Acta Oncologica Vol. 35, No. 2, pp. 193–199, 1996

VARIANTS OF KAPOSI'S SARCOMA IN SOUTHERN AFRICA

A retrospective analysis (1980–1992)

MOSHE E. STEIN, JESSE LACHTER, DAVID SPENCER, LARRY MARGOLIUS and WERNER R. BEZWODA

All types of Kaposi's sarcoma (KS) are represented in the Southern African region. We present a retrospective analysis of patients with KS, treated and followed up at the Johannesburg General Hospital over a 12-year period (1980–1992). One hundred and nineteen patients with KS, divided into four groups according to their etiology (classical; endemic African; renal transplant recipients; epidemic AIDS-related) were analyzed. Choice of treatment (radiotherapy or chemotherapy) was individualized and based on clinical criteria, extent of disease and severity of symptoms. Kaposi's sarcoma showed a very high response rate to radiation therapy, regardless of variant, radiation modality or schedule. Chemotherapy was also effective in the more aggressive pattern of endemic African KS. Epidemic Kaposi's sarcoma showed the same poor outcome as demonstrated by its Western counterpart. We conclude that radiation therapy can provide excellent palliation with only minimal side-effects in all variants of KS seen in Southern Africa.

Since the initial description of the classical type of Kaposi's Sarcoma (CKS), other clinical variants of Kaposi's sarcoma (KS) have been described (1). Kaposi's sarcoma is the most common neoplasm among the Black population in equatorial Africa and accounts for about 9% of all cancers in the sub-Saharan region (2). In renal transplant recipients (RTR), the incidence of KS is reported to be 3.4–6%, a 400–500-fold increase over that seen in the general population (3). Recently, KS became the major indicator of malignancy in patients with acquired immunodeficiency syndrome (AIDS) (1, 4). Morphologically and ultrastructurally, there are no differences between the various types of KS (4).

Received 17 July 1995.
Accepted 3 September 1995.
From the Northern Israel Oncology Center (M.E. Stein), and Institute of Gastroenterology Rambam Medical Center, (J. Lachter) Haifa, Israel, and Department of Medical Oncology and Clinical hematology (M.E. Stein, D. Spencer, W.R. Bezwoda) and Renal Transplant Unit Faculty of Medicine, Univeristy of the Witwatersrand, and Johannesburg General Hospital (L. Margolius), Johannesburg, South Africa.
Correspondence to: Dr. M.E. Stein, Northern Israel Oncology Center, Rambam Medical Center, P.O.B. 9602 Haifa, Israel 31096.

The agressive variants of the endemic African KS and, especially, the epidemic AIDS-related KS, pose significant challenges to medicine in the Third World countries (5, 6). In Africa, this disease makes enormous demands on the already overburdened health care system. Increased morbidity and mortality in the most productive age groups is expected to undermine Africa's traditional family-based economic relationships (7–9).

In this retrospective analysis, we present our experience from 119 KS patients from various Southern-African regions, treated and followed at the Department of Radiation Therapy of Hillbrow Hospital and the Department of Medical Oncology & Clinical Hematology of Johannesburg General Hospital over a period of 12 years.

Material and Methods

Between 1980 and 1992, 119 adult patients with histologically proven KS were referred to our department. All patients were divided into four groups according to their clinical presentation: classical KS; KS in renal transplant recipients (RTR); endemic, African KS (AKS); and the epidemic AIDS-associated type (EKS). Data were analyzed retrospectively from patients' files. Patients with

 ISSN 0284-186X

EKS fulfilled the criteria of the Center for Disease Control for the Diagnosis of AIDS.

All patients underwent physical examination, hematological and biochemical studies and chest radiography. Where clinically appropriate, gastrointestinal studies, abdominal sonography and/or computerized tomography were performed. All patients were screened for the presence of human immunodeficiency virus (HIV) by standard serologic tests.

Treatment modalities

The choice of treatment was individualized and based on clinical criteria, including performance and nutritional status, severity of symptoms, accompanying diseases, localization, distribution, extent and depth of lesions.

