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Research Article

Clinical Outcomes of Kaposi's Sarcoma Treated with Systemic Chemotherapy

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Abstract

Objectives: We aimed to examine the clinical and epidemiological features of the patients diagnosed with Kaposi's sarcoma, who were treated with systemic chemotherapy.

Methods: Patients with age of 18 years or older and histopathologically confirmed Kaposi sarcoma, were included in the study. Demographic data, tumor histology and characteristics, Kaposi's sarcoma subtype and treatment modalities were retrospectively evaluated.

Results: A total of 20 patients were included in the study. Fourteen patients (70%) were found to be related with HHV-8. Five patients (25%) were HIV-positive. The lesions were located in the lower extremities in 19 patients (95%), upper extremities in 11 patients (55%), head and neck in 11 patients (55%) and trunk in 6 patients (30%). All 20 patients unresponsive to the local treatments including two patients with visceral metastases received chemotherapy. Complete remission was achieved in seven patients (35%), partial response was achieved in seven patients (35%) and stable response was achieved in four patients (20%) with the systemic chemotherapy.

Conclusion: The success rate is high with the practice of local treatments. The aggressive state of the disease which is ineligible for local treatment can be controlled by systemic chemotherapy.

Keywords: Chemotherapy, Kaposi's sarcoma, systemic treatment

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The Kaposi's sarcoma (KS) which was defined for the first time in 1872 by Moritz Kaposi is a disease characterized by vascular proliferation associated with Human herpes virus-8.[1] Although HHV8 is necessary in the pathogenesis of Kaposi's sarcoma, it is not the sole element for its development. Genetic, immunologic and environmental factors are also mandatory. Clinically, one or more, asymptomatic red, purple or brown patches, plaques or nodular skin lesions are generally observed in the lower extremities in Kaposi's sarcoma. These lesions are characterized by the presence of angiogenesis and spindle cell-shaped cells histologically.[2] Kaposi's sarcoma shows considerable clinicopathologic variation according to the lesions' location (lymph node, viscera or cutaneous tissue), clinical phase (patch, plaque, nodule) and epidemiological features. Kaposi sarcoma includes four different subtypes epidemiologically. Classic KS, endemic KS, human immune deficiency virus (HIV) related KS (epidemic KS) and iatrogenic KS (related with immunosuppression).[3] Classic KS is the type mainly observed in Mediterranean countries such as Italy, Greece and Turkey and it has predilection for elderly men. The endemic type is observed in equatorial regions in Africa and presents with aggressive course

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in children. The iatrogenic subtype, typically, occurs as a consequence of exogenic immunosuppression such as solid organ transplantation and can regress with the modification of the immunosuppression. On the other hand, epidemic KS is related with HIV infection and it is the subtype, which has the potential to be controlled by antiretroviral drugs.[4]

Today, there is no single standard treatment approach for the treatment of KS. The treatment decision making should be performed according to the speed of the tumor growth, extensiveness of the disease and the patient's symptoms as well as relation with HIV infection. Treatment options include multidisciplinary methods such as local treatments, electrochemoterapy, systemic chemotherapy, radiotherapy and molecularly targeted therapy.

Systemic chemotherapy is one of the most important elements of the treatment of aggressive Kaposi's sarcoma.[5] In this study, we aimed to examine the clinical and epidemiological features of the patients who were treated with systemic chemotherapy.

Methods

Twenty patients who were treated in the departments of medical oncology of University of Health Sciences Ümraniye Training and Research Hospital and Dr. Lütfi Kırdar Kartal Training and Research Hospital, between 2010-2020 were included in the study. Inclusion criteria were as follows: histopathologically confirmed Kaposi's sarcoma, age of 18 years or older and absence of secondary primary cancer. Demographic data, tumor histology and characteristics, Kaposi's sarcoma subtype and treatment modalities were evaluated. All data were collected from the patient files retrospectively. The clinicodemographic features of patients were evaluated by use of descriptive analysis.

