

Hodgkin disease in the HIV setting

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ABSTRACT

Recent studies have shown an increased incidence of Hodgkin disease in individuals with Human Immunodeficiency Virus (HIV), especially among intravenous drug users and homosexual men. These patients have a poorer prognosis when compared to non-infected individuals with Hodgkin disease. They tend to present with more advanced disease, with more unfavorable histology, and have a poorer response to chemotherapy. Highly active antiretroviral therapy may permit the use of aggressive chemotherapeutic regimens that were overly toxic in the previous era. However, relapse rates remain high. With the use of various combinations of chemotherapeutic agents, median survival in patients with HIV-associated Hodgkin disease ranges from only 12 to 18 months. Given the shared clinical features of these patients, familiarity with its presentation and early diagnosis may improve survival.

Keywords

Hodgkin disease; HIV; AIDS

INTRODUCTION

The immune system is believed to play an important role in the development of cancers,¹ therefore it is no surprise that immunodeficiency increases the risk of certain types of cancers. Kaposi sarcoma (KS) and Non Hodgkin Lymphoma (NHL) are the most common malignancies associated with Acquired Immune Deficiency Syndrome (AIDS). In fact, they are considered to be among the so-called 'AIDS defining illnesses'. Although Hodgkin Disease (HD) is not part of the US Centers for Disease Control and Prevention (CDC) definition of AIDS, there is increasing evidence of an association between HD and HIV infection. KS and NHL have a much higher relative risk of development in HIV infected patients (73,000 and 165 respectively). However, studies have established an association between HD and HIV infection with a relative risk of 8.² More than 300 cases have been reported mainly from European countries, most of these patients being homosexual men and/or intravenous drug users.³ Heightened knowledge among clinicians about epidemiology, symptoms, and treatment options may help improve the poor survival in these patients.

Results from cohort studies of homosexual men enrolled in the San Francisco City Clinic⁴ and in the Multicenter AIDS Cohort Study⁵ conveyed that Hodgkin's disease is more prevalent among HIV- infected homosexual men compared to the general population. Reports from the Italian Cooperative Group for AIDS-Related Tumors⁶ and from Spanish researchers Rubio *et al.*⁷ suggest that intravenous drug users were at

Neka Dunlap completed her undergraduate education at the University of California, Berkeley where she received a BA in Psychology. While writing this article, she was influenced by an African female patient with HIV associated Hodgkin's disease who she encountered during her third year internal medicine rotation. As an African American woman in medicine, she feels that it is her duty to educate as many people as possible about the AIDS epidemic.

exceptionally high risk of developing HIV associated HD. In these studies, the incidence of HD in HIV increased with AIDS diagnosis, suggesting that the probability of developing HD is proportional to the degree of immunosuppression. These studies also showed an association between Epstein-Barr virus (EBV) and HIV-HD 70-100 per cent. Although the etiology of HIV-HD remains unknown, EBV infection is seen as important in its pathogenesis.^{8,9}

Clinical presentations of Hodgkin disease in the HIV setting

Hodgkin disease in HIV infected patients tends to present differently from that in non HIV infected patients. Mediastinal disease is less frequent and the disease often presents with B symptoms which include fever, night sweats, and weight loss.¹⁰ Advanced stages (stages III and IV) at diagnosis as well as extranodal involvement are also typical in HIV positive patients.^{4, 6-7, 10-15} Among the extranodal sites, bone marrow and gastrointestinal (GI) involvement were commonly reported, which usually manifested itself as colicky abdominal pain and/or bright red blood per rectum. Other unusual extranodal sites in HIV infected patients include skin, central nervous system, tongue, and lung. Prognostically poorer subtypes such as lymphocyte-depleted and mixed-cellularity HD are the most common among HIV patients as opposed to nodular sclerosis which is the most common in immunocompetent patients in the United States.¹⁶⁻¹⁹ In addition, HIV infected individuals present at a younger age with HD with the majority falling between the ages of 35 and 49 years compared to the bimodal age distribution observed with non HIV-infected individuals. Hodgkin disease should be thought of and ruled out in any HIV-infected patient with low CD4 counts, B symptoms, and GI complaints.

