Clinical aspects of AIDS-associated lymphomas

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It is clear from a number of studies \[22.1\] that there is an increased incidence of neoplastic complications in HIV disease. In the Concorde and the ACTG019 studies of patients with early HIV disease, from Europe and the U.S. respectively, about a quarter of all patients developed a malignancy as their AIDS-defining illness. In the ACTG196 study of patients with more advanced immunosuppression who were receiving a prophylactic anti-mycobacterial agent, there was approximately the same frequency of death from a neoplastic disease. Furthermore, as infectious disease physicians become more successful in controlling opportunistic infection, the frequency of neoplasms is rising. It is estimated that as many as 40% of HIV-positive patients will develop a malignancy at some stage. These lesions represent a link between infectious disease and oncology, since each of the major tumor types seen in HIV-positive patients is associated with at least one infectious agent. Non-Hodgkin’s lymphomas are associated not only with Epstein-Barr (EB) virus, but also with the herpes virus, HHV-8, which has also been associated with Kaposi’s sarcoma. The list in \[22.2\] is probably incomplete and it is likely that other infectious agents will in the future be implicated in subsets of AIDS-associated tumors.

About a quarter of these malignancies were lymphomas, and it is estimated that in 6 - 10% of patients with AIDS death is due to lymphoma. A very dramatic increase in the incidence of lymphoma was noted in the early 1980s in particular geographic areas and demographic subsets, and as a result non-Hodgkin’s lymphoma was designated in 1987 as an AIDS-defining illness \[22.3\].

There have been varying estimates of the frequency with which AIDS patients will develop non-Hodgkin’s lymphoma. The most comprehensive of these studies is from Moore et al.\[22.4\] who estimated the incidence of non-Hodgkin’s lymphoma in patients with symptomatic HIV disease to be 1.6% per year. This is fairly consistent over time. However, other estimates have been as high as 8% per year. Lymphomas are more common in patients who have late HIV disease, but risk is not exclusively restricted to patients with advanced immunosuppression, and lymphoma may indeed be the presenting manifestation of HIV infection.

HIV disease differs in its epidemiology from Kaposi’s sarcoma, whose occurrence may be related to particular sexual practices, since it is generally...
restricted to homosexual or bisexual partners of homosexual men. In contrast, there is a fairly even distribution of risk of lymphomas regardless of the mode of HIV transmission [22.5]. However, there are some minor differences between patient groups that may reflect aspects of care, such as the reduced incidence in IV drug abusers, perhaps due to higher likelihood of death from infection in this group. In addition, there are some patients, such as hemophiliacs, in whom there may be an increased incidence, possibly reflecting true biologic differences. One hopes that more detailed analysis of differences between these groups may shed light on the pathophysiologic mechanisms underlying these neoplasms.

There are two distinct clinical subsets of patients with AIDS lymphoma: those who present with a parenchymal mass lesion exclusively restricted to the CNS, and patients who have systemic involvement that may or may not also include the CNS [22.7]. The patients who present with primary CNS lymphoma typically have more advanced stage HIV disease, lower CD4 counts, and a higher frequency of opportunistic infections or other AIDS-defining illness. The lymphomas in these patients are virtually all of immunoblastic type and they are associated with the presence of the EB virus genome. The EB virus latency genes expressed in these tumors EBNA2 through 5 and LMP1 and 2 are similar to those seen in post-transplant lymphomas.

In contrast, the systemic lymphoma patients tend to have higher CD4 counts and a lower incidence of prior AIDS-defining illnesses [22.7]. Immunoblastic lymphoma is not the only subtype and the EB genome is less frequently found. Furthermore, the EB virus latency genes expressed within this subset of lymphoma vary, about half of the cases expressing EBNA2 and virtually all expressing EBNA1.

Summarized in [22.8] are 12 different studies which have reviewed the histologic subtypes of lymphomas in AIDS patients. The great majority are of large cell, immunoblastic or anaplastic large cell type, but fully a third of patients have neoplasms with a small non-cleaved cell or Burkitt-like histology. This spectrum of histologic types differs not only from age-matched controls in the world population, but also from immunosuppressed transplant patients.