Generally, radiation therapy (orthovoltage x-rays, ^{60}Co unit and electron beam) was considered for indolent, slow-growing disease. Local field radiotherapy ('involved field') was delivered to the tumor and its immediate surroundings ($\sim$2 cm). More extensive disease demanded a larger field, tailored to the extent of lesions. field sizes ranged from 2.5 x 3.5 cm to 20 x 25 cm. Total administered doses ranged from 8–12 Gy, given in a single fraction to 24–30 Gy fractionated over 2–3 weeks, in daily fractions of 2 Gy. All fields were treated daily.

Oropharyngeal lesions were treated with 10 MV photons through two opposed lateral fields encompassing the involved area alone. The total dose ranged from 12 to 14 Gy, delivered in 1.5–2 Gy fractions. The dose was calculated at the midplane.

Indications for chemotherapy included rapidly progressing, symptomatic disease (ulcerating, fungating, bleeding lesions), failure of or intolerance to radiotherapy. The agents mostly used were bleomycin (20 units) or vinblastine (6–8 mg) on a weekly basis, and etoposide (VP-16) 150 mg intravenously daily for 3 days every 3–4 weeks. Combination chemotherapy consisted of doxorubicin (20–40 mg/m^2)/bleomycin (30 units)/vinblastine (4 mg/m^2) every 3–4 weeks or actinomycin-D (1-1.5 mg/m^2) every 3 weeks and vincristine (2 mg) weekly.

Staging

The patient population was divided by convenience into two major groups: early KS, i.e. patients with limited disease, encompassable within 1–2 radiation fields, minimally symptomatic, slow-growing, non-ulcerating or fungating, and advanced KS, i.e. patients with extensive skin + lymphadenopathy + visceral organ involved and very pronounced symptoms.

Response criteria

Complete remission was defined as complete regression of lesions. Partial remission required a >50% decrease in number of lesions. An increase in size/number/severity of symptoms was listed as no response. Side-effects of therapy were assessed clinically (10, 11).

Results

Group I: Classical Kaposi's sarcoma (CKS)

Fifteen patients presented with the clinical features of CKS. Ten (67%) patients were males and 5 (33%) were females. Mean age at diagnosis was 70 years (range 26–81 years). Then (66%) of the 15 patients were Jews of East European (Ashkenazi) origin, one patient was Italian-born and the remainder were South African Caucasians. Clinical characteristics are presented in Table 1. The disease was limited to the lower extremities in 9 patients and the upper limbs in one patient. One patient with limited skin lesions presented with biopsy-proven inguinal lymph nodes. Five patients demonstrated lesions on multiple sites. In addition to their skin disease, two patients had oral cavity (tongue, buccal mucosa, soft palate) and small bowel involvement. Five patients achieved complete remission and four patients partial remission, at an overall response rate of 60%. After a mean follow-up of 50 months (range 7–168 months), two patients are alive with no disease, one patient is alive with stable disease and one patient still has active disease in his lower limbs. Two patients died from metastatic disease. five patients died of diseases unrelated directly to KS; heart failure (n = 1), diabetic ketoacidosis (n = 1), sepsis (n = 1), Hodgkin's disease (n = 1) and unknown cause (n = 1). All patients had stable, asymptomatic KS or no disease at their last follow-up visit. Three patients were lost to follow-up but had minimal or no disease when last assessed. Only one patient died of sepsis due to active KS.

Group II: Kaposi's sarcoma in renal transplant recipients

Nine hundred and eighty-nine RTR were followed by the Renal Transplant Unit at the Johannesburg General Hospital from August 1966 to December 1989. All transplanted patients received various schedules of immunosuppressive drugs (azathioprin, cyclosporin-A and steroids). Five (0.5%) adult male RTRs developed KS (Table 1). Mean age at the time of diagnosis was 47 years (range 43–53 years). The mean interval between transplantation (and onset of the immunosuppressive medication) and the development of KS was 18 months (range 8–38 months). One patient had KS limited to the skin. The four others presented with advanced KS: necrotic mouth ulcers without skin disease (n = 1); disseminated skin and lung involvement (n = 1); disseminated skin lesions and inguinal lymphadenopathy (n = 2). All patients were treated with immediate withdrawal of the immunosuppressive drugs. Additional therapeutic approaches used included palliative

