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Original Article

Epidemiological and Survival Characteristics of Childhood Lymphomas and Solid Organ Tumors Treated at Our Center

Merkezimizde Tedavi Edilen Çocukluk Çağı Lenfomaları ve Solid Organ Tümörlerinde Epidemiyoloji ve Sağkalım Özellikleri

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ABSTRACT

Objective: Childhood cancers constitute 2% of all cancers seen in the world. Overall 5-year survival rate for childhood cancers is 80% in developed, but it is only 30% in underdeveloped countries. In our study have we aimed to analyze the childhood cancer cases treated in our hospital, and to compare the epidemiological characteristics of the patients followed in our center, the distribution of cancer types in our center and the overall survival rates, with the data obtained from our national, and international literature.

Method: The records of patients aged 0-19 years with lymphomas and malignant solid tumors, who were followed up and treated between December 25,1987 and January 28, 2021 in our department of pediatric oncology were examined. Hospital files of 1326 patient were reviewed retrospectively, and 1175 patients were included in the study. The data were analyzed in SPSS 25.0 package program.

Results: In our study, the male/female ratio was 1.2 among 1175 patients diagnosed with lymphoma and malignant solid organ tumor with a mean age of 7.75 years at the time of diagnosis. Considering the subgroup distribution of childhood cancers other than leukemias; central nervous system tumors (23.6%), lymphomas (19.5%) and neuroblastomas (12%) were found to be the most common malignant diseases. The mean follow-up time of our patients was 62.31±55.3 months, and the mean event-free follow-up period was 50.20±49.681 months. Five- and 10-year overall survival, and event-free survival rates were 74% vs. 68.9%, and 50.5%, vs. 39%, respectively.

Conclusion: In general, survival rates in childhood cancers in our center are close to the average of our region, our country and European countries, but it was found to be lower in some subgroups of our patients compared to developed countries.

Keywords: Childhood cancers, epidemiology, overall survival rate, event-free survival rate

ÖZ

Amaç: Çocukluk çağı kanserleri, dünyada görülen tüm kanserlerin %2'sini oluşturmaktadır. Gelişmiş ülkelerde çocukluk çağı kanserlerinde genel beş yıllık sağkalım oranı %80 iken, az gelişmiş ülkelerde bu oran %30'dur. Bu çalışmanın amacı, merkezimizde takip edilen hastaların epidemiyolojik özelliklerini, kanser türlerinin merkezimizdeki dağılımını ve genel sağkalım oranlarını, dünyadan ve ülkemizden elde edilen verilerle karşılaştırmak ve hastanemizdeki çocukluk çağı kanser vakalarını analiz etmektir.

Yöntem: 25.12.1987 ve 28.01.2021 tarihleri arasında hastanemiz çocuk onkoloji kliniğinde takip ve tedavi edilen, lenfoma ve malign solid tümörleri olan 0-19 yaş arasındaki hastaların kayıtları incelendi. Toplamda 1326 hasta kaydı retrospektif olarak gözden geçirildi. Çalışmaya 1175 hasta dahil edildi. Veriler SPSS 25.0 paket programında analiz edildi.

Bulgular: Çalışmamızda, lenfoma ve malign solid organ tümörü tanısı konulan 1175 hastanın epidemiyolojik cinsiyet dağılımı erkek/kadın: 1,2, tanı anındaki ortalama yaş ise 7,75 yıl olarak bulundu. Lösemiler dışındaki çocukluk çağı kanserlerinin alt grup dağılımları dikkate alındığında, merkezi sinir sistemi tümörleri (%23,6), lenfomalar (%19,5) ve nöroblastom (%12) en yaygın görülen malign hastalıklar olarak tespit edildi. Hastalarımızın ortalama takip süresi 62,31±55,3 ay, ortalama olaysız takip süresi ise 50,20±49,681 ay idi. Beş yıllık genel sağkalım %74 ve 10 yıllık genel sağkalım %68,9; beş yıllık olaysız sağkalım oranı (EFS) %50,5 ve 10 yıllık EFS %39 olarak bulundu.

Sonuç: Genel olarak, merkezimizdeki çocukluk çağı kanserlerinde sağkalım oranları, bölgemiz, ülkemiz ve Avrupa ülkeleri ortalamasına yakın olmakla birlikte, gelişmiş ülkelerle kıyaslandığında bazı alt gruplarda daha düşük bulunmuştur. Daha yüksek yaşam hızları için multidisipliner bir yaklaşıma ihtiyaç duyulmaktadır.

