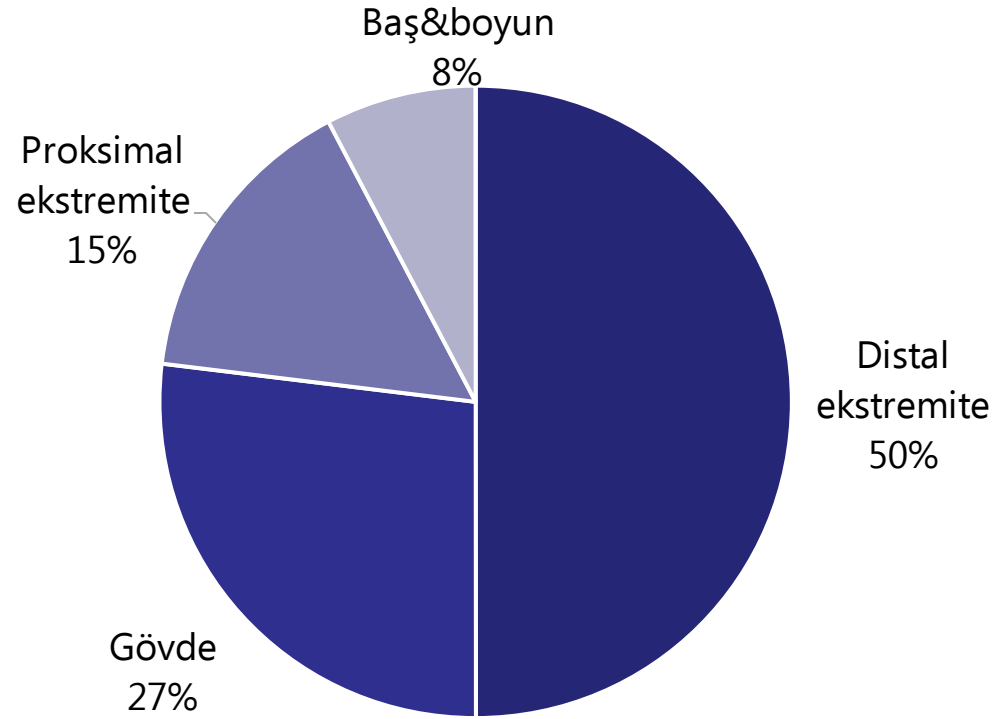
- İmmünohistokimya
 - Leica Bond Otomatik Boyama
 - INI1
 - (ZETA Corporation, Clone 25, 1:50-100)
 - Kayıp/Mozaik/Korunmuş
 - CD34
 - (Novocastra, QBEnd/10, 1:100)
 - Negatif/Pozitif (Fokal/Diffüz)
 - SALL4
 - (Biocare Medical, 6E3, 1:100-1:200)
 - Negatif/Pozitif (Fokal/Diffüz)
 - CyclinD1
 - (Biocare Medical, EP12, 1:200-1:400)
 - >%10 pozitif

Bulgular

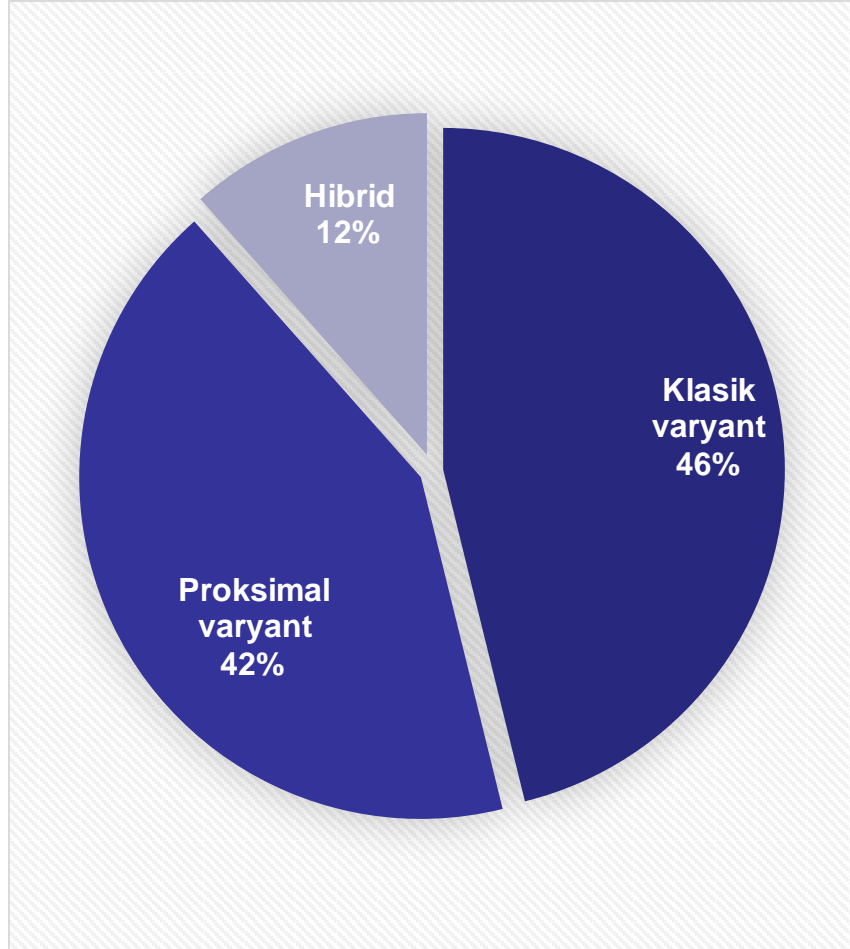
- Ortalama yaş : 33 (2-62)
- Erkek/Kadın : 3,3 (20:6)
- Tümör çapı ortalama 2,7 cm (0,3-6)



