

KAPOSI'S SARCOMA IN HOMOSEXUAL MEN—A REPORT OF EIGHT CASES

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Summary The clinical findings in eight young homosexual men in New York with Kaposi's sarcoma showed some unusual features. Unlike the form usually seen in North America and Europe, it affected younger men (4th decade rather than 7th decade); the skin lesions were generalised rather than being predominantly in the lower limbs, and the disease was more aggressive (survival of less than 20 months rather than 8–13 years). All eight had had a variety of sexually transmitted diseases. All those tested for cytomegalovirus antibodies and hepatitis B surface antigen or anti-hepatitis B antibody gave positive results. This unusual occurrence of Kaposi's sarcoma in a population much exposed to sexually transmissible diseases suggests that such exposure may play a role in its pathogenesis.

Introduction

Kaposi's sarcoma is rare in the United States, where the annual incidence is 0·021–0·061 per 100 000 population.^{1,2} In North America and Europe, this disease commonly presents as tumours of the lower extremities, and the clinical picture is that of a localised disease with an indolent course. Most patients are in their seventh decade. This form of the disease is commonest among Ashkenazi Jews and those of Mediterranean origin, and especially in men.^{3,4}

The incidence of Kaposi's sarcoma in African Blacks residing in an endemic region is much higher than among Blacks and Caucasians in North America and Europe. Kaposi's sarcoma makes up 9·1% of all malignancies diagnosed in Uganda.¹ In Africa, about 10% of patients with Kaposi's sarcoma present with the lymphadenopathic form of the disease.⁵ They have few skin lesions, which may occur on any part of the body, but extensive lymph node and visceral involvement. Most of the patients are less than 20 years of age, and all reported cases have died within 3 years of presentation.^{3,5}

We describe here the features of Kaposi's sarcoma seen in eight young homosexual men in the New York City area.

Methods

Eight patients with Kaposi's sarcoma were seen between March, 1979, and March, 1981, inclusive, at the New York University Medical Center, Brooklyn Veterans Administration Medical Center, and the Mount Sinai Hospital. All were seen and evaluated by at least one of the authors. Routine investigations done in all patients included complete and differential blood counts, serum electrolytes, liver-function tests, and the Venereal Disease Reference Laboratory (VDRL) test. Biopsy specimens and specimens of necropsy tissue were examined by the departments of pathology at the respective institutions. Hepatitis B surface antigen (HBsAg) and anti-hepatitis B surface antibody (anti-HBs) were determined by radioimmunoassay. Cytomegalovirus (CMV) titres

were measured by the complement fixation technique in the New York City Health Department Laboratories.

Clinical Observations

All eight patients with Kaposi's sarcoma reported in this study were homosexual men aged 27–45 years and had multiple sexual partners. All had histories of a variety of sexually transmitted diseases including syphilis, gonorrhoea, viral hepatitis, amoebiasis, *Herpes progenitalis* infection, and condyloma acuminatum. Four of the eight patients were Jewish and one was Italian. The only Black patient in our study was born in America and had never been to Africa. The accompanying table summarises some of the clinical features.

Seven of the eight patients sought medical attention because of skin lesions. The eighth (case 8) presented with *Pneumocystis carinii* pneumonia, and the skin lesions were detected at the first physical examination. In all patients the skin lesions appeared gradually. In six, the skin lesions were numerous when first seen. Case 8 had two discrete lesions on admission but more than twenty new lesions developed during his 3 months in hospital. The skin lesions consisted of nodules and papules in seven patients, and of plaques in case 8. All the skin tumours were non-tender, purplish, and non-ulcerating, and ranged in size from several millimetres to several centimetres in diameter. In several patients the lesions tended to coalesce. Lesions were found in the head and neck in four patients, but no patient showed predominant involvement of the lower extremities.

All eight patients had histologically proven cutaneous and lymph-node involvement. The histological features were typical of Kaposi's sarcoma. Skin lesions showed proliferation of small vessels lined by endothelium and interspersed groups of spindle-shaped pleomorphic cells. There were red blood cells within slit-like spaces not lined by endothelial cells, and haemosiderin-laden macrophages. Lymph-nodes showed similar features, with partial to complete effacement of normal nodal architecture and invasion of the capsule. A recent study details the histopathology of this disease.⁶

Seven patients had clinically detectable generalised lymphadenopathy. Six had visceral involvement (spleen, bone, lung, pleura, liver, or gastrointestinal tract) as shown by radionuclide scans, radiographic studies, or histological examination. In case 3 the frontal lobe mass detected by computerised axial tomography (CAT) could represent brain involvement by Kaposi's. Case 8 underwent necropsy.

All the four patients in whom CMV titres were measured had detectable antibody to the virus, but none presented with a mononucleosis-like illness.

Hepatitis B surface antigen was present in one patient and antibody to hepatitis B surface antigen in four.

