Accelerated atherosclerosis in a human immunodeficiency virus infected patient not on highly active anti-retroviral therapy: An autopsy case report

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ABSTRACT

The pandemic spread of human immunodeficiency virus (HIV) has been the greatest challenge to public health in modern times. However today, people infected with HIV are living longer due to highly active antiretroviral therapy (HAART). This has resulted in age related complications like cardiovascular diseases, causing increased morbidity and mortality. The relative contributions of HIV infection versus potential adverse effects of HAART to coronary heart disease risk remains unclear. Recent reports implicate both HIV infection per se and HAART therapy to cause metabolic derangements which are pro-atherogenic. Here, we report a case of HIV infected young patient never exposed to HAART, presenting with accelerated atherosclerosis in aorta, coronary and carotid arteries.

Key words: Accelerated atherosclerosis, autopsy, highly active anti-retroviral therapy, human immunodeficiency virus

INTRODUCTION

Human immunodeficiency virus (HIV) infected individuals have an increased risk of coronary heart disease (CHD).[1-3] The cause might be the viral infection itself, the use of highly active antiretroviral therapy (HAART) or altered immune responses seen in these patients.[2] The risk is influenced by traditional factors such as age, smoking, diabetes and dyslipidemia as well as non-traditional factors like local and systemic inflammation. Clinical presentation of CHD in HIV infected patients tends to be different from CHD due to traditional risk factors in that they present at an age which is almost a decade younger, with a mean age of 50 years, compared with non- infected controls.[2] Early diagnosis of CHD is of paramount importance in the present day scenario where HIV infection has become a manageable but not yet curable, chronic condition.

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CASE REPORT

A 36 year old man, who met with a road traffic accident, was admitted to the hospital with severe head injuries. During his stay in the hospital he was diagnosed to be infected with HIV. He was a smoker, non alcoholic, non-diabetic and had no past history of CHD symptoms or family history of CHD. He died on the 8th day of admission and an autopsy was conducted. Grossly, the aorta showed extensive areas of atherosclerosis [Figure 1]. Coronary [Figure 2] and carotid arteries showed atherosclerotic plaques and narrowing of the lumen. Microscopy and histopathological examination with hematoxylin and eosin staining showed well formed atherosclerotic plaques in the aorta [Figures 3 and 4], circumferential involvement of all the

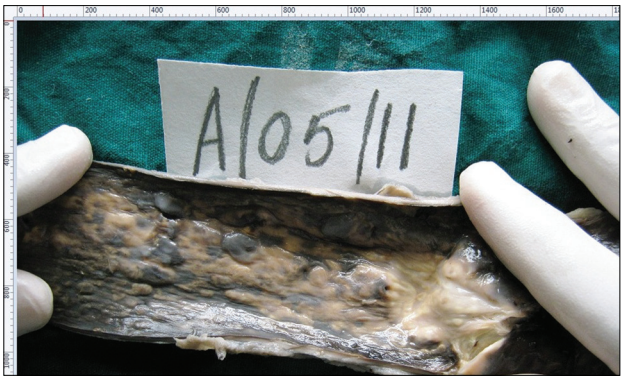

Figure 1: Gross photograph of aorta showing marked large atheromas

Figure 2: Gross photograph of coronary arteries showing marked narrowing with atheroma in the wall

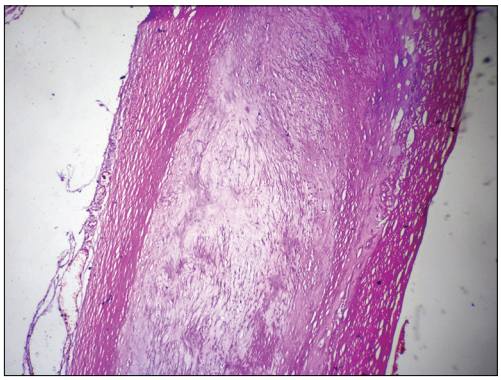

Figure 3: Microphotograph of aorta showing well formed atheromatous plaque with lipid core (hematoxylin and eosin stain, 100×)

