J Surg Med. 2020;4(8):636-639.
DOI: 10.28982/josam.767956

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN=2602-2079

Rhabdomyosarcoma as a very rare tumor in adult: Case series

Erişkinde nadir bir tümör olarak rabdomiyosarkom: Vaka serisi

Ferit Aslan [1], Erkan Erdur [2], Fatih Yıldız [3]

[1] Yüksek İhtisas University, Medicalpark Ankara Hospital, Department of Medical Oncology, Ankara, Turkey
[2] Health Sciences Unıversity, Gazi Yaşargil Training and Research Hospital, Department of Medical Oncology, Diyarbakır, Turkey
[3] Health Sciences Unıversity, Ankara Dr Abdurrahman Yurtaslan Oncology Training and Research Hospital, Department of Medical Oncology, Ankara, Turkey

ORCID ID of the author(s)
FA: 0000-0002-9153-6921
EE: 0000-0002-9123-2688
FY: 0000-0003-2295-7332

Corresponding author/Sorumlu yazar:
Ferit Aslan
Address/Adres: Yüksek İhtisas Üniversitesi, Medicalpark Ankara Hastanesi, Tıbbi Onkoloji Kliniği, Ankara, Türkiye
E-mail: feritferhat21@gmail.com

Ethics Committee Approval: Ethics committee approval was not received due to retrospective design of the study. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif dizaynından dolayı alınmamıştır. İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 8/30/2020
Yayın Tarihi: 30.08.2020

Abstract

Aim: Rhabdomyosarcoma is more frequent and has a better prognosis in children. In adults, it is relatively rare and has a worse prognosis. The most effective treatment is achieved with a multimodal approach. We aimed to share the clinical, pathological and survival results of 14 patients with adult rhabdomyosarcoma.

Methods: In our study, we evaluated 14 patients with RMS who were followed up and treated between January 2000 and January 2018 in three medical oncology departments in Turkey. The uses of surgery, chemotherapy and radiotherapy for curative and palliative purposes were considered multimodal in all patients.

Results: The median age of all patients was 44.5 years (range: 16-83). Ten (71.4%) of our patients were male. The tumors of nine (64.3%) of 14 patients were localized and 5 (35.7%) patients had metastatic disease. Five (55.6%) of 9 patients with localized disease developed relapse. Histological examination of the patients revealed that 10 (71.4%) had pleomorphic, 3 (21.4%) had alveolar and 1 (7.1%) had undifferentiated RMS. The median follow-up period of all patients was 14.6 (range; 2.3-267) months. Relapse-free survival (RFS) was 15.17 months (95% CI; 1.1-29.2). The time to progression of disease after metastatic first-line treatment (PFS) was 10.18 (95% CI; 7.08-13.2) months. At evaluation of the data, 9 patients had died. Median overall survival (OS) at local and metastatic stages were 29.3 months (95% CI; 20.8-37.9) and 11.2 months (95% CI; 9.29-13.1), respectively, while the OS of all participants was 22.8 months (95% CI; 0-47). Five-year OS was 28.2% (Standard error (SE); 13.4%) and 5-year relapse-free survival was 41.2% (SE; 17.3%).

Conclusions: The multimodal approach is the best option in early and advanced stage rhabdomyosarcoma. Among our few patient series, clinic and survival results are consistent with the literature.

Keywords: Adult rhabdomyosarcoma, Multimodality, Survival, Clinic and pathology

Öz

Amaç: Çocuklarda daha sık ve daha iyi prognozlu olan rabdomiyosarkom, erişkinlerde çocukların aksine daha nadir ve daha kötü prognozludur. En etkili tedavi yöntemi multimodaliter yaklaşımdır. Bu çalışmamızda 14 hastalık erişkin rabdomiyosarkom hastamızın klinik, patolojik ve sağkalım sonuçlarını paylaşmayı amaçladık.

Yöntemler: Çalışmamızda, Türkiye'nin üç tıbbi onkoloji bölümünde 2000 Ocak ve Ocak 2018 tarihleri arasında takip edilen ve tedavi edilen 14 RMS hastası değerlendirildi. Hastaların tamamında, küratif ve palyatif amaçlı cerrahi, kemoterapi ve radyoterapinin kullanılması multimodaliter olarak benimsenmiştir.

