MEDICAL SCIENCE

Kaposi's sarcoma among persons with AIDS: a sexually transmitted infection?

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In the United States Kaposi's sarcoma is at least 20 000 times more common in persons with acquired immunodeficiency syndrome (AIDS) than in the general population and 300 times more common than in other immunosuppressed groups. Among persons with the acquired immunodeficiency syndrome (AIDS) reported to Centers for Disease Control by March 31, 1989, 15% (13 616) had Kaposi's sarcoma. Kaposi's sarcoma was commoner among those who had acquired the human immunodeficiency virus (HIV) by sexual contact than parenterally, the percentage with Kaposi's sarcoma ranging from 1% in men with haemophilia to 21% in homosexual or bisexual men. Women were more likely to have Kaposi's sarcoma if their partners were bisexual men rather than intravenous drug users. Kaposi's sarcoma risk was not consistently related to age or race but varied across the United States, being greatest in the areas that were the initial foci of the AIDS epidemic. Thus Kaposi's sarcoma in persons with AIDS may be caused by an as yet unidentified infectious agent, transmitted mainly by sexual contact.

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Introduction

One of the first manifestations of the acquired immunodeficiency syndrome (AIDS) epidemic was the unusual appearance of Kaposi's sarcoma in young homosexual men. Since then 24 different disorders have been included in the Centers for Disease Control's (CDC) surveillance definition of AIDS. Most of these disorders are caused by opportunistic infections.[1] Kaposi's sarcoma remains a common manifestation of AIDS but its cause is unknown.

Since the start of the epidemic, the pattern of occurrence of Kaposi's sarcoma in people with AIDS was recognised as providing important clues to its aetiology. That Kaposi's sarcoma was ten times more common in homosexual or bisexual men than in other men with AIDS led to suggestions that it might be caused by a sexually transmitted infection, or by an environmental agent, such as nitrite inhalants (poppers), to which homosexual men are preferentially exposed.[2–5] These suggestions are reminiscent of some of the initial proposals of the cause of AIDS itself.[6]

We analysed data on the occurrence of Kaposi's sarcoma among persons with AIDS reported to CDC to evaluate the existing hypotheses and to provide further clues about the aetiology of Kaposi's sarcoma.

Methods

AIDS surveillance at CDC began in 1981 and since then data have been continually collected on persons diagnosed as having AIDS.[7] Kaposi's sarcoma is included among the reportable manifestations of AIDS. Generally it is not reported if it occurs after the case has been reported to CDC. Individuals were assigned to HIV transmission groups according to the criteria defined by CDC.[7] Those whose risk group was "heterosexual contact" were separated according to whether or not they were born in "pattern II countries", as defined by WHO, which includes certain African and Caribbean countries where heterosexual spread predominates.[8]

The expected number of cases of Kaposi's sarcoma among persons with AIDS was estimated from (i) the age-specific and sex-specific incidence rate of Kaposi's sarcoma in the United States from 1973–79,[9] on the assumption that the average time from onset

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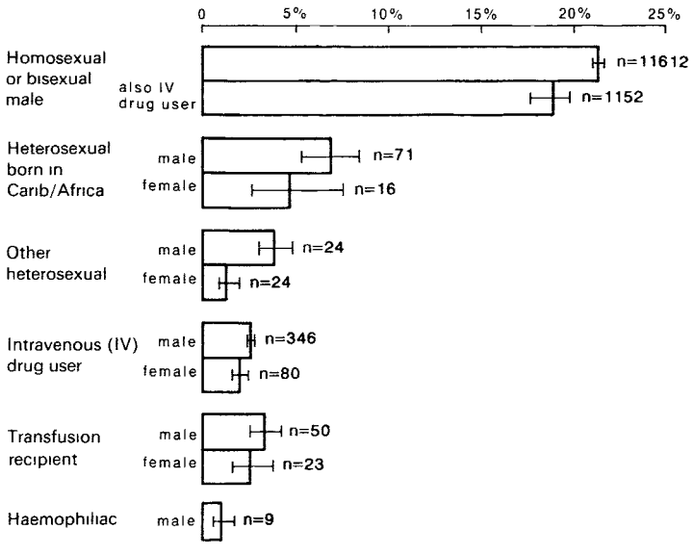

Fig 1—Percentage of AIDS patients with Kaposi's sarcoma by HIV transmission group and sex.

