

Kaposi sarcoma in HIV Patients: Case study and literature review

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World Journal of Advanced Research and Reviews, 2024, 22(02), 326–331

Publication history: Received on 04 March 2024; revised on 24 April 2024; accepted on 26 April 2024

Article DOI: <https://doi.org/10.30574/wjarr.2024.22.2.1142>

Abstract

Introduction: Kaposi sarcoma (KS), a malignancy originating from endothelial cells and linked to human herpesvirus 8 (HHV-8), disproportionately affects individuals with human immunodeficiency virus (HIV). Despite decreased incidence in high-income countries due to antiretroviral therapy, KS remains a significant concern in sub-Saharan Africa. This article presents a case study of an HIV-positive patient treated exclusively with radiation therapy and provides a comprehensive literature review on KS management.

Case Presentation: A 46-year-old HIV-positive patient, under well-controlled infection, exhibited nodular skin lesions, hyperpigmentation, and lymphedema primarily on the lower left limb. Histological analysis confirmed the diagnosis of KS. The patient underwent radiation therapy (36 Gy in 12 sessions) with subsequent topical imiquimod. Nine months post-treatment, no nodular lesions were observed, indicating a positive response.

Conclusion: In the antiretroviral era, radiation therapy emerges as a crucial loco-regional treatment in the multimodal management of epidemic KS. With a focus on controlling disease within irradiated areas, excellent response rates and acceptable toxicity levels highlight the efficacy of this approach.

Keywords: Kaposi Sarcoma; Human Herpesvirus 8 (HHV-8); HIV; Radiation Therapy; Antiretroviral Therapy

1. Introduction

Kaposi sarcoma is a malignant tumour of endothelial cells caused by human herpesvirus type 8. It may affect the skin, lymph nodes and/or viscera, especially in patients infected with the human immunodeficiency virus. Indeed, Human Immunodeficiency Virus-related immunodeficiency is a significant risk factor for co-infection with Kaposi Sarcoma Herpes Virus, and Kaposi sarcoma remains one of the most common cancers in people living with Human Immunodeficiency Virus (1). It is encouraging to note that, despite persistent challenges, highly active antiretroviral therapies have contributed to a substantial decrease in the incidence and mortality of Kaposi sarcoma in high-income countries. However, the situation in sub-Saharan Africa remains challenging due to the high prevalence of Human Immunodeficiency Virus. In 2018, there were an estimated 19,902 Kaposi sarcoma-related deaths worldwide, with Africa accounting for around 90% of these deaths (2). This epidemiological evolution has introduced new challenges in the management of Kaposi sarcoma, regarding the use of radiation therapy in combination with other therapeutic modalities. (3).

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The established radiosensitivity of Kaposi sarcoma since the beginning of the 20th century has enabled radiotherapy to be significantly integrated into therapeutic management (4). Radiotherapy has therefore become an integral part of the therapeutic management of Kaposi Sarcoma and can be exclusive in the case of solitary lesions, or palliative in disseminated forms. Radiotherapy is effective in treating cutaneous and mucosal lesions (5). This efficacy was demonstrated in two randomised trials evaluating different irradiation regimens in patients with Human Immunodeficiency Virus-related Kaposi Sarcoma (6,7). The results of these trials have provided crucial information to guide practitioners towards treatment options that are effective while minimising adverse effects, particularly in this complex population.

Despite the progress made in management, the local and sub-regional literature on this epidemic form of Kaposi Sarcoma remains limited. The case of a patient treated with exclusive radiotherapy is discussed and analysed in the light of contemporary literature.

2. Case presentation

The patient, aged 46, had been HIV positive for 10 years with a well-controlled infection. She presented with several firm, nodular, painless skin lesions associated with hyperpigmentation of the overlying skin and lymphoedema. These lesions affect the lower two-thirds of the left leg and foot (dorsal side and sole), including two plantar lesions measuring 3 cm each (Figure 1).



Figure 1 Nodular lesions of Kaposi's Sarcoma



Figure 2 Centring foot forward with bolus and heated sock.

