Original Article on Palliative Radiotherapy

Radiation therapy for the treatment of skin Kaposi sarcoma

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Background: Kaposi sarcoma (KS) lesions are purplish, reddish blue or dark brown/black macules, plaques or nodules which involve the skin and occasionally internal organs. Most patients with KS have a long indolent chronic course.

Methods: A retrospective review was undertaken for all KS skin patients treated with radiotherapy at a tertiary cancer centre from Jan. 2, 1999 to Dec. 31, 2014 (inclusive).

Results: A total of 47 patients with KS (43 classical, 0 African, 1 iatrogenic, 3 AIDS related) were seen in the multidisciplinary clinic. Out of this group, 17 patients (5 females and 12 males, 14 classical, 0 African, 0 iatrogenic, 3 AIDS related) with 97 KS skin sites were treated with local external beam radiotherapy. An additional 18 skin sites were treated with repeat radiotherapy. The radiotherapy dose ranged from 6 Gy in 1 fraction to 30 Gy in 10 fractions with the most common dose fractionation scheme being 8 Gy in 1 fraction or 20 Gy in 5 daily fractions. For the previously untreated KS sites, 87% responded to radiation [30% complete response (CR) and 57% partial response (PR)]. Thirteen percent of KS sites treated with radiation progressed. For the skin sites which were treated with repeat radiotherapy, 0% showed CRs, 50% PRs and 50% had continued progression.

Conclusions: The majority of KS skin lesions (87%) responded to radiotherapy. Patients experience minimal side effects from the palliative radiation regimens used. KS skin lesions which progress despite radiation are unlikely to show CR with repeat radiotherapy. In our experience 50% of skin KS will have partial regression with repeat radiotherapy and 50% will have continued progression.

Keywords: Kaposi sarcoma (KS); skin; radiotherapy

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Introduction

Kaposi sarcoma (KS) is a non-curable malignancy caused by infection with human herpes virus 8 (HHV8) which can present as skin lesion with or without internal organ involvement (1,2).

KS lesions are purplish, reddish blue or dark brown/black macules, plaques or nodules which involve the skin and mucous membranes. These lesions may bleed, ulcerate and may be associated with lymphedema, pain and secondary infection (3). Most patients with KS have a long indolent chronic course.

There are four subtypes of KS (4):

(I) Classical KS affecting those of Mediterranean descent or Eastern European descent;
(II) African endemic KS;
(III) Iatrogenic immunosuppressed KS;
(IV) AIDS (epidemic) related KS.

Localized cutaneous KS may be treated with radiotherapy, cryotherapy, intralesional injections of vinblastine or topical

immunotherapy. Extensive skin or internal involvement with KS may be treated with chemotherapy or immunotherapy. Highly active antiretroviral therapy (HAART) is considered first-line therapy for AIDS related KS. For iatrogenic KS due to immunosuppression, reduction or discontinuation of immunosuppressive therapy is recommended (5).

Radiation therapy is used to help regress KS skin lesions causing local symptoms such as bleeding or pain (6).

Methods

A retrospective review was undertaken for all KS patients treated with radiotherapy at a tertiary cancer centre from Jan. 2, 1999 to Dec. 31, 2014 (inclusive). This study was approved by the local hospital Research Ethics Board.

Demographic information (date of birth, sex, co-morbidities) were retrieved, radiotherapy treatment details, symptom and side-effects outcomes were recorded.

Complete response (CR) was defined as complete visual disappearance. Partial response (PR) was defined as 50% or more regression and progressive disease defined as growth of the lesion.

Results

A total of 47 patients with KS (43 classical, 0 African, 1 iatrogenic, 3 AIDS related) were seen in the multidisciplinary clinic. Nineteen patients with asymptomatic cutaneous skin KS were observed. Four patients were treated with surgery. Three patients were treated with cryotherapy and two patients were treated with electrodessication and curettage. One patient was treated with Aldara cream. One patient had iatrogenic KS due to immunosuppressive drugs. With the withdrawal of the immunosuppressive, the KS lesions regressed.