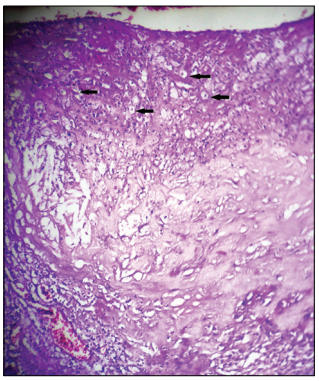

Figure 4: Microphotograph of aorta showing foamy macrophages (arrows) in athermatous plaque (hematoxylin and eosin stain, 400×)

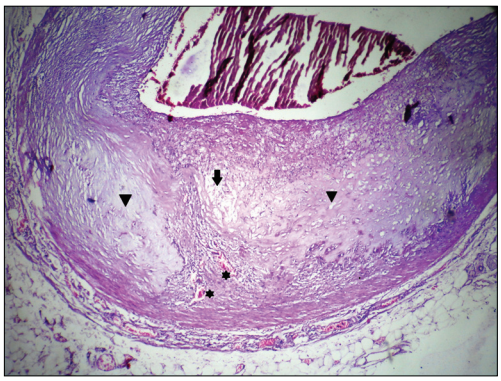

Figure 5: Microphotograph of coronary artery showing well formed athermatous plaque with lipid core (arrow heads), cholesterol crystals (arrow) and angiogenesis (star) (hematoxylin and eosin stain, 100×)

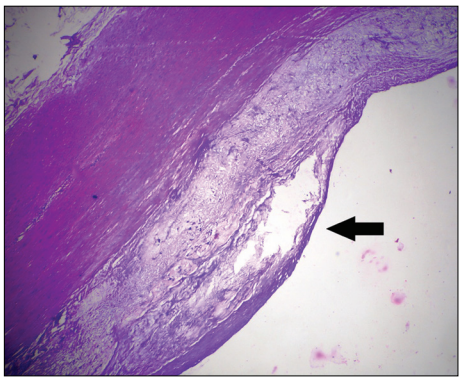

Figure 6: Microphotograph of coronary artery showing athermatous plaque with a thin cap (hematoxylin and eosin stain, 100×)

three coronary vessels [Figures 5 and 6] and carotid arteries with large lipid cores, intense inflammation, abundant foam cells, speckled calcification, thin cap atheroma and lack of normal vessel wall between the atheromas.

DISCUSSION

With advancements in medicine and HAART therapy, people with HIV infection are now living longer and an understanding of its relationship with development of atherosclerosis is the need of the hour. Whether HIV infection per se is an independent CHD risk factor, or it is solely due to HAART remains controversial.[4] Clinical and epidemiological studies have shown relation between HIV infection and increased risk of CHD across large cohorts.[1] People with HIV infection have 1.5 to 2 fold higher incidence of cardiovascular events reported, compared with uninfected individuals.[1-4] When first reports of myocardial infarction in young HIV infected patients surfaced, the initial focus was primarily on the

dyslipidemic effects of antiretroviral therapy.[5] Only recently, the broader appreciation of the complex interplay between traditional risk factors for CHD and HIV infection has emerged.[5]

The mechanisms by which HIV causes increased atherosclerosis and CHD has been the topic of great interest to physicians, pathologists and cardiologists. Although exact pathogenesis needs to be proved and verified, many possible mechanisms have been proposed with significant evidence to back them. Traditional risk factors like age, smoking, hypertension and diabetes are all strong predictors of CHD risk in HIV infected patients. HIV serves as a marker for a subgroup of the general population with an altered prevalence of traditional risk factors in particular, with the rate of smoking in HIV populations being consistently high and exceeding that for age-matched controls in several studies.[5] A French cohort study reported smoking prevalence rate of 56.6% in HIV infected men Vs 32.7% in HIV negative men.[3] The prevalence of hyperlipidemia in HIV patients is between 28-80% in different studies.[2] In the early stages of HIV infection before treatment is instituted, the predominant changes in the lipid profile are: hypertriglyceridaemia, low high density lipoproteins and high LDL (low density lipoprotein) values with predominant small, dense LDL particles which are highly atherogenic, compared with controls.[1-5] The overall effect of HIV infection on the lipid profile is atherogenic.[2,5] The proposed mechanisms for the lipid abnormalities include increased hepatic lipogenesis, impaired clearance of lipids from the blood stream and potential effects on immunologic status.[2]

