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Treatment of AIDS-related Kaposi's Sarcoma With Low-dose Radiotherapy – Follow-up on 2,305 Tumours

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Abstract. *Background/Aim: We aimed to report our experience obtained by treating AIDS-related Kaposi's sarcoma (KS) with radiotherapy before the era of antiretroviral therapy. Patients and Methods: This investigation was performed as a quality control of KS patients treated with low-dose radiotherapy at our department. KS patients referred to our section from 1983 up until 1990, were treated three times with radiotherapy (29-50 kV, 2-4 Gy), once every second week. Results: Initially, 74 skin KSs were treated three times with 2 Gy, of which 70% were treated successfully. Hereafter, other 2,066 KSs on the skin were treated three times with 4 Gy with a very high success rate of 93%. Additional 165 mucous KSs were treated three times with 4 Gy, of which 91% were treated successfully. Conclusion: Low-dose radiotherapy is effective for the treatment of many AIDS-related KS patients.*

AIDS-related Kaposi's sarcoma (KS) was a common cancer type in HIV-infected persons before the introduction of combined potent antiretroviral therapy (ART) (1). After the extensive use of ART, there has been a substantial reduction in the number of AIDS-related KS and the tumour is now mostly seen in patients who are not taking ART or have just initiated ART treatment within the last half a year (2, 3). AIDS-related KS is sensitive to radiotherapy like the other forms of KS (4, 5). The historical use of radiotherapy for KS has been well documented (6). The purpose of the present article was to report our experience obtained by treating a total of 2,305 AIDS-related KS with radiotherapy before the era of ART.

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Key Words: Acquired immune deficiency syndrome, Kaposi's sarcoma, radiotherapy.

Patients and Methods

This investigation was performed as a quality control and included KS patients treated with low-dose radiotherapy at our department from 1983 up until 1990. The KS patients were treated three times with radiotherapy, once every second week. The regime could be repeated in case of unsatisfactory treatment response. All treatments were performed using a Siemens Dermopan X-ray unit (Erlangen, Germany) with fixed settings at 12 kV, 29 kV, 43 kV, and 50 kV.

The dose was originally 2 Gy per treatment and later 4 Gy per treatment. The clinically estimated thickness of each tumour determined the choice of kV setting according to half-value depth. Twenty-nine kV were used for tumours with a thickness of up to 2 mm, 43 kV for tumours 2-6 mm, and 50 kV for tumours thicker than 6 mm. The treatment area included not only the visible KS but also the surrounding, palpable tumour, and a 10 mm rim of normal skin.

Treatment was considered successful if complete clinical disappearance of the tumour was obtained (Figure 1). Alternatively, patients experienced partial response and/or recurrence (Figure 2).

The patients were all male, suffering from AIDS, and with an average age of 41 years (range=26-63 years). The observation time was limited by the life span of the patients. All patients died.

Statistics. The Pearson Chi-Square test was used to test the difference in treatment response after initial treatment of skin KS with 2 Gy or 4 Gy. We assumed homogeneity in treatment response and included each KS independently.

Results

Skin KS. Patients referred to our clinic with KS on the skin were treated with low-dose radiotherapy and afterwards, observed for 62 weeks in average. Nine patients had a total of 74 skin KSs treated with the 2 Gy regimen (Table I). Fifty-two tumours (70%) were successfully treated. Recurrences were found in 6 patients within an average of 17 weeks (range=12-48 weeks) after treatment. After retreatment with the 4 Gy regimen, no recurrences were observed for 159 weeks (range=23-190 weeks).

A total of 2,066 KS on the skin were treated with the 4 Gy regimen and the treatment had a very high success rate

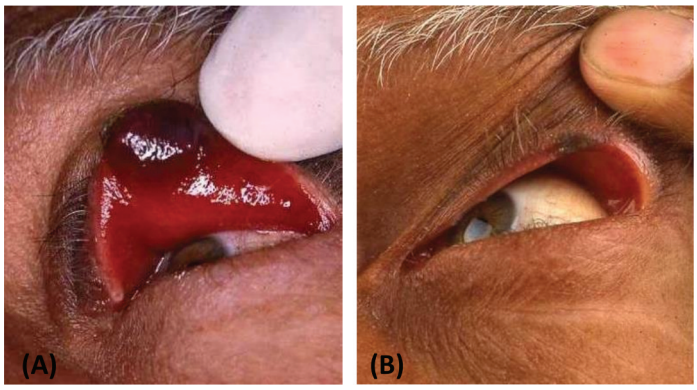

Figure 1. *Kaposi's sarcoma (KS) successfully treated with radiotherapy. (A) KS affecting the upper eyelid. (B) After 3 treatments with 40 kV 4 Gy the KS is regressed.*