Results

A total of 20 patients were included in the study. Male to female ratio was 1.9 (13/7). Median age was identified as 64.1 (range 29.8-90). Fourteen patients (70%) were found to be related with HHV-8. Five patients (25%) were HIV-positive. The lesions were located in the lower extremities in 19 patients (95%), upper extremities in 11 patients (55%), head and neck in 11 patients (55%) and trunk in 6 patients (30%). Four patients (20%) were in the patch phase, 11 patients (55%) were in the plaque phase and 5 patients (25%) were in the nodule phase of the disease. Regarding comorbidities: 8 patients (40%) had hypertension, 6 patients (30%) had diabetes, 2 patients (10%) had cardiac insufficiency. Family history of KS was not identified in any of the patients. All 20 patients unresponsive to the local treatments including two patients with visceral metastases received chemotherapy. The involved organs were lung and stomach. Surgical treatment was performed for one patient (5%), interferon treatment was performed for three patients (15%) and radiotherapy was performed for nine patients (45%) in addition to chemotherapy. Chemotherapy was the first-line treatment in 7 patients whereas it was used in second-line setting in 13 patients. Complete remission was achieved in seven patients (35%), partial response was achieved in seven patients (35%) and stable response was achieved in four patients (20%) with the systemic chemotherapy. Clinicodemographic characteristics of patients were presented in Table 1. Five patients died during the follow-up.

Discussion

Frequency of Classic Kaposi's sarcoma varies according to the ethnical and geographical features. Male to female ratio varies from 10:1 to 15:1 in the literature.[6] However, recent studies reported that this ratio was lower. The ratio was determined as 3:1 in the study conducted by Lospalluti et al.[7] in Italy. Su et al. and Oysul et al. found the ratio as 2:1 in their research in Turkey.[8,9] Male to female ratio was identified as 1.9 in our study.

In the literature, Classic Kaposi's sarcoma has been observed generally in old patients and median age varies from 50 to 80 years old.[6] Classic Kaposi's sarcoma has been mostly observed in men in their sixth and seventh decade of life in the studies conducted in Turkey as well.[8–10] Median age was identified as 64.1 (range 29.8-90) in our study compliant with the literature.

All forms of Kaposi's sarcoma are known to be related with HHV-8. In the study conducted by Chang et al. HHV-8 positivity was reported to be over 90% in all Kaposi subtypes.[11] Frequency of HHV-8 positive cases varies according to age and geographical features. While low rates are being observed in the North European countries,[12] HHV-8 presence, was identified as 35% in the study performed by Whitby et al.[13] in Italy. Demirel et al. found HHV-8 positivity in 89.2% of patients in their work.[14] Similarly, in the present study, we detected the rate of HHV-8 presence as 70%.

The association of Kaposi's sarcoma with HIV is well-known. The rate of HIV positivity varies across the studies. There were five HIV related Kaposi's sarcoma patients in our study. These cases were mostly young men which is consistent with literature, and they were characterized by multiple lesions in the body including oral mucosa.[15,16] In addition to antiretroviral treatment, four patients received liposomal doxorubicin, and one patient was given interferon. Complete remission was achieved in three patients, partial response was noted in one patient and progressive disease was observed in one patient.

