Kocaeli Üniversitesi Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları Anabilim Dalı Çocuk
Onkoloji Bilim Dalı

6 Ekim 2021 Çarşamba

İnt Dr Bengisu GENÇ
Arş. Gör. Halime ASLAN

15 yaş 6 aylık erkek

- Şikayet: Sağ göğüs üst dış tarafta şişlik

- Hikaye: 15 Mayıs 2021 tarihinde sağ göğsünün üst dış tarafında ani gelişen ve hızlıca büyüyen yaklaşık portakal büyüklüğünde ağrısız, sınırları belirli ve dokunmak ile hareket eden kitle şikayeti ile Derince Eğitim ve Araştırma Hastanesi'nde çocuk cerrahisine başvurmuş.

- Hastamız 120.8 kg ile bize başvurduğunda fitness sporu ile ilgilenmeye yeni başlamış ve bir ayda 6 kg kaybı olmuş.

- Gece terlemeleri aralıklı az miktarda olmuş.

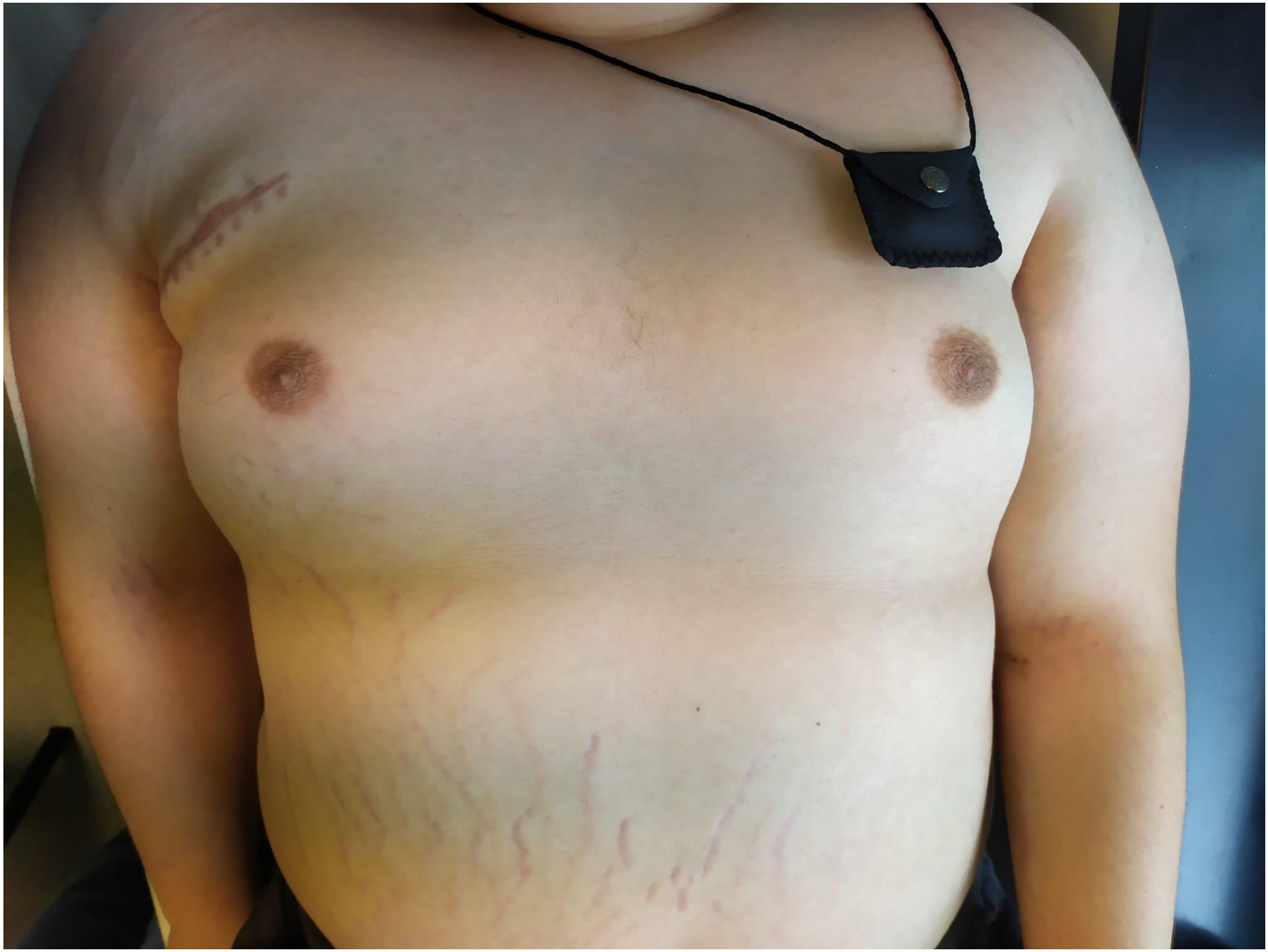
- Ateşlenmesi olmamış.