Anahtar kelimeler: Çocukluk çağı kanserleri, epidemiyoloji, genel sağkalım oranı, olaysız sağkalım oranı

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INTRODUCTION

Incidence, mortality, and survival rates of childhood cancers vary by country due to factors related to the local culture, environment, and socioeconomic status of the patients. Major disparities stem from unequal distribution of resourcen between and within countries. Individuals with higher socioeconomic status typically have better health literacy, greater financial resources, and easier access to healthcare services. Consequently, they are more likely to benefit from cancer prevention services, receive earlier diagnoses, and access higher-quality treatment than those with lower socioeconomic status[1].

Childhood cancers account for approximately 2% of all cancers diagnosed worldwide. Cancer remains one of the leading causes of death among children worldwide, with observed incidence rates generally rising over time. There are limited comparative data in the national and international literature on the incidence of childhood cancers diagnosed within the last 20 years[2]. According to 2019 data from the United States, cancer is the leading cause of death among children and ranks among the top four causes of mortality in developing countries like ours[3]. While the incidence of cancer and cancer-related deaths among children is increasing globally, 5-year overall survival (OS) rates have risen up to 80% in developed countries thanks to advances and innovations in its diagnosis and treatment, compared to survival rate of only 30% in developing countries. In the United States, the overall 5-year survival rate for all childhood cancers was reported to be 84.1% in 2015[4].

In the light of these data, the World Health Organization now emphasizes that childhood cancers have become a significant public health issue in the developing world. In our country and other developing nations, understanding the distribution and prevalence of cancer, as well as determining OS rates, is crucial for improving survival rates and living standards of people. Achieving this target is only possible through the regular maintenance of cancer registries and consistent reporting.

The aim of this study is to evaluate the epidemiological characteristics, distribution of cancer types, and OS rates of patients diagnosed with lymphoma and childhood solid organ tumors, treated at our pediatric oncology clinic, between December 25, 1987, and January 28, 2021. We aim to compare these findings with data obtained from both global and national sources, thereby assessing the status of pediatric cancer cases in our hospital.

MATERIALS and METHODS

This research was conducted after obtaining ethical approval from the Clinical and Laboratory Research Ethics Committee of the Dokuz Eylül University (approval number: 2021/24-13, dated: 25.08.2021). The epidemiological data, diagnostic methods used, treatments provided, and OS status of all patients aged 0-19 years who were followed up and treated for lymphoma and malignant solid organ tumors in our pediatric oncology clinic, between December 25, 1987, and January 28, 2021, were retrospectively recorded.

Hospital records of a total of 1,326 patients were retrospectively reviewed. Patients with missing data (n=130) and those who applied to our clinic only once or for consultation purposes (n=21) were excluded from the analysis. The remaining 1,175 patients were included in the study. The study population consisted of 54 patients who applied to our center after they experienced relapse while being treated at another center, 383 patients who were diagnosed at another centers, and referred to our department for follow-up and treatment, and the remaining 738 patients applied firstly to our center, received their histopathological diagnosis, and then treated at our center. The last date of patient follow-up was set as December 31, 2021.

Event-free survival (EFS) and OS curves for the patients were also drawn. The OS of the patients was calculated by subtracting the date of diagnosis from the last follow-up date, while EFS was estimated by subtracting the date of diagnosis from the date of the first event experienced. Patients who were lost to follow-up or unreachable were classified as "lost to follow-up", those who transferred to another center for subsequent follow-up were labeled as "transferred to another center", and cases refractory to treatment or presence of progressive disease, recurrence, death, or secondary cancer development were defined as "events".Cancer types were classified according to the International Classification of Childhood Cancer (ICCC-3, 2005)[5].

