HIV- and AIDS-Associated Cancers

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One of the most significant world epidemics in history, HIV/AIDS, has been a research priority since its discovery in 1981. This review article provides an update on HIV/AIDS, with a specific focus on the diagnosis and care of patients with HIV- and AIDS-associated cancers.

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Since HIV/AIDS was first identified in 1981, researchers have established several significant breakthroughs in treatment (AIDSinfo, 2013; Centers for Disease Control and Prevention [CDC], 2012; Office of AIDS Research Advisory Council [OARAC], 2013). In addition, activists, policy makers, and the healthcare establishment have worked to better characterize those at risk for HIV infection, improve testing, clarify the HIV/AIDS diagnoses, and mobilize systems to improve patient access to care and treatments. The results of these efforts have made inroads in the myriad challenges presented by the epidemic. HIV attacks the immune system’s white blood cells, thus jeopardizing the body’s ability to fight infections and certain types of malignancies. An estimated 33.2 million people were HIV-positive (HIV+) in 2012 (Nokta, 2011). By the time a person is given an AIDS diagnosis, the HIV infection is in an advanced stage (Malfitano, Barbaro, Perretti, & Barbarini, 2012; National Cancer Institute [NCI], 2013a). Figure 1 shows AIDS diagnoses and deaths in the United States from 1985–2009.

In addition to prevention strategies, other key strategies to address the HIV/AIDS epidemic have included the development of effective antiretroviral drugs and therapies for those already affected. Coupled with drug development have been efforts to ensure patient access to drugs, the prompt start of treatment, and patient compliance when taking medications long-term.

Starting HIV+ treatment early may have a number of potential benefits, including a decreased risk for the occurrence of HIV-associated nephropathy, liver disease progression from hepatitis B or C, cardiovascular disease, malignancies, and neurocognitive decline (OARAC, 2013). In addition, early treatment may decrease the risk of sexual, blood-borne, and mother-to-child transmission of HIV (OARAC, 2013). The improved effectiveness of treatment, anchored by highly active antiretroviral therapy (HAART), began in 1996. Data have shown steady therapeutic progress toward suppressing the virus and slowing the development of AIDS and AIDS-related malignancies (NCI, 2012b; Nokta, 2011). For more information about U.S. Food and Drug Administration (FDA)-approved HAART agents, visit http://bit.ly/tvXVTc.

A number of AIDS-associated malignancies are termed AIDS-defined cancers and non-AIDS-defined cancers. In fact, about 80,000 patients with AIDS were diagnosed with cancer from 1991–2005 (Shiels et al., 2011). As HAART has reduced the number of deaths from AIDS, the HIV+ population has grown and aged. The fastest-growing proportion of HIV-infected individuals is the group aged older than 40 years. Therefore, patients who are HIV+ now are developing cancers common of aging, referred to as non–AIDS-defined cancers (NCI, 2011; Shiels et al., 2011). Diagnoses of non-AIDS-defining cancers have increased threefold from 1991–2005 (Shiels et al., 2011). With HAART as an initial strategy for treatment, cancer is now the most common cause of death in patients who are HIV+ (Notka, 2011).

AIDS-Defined Cancers

People with AIDS may develop specific cancers, particularly those caused by viruses, such as Kaposi sarcoma (KS) and cervical cancer, or cancers of the immune system (i.e., lymphomas). Those cancers usually are more aggressive and difficult to treat in patients with AIDS because of the morbidities caused by these viruses (e.g., human herpesvirus, Epstein Barr virus [EBV], human papillomavirus [HPV], hepatitis B virus, hepatitis C virus [HCV]). Researchers have implicated these viruses, at the very least, as contributors to the metabolic environment that prompts these cancers to occur (NCI, 2011; Nokta, 2011).

Kaposi Sarcoma

Along with non-Hodgkin lymphoma (NHL), KS is one of the most common cancers in the U.S. AIDS population (Shiels et al., 2011). In the United States, most cases of epidemic KS have been diagnosed in HIV+ individuals from the risk groups of homosexual or bisexual men (NCI, 2012b). HAART protocols have greatly reduced the incidence of KS in the HIV+ population and increased overall survival; however, the risk of patients who are HIV+ to be diagnosed with KS still is higher than for the general population (Malfitano et al., 2012; NCI, 2011).
KS appears as skin lesions and lesions in the lining of the mouth, lymph nodes, stomach, intestines, lungs, liver, and spleen. KS lesions in light-skinned people are round brown, reddish, or purple spots; in dark-skinned people, the spots are more pigmented (NCI, 2012b). FDA-approved drugs to treat AIDS-related KS include various liposomal formulations of doxorubicin, daunorubicin, and paclitaxel (NCI, 2012b, 2013b). In the later stages of KS, life-threatening infections, manifested as fever, weight loss, and diarrhea, are common and are treated with antimicrobials (NCI, 2011).