- Özgeçmiş: Miadında 3750 gr CS ile doğmuş. YDYBÜ ve sarılık öyküsü yok. Fototerapi almamış. Aşıları takvimine uygun olarak zamanında yapılmış. 2015 yılında sünnet olmuş. **10 Haziran 2021 kitle eksizyonu yapılmış.** Bilinen allerji öyküsü yok.
- Soygeçmiş: Anne: 40 yaş, sağ-sağlıklı
  Baba: 42 yaş, sağ-sağlıklı
  1. Çocuk: Hastamız
  2. Çocuk: 10 yaş, erkek, sağ hidronefroz
  3. Çocuk: 8 yaş, erkek, sağ gözde kayma

  Anne ve baba arasında akraba evliliği mevcut. (Dayı-Hala çocukları)
  Ailede erken yaşta malignite öyküsü mevcut. (Dede ve babaanne kolon ve kemik kanserinden vefat etmiş)

- Vücut Ağırlığı: 120.8 kg
- Boy: 181 cm
- Vücut Yüzey Alanı: 2.4 m2

- Fizik Muayene: Cilt turgor ve tonusu doğal. Döküntü izlenmedi. **Sağ klavikula altında laterale uzanan yaklaşık 6 cm büyüklüğünde akıntı izlenmeyen operasyon skarı mevcut.**
- Lenfoadenopati izlenmedi.
- Orofarenks doğal, mukozit izlenmedi. Bilateral akciğer sesleri doğal, ral ve ronküs yok. S1 (+) S2 (+) Ek ses ve üfürüm yok.