Statistical Analysis

The data were analyzed using the SPSS 25.0 software package program. Categorical variables were analyzed using the chi-square test, while continuous variables were analyzed using the t-test. Correlation analyses were conducted with multivariate logistic regression test. Survival analyses were performed using the chi-square test and Kaplan-Meier analysis, and survival curves were compared using the log-rank test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

In this study, hospital files of a total of 1,175 cases including 536 (45.6%) female, and 639 (54.4%) male (Male/Female:1.2:1) patients who were followed up in our pediatric oncology clinic, between December 25, 1987, and January 28, 2021, were reviewed. The mean age of our patients at the time of diagnosis was 7.75 years. Our study population consisted of patients (n=738:63%) who received their histopathological diagnosis at our center or at other centers and referred to our department (n=383, 32%). While 54 (5%) patients were under follow-up at other centers before presenting to us with relapsed disease. Metastasis was detected in 246 (20.9%) patients, and the site of metastasis was identified in 237 of these patients. Specifically, metastatic lesions were observed in the skeleton in 6.9% (n=81), in the lung in 6.6% (n=77), in the bone marrow in 3.2% (n=37), in the liver in 2% (n=23), in the central nervous system in 0.6% (n=7), and in distant lymph nodes in 0.4% (n=5) of the patients.

The mean duration of follow-up for the patients included in this study was 62.31±55.327 months, while the mean duration of event-free follow-up was 50.20±49.681 months. A pathological event occurred in 50.9% of the patients. Considering the final medical outcome of the study population, patients had died (n=300; 25.5%), were lost to follow-up (n=193; 16.4%) livied with (n=68: 5.8%) and without the disease (n=565; 48.1%), and had been transferred to another center (n=49: 4.2%). The most common cause of mortality was cardiopulmonary arrest due to disease progression.

The information regarding the types of cancer diagnosed in our patients was evaluated, and the results are presented in Table 1.

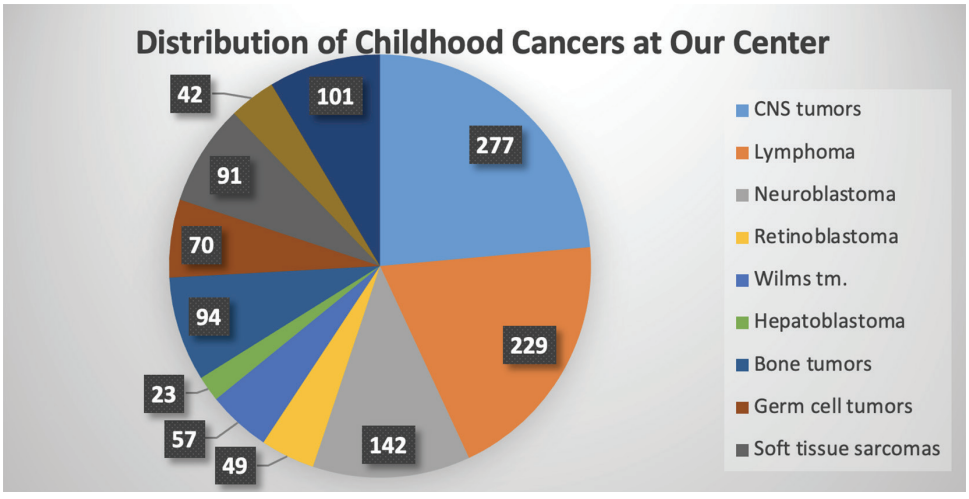
The five-year and 10-year OS rates for patients diagnosed with lymphoma and solid organ tumors followed at our center were found to be 74%, and 68.9%, respectively (Figure 1). The five-year, and 10-year EFS rates for our patients were 50.5%, and 39%, respectively (Figure 2).

We investigated the average follow-up duration, five-year OS, and five-year EFS rates according to tumor subgroups in our patients. In patients diagnosed with central nervous system tumors, the five-year OS rate was found to be 65%, while specific 5-year OS rates for astrocytomas (72%), medulloblastomas (64%) and ependymomas (51%) were also determined. The respective average follow-up times, 5-year OS, and EFS rates for patients diagnosed with Hodgkin lymphoma (86 mos, 90%, and 76.6%). non-Hodgkin lymphoma (63 mos, 75%, and 52%), neuroblastoma (60 mos, 70%, and 48%), hepatoblastoma (68 mos, 75%, and 70%), osteosarcoma (44.8 mos, 56.9%, and 41.9%), Ewing sarcoma (54.7 mos, 60.7%, and 37.8%), rhabdomyosarcoma (65.4 mos, 57.8%, and 42%), and Wilms tumor (65.9 mos, 77%, and 54%) were as indicated (Figures 3-5).