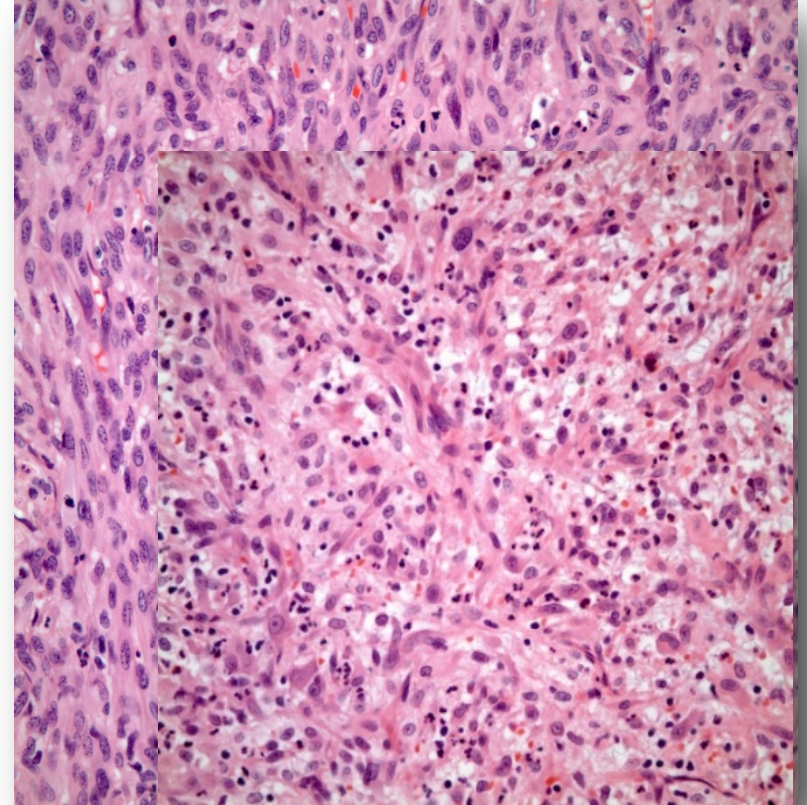
Yerleşim



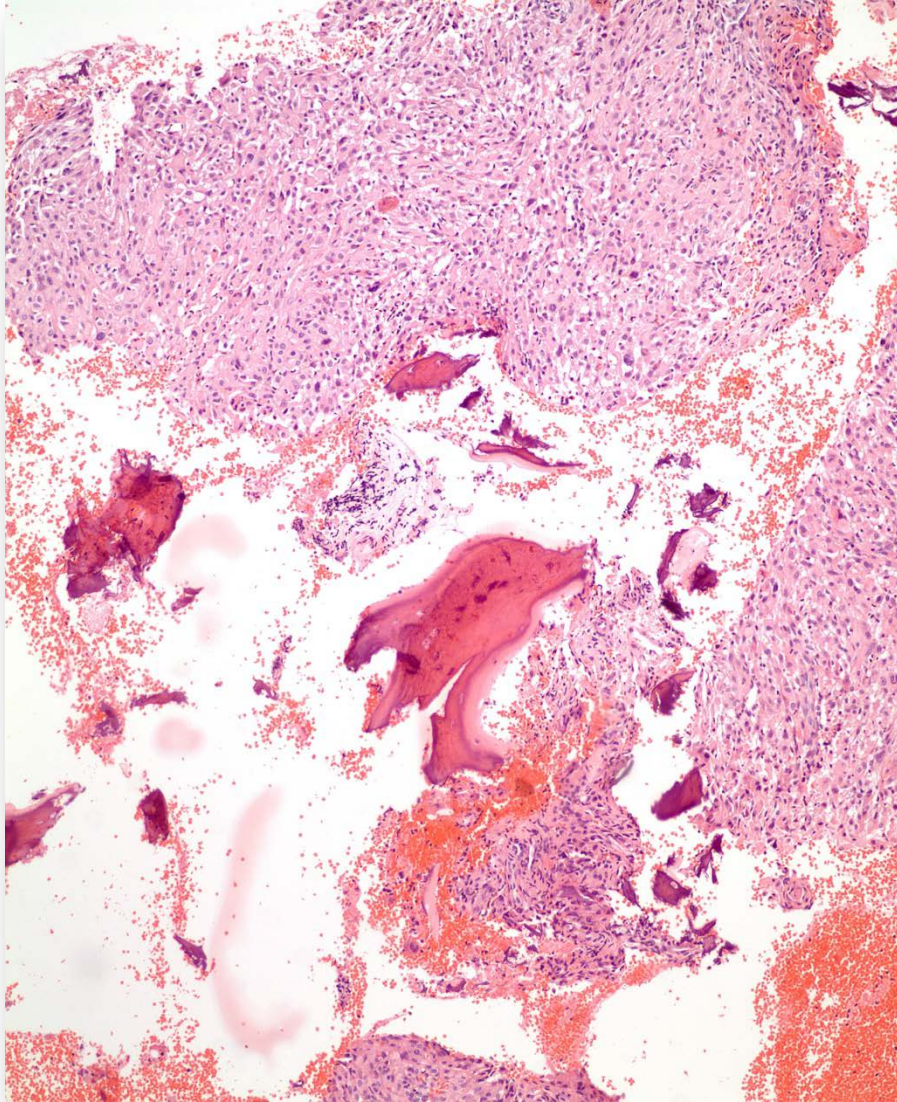
Bulgular



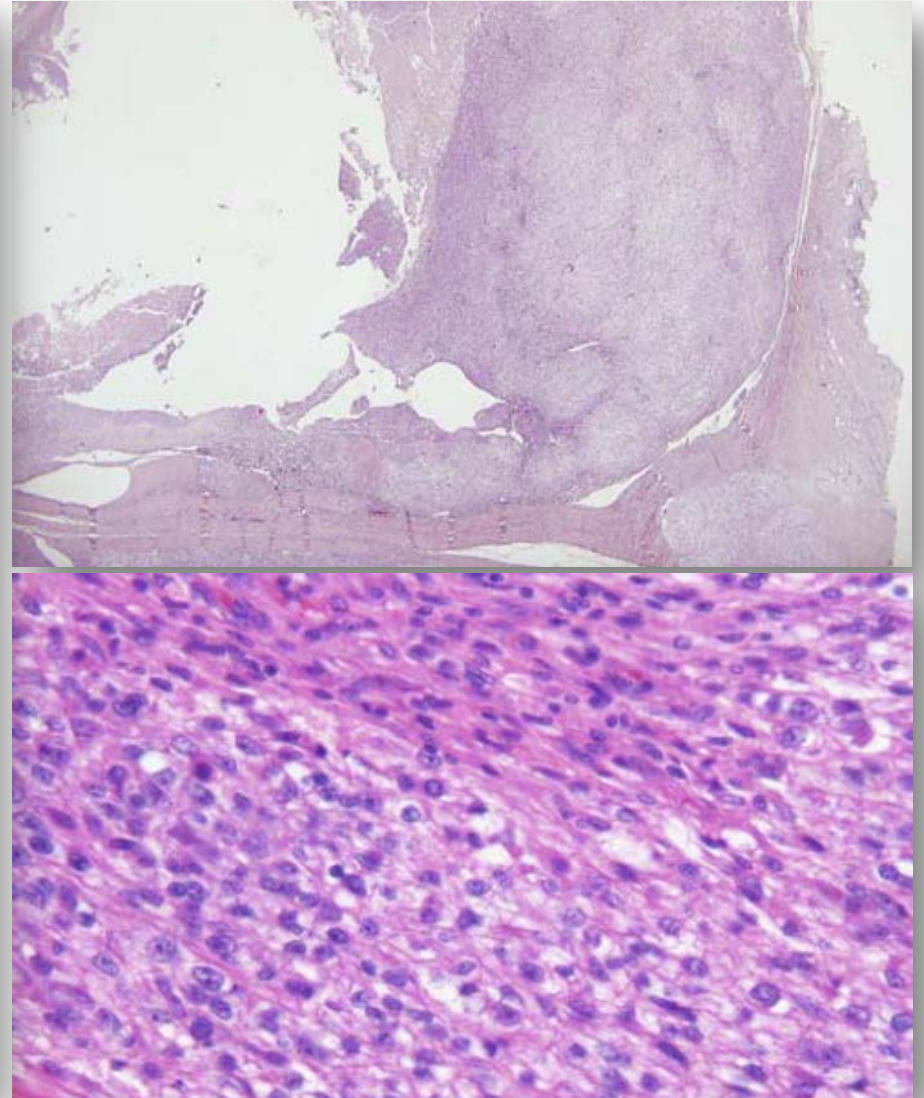
- Proksimal varyant olgularının 3' ünde MERT de ayırıcı tanıya girmektedir.



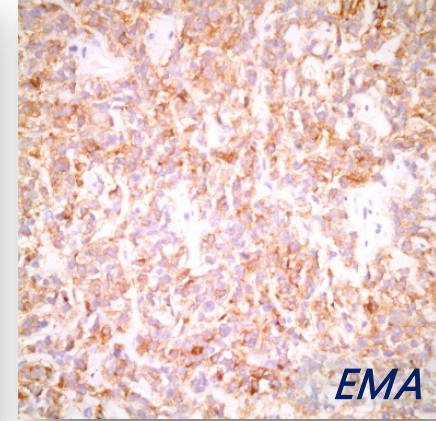
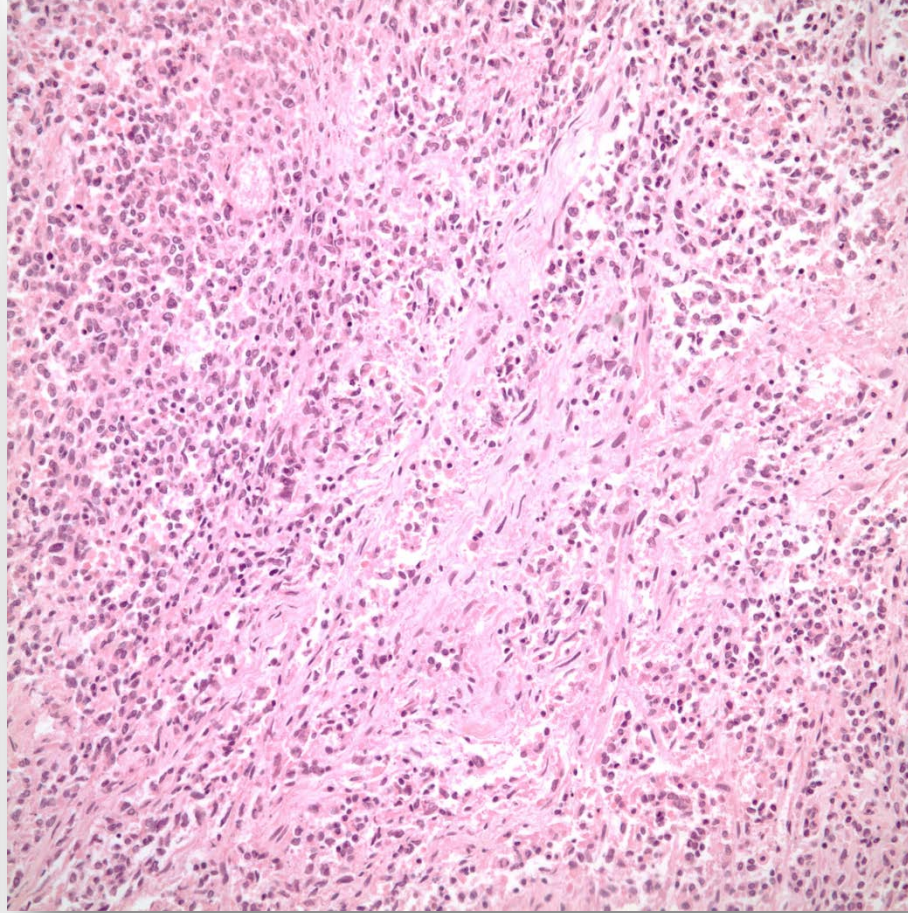
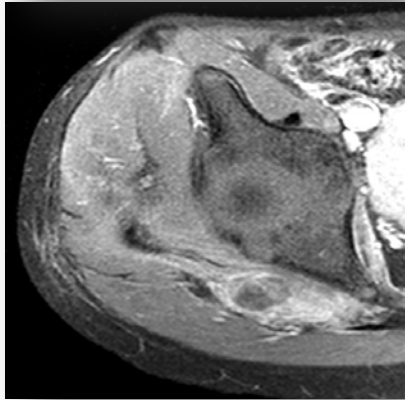
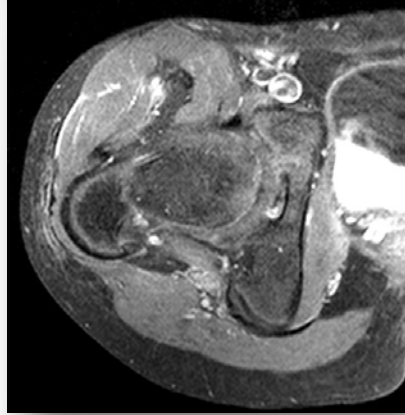
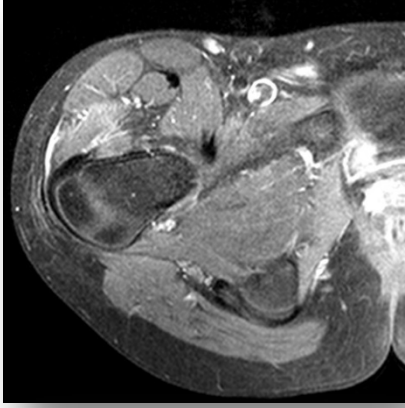
İntraosseöz (1 olgu)