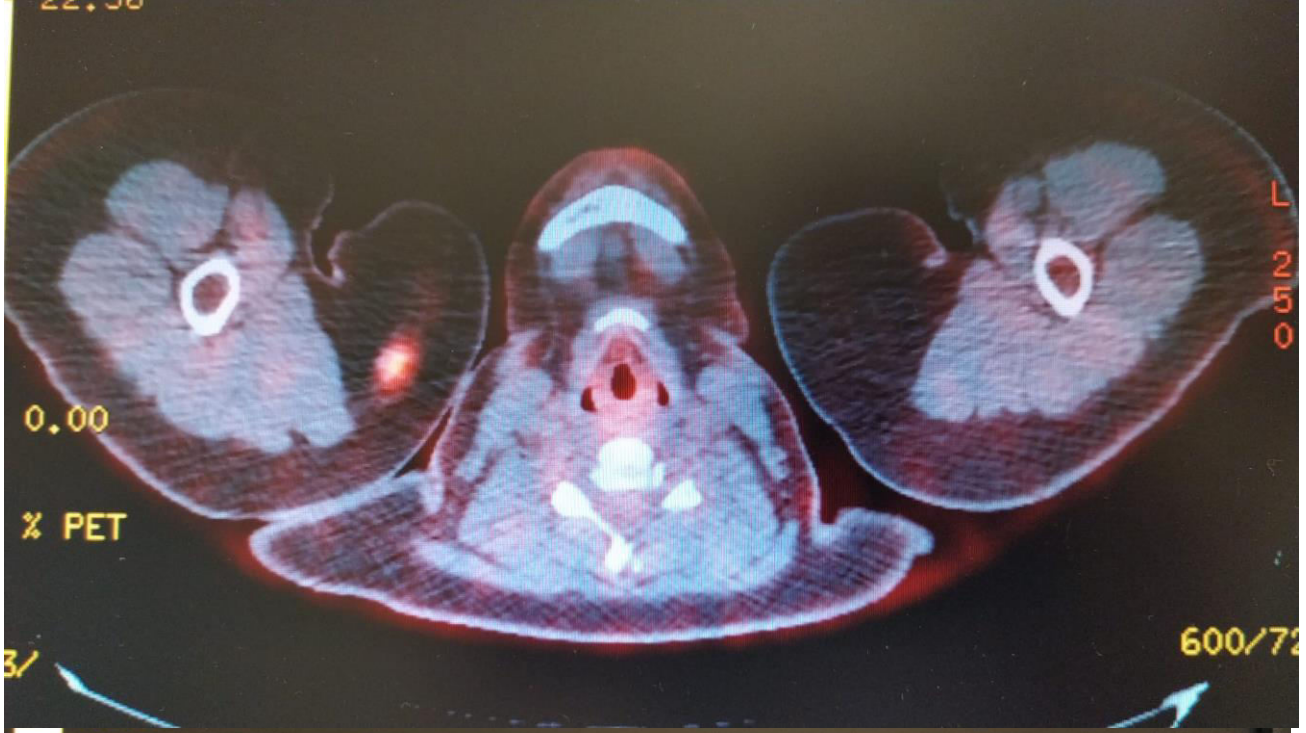


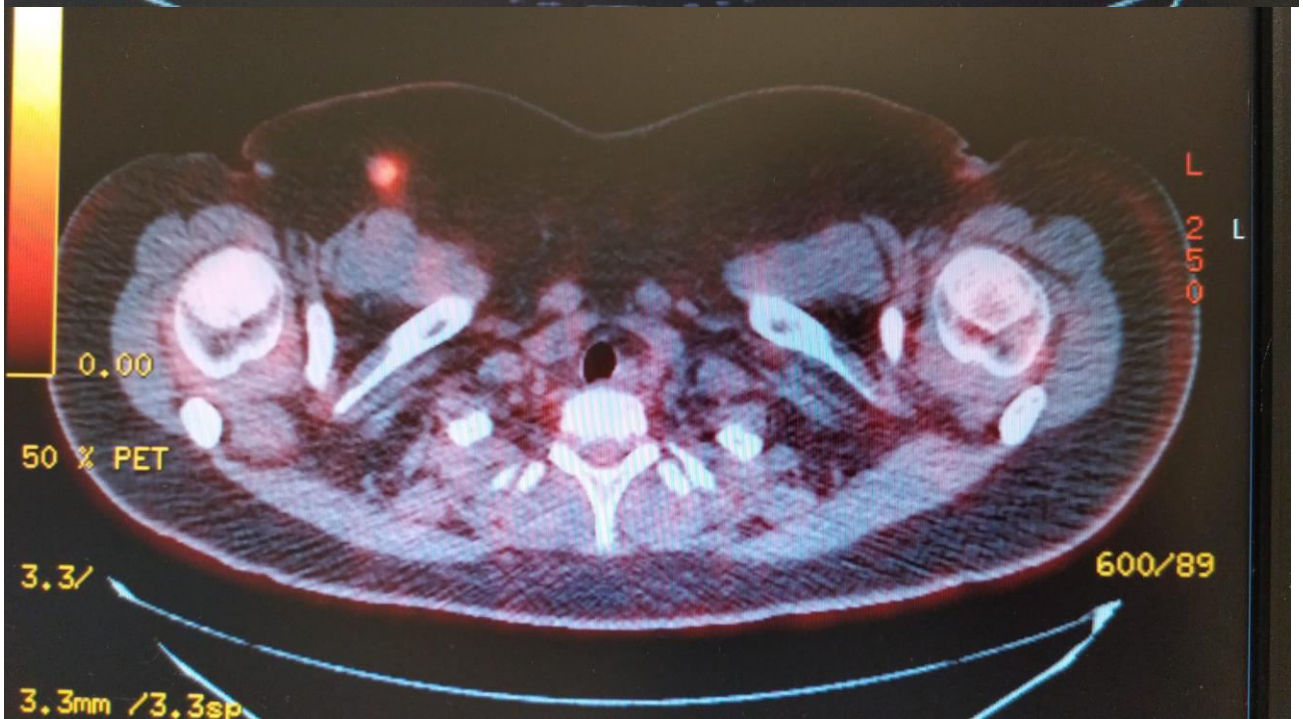
- **AKŞ: 117.7 mg/dL**
- Üre: 15.1 mg/dL
- Ürik Asit: 5.2 mg/dL
- Kreatinin: 0.69 mg/dL
- Total Bil: 0.5 mg/dL
- Direkt Bil: 0.16 mg/dL
- AST: 37.4 U/L
- ALT: 36.7 U/L
- LDH: 246 U/L
- Total Protein: 68.9 g/L
- Albumin: 46.2 g/L
- Globulin: 22.7 g/L

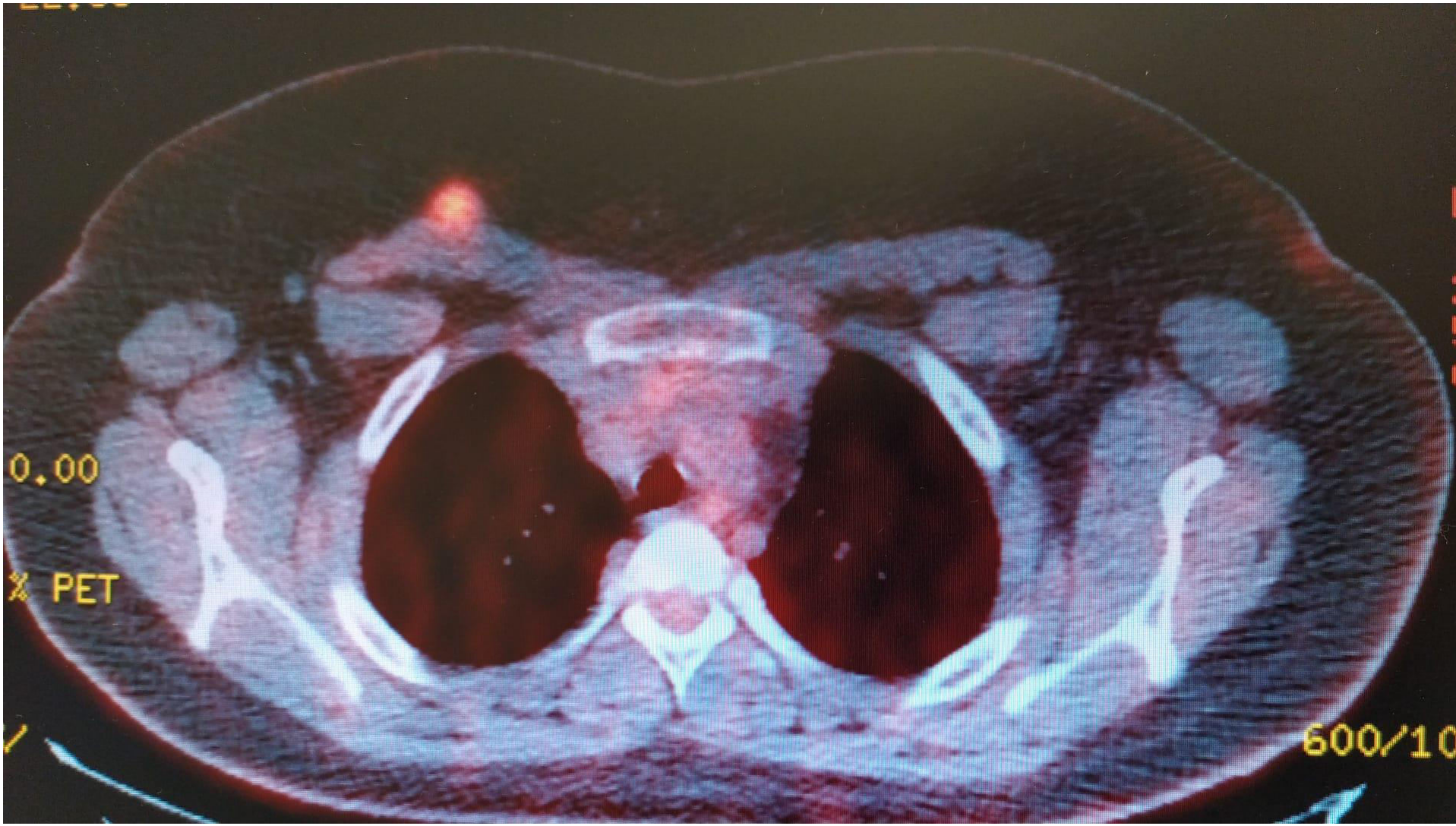
- Düzeltilmiş Na: 140.3 mmol/l
- K: 4.61 mmol/L
- Cl: 100 mmol/L
- Düzeltilmiş Ca: 9.63 mg/dL
- Mg: 2.29 mg/dL
- P: 3.61 mg/dL

