HIV Infection With Hodgkin’s Disease: The Virus Makes a Difference

People infected with the human immunodeficiency virus may have a greater risk of Hodgkin’s disease, display an unusual form of this rare cancer, and require a different approach to therapy than the usual Hodgkin’s patient, according to data presented recently at the first National AIDS Malignancy Conference, sponsored by the National Cancer Institute and held in Bethesda, Md.

Two other cancers — Kaposi’s sarcoma and non-Hodgkin’s lymphoma — have long been associated with HIV or AIDS. But only in the last few years have published accounts begun to suggest a connection between AIDS and other malignancies, including Hodgkin’s disease, anal cancer, melanoma, and more (see Stat Bit).

Among these “other” cancers, Hodgkin’s disease has one of the strongest and most consistently reported links with HIV, according to NCI’s Charles S. Rabkin, M.D. Rabkin told the meeting participants that four major studies seeking links between AIDS and cancer have revealed an increased risk of Hodgkin’s disease that is “relatively small but statistically significant.”

Evidence of a heightened risk has grown rapidly in the 5 years since

Nancy Hessol, M.D., first reported what seemed to be a higher rate of Hodgkin’s disease among AIDS patients at San Francisco General Hospital. Since then, supporting data have come from sources as diverse as NCI’s Multicenter Hemophilia Cohort; the Multicenter AIDS Cohort Study at the University of Pittsburgh, which is following more than 5,000 gay men; and a study in Australia, which linked the New South Wales cancer and AIDS registries.

Common Age Group

Researchers are still careful to point out that the increased incidence of Hodgkin’s disease in HIV cohorts could be at least partly independent of HIV. For instance, Hodgkin’s disease tends to occur most frequently among young adults, the same age group in which HIV infection is most common, said Rabkin.

Nevertheless, consensus seems to be growing that the association between Hodgkin’s disease and HIV infection is real. “To prove the connection, we need to see a consistent association in a lot of different studies,” Rabkin said, “and that is beginning to roll in.”

Also emerging are more and more data supporting the observation that Hodgkin’s disease tends to look different in HIV-positive patients. Alexandre Levine, M.D., at the University of Southern California School of Medicine, Los Angeles, reported that AIDS patients with Hodgkin’s are more likely to have types of the disease that are otherwise less common in the United States — the so-called “mixed cellularity” and “lymphocyte depleted” types. Both carry a poorer prognosis than the more common “nodular sclerosis” and “lymphocyte predominant” types.

Other Differences

Other differences involve the Epstein-Barr virus, which is much more common in Hodgkin’s patients with HIV infection than in other Hodgkin’s patients in the general U.S. population; the stage at diagnosis — more often stage III or IV in HIV patients; and the occurrence of a set of systemic symptoms — fever, night sweats, and weight loss — that are also more common in HIV-infected Hodgkin’s patients.

Finally, an unusually high proportion of AIDS patients with Hodgkin’s have bone marrow involvement. In some it is the only site affected, Levine said. The cancer can also occur in the central nervous system, skin, rectum, lung, liver, and tongue in HIV patients, all sites unusual for Hodgkin’s disease.

The differences between Hodgkin’s disease with HIV and Hodgkin’s without HIV may extend to therapy. At the April meeting, Levine reported preliminary findings from a trial with 21 HIV-infected patients with advanced Hodgkin’s disease who had received the standard ABVD chemotherapy regimen (Adriamycin [doxorubicin], bleomycin, [text continues on next page])
vinblastine, and dacarbazine). The response rates were “reasonable,” Levine said, if a little lower than might be expected in the general population of Hodgkin’s disease patients.

Survival rates, though, were another matter. Median survival for the HIV patients in this study was only 78 weeks, whereas the majority of Hodgkin’s disease patients, even those diagnosed at an advanced stage, now survive for many years.

More Striking

Even more striking was the high number of adverse reactions to treatment drugs among the HIV-infected patients. Despite the use of colony stimulating factor (Neupogen®), neutropenia occurred in 71% of the patients, thrombocytopenia in 48%, and anemia in 62%. Liver toxicity was also common, and a sizable proportion of patients died of infection.

“The toxicity was truly significant,” Levine said. “We need to do better.”

Other chemotherapy regimens have had similar results. Levine reported that in six retrospective studies of patients with HIV and Hodgkin’s disease, treated with various drugs and drug combinations, median survival has ranged from 8 to 18 months. Opportunistic infections were reported in 30% to 50% of large series of patients and bacterial infections caused death in an additional 13% of cases.

In another study presented at the conference by U. Tirelli, M.D., and colleagues of Italy’s National Cancer Institute in Aviano, Hodgkin’s patients infected with HIV received anti-retroviral therapy (AZT) along with chemotherapy (cyclophosphamide, vincristine, and vinblastine) and colony stimulating factor. Toxicity was moderate and response rates good, they reported, but again, median survival was only 14 months. “Taking into considerations the moderate toxicity, we are currently considering higher doses of chemotherapy at shorter intervals with the support of [colony stimulating factor],” this group reported.

For Levine, on the other hand, the next steps will probably involve lower doses of chemotherapy. In an interview, she noted that lower drug doses could be combined with other strategies.

For instance, since the Epstein-Barr virus is a common feature of Hodgkin’s disease in HIV-infected patients, she said, one possibility might be to use an anti-EBV agent in combination with chemotherapy.

Next steps will be discussed at a meeting with investigators in the AIDS Malignancy Consortium in the near future, according to Levine. “We’re re-grouping,” she said. “We have to explore new regimes.”

— Caroline McNeil

![Stat Bite](HIV-Associated Malignancies)

Kaposi’s sarcoma and non-Hodgkin’s lymphoma were among the earliest manifestations of the AIDS epidemic. HIV-infected persons have an estimated 530-fold increased risk of KS and an 81-fold increased risk of NHL, according to National Cancer Institute studies of hemophiliacs. HIV infection may also be related to other cancers. The graph below includes selected findings from various studies that have estimated risks of cancer for patients with HIV infection or AIDS compared with non-HIV-infected persons or a general population. Some associations were not statistically significant and will need to be confirmed in further studies.

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* Relative risk

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<th>Hodgkin's disease†</th>
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