Number of cases of Kaposi's sarcoma (n) and 95% confidence intervals shown

of immunosuppression to death is 5 years; and (ii) the percentage of transplant recipients in whom Kaposi's sarcoma develops (0·05%: cancer develops after 1%–2% of renal transplants[10,11] and 3% of the cancers are Kaposi's sarcoma[12]), on the assumption that the transplant recipients and persons with AIDS were immunosuppressed for a similar length of time.

Among persons with AIDS the differences between various risk groups in percentage with Kaposi's sarcoma was examined. The numbers on which the percentages are based are stated when there are fewer than 10 cases of Kaposi's sarcoma. Other numbers are available from the authors on request. Where necessary the effects of age, sex, race, and year of diagnosis of AIDS were modelled by use of logistic regression methods.

Results

By March 31, 1989, 90 990 persons with AIDS had been reported to CDC; of these 88 739 were residents of the USA. 15% (13 616) of those who were US residents were reported to have Kaposi's sarcoma, 93% of which were reported to have been histologically confirmed. The expected number of cases of Kaposi's sarcoma in this population is 0·5 cases, on the basis of incidence rates in the United States from 1973–79; on the basis of proportion of transplant recipients with Kaposi's sarcoma, the expected number was 45·4. Thus the overall risk of Kaposi's sarcoma in patients with AIDS is at least 20 000 times greater than that in the general population and 300 times greater than that in other immunosuppressed populations.

Transmission group

Among persons with AIDS the percentage with Kaposi's sarcoma ranges from 1% in haemophilic men to 21% in homosexual or bisexual men (fig 1); the differences in risk between most HIV transmission groups are highly statistically significant, as indicated by the 95% confidence intervals. Homosexual or bisexual men, irrespective of whether they were also intravenous drug users, had substantially higher risks of Kaposi's sarcoma than did any other group. People born in Caribbean and African countries whose HIV was acquired by heterosexual contact had the next highest risk, 6% having Kaposi's sarcoma. Men with haemophilia and women who acquired HIV by heterosexual contact had the lowest risks of Kaposi's sarcoma.

TABLE I—KAPOSI'S SARCOMA IN WOMEN WITH AIDS ACCORDING TO THEIR SEXUAL PARTNER'S REPORTED HIV TRANSMISSION GROUP

Woman's HIV transmission group	Sexual partner's HIV transmission group	Percent (numbers) with Kaposi's sarcoma
Heterosexual contact	Bisexual male	3·0% *(9/303)*
	Intravenous drug user	0·7% *(9/1238)*
	Transfusion recipient or haemophiliac	0·0% *(0/71)*
Intravenous drug user	Bisexual male	4·1% *(3/74)*
	Intravenous drug user	1·1% *(6/531)*

Gender and sexual contact

Within each HIV transmission group Kaposi's sarcoma was generally slightly commoner among males than among females (fig 1). The only group with a striking excess among males was those whose AIDS was attributed to "other heterosexual contact".

Among women who had acquired HIV by heterosexual contact, Kaposi's sarcoma was four times commoner in women reported to have had sex with bisexual men than in women whose partners were from other HIV transmission groups ($p < 0·05$, table I). For 17% of female intravenous drug users details about their sexual partner(s) were recorded; and Kaposi's sarcoma was also four times commoner in women who were reported to have had sex with bisexual men than those whose partners were intravenous drug users (table I).

Race

The percentage with Kaposi's sarcoma varied by race within each transmission group, but the differences between the races were not consistent from one transmission group to another. Among homosexual or bisexual men, the percentage with Kaposi's sarcoma was twice as great in whites as in blacks (24% versus 11%, $p < 0·001$). In contrast, among transfusion recipients the percentage of whites with Kaposi's sarcoma was half that for blacks (2·5% versus 5·4%, $p < 0·01$, adjusting for sex). Among intravenous drug users there was a slight and non-significant excess among whites compared with blacks (3·5% versus 2·4%).

