

HTLV-1 Seropositivity and Unexplained Dilated Cardiomyopathy in Jamaican Patients



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Abstract

Background: Viruses have been implicated in the aetiology/pathogenesis of unexplained dilated cardiomyopathy. 6% of adult Jamaicans are HTLV-1 seropositive. We therefore explored the relationship between HTLV-1 infectious cases and unexplained dilated cardiomyopathy in Jamaica.

Methods: Thirteen patients were recruited from Kingston Public Hospital Cardiology clinic, to study HTLV-1 seroprevalence in patients with unexplained dilated cardiomyopathy (WHO criteria: LVEF < 45 %, LVIdD > 117% of upper limit for age and BSA without evidence of coronary disease, severe hypertension, excess alcohol intake, valvular heart disease and HIV infection). The HTLV-1 seroprevalence in a group of patients without dilated cardiomyopathy registered in the cardiology clinic was then compared. HTLV-1 antibodies were detected by ELISA and confirmed where positive by Western Blot. Logistic regression was used to assess the association between HTLV-1 seropositivity and unexplained dilated cardiomyopathy.

Results: HTLV1 seroprevalence in 11 patients (7 males, 3 females) with unexplained dilated cardiomyopathy and 30 (11 males, 19 females) controls were compared. Three (27%) patients with cardiomyopathy and 3 (10%) of controls had HTLV-1 antibodies the crude OR (95%CI) for HTLV1 seropositivity was 3.36 (0.57-20.10). The age and sex adjusted OR (95%CI) was 2.71 (0.43-17.19).

Conclusion: There may be an association between HTLV-1 infection and unexplained dilated cardiomyopathy in Jamaica. A larger study is required to further explore this potential relationship.

Category: Epidemiology.

Background

Dilated cardiomyopathy refers to heart muscle disease characterized by increased mass of the heart as well dilatation and systolic dysfunction involving the left ventricle or both ventricles. Idiopathic cardiomegaly was first described as a clinicopathological entity in Jamaica in 1967 [1,2]. Patients with an antecedent history of heart failure who were not known to be hypertensive but at autopsy had heavy and dilated hearts without evidence of valvular heart disease or epicardial coronary heart disease. The advent of 2D echocardiography has made the antemortem diagnosis of dilated cardiomyopathy straightforward. Of the large percentage of cases that still remain “unexplained” a large proportion are thought to be either viral or familial. For the purpose of this study unexplained dilated cardiomyopathy refers to patients who meet WHO criteria for dilated cardiomyopathy i.e. LVEF < 45% and dilation of left

ventricular dilatation > 117% of the upper limit for age, sex and BSA without known coronary heart disease, severe hypertension, history of excessive alcohol intake or HIV/AIDS [3].

The role of viruses in the pathogenesis of dilated cardiomyopathy has long been recognized. Recent studies by German and Japanese groups have demonstrated the high prevalence of viral particles in patients with dilated cardiomyopathy [4,5]. These studies have renewed interest in the search for virus implicated in the aetiology and pathogenesis of this condition. HTLV1 has an extremely high seroprevalence in the Jamaican population affecting some 6% of adults [6]. The virus has been implicated in human diseases affecting many different organ systems. It has been identified as the cause not only of Adult T-Cell Leukemia/Lymphoma (ATLL) and HTLV-1-Associated Myelopathy/ Tropical Spastic Paraparesis/

(TSP/HAM) but also affects the skin and lungs. Moreover, HTLV-1 not only affects organ-systems directly but also facilitates infection by other agents including bacteria, fungi, helminthes and other virus [7]. It is not inconceivable therefore that HTLV-1 may also be implicated in the pathogenesis of dilated cardiomyopathy in Jamaica. given the unusually high incidence of both conditions in our population.