Bulgular: Tüm hastaların ortanca yaşı 44,5 (dağılım: 16-83) yıl olarak bulundu. Hastalarımızın 10'u (%71,4) erkektir. On dört hastanın 9'unda (%64,3) lokalize, 5'inde (%35,7) metastatik hastalık mevcuttu. Lokalize hastalığı olan 9 hastanın 5 (%55,6) inde nüks gelişti. Hastaların histolojik özelliklerine bakıldığında 10 (%71,4) hasta pleomorfik, 3 (%21,4) alveoler ve 1 (%7,1) hastada pleomorfik rabdomiyosarkom (RMS)vardı. Tüm hastaların ortanca takip süresi 14,6 (dağılım; 2.3-267) aydı. Nükssüz geçen sağkalım (RFS) 15,17 aydı (%95 Güvenlik Aralığı (GA); 1,1-29,2). Metastatik hastalarda birinci basamak tedavi için progresyonsuz sağkalım süresi (PFS) 10,18 (%95 CI; 7,08-13,2) ay olarak saptandı. Hastalardan 9 unda ölüm gerçekleşmişti. Lokal evrede toplam sağkalım (OS) 29,3 ay (%95 GA; 20,8-37,9), metastatik evrede 11,2 ay (%95 GA; 9,29-13,1) ve tüm hasta grubunda 22,8 (%95 GA; 0-47) ay olarak bulundu. Beş yıllık OS %28,2 (Standart hata (SH); %13,4) ve 5 yıllık RFS %41,2 (SH; %17,3) idi.

Sonuç: Multimodaliter tedavi yaklaşımı erken ve ileri evre rabdomiyosarkom için en iyi seçenektir. On dört hastalık serimizin klinik ve sağkalım sonuçları literatürle uyumludur.

Anahtar kelimeler: Yetişkin rabdomiyosarkom, Multimodalite, Sağkalım, Klinik ve patoloji

Introduction

Soft tissue sarcomas constitute 1% of all adult malignancies [1,2]. Although rhabdomyosarcoma (RMS) is common in children, it is very rare in adults [3]. In a study in Europe where adult sarcomas were evaluated retrospectively, rhabdomyosarcomas constituted 10.6% of all soft tissue sarcomas [4,5].

While the overall 5-year overall survival (OS) in localized RMS in children exceeds 70%, the prognosis is worse in the adult age group. Five-year overall survival in localized disease in RMS in the adult age group is around 20-43%, while this rate is around 5% in metastatic disease. Treatment of RMS in adult patients is difficult, the most important reasons being its rarity and heterogeneous distribution [6,7].

Alveolar and embryonic RMS are treated according to pediatric guidelines. RMSs seen in the adult age group are treated by adhering to pediatric treatment protocols and with multidisciplinary approaches [8,9].

In systemic treatment of alveolar and embryonic RMS, agents such as doxorubicin, actinomycin, cyclophosphamide, vincristine, ifosfamide and etoposide are used. Pleomorphic RMS is treated like other soft tissue sarcomas in the adult age group [4,10,11].

We aimed to share the clinical features, treatment, and follow-up results of 14 adult rhabdomyosarcoma patients, 9 of which had localized and 5 had metastatic disease.

Materials and methods

This study involved the evaluation of 14 patients who were treated for and followed-up with a diagnosis of RMS at three medical centers between January 2000 and December 2018.

Soft tissue sarcoma staging of the American joint committee on cancer (AJCC, 2017, 8th edition) staging system was used. The classification determined by the World Health Organization was utilized for side effect assessment. Treatment choices were made taking into account the studies of international sarcoma study groups and the National Comprehensive Cancer Network guideline (NCCN).

VAC (vincristine, actinomycin, cyclophosphamide, mesna), ICE (ifosfamide, carna, adriamycin) and oral pazopanib were used for chemotherapy. Multidisciplinary treatment, including surgery, adjuvant chemotherapy and radiotherapy, was required in 9 patients with localized disease. Considering adjuvant treatment protocols, 7 pleomorphic RMS and 1 alveolar RMS patients received VAC chemotherapy, while 1 alveolar RMS patient received IMA. When all stage 4 patients were evaluated in terms of 1st line treatment, 1 undifferentiated RMS, 2 alveolar RMS and 4 pleomorphic RMS patients were administered VAC chemotherapy, and 3 pleomorphic RMS patients, IMA chemotherapy. Total anthracycline dose was decisive in the selection of first-line treatment in patients with recurrence. In the second line treatment of stage 4 patients, 2 patients with pleomorphic RMS received oral pazopanib treatment and 1 patient with alveolar RMS received ICE chemotherapy. No patients received third-line treatment.