Age and country of birth

Among homosexual or bisexual men who were not intravenous drug users, the overall percentage with Kaposi's sarcoma increased with age up to 35–44 years, then declined (fig 2). The shape of the age curve in these men has changed over time, with the peak moving to progressively older ages. Among adults in other risk groups there is little variation in the percentage with Kaposi's sarcoma by age (fig 2). The data for males and females were combined since there was no difference in the age pattern between the sexes.

Kaposi's sarcoma is rare before the age of 15 years. Overall the proportion of patients with Kaposi's sarcoma was 1·6% (9 patients) for those aged less than 1 year, 0·5% (3) for those aged 1–4 years, and 0·4% (1) for those aged 5–14 years. These percentages cannot be compared directly with those at older ages since many HIV transmission groups are not represented at all ages. Only transfusion recipients and persons with haemophilia span a wide age

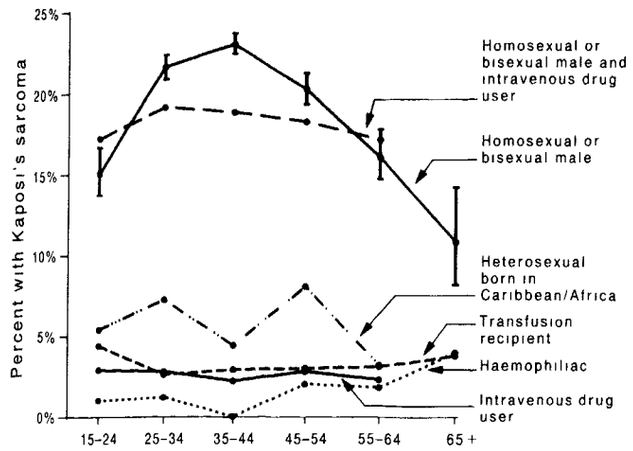

Fig 2—Percentage of AIDS patients with Kaposi's sarcoma by age and HIV transmission group.

95% confidence intervals shown for homosexual or bisexual men. There are insufficient numbers (fewer than 100 persons with AIDS) at ages 65+ for certain HIV transmission groups.

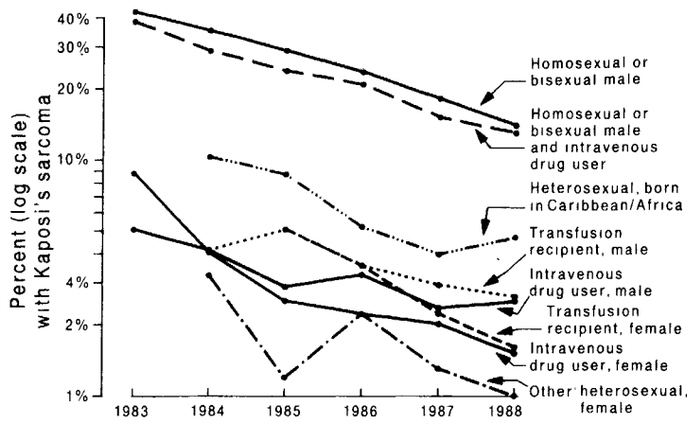

Fig 3—Percentage of AIDS patients with Kaposi's sarcoma by year of diagnosis of AIDS and HIV transmission group 1983–88.

There are insufficient numbers (fewer than 100 persons with AIDS) in 1983 and 1984 for certain HIV transmission groups.

range. In these groups Kaposi's sarcoma was less common among those aged under 15 years than among older patients—0·6% (1 patient) and 3·3% (72), respectively, for transfusion recipients ($p < 0·05$); and 0% (0/111) and 1·2% (10 cases), respectively, for those with haemophilia. All 12 children with Kaposi's sarcoma who were younger than 5 years were from Florida and all but 1 were the children of Haitian women. The only child aged between 5 and 14 years reported to have Kaposi's sarcoma was a transfusion recipient born in Central America but resident in the USA.

For US residents who had acquired HIV heterosexually, those born in the US were less likely to have Kaposi's sarcoma (1·8%, 37 patients) than those born in Haiti (6·3%, 85 patients), other Caribbean countries (9·0%, 3 patients), Mexico or Central America (7·4%, 2 patients), or Africa (7·7%, 2 patients). The difference in risk between those born in the US and other countries was statistically significant both for men (3·2 versus 7·0%) and women (1·3% versus 5·0%). Similar differences in risk were not found for homosexual or bisexual men, among whom the percentages with Kaposi's sarcoma were 21% for the US-born, 9% for the Haiti-born, and 25% for men born in the other countries named above. For residents of Puerto Rico with AIDS, Kaposi's sarcoma was reported in 4·5% (5 patients) of heterosexual women, 14% (4) of heterosexual men, and 18% (73) of homosexual men.

