The unique epidemiology of Kaposi's sarcoma among patients with the acquired immunodeficiency syndrome suggests a multifactorial cause. Although the human immunodeficiency virus (HIV) plays a major role in the

Introduction

Kaposi's sarcoma (KS) is best known in the United States in association with acquired immunodeficiency syndrome (AIDS). Worldwide, however, the AIDS-related form is only one of four clinical presentations of the disease. Much remains unknown about the pathogenesis of AIDS-related KS. Some aspects of the epidemiology of the four types, as well as the changing picture of AIDS-related KS, may provide important leads to understanding the etiology(ies) of these neoplasms.

The Four Types of KS

The four types of KS are the classic form, the African form, the form associated with iatrogenic immunosuppression, and the AIDS-related form. The classic form of KS was first described as "idiopathic, multiple pigmented sarcomas of the skin" in 1872 by Moritz Kaposi, a Viennese dermatologist[1]. Kaposi's description was based on the examination of three elderly men who had lesions on their extremities. Since the publication of Kaposi's original paper, this form of KS has been observed worldwide, although it seems to be more prevalent in people of Mediterranean origin. It is not rapidly progressive, and the male-to-female ratio is 10 to 15:1. A typical patient might present with KS in his 60s and live another 10 or 15 years before dying of some unrelated cause [2].

The African endemic form of KS was first described in 1914, but its prevalence in Africa was only appreciated approximately 20 years later, when a review of 500 tumors in Nigerian patients showed 2% to be KS [3,4]. The African form occurs predominantly in young, black adults 25 to 40 years of age. The male-to-female ratio for this form is 17:1. The presentation is variable. Benign, nodular lesions limited to the extremities form one end of the spectrum; florid, disseminated lesions are at the other end. Survival ranges from 3 to 10 years following presentation. There is also a lymphadenopathic subvariant of the African form that affects children at a mean age of 3 years. The male-to-female ratio for this pediatric subvariant is 3:1 [2].

In the 1970s, a third form of KS was observed in immunocompromised patients. Such patients who are at risk for this form of KS include recipients of renal transplant, patients on long-term corticosteroids for various disorders, and patients who are immunosuppressed as a result of some other therapeutic regimen or malignancy. As with the African form, with the immunocompromised form, lesions are often localized, although rapid dissemination is seen in some cases. The male-to-female ratio for this form is 2.3:1. One unique aspect of this form of KS is that some lesions resolve when iatrogenic immunosuppression is stopped [2].

In 1981, a major epidemic of the fourth type of KS was discovered. The AIDS-related form occurs in conjunction with human immunodeficiency virus (HIV) infection and is found predominantly among white, homosexual/bisexual men. In contrast to the other three forms, in which lesions tend to appear on the legs, AIDS-related KS may appear on the extremities but also commonly appears on the chest and face (Figure 1) as well as in the gastrointestinal tract and lungs. Disease is also more virulent with this form than with the other three forms, and most patients die of KS or other AIDS-defining illnesses within 1 to 3 years of presentation. The male-to-female ratio for the AIDS-related form is 100:1 [2].

There may be some confusion about presentation when forms of KS intersect. For example, as the AIDS epidemic spreads in Africa, AIDS-related KS is overtaking the endemic African form in frequency. Researchers from Zambia report that the prevalence of KS is increasing in tandem with
that of HIV infection. The male-to-female ratio for all cases of KS dropped from 10:1 in 1985 to 2.3:1 in 1993. The HIV seroprevalence in Zambian cases of KS is 97% [5]. Another example is the juxtaposition of HIV-positive and HIV-negative patients with KS among homosexual men in the United States. Compared with HIV-positive patients, HIV-negative patients are older (median age, 49 years vs 37 years), less immunosuppressed (median CD4 counts, 768 vs 226 cells/mm³), and have more indolent clinical courses (less than 10 skin lesions for all HIV-negative patients) [6].

National Surveillance for AIDS-Related KS

In 1981, the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, initiated surveillance of AIDS in the United States. Between June 1981 and December 31, 1992, a total of 253,322 cases of patients with AIDS were reported. Presumptive or definitive KS was reported in 33,170 patients (13%). There are three caveats regarding the interpretation of these figures. First, the definition of AIDS and AIDS-related KS changed several times during the surveillance process. Second, approximately 20% of cases of KS are diagnosed without benefit of biopsy; this is particularly common in patients with other manifestations of AIDS, who are often diagnosed with KS on clinical grounds alone. Third, there are cases of KS that go unreported when patients with AIDS develop KS in the later stages of disease, after AIDS has already been reported [7].

Despite these limitations, several observations can be made from the surveillance data. First, homosexual/bisexual men are much more likely to develop KS than are patients from other groups (Table 1). More than 30,000 of the 33,170 AIDS-related cases of KS have occurred among homosexual/bisexual men, a rate of KS of 19.2% in the homosexual/bisexual patient population with AIDS. In other groups, the rate ranges from 0.5% to 5.6%. This difference is highly significant.

Second, the incidence of AIDS-related KS increased each year from 1981 through 1990. However, unlike total cases of AIDS, which have continued to increase, the incidence of AIDS-related KS declined in 1991 and 1992. In fact, the proportion of cases of AIDS with KS has declined each year since surveillance began (Table 2).

Third, among blood transfusion-related cases of AIDS, 42 donor-recipient pairs developed AIDS. There were no cases in which the recipient developed KS after receiving transfusion from donors who later developed KS. In one case, a recipient developed KS after receiving HIV-infected blood from a donor who did not develop KS. If AIDS-related KS was caused by HIV alone or a special strain(s) of HIV, some concordance of KS between donors and recipients would be expected [7].

Fourth, among homosexual/bisexual men with AIDS, KS is more common in white men than in black men (22% vs 10%) [7,8].

Fifth, initial data showed that women who were sexual partners of homosexual men were more likely to develop KS than women sexually linked to injection drug users (3% vs 0.9%) [9]. The gap between these groups is narrowing, however, and is no longer statistically significant (Table 3) [7]. Women who reported intravenous drug abuse or a history of blood transfusion prior to the diagnosis of AIDS were excluded from analysis.

Finally, the rate of KS among patients with AIDS varies with location. The proportion of white, homosexual patients with AIDS and KS is more than 20% in California, Connecticut, the District of Columbia, Massachusetts, New Mexico, New York, and South Carolina but less than 10% in Alabama, Arkansas, Iowa, Nevada, and Utah [7].

Conclusion

The unique epidemiology of KS among patients with AIDS suggests that its cause is multifactorial. Although HIV plays a major role in its pathogenesis, HIV alone is not its cause. Data suggest that a necessary factor(s), and/or enhancing factor(s), associated with a homosexual life-style predisposes HIV-infected persons to KS. A second sexually transmitted organism, a fecal-orally transmitted organism, genetics, and nitrite inhalant use have been proposed as cofactors. The current epidemic of AIDS-related KS provides a unique opportunity to decipher the pathogenesis of a malignancy that is multifactorial in etiology.

References:
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