

Multiple Cerebrovascular Accidents Associated with Intracranial HIV Vasculopathy: A Case Report

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Received May 06, 2019; Revised June 24, 2019; Accepted July 04, 2019

Abstract HIV disease continues to be a major public health concern with 36.9 million people reported living with HIV in 2017 [1]. Cardiovascular disease (CVD) is one of serious complications of HIV disease. While control of HIV disease with antiretroviral therapy (ART) has been shown to unequivocally reduce all-cause mortality, ART in itself can paradoxically increase CVD risk in the HIV population. In this report we present a case of 32 year old African American woman with long standing uncontrolled HIV disease resulting in multiple cerebral aneurysms with aneurysmal rupture leading to recurrent strokes. We