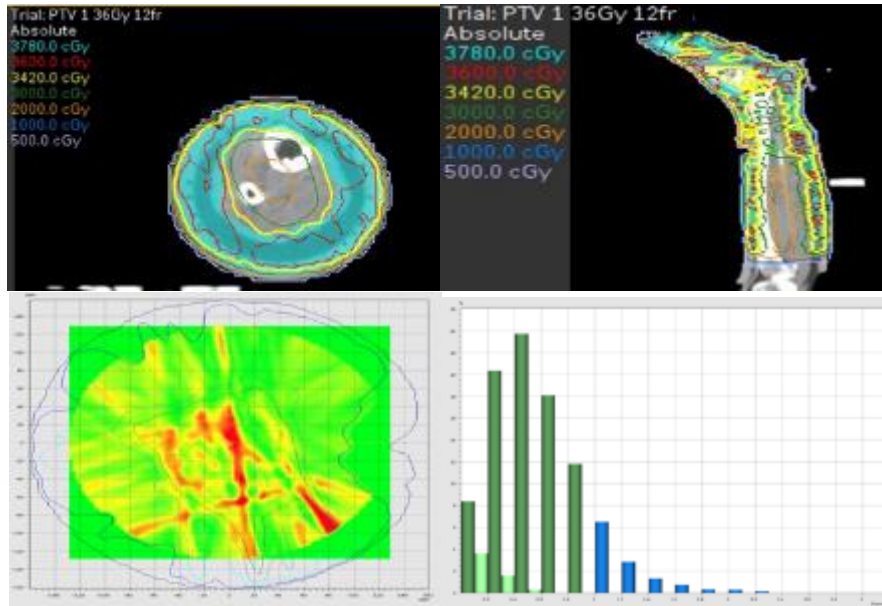


Figure 3 A - Dose distribution (transverse and sagittal sections) B - Gamma-index distribution and histogram



Figure 4 Post-irradiation clinical outcome

A lymphoscintigraphy performed on 08 April 2022 revealed scanographic features suggesting primary lymphoedema affecting the left lower limb, attributable to hypoplasia of the lymphatic channels. A biopsy of the skin lesion was carried out on 13 April 2022 without incident.

Histological analysis of the excised skin lesions confirmed the presence of Kaposi sarcoma. Her physician in Nairobi prescribed Mupirocin-based antibiotic therapy for topical application to wounds on the left lower limb. The patient was called for a follow-up consultation two weeks later

She then consulted an oncologist in Dakar in April 2023, where an extension work-up was carried out, classifying the cancer as stage T3N0M0. Following a multidisciplinary consultation meeting, a treatment plan was decided, including radiotherapy followed by topical application of Imiquimod 5% cream.

The RT centring scan was performed in the supine position with the foot forward. To optimise the dose to the skin, we covered the leg with a 1 cm thick bolus, which moved the maximum dose to the target volume on the surface. A heated sock was then used to avoid air gaps between the leg and the bolus. (Figure 2).

Dosimetric planning was carried out using a technique combining dynamic arc therapy and intensity modulation (VMAT). Qualitative analysis using iso-dose curves showed good dose distribution. As for the quantitative analysis, we noted that 95% of our target received 80% of the prescribed dose. Under-dosing was observed in the extremities in healthy areas.

Quality control of the treatment plan using gamma-index analysis showed good consistency between the calculated and measured plans. The overall absolute pass rate of the gamma-index was 93% for a pass criterion of 3% / 3mm.

External radiotherapy was administered on an Elekta Synergie accelerator at a dose of 36 Gy over 12 sessions, from 19 April 2023 to 08 May 2023. The accuracy of the ballistics was checked daily using an on-board scanner (CBCT). During treatment, the patient experienced grade 3 skin toxicity, which was successfully managed using Cicalfate cream, showing significant improvement. At the end of radiotherapy, the patient began treatment with Imiquimod 5%, after a period without skin toxicity, continuing treatment for 6 weeks.

Currently, at 9 months post-radiotherapy, there are no nodular lesions, the skin is smooth and has a similar appearance to that of the right leg, which was not initially affected. (Figure 4).