Table 1. Characteristics and outcomes of the patients with Kaposi sarcoma

	n (%)
M:W sex ratio	1.9
Median (years)	64.1 (29.8-90.0)
Localization on the skin	
Upper limbs	11 (55.0)
Lower limbs	19 (95.0)
Trunk	6 (30.0)
Head	11 (55.0)
Genitalia	0
Lymphedema	0
Management	
Surgery	1 (5.0)
Chemotherapy	20 (100.0)
IFN	3 (15.0)
Radiotherapy	9 (45.0)
Visceral involvement, prevalence, no.	2 (10.0)
Type of skin/mucosal lesions, prevalence, no.	
Nodules	5 (25.0)
Plaques	11 (55.0)
Macules and patches	4 (20.0)
HIV positivity	
Yes	5 (25.0)
No	15 (75.0)
HHV8 positivity	
Yes	14 (70.0)
No	6 (30.0)
Comorbidities	
Hypertension	8 (40.0)
Diabetes mellitus	6 (30.0)
Heart failure/pretibial edema	2 (10.0)
Malignancy	0
Outcomes, prevalence	
Complete remission	7 (35.0)
Partial response	7 (35.0)
Stable disease	4 (20.0)
Progressive disease	1 (5.0)
Follow-up not available	1 (5.0)
Chemotherapy lines	
1	12 (60.0)
2	5 (25.0)
≥3	3 (15.0)

IFN: interferon; HHV8: Human herpes virus 8; HIV: Human immunodeficiency virus.

The characteristics of Kaposi's sarcoma lesions are development of patch in the early phase, plaque, in the intermediate phase and nodule, in the late phase. The mostly encountered lesion is the nodule phase in a wide variety of studies. Demirel et al. and Errihani et al. in their studies, reported that nodule phase was the most frequently observed phase in the disease course.[14,17] In contrary to this, Mohana and colleagues, revealed that the lesions were mostly observed in the plaque phase.[18] In our study, the lesions were mostly presented with the plaque phase as well. The lesions of the Kaposi's sarcoma are known to be localized most frequently in the lower extremity.[10,14,19] In parallel to this, lower extremity involvement (95%) was predominant in our study.

Diabetes mellitus is observed more often in classic Kaposi's sarcoma patients compared with the general population.[20] Anderson et al. stated that corticosteroid use and diabetes were the independent risk factors in the KS development.[21] The incidence of Diabetes mellitus was reported to be 30% in our study. This finding is in parallel with the literature.

Systemic chemotherapy is recommended particularly for the patients who have extensive disease; rapidly progressing lesions with visceral involvement and are not eligible for local treatments. Systemic treatment of Classic Kaposi's sarcoma varies among institutions. Dogan et al. used Vincristine-Bleomycin-Doxorubicin combination regimen in the study they performed.[10] There are several studies with single agent chemotherapeutics (Vincristine, Vinblastine, Etoposide, Paclitaxel etc.). The response rate with these agents varies from 30% to 70%. Krown et al. and Henge et al. reported that liposomal doxorubicin was effective and safe in concurrent use with highly active anti-retroviral therapy (HAART) especially in HIV related Kaposi's sarcoma in the two separate studies they conducted.[22,23] In the present study, Liposomal Doxorubicin was given to four patients who had HIV-related Kaposi's sarcoma and the clinical benefit was found to be 100%.

Paclitaxel monotherapy was found to be effective both in the first and second lines in the treatment of non-HIV related Kaposi's sarcoma. Athanasia et al. identified the response rate with paclitaxel, in the setting of first line, as 94.6% (complete response+partial response).[24] Brambilla et al. ended up with complete response and partial response in 14 out of 17 patients involved in their study.[25] Four non-HIV related patients were given paclitaxel as the first line treatment in our study and the overall response rate was 100% (complete response+partial response). Five patients died in the follow-up. Since the patients were diagnosed in older age and had co-morbidity, their deaths were not found to be associated with the Kaposi's sarcoma.

The most significant limitations of the study were the limited number of patients and the retrospective design of the study. Another limitation includes, the lack of standardization of the systemic treatments which precludes comparison among them.

Conclusion

Classic Kaposi's sarcoma has a benign course, and it is generally limited to the skin with uncommon visceral involvement. It is mostly observed in elderly men. The success rate is high with the practice of local treatments. In aggressive state in which local treatment is not applicable, the disease can be controlled by systemic chemotherapy.

Disclosures

Ethics Committee Approval: The study protocol was approved by University of Health Sciences, Umraniye Training and Research Hospital Clinical Research Ethics Committee with 11/06/2020 and 238 number and Helsinki Declaration decision.

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