This left a total of 17 patients (5 females and 12 males) with 97 KS skin sites treated with local external beam radiotherapy (*Table 1*). There were an additional 18 skin sites which were treated with repeat radiotherapy (*Table 2*). The subtypes of KS treated with radiotherapy were 14 classical, 0 African, 0 iatrogenic, 3 AIDS related. Ages at the time of initial radiotherapy ranged from 44–93 years of age. The radiotherapy dose ranged from 6 Gy in 1 fraction to 30 Gy in 10 fractions, with the most common dose fractionation scheme being 8 Gy in 1 fraction or 20 Gy in 5 daily fractions. The number of KS sites treated with radiotherapy per patient ranged from 1–22 sites (including repeat radiotherapy sites). The median follow-up time was 26.1 months (range, 0.3 months to 28.5 years).

For 97 previously untreated KS sites, 87% responded to radiation (30% CR and 57% PR). Thirteen percent of KS sites treated with radiation progressed.

Of the 13% (n=13) KS skin sites which progressed despite radiation, all were treated with repeat radiotherapy except one was treated with liquid nitrogen. There were a total of 18 repeat radiotherapy fields (as some of the originally treated fields were broken up into smaller fields). The CR, PR and progression rates for repeat radiotherapy KS sites were 0%, 50% and 50% respectively. One patient with two skin sites treated with repeat radiation was lost to follow-up.

No fatal toxicities occurred. The most common side effects were dry desquamation, hyperpigmentation and lymphedema.

Discussion

KS was first described in 1872 by Moritz Kaposi. Microscopic characteristics include disorganized endothelial cell proliferation and blood-filled vascular clefts with areas of organized micro-neovascularizations. An inflammatory infiltrate is also commonly seen (1). Since the description of KS (a classical or Mediterranean type) by Moritz Kaposi, two additional forms were identified (African endemic KS and post-transplantation or iatrogenic KS). With the emergence of the AIDS epidemic in the early 1980s, the 4th type AIDS (epidemic) emerged.

In this present series, the most common KS type was classical. While epidemiologic studies indicate that the incidence of classic KS has remained stable over the years, the incidence of AIDS related KS began to fall in the late 1980s with the use of HIV directed treatments. Subsequently with the use of HAART, which partially restores the immune system, the incidence of AIDS related KS has dropped dramatically (7). Our radiation series did not include any patient with iatrogenic/post-transplantation KS. The incidence of KS after transplantation is low at 8.8 per 100,000 person years among transplant recipients in North America (8).

A systematic review published in 2012 regarding the management for classic KS was undertaken by Régnier-Rosencher *et al.* (6). There were only 26 articles with at least five patients included in the systematic review. Of these included studies, only four were radiotherapy publications (9-12). The number of patients included in these radiotherapy series ranged from 27 patients to

Table 1 Radiotherapy sites (no previous radiation)

Patient number	KS type	Age at time of initial radiotherapy (years)	Sex	Irradiated sites of disease	Clinical response
1	Classical	93	M	(I) Left foot; (II) right foot	2 skin sites: CR
2	Classical	78	F	(I) Bilateral lower legs; (II) right medial thigh; (III) right medial calf; (IV) right thigh	3 skin sites: PR; 1 skin site: progression
3	AIDS (epidemic)	44	F	Right lower eyelid	1 skin site: CR
4	Classical	83	M	11 different skin sites	11 skin sites: CR
5	Classical	63	M	Right foot	1 skin site: CR
6	Classical	88	M	17 different skin sites	9 skin sites: PR; 8 skin sites: progression
7	AIDS (epidemic)	49	M	(I) Right leg; (II) left lower leg; (III) left posterior calf; (IV) left second toe; (V) upper left leg; (VI) left hand	6 skin sites: PR
8	Classical	93	M	13 different skin sites	11 skin sites: PR; 2 skin sites: progression
9	Classical	87	M	(I) Right foot; (II) left leg	1 skin site: PR; 1 skin site (right foot) progressed with bleeding treated with liquid nitrogen and curettage
10	Classical	64	M	10 different skin sites	10 skin sites: PR
11	Classical	77	M	14 different skin sites	13 skin sites: PR; 1 skin site: progression
12	AIDS (epidemic)	44	M	Right earlobe	1 skin site: CR
13	Classical	89	M	(I) Right foot; (II) left foot; (III) left hand/arm; (IV) left elbow; (V) left lower leg; (VI) right lower leg	CR
14	Classical	73	F	Left ankle	CR
15	Classical	88	F	(I) Left foot; (II) right foot	CR
16	Classical	92	F	(I) Superior medial right foot; (II) superior mid right foot; (III) centre right foot; (IV) right foot posterior heel	CR
17	Classical	82	M	(I) Left foot; (II) right foot	PR