3. Discussion

Clinically, Kaposi Sarcoma mainly manifests itself as violet-blue pigmented macules, plaques, or nodules on the skin (8). However, the Human Immunodeficiency Virus-associated form is generally more disseminated in the skin, with frequent involvement of mucous membranes, lymph nodes and viscera. In the case of our patient, who had been HIV-positive for 10 years and whose disease appeared to be under control, a less aggressive form of Kaposi Sarcoma was diagnosed. This phenomenon has already been reported in the literature (9). This suggests that antiretroviral treatment influenced the clinical expression of Kaposi Sarcoma in our patient.

Another clinical skin manifestation is lymphoedema, which predominates in the lower limbs. Lymphoedema of the limbs accounts for around 17% of cutaneous manifestations in endemic forms of Kaposi Sarcoma (10). Human Herpes Virus type 8 can infect different cell types but has a particular tropism for lymphatic endothelial cells. It induces multicentric endothelial proliferation, leading to occlusion of the lymphatic vascular lumen, which in turn causes lymph stasis and, consequently, lymphoedema. Lymphoedema mainly affects the lower limbs affected by Kaposi Sarcoma. It can develop simultaneously with or after the appearance of Kaposi Sarcoma lesions, but it can also be the first sign of Kaposi Sarcoma, long before the appearance of Kaposi Sarcoma skin lesions. The diagnosis of lymphoedema is clinical and lymphoscintigraphy can confirm it if necessary (11).

The treatment of Kaposi Sarcoma depends on the clinical category, the extent of the lesion and the patient's pre-existing medical conditions (3). For patients with cutaneous Kaposi Sarcoma, recent clinical guidelines have recommended radiotherapy, surgical excision, cryosurgery, laser therapy and intra-lesional agents as treatment modalities(12).

Topical agents represent a more appropriate therapeutic option for certain clinical forms of cutaneous Kaposi Sarcoma (symptomatic and aesthetically unacceptable). They have the potential to achieve a higher concentration of the drug at the tumour site, relieve pain and promote healing, and therefore have a better safety profile (3). Eight case reports, one phase II prospective cohort study and one single-blind, uncontrolled, comparative clinical study used topical imiquimod as a treatment for cutaneous Kaposi Sarcoma (13–15). (13-15). All these studies used imiquimod 5% cream and the duration of treatment ranged from 6 to 83 weeks, with a median of 17 weeks, with response rates of up to 47% (13). Eight studies reported no recurrence of Kaposi Sarcoma skin lesions after a median follow-up of 12 months (range: 6-15 months) (14,16). However, imiquimod has not been extensively studied as a reference treatment in patients with HIV/AIDS-related skin Kaposi Sarcoma. It may represent a therapeutic option based on extrapolation of data presented previously in other contexts, expert consensus.

According to NCCN guidelines (3), radiotherapy is indicated for limited skin lesions that are symptomatic and/or cosmetically unacceptable. It is effective in relieving pain, stopping bleeding, and reducing oedema. In the case of extensive disease, radiotherapy improves symptoms, the aesthetic appearance of lesions and quality of life, and is very well tolerated. The recognised sensitivity of Kaposi Sarcoma to moderate doses explains why response rates vary from 47% to 99% for doses of 20 to 40 Gy (12,17). Due to the lack of prospective randomised studies, there is no standard approach to optimal radiotherapy techniques (18). Low-energy electrons and photons are often preferred for radiotherapy of Kaposi sarcoma (19). Three-dimensional conformal radiotherapy with and without intensity modulation (IMRT) and volumetric arctherapy (VMAT) can also be used for treatment planning. Dosimetric comparison of these different techniques has shown a significant benefit in terms of dose coverage and treatment time for volumetric arctherapy (20,21). The irregularity of the limb surface requires the use of devices such as boluses to homogenise dose distribution (22,23).

After irradiation, Kaposi Sarcoma lesions may take up to 4 months to regress clinically, while oedema may take up to 6 to 12 months to disappear completely (24). There is a risk of recurrence outside the irradiation field, which is why patients need to be regularly monitored by a dermatologist.

4. Conclusion

In the era of highly active antiretroviral therapy, radiotherapy is a locoregional treatment that forms part of a multimodal management strategy for the epidemic form of Kaposi disease. Its sole aim is to control the disease in the irradiated areas. Complete response rates are excellent, with extremely acceptable toxicity.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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