Table 1

Clinical characteristics of patients with Kaposi's sarcoma

	AKS	EKS	CKS	RTR-KS
No. of patients	47	52	15	5
Age				
Mean	68	36	70	47
Range	23–82	23–67	26–81	43–53
Total number/percentage (%)				
Sex				
Male	47 (100)	37 (71)	10 (67)	5 (100)
Female	0	15 (29)	5 (33)	0
Prior 01	1 (2)	18 (24)	Nil	Nil
Sites of skin lesions				
Lower limbs [limited]	26 (55)	24 (46)	9 (60)	1 (20)
Upper limbs [limited]	Nil	Nil	Nil	Nil
Multiple sites	21 (45)	28 (54)	5 (33)	3 (60)
Stage				
Early	41 (87)	14 (27)	12 (80)	1 (20)
Advanced	6 (13)[1]	38 (73)[2]	3 (20)[3]	4 (80)[4]

Abbreviations
EKS = Epidemic Kaposi's sarcoma [AIDS-related], AKS = Endemic African Kaposi's sarcoma [non-AIDs-related], CKS = Classical Kaposi's sarcoma, RTR-KS = Kaposi's sarcoma in renal transplant recipients, OI = Opportunistic infections
1. Lymphadenopathy (n = 4), lungs/pleural effusion (n = 1) and oral cavity (n = 1).
2. Oral cavity, lymph node and large bowel involvement. One patient presented with liver metastases.
3. Lymphadenopathy (n = 1), oral cavity (n = 1) and small bowel involvement (n = 1).
4. Lungs (n = 1), oral cavity (n = 1) and lymphadenopathy (n = 2)

radiation therapy and single agent chemotherapy (cyclophosphamide) (n = 3). Only one patient died of disseminated KS. The other four patients experienced total disappearance of the lesions upon discontinuation of the immunosuppressive therapy. After a mean follow-up of 18 months (range 15–24 months), one patient is alive with no evidence of recurrent KS, while the other three patients have died of unrelated causes: sepsis (n = 2) and intracerebral hemorrhage of unknown etiology (n = 1). Autopsies performed on these patients did not reveal any evidence of KS.

Table 2

Clinical characteristics and patients' outcome in the endemic African variant of Kaposi's sarcoma

	Radiotherapy (n = 30)	Chemotherapy (n = 17)
	n (%)	n (%)
Age, years		
Mean	56	41
Range	29–82	23–59
Stage		
Early	29 (97)	12 (70)
Advanced	1 (3)	5 (30)
Response to treatment		
Complete remission	10 (33)	4 (23)
Partial remission	16 (53)	10 (58)
No response	4 (14)	3 (19)

Group III: Endemic African Kaposi's sarcoma (AKS)

Forty-seven Black patients domiciled in the Southern African region (including South Africa, Zimbabwe, Mozambique, Namibia and Malawi) were included in this study. Mean age was 68 years (range 23–82 years). Clinical characteristics are shown in Table 1. All patients were HIV negative and all presented with cutaneous disease, either confined to the lower limbs alone or present on multiple sites. Main symptoms were local pain, itching and burning. Two patients had clinical and radiologic evidence of underlying bone involvement; both presented with painful, tender and swollen affected limbs. Six (13%) patients demonstrated extracutaneous as well as cutaneous involvement: oral cavity (n = 1), lung (n = 1) and lymph nodes (n = 4). Therapy details are shown in Table 2. The response rates are similar for the two treatment modalities. Fourteen (30%) patients achieved complete remission and 26 (55%) attained partial remission. Complete symptomatic relief was achieved in 38 (81%) patients. Age, appearance of lesions (nodular vs macular) radiation modality, total dose and daily fractionation had no influence on response rate or duration of response. Due to the

Table 3

Treatment outcome in patients with the epidemic, AIDS-related type of Kaposi's sarcoma

	Radiotherapy	Chemotherapy
	n (%)	n (%)
Number	20 (38%)	32 (62%)
Mean age (range)	38 (23–67)	35 (25–45)
Lesions/no. of fields		
Lower/upper extremities	8	Extensive
Trunk	4	Extensive
Oral cavity	8	
Eyelid	1	
Visceral involvement	—	Extensive
Response rate/n (%)		
Complete remission	9 (45%)	Nil
Mean RFD*	5 months	Nil
Partial remission	9 (45%)	12 (38%)
Tumor progression	2 (10%)	20 (62%)
Symptomatic relief	17 (80%)	3 (9%)