KS, Kaposi sarcoma; M, male; F, female; CR, complete response; PR, partial response.

209 patients. All the series were retrospective except one (9).

The Yildiz *et al.* publication (9) was a prospective non-randomized study of 8 Gy given prior to 1998 and then 6 Gy given in 1998 to 2004. The authors reported that CR at 12 months was 93% with 8 Gy and 60% with 6 Gy, P<0.0001. It was concluded that a single 8 Gy is more effective for CR as compared to a single 6 Gy. From the four included radiotherapy studies (9-12), the CR plus PR rates ranged from 85–99.5%.

There is a lack of controlled prospective studies which examine the optimal radiation dose fractionation schedule for response and symptom control. Reported dose fractionation schedules range from 6 Gy in 1 fraction to radical dose fractionation schemes to a total of 45 Gy (9). A randomized trial was reported for AIDS associated KS. Sixty patients with 65 sites of AIDS related KS skin sites

Table 2 Repeat radiation sites

Patient number	KS type	Repeat radiotherapy sites	Clinical response
2	Classical	(I) Left lateral calf; (II) bilateral lower legs	2 skin sites: further progression treated with chemotherapy etoposide and intralesional injections vinblastine
6	Classical	(I) Right toes; (II) right medial calf; (III) right lateral heel; (IV) right upper sole; (V) right foot	5 skin sites: PR
8	Classical	(I) Right foot; (II) left foot; (III) right foot; (IV) left foot; (V) right hand; (VI) right posterior thigh; (VII) right posterior thigh; (VIII) right posterior thigh	#1, #2, #6, #7, #8 skin sites: further progressed; #3, #4, #5 skin sites: PR
11	Classical	(I) Left forearm; (II) left hand; (III) left arm	#1 skin site: further progressed; #2, #3 skin sites lost to follow-up

KS, Kaposi sarcoma; PR, partial response.

were randomized to 24 Gy in 12 fractions versus 20 Gy in 5 fractions. The authors concluded that response and local control rates were not statistically different between the two arms. Acute and late skin toxicity were also not statistically different between the two arms (13).

Our series of patients had similar high response rates (87% CR and PR) after radiation as compared to the published literature. In addition to the existing literature, we were able to report on a subset of patients treated with repeat radiotherapy for KS skin lesions which failed initial radiotherapy. In this subgroup, none of the patient had CR, half showed PR and half showed continued progression.

The limitations of this study include the retrospective nature of the analysis, the lack of validated quality of life and symptom control outcomes. In addition various radiotherapy dose fractionation schedules were used.

Conclusions

In this cohort of patients, the majority of KS skin lesions (87%) responded to radiotherapy. Patients experience minimal side effects from the palliative radiation regimens used. KS skin lesions which progress despite radiation are unlikely to show CR with repeat radiotherapy. In our experience 50% of repeat radiotherapy KS skin lesions will have partial regression and 50% will have continued progression.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by institutional ethics board of Sunnybrook Health Sciences Centre (REB project identification number 464-2014) and written informed consent was obtained from all patients.

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