DISCUSSION

The average age of 1,175 patients diagnosed with malignant childhood cancers who presented to our hospital was found to be 7.75 years, with a male-to-female (M/F) ratio of 1.19. This distribution was found to be similar to the data collected from across Turkey by the Turkish Pediatric Oncology Group (TPOG) between 2009 and 2021. In the TPOG 2009-2021 report, the median age of the patients was reported as 6.7 years, with a M/F ratio of 1.27[6]. According to an alliance of

Table 1. Distribution of non-leukemic pediatric tumor subgroups followed at our center, 1987-2021



non-governmental and public health organisations with member organisations across European countries (EUROCARE) and the Automated Childhood Cancer Information System data from 2010 in Europe, the median age of patients was reported as 5.8 years, with a M/F ratio of 1.2[3]. It was determined that the epidemiological analysis of our patients in terms of age and gender is consistent with the literature data.

In the study conducted in our center, excluding leukemias, the most common childhood cancers in decreasing frequency were found to be central nervous system tumors (23.6%), lymphomas (19.5%), and neuroblastoma (12%), respectively.

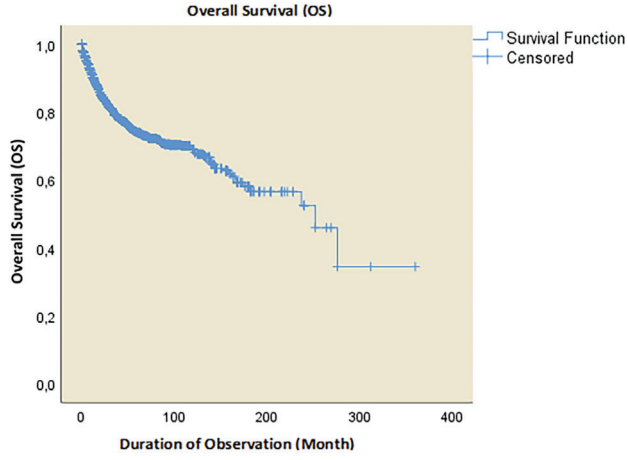


Figure 1. OS rates in childhood cancers
OS: Overall survival

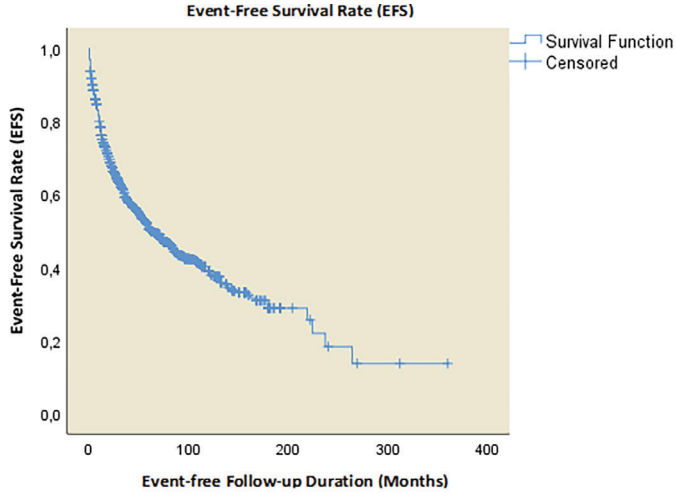


Figure 2. EFS rates in childhood cancers
EFS: Event-free survival

According to the 2021 TPOG report, the most common subgroups of childhood cancers in our country were lymphomas (18.8%), central nervous system tumors (15.0%), and neuroblastoma (8.2%)[6]. In contrast, at our center, the most common cancers are central nervous system tumors (23.6%), followed by lymphomas (19.5%) and neuroblastoma (12%). This discrepancy may be attributed to our center's status as a referral center for Neurosurgery and Radiation Oncology, particularly in our region.

Additionally, the incidence of neuroblastoma at our center (12%) was found to be higher than that reported in both national and European literatüre (7-8%). This