Statistical analysis

The SPSS 18.0 program was used to estimate survival rate, and descriptive data were calculated through the use of the same program. Kaplan-Meier curves and a Log-rank test were used to analyze the survival data, and *P*-values of <0.05 were considered statistically significant.

Results

The median age of all patients was 44.5 (Range: 16-83) years. Ten (71.4%) patients were male. Nine (64.3%) of 14 patients had localized tumors, while 5 (35.7%) were in stage 4 at diagnosis. Five localized patients (35.7%) had stage 2, 4 patients (28.6%) had stage 3 disease. During the diagnosis, 1 (20%) RMS patient with a single metastatic nodule in the lung underwent metastasectomy. In 4 (80%) patients with metastatic disease, surgery could not be performed due to extensive metastasis. R1 resection was performed in 2 (22%) of 9 patients with localized disease, while R0 resection was performed in the remaining 7 (88%) patients. The primary sites of 5 patients (35.7%) were lower limbs, 2 patients (14.3%), upper limbs, 2 patients (14.5%), the head and neck, 2 patients (14.5%), the trunk, 2 patients (14.5%), the genitourinary system, and 1 patient (7.1%), the ophthalmic area. Histopathologically, 10 (71.4%) patients had pleomorphic, 3 (21.4%) patients had alveolar, 1 (7.1%) patients had undifferentiated RMS (Table 1, 2).

Recurrence occurred in 5 (55.6%) of 9 patients with localized disease. Local recurrence was more common, followed by inguinal region and lung recurrence. Considering the metastasis sites in patients who had metastases at diagnosis or later, 5 patients (55.6%) had metastasis in the lung, 2 patients (22.2%), in the skin, 3 patients (33.3%), in the bone, 1 patient (11.1%) in the breast, and 1 (11.1%) in the inguinal lymph node.

Primary GCSF prophylaxis was performed in the treatment of VAC, IMA and ICE. Hematological toxicity was grade 3-4 in seven patients and grade 1-2 in 5 patients. Among non-hematologic toxicities, 4 patients had grade 3 mucositis and one patient using VAC developed severe type demyelinating polyneuropathy. The use of pazopanib in the second-line treatment of metastatic pleomorphic sarcoma was well tolerated.

Median overall survival (OS) at local and metastatic stages were 29.3 months (95% CI; 20.8-37.9) and 11.2 months (95% CI; 9.29-13.1), respectively, while the OS of all participants was 22.8 months (95% CI; 0-47). Five-year OS was 28.2% (Standard error (SE); 13.4%), the median survival time to relapse (RFS) was 15.17 months (95% CI; 1.1-29.2), and 5-year RFS was 41.2% (SE; 17.3%). Progression-free survival (PFS) was 10.18 (95% CI; 7.08-13.2) months after first-line treatment in metastatic disease. Three patients were able to receive second-line treatment in metastatic disease: Two patients with Pleomorphic RMS received pazopanib, and PFS was 3.2 and 7.2 months. The PFS of the patient with alveolar RMS who received ICE chemotherapy in the second line was 7.2 months (Tables 1, 2).

Table 1: Underwent surgery patients who are early stage (stage 2-3) at diagnosis

Patient Number	Age	Gender	Localization	Pathology	Stage	Adjuvant Treatment	Recurrence Area	RFS (Month)	Name and Response of First line Treatment in advance disease	PFS of First line Treatment in advance disease (Month)	Name and Response of second line treatment of advance disease	PFS of second line treatment of advance disease	OS (Month)	Exitus
1	30	Male	Genitourinary	Alveolar	Stage 3	6×IMA Local RT	Local Recurrence Lung	15.1	4×VAC SD	4.99	3×ICE SD	7.23	28.85	Yes
2	53	Male	Trunk	Pleomorphic	Stage 3	6×VAC Local RT	İnguinal LAP	8.8	6×IMA PR	8.28	6 ×Pazopanib (Month) SD	7.2	29.37	Yes
3	43	Male	Limbs	Pleomorphıc	Stage 2	6×VAC Local RT	No						59.3	No
4	16	Male	Genitourinary	Alveolar	Stage 2	6×VAC Local RT	No						215.1	No
5	68	Male	Limbs	Pleomorphıc	Stage 2	5×VAC Local RT	No						13.37	No
6	33	Female	Limbs	Pleomorphıc	Stage 2	6×VAC Local RT	Lung	7.26	6×IMA SD	8.05	3 ×Pazopanib (Month) PD	3.22	23.85	Yes
7	46	Male	Head and Neck	Pleomorphıc	Stage 2	3×VAC		9.43					10.3	Yes
8	16	Male	Head and Neck	Pleomorphıc	Stage 3	6×VAC	No						267	No
9	83	Female	Limbs	Pleomorphıc	Stage 3	No	No	2.43					2.43	Yes