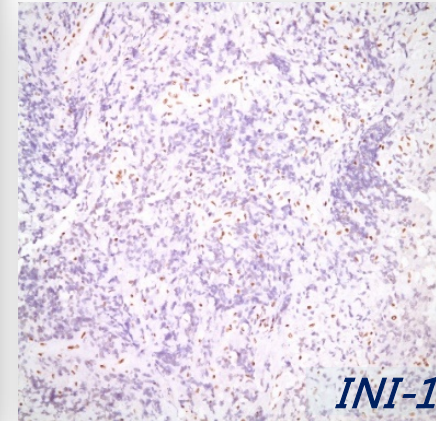
İntraartiküler (1 olgu)



2 olgu periferik sinir kökenlidir

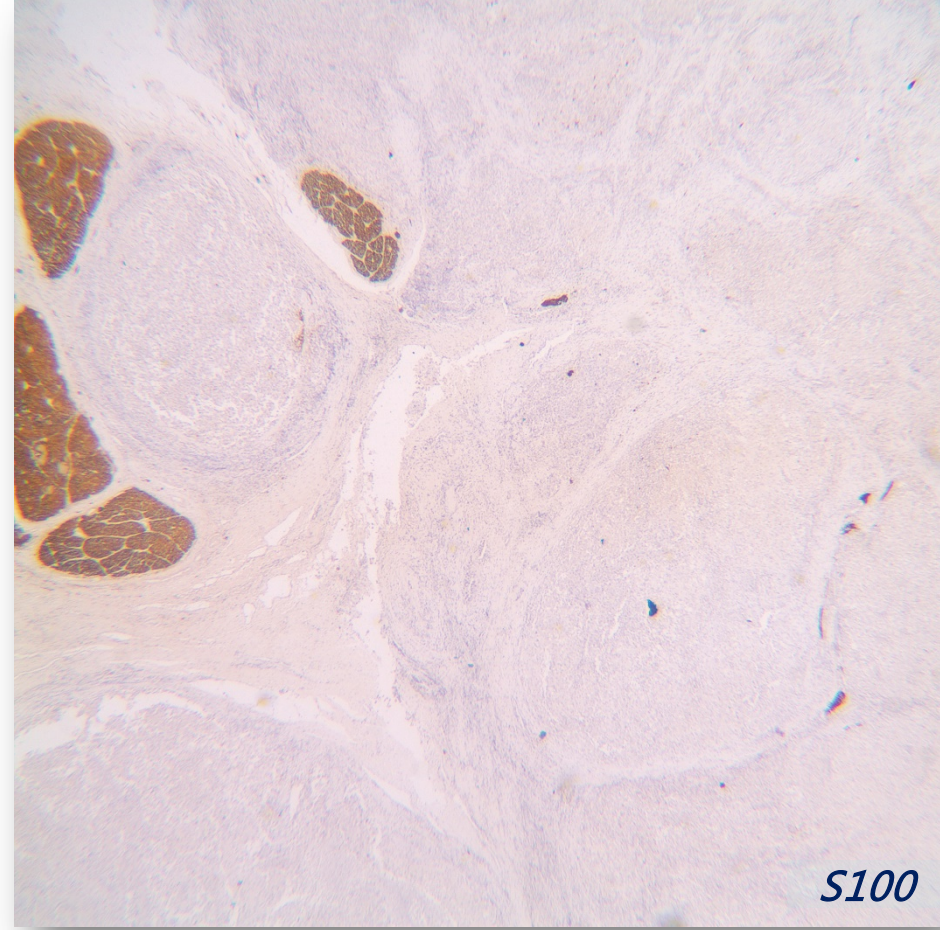
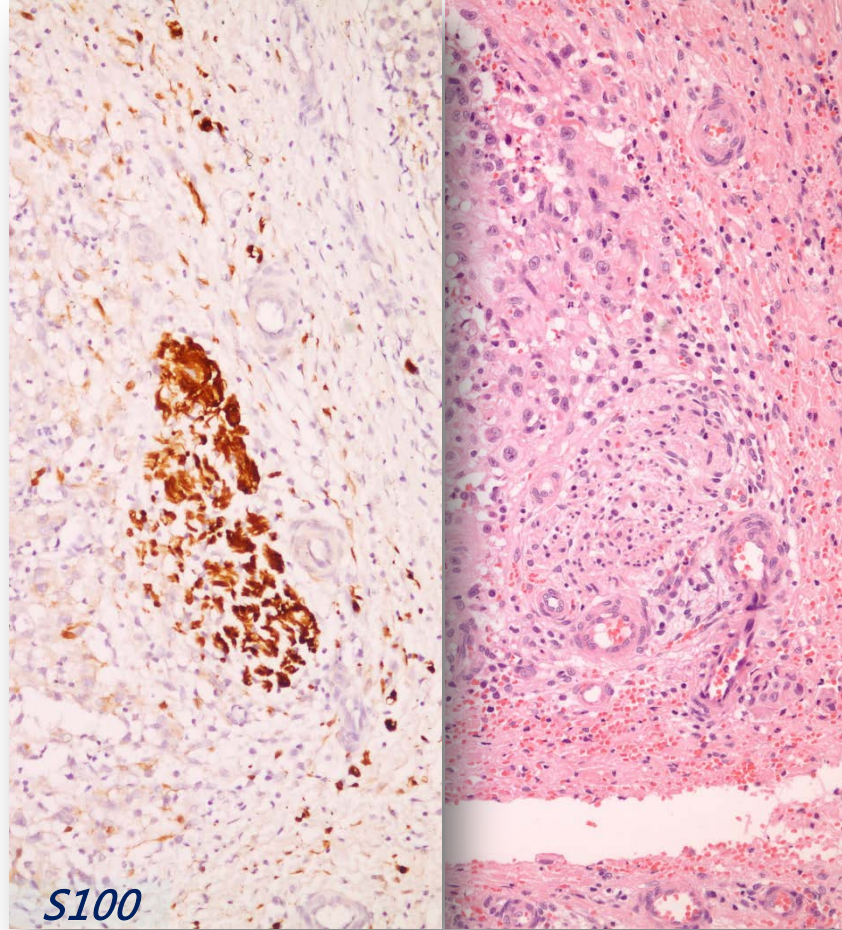


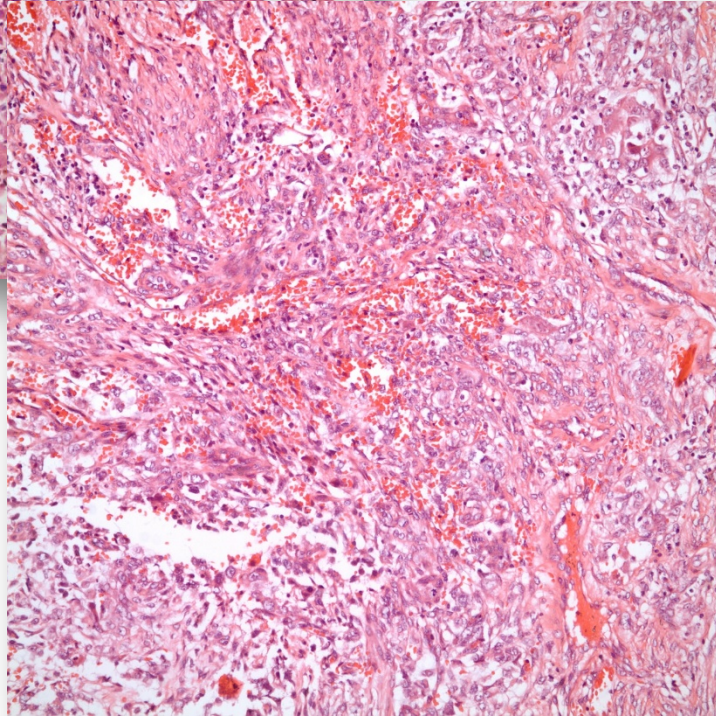
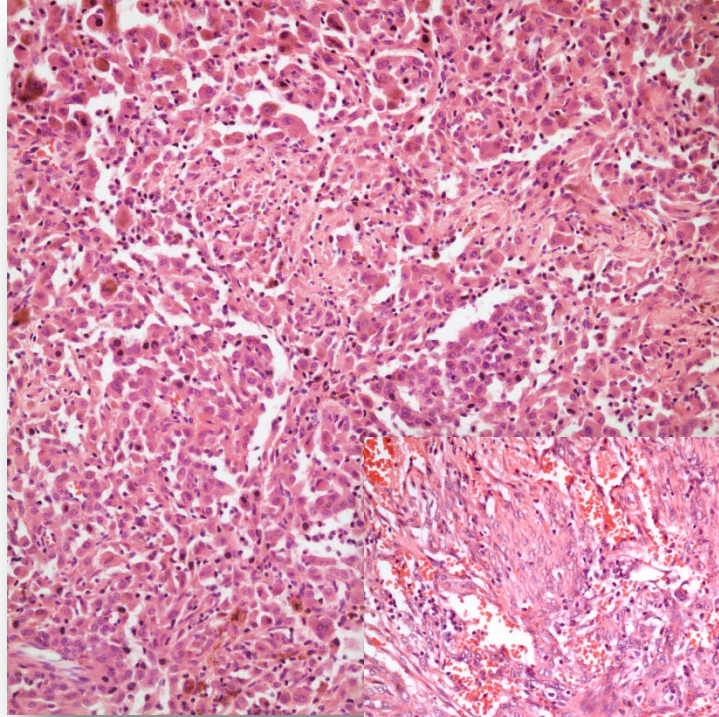
EMA