Trend with time and incubation period

The percentage of persons with AIDS reported to have Kaposi's sarcoma has declined over time (fig 3). The relative decline, estimated by use of a logistic model, has been 26% per year in homosexual men and 20% per year in other AIDS transmission groups. The decline might be an artifact due to the broadening of the CDC definition of AIDS. Two conditions, Kaposi's sarcoma and *Pneumocystis carinii* pneumonia, have always been part of the CDC definition of AIDS, and when persons with all other conditions were excluded, Kaposi's sarcoma still declined relative to pneumocystis pneumonia, but less so than before. The estimated relative decline was 20% per year in homosexual men and 10% per year in other HIV transmission groups. In homosexual men, but not in other HIV transmission groups, the decline in Kaposi's sarcoma relative to pneumocystis pneumonia was steeper in whites than others (annual relative decline of 22% in whites, 17% in blacks, and 14% in Hispanics); and it was steeper in younger than older men (annual relative decline, adjusted for race/ethnic group, of 22% under the age of 30, 20% at age 30–49 years, and 17% over the age of 50).

Because the percentage of AIDS patients with Kaposi's sarcoma declined over time, all findings described above were reanalysed, adjusting for year of diagnosis of AIDS. The findings remained unchanged.

Transfusion recipients with AIDS are three times more likely to have Kaposi's sarcoma than are persons with haemophilia or other clotting disorders (3% versus 1%, $p < 0·05$, adjusted for age, race, sex, and year of diagnosis). The time between transfusion and onset of AIDS was compared in subjects who had Kaposi's sarcoma and those who had pneumocystis pneumonia. (People with other clinical manifestations of AIDS were excluded because the changing definitions of AIDS could cause bias in the comparisons.) For each year of transfusion AIDS was consistently diagnosed earlier in those with Kaposi's sarcoma than in those with pneumocystis pneumonia. The incubation period was 6·6 months shorter for Kaposi's sarcoma (adjusted for year of transfusion). Half the AIDS patients with haemophilia or clotting disorders had at least one blood transfusion since 1979, and the proportion with Kaposi's sarcoma was similar in those who did not have a transfusion (1%, based on 5 cases, in each group).

TABLE II—KAPOSI'S SARCOMA IN RESIDENTS OF DIFFERENT STATES OF THE US, CLASSIFIED ACCORDING TO THE FREQUENCY OF KAPOSI'S SARCOMA IN HOMOSEXUAL MEN

HIV transmission group	Sex	Percent with Kaposi's sarcoma in states where. 20% or more homosexual men have Kaposi's sarcoma*	Fewer than 20% of homosexual men have Kaposi's sarcoma
Heterosexual contact			
With a bisexual partner	F	3·9% *(6)*	2·0% *(3)*
Without a bisexual partner	F	0·7% *(5)*	0·7% *(4)*
Intravenous drug user	F	2·5% *(57)*	1·5% *(23)*
	M	3·0% *(237)*	2·2% *(109)*
Transfusion recipient	F	3·3% *(12)*	2·1% *(11)*
	M	4·1% *(27)*	2·8% *(23)*

*States included. California, Connecticut, Florida, Massachusetts, New York, Oregon, and Rhode Island
Numbers in parentheses refer to cases of Kaposi's sarcoma

Geographical distribution in the USA

The percentage of white homosexual or bisexual men with AIDS who have Kaposi's sarcoma varied tenfold across the United States, ranging from 3% (5 cases) in Kansas and 6% (5 cases) in Iowa to 30% (3116 cases) in California and 31% (1929 cases) in New York (the percentages are adjusted for year of diagnosis of AIDS). The highest percentages were in northeastern states and along the west coast and the lowest percentages were in central US. A similar geographical distribution was found for black homosexual or bisexual men. For other HIV transmission groups the percentage with Kaposi's sarcoma was also higher in the states where Kaposi's sarcoma was most common among homosexual men (table II). None of the 23 other clinical manifestations of AIDS reported to CDC showed a geographical pattern similar to Kaposi's sarcoma.

