HIV Infections- Acquired Immuno Deficiency Syndrome Malignancies

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Abstract

Persons infected with HIV are at increased risk for all cancers known as HIV infections or AIDS malignancies. Acquired immune deficiency syndrome (AIDS) is a disease of the immune system caused by human immunodeficiency virus (HIV). Treatment for HIV/AIDS can slow the course of the disease but there is no known cure or vaccine. Infection with HIV weakens the immune system and reduces the body's ability to fight infections that may lead to cancer. Three of these cancers are known well, Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer. Kaposi’s sarcoma (KS) is a multicentric vascular tumor. Non-Hodgkin’s lymphoma is cancer of the lymphoid tissue. Human Papilloma viruses which cause cervical cancer are not-enveloped double stranded DNA viruses that infect preferentially epithelial cells.

Keywords: CD4+ cells; Kaposi sarcoma; Non-Hodgkin lymphoma; cervical cancer; Human Papilloma Virus; Natural killer

Abbreviations: HIV: Human Immunodeficiency Virus; AIDS: Acquired Immune Deficiency Syndrome; KS: Kaposi Sarcoma; ARVs: Antiretroviral Drugs; HAART: Highly Active Antiretroviral Therapy; ART: Antiretroviral Therapy; HPV: Human Papilloma Virus; NHL: Non-Hodgkin Lymphoma; NK: Natural Killer Cells; cART: Combination Antiretroviral Therapy; KSHV: Kaposi’s Sarcoma-Associated Herpes Virus

Introduction

Acquired immune deficiency syndrome (AIDS) is a disease of the immune system caused by human immunodeficiency virus (HIV). HIV is a virus that gradually attacks immune system cells. As HIV progressively damages these cells, the body becomes more vulnerable to infections, which it will have difficulty in fighting off. Very advanced HIV infection that a person is said to have is said to be AIDS. A person with HIV is highly vulnerable to life-threatening conditions because HIV severely weakens the body's immune system. When HIV infection causes symptoms and specific disease syndromes, the disease is called AIDS [1,2]. By December 2000, 21.8 million people worldwide had died of the disease, including more Americans (438,795) than died in World War I and World War II combined [3]. The spread of the disease in Haiti was postulated to be a result of voodoo practices rather than heterosexual sex [4]. Today, most human immunodeficiency virus (HIV) infections in the world derive from heterosexual transmission, a fact that is still overlooked by many. HIV is transmitted in many ways, such as anal, vaginal or oral sex, blood transfusion, contaminated needles, exchange between mother and baby during pregnancy, childbirth, and breastfeeding [5]. It can be transmitted by any contact of a mucous membrane or the bloodstream with a bodily fluid that has the virus in it, such as the blood, semen, vaginal fluid, preseminal fluid, or breast milk from an infected person [6]. HIV infection in the age group of 15-30 years is responsible for over 65% of all new cases disease in India [7]. Sexual assaults in children were reported all over and only little HIV prophylaxis was done. The Red Cross War Memorial Children’s Hospital (RCWMCH) in Cape Town has the only trauma unit in Africa dedicated to the care of children under the age of 13 years and in 2000, became the first hospital in South Africa to routinely prescribe HIV post-exposure prophylaxis (HIV PEP) to children who are victims of sexual assault [8]. Risky drug use behaviors such as injection, as well as risky sexual behaviors such as having multiple sexual partners, can put drug users at risk of both acquiring and transmitting HIV and other blood-borne diseases [9].

Treatment for HIV/AIDS can slow the course of the disease but there is no known cure or vaccine. Antiretroviral treatment reduces both the deaths and new infections from HIV/AIDS, but these drugs are expensive and the medications are not available in all countries [10]. Risk reduction is occurring more frequently through the modification of sexual or drug-use behavior than through its elimination [11]. HIV-infected patients may develop a variety of muscular disorders such as polymyositis, inclusion-body myositis, myopathy secondary to HIV therapy, HIV wasting syndrome, and rhabdomyolysis [12]. Opportunistic infections are common in people with AIDS [13]. These infections affect nearly every organ system. People with AIDS also have an increased risk of developing various cancers such as Kaposi’s sarcoma, cervical cancer, and cancers of the immune system known as lymphomas. Additionally, people with AIDS often have systemic symptoms of infection like fevers, [14] sweats, swollen glands, chills, weakness, and weight loss [15,16]. Risk factors contributing to virologic failure and drug resistance [17,18] are more frequent.

