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Kaposi Sarcoma: Single Center 10 Years Of Experience

Kaposi Sarkomu: Tek Merkezde 10 Yıllık Deneyim

Şeyhmus Kaya[1], Sedanur Aydın[1] , Ramazan Oğuz Yüceer[1], Tülay Koç[1] , Hatice Reyhan Eğilmez[1]

[1] Sivas Cumhuriyet University, School of Medicine, Department of Pathology, Sivas, Turkey

e-mail: drseyhmuskaya21@gmail.com, ksedanur@gmail.com, r.yuceer66@hotmail.com, tkoc@cumhuriyet.edu.tr, egilmezreyhan@gmail.com
ORCID: 0000-0003-4059-9946
ORCID: 0009-0009-9878-7983
ORCID: 0000-0002-9418-8862
ORCID: 0000-0001-8612-0238
ORCID: 0000-0001-9666-0246

*Sorumlu Yazar / Corresponding Author: Şeyhmus Kaya
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Öz

Giriş ve Amaç: Kaposi sarkomu, insan herpes virüs-8 (HHV-8) ile güçlü bir şekilde ilişkili nadir bir anjiyoproliferatif bozukluktur. Ülkemizde bu hastalığın epidemiyolojisi ve klinik özelliklerine dair veriler sınırlıdır. Bu çalışma, Sivas Cumhuriyet Üniversitesi Uygulama ve Araştırma Hastanesi Tıbbi Patoloji Anabilim Dalı'nda tanı alan Kaposi sarkomu olgularını analiz etmeyi amaçlamaktadır.
Gereç ve Yöntemler: 1 Ocak 2013 ile 30 Haziran 2023 tarihleri arasında Kaposi sarkomu tanısı alan hastaların (n=18) tıbbi kayıtları retrospektif olarak incelenmiştir. Tekrarlayan vakalar da dahil edildiğinde, toplam tanı sayısı 27'ye ulaşmıştır. Klinik, histopatolojik ve demografik özellikler değerlendirilmiştir.
Bulgular: Hastaların ortalama yaşı 69,3±13,3 yıl (aralık: 32–88) olarak bulunmuştur. On üç hasta (%72,2) erkek, beş hasta (%27,7) kadındır. Hiçbir hastanın HIV enfeksiyonu öyküsü bulunmamaktadır. Lezyonlar en sık alt ekstremitelerde (%66,6, n=12), ardından üst ekstremitelerde (%22,2, n=4) ve ekstremite dışı bölgelerde (%11,1, n=2) yerleşmiştir. Histopatolojik evrelemeye göre hastalar %72,7'si (n=13) tümör (nodül) evresinde, %22,2'si (n=4) yama evresinde ve %5,6'sı (n=1) plak evresinde bulunmuştur. Tüm hastalar cerrahi tedavi almıştır. Tekrarlayan vakalar arasında beş hastada dokuz nüks oluşmuştur. Gözlenen komorbiditeler arasında kardiyovasküler hastalık, hipertansiyon ve diabetes mellitus yer almaktadır.
Sonuç: Ülkemizde Kaposi sarkomunun demografik ve klinik özelliklerinin daha iyi anlaşılabilmesi için çok merkezli çalışmalara ihtiyaç duyulmaktadır. Ayrıca, hastalığın zamanında tanı alınması ve hastalığın klinik yönetimi için klinisyenler arasında farkındalığın artırılması gereklidir.

Anahtar kelimeler: Kaposi sarkomu, HHV-8, histopatoloji

Abstract

Aim; Kaposi sarcoma is a rare angioproliferative disorder strongly associated with human herpesvirus-8. Data on its epidemiology and clinical features in our country are limited. This study aims to analyze cases of Kaposi sarcoma diagnosed at the Department of Pathology, Sivas Cumhuriyet University Practice and Research Hospital.
Method; A retrospective review was conducted on the medical records of patients diagnosed with Kaposi sarcoma (n=18) between January 1, 2013, and June 30, 2023. Including recurrent cases, the total number of diagnoses reached 27. Clinical, histopathological, and demographic characteristics were examined.
Results; The mean age of the patients was 69.3±13.3 years (range: 32–88). Thirteen patients (72.2%) were male, and five (27.7%) were female. None of the patients had a history of HIV infection. The lesions were predominantly located on the lower extremities (66.6%, n=12), followed by the upper extremities (22.2%, n=4) and non-extremity

regions (11.1%, n=2). Histopathological staging revealed that 72.7% (n=13) of the patients were in the tumor (nodule) stage, 22.2% (n=4) in the patch stage, and 5.6% (n=1) in the plaque stage. All patients underwent surgical treatment. Among recurrent cases, five patients accounted for nine recurrences. Comorbidities observed included cardiovascular disease, hypertension, and diabetes mellitus.
Conclusion; To improve the understanding of the demographic and clinical features of Kaposi sarcoma in our country, multicenter studies are warranted. Additionally, enhanced awareness of this disease among clinicians is essential for timely diagnosis and management.