IMA: Iphosphamide-Mesna-Adriamycin, VAC: Vincristin-Actynomycin-Cyclophosphamide-Mesna, ICE: Iphosphamide-Carboplatin-Etoposide-Mesna, RT: Radiotherapy, LAP: Lymphadenopathy, RFS: Recurrence Free Survival, PFS: Progression Free Survival, OS: Overall Survival, PR: Partial Response, SD: Stabil Disease, PD: Progression Disease

Table 2: Patients who are advance disease at diagnosis

Patient Number	Age (Years)	Gender	Primary Localization	Pathology	Palliative RT	Metastasıs Area	Name and response of firstline in advance disease	PFS of Firstline in advance disease (Month)	OS	Exitus
10	26	Female	Ophthalmic	Undifferentiated	Bone	Bone	6×VAC PR	9.17	10.32	Yes
11	68	Male	Scapula	Pleomorphıc	Bone	Lung Skin	1×VAC PD	0.43	0.79	Yes
12	32	Female	Limbs	Alveolar	Bone	Bone Breast	3×VAC PD	4.47	14.52	No
13	52	Male	Limbs	Pleomorphic	Bone	Bone	6×VAC PR	11.20	11.20	Yes
14	48	Male	Limbs	Pleomorphic	No	Lung	6×VAC PD	8.02	11.96	Yes

Discussion

We shared the clinical, follow-up and treatment results of 14 patients with adult rhabdomyosarcoma. In this case series, the 5-year OS was 28%. In the literature, the 5-year OS in adults is reported as 27%, regardless of stage [3]. Among histologic sub-types, alveolar and pleomorphic RMS were the majority in our case series. While alveolar histology was seen in early ages, pleomorphic histology was dominant in later years, which was coherent with the literature. Since RMS is less common in the adult age group, chemotherapy protocols used in childhood were predominantly applied in our cases. A multidisciplinary approach was demonstrated in all of our patients. Combined treatment approach including surgery, radiotherapy and chemotherapy was adopted in those with localized disease. While median OS was 22.8 months in all patient groups, it was 11.2 months in the metastatic group. Although the number of patients in our study was low, survival data were similar to the literature. The OS of one patient was 17.9 years, and he was still alive. Even though grade 3-4 toxicities developed from time to time with the chemotherapy protocols applied, they were manageable.

In the study with the largest patient series regarding adult RMS and comparing adult and child age group RMS, the 5-year OS was around 82% in children with localized disease, and around 47% in adults. Age, histological subtype, primary location, stage, surgery and radiotherapy and local control were the most important predictors for survival in multivariate analysis [3].

In a study in which French national data were compiled, when survival according to histopathologic subtypes were examined, the median OS in localized disease was 24, 42, 66 months for alveolar, pleomorphic, and embryonic RMS, respectively, and 9, 13 and 28 months for metastatic alveolar, pleomorphic and embryonic RMS, respectively. In the Multivariate analysis performed for OS in localized disease, it was observed that patients with non-alveolar histology, young age, R0 resection, radiotherapy and pediatric KT protocol had better survival. In the multivariate analysis for advanced RMS, non-alveolar histology, R0 resection and RT use were found to have better OS [6].

In the study from MD Anderson cancer center involving 239 patients, median OS was 3.8 years in the nonmetastatic group. In multivariate analysis of localized disease, age >50 years was associated with shorter OS and RFS. Median OS in metastatic disease was 1.4 years. Multimodal therapy has been shown to be associated with longer survival in localized and metastatic disease [7].