AIDS-Related Lymphomas

AIDS-related lymphomas typically are aggressive B cell tumors, which include diffuse large B cell lymphoma, B cell immunoblastic lymphoma, and small nonecleaved lymphoma (either Burkitt or Burkitt-like) (NCI, 2012a). The HIV-associated aggressive B-cell lymphomas also include primary central nervous system lymphoma (PCNSL), primary effusion lymphoma, plasmablastic multicentric Castleman disease, and Hodgkin lymphoma (NCI, 2012a). Patients who are HIV+ and have aggressive lymphoma usually present with advanced-stage disease that is frequently extranodal, typically appearing in the bone marrow, liver, meninges, and gastrointestinal tract (NCI, 2012a). HAART as treatment for patients who are HIV+ has contributed to much of the decline in incidence of HIV-associated lymphomas (Malfitano et al., 2012).

Non-Hodgkin lymphoma: In the United States, NHL is the other most common cancer in the AIDS population (Shiels et al., 2011). The diagnosis of AIDS precedes the onset of NHL in about 57% of patients who are HIV+, but the diagnosis of AIDS is made at the time of the diagnosis of NHL in 30% of patients (NCI, 2012a). In patients who are HIV+, HAART has contributed to the decreasing risk of advancement to NHL, in addition to increasing overall survival. In one study of NHL in the HIV/AIDS population, the decline in incidence was estimated at 42% from 1992–1996 to 1997–1999. Even so, HIV can develop resistance to HAART protocols over time, prompting malignancies to develop (NCI, 2011).

Standard NHL treatment protocols include cyclophosphamide, doxorubicin, etoposide, prednisone, vincristine, cyclophosphamide, and rituximab (Malfitano et al., 2012). Rituximab, although controversial, has been shown to be effective as a treatment option (Wyen et al., 2012). NHL treatment also includes prophylaxis for opportunistic infections and rapid recognition and treatment of infections.

Primary central nervous system lymphoma: PCNSL is a rare variant of extranodal NHL that accounts for 1%–5% of all primary brain tumors and 1% of all lymphomas. An estimated 20% of all NHL cases in patients with AIDS are diagnosed with PCNSL (González-Aguilar & Soto-Hernández, 2011). Patients with AIDS-related PCNSL appear to have more severe underlying HIV-related disease than patients with systemic lymphoma.

Patients with AIDS have a 3,600-fold risk to develop PCNSL compared to the general population (González-Aguilar & Soto-Hernández, 2011). AIDS-associated PCNSL is linked to infection from EBV; therefore, treatment includes ganciclovir (González-Aguilar & Soto-Hernández, 2011). Patients usually have evidence of far-advanced AIDS, are severely debilitated, and present with focal neurologic symptoms such as seizures, changes in mental status, and paralysis (NCI, 2012a).
PCNSL incidence has decreased with HAART and aggressive initial treatment targeted to the malignancy—high-dose methotrexate or whole-brain radiotherapy alone or combined therapies (González-Aguilar & Soto-Hernández, 2011). Other chemotherapy treatment protocols include procarbazine, thiopeta, bleomycin, doxorubicin, cyclophosphamide, vincristine, and dexamethasone accompanied by granulocyte macrophage-colony-stimulating factors (NCI, 2012a).

Cervical Cancer

Although HAART has contributed to the lower incidence of KS and NHL among patients who are HIV+, it has not reduced the incidence of cervical cancer, which has remained essentially unchanged in this population (NCI, 2011). Those diagnosed with cervical cancer have a low CD4 count and a higher prevalence of HPV infection; their disease is more advanced when diagnosed (Malfitano et al., 2012). Treatment for cervical cancer is surgery, then concomitant chemoradiotherapy with cisplatin-based protocols for advanced disease.