Four of the eight patients died. Three died from Kaposi's sarcoma despite chemotherapy; the fourth (case 8) died of overwhelming cryptococcosis unresponsive to antifungal therapy before chemotherapy for Kaposi's sarcoma could be started. The average survival of these four patients was 15 months (range 3–20 months).

Four patients are alive 2–30 months after diagnosis. Two patients (cases 1 and 7) are in clinical remission, and one (case 3) has responded partially to chemotherapy. The fourth patient has not yet been treated for his tumour.

The two case-summaries presented below are representative of the clinical spectrum of Kaposi's sarcoma among our patients.

CLINICAL FEATURES OF EIGHT HOMOSEXUAL MEN WITH KAPOSI'S SARCOMA

Age at onset (yr)	Ethnic group	Site of skin lesion*	Other Sites	CMV titre‡	HBsAg‡	Anti-Bs‡	Disease duration (mo)	Chemotherapy§	Outcome
27	Jewish	Head (1)	Nodes Spleen† Bone†	1/32	Absent†	Present	>30	Doxo/Bleo/Vbl/Dacarb	Remission
33	Jewish	Head, trunk, Arm	Nodes Lung Pleura†	1/64	ND	ND	18	Vbl→Bleo/Vbl→ VP16/Doxo	Death
32	Scand.	Head, trunk, arms	Nodes Liver† Lung† ?Brain†	ND	Present†	Absent†	>7	Bleo/Vcr	Response
45	Irish	Trunk, arms, legs	Nodes	ND	Absent†	ND	20	Bleo	Death
38	Black	Chest, arms	Nodes	ND	Absent†	Present†	>2	None	Alive
39	Anglo-Irish	Trunk, arms, legs	Nodes Liver† Spleen† Lung	1/32	Absent†	Present†	14	Vcr/Dacarb/Act-D →Cyc/Doxo/Pred	Death
34	Italian	Trunk, arms, legs	Nodes Liver†	ND	ND	ND	>17	Doxo/Bleo/Vbl/Dacarb	Remission
34	Jewish	Head, back (2)	Nodes G.I. Lung	1/64	Absent†	Present†	3	None	Death

‡ND=Not done

†=organ involvement determined by nuclide scans and radiographic studies

*When patient was first seen; number of lesions "many," except where shown in parentheses.

§Drug: Doxo=doxorubicin; Bleo=bleomycin; Vbl=vinblastine; Dacarb=dacarbazine; Vcr=vincristine; Cyc=cyclophosphamide; ActD=actinomycin D; Pred=prednisolone; VP-16=Epipodophyllotoxin.

Case-reports

Case 1

This 27-year-old homosexual man noted a mass behind his right ear enlarging over 6 months. Pathological examination of the biopsied mass revealed Kaposi's sarcoma. He had had multiple episodes of gonorrhoea and condyloma acuminatum. Two cousins had leukaemia. The patient had very slight weight loss and anorexia for 1 year, and frequent upper respiratory infections. The lump behind his right ear was a 1.5×0.5 cm non-tender, purplish, cutaneous nodule. There were firm, non-tender, and mobile lymph nodes in the cervical, axillary, supraclavicular, and inguinal regions. The spleen was palpable.

Results of routine blood tests were unremarkable. Examination of a lymph-node biopsy (axillary) specimen revealed Kaposi's sarcoma. Lymphangiography showed inguinal and para-aortic lymph node involvement. A technetium-99 radionuclide study showed a photon-deficient lesion in the spleen; a bone scan and X-ray evaluation showed a lesion in the right iliac crest; and bone marrow biopsy was normal.

After six cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine the patient went into complete clinical remission. He has remained apparently disease-free at 2 years.

Case 2

This 33-year-old homosexual man first noted purple, raised, non-tender lesions behind both ears. 3 months later an examination of a biopsy specimen revealed Kaposi's sarcoma. He had had multiple episodes of gonorrhoea and amoebiasis. Physical examination revealed more than seventy-five discrete, violaceous, raised, and non-tender skin lesions on the head, neck, trunk, and arms; generalised lymphadenopathy; and no hepatic or splenic enlargement.

Routine blood tests were unremarkable. Examination of a biopsy specimen of the right axillary node revealed Kaposi's sarcoma. An abdominal CAT scan suggested retroperitoneal lymphadenopathy.

Vinblastine given weekly induced marked regression of the skin lesions. 3 months later bleomycin was added because of progression of the disease. 8 months after that treatment was stopped because

there was a complete response, but 2 months later the patient relapsed with new skin lesions and bilateral pleural effusions, which partly responded to readministration of bleomycin and vinblastine. Within 2 months there were progressive pulmonary infiltrates, large bilateral pleural effusions, and lower extremity lymphoedema. Treatment was changed to VP-16 (epipodophyllotoxin) and then doxorubicin but the patient did not respond and died of respiratory failure 18 months after the onset of his illness.