- WBC: 7940/mm^3
- NEU: 3760/mm^3
- LYM: 3460/mm^3
- HGB: 13.7 g/dL
- HCT: %39.4
- MCV: 76 fL
- PLT:257000/mm^3

- 26 Ağustos 2021 tarihinde PET çekilen hastamızda; **sağ omuz ve aksilla anteriorunda cilt altı yağlı doku içerisinde bulunan nodüler lezyonlarda ve sağ pektoral kas anteriorunda yağ dokusu içinde bulunan nodüler lezyonda izlenen anormal artmış FDG tutulumları büyük olasılıkla malign doku ile ilgilidir**. Diğer vücut bölgelerinde malign doku varlığını düşündürecek tarzda artmış metabolik aktivite tutulumu gösteren bir odak izlenmemiştir.


L
250
0.00
% PET
600/72


0.00
50 % PET
L
250
L
3.3/
600/89
3.3mm /3.3sp


0.00
% PET
600/10

PATOLOJİK BULGULAR

- Sağ göğsünün üst dış tarafında ani gelişen ve hızlıca büyüyen yaklaşık portakal büyüklüğünde ağrısız, sınırları belirli ve dokunmak ile hareket eden, ele gelen kitle.

- Bir ayda 6 kg kaybı.

- PET: Sağ omuz ve aksilla anteriorunda cilt altı yağlı doku içerisinde bulunan nodüler lezyonlarda ve sağ pektoral kas anteriorunda yağ dokusu içinde bulunan nodüler lezyonda izlenen anormal artmış FDG tutulumları büyük olasılıkla malign doku ile ilgilidir

ÖN TANILARINIZ NELER?

- Derince Eğitim ve Araştırma Hastanesi

Patoloji Bölümü: **Nodüler ve lobüler gelişim gösteren küçük belirgin nükleollü, veziküler nükleuslu, sitoplazmik sınırları belirsiz,uniform küçük hücre tabakalarından oluşan tümoral lezyon izlenmiştir.**

- Fokal alanlarda belirgin miksoid zemin ve makro-mikrokistik alanlar dikkati çekmiştir. Belirgin pleomorfizm veya nekroz görülmemiştir.

- Mevcut morfolojik ve immunohistokimyasal inceleme sonuçları ile olguda ön planda:

Az differansiye sinoviyal sarkom veya BCOR genetik değişiklikli sarkom

başta olmak üzere undifferansiye yuvarlak hücreli sarkom ayırıcı tanıya alınmıştır.

KONSÜLTASYON- (B-6552-2021 KODLU20 ADET HAZIR BLOK,44 ADET HAZIR LAM)- TORAKS ÖN DUVARI, KİTLE, EKSİZYON MATEYALİ:
Küçük yuvarlak mavi hücreli tümör, lütfen yorumu okuyunuz

Kesitlerde; nodüler ve lobüler gelişim gösteren, küçük belirgin nükleollü, veziküler nükleuslu, sitoplazmik sınırları belirsiz, uniform küçük hücre tabakalarından oluşan tümöral lezyon izlenmiştir. Fokal alanlarda belirgin mikzoid zemin ve makro-mikrokistik alanlar dikkati çekmiştir. Belirgin pleomorfizm veya nekroz görülmemiştir.