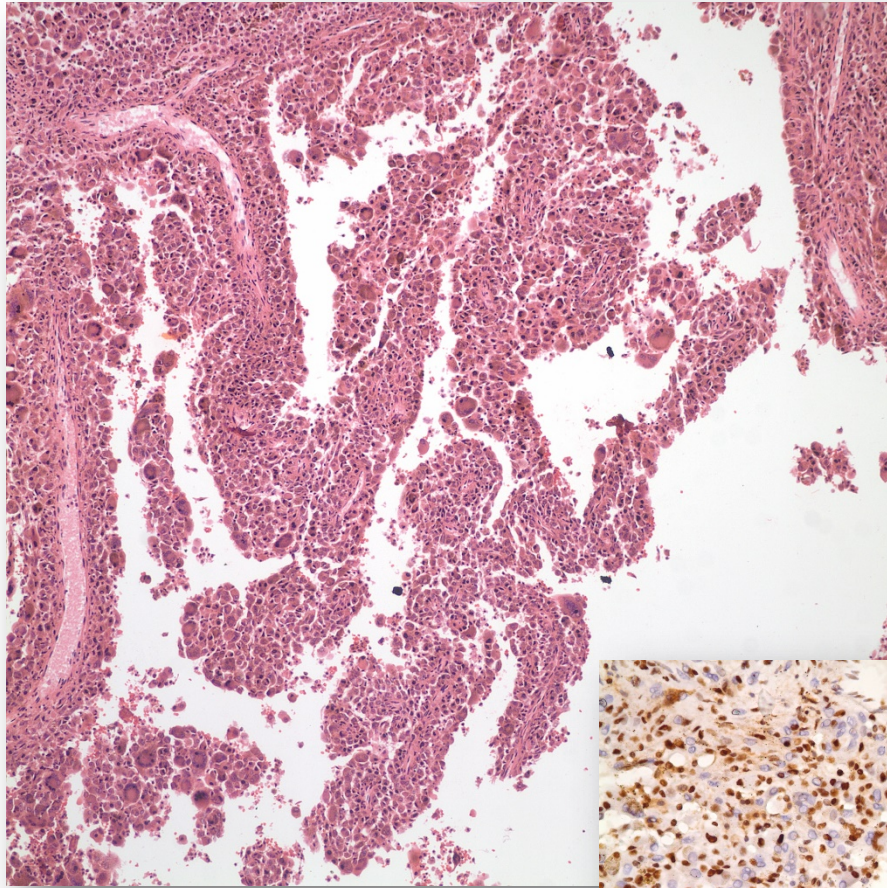
INI-1

2 olgu periferik sinir kökenlidir

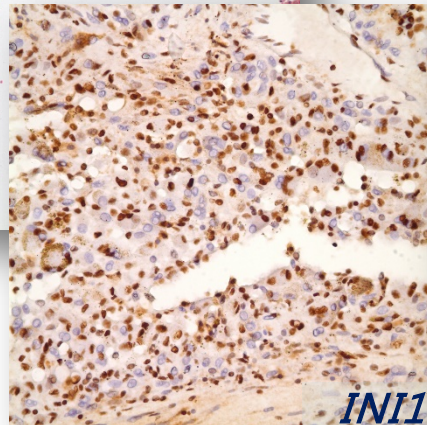




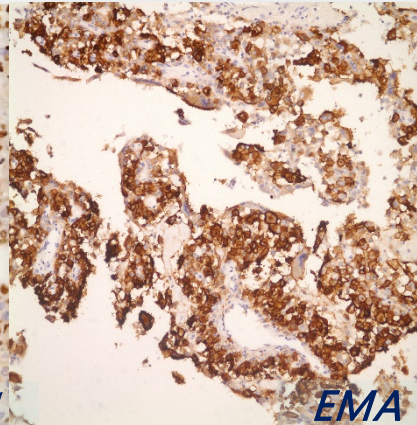
5 olguda (%20)
anjiosarkom benzeri
görünüm ve kanama
alanları



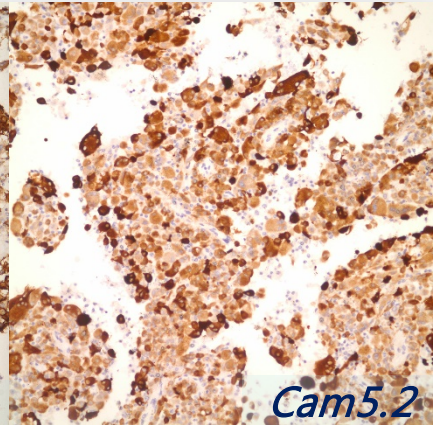
3 olguda diffüz tip
tendon kılıfının dev
hücreli tümörü (PVNS)
benzeri görünüm



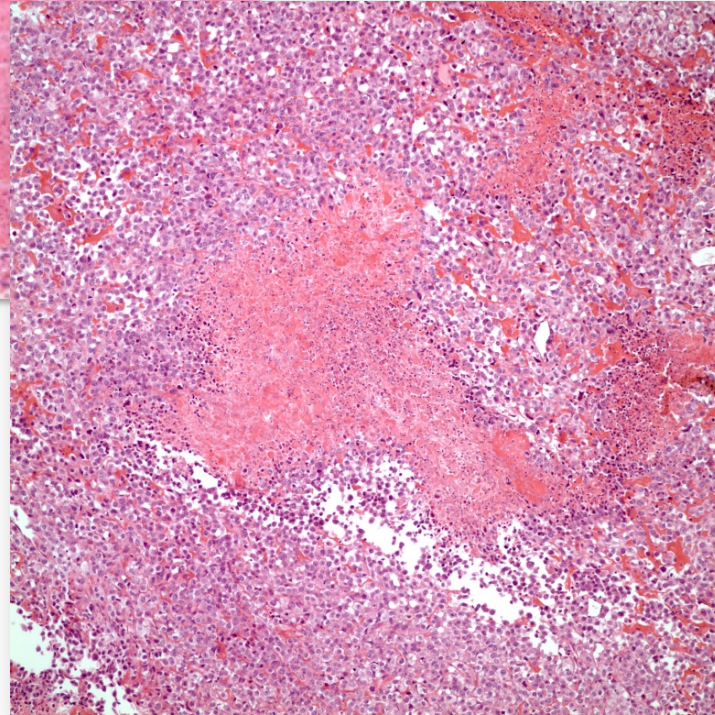
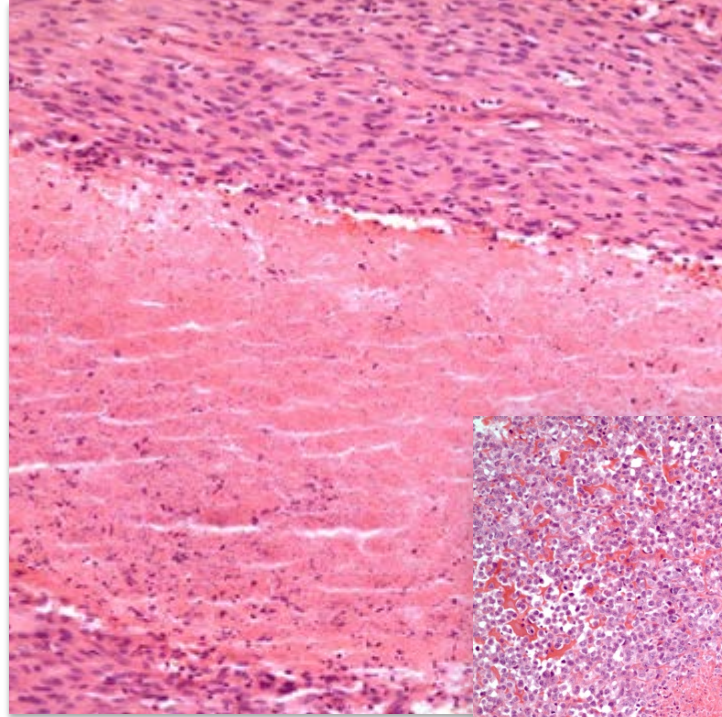
INI1