The effects of HIV on non-traditional risk factors like local and systemic inflammation and endothelial function have gained importance in recent times. Chronic inflammation plays a central role in the development of atherosclerosis. Increased vascular inflammation seen in HIV infection might be due to direct viral infection or due to the associated metabolic defects.[2] Vascular inflammation causes endothelial cell activation leading to an increased expression of adhesion molecules and also causes activation of the monocytes.[1,2] This in turn leads to an increased migration of monocytes into the atherogenic lesion, maturation into macrophages and conversion into lipid rich foam cells.[1] Activated macrophages are a major source of cytokines and chemokines that direct monocytes into the vascular lesions, creating a positive feedback loop.[1,6] More recently, HIV infection has been shown to interfere with the cholesterol efflux from the macrophages resulting in accumulation of many foam cells, subsequent necrosis and apoptosis of these cells leading to the formation of the lipid core of the atheroma.[1] HIV infection impairs reverse cholesterol transport whereas HAART affects mostly forward cholesterol transport (increasing cholesterol delivery to cells).[1]

The present case highlights the role of traditional risk factors like male sex and smoking in the causation of atherosclerosis which seems to be accelerated by the HIV infection induced inflammation. Since the patient was never exposed to HAART nor did he have a positive family history of CHD, the accelerated atherosclerosis was most probably caused by smoking and HIV infection. Histopathological examination showed circumferential atheromas with complication in all the three coronary vessels, carotid arteries and aorta. Lesions with large lipid core and thin cap carry a higher risk of rupture and thrombosis.

CONCLUSION

HIV related cardiovascular disease is an under-recognized cause for symptomatic illness.[7] A high degree of suspicion and early screening may allow appropriate intervention and improved quality of life in those affected. Observations in the present case highlight the fact that traditional factors such as smoking need to be controlled for reducing CHD. These patients should be prescribed statins and platelet anti-aggregants along with antiretroviral regimens.[8] Strategies to decrease cardiovascular risk in HIV infected patients will be important in the public health perspective.

REFERENCES

1. Crowe SM, Westhorpe CL, Mukhamedova N, Jaworowski A, Sviridov D, Burkinsky M. The macrophage: The intersection between HIV infection and atherosclerosis. J Leukoc Biol 2010;87:589-98.
2. Ho JE, Hsue PY. Cardiovascular manifestations of HIV infection. Heart 2009;95:1193-202.
3. Malvestutto CD, Aberg JA. Coronary heart disease in people infected with HIV. Cleve Clin J Med 2010;77:547-56.
4. Schambelan M, Wilson PW, Yarasheski KE, Cade WT, Davila-Roman VG, Agostino RB Sr, *et al.* Development of appropriate coronary heart disease risk prediction models in hiv-infected patients. Circulation 2008;118:48-53.
5. Currier JS, Lundgren JD, Carr A, Klein D, Sabin CA, Sax PE, *et al.* Epidemiological evidence for cardiovascular disease in HIV-infected patients and relationship to highly active antiretroviral therapy. Circulation 2008;118:29-35.
6. Bukrinsky M, Sviridov D. HIV and cardiovascular disease: Contribution of HIV-infected macrophages to development of atherosclerosis. PLoS Med 2007;4:e43.
7. Dubé MP, Lipshultz SE, Fichtenbaum CJ, Greenberg R, Schecter AD, Fisher SD. Effects of HIV infection and antiretroviral therapy on the heart and vasculature. Circulation 2008;118:36-40.
8. Alonso-Villaverde C, Coll B, Parra S, Montero M, Calvo N, Tous M, *et al.* Atherosclerosis in Patients infected with HIV Is influenced by a mutant monocyte chemoattractant protein-1 allele. Circulation 2004;110:2204-9.

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