Dış merkezde yapılarak gönderilen 24 adet immunohistokimya boyalı preparat incelenmiş olup tüm hücrelerinde ;

CD56 ile diffüz orta şiddette membranöz boyanma izlenmiştir.
Vimentin ile diffüz kuvvetli sitoplazmik boyanma izlenmiştir.
CD99 ile fokal, gruplar hinde veya tek tek dağınık membranöz boyanma izlenmiştir.
Pansitokeratin ile negatif reaksiyon izlenmiştir.
EMA ile negatif reaksiyon izlenmiştir.
SMA ile negatif reaksiyon izlenmiştir.
Desmin ile negatif reaksiyon izlenmiştir.
Myogenin ile negatif reaksiyon izlenmiştir.
CD68 ile seeyrek dağınık tek tek boyanma izlenmiştir.
Sinaptofizin ile negatif reaksiyon izlenmiştir.
Kromogranin ile negatif reaksiyon izlenmiştir.
LCA ile negatif reaksiyon izlenmiştir.
CD3 ile negatif reaksiyon izlenmiştir.
CD20 ile negatif reaksiyon izlenmiştir.
CD45 ile negatif reaksiyon izlenmiştir.
CD30 ile negatif reaksiyon izlenmiştir.
SALL4 ile negatif reaksiyon izlenmiştir.
Tdt ile negatif reaksiyon izlenmiştir.
CD117 ile fokal zayıf membranöz pozitif reaksiyon izlenmiştir.
Melan A ile negatif reaksiyon izlenmiştir.
CD34 ile negatif reaksiyon izlenmiştir.
CD31 ile negatif reaksiyon izlenmiştir.
Ki67 ile proliferasyon indeksi %20-30 olarak değerlendirilmiştir.

Bölümümüzde yapılan immünohistokimyasal incelemelerde;
BCL-2 ile diffüz kuvvetli sitoplazmik boyanma izlenmiştir.

Desmoid Fibromatosis

Kaposiform hemangioendothelioma

Myofibroma

Angiomatoid fibrous histiocytoma

Dermatofibrosarcoma protuberans, giant cell fibroblastoma

Gastrointestinal stromal tumor

Infantile fibrosarcoma

Inflammatory myofibroblastic tumor

Myoepithelioma

Plexiform fibrohistiocytic tumor

Angiomatoid fibrous histiocytoma

Alveolar soft-part sarcoma

Clear cell sarcoma of soft tissue

Desmoplastic small round cell tumor

Embryonal sarcoma of the liver

Epithelioid sarcoma

Fibrosarcoma (adult-type)

Leiomyosarcoma

Liposarcoma

Malignant peripheral nerve sheath tumor

Malignant rhabdoid tumor

Synovial sarcoma

Undifferentiated sarcoma

histotype	pts	groups	treatment	results	Conclusions, comments
SYNOVIAL SARCOMA *Ocku et al. J Clin Oncol 2003;21:1601-1612*	220	MD Anderson, St. Jude, CWS, INT Milan	82% received CT 60% RT	5yr EFS = 72%, 5yr OS = 80% CT response rate = 61%	CT: no impact on survival in Group I-II pts RT improved LRFS and OS Prognostic factors: SIZE
MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR *Carli et al. SIOP Meeting 2001*	166	ICG, CWS	80% CT 40% RT	10yr OS = 45% (5% in NF1) CT response = 47%	Local control is the main challenge RT improve local control IRS I-II pts Unexpected response to CT
FIBROSARCOMA *Cecchetto et al, J Surg Oncol 2001;78:255-231* *Ladenstein et al. SIOP Meeting 2001*	25 52	ICG CWS	72% CT, 24% RT 54% CT, 10% RT	5yr OS 78% for infantile type, 51% adult type CT response 3/8 5yr OS 92% for infantile type, 60% adult type	Infants: better outcome, surgery alone Adult type: SIZE and IRS group as prognostic factors
EPITHELIOID SARCOMA *Mattke et al, SIOP Meeting 2001*	44	CWS, ICG	not reported	OS = 89% for IRS Group I, 41% II-III, 0% IV 81% <5cm, 33% >5cm CT response 3/8	Prognostic factors: IRS group, T, SIZE Surgery mainstay of treatment
LEIOMYOSARCOMA *Ferrari et al. Ann Oncol 2001;12:1163-1168* *Kunz et al. SIOP Meeting 2001*	16 54	ICG CWS, ICG	56% CT, 19% RT 60% CT, 18% RT	5yr OS = 73% (SIZE 100% vs 45%) OS 85%, CT response rate 43%	Role for RT Quite unexpected response to CT
MALIGNANT FIBROUS HISTIOCYTOMA *Kunz et al. SIOP Meeting 2001*	45	CWS, ICG	55% CT 33% RT	5yr OS = 89%, 100% in IRS Group I-II CT response 3/7	Gross surgical is the treatment of choice
LIPOSARCOMA *Mattke et al. SIOP Meeting 2001*	34	CWS, ICG	65% CT 50% RT	5yr OS: 100% IRS I, 67% II, 22% III, 33% IV 100% <5cm CT response 7/13	Prognostic factors: surgery, SIZE, age (?) Quite good response to CT