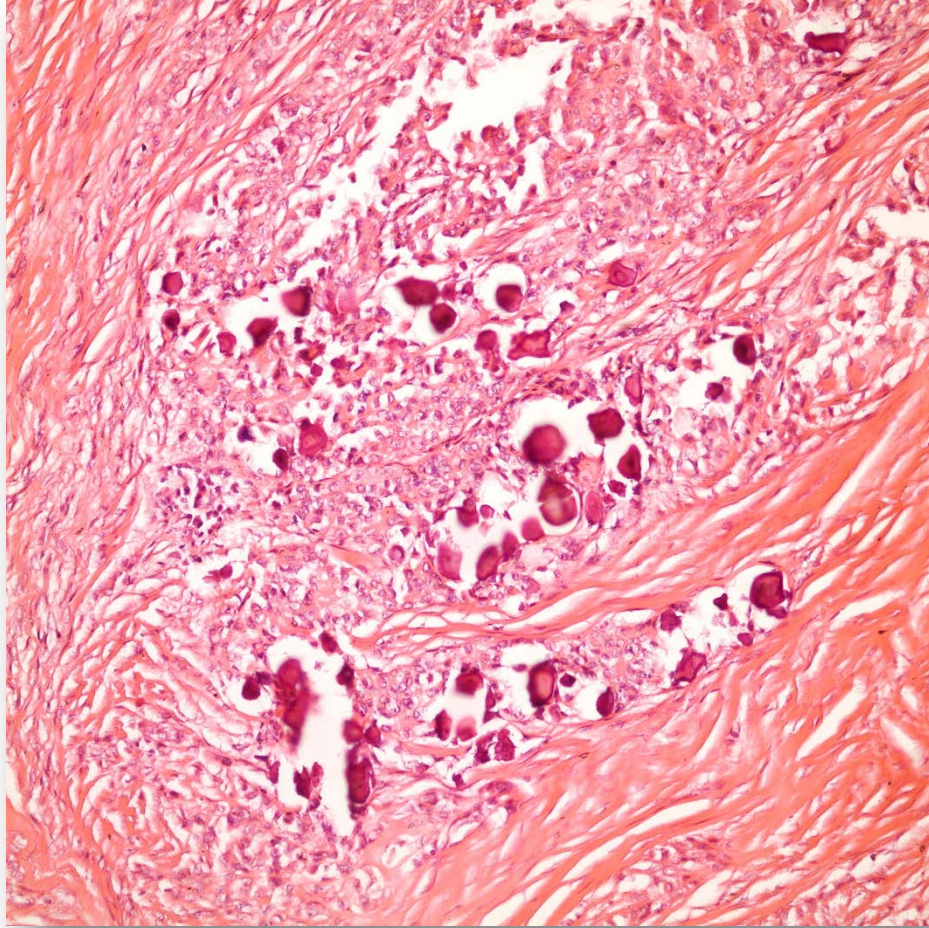
EMA



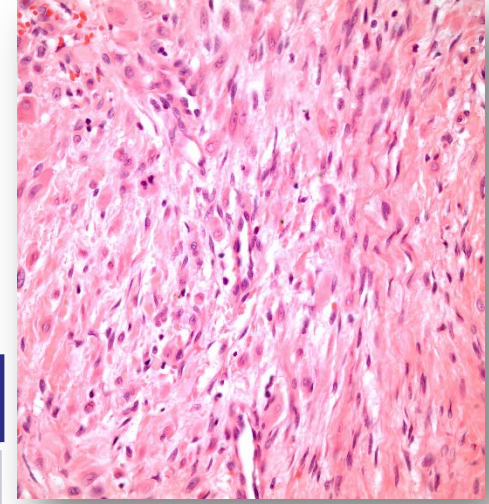
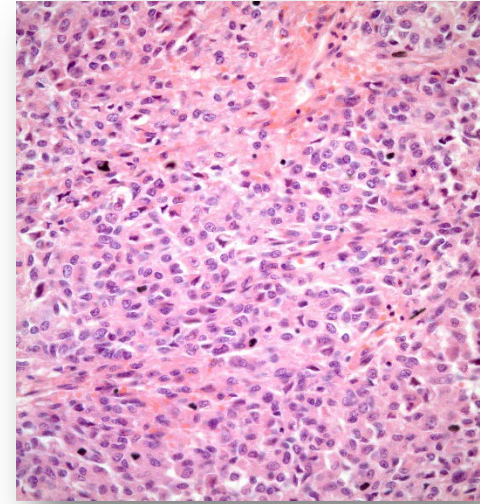
Cam5.2



Olguların
%69'unda en
azından odaksal
nekroz



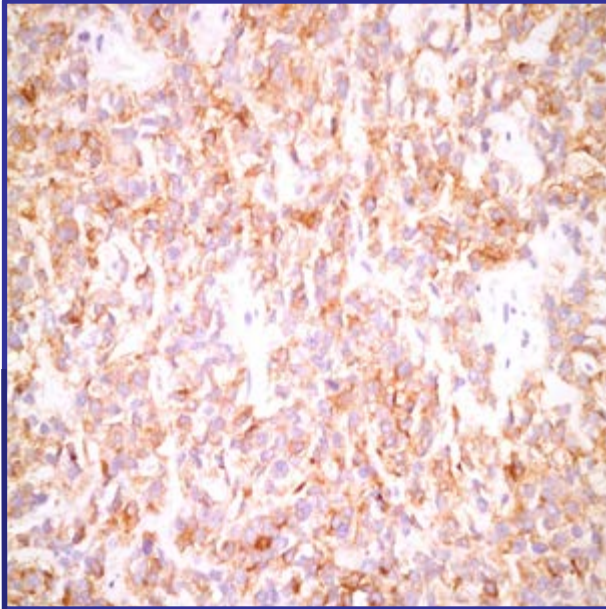
Psammomatöz
Kalsifikasyon



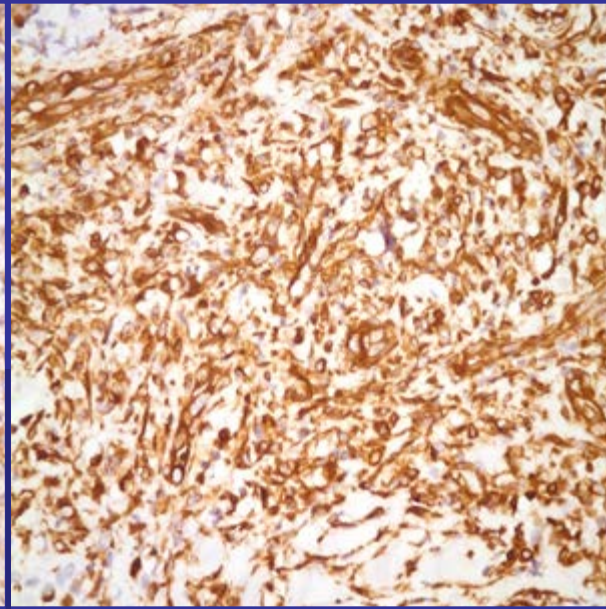
Morfolojik Patern

	Epitelioid baskın	İğsi baskın	Eş baskın	
Klasik	7	4	1	12
Proksimal	11	0	0	11
Hibrit	2	0	1	3
	20	4	2	26

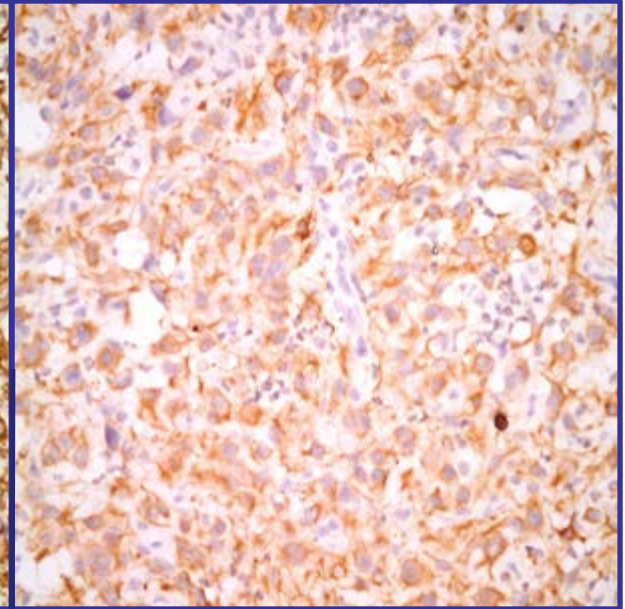
İlk tanı anında uygulanan immünohistokimya



EMA %100
(14/14)