People infected with HIV have a substantially higher risk of some types of cancer compared with uninfected people of the same age [19]. Infection with HIV weakens the immune system and reduces the body’s ability to fight infections that may lead to cancer. Traditional risk factors [20] play a significant role in the increased risk of non-AIDS-defining malignancies for HIV-infected individuals, but do not entirely explain the excess cancer risk. Non-AIDS-defining malignancies account for more morbidity and mortality than AIDS-defining malignancies in the antiretroviral therapy era [21,22]. The fast growth of HIV resistance to
antiretroviral drugs (ARVs) is one of the main limitations in treating the disease [23,24]. Antiretroviral therapy is effective in preventing perinatal HIV transmission but may be associated with adverse long-term side effects in exposed infants [25,26]. Ability of the patients to both consistently take the drugs without fail at exactly or approximately the same times of the day depends on the individuals' frame of mind, his/her family members support, as well as people around them and the community at large [27]. The AIDS virus is a neurotropic virus which is present in approximately ten percent of cases of HIV infection [28]. Natural killer (NK) cell function was investigated in Malaysian HIV patients beginning antiretroviral therapy (ART) with advanced immunodeficiency [29,30]. Nowadays Human Immunodeficiency Virus (HIV) is considered as a chronic disease because individuals have the potential to live upward of 20 years on highly active antiretroviral therapy [31].

AIDS Malignancies

Persons infected with HIV are at increased risk for all cancers known as HIV infections [32] are suspected to have an infectious diseases, an effect believed to be primarily mediated by lowered host immunity via the depletion of CD4+ cells [33]. Three of these cancers are known as "acquired immunodeficiency syndrome (AIDS)-defining cancers" or "AIDS-defining malignancies": Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer [34]. People infected with HIV are several thousand times more likely than uninfected people to be diagnosed with Kaposi sarcoma, at least 70 times more likely to be diagnosed with non-Hodgkin lymphoma, and, among women, at least 5 times more likely to be diagnosed with cervical cancer. People infected with HIV are at least 25 times more likely to be diagnosed with anal cancer than uninfected people, 5 times as likely to be diagnosed with liver [35] cancer, 3 times as likely to be diagnosed with lung cancer, and at least 10 times more likely to be diagnosed with Hodgkin lymphoma [34]. Despite the impact of combination antiretroviral therapy (cART) on HIV-related mortality, malignancy remains an important cause of death in the current era [36]. Although the advent of cART has resulted in reductions in the incidence of Kaposi's sarcoma and non-Hodgkin's lymphoma, non-AIDS-defining malignancies present an increased risk for HIV-infected patients [37,38]. Although the incidence of AIDS-defining cancers (Kaposi sarcoma, non-Hodgkin lymphoma, and invasive cervical carcinoma) [39] has decreased with the use of antiretroviral therapy, non-AIDS-defining cancers have increased in HIV-infected patients, as suggested by numerous studies. These malignancies have increased as has the proportion of mortality associated with non-AIDS-defining malignancies in HIV-infected patients [40]. Some studies have shown that HIV increases susceptibility to such cancers through the direct effects of the virus (genetic instability and increased susceptibility to carcinogens, for instance) and long-term immunosuppression [41]. Effective screening and treatment options need to be established. It is crucial that we get a better understanding of the interactions among chemotherapy, HAART [42,43,44] (Highly active antiretroviral therapy) and other medications used by HIV-infected patients [45].

Kaposi Sarcoma (KS): Kaposi's Sarcoma–Associated Herpesvirus (KSHV)

Kaposi's sarcoma (KS) is a cutaneous tumor, in some cases also found in visceral tissue [46]. The etiologic agent of KS is Kaposi's sarcoma-associated herpesvirus (KSHV) or human herpesvirus 8. AIDS-associated KS arises in the setting of poor immunemediated control of this γ-herpesvirus [47]. Classic Kaposi's sarcoma occurred on the lower limbs and lacked visceral involvement [48]. KSHV was identified in Kaposi's sarcoma lesions from human immunodeficiency virus, positive (HIV+)[49] and negative (HIV-) individuals [50]. KSHV infection is uncommon in some populations in the Western Hemisphere and that KSHV is largely confined to patients with AIDS-associated KS [51]. Kaposi's sarcoma (KS) is a multicentric vascular tumor caused by herpesvirus type 8. It can occur in classic, AIDS-associated, endemic, and iatrogenic forms. The tumor cells have a spindle shape, [52] resembling smooth muscle cells, fibroblasts, and myofibroblasts. The symptoms include cutaneous lesions which are asymptomatic purple, pink, or red macules that may coalesce into blue-violet to black plaques and nodules, sometimes edema is also seen. Occasionally, nodules fungate or penetrate soft tissue and invade bone. Mucosal lesions appear as bluish to violaceous macules, plaques, and tumors. GI lesions can bleed, sometimes extensively, but usually are asymptomatic. KSHV is a widespread virus in urogenital tissues of healthy individuals [53]. KS is more common among individuals who acquired HIV infection by sexual transmission rather than parenterally, and that the incidence of this neoplasm is declining over time [54]. The three major diseases associated with the KSHV infection are Kaposi Sarcoma, Primary effusion Lymphoma and Multicentric Castleman Disease [55,56]. Highly active antiretroviral therapy (HAART) for HIV infection restores immune function and reduces Kaposi's sarcoma incidence [57,78].