histotype	pts	groups	treatment	results	Conclusions, comments
CLEAR CELL SARCOMA *Ferari et al. Cancer 2002;94:3269-3276*	28	ICG, CWS	71% CT 25% RT	5yr OS = 69% CT response 1/7 Univariate analysis: surgery, size, site	Only surgery for small resected tumour Uncertain role for CT and RT
ANGIOSARCOMA *Ferrari et al. Med Pediatr Oncol 2002;39:109-114*	18	ICG, CWS	78% CT 33% RT	5yr OS = 31%, EFS = 21% CT response 3/9	Poor prognosis – high rate of metastatic relapses Surgery not sufficient
HEMANGIOPERICYTOMA *Ferrari et al. Cancer 2001;92:2692-2698*	27	ICG, CWS	85% CT 55% RT	Infants: 5/6 CT response, OS 85% Adult-type: CT response 70%, OS 69%	Infants: myofibroblastic lesions? Adult-type: CT and RT seem effective, SIZE as prognostic factor
HEMANGIOHENDOTELIOMA *Ferrari et al. Ital J Pediatr 2001;27:774-778*	18	ICG, CWS	72% CT (4 pts received α-IFN)	OS = 83%, EFS 60% No response to CT 2 PR + 2 SD with α-IFN	Heterogeneous group CT completely uneffective, role for α-IFN
ALVEOLAR SOFT PART SARCOMA *Casanova et al. Ann Oncol 2000;11:1445-1449*	19	ICG	79% CT 42% RT	5yr OS = 80%, 92% for localized disease, 100% <5 cm, 31% >5 cm CT response 2/7	More favourable prognosis than adults Surgery mainstay of therapy SIZE strongly correlates with outcome
DESMOPLASTIC SMALL ROUND CELL TUMOUR *Bisogno et al. Med Pediatr Oncol 2000;34:338-342* *Kunz et al, SIOP Meeting 2001*	6 12	ICG CWS	All pts received CT	Alive in CR 4/18 (with short follow-up)	Disappointing survival Complete resection + intensive CT ± RT → crucial for good prognosis

TABLE 1. Selected New Tumor Entities and Subtypes in the 2020 WHO Classification of Soft Tissue Tumors

Tumor Category	Biological Potential	New Entities and Subtypes	Clinical Features	Histologic Features	Immunohistochemical Markers	Molecular Features
Adipocytic tumors	Benign	Atypical spindle cell/ pleomorphic lipomatous tumor	Middle-aged adults, slight male predominance, wide anatomic location, most common locations are hand, foot, thigh	Atypical spindle cells, adipocytes, lipoblasts, pleomorphic cells, myxoid to collagenous extracellular matrix	CD34 (+), S100 protein (±), loss of RB expression in 50%-70%, MDM2 (−)	Deletions or losses of 13q14, including *RB1*, lack of *MDM2* amplification
	Malignant	Myxoid pleomorphic liposarcoma	Children and young adults, female predominance, a predilection for mediastinum	Admixture of areas resembling low-grade myxoid liposarcoma and areas resembling pleomorphic liposarcoma	MDM2 (−), CDK4 (−), S100 protein (±)	Absence of *DDIT3* rearrangement and *MDM2* amplification, inactivation of *RB1*
Fibroblastic and myofibroblastic tumors	Benign	*EWSR1-SMAD3*–positive fibroblastic tumor (emerging)	A broad age range, female predominance, small superficial nodule in hand and foot	Distinctive zonation pattern with central acellular hyalinized area and peripheral bland spindle cells' proliferation	ERG (+), SMA (−), CD34 (−)	*EWSR1-SMAD3* fusion
	Benign	Angiofibroma of soft tissue	Middle-aged adults, female predominance, lower extremities, often adjacent to large joint such as knee	Bland and uniform short spindle cells, myxoid or collagenous stroma, small thin-walled branching blood vessels	EMA (±), CD34 (±)	*AHRR-NCOA2* fusion
	Intermediate (rarely metastasizing)	Superficial CD34-positive fibroblastic tumor	Middle-aged adults, slight male predominance, lower extremities, especially thigh, arm, buttock, shoulder	Superficial location, large pleomorphic cells with granular to glassy cytoplasm, but very low mitotic count	Diffuse CD34 expression, cytokeratin (+) in ~70%	*PRDM10* rearrangements (subset)
Vascular tumors	Benign	Anastomosing hemangioma	Predominantly adults, but can arise in pediatric age, genitourinary tract, retroperitoneum, paravertebral soft tissue	Anastomosing vessels lined by hobnail endothelial cells, intracytoplasmic hyaline globules, extramedullary hematopoiesis	CD31 (+), CD34 (+), ERG (+)	Mutation in *GNAQ* or *GNA14*
Smooth muscle tumors	Intermediate	EBV-associated smooth muscle tumor	Wide age range, arise in patients with immunosuppression, visceral organs, soft tissue, skin	Fascicles of spindle cells with elongated nuclei and eosinophilic cytoplasm, but more primitive-appearing round cells in about 50%	SMA (+) diffusely, desmin (+), caldesmon (+), EBER (+) by in situ hybridization	MYC overexpression, AKT/mTOR pathway activation
	Malignant	Inflammatory leiomyosarcoma	Adults, with a male predominance, lower limb, trunk, retroperitoneum, visceral organs	Eosinophilic spindle cells with blunt-ended nuclei, diffuse inflammatory cell infiltrate, predominantly lymphoplasmacytic cells	SMA (+) diffusely, desmin (+), caldesmon (+)	Near-haploid genotype, with or without subsequent whole-genome doubling(s)
Skeletal muscle tumors	Malignant	Congenital spindle cell RMS with *VGLL2/ NCOA2/CITED2* rearrangement	Infants or below 3 y of age, located in the soft tissues	Spindle cells with ovoid, monomorphic nuclei and pale eosinophilic cytoplasm, fibrous stroma, but more cellular (subset)	Desmin (+) diffusely, myogenin (+) variably	Gene fusions involving *VGLL2*, *SRF*, *TEAD1*, *NCOA2*, and *CITED2*
	Malignant	*MYOD1*-mutant spindle cell/sclerosing RMS	Any age, affect equally children and adults, female predominance, head and neck, extremities, trunk	Spindle cells with ovoid monomorphic nuclei and eosinophilic cytoplasm, fascicular pattern, necrosis, brisk mitotic activity	Desmin (+) diffusely, MYOD1 (+) diffusely, myogenin (+) patchy	*MYOD1* p.Leu122Arg mutation