Discussion

Kaposi's sarcoma is exceptionally common among patients with AIDS. It is at least 20 000 times more common than would be expected from the incidence rates of Kaposi's sarcoma in the United States before the AIDS epidemic began. Although our estimate of the incidence of Kaposi's sarcoma in people with AIDS was made on several assumptions, an incidence of similar magnitude was found in a cohort of HIV-positive homosexual men.[13] Such a massive increase in risk itself provides a clue to the aetiology of Kaposi's sarcoma. Few known human carcinogens increase risk by more than 100 fold and, in the best documented example, hepatitis B infection and hepatoma,[14] the cause of the cancer is an infection. The association of Kaposi's sarcoma with immunosuppression is further indicative of its probable infectious aetiology. The risk of only a few specific types of cancer, including Kaposi's sarcoma, is increased in immunosuppressed subjects, and a shared feature of those cancers is that they may all have an infectious cause.[15] Kaposi's sarcoma is, however, still 300 times more common in people with AIDS than in other immunosuppressed groups.' This contrasts with non-Hodgkin lymphoma, which occurs in 3% of those with AIDS,[16] a risk of similar magnitude to that found in immunosuppressed groups who do not have AIDS.[10,11]

The data presented here are consistent with Kaposi's sarcoma in people with AIDS being caused by an as yet unidentified sexually transmitted infection. The risk of Kaposi's sarcoma is generally greater among those who acquired HIV by sexual contact than parenterally. The risk is greatest of all in homosexual and bisexual men. And among homosexual or bisexual men the risk is greatest among those living in California and New York, the initial foci of the AIDS epidemic, and lowest among those living in central USA, where the incidence of AIDS is low. Among women with heterosexually acquired HIV, the partners of bisexual men had risks of Kaposi's sarcoma four times higher than for women with other sexual partners. It is often difficult to differentiate between sexual and faecal-oral spread of an infection but Kaposi's sarcoma is rare before the age of 5 years, when faecal-oral contact is common.

1% to 3% of patients with parenterally-acquired HIV have Kaposi's sarcoma, which is still at least 20 times as common as in immunosuppressed patients who do not have AIDS. The observation that Kaposi's sarcoma is less frequently associated with parenterally than with sexually transmitted HIV suggests that the causative agent may not normally be present in the blood. If it persisted in the blood it might be expected, for example, that more than 3% of transfusion recipients with AIDS would have Kaposi's sarcoma since almost all transfusion recipients with AIDS acquired HIV from the blood of homosexual men,[17] in at least 20% of whom Kaposi's sarcoma develops. Perhaps the agent remains in the blood longer than transiently only in immunosupppressed patients but other explanations are also plausible. For example, since the percentage of transfusion recipients with Kaposi's sarcoma is lower before the age of 15 years than at older ages transmission may be by routes other than the blood. It is not clear why Kaposi's sarcoma occurs three times less often in AIDS patients with haemophilia or clotting disorders than in transfusion recipients, especially since haemophiliacs receive plasma from large numbers of donors and are known to be at specially high risk of acquiring parenterally transmitted infections. Perhaps the agent is highly cell-associated.

Perinatal spread of the agent may occur since Kaposi's sarcoma has been reported in children with maternally transmitted HIV in the USA,[18] Africa,[19] and Mexico.[20] All but 1 of the 12 children with maternally transmitted HIV and Kaposi's sarcoma reported to CDC were offspring of women born in Haiti. Since the clinical manifestations of Kaposi's sarcoma are atypical in children,[18] and all the affected children were reported from Florida, diagnostic biases might exist.

The high frequency of Kaposi's sarcoma among adults with heterosexually acquired HIV from Puerto Rico and those born in Haiti, other Caribbean countries, Mexico, Central America, or Africa suggests that the agent responsible for Kaposi's sarcoma may be more prevalent among heterosexuals in those countries than in the United States. The percentage with Kaposi's sarcoma in AIDS patients born in those countries is similar to the percentages reported for AIDS patients living in Africa.[21-23] These observations and the accompanying report (p 168)[25] of benign and localised Kaposi's sarcoma in 6 HIV-negative homosexual or bisexual men from New York suggest that the agent that causes Kaposi's sarcoma must be the same irrespective of whether there is an associated HIV infection. Before the advent of AIDS, Kaposi's sarcoma was more common in Africa and Puerto Rico than in the US.[9,24] Perhaps the circumstances responsible for the heterosexual spread of AIDS in those countries also facilitate the spread of the agent causing Kaposi's sarcoma.