Non–AIDS-Defined Cancers

Although the incidence of some AIDS-defined cancers has decreased in the United States, non–AIDS-defined cancers are increasing as patients with HIV and AIDS live longer and are relatively healthier than in the past (Nokta, 2011; Shiels et al., 2011).

The non–AIDS-defined malignancies include anal, liver, and lung cancers, as well as Hodgkin lymphoma (see Table 1). The rising incidence of these cancers in the HIV+ population is considered multifactorial and is not well understood. In addition to HAART extending the lives of patients who are HIV+, non–AIDS-defined cancer incidence is related to standard cancer environmental and behavioral risk factors that may be more prevalent in the HIV+ population (e.g., smoking, alcohol abuse, exposure to hepatitis virus) (Malfitano et al., 2012, NCI, 2011).

Implications for Nursing

Nurses have many broad and specific opportunities to make an impact with the HIV/AIDS patient population, including cancer prevention and screening related to patients with HIV/AIDS at higher risk for certain malignancies. For example, because HIV-infected women have a higher risk of developing cervical cancer, regular screening for cervical cancer is particularly important for this population (NCI, 2011). Patient and community teaching about HIV risk factors, testing, diagnosis, treatments, and access to care have increased. However, vigilance and heightened advocacy based on facts are needed to reduce the stigma that HIV/AIDS still holds in society (NCI, 2012h). Specific patient teaching related to HIV status and AIDS can be used. For example, because HIV-infected people have a higher risk for developing lung cancer, they should not smoke. Therefore, smoking cessation initiatives are crucial (Shiels et al., 2011). The higher incidence of liver cancer among HIV-infected people appears to be related to hepatitis virus infection (particularly HCV) and alcohol abuse or dependence. Therefore, patients who are HIV+ should know their hepatitis status (NCI, 2011). Finally, HAART and chemotherapy interactions remain ill defined, so nurses can help focus attention on potential interactions when patients are on combined treatment protocols (NCI, 2011; Rudek, Flexner, & Ambinder, 2011). Figure 2 reviews components of the National HIV/AIDS Strategy, which nurses can use as a guide in their care of patients with HIV/AIDS.

1. Reduce new HIV infections.
   a. Lower the annual number of new infections by 25%.
   b. Reduce HIV transmission by 30%.
   c. Increase the percentage of people living with HIV who know their serostatus from 79% to 90%.

2. Increase access to care and improve health outcomes for people living with HIV.
   a. Increase the proportion of newly diagnosed patients linked to clinical care from 65% to 85%.
   b. Increase the proportion of Ryan White HIV/AIDS Program clients who are in continuous care from 73% to 80%.
   c. Increase the number of Ryan White clients with permanent housing from 82% to 86%.

3. Reduce HIV-related health disparities.
   a. Improve access to prevention and care services for all Americans.
   b. Increase the proportion of HIV-diagnosed gay and bisexual men with undetectable viral load by 20%.
   c. Increase the proportion of HIV-diagnosed Blacks with undetectable viral load by 20%.
   d. Increase the proportion of HIV-diagnosed Latinos with undetectable viral load by 20%.


TABLE 1. Increased Risks of AIDS- and Non–AIDS-Defined Cancers

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Increased Risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS-defined</td>
<td></td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>3,640 times</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>77 times</td>
</tr>
<tr>
<td>Cervical</td>
<td>6 times</td>
</tr>
<tr>
<td>Non–AIDS-defined</td>
<td></td>
</tr>
<tr>
<td>Anal</td>
<td>29 times</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>11 times</td>
</tr>
<tr>
<td>Liver</td>
<td>5 times</td>
</tr>
<tr>
<td>Lung</td>
<td>3 times</td>
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</tbody>
</table>

*Compared to individuals not infected with HIV.

Note. Based on information from Malfitano et al., 2012; National Cancer Institute, 2011, 2013a; Nokta, 2011; Shiels et al., 2011.

Conclusion

Characteristics of the HIV/AIDS epidemic are the basis for HIV+ and AIDS patient care. Among key strategies to address the epidemic have been the development of antiretroviral drug protocols, prompt and compliant treatment of patients who are HIV+, and treatment of AIDS-associated malignancies. Knowing the trajectory of the HIV/AIDS epidemic and its associated treatment strategies provides many opportunities for nurses to make an impact on the HIV/AIDS population.

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