TABLE 1. (*continued*)

Tumor Category	Biological Potential	New Entities and Subtypes	Clinical Features	Histologic Features	Immunohistochemical Markers	Molecular Features
	Malignant	Intraosseous spindle cell RMS (with *TFCP2*/*NCOA2* rearrangements)	Wide age range, mainly located in bones, especially craniofacial bones, may invade soft tissue, aggressive subtype	Spindle cells with vesicular nuclei and abundant eosinophilic cytoplasm, obvious rhabdomyoblastic differentiation is absent	Cytokeratin (AE1/AE3) (+), desmin (+), myogenin (+), MYOD1 (+)	*EWSR1* or *FUS* gene fused to the *TFCP2* gene, *MEIS1*-*NCOA2* fusion
Peripheral nerve sheath tumor	Malignant	Malignant melanotic nerve sheath tumor	Middle-aged adults, associated with Carney complex (subset), arise from spinal or autonomic nerve, bone, soft tissues	Fascicles or sheets of spindle to epithelioid Schwann cells, nuclear groove, melanin pigments, psammoma bodies	S100 protein (+), SOX10 (+), HMB45 (+), Loss of PRKAR1A expression	*PRKAR1A* mutation
Tumors of uncertain differentiation	Malignant	NTRK-rearranged spindle cell neoplasm (emerging)	Children and young adults, most tumors present as superficial and deep tumors in the extremities or trunk	Monomorphic spindle cells, stromal and perivascular hyalinization, infiltrative growth, but variable histologic features	S100 protein (+), CD34 (+), Pan-TRK (+), SOX10 (−)	*NTRK1* fusions with a variety of partners

− indicates negative staining; +, positive staining; ±, variable staining; EBER, Epstein-Barr virus-encoded RNA; RMS, rhabdomyosarcoma; RNA, ribonucleic acid.

TABLE 4. Undifferentiated Small Round Cell Sarcomas of Bone and Soft Tissue in the 2020 WHO Classification

	Clinical Features	Histologic Features	Immunohistochemical Marker	Molecular Features
Ewing sarcoma	Children and young adults, long bones, pelvis, and ribs, about 12% arise in extraskeletal regions, including extremities, paravertebral region, mediastinum	Classic ES; uniform, small round cells and scant clear or eosinophilic cytoplasm Atypical ES; larger, prominent nucleoli, and irregular contours	CD99 (+) diffusely membranous expression, NKX2.2 (+) diffusely nuclear expression, FLI1 (+), ERG (+)	Gene fusions involving one member of the FET family of genes (usually *EWSR1*) and a member of the ETS family
Round cell sarcoma with *EWSR1*–non-ETS fusions	*EWSR1/FUS-NFATC2* sarcoma; children and adults, with a male predominance, long bones *EWSR1-PATZ1* sarcoma; wide age range, chest wall, abdomen, extremities, head and neck	Spindled to rounded cells arranged in nests, pseudoacinar, cords, or sheet pattern, fibrohyaline stromal changes, mostly low-grade features, but high-grade cases are reported	*EWSR1/FUS-NFATC2* sarcoma; CD99 (+) in 50%, PAX7 (+), NKX2.2 (+) *EWSR1-PATZ1* sarcoma; coexpression of myogenic and neurogenic markers	*EWSR1-NFATC2*, *FUS-NFATC2*, *EWSR1-PATZ1*
CIC-rearranged sarcoma	Young adults, but a wide age distribution, deep soft tissues of the limbs or trunk, about 10% arise in visceral organs (kidney, gastrointestinal tract)	Predominant round cell phenotype, mild nuclear pleomorphism, epithelioid and/or spindle cell components, variably myxoid stroma	ETV4 (+), WT1 (+), NKX2.2 (−), CD99 (+) patchy	*CIC-DUX4* (95%), *CIC-FOXO4*, *CIC-LEUTX*, *CIC-NUTM1*, *CIC-NUTM2A*
Sarcoma with *BCOR* genetic alterations	Children, male predominance, more often in bone than in soft tissue, pelvis, lower extremities, paraspinal region, trunk	Primitive round to spindle cells arranged in nests, sheets, or fascicular pattern, variably myxoid stroma with delicate vasculature	BCOR (+), SATB2 (+), TLE1 (+), CD99 (+) heterogenous staining in about 50%	*BCOR-CCNB3*, *BCOR-MAML3*, *BCOR3-ZC3H7B*

