HIV INFECTION, ACQUIRED IMMUNODEFICIENCY SYNDROME, AND THE HEART

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THE HUMAN IMMUNODEFICIENCY VIRUS (HIV) epidemic continues in most parts of the world and it eventually results in progressive immunodeficiency, clinically defined as the acquired immunodeficiency syndrome (AIDS). The morbidity and mortality associated with HIV disease primarily involve the lymphoreticular, pulmonary, central nervous, and alimentary systems. However, cardiac involvement is an important complication of AIDS that is being reported in 28% to 78% of such patients.1-6 Based on published American and European reports, it is predicted that between 2860 and 5032 AIDS patients in the United States will develop clinical heart disease each year for the next several years.7 During this period, between 324 and 3465 patients can be expected to die of cardiac complications of AIDS each year. Symptomatic heart disease has only been reported among AIDS patients and occurred in 6.5% to 6.8% of patients studied.1-7 However, at autopsy, cardiac dysfunction as a cause of death occurred in up to 6.3% of reported cases.8-13 As the number of patients with HIV infection increases and other causes of morbidity and mortality, such as secondary infection, become less of a problem because of effective treatment, cardiac disease due to HIV infection may become more familiar to all cardiologists.

Pathogenesis

Cardiac involvement in HIV-infected patients appears to be common, to occur during various stages of the disease, and to affect patients in all major risk groups.14 The natural history and association of cardiac dysfunction in an entire range of adult groups infected with HIV have been widely reported7,13-17 and attributed directly to HIV itself,18 cardiotoxic agents used to treat HIV or HIV-associated opportunistic infection,17,19 nutritional deficiency,20,21 neoplasm,5,8,9,14,22,23 activation of autoimmune process,10,17 or by means of a bystander effect.24 Catecholamine-induced myocarditis has been shown to contribute to AIDS-associated myocardial necrosis25,26 and nonbacterial thrombotic endocarditis which are rarely diagnosed before death.5 It has, however, also been reported that persons infected with HIV who have not yet developed AIDS are less likely to have pericardial effusion than are patients with AIDS.13,27

In several cross-sectional studies,13,14,28 left ventricular dilatation and/or wall motion abnormalities have been documented in 27% of HIV-infected patients without symptomatic heart disease, but 90% of these patients had HIV combined with an opportunistic infection and a CD4 lymphocyte count of less than 100/mm3.29 Such a combination is, by definition, AIDS syndrome. Furthermore, an interesting finding of circulating cardiac autoantibodies was reported in AIDS patients with cardiomyopathy but in none of the HIV-positive patients without opportunistic infection.30 In keeping with these findings, we have recently reported a much higher prevalence of cardiovascular abnormalities in HIV-infected patients in the presence of opportunistic infections.31 We have also shown that, when compared with HIV-infected subjects, patients with AIDS had a much stronger correlation between degree of immunosuppression and presence of cardiac involvement. It is therefore not unreasonable to
assume that HIV itself is not solely responsible for the development of AIDS-associated heart disease, but the opportunistic disease may have a significant pathognomonic role. Cardiac dysfunction occurs late in the course of AIDS but as the treatment of opportunistic infection becomes increasingly successful, HIV infection may result in more patients surviving to develop such pathology.

Myocardial Dysfunction

Echocardiographic features of dilated cardiomyopathy have been described in a wide range (16.6% to 41%) of patients with AIDS. However, the pathogenesis of left ventricular dysfunction in HIV-infected patients remains uncertain. Myocarditis, toxic agents, malnutrition, and tumor necrosis factor have all been suggested to be the cause of myocellular damage, but the HIV and coxsackie B viruses have only sporadically been directly demonstrated in the myocardium of HIV-infected patients.