Methods

Thirteen patients who met the WHO criteria for dilated cardiomyopathy without an identifiable underlying cause were selected. The patients were recruited from the Kingston Public Hospital Cardiology clinic and approved by the institution's ethics committee. Patients were all seronegative for HIV (within 3 months of entry), which is a known cause of dilated cardiomyopathy. Other exclusion criteria included excessive alcohol intake, hypertension with blood pressures > 160/95mm Hg. Patients with known coronary heart disease, chest pain as the predominant symptom, dynamic ECG changes and multiple segmental wall motion abnormalities were excluded unless they had undergone stress imaging which was negative for ischaemia. Patients with symptoms for greater than one year were also excluded because of patients concern that HTLV-1 could also be a prognostic determinant. These patients were recruited between April 2003 and December 2004. Controls were selected from the remainder of the cardiology clinic population who did not meet clinical and echocardiographic criteria for dilated cardiomyopathy. These comprised of persons mainly with valvular, coronary hypertensive and grown-up congenital heart disease. The ratio of cases to controls was 3:1. Echocardiography for determination of left ventricular ejection fraction and chamber dimensions was done for cases and controls using a GE Logic 500 Ultrasound system with echocardiography package. The same operator did all image acquisition and interpretation. Diastolic function was also assessed by mitral spectral flow from pulse wave Doppler interrogation in 4-chamber apical view. Blood was drawn from cases and controls for HTLV-1. Abbott Murex performed assays and Western Blot Analysis confirmed positive cases. Statistical Analysis was carried out using Intercooled Stata Version 7. Logistic regression was done to compare seroprevalence in cases and controls and to appropriate adjust for potential confounders. Data was presented as mean +/- one standard deviation.

Result

HTLV-1 antibodies were measured in 11 patients (7 males, 4 females) with unexplained dilated cardiomyopathy and 30 control subjects (11 males, 9 females) without dilated cardiomyopathy. The median duration of symptoms prior to presentation was 8.95 months among cases. Mean LVEF was 20.8±4.5 % for cases versus 63.5±11.4 % among controls while mean LVIDd was 62.0±7.1mm among cases and 49.8±11.4mm among controls (p= 0.0055, Mann-Whitney). HTLV1 seroprevalence in 11 patients with unexplained

dilated cardiomyopathy and 30 controls were compared. Three (27%) patients with cardiomyopathy and 3(10%) of controls had HTLV-1 antibodies. The crude odds ratio (OR) for HTLV1 seropositivity was 3.36, 95% CI [0.57-20.10]. The age and sex adjusted OR was 2.71, 95% CI [0.43-17.19].

Discussion

It is reasonable to consider the possibility that HTLV1 may be implicated in the aetiology or pathogenesis of dilated cardiomyopathy in Jamaica, either by acting in concert with other factors which cause heart muscle injury including immune activation or facilitating other viruses already implicated in the aetiology of dilated cardiomyopathy. The high prevalence of HTLV1 in the Jamaican population implies that if a causal relationship is established that this virus could contribute significantly to the comparatively large number of cases, which have been noted in our population over the last three to four decades. The major limitation of the study was of course insufficient numbers of cases to demonstrate a statistically significant association. It was not possible to exclude the possibility that cases may have been ischaemic cardiomyopathy as coronary angiography or stress imaging for coronary heart disease was not routinely done. However, in order to reduce the likelihood of inadvertently including patients with ischaemic cardiomyopathy, patients with chest pain as the predominant symptom, isolated left ventricular dilatation and important regional wall motion abnormalities were excluded even though all these patients certainly would not all have had coronary heart disease. One could therefore consider the possibility of either combining data from multiple sites in the Caribbean with comparable incidences of both conditions to overcome 'small numbers' issue from a single site or perhaps approaching the problem from the other direction: screening a larger population of HTLV 1 seropositive persons for asymptomatic left ventricular dysfunction in order to prove the study hypothesis.

Conclusion

There may be an association between HTLV1 seropositivity and unexplained dilated cardiomyopathy in Jamaica. However a larger study is required to establish this potential relationship. An established association and the identification of a biologically plausible causal relationship would have important implications for reducing the burden of unexplained cardiomyopathy in Jamaica, the Caribbean and perhaps the wider world. It would also serve to strengthen the resolve to reduce the incidence of new HTLV 1 infection by greater application of validated prevention methods as well as to develop effective specific antiviral therapies for this important viral disease agent.

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