ES indicates Ewing sarcoma.

Am J Surg Pathol. 2017 July ; 41(7): 941–949. doi:10.1097/PAS.0000000000000846.

Sarcomas with CIC-rearrangements are a distinct pathologic entity with aggressive outcome: A clinicopathologic and molecular study of 115 cases

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CIC-DUX4 gene fusion, resulting from either a t(4;19) or t(10;19) translocation, is the most common genetic abnormality detected in *EWSR1*-negative small blue round cell tumors (SBRCTs). Following their discovery it was debated if these tumors should be classified as variants of Ewing sarcoma (i.e. atypical Ewing sarcoma) or as a stand-alone pathologic entity. As such the WHO classification temporarily grouped the *CIC*-rearranged tumors under undifferentiated sarcomas with round cell phenotype, until further clinical evidence was available. However, most studies reported so far include small series with limited follow-up information which preclude a more definitive assessment. The present work investigates the clinicopathologic features of a large cohort of sarcomas with *CIC* gene rearrangement, in order to define their clinical presentation, morphologic spectrum, and outcome. Our study further examines the overall survival of the *CIC*-positive cohort compared to a control group of *EWSR1*-rearranged Ewing sarcoma matched for age and stage. The study cohort included 115 patients, with a mean age of 32 years and a slight male predominance. Most tumors occurred in the soft tissue (86%), predominantly deep-seated and equally divided among trunk and extremity, followed by visceral locations (12%) and rarely in the bone (3%). Microscopically, most tumors showed round to ovoid cytomorphology but half of the cases showed also focal areas of spindling and epithelioid/ rhabdoid phenotype, with frequent myxoid stromal changes. Variable CD99 reactivity was seen in 84% cases, with a diffuse pattern only in 23% of cases, while nuclear WT1 was seen in 92%. A *CIC-DUX4* fusion was detected in 57% of cases, with either *DUX4* on 4q35 (35%) or on 10q26 in 25 (22%) cases. No *FOXO4* gene rearrangements were present in 39 cases tested. Clinical follow-up was available in 57 patients, with a 5-year survival of 43%, which was significantly lower than the 77% 5-year survival in the control Ewing sarcoma group (p=0.002). Our findings show that *CIC-DUX4* sarcomas occur most commonly in young adults within the somatic soft tissues, having a wide spectrum of morphology including round, epithelioid and spindle cells, and associated with an aggressive clinical course, with an inferior overall survival compared to Ewing sarcoma. The results support the classification of *CIC*-rearranged tumors as an independent molecular and clinical subset of SBRCTs distinct from Ewing sarcoma.

Hindawi
Sarcoma
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Research Article

Survey of Paediatric Oncologists and Pathologists regarding Their Views and Experiences with Variant Translocations in Ewing and Ewing-Like Sarcoma: A Report of the Children's Oncology Group

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Advances in molecular diagnostics have identified subsets of Ewing and Ewing-like sarcomas driven by variant translocations with unique biology. It is likely that patients with these tumours will have different clinical features and therapeutic outcomes. Nevertheless, the management of these patients both locally and within cooperative group trials depends on the local pathological diagnosis. It is not known what molecular diagnostic approaches are employed by local pathologists or if the exact translocation is commonly determined. In addition, it is not known what therapeutic approaches are employed for these patients or what cooperative trials are deemed appropriate for these patients by expert consensus. To answer these questions, we performed an international survey of oncologists and pathologists to better understand the diagnostic approaches used to identify variant translocations and the influence the findings have on therapy and clinical trial eligibility. An online survey was distributed to oncologists and pathologists primarily in North America. A total of 141 surveys were completed, representing a 28% response rate. The majority of respondents considered EWSR1-ETS gene family translocations (range 61–96%) to be Ewing sarcoma and would include them on the primary arm of a Ewing sarcoma clinical trial. There was a lack of consensus on how to classify and stratify BCOR-CCNB3, CIC-DUX4, and EWSR1+ with non-ETS partner fusions. Most respondents were either unsure how their institution tested, or their institution did not perform the test. In cases with atypical Ewing morphology, most respondents favoured additional fusion transcript testing. There is a lack of consensus regarding the classification and stratification of rare molecular subtypes in Ewing sarcoma. It is not clear how these alternative translocations have impacted outcomes for past clinical studies. This suggests a need for molecular confirmation of diagnoses and centralized or minimum standardization of testing for future trial enrolment.

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