Furthermore, left ventricular dysfunction and other cardiac abnormalities have been recently reported in HIV-seronegative patients with intercurrent infection. Although the etiology of left ventricular dysfunction in HIV-infected patients is probably multifactorial, a higher prevalence of dilated cardiomyopathy was reported in patients with more advanced disease and was more frequently observed in those patients with active opportunistic infection. Furthermore, the degree of immunosuppression in these patients, as manifested by the significantly lower total and percentage CD4 lymphocyte count, correlated strongly with the presence of echocardiographic features of dilated cardiomyopathy. Sepsis may present diagnostic difficulties, but patients in septic shock with reduced ejection-fraction and transient ventricular dilatation have normal-to-increased cardiac index when compared to HIV-infected patients.

Nondilated left ventricular systolic dysfunction has also been reported with higher incidence in HIV-infected patients with active opportunistic infections, neoplastic infiltration of the myocardium (Kaposi's sarcoma, non-Hodgkin's lymphoma), or idiopathic. In a study by Anderson and Virmani, the overall nondilated heart failure accounted for 13 of 42 (31%) cases of death among all HIV-autopsy patients. Isolated right ventricular dysfunction and dilatation were reported in 4% of HIV-infected subjects with opportunistic infection (recurrent pneumocystis carinii pneumonia and/or pulmonary disease) and in 4% without evidence of opportunistic infection.

Endocardial Manifestations

The frequency of infective endocarditis and myocardial abscess appears to depend upon the characteristics of each study population. It can involve all four valves, but left-sided lesions are the most common. However, endocarditis occurs in drug addicts who constitute 75% of HIV-affected patients in southern Europe. Conversely, it is uncommon in North America, where most HIV-infected subjects (80% to 85%) are homosexual. But in a recent European study of HIV-infected homosexual subjects, the incidence of infective endocarditis was reportedly very small. Nonbacterial thrombotic endocarditis is known to be associated with chronic wasting disease, malignancies, and hypercoagulable states. In AIDS, Cammarosano and Lewis maintain that nonbacterial thrombotic endocarditis is the most common form of cardiac involvement during HIV infection.

Pericardial Involvement

Pericardial effusion is a frequent cardiac manifestation of AIDS, usually diagnosed by echocardiography which is also used for monitoring its progress. Patients infected with HIV who had not yet developed AIDS are less likely to have effusions than patients with AIDS. In only a few patients of those reported studies has pericardiocentesis been deemed necessary. However, in one study severe effusion was reported in a large percentage of HIV-infected patients, most of whom (71%) required pericardiocentesis.

Symptomatic effusions are commonly associated with ventricular dysfunction, heart
failure, and echogenic masses. However, the precise etiology of most asymptomatic effusions, aside from those due to malignancies, remains uncertain. Pericarditis with fibrinous and/or exudative effusion of a variable amount has been reported in HIV-infected patients. Furthermore, a variety of infectious agents has been identified by a positive culture of pericardial fluids and was treated in the usual way. Other effusions can be treated successfully with nonsteroidal antiinflammatory drugs or antifailure therapy alone.

Cardiac Neoplasm

Kaposi's sarcoma of the heart was first described in an autopsy report by Autran et al in 1983. It has a predilection for the epicardium and subepicardial fat, and few studies reported both pericardial and myocardial involvement. It has been reported at autopsy in 20% to 28% of patients with AIDS and was not usually associated with clinical cardiac manifestations. However, a case report of pericardial constriction and two cases of fatal cardiac tamponade in AIDS with epicardial Kaposi's sarcoma have been reported. Malignant lymphoma involving the heart has also been described in patients with AIDS. Intracardiac echo genic masses (Kaposi's sarcoma, tuberculoma, and non-Hodgkin's lymphoma) affecting the left and right ventricular myocardium were recently reported in 6.5% of HIV-infected patients.

Conclusion

Cardiac involvement (myocardial, endocardial and/or pericardial) was, until recently, an autopsy finding in patients with AIDS. However, it is being increasingly identified and reported clinically. It is now common in the later stages and can complicate the course of the disease. Some of the reported abnormalities are independent of HIV infection, such as those found in drug abusers. Other cardiac pathologies are clearly related to opportunistic infections; better treatment of their pathogens and HIV disease will result in more patients surviving to develop cardiac pathology.

References

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