*RFD = recurrence-free duration

nature of the study population (e.g., non-compliance, distance from treatment centers, repatriation of migrant laborers), complete follow-up could not be obtained for all patients, but all were evaluable for response. The median duration of response for the complete responders was 8 months. With a median follow-up period of 29 months (range 1–181), two patients were in complete remission for 15 and 18 months respectively. Ten (32%) patients from the radiotherapy arm developed slight dermatitis and subcutaneous atrophy (RTOG grade 1). Side-effects in the chemotherapy arm included vomiting, nausea, and diarrhea (n = 3). Four patients presented with simultaneous Kaposi's sarcoma and non-Hodgkin's lymphoma. These patients responded significantly, although incompletely, to chemotherapy and died due to progressive disease.

Group IV: Epidemic AIDS-related Kaposi's sarcoma (EKS)

A total of 52 patients were retrospectively analyzed. thirty-eight (73%) patients were Black and 14 (27%) White, with a male:female ratio of 2.8:1. Eighteen (34%) patients had prior or co-existent opportunistic infections (pneumocystis carinii pneumonia, fungal diseases, tuberculosis). Clinical characteristics are shown in Table 1. All patients presented with skin disease, either localized or disseminated. Other sites of involvement were the oral cavity, regional lymph nodes and the large bowel. One patient presented with liver metastases. Local symptoms included pain, burning, itching, local infection, oozing and lymphedema. One patient presented with KS involving the right side of the face, causing facial palsy. Complete remission of skin disease could be achieved in nine (45%) of the irradiated patients for a mean recurrence-free interval of seven months (Table 3). Most lesions disappeared within 3–5 weeks after the end of the radiotherapy course. Seventeen (80%) irradiated patients had marked symptomatic relief. Response rate was independent of radiotherapeutic equipment or schedule (single vs fractionated dose). Only two patients did not respond to radiotherapy. Side-effects of radiation therapy included grade I RTOG dermatitis or subcutaneous sequelae (n = 4) and grade II RTOG dermatitis (n = 2). Radiation-induced mucositis (moderate to severe grade) developed in five patients. Due to frequent loss to follow-up, the exact calculation of the duration of response became impossible; hence, the most reliable measure of treatment was response rate only. The response rate in the chemotherapy arm was very poor (Table 3). In the majority of patients, discontinuation of chemotherapy was necessary because of rapid deterioration and/or severe side-effects (debilitating mucositis, neutropenic sepsis). No patient entered complete remission and the rate of symptomatic relief was very low and of brief duration. All non-responders died rapidly, either from progressive disease and/or from exacerbating opportunistic infections.

Discussion

Classical Kaposi's sarcoma (CKS)

Classical Kaposi's sarcoma (CKS) is characterized by a protracted course and is rarely fatal. Most deaths occurring in CKS patients result from intercurrent diseases. In a few instances, a more agressive course with involvement of underlying bone, lymph nodes and/or visceral involvement is seen (1, 4). CKS has been predominantly described in elderly males of Ashkenazi Jewish or Mediterranean descent (2). Our patients were typical both in the preponderance of Eastern Europeans (10/66%) and in displaying a 2:1 male:female ratio (1, 2). However, our patients were of special interest in that they were Caucasians from Southern Africa where the endemic African, non-AIDS related KS (AKS) is the most common neoplastic disorder (9). The low incidence of KS in white Europeans and Asians living in this region is similar to that observed in their native lands (1, 12). Radiation therapy is the treatment of choice for symptomatic CKS (13, 15). Chemotherapeutic agents, such as vincristine, vinblastine, actinomycin-D, bleomycin and interferon-alpha, or combination chemotherapy are also very effective in the treament of progressive symptomatic CKS (16–19).