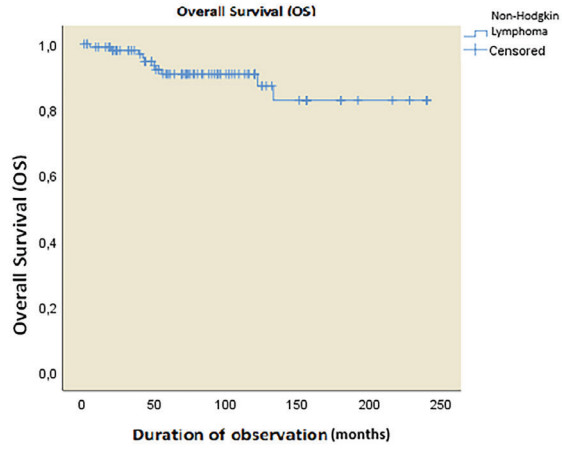


Figure 3. OS rates in Hodgkin lymphoma patients
OS: Overall survival

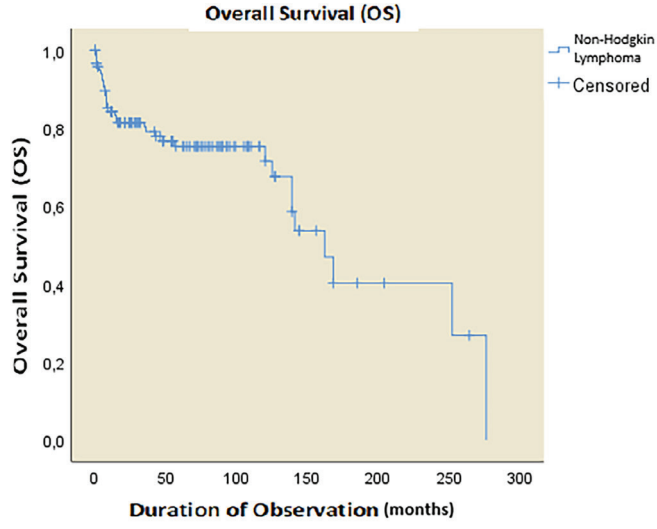


Figure 4. OS rates in non-Hodgkin lymphoma patients
OS: Overall survival

difference in incidence rates may be related to our center becoming a referral center for neuroblastoma cases coming from the Aegean region and even across Turkey, particularly following the implementation of the TPOG-NB-2003 protocol and the initiation of molecular and cytogenetic studies at our center. While the incidence of retinoblastoma and bone tumors was comparatively higher at our center, the incidence rates of kidney tumors, liver tumors, soft tissue sarcomas, and germ cell tumors were comparable to those reported in the literature.

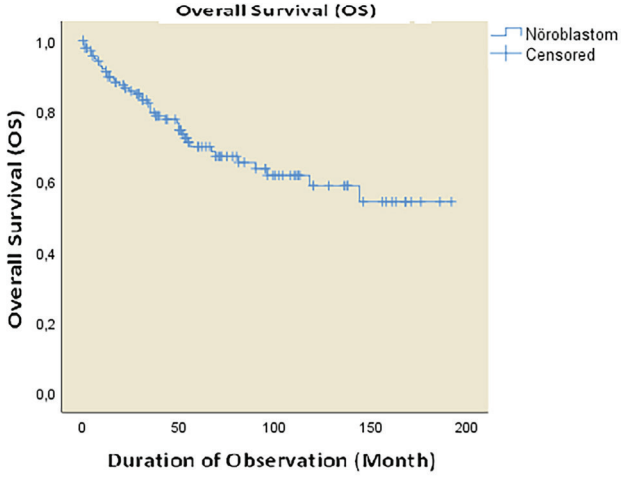


Figure 5. OS rates in Neuroblastoma patients
OS: Overall survival

The 5-, and 10-year OS rates for patients diagnosed with lymphoma and solid organ tumors followed at our center were 74%, and 68.9%, respectively. Whereas, 5-, and 10-year EFS rates for these patients were 50.5%, and 39%, respectively. In our study, 20% of the patients had metastasis at the time of diagnosis. The five-year OS rate for patients with metastatic disease at diagnosis was 52.3%, compared to 79.8% for those without. Statistically, a significant difference in survival rates was observed based on the presence of metastasis at diagnosis. This result is a critical indicator of the importance of early diagnosis and treatment in improving survival rates.

In a study conducted by Ege University Medical Faculty Hospital, which analyzed childhood cancers between 1992 and 2017, 5-year OS rate was found to be 74%[7]. According to data from the Oncology Institute of İstanbul University, 5-year OS rate for childhood cancers treated between 1990 and 2012 was reported to be 74.4%[8]. According to TPOG data, 5-year OS rate for childhood cancers increased from 65% between 2002 and 2008 to 72% between 2009 and 2020[6,9]. According to the data from the Middle East Cancer Consortium whose member countries are Jordan, Iraq, Egypt, Israel, Lebanon, Palestine, Pakistan, and Turkey, leukemias are the most common childhood cancers, followed by central nervous system tumors and lymphomas. The five-year OS rates were reported to be the lowest in Morocco at 30%, followed by at an ever-increasing rate by Pakistan (55%), Egypt (40-60%), Iraq (62%), Jordan,