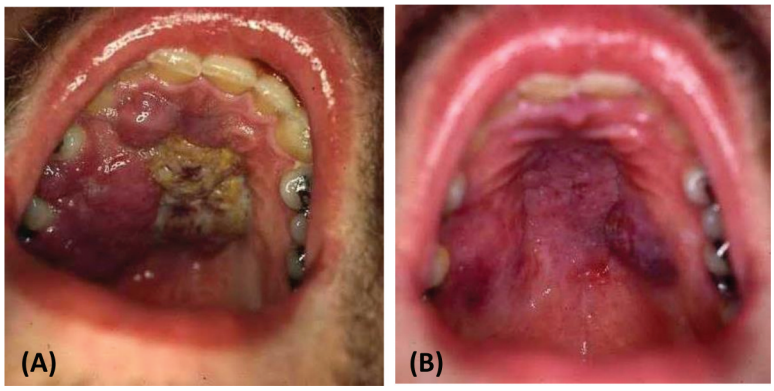

Figure 2. *Partial response after radiotherapy of Kaposi's sarcoma (KS). (A) KS of the palate. (B) After 3 treatments with 50 kV 4 Gy the KS is nearly regressed. Illustrating the difficulty associated with the uniformity of the X-ray field when treating dome-shaped fields such as the oral cave.*

Table I. *Treatment results after the first radiotherapy series of AIDS-related Kaposi's sarcoma depending on tumour site and X-ray dose. A radiotherapy series consisted of 3 treatments given 2 weeks apart.*

Regimen	Patients, n	KS, n	Complete response, n (%)	Partial response or recurrence, n (%)
2 Gy × 3. Skin KS	9	74	52 (70%)	22 (30%)
4 Gy × 3. Skin KS	53	2066	1928 (93%)	138 (7%)
4 Gy × 3. Mucous KS	32	165	150 (91%)	15 (9%)

KS: Kaposi's sarcoma.

of 93% (Table I). Seven % of tumours had partial response or recurrences. Time to recurrence was 32 weeks in average (range=9-76 weeks). The average observation time after retreatment was 66 weeks (range=7-190 weeks) in 34 patients, and a second recurrence appeared after 30 weeks (range=8-52 weeks) in 11 patients. In 10 patients, 29 KSs recurred more than twice. Moreover, the 4 Gy regimen was significantly superior to the 2 Gy regimen as initial treatment ($p<0.0001$). Post-treatment hyperpigmentation was pronounced in the KS area, but only weak erythema was found in cases with overlapping treatment fields.

Mucous KS. Patients (n=32) with KS on mucous membranes were observed for a mean of 57 weeks after treatment.

The 4 Gy treatment turned out to be just as effective on KS in mucous membranes as on the skin (Table I). In total, 165 mucous KS were treated, of which 150 were treated successfully. Eight patients had 15 KSs, which were not treated satisfactorily. Recurrences occurred after an average of 21 weeks (range=9-48 weeks). Four KSs were retreated and observed for an average of 58 weeks (range=6-98 weeks) without recurrence. In 3 KSs a second recurrence was seen after 13 weeks. No objective side effects were observed except in one case where ulceration occurred.

Discussion

The AIDS patients referred to our clinic with KS before the introduction of ART were offered radiotherapy following the guidelines for classical, non-AIDS-related KS. This modality normally uses 1-2 Gy doses repeated weekly (7). Most patients had rather thick tumours, especially at the beginning of the treatment period. Later, when the treatment modality became more widely known, patients with smaller tumours were referred. The advantages of using higher single doses and longer time intervals between treatments were soon clear, and fractionated single doses of 4 Gy were then chosen as standard. As time was an important factor in tumour regression, the interval of 2 weeks between the single fractions proved optimal. After the introduction of ART, the incidence of AIDS-related KS has decreased to a very small number (1), and today, it would take a long time to collect similar data on the number of AIDS-related KSs presented here.

We found our choice of fractionated irradiation of KS with a total dose of 12 Gy to be highly effective. Similar success with low-dose radiotherapy (8, 9) was reported in other studies. Treatment with up to double or more Gy compared to our dose (5, 10) produced good results as well.

When performing radiotherapy of KS, it is very important to treat both the visible and the palpable tumour as well as a margin of approximately 10 mm. Satellite elements may occur around the treated area if only the visible tumour is treated. When treating areas of the skin with hair growth, the patient must be informed that total hair loss may occur as a side effect of the treatment.

The recommended doses may be used on mucous membranes of the mouth and eyes without risk of ulceration. In cases of overlapping radiation fields, skin irritation may occur, but the treatment led to ulceration in only one case. Patients suffering from candida infection plaques may experience a temporary improvement. The radiotherapy treatment often leads to months of altered skin pigmentation. The KS tumours of the skin will regress to the level of the normal skin and the blueish colour changes to dark pigmentation or depigmentation.

In conclusion, the treatment and follow-up on many AIDS-related KSs confirm that low-dose radiotherapy is a highly effective and safe treatment strategy.

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

Study concepts and design: Both Authors; Data acquisition: HW; Data analysis and interpretation: HW; Manuscript preparation: Both Authors; Manuscript editing and approval of the final article: Both Authors.

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