Editorial Comment: Reducing the Risk of Non–AIDS-Defining Cancers

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By AIDS Reader [1]

Cinti and colleagues call further attention to an increasing concern for people living with HIV infection and those providing their care: the increased risk of cancers that are not considered AIDS-defining events.

Although the authors refer to these cancers as non-opportunistic, many such cancers apparently capitalize on lowered host resistance and, as such, can be considered opportunistic in the broader sense, although not fulfilling the narrow CDC criteria used to designate malignancies as AIDS-defining. It is noteworthy that of the 5 cancers highlighted in this review, 4 are strongly associated with viral infections. In this respect, they are similar to the 3 malignancies (Kaposi sarcoma, high-grade non-Hodgkin lymphomas, and cervical cancer) included in formal definitions of AIDS and for which a decreased host immune response to viral infection has been linked to tumorigenesis. Also noteworthy is that some of the AIDS-defining malignancies (notably, Kaposi sarcoma and Burkitt-like lymphomas) are not infrequently diagnosed in HIV-infected persons with CD4 counts well above the threshold that places patients at increased risk for opportunistic infections. This suggests that a failure of immune surveillance can occur at CD4 levels far above those associated with other HIV disease complications. For the virus-associated malignancies that are not considered diagnostic of AIDS, a similar breakdown in immunological control of oncogenic viruses may be important.

Not all cancers that show an increased incidence in HIV-infected persons are associated with infectious agents. For lung cancer, tobacco use is the single most significant risk factor for both HIV-infected and uninfected persons, but there is evidence that HIV-positive persons with lung cancer develop this cancer after a shorter history of smoking exposure than their HIV-negative counterparts. In addition, while human papillomavirus infection may be implicated in some oral cancers, tobacco and alcohol use are also important behavioral risk factors for oral cancer.

For those cancers without an infectious cause (and perhaps also for those in which viruses have been implicated), it may be that HIV infection influences cancer susceptibility by mechanisms that are unrelated to CD4 levels. For example, some years ago Wistuba and colleagues reported that microsatellite alterations, which reflect widespread genomic instability, occur at a greatly increased frequency in the lung cancers of HIV-infected persons. Microsatellite instability has also been described in other AIDS-defining tumors, including Kaposi sarcoma and high-grade B-cell lymphomas. The mechanisms underlying the increased genomic instability of tumors in HIV-infected persons are unknown as is the stage in tumorigenesis in which these alterations develop. Based on what is known at present, it is not possible to predict whether earlier institution of antiretroviral therapy might decrease the risk of cancers, whether they are deemed “AIDS-defining” or not. What clearly can be recommended is increased education and intervention to reduce risk behaviors (eg, smoking, excessive alcohol consumption) that predispose to cancer. More widespread use of established methods of cancer screening in high-risk patients, while not preventing cancers, might help decrease the proportion of HIV-positive persons presenting with advanced-stage disease.
And finally, both large-scale studies to evaluate whether earlier institution of antiretroviral therapy decreases cancer risk and small-scale studies to explore the mechanisms by which HIV infection enhances tumorigenesis are warranted.

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References


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