Keywords: Kaposi sarcoma, HHV-8, histopathology

1.Introduction

Kaposi Sarcoma (KS) is a rare angioproliferative tumor caused by human herpesvirus 8 (HHV-8), first described by Moritz Kaposi in 1872 [1]. HHV-8 is a double-stranded DNA virus, with sexual transmission being the most common and significant route of infection [2]. KS predominantly affects men and is typically diagnosed after the age of 50. The lesions appear as blue, red, or purple discolorations, primarily on the distal extremities, often presenting as a single lesion during the early stages. As the disease progresses, additional lesions may develop in other areas, typically exhibiting slow growth. KS can involve multiple organ systems, including the skin, conjunctiva, oral cavity, gastrointestinal tract, and respiratory system [3].

There are four clinical variants of KS: classic, African endemic, iatrogenic, and AIDS (HIV)-associated (epidemic). Despite the clinical differences, histomorphological features are consistent across these variants and progress through three distinct stages: patch, plaque, and tumor. Diagnosis and staging rely on biopsy [4], which typically reveals vascular proliferation, inflammatory infiltrates, and the presence of HHV-8 [5].

Treatment options for KS depend on the location, size, and number of lesions, but a definitive consensus on the most effective therapeutic approach has yet to be established. Current treatments include clinical observation, surgical excision, physical destruction methods, and intralesional or topical therapies [5].

In our country, limited studies and case reports are available regarding the epidemiology of KS. This study aims to provide a comprehensive overview of the demographic characteristics of KS cases diagnosed at our center over a 10-year period, with the goal of increasing awareness about this rare disease.

The necessary ethics committee approval for this study was obtained from the Sivas Cumhuriyet University Medical Faculty Research Hospital Clinical Research Ethics Committee on July 18, 2024, with report number 2024/07-35.

2.Materials and Methods

This cross-sectional study included patients diagnosed with KS at the Pathology Department of Sivas Cumhuriyet University Practice and Research Hospital between January 1, 2013, and June 30, 2023. No sampling method was applied; all patients diagnosed with KS during this period were included in the study. Patient information was obtained from pathology reports.

The dependent variable of the study was the diagnosis of KS, while the independent variables included patients' age, gender, year of biopsy, HIV status, lesion localization, recurrence status, disease stage, treatment type, whether patients received treatment, and the presence of comorbid diseases.

Data were analyzed using SPSS-22 statistical software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as counts and percentages for categorical variables and as means with standard deviations (minimum and maximum values) for continuous variables. The Chi-square test was used for the evaluation of categorical data, with a significance level of $p<0.05$ considered statistically significant.

3.Results

Eighteen patients diagnosed with KS during the specified period were included in the study. When recurrences were accounted for, the total number of cases increased to 27. The mean age of the patients was 69.3 ± 13.3 years (range: 32–88). Among these patients, 13 (72.2%) were male, and 5 (27.7%) were female. None of the patients tested positive for HIV serology (Table 1).

Regarding lesion localization, 66.6% (n = 12) of the patients had lesions in the lower extremities, 22.2% (n = 4) in the upper extremities, and 11.1% (n = 2) in other regions**.** Microscopic examination of the lesions revealed thin, elongated vascular proliferations with prominent endothelial cells and small lumens containing erythrocytes, accompanied by extravasated erythrocytes and inflammatory cells. Immunohistochemical analysis showed dot-like positive staining in endothelial cells using the HHV-8 marker (Figure 1). Histopathologically,

72.7% (n = 13) of the patients were in the tumor stage, 22.2% (n = 4) in the patch stage, and 5.6% (n = 1) in the plaque stage (Table 1). When all 27 cases were analyzed, 20 (74.1%) were classified as tumor stage, 5 (18.5%) as patch stage, and 2 (7.4%) as plaque stage. All patients were treated surgically, with no additional treatment methods employed.

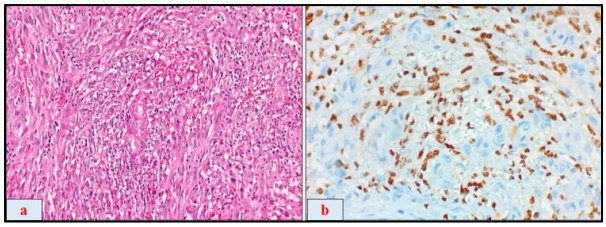

Figure 1. Skin tissue. Microscopic examination of Kaposi Sarcoma shows vascular proliferation characterized by thin lumens lined with prominent endothelial cells. Erythrocytes are observed both within and outside the lumens, accompanied by inflammatory cells within the lesion (a, hematoxylin & eosin staining, x200). In Kaposi Sarcoma, dot-like specific positive staining for HHV-8 is evident in the endothelial cells of the vascular lesions (b, immunoperoxidase, x400).