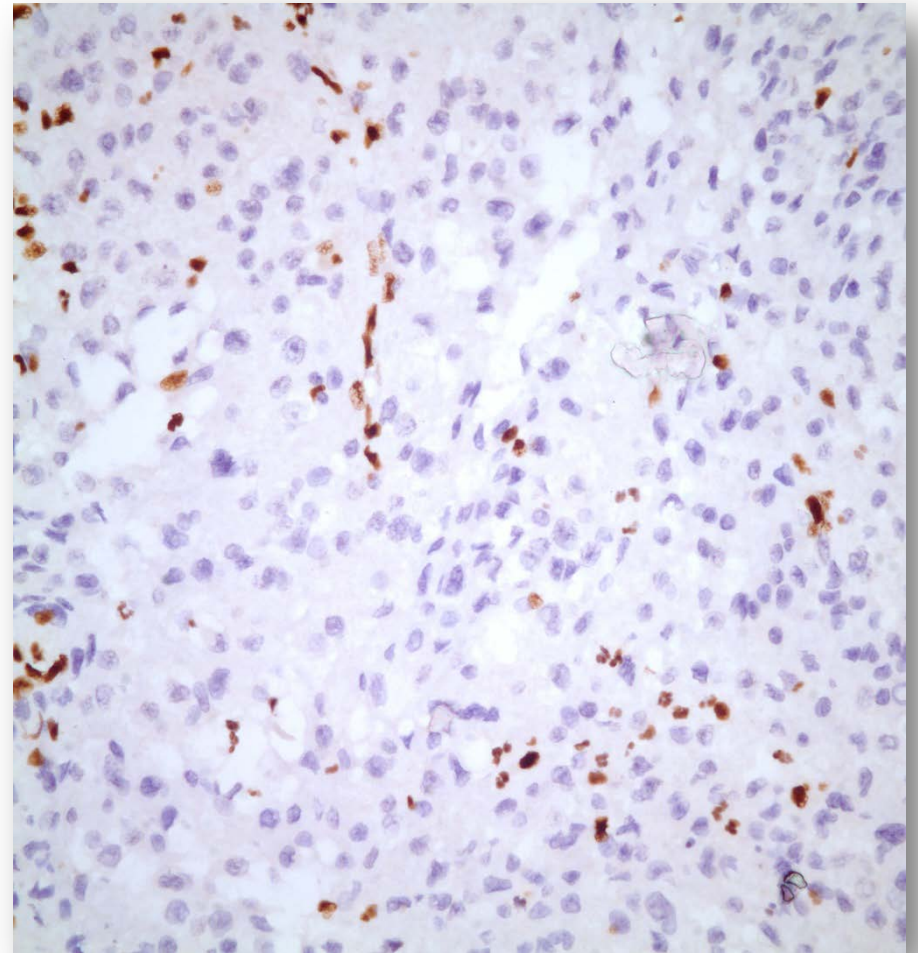
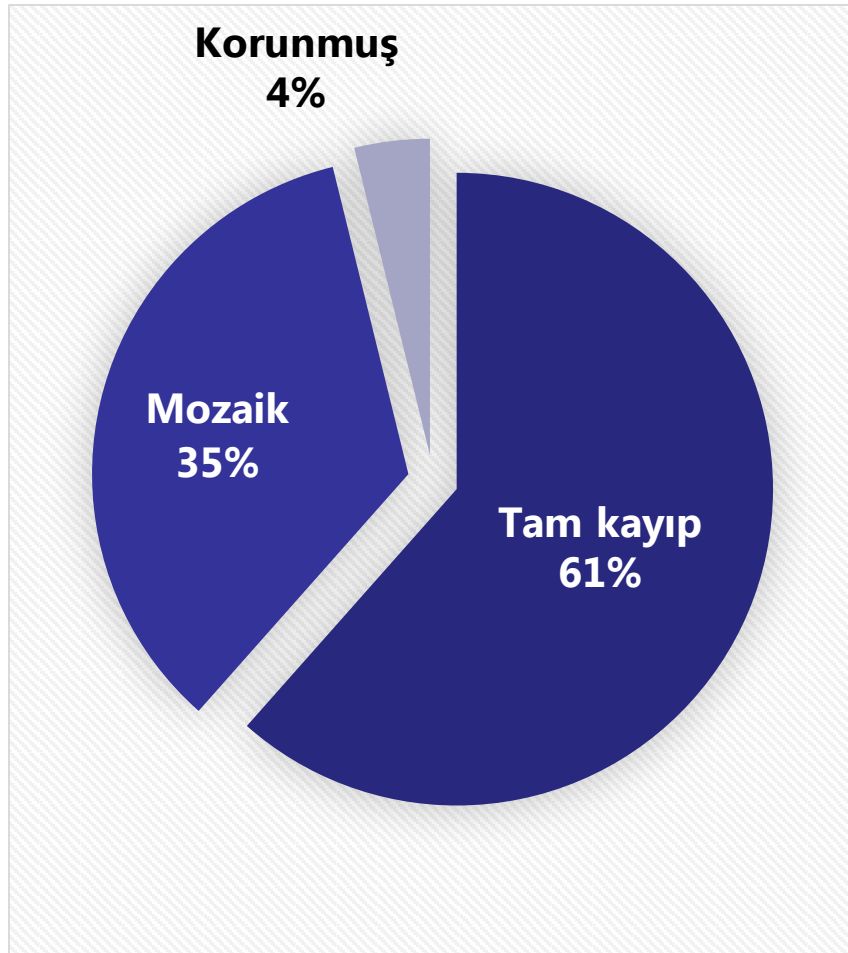


Vimentin %92
(22/24)



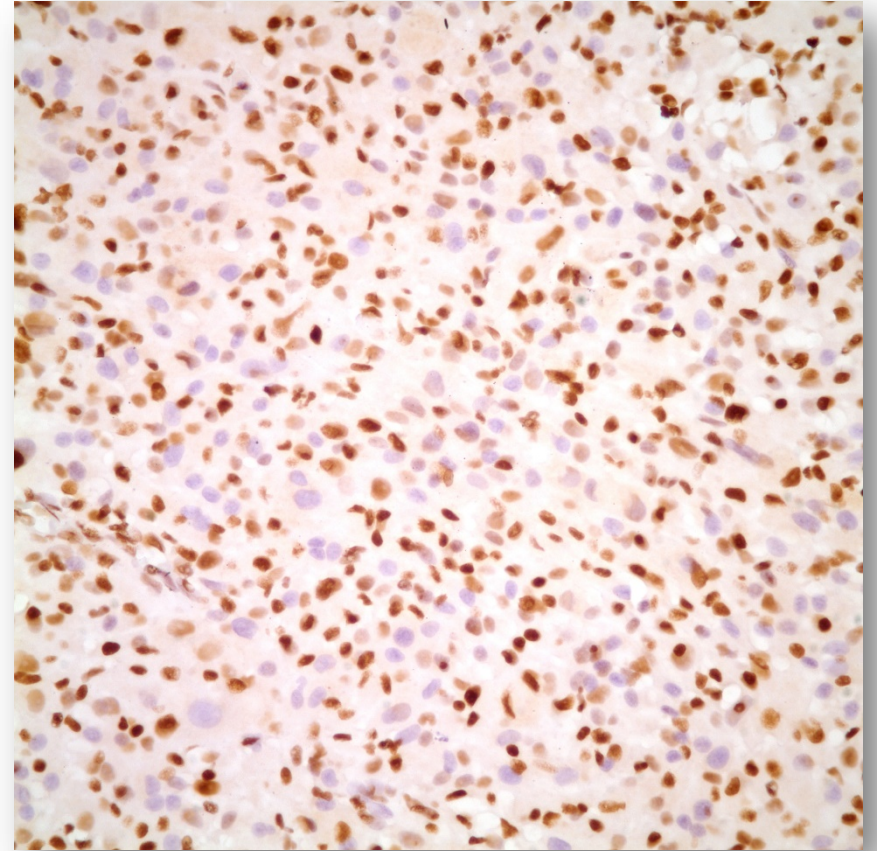
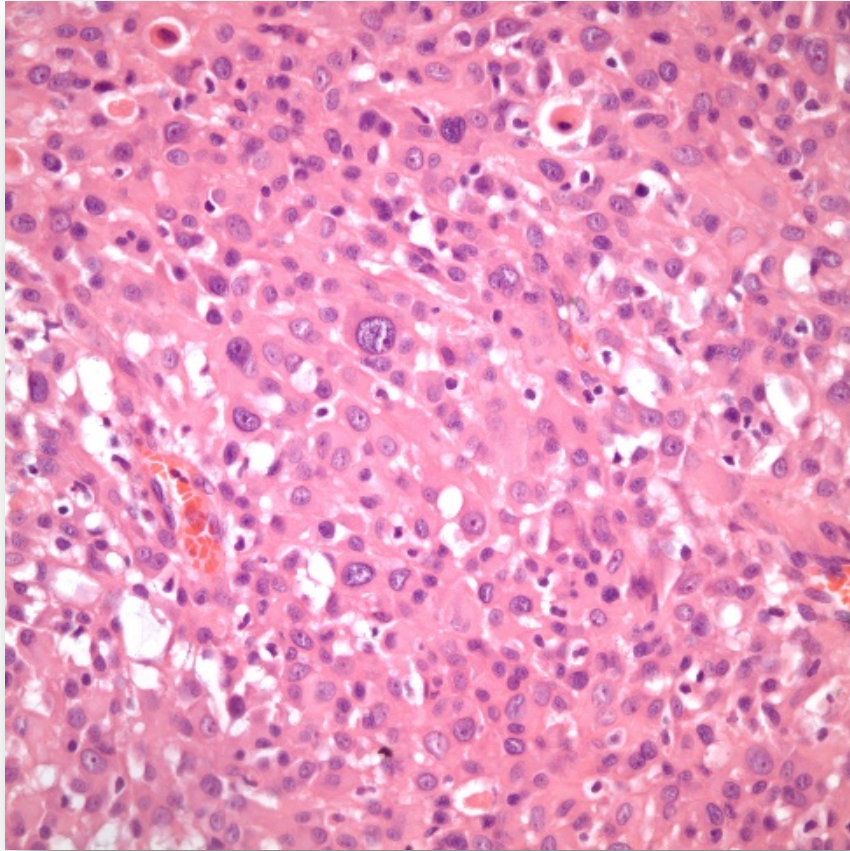
Pan-sitokeratin %57
(13/23)