Table 2. Five-year OS rates by tumor subgroups

Five-year OS rates							
	Our pediatric oncology clinic (%)	**EUMF* pediatric oncology (7) (%)**	**İstanbul Oncology Institute (8) (%)**	**TPOG-TPHS** (9) (%)**	**ACCIS (12) (%)**	**EUROCARE-5 (3) (%)**	**SEER (11) (%)**
All patients	74	74	74.4	72	72	78	83
Hodgkin lymphoma	91	95	98	78	93	-	97
Non-Hodgkin lymphoma	75	83.5*	92		79	-	85
CNS tumors	65	67	63	47	76		75
Neuroblastoma	70	60	70	55.6	59	70	79
Osteosarcoma	56	57	-	45		64	71
Ewing sarcoma	61	54	-			66	72
Rabdomyosarcoma	58	62	70	52	65	68	64
Wilms tumor	77	76	92	74	84	90	90
Liver tumors	75		48	53	-	-	74

*EUMF: Ege University Faculty of Medicine, **TPOG: Turkish Pediatric Oncology Group, CNS: Central nervous system, TPHS: Turkish Pediatric Hematology Society, ACCIS: The Automated Childhood Cancer Information System, SEER: The Surveillance, Epidemiology, and End Results, EUROCARE: An alliance of non-governmental and public health organisations with member organisations across European countries, OS: Overall survival

Lebanon (75%), and Israel (84%)[10]. Between 1999 and 2007, the EUROCARE-5 study analyzed approximately 58,000 pediatric cancer patients from 29 countries, finding a 5-year OS rate of 77.9%[3]. According to data from the United States, the National Cancer Institute's Surveillance, Epidemiology, and End Results program, 5-year OS rate for pediatric cancers increased from 63% between 1975 and 1979 to 83% between 2003 and 2009[11]. According to these data, although the survival rates for childhood cancers at our center are comparable to the averages in our region, country, and European countries, they are lower than those reported in developed countries like the United States.

When compared to the literature data, 5-year OS rates of central nervous system tumors in our region were found to be consistent with local data. Although these rates were higher than those reported by TPOG, they remained at lower levels when compared to developed countries. The five-year survival rates for Hodgkin lymphoma and non-Hodgkin lymphoma at our center were found to be lower than those reported in other studies conducted in our country and in developed countries. The survival rates for neuroblastoma, hepatoblastoma, and Wilms tumor were found to be consistent with those reported in studies from both developed countries and our country. For the subgroups of osteosarcoma, Ewing sarcoma, and rhabdomyosarcoma, the survival rates of patients treated at our center were comparable to those indicated in our national registry, but lower compared to data reported from developed countries. Five-year OS rates of institutions by tumor subgroups are presented in Table 2.

CONCLUSION

With the exception of certain tumor groups, the survival rates of the patients treated at our center were found to be at comparable levels with those reported in national and international literature. These results are not limited to a single department; rather, they represent a collective outcome of a multidisciplinary team, including the intensive care units involved in the diagnosis, follow-up, and treatment of pediatric oncology patients at our hospital, as well as all branches of pediatric health and diseases, pediatric surgery, radiology, pathology, radiation oncology, nuclear medicine, laboratory services, nursing services, child and adolescent mental health, physical therapy and rehabilitation, social services, and management units. Multidisciplinary approaches to childhood cancers, adherence to specific treatment protocols, and good supportive care are crucial factors for achieving therapeutic success. In order to attain higher survival rates, there is a need for targeted antineoplastic agents developed alongside advancing technology, new treatment protocols, and effective supportive care within a multidisciplinary approach[13].

Ethics

Ethics Committee Approval: This research was conducted after obtaining ethical approval from the Clinical and Laboratory Research Ethics Committee of the Dokuz Eylül University (approval number: 2021/24-13, dated: 25.08.2021).

Informed Consent: Retrospective study.

Footnotes

Author Contributions

Surgical and Medical Practices: E.Ç., Concept: N.O., Design: N.O., Data Collection or Processing: B.A, Analysis or Interpretation: D.İ., Literature Search: B.A., D.K., Writing: B.A.

Conflict of Interest: The authors have no conflict of interest to declare.

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