Discussion

The eight patients with Kaposi's sarcoma reported here have several distinctive and unusual features. Their median age was 34 years at the time of diagnosis, instead of the seventh decade as in other series.^{2,4} The generalised distribution of their skin lesions, the presence of lesions on the head and neck, and the absence of predominantly lower extremity involvement is atypical of the form of Kaposi's sarcoma encountered in North America and Europe. The generalised lymphadenopathy and visceral involvement that we observed is also unusual; so is the aggressive nature of the tumour in our patients. The duration of survival after diagnosis is usually 8–13 years,⁷ but half our patients were dead within 20 months of diagnosis, and only 2 went into remission after chemotherapy. This rapid clinical course closely resembles that of the lymphadenopathic form of Kaposi's sarcoma seen in Africa.

The aetiology and pathogenesis of Kaposi's sarcoma is unknown. Several mechanisms have been proposed for the development of this tumour—the effects of an oncogenic virus,^{8,9} an immunosuppressed state resulting in impaired tumour surveillance,¹⁰ or a combination of both. Observations supporting immunosuppression as the underlying factor are the high incidence of Kaposi's sarcoma in renal transplant patients^{11,12} and in patients receiving corticosteroids or cytotoxic drugs,¹³ and the anergy and depressed cellular immune function in patients with this

tumour.¹⁴ Of interest is the observation that a considerable proportion of patients in whom Kaposi's sarcoma develops after organ transplantation have visceral involvement similar to that seen in our patients.^{11,12} The evidence for a viral aetiology includes the high prevalence of CMV antibodies among patients with Kaposi's sarcoma.^{15,16} Also, virions have been seen by electron microscopy of tissue cultures of Kaposi's tumours,⁹ and DNA/DNA association kinetics suggest incorporation of the CMV genome into Kaposi's tumour cells.¹⁷

We do not know of reports of an increased risk of Kaposi's sarcoma in homosexuals. Furthermore, there have been no studies of immune function in this population. The high prevalence of sexually transmitted diseases in homosexuals is well established. It has been suggested that CMV may be venereally transmitted.^{18,19} Homosexuals attending a venereal disease clinic seem to have a high prevalence of CMV antibodies as well as viruria.²⁰ It is of interest that all of our patients who were studied for CMV antibodies had positive titres. In addition, all who were studied for hepatitis B surface antigen or antibody had serological evidence of prior infection with this virus. As noted previously, all of our patients had histories of a variety of sexually transmitted illness.

This study suggests that the homosexual population may have an increased risk of Kaposi's sarcoma. Although CMV and chronic or recurrent infections with other sexually transmitted agents were common to our patients and may have been related to the pathogenesis of Kaposi's sarcoma in this group of patients, other as yet undefined factors may be equally important. Certainly further epidemiological, serological, and immunological studies are needed to further understand this association.

ADDENDUM

Patient 3 died of progressive Kaposi's sarcoma despite continued chemotherapy, 9 months after his illness was diagnosed. Necropsy was not done.

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PLACEBO-CONTROLLED STUDY OF PHENOBARBITONE AND PHENYTOIN IN THE PROPHYLAXIS OF FEBRILE CONVULSIONS

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Summary Of 138 children who had a first febrile convulsion before their second birthday, 48 were treated with phenobarbitone, 47 with phenytoin, and 43 with a placebo for 12 months. Drug levels were monitored and adverse effects of the drugs were noted. Compared with placebo, phenobarbitone significantly reduced recurrences among children under 14 months old at the time of their first convulsion, but not among older children. Phenytoin was an ineffective prophylactic agent. Ideal drug levels were difficult to maintain, and many recurrences occurred when concentrations were suboptimal. Behavioural disturbance in children taking phenobarbitone was not a serious problem. The decision to give continuous prophylaxis for febrile convulsions is complex, and each case must be judged on its merits. For children who have a first seizure before 14 months of age prophylaxis may be advisable and phenobarbitone is effective.

Introduction

FEBRILE convulsions are experienced by 2-3% of children.¹ Although they frighten the family, constitute a burden on health services, and if prolonged carry a small but definite risk of brain damage,²⁻⁴ a consensus on management has not been reached—especially concerning continuous anticonvulsant prophylaxis. Several workers⁵⁻⁸ have found that phenobarbitone reduces recurrences, but others⁹ have been doubtful. In one study,¹⁰ in which phenytoin levels were monitored, recurrent seizures were reduced in duration but not in frequency. More recently, sodium valproate has been shown to provide protection,⁸⁻¹¹ but the adverse effects¹²⁻¹⁴ of this drug, though rare, may disqualify it for use in a common condition.

None of these studies has been placebo-controlled. This is a defect in design, because a mother who is giving medication

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