INI1



INI1

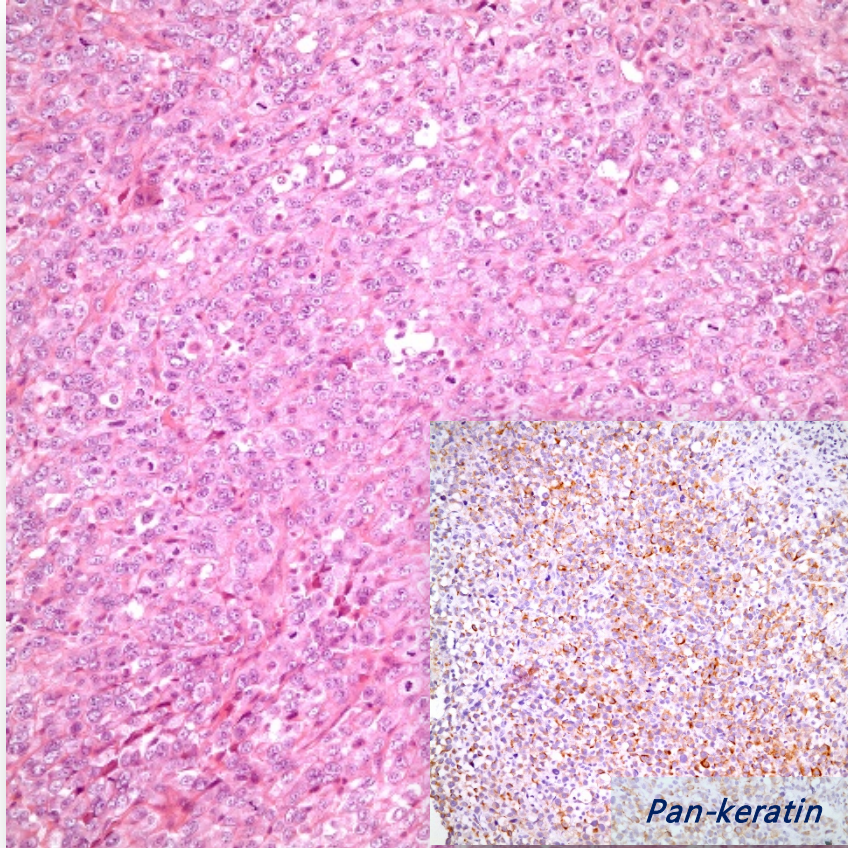
Mozaik INI1 kaybı



INI1

INI1 korunmuş

26 y E, sol alt proksimal ekstremitte yerleşimli

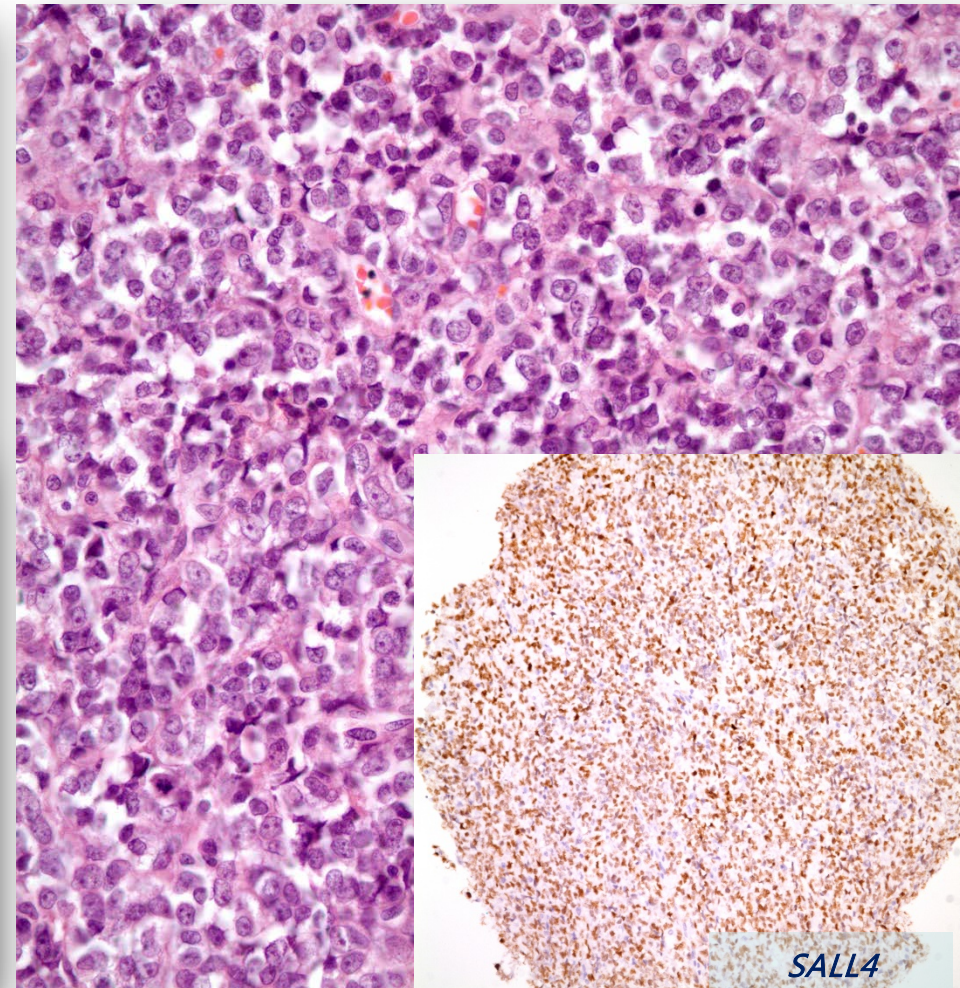
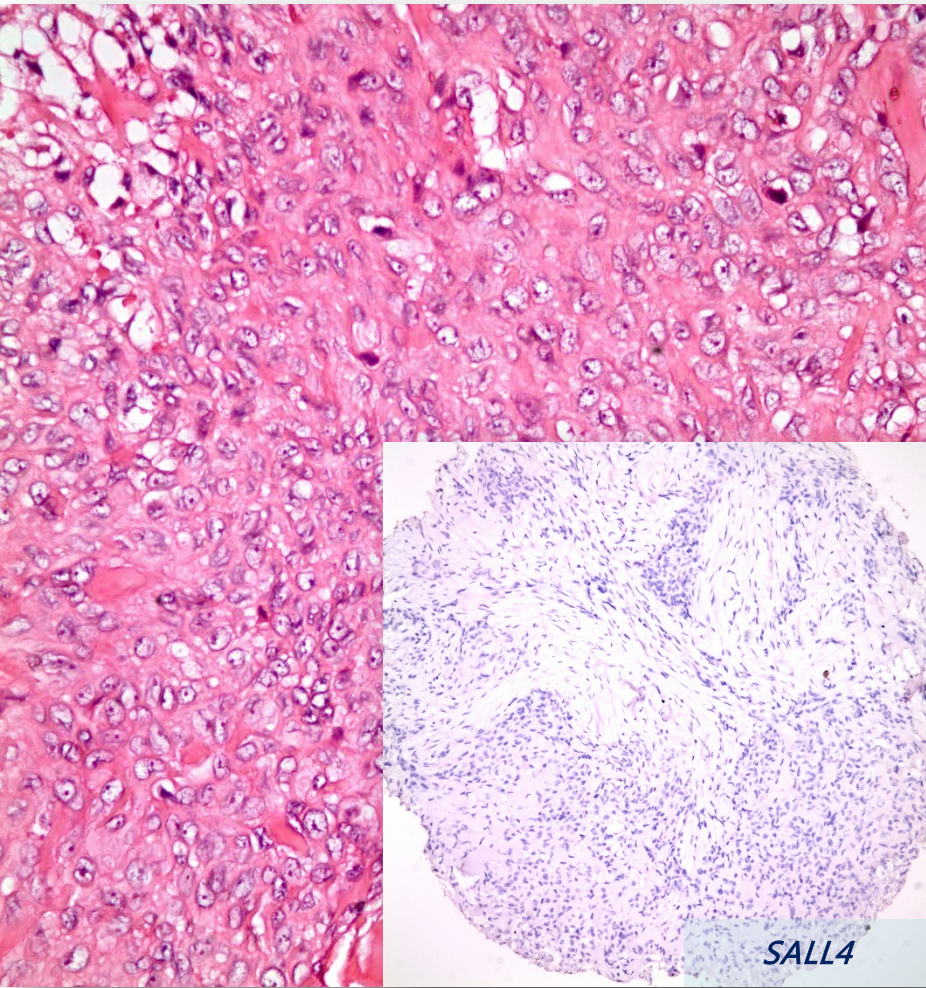