Kaposi's sarcoma in renal transplant recipients (RTR)

In RTR, the incidence of KS is reported to be 3.4–6%, a 400–500-fold increase over that seen in the general

population. The risk of KS following renal transplantation is the same as in patients with other forms of acquired immunodeficiency states, such as lymphoproliferative malignancies, long-term steroid therapy and patients with AIDS (3, 20–22). The widespread use of cyclosporin-A (CS-A) has improved the engraftment and graft survival among RTR. Unfortunately, an apparent increase in the incidence of lymphoma, skin cancer, mycosis fungoides and thymoma has been noted following the usage of this drug (23). Recently, KS has been described more frequently in CS-A treated patients than in patients treated with the conventional immunosuppressive therapy (steroids, azathioprine) (24–26). Discontinuation of immunosuppressive drugs and local radiotherapy is the treatment of choice for symptomatic KS (13, 14).

Endemic African Kaposi's sarcoma (AKS)

The endemic African variant of Kaposi's sarcoma was initially recognized during the beginning of the 20th century (27) and is the most common neoplasm among Black adults in sub-Saharan Africa (2). Three clinical entities of AKS among adults are recognized. Elderly patients usually present with the indolent/nodular type, which resembles the classical KS in its clinical behavior and radiosensitivity. The florid (infiltrative, locally agressive) AKS denotes a more agressive and less radio- or chemotherapy responsive pattern (1, 4, 28). Metastatic lymphadenopathy, either in its pediatric or adult form, is a very poor sign. Non-responsiveness to any form of treatment and fatal outcome characterizes this entity (1, 4, 29).

During recent years, there has been confusion related to the overlap of the concurrent presence of AIDS-associated KS and the endemic, HIV-negative variant seen in equatorial Africa. Retrospective serologic studies have revealed that nearly 17% of the Ugandan and Zambian patients tested had serum antibodies to HIV (30). The rapid spread of HIV infection throughout Africa will further complicate the ability to differentiate patients with very aggressive forms of endemic AKS from HIV infected patients who may also develop this neoplasm (5).

A thorough literature search revealed only a few studies evaluating the role of radiation therapy as the sole modality of treatment in AKS (31–34). This is due to the acute lack of skilled radiotherapists and modern radiotherapeutic facilities in many African countries. Generally, doses ranging from 8–10 Gy in a single exposure to 25 Gy fractionated over 3–4 weeks can successfully control AKS (31). Radiaion therapy in AKS has been reported to give poor results and a high complication rate. In the reports published over the past 30 years, patients were treated with old orthovoltage facilities with a clinical set-up only. Poor radiation quality control, large portal size, short treatment time and high daily fraction aggravated the side-effects. Follow-up was short and non-compliance of patients made conclusions sometimes impossible. Patients often presented with chronic and tropical infections (e.g., malaria, hepatitis), lymphedema (e.g., filarial), and protein malnutrition (31, 32). Additional contributing factors for the poor results achieved and severe tissue reactions (extensive fibrosis, endarteritis) noted include the concomitant use of dermatotoxic agents, such as actinomycin-D, vinblastine, bleomycin and nitrogen mustard (32, 35, 36). Up-to-date, modern megavoltage therapy and meticulous planning can significantly reduce the rate of severe side-effects.

Chemotherapy is also widely used in AKS (2). High response rates (80–90%) have been reported with weekly vinblastine and actinomycin-D as single drugs. Other effective drugs are bleomycin, carmustine, vincristin and intralesional nitrogen mustard (16, 28, 35, 37–40). These responses, however, were of brief duration. Low-dose recombinant interferon-alpha-2b has been shown prospectively to be very effective in AKS patients (18). Combined regimen have been proven to be effective in aggressive AKS, with an overall response rate of >80%. However, there is a lack of long-term follow-up studies.