Although the data are consistent with an infectious cause for Kaposi's sarcoma, other explanations need to be considered. Nitrite inhalants (poppers) or other substances to which homosexual men have been preferentially exposed have been suggested as a cause of Kaposi's sarcoma.[4] The use of poppers is highly correlated with behaviours that provide opportunities for acquiring sexually transmitted infections. Kaposi's sarcoma has been associated with both sexual practices and the use of poppers.[4,26,27] Under such circumstances it is difficult to disentangle the effects of two highly correlated exposures, similar problems having been encountered in early studies of AIDS.[6] The occurrence of Kaposi's sarcoma in children and elderly people with parenterally transmitted HIV and in one-tenth of AIDS patients in Africa, where poppers are not used, suggests that poppers cannot account for the pattern of occurrence of Kaposi's sarcoma in AIDS patients.

A further proposal for the high frequency of Kaposi's sarcoma in AIDS patients is that there may be a special genetic susceptibility to the disease. The genetic hypothesis

is not supported by detailed HLA studies.[28] Nor are there consistent differences in risk by race. In addition, genetic differences between the HIV transmission groups are unlikely to be of sufficient magnitude to explain the wide diversity of risk of Kaposi's sarcoma in patients with AIDS. Suggestions that Kaposi's sarcoma might be a manifestation of HIV infection itself[29] are not supported by the reports of Kaposi's sarcoma in HIV-negative homosexuals;[25] nor by the 20-fold differences in risk of Kaposi's sarcoma, unless the groups at risk of AIDS are infected with HIV strains having different biological properties, a hypothesis for which there is currently no support.

Variations in the risk of Kaposi's sarcoma in different groups are not due to differences in diagnostic or reporting practices, except perhaps in children. If Kaposi's sarcoma occurs in patients with AIDS, it is generally the presenting symptom,[30] and the large majority of cases reported to CDC were confirmed histologically. Although it is possible that adults in certain HIV transmission groups might have better access to medical care and be more likely to have Kaposi's sarcoma reported than others, this could not explain the 20-fold range in risk described here. The most likely source of bias is the misclassification of homosexual or bisexual men, who have the highest risks of Kaposi's sarcoma, into the wrong HIV transmission group. In intravenous drug users and transfusion recipients, there is little to suggest such misclassification, but it may have occurred for some men whose AIDS was classified as being due to "other heterosexual contact".

The percentage of AIDS patients with Kaposi's sarcoma has declined in all risk groups from 1983 to 1988, as others have reported,[30-32] a trend that can be only partly explained by the broadening of the CDC definition of AIDS. Even after taking the changes in definition and reporting into account, the relative decline in Kaposi's sarcoma was 20% per year in homosexual men and 10% per year in other transmission groups. The relative decline may be in part attributable to a shorter incubation period for Kaposi's sarcoma than for *Pneumocystis carinii* pneumonia. The shorter incubation period[30] is supported by laboratory evaluations and survival studies which suggest that patients with Kaposi's sarcoma are less severely immunosuppressed and survive longer than do other AIDS patients.[4,33] The steeper decline in occurrence of Kaposi's sarcoma in homosexual men than in other risk groups, especially in young people and in whites, might reflect different trends in exposure to the causal agent resulting from the altered sexual behaviour of homosexual men.[34,35] How much of the decline can be attributed to these factors is, however, unclear.

Cytomegalovirus and other viruses have been investigated as possible specific causes of Kaposi's sarcoma. The viruses studied are generally ones that are widely prevalent and the findings have been inconsistent.[4,26,31,36] It is likely, however, that infection with the agent responsible for Kaposi's sarcoma was rare in most western countries until recently. The occurrence of benign Kaposi's sarcoma in HIV-negative homosexual men[25] coincides with the epidemic of AIDS. Furthermore, in immunosuppressed populations who do not have AIDS, most of whom were studied in the 1970s, no more than 0·05% acquired Kaposi's sarcoma and those who did were often from developing countries, the Caribbean, or the Middle East.[11,12]

In searching for the causal agent, emphasis should be placed on organisms whose prevalence is low in the United States except among homosexual men or heterosexuals born in Africa, Central America, or the Caribbean. Its main route of transmisssion is likely to be sexual. Transmission by whole blood may be rare, and by clotting factor concentrates rarer still.