Hodgkin disease and immunosuppression

Hodgkin Lymphoma tends to be more common in individuals with low CD4 cell counts.²⁰ The majority of people with HIV who have developed HD have had CD4 cell counts around 200 to 300 cells/mm³. It is therefore suggested that reconstituting the immune system with HAART will aid in controlling the lymphoma. Dr Ribera and colleagues²¹ reported that patients with HIV-related Hodgkin's disease who receive HAART have a better response to therapy and improved survival compared with similar patients who have not received HAART. The Spanish researchers studied 45 patients with HIV associated Hodgkin disease. Patients were divided into two groups; those who received HAART before or started HAART shortly after Hodgkin disease diagnosis, and those who had not received HAART or started HAART after completing treatment for Hodgkin disease. The researchers found that among patients who received HAART before or shortly after Hodgkin disease diagnosis, the response rate to treatment was significantly higher than in the other group. Multivariate analysis showed that only HAART was independently associated with a complete response to treatment (odds ratio 5.3, p = 0.026). Both disease-free and overall survival were also significantly better among patients who had received HAART. Multivariate analysis found HAART predicted better survival in these patients (odds ratio 8.6, p = 0.002).

Prognosis

In non HIV- infected patients with advanced stage III or IV disease, HD is potentially curable with complete remission rates of 70 to 80 per cent with ABVD (doxorubicin, bleomycin, vinblastin, dacarbazine) and relapse-free long-term survival in 60 to 70 per cent of cases.²² The prognosis of HD in HIV population is significantly worse by comparison. In patients with HIV-HD, complete response rates to a variety of combination chemotherapeutic regimens have ranged from 20 to 100 per cent and median survivals generally in the 12 to 18-month range.^{6-7, 12, 16, 23-24}

Treatment

The optimal treatment regimen for Hodgkin disease in the setting of HIV infection remains unclear. For advanced-stage disease, ABVD was shown to be superior to chlormethine, vincristine, procarbazine, and prednisolone therapy (MOPP) in freedom from progression in two trials^{22,25} and in overall survival in one trial.²⁶ Table I contains chemotherapeutic combinations and outcomes reported in HIV positive patients with Hodgkin disease. For those individuals with severe immunocompromise, consideration may be given to dose-modified standard regimens. Autologous hematopoietic stem cell transplantation and granulocyte colony-stimulating factor (G-CSF) has been determined safe and effective when used adjunctively with chemotherapy. Both methods help rebuild the immune system by replacing cells that are killed during the course of drug treatment.^{24,28}

CONCLUSION

Recent studies suggest an elevated incidence of Hodgkin Disease in the setting of HIV when compared to the HIV negative population. The presentation and prognosis of HD differ greatly between HIV-infected and non-infected patients. Because the prognosis in HIV associated HD is poor, familiarity of how it presents and early diagnosis can help improve the survival. Although various treatment regimens have been studied, data regarding the most efficacious combination are still lacking. As the incidence rate of HIV infection remains steady and people are living longer with the disease, research on concomitant infections and malignancies in the setting of HIV specifically are becoming more crucial.

Table I. Summary of treatment and outcomes in studies of HIV associated Hodgkin's disease

Reference	Sample size	Chemotherapy	CR ¹ (%)	Median Survival (Months)
6	21	MOPP ² alone or MOPP/ABVD ³	65-MOPP/ABVD 46-MOPP alone	15
23	17	Epirubicin, vinblastin, & bleomycin	53	11
24	21	ABDV and G-CSF ⁴	56	18
27	20	Stanford V ⁵ plus antiretroviral therapy	80	18
29	12	BEACOPP ⁶	100	Could not be calculated

Key to Table I

- CR Complete Remission
- ² MOPP chlormethine, vincristine, procarbazine, and prednisolone
- ³ ABVD doxorubicin, bleomycin, vinblastine, and dacarbazine
- ⁴ G-CSF granulocyte colony-stimulating factor
- ⁵ Stanford V mechlorethamine, doxorubicin, vinblastine, vincristine, bleomycin, etoposide, and prednisolone
- ⁶ BEACOPP bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone

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ARTICLE : REVIEW

Telemedicine: rural health and beyond

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Rural health care: a global problem

In a recent televised open debate program in Nepal, people from Achham, a remote district, complained that a doctor was at service in their district hospital for hardly 6 months in the last 6 years. The Public Service Commission of Nepal, which is responsible for the recruitment of doctors in such governmental hospitals, never gets enough applicants in the first place and the situation gets progressively worse with every further step such as the examination and appointment to the vacant posts at such remote hospitals. The country has seen a significant increase in the number of medical graduates after the 1990 re-establishment of democracy but there is still a lack of doctors in rural hospitals. Is the number of doctors serving in rural areas only a problem of developing countries? No, every country is facing this problem, the difference being only of magnitude. The geographical distribution of doctors is skewed towards urban areas in every country. In India, about 75 percent of modern (allopathic) medical practitioners are concentrated in urban areas¹, which cover 27 percent of the population. New Zealand also has the problem of retaining health care workforce in rural areas despite their enviable environment. The strain on the practitioners who remain threatens to compromise the availability and quality of the services they provide.² Even the United States of America is not free of such problems. Rural America has 20 percent of the nation's population but less than 11 percent of physicians.³ Similar to the scenario elsewhere in the world, the smaller and the more remote the place, the more difficult it is to attract and retain physicians in the USA.⁴

Developed countries like the USA and UK have partially solved the problem by recruiting doctors coming from developing countries in rural areas, but this has cost more to rural health of developing nations. To overcome the disparities in health care of rural people due to geographical barrier, telemedicine has been developed as a new system of health care.

Telemedicine: a promising solution

WHAT IS TELEMEDICINE?

Telemedicine is the delivery of health care services, where distance is a critical factor. Health care professionals use information and communication technologies to exchange information relevant to diagnosis, treatment and prevention of disease and injuries, research and evaluation, and the continuing education of health care providers. This is all in the interest of advancing the health of individuals and their communities.⁵

A BRIEF HISTORY OF TELEMEDICINE

Telemedicine has long been practised in one form or another, but in the real sense the development of telemedicine occurred in NASA's manned space flight program. "Telemedicine is really an outgrowth of the space program", as said Daniel Johnson former president of AMA⁵.

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During the early stage of manned space program NASA's scientists were concerned about the physiological ill effects of zero gravity on astronauts' vital functions. They developed a telemedical system to monitor vital functions in the astronauts (telemetry). Telemedical capabilities for diagnosis and treatment of medical emergencies, establishment of health maintenance systems and biomedical experimentation developed as the space program needed longer flight time and orbital stations.⁷ Then, being virtually out of the scene for some time, telemedicine resurged in the 1990s because of rapid expansion of information and telecommunication technologies. Telehealth and telemedicine have become the WHO strategy for achieving equal healthcare for all since 1997.⁸

HOW DOES TELEMEDICINE WORK?

Telemedicine basically works using information and communication technologies in various forms and for various purposes. And accordingly are the services it provides.

- **Teleconsultation:** General Practitioner or any trained health care worker in the rural area transfers the patient's data, including images, through the Internet to an expert (consultant) for a second opinion. The expert, based on the information, can make diagnosis and write a prescription for the patient and relay it back to the patient. Through video conferencing, live interaction between the two parties can be organized and the health care worker can elicit the required information and perform examination of the patient as per the need of the expert.

- **Teleradiology:** In a rural area, specialist opinion can be sought from an expert radiologist in a city by transmission and display of digital radiological images. These include x-rays, CT scan and MRI images.

- **Telepathology:** Similar to the concept of teleradiology, here the histopathological diagnosis is made by an expert seeing the digital image of the slide sent via the internet.

- **Telehome nursing:** It is mostly applied to the patients suffering from chronic illness, in place of the traditional home visits. Here the patients are monitored and nursed from distance away while they are at home using electronic devices to measure the clinical parameters and advised via videophone.

- **Telesurgery:** Telesurgery is probably the most amazing development made possible by the modern day technology. Success in this regard came in 2001, when surgeons in New York performed