At the 2018 American Society of Clinical oncology (ASCO) congress, the European Pediatric Soft Tissue Sarcoma Study Group (EpSSG) phase 3 study showed that maintenance metronomic chemotherapy increased OS in patients with high-risk RMS after standard chemotherapy in patients aged 6-21 years. Additional studies and time are needed to evaluate this as a standard approach [12].

Limitations

The main deficiencies in our study are the low number of patients, lack of multi-center data and retrospective evaluation. Due to the low number of patients, a complete statistical evaluation of the factors affecting treatment efficacy and survival could not be made. Case reports and case series on adult rhabdomyosarcoma have an important place in the literature. The number of studies with large patient series and prospective studies is very low. For these reasons, we think that our series of 14 cases will contribute to the literature.

Conclusion

In our series of patients with rhabdomyosarcoma, which we rarely see in adults, we have seen that our patients with multimodal approach can have better results on a case-by-case basis. In our patients, we experienced that multimodal treatment was tolerable with a manageable toxicity profile.

References

1. Wibmer C, Leithner A, Zielonke N, Sperl M, Windhager R. Increasing incidence rates of soft tissue sarcomas? A population-based epidemiologic study and literature review. Ann Oncol. 2010 May;21(5):1106-11.
2. Allouche F, Mazti A, Terrab F, Ghammad S, Bouhafa T, El Mazghi A, Hassouni K. Kidney clear cell sarcoma: About one case. J Surg Med. 2018;2(3):380-2.
3. Sultan I, Qaddoumi I, Yaser S, Rodriguez-Galindo C, Ferrari A. Comparing adult and pediatric rhabdomyosarcoma in the surveillance, epidemiology and end results program, 1973 to 2005: an analysis of 2,600 patients. J Clin Oncol. 2009 Jul 10;27(20):3391-7.
4. Nagar SP, Mytelka DS, Candrilli SD, Dyachkova Y, Lorenzo M, Kasper B, et al. Treatment patterns and survival among adult patients with advanced soft tissue sarcoma: a retrospective medical record review in the United Kingdom, Spain, Germany, and France. Sarcoma, 2018 May;2018:5467057. 10.1155/2018/5467057
5. Demirli Atıcı S, Yeşilyurt D, Dikmeer E, Salimoğlu S, Ayaz D, Aydın C. Biphasic synovial sarcoma: A rare cause of axillary mass. J Surg Med. 2019; 3(7): 533-535.
6. Bompas E, Campion L, Italiano A, Le Cesne A, Chevreau C, Isambert N, et al. Outcome of 449 adult patients with rhabdomyosarcoma: an observational ambispective nationwide study. Cancer Med. 2018 Aug;7(8) 4023–35.
7. Elsebaie MA, Amgad M, Elkashash A, Elgebaly AS, Shash E, Elsayed Z. Management of low and intermediate risk adult rhabdomyosarcoma: a pooled survival analysis of 553 patients. Sci Rep. 2018 Jun 19;8(1):9337. doi: 10.1038/s41598-018-27556-1.
8. Kojima Y, Hashimoto K, Ando M, Yonemori K, Hirakawa A, Kodaira M, et al. Clinical outcomes of adult and childhood rhabdomyosarcoma treated with vincristine, d-actinomycin, and cyclophosphamide chemotherapy. J Clin Oncol. 2009 Nov 1;27(31):5182–8.
9. Ferrari A, Dileo P, Casanova M, Bertulli R, Meazza C, Gandola L, et al. Rhabdomyosarcoma in adults: a retrospective analysis of 171 patients treated at a single institution. Cancer. 2003 Aug 1;98(3):571-80
10. Schöffski P, Cornillie J, Wozniak A, Li H, Hompes D. Soft tissue sarcoma: an update on systemic treatment options for patients with advanced disease. Oncol Res Treat. 2014;37(6):355-62
11. Garcia del Muro X, de Alava E, Artigas V, Bague S, Brana A, Cubedo R, et al. Spanish Group for Research on Sarcoma. Clinical practice guidelines for the diagnosis and treatment of patients with soft tissue sarcoma by the Spanish group for research in sarcomas (GEIS). Cancer Chemother Pharmacol. 2016 Jan;77(1):133-46.
12. Dumont SN, Araujo DM, Munsell MF, Salganick JA, Dumont AG, Raymond KA, Linassier C, Patel S, Benjamin RS, Trent JC. Management and outcome of 239 adolescent and adult rhabdomyosarcoma patients. Cancer Med. 2013 Aug;2(4):553-63.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.