Epidemic AIDS related Kaposi's sarcoma (EKS)

Retrospective sero-epidemiological and clinical studies have shown that AIDS and Kaposi's sarcoma as one of its major indicator diseases began to spread in the large cities of Central Africa in the late 1970's and early 1980's (7, 8, 41). Its clinical manifestations are distinct from the endemic African variant of KS (AKS). The EKS seen in adult Africans follows an agressive course and is less responsive to treatment than its endemic counterpart (1). The highest prevalence rates of AIDS-associated KS have been reported from Zaire, Uganda and Southern African countries. Available data suggest that approximately 5–15% of African AIDS patients present with KS (42). The pattern is agressive and outcome is dismal. Systemic treatment does not alter the ultimate course of disease. African patients with EKS often need palliative treatment because of the disfiguring and stigmatic nature of the disease. Delays in seeking medical help and the shortcomings of appropriate oncological facilities might aggravate the condition of these patients. Extreme hopelessness, social decline and tribal rejection are the common reactions which patients with EKS face in the traditional African society.

Based on comparisons of EKS with the non-AIDS type, some authors (10, 43, 44) found that radiation sensitivity and responsiveness are identical in both groups. Complete remission rates ranging from 50–90% and symptomatic relief of about 100% can be achieved with single doses of 8–10 Gy or biologically equivalent fractionated doses in the range of 15–25 Gy. Disease stage, irradiation technique or schedule did not have a major impact on remission rate.

To the best of our knowledge, there are no published studies evaluating the exact role of modern radiation therapy in African EKS; however, our study demonstrated that radiation sensitivity and responsiveness are similar to the Western type of EKS (1, 10, 45).

Severe skin reactions were not observed among our patients. Berson et al. (46) showed in his American population that the large dose per fraction scheme is more likely to be associated with greater normal tissue reaction. He, as well as Dewit et al. (47), recommended Gy/1 fraction schedule as the most appropriate for all cutaneous EKS lesions. The etiology of excessive skin reactions noted in African patients irradiated for KS is unclear. In many Third World countries, old radiotherapeutic facilities, poor radiation quality, incorrect dose calculation and irradiation of large skin volumes should be blamed for severe skin reactions (1, 31, 34, 36). Contributing factors include the above-mentioned tropical and parasitic disorders and malnutrition commonly seen in many Central and East-African countries (32, 34–36).

Five of our irradiated patients developed mucositis of the oropharyngeal region. Usually, total doses greater than 14 Gy and daily fractionation over 1.8 Gy produce mucositis, necessitating temporary or permanent termination of radiation therapy (46, 48, 49). Radiobiologically, the ability of the cells lining the oropharyngeal cavity to repair radiation damage appears to be impaired in AIDS patients (49, 50). Contributing factors to the slow healing of the radiation-induced mucositis seen among AIDS patients include subclinical infections and devastating malnutrition.

Marrow-sparing agents, such as bleomycin and vincristine, form the backbone of chemotherapeutic treatment in EKS. Other effective drugs are etoposide (VP-16), vinblastine and doxorubicin (4, 16, 51). Combination chemotherapy can achieve an objective tumor regression rate ranging between 50–90%, but also significant myelotoxicity and a high incidence of opportunistic infections (16, 52–54). Trials combining aggressive chemotherapy with hematopoeitic growth factors may allow optimal chemotherapy drug delivery [55].

ACKNOWLEDGEMENTS

The authors wish to express their appreciation to Mrs. M. Perlmutter for her assistance in preparing this manuscript.