Non-Hodgkin Lymphoma (NHL): HIV-Associated Non-Hodgkin Lymphoma

Non-Hodgkin Lymphoma (NHL) is a well-recogized complication of infection with the human immunodeficiency virus (HIV) [58]. NHL is one of the common cancers in urban populations in India; it is the 6th most common cancer in the US. NHL is not one disease but it's rather lymphocyte cancers. Incidence increases with age (median age, 50 yr). It is more common in India compared to Australia and western countries [59]. Most lymphomata are of high-grade B-cell origin, with large cell immunoblastic lymphoma and small, noncleaved cell lymphoma dominant histologic types [60]. Non-Hodgkin's lymphoma is cancer of the lymphoid tissue, which includes the lymph nodes, spleen, and other organs of the immune system. Symptoms include Night sweats (soaking the bed sheets and pajamas even though the room temperature is not too hot), Fever and chills that come and go, Itching, Swollen lymph nodes in the neck, underarms, groin, or other areas and Weight loss [61,62]. AIDS-NHL is almost invariably derived from B cells's-12, [63]. They usually present as a systemic NHL, although the gastrointestinal (GI) tract and the central nervous system (CNS) represent the primary site of the tumor in a significant fraction of cases. AIDS-NHL are associated with multiple genetic lesions that involve both proto-oncogenesis and tumor suppressor genes and may accumulate in the relatively short period of time (4 to 6 years) between human immunodeficiency virus infection and AIDS-NHL development. These genetic lesions differ in the various AIDS-NHL subtypes, suggesting the involvement of distinct molecular pathway [64]. An increased risk arises from the complex combination of immunosuppression and inflammatory activation. Other factors such as possible effects of HIV insertional mutagenesys are still unknown, but have been proposed [65]. The prognosis of HIV-NHL was poor, despite a high response rate, owing to aggressive tumor behavior, increased hematomal toxicity and a high rate of opportunistic infections. Historically, patients with NHL and AIDS have been more likely to present with extranodal NHL and high grade histological findings, they have been less likely to respond to chemotherapy, with shorter overall survival [66]. Inappropriate treatment and inability to maintain dose density and intensity in the
background of aggressive disease are determinants of poor response to therapy [67].

Cervical Cancer: HIV-Associated Human Papilloma Virus

Invasive cervical cancer in HIV-infected women is also considered AIDS-defining cancer; it is caused by Human Papilloma virus [68]. Human Papillomavirus (HPV) infection is a necessary factor in the development of almost all cases of cervical cancer [69]. HPV silently grows in the cervix and later develops to invasive cervical cancer. HPV related cell changes are related to the functioning of the immune system thus when the immune function declines or CD4 count lowers in HIV-positive people the HPV cell changes increases [71]. Human Papilloma viruses are non-enveloped double stranded DNA viruses that infect preferentially epithelial cells [72]. HPV-infected people have greater diversity of Human Papilloma virus types and also greater prevalence of multiple HPV types. Human Papilloma virus is sexually transmitted [73]. HPV can cause Genital Warts, Genital warts usually appear as a small bump or groups of bumps in the genital area. They can be small or large, raised or flat, or shaped like a cauliflower [74]. The genital HPV types can be divided into three groups as “high-risk” or “carcinogenic” associated with a high relative risk of cervical cancer; “low-risk” types associated with benign epithelial proliferations in the genital area, but not associated with invasive cervical cancer and a group of six types that is classified as “probably carcinogenic” since there is limited data associating these HPV types with cervical cancer [75]. At least 15 types of HPV have been associated with cervical cancer, but current HPV vaccines confer only type-specific immunity [76]. Cervical cancer is largely preventable through screening programmes designed to diagnose and treat cervical lesions that may progress to invasive cancer [77].

Conclusion

HIV is very much prevalent in India which causes AIDS. Majorly HIV leads to various cancer diseases. The major three diseases are the Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer. There is general agreement that KSHV called as Kaposi Sarcoma associated Herpes virus is sexually transmitted among homosexual men although the precise mode of transmission is still hotly contested. KSHV has been associated with a number of other diseases. The presence of KSHV identifies a population at highest risk of the disease. An increased risk arises from the complex combination of immunosuppression and inflammatory activation in Non-Hodgkin lymphoma. This is one of the common cancers occurring in India. Human Papilloma virus leads to HIV infection called cervical cancer which is predominant in women. All the three diseases are mostly transmitted through sexual transmission.

References