CD34 ve SALL4

CD34 ve SALL4					
	CD34 + SALL4 -	CD34 - SALL4 -	CD34 + SALL4 +	CD34 - SALL4 +	
Klasik	9 (75)	2 (17)	1 (8)	0	12
Proksimal	1 (9)	5 (46)	3 (27)	2 (18)	11
Hibrit	2 (67)	1 (33)	0	0	3
	12	8	4	2	26

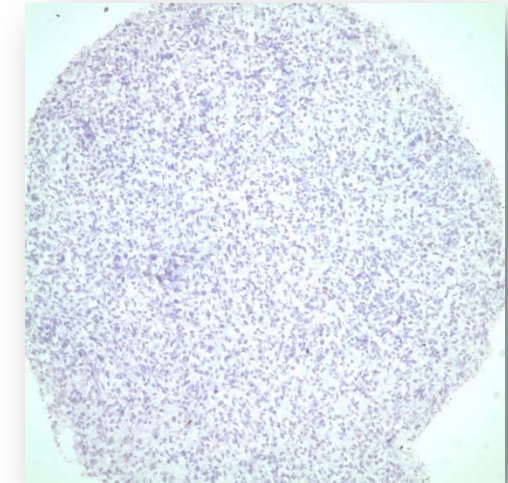
- CD34 %62 pozitif, SALL4 %23 pozitif
- Klasik (%75) ve hibrit (%67): CD34+/SALL4-
- Proksimal (%45): CD34±/SALL4+





Cyclin D1

	Cyclin D1		
	+	-	
Klasik	10	2	12
Proksimal	7	4	11
Hibrit	3	0	3
	20	6	26





Klinik

- 13/26 (%50) olguda klinik takip mevcuttur
 - 1 ay – 30 yıl (5 olgu 8 seneden fazla takipte)
 - 4 (%31) olguda rekürrens
 - 8 (%60) olguda metastaz
 - 7 (%95)' si proksimal veya mikst
 - 2/8 (%25) lenf nodu metastazı
 - Akciğer, beyin ve karaciğer
 - 2 (%15) olgu Ex (MERT?)
- 6 olguda dış merkez yanlış tanı ile takip
 - Epitelioid hemangioendotelyom (2)
 - Benign fibröz histiyositom
 - Skuamöz hücreli karsinom
 - Şeffaf hücreli sarkom
 - Adenokarsinom
 - Sinovyal sarkom

Expression profile and molecular genetic regulation of cyclin D1 expression in epithelioid sarcoma

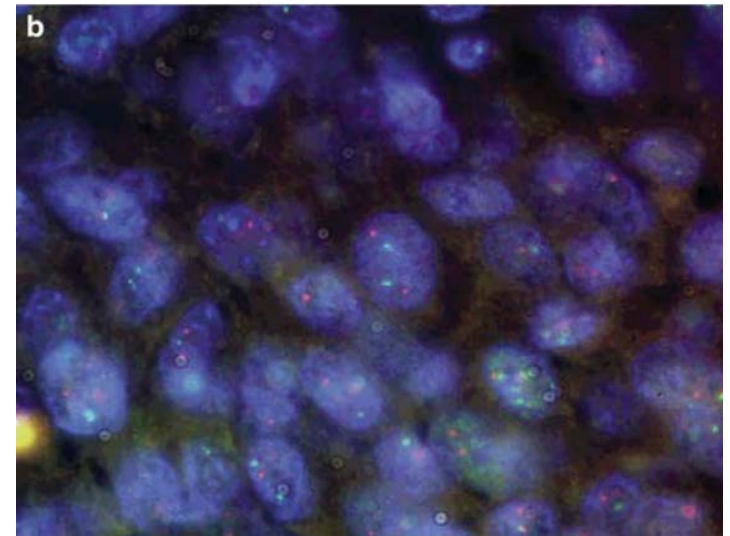
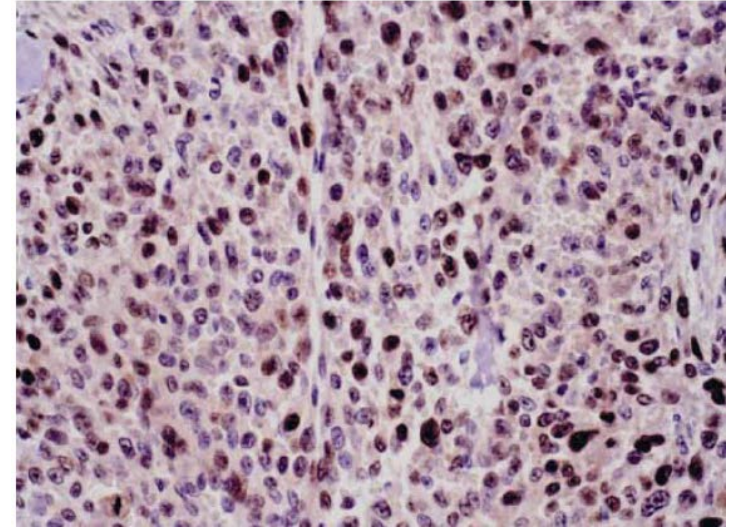
Lin Lin¹, David Hicks¹, Bo Xu¹, Jessica E Sigel¹, Wilma F Bergfeld¹, Elizabeth Montgomery², Cyril Fisher³, Marybeth Hartke¹, Raymond Tubbs¹ and John R Goldblum¹

Modern Pathology (2005) 18, 705–709

Table 1 Cyclin D1 immunoreactivity in epithelioid sarcoma

<i>Immunostaining</i>	<i>Epithelioid sarcoma</i>
Negative (0)	1/24 (4%)
Positive	23/24 (96%)
1+	6/24
2+	5/24
3+	10/24
4+	2/24

- %96 upregülasyon
- Amplifikasyon yok



Histopathology



Histopathology 2015, 66, 252–261. DOI: 10.1111/his.12460

Differential SALL4 immunoexpression in malignant rhabdoid tumours and epithelioid sarcomas

Akihiko Yoshida, Naofumi Asano,¹ Akira Kawai,¹ Hiroshi Kawamoto,² Atsuko Nakazawa,³ Hiroshi Kishimoto⁴ & Ryoji Kushima
Pathology and Clinical Laboratory, National Cancer Centre Hospital, Tokyo, Japan, ¹*Musculoskeletal Oncology, National Cancer Centre Hospital, Tokyo, Japan,* ²*Paediatric Oncology, National Cancer Centre Hospital, Tokyo, Japan,* ³*Pathology, National Centre for Child Health and Development, Tokyo, Japan, and* ⁴*Pathology, Saitama Children's Medical Centre, Saitama, Japan*

	Epitelioid Sarkom	MERT
SALL4 (+)	1	10
SALL4 (-)	35	5
Toplam	36	15

Human Pathology (2015) 46, 225–230



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Original contribution

ERG and SALL4 expressions in SMARCB1/INI1-deficient tumors: a useful tool for distinguishing epithelioid sarcoma from malignant rhabdoid tumor[☆]



Kenichi Kohashi MD, PhD^a, Yuichi Yamada MD^a, Yuka Hotokebuchi MD^a, Hidetaka Yamamoto MD, PhD^a, Tomoaki Taguchi MD, PhD^b, Yukihide Iwamoto MD, PhD^c, Yoshinao Oda MD, PhD^{a,*}

	Epitelioid Sarkom (Klasik)	Epitelioid Sarkom (Proksimal)	MERT
SALL4 (+)	0	5 (%25)	4(≈%50)
SALL4 (-)	24	15	3
Toplam	24	20	7

Sonuçlar

- Klinik ve morfolojik spektrum geniştir:
 - İntraosseöz, intraartiküler, vulva yerleşimi
 - Prognoz değişken
 - Anjiosarkom veya PVNS benzeri görünüm
- Tam INI1 kaybı yanı sıra azımsanmayacak ölçüde (%35) mozaik kayıp varlığı saptanmıştır
- Yüksek oranda cyclinD1 ekspresyonu mevcuttur
- “Klasik” ve “proksimal” varyant ayrımında morfolojik bulgular yanı sıra CD34 ve SALL4’ün panel halinde uygulanması yararlı olabilir
- Bazı olgularda hem “klasik” hem de “proksimal” varyant özellikleri bir arada görülebilir (hibrit olgular)
- Hibrit olgular klinik olarak «proksimal», immünofenotip olarak «klasik» varyant özellikleri göstermektedir



Teşekkürler