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Epstein-Barr virus in nasal T-cell lymphomas in patients with lethal midline granuloma

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Five cases of lethal midline granuloma were identified histologically and phenotypically as peripheral T-cell lymphomas. Epstein-Barr virus (EBV) DNA was detected in the nasal tumour biopsy specimens by Southern blotting and in-vitro hybridisation with simultaneous detection of EBV-determined nuclear antigen (EBNA) and T-cell surface markers by two-colour immunofluorescence. Further immunofluorescence and northern blotting revealed that EBNA2 gene and also latent membrane protein gene were expressed in the nasal tumour cells. The patients had high titres of antibodies to EBV. These findings suggest that lethal midline granuloma is causally associated with EBV.

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Introduction

Histological examinations and surface marker tests show that lethal midline granuloma is a peripheral T-cell lymphoma.[1,2] Epstein-Barr virus (EBV) immortalises B-lymphocytes in vitro and is causally associated with benign and malignant diseases of B-cell origin, such as infectious mononucleosis, Burkitt's lymphoma, and opportunistic lymphomas in immunodeficiency. EBV genomic DNA, the virus-determined nuclear antigen (EBNA), and high EBV antibody titres[3,4] can be detected in B-cell lesions in such patients. Uncontrolled lymphoproliferation carrying the EBV genome has also been observed in T cells in two cases of chronic active EBV infection.[5,6] We report five cases of lethal midline granuloma, all of which were T-cell lymphomas positive for EBV DNA, EBV-transforming footprint EBNA, especially EBNA2 with latent membrane protein (LMP), and high-titre EBV antibodies.

Patients and methods

Five Japanese patients with lethal midline granuloma, one man and four women (mean age 39 years), were studied. Serum samples were assayed on admission for antibodies to EBV capsid antigen (VCA) (IgG, IgM, and IgA),[7,8] early antigens (EA) (IgG and IgA),[8,9] and EBNA (IgG)[10] by immunofluorescence. Surface phenotypes of nasal tumour biopsies were assessed on frozen sections by avidin-biotin immunoperoxidase.[11] The monoclonal antibodies that we used are shown in table I.

TABLE I—SURFACE PHENOTYPES IN FIVE CASES OF LETHAL MIDLINE GRANULOMA

Surface antigen	Surface antigen positive cells (%)				
	1	2	3	4	5
CD2 (pan T)	90	80	80	78	82
CD3 (mature T)	25	80	80	76	ND
CD4 (T subset)	25	20	75	70	ND
CD5 (pan T, B subset)	28	7	78	78	ND
CD8 (T subset)	1	7	23	25	ND
CD11b (C3 bR)	0	20	7	5	ND
CD19 (pan B)	0	0	0	0	ND
CD20 (peripheral B)	0	0	0	0	ND
CD21 (C3dR, EBVR)	0	0	0	0	ND
CD23 (FcεR)	0	0	0	0	ND
CD25 (IL2R)	0	0	0	0	ND
Leu8 (T subset, B subset)	0	10	60	ND	ND
Leu18 (T subset, B subset)	0	3	7	ND	ND
Ia	85	83	25	80	ND
sIg	0	0	0	0	ND
CD45RO (pan T)	85	85	80	75	85
L26 (pan B)	0	0	0	0	0

ND = not done

EBV was detected by Southern blotting, in-situ hybridisation,[12] and EBNA immunofluorescence.[10] Southern blot hybridisation was done for EBV DNA extracted from biopsy specimens with ^{32}P-labelled *Bam* HI-W as a probe. In-situ hybridisation was also done for EBV DNA on frozen sections with biotinylated *Bam* HI-W or ^{3}H-labelled *Bam* HI-A, HI-B, HI-C, and HI-W mixture as probes. EBNA was stained on frozen sections by the anti-complement method. In addition, EBNA2[13] and LMP[14] gene

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