In the analysis of recurrence cases, 9 instances of recurrence were observed among 5 patients, including 1 female and 4 males. This analysis of the clinical and histopathological characteristics associated with relapses highlights key features of relapse in patients with KS. The mean relapse duration was calculated as 18.80 ± 7.60 months, and this duration was found to be statistically significant ($p = 0.02$). Regarding gender, 80% of the patients with relapse were male, and 20% were female, with relapse rates significantly higher in males ($p = 0.04$). Relapse localization analysis showed that 40% of relapses occurred in the same region, while 60% occurred in different regions, and this difference was also statistically significant ($p = 0.03$). Initial lesion localizations were typically found in the distal extremities, while relapses predominantly occurred in different regions. In one patient, the lesion initially located in the left hand relapsed in the same region. However, in other cases, the lesion in the left foot relapsed in the right foot, and the lesion in the perianal region relapsed in the right thoracic region. An analysis of histopathological stages revealed that most relapses occurred within the same stage; however, stage changes were observed in some cases. Relapse durations varied among patients. One patient with multiple relapses experienced relapses at 46, 65, 77, 90, and 96 months. In contrast, other cases showed shorter and singular relapse durations, occurring at 24, 5, 13, and 6 months, respectively.

When evaluating comorbidities, 4 out of 18 patients had no additional medical conditions. Among the remaining 14 patients, 5 had more than one comorbidity, while 9 had a single comorbid condition. The most common comorbidities were heart disease, hypertension, and diabetes.

Table 1: Demographic data of patients

Categorical features	n	%
Gender		
Female	5	27,7
Male	13	72, 2
Localization		
Upper extremity	4	22,2
Lower extremity	12	66,6
Others	2	11,1
Relapse		
Yes	5	27,7
No	13	72,3
Histopathological tumor stage		
Tumor	13	72,2
Patch	4	22,2
Plaque	1	5,6
Treatment		
Surgical	18	100,0
Medical	0	0
Comorbidity disease		
Yes	14	77,8
No	4	22,2

4.Discussion

Kaposi Sarcoma, more prevalent in Mediterranean countries, is reported to have the highest incidence in southern Italy [6]. In our country, the exact incidence of KS remains unclear due to the limited number of studies on the Turkish population [7,8]. This study aimed to present the demographic characteristics of KS patients at our center, with the goal of raising awareness of the disease among healthcare professionals.

Globally, KS incidence rates vary between 0.02 and 0.20 per 100,000. The disease is more common in men than in women [9,10], potentially due to the protective effects of luteinizing hormone in women, which has been suggested to inhibit HHV-8, the virus linked to KS [11]. Consistent with the literature, the majority of patients in our study were male.

The pathogenesis of KS is not fully understood, but HHV-8 is recognized as the primary causative agent. However, cases of KS with negative HHV-8 findings have been reported, which could result from factors such as low viral copy numbers, tissue

preparation issues, or sequence polymorphisms in the virus's binding regions [12,13]. In pathology departments, immunohistochemical methods are routinely used to confirm the presence of HHV-8. In our study, immunohistochemical analysis using the HHV-8 (clone LNA-1) monoclonal antibody revealed HHV-8 positivity in all cases.

A previous study of 2,177 KS patients reported the youngest case as 5 years old [10]. KS is known for its slow progression and is typically localized to the lower extremities [6]. Our findings align with these observations, as more than half of our patients presented with lesions in the lower extremities.

Risk factors for KS may include exposure to volcanic waste, diabetes, and corticosteroid use [1,15]. In our study, 4 out of 18 patients had no comorbidities, while the remaining 14 had at least one comorbid condition. The most common comorbidities were heart disease, hypertension, and diabetes.

KS lesions generally present as red-purple macules, plaques, or nodules. Mucosal, lymph node, and internal organ involvement occurs in 10–15% of cases [12]. Some studies have also reported an association between KS and other primary malignancies, particularly lymphoproliferative disorders [9]. However, none of our patients exhibited metastases or additional malignancies.

The size, location, and number of KS lesions are crucial factors in determining the treatment approach. Treatment options include surgical excision, intralesional drug administration, radiotherapy, and chemotherapy [6]. Recurrence is reported to be more common in patients treated with surgical excision, and studies suggest that achieving tumor-free surgical margins does not guarantee prevention of recurrence [16]. Moreover, there is no standardized approach to defining tumor-free margins in KS. In our study, recurrences were more frequent in men, and this gender difference was statistically significant. Most recurrence cases were in the tumor (nodule) stage. Among the five patients with recurrences, two experienced recurrences at the same site, while three had recurrences at different locations.

Overall, our findings are consistent with the existing literature regarding the demographic characteristics, clinical presentation, and histopathological features of KS. We believe that multicenter studies focusing on the demographic, clinical, and histopathological aspects of KS are essential to increasing awareness among healthcare providers, ultimately leading to improved diagnosis and management of the disease.

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