REFERENCES

1. Friedman-Kien AE, Saltzman BR. Clinical manifestations of classical, endemic African and epidemic AIDS-associated Kaposi's sarcoma. J Am Acad Dermatol 1990; 22: 1237–50.
2. Safai B, Anhalt TS. Kaposi's sarcoma. Semin Dermatol 1984; 3: 69–77.
3. Penn I. Kaposi's sarcoma in organ transplant recipients. Transplantation 1981; 27: 8–11.
4. Stickler MC, Friedman-Kien AE. Kaposi's sarcoma. Clin Dermatol 1991; 9: 39–47.
5. Bayley AC. Aggressive Kaposi's sarcoma in Zambia. Lancet 1984; 1: 1318–20.
6. Biggar RJ. The AIDS problem in Africa. Lancet 1986; 1: 79–82.
7. Downing RG, Eglin RP, Bayley AC. African Kaposi's sarcoma and AIDS. Lancet 1984; 1: 478–80.
8. Piot P, Plummer FA, Rey M. Retrospective sero-epidemiology of AIDS verus infection in Nairobi populations. J Infect Dis 1987; 155: 1108–12.
9. Desmond-Hellman SD, Katongole-Mbidde E. Kaposi's sarcoma: recent developments. AIDS 1991; 5: (Supp): 135–42.
10. Chang LFL, Reddy S, Shidnia H. Comparison of radiation therapy of classic and epidemic Kaposi's sarcoma. Am J Clin Oncol 1992; 15: 200–6.
11. World Health Organization: WHO Handbook for Reporting Results of Cancer Treatment. Geneva; WHO Offset Publication 98, 1979.
12. Hood AF, Farmer ER, Weiss RA. Kaposi's sarcoma. Johns Hopkins Med J 1980; 151: 222–30.
13. Lo TCM, Salzman FA, Smedal MI, Wright KA. Radiotherapy for Kaposi's sarcoma. Cancer 1980; 45: 682–4.
14. Hamilton CR, Cummings BJ, Harwood AR. Radiotherapy of Kaposi's sarcoma. Int J. Radiat Oncol Biol Phys 1986; 12: 1931–5.
15. Holecek MJ, Harwood AR. Radiotherapy of Kaposi's sarcoma. Cancer 1978; 41: 1733–8.
16. Volberding P, Conant MA, Sticker RB, Lewis BJ. Chemotherapy in advanced Kaposi's sarcoma. Implications for current cases in homosexual men. Am J Med 1983; 74: 652–6.
17. Salan AJ, Greenwald ES, Silvay O. Long-term complete remissions in Kaposi's sarcoma with vinblastine therapy. Cancer 1981: 47: 637–9.
18. Rybojad M, Borradori L, Verola O, Zeller J, Puissant A, Morel P. Non-AIDS associated Kaposi's sarcoma (classical and endemic African types): treatment with low doses of recombinant interferon-alpha. J Invest Dermatol 1990; 95: 176–9.
19. Lanzotti VJ, Campos LT, Sinkorics JG, Samuels ML. Chemotherapy for advanced Kaposi's sarcoma. Arch Dermatol 1975; 111: 1331–3.
20. Qunibi A, Akhtar M, Steth K. Kaposi's sarcoma: the most common tumor after renal transplantation in Saudi Arabia. Am J Med 1988; 84: 232–55.
21. Sheil AGR. Cancer in organ transplant recipients: part of an induced immunodeficiency syndrome. Br Med J 1984; 288: 659–61.
22. Revillard JP. Immunologic alterations in chronic renal deficiency. Adv Nephrol 1979; 8: 365–82.
23. Abel EA. Cutaneous manifestations of immunosuppression in organ transplant recipients. J Am Acad Dermatol 1989; 21: 167–79.
24. Beveridge T. Cyclosporin-A, an evaluation of clinical results. Transplant Proc 1983; 15: 433–7.
25. Bencini PL, Marchesi L, Cainelli T. Kaposi's sarcoma in kidney transplant recipients treated with cyclosporin. Br J Dermatol 1988; 118: 709–14.
26. Penn I. Cancers following cyclosporin therapy. Transp 1987; 43: 32–5.
27. Hallenberger O. Multiple Angiosarskome der Haut bei einem Kamerunneger. Arch Schiffs Top Hyg 1918; 18: 647–50.
28. Taylor JR, Templeton AC, Vogel CL, Ziegler JL, Kyalwazi SK. Kaposi's sarcoma in Uganda: a clinico-pathological study. Int J Cancer 1971; 8: 122–35.
29. Salvin G, Cameron H, Forbes C. Kaposi's sarcoma in East African children: a report of 50 cases. J Pathol 1970; 100: 1987–99.

30. Bayley AC, Cheingsong-Popov R, Dalgleish AG, Downing RG, Teddens RS, Weis RA. HTLV-III serology distinguishes atypical and endemic Kaposi's sarcoma in Africa. Lancet 1984; 1: 359–61.
31. Cohen L. Dose, time and volume parameters in irradiation therapy of Kaposi's sarcoma. Br J Radiol 1962; 35: 485–9.
32. Duncan JTK. Radiotherapy in the management of Kaposi's sarcoma in Nigeria. Clin Radiol 1977; 28: 503–9.
33. Cohen L, Palmer PES, Nickson JJ. Treatment of Kaposi's sarcoma by radiation. Acta Union Int Contra Cancer 1962; 18: 502–9.
34. MaClean CM. Kaposi's sarcoma in Nigeria. Br J Cancer 1963; 17: 195–205.
35. Cook J. Treatment of Kaposi's sarcoma with nitrogen mustard. Acta Clin Int Cancer 1962; 18: 494–501.
36. Gordon JA. Kaposi's sarcoma: a review of 136 Rhodesian African cases. Postgrad Med J 1967; 43: 513–9.
37. Odom RB, Goette DK. Treatment of cutaneous Kaposi's sarcoma with intralesional vincristine. Arch Dermatol 1973; 144: 1693–4.
38. Kyalwazi SK. Chemotherapy of Kaposi's sarcoma: experience with trenimon. East Afr Med J 1968; 45: 17–26.
39. Kyalwazi SK, Bhana O, Master SP. Actinomycin-D in malignant Kaposi's sarcoma. East Afr Med J 1971; 48: 16–26.
40. Olweny CLM, Toya T, Katongole-Mbidde E. Treatment of Kaposi's sarcoma by combination of actinomycin-D, vincristine and imidazole-carboxamide [NSC-453–88]. Int J Cancer 1974; 14: 649–56.
41. Piot P, Kapita BM, Ngugi EN, Mann J. AIDS in Africa—a manual for physicians. Geneva, WHO, 1992.
42. Sher R. HIV infection in South Africa [1982–1988]—a review. S Afr Med J 1989; 76: 314–8.
43. Cooper JS, Fried PR. Defining the role of radiation therapy in the management of epidemic Kaposi's sarcoma. Int J Rad Oncol Biol Phys 1987; 13: 35–9.
44. Harris JW, Reed TA. Kaposi's sarcoma in AIDS: the role of radiation therapy. Front Radiat Therap Oncol 1985; 19: 126–32.
45. Cooper JS. Optimal treatment of epidemic Kaposi's sarcoma. Int J Rad Oncol Biol Phys 1990; 19: 807–8.
46. Berson AM, Quivey JM, Harris JW, Wara WM. Radiation therapy for AIDS related Kaposi's sarcoma. Int J Rad Oncol Biol Phys 1990; 19: 569–75.
47. Dewit R, Smit WGJM, Veenhof KHW. Palliative radiation therapy for AIDS-associated Kaposi's sarcoma using a single fraction of 800 cGy. Radioth & Oncol 1990; 19: 131–6.
48. Watkins EB, Findlay P, Gelman E, Lare H, Zobell A. Enhanced mucosal reactions in AIDS patients receiving oropharyngeal irradiation. Int J Rad Oncol Biol Phys 1987; 13: 1403–8.
49. Ficara G, Berson AM, Silverman S et al. Kaposi's sarcoma of the oral cavity: a study of 134 patients with a review of the pathogenesis, epidemiology, clinical aspects and treatment. Oral Surg Oral Med Oral Path 1980; 66: 543–55.
50. Papadopulos-Eleopulos E, Hedland-Thomas B, Causer DA, et al. An alternative explanation for the radio-sensitization of AIDS patients. Int J Rad Oncol Biol Phys 1989; 17: 695–7.
51. Groopman JE. AIDS-related Kaposi's sarcoma: therapeutic modalities. Sem Hemat 1987; 24: 5–8.
52. Northfelt DW, Volberding PA. AIDS-related Kaposi's sarcoma: clinical presentation, biology and therapy. Adv Oncol 1992; 7: 917.
53. Northfelt DW, Kahn JD, Volberding PA. Treatment of AIDS-related Kaposi's sarcoma. Hematol Oncol Clin North Am 1991; 5: 297–310.
54. Tapero JW, Conant MA, Wolfe SF, Berger TG. Kaposi's sarcoma: epidemiology, pathogenesis, histology, clinical spectrum, staging criteria and therapy. J Am Acad Dermatol 1993; 28: 371–95.
55. Gill PS, Rarick M, McCutcheon JE, et al. Systemic treatment of AIDS-related Kaposi's sarcoma: results of a randomized trial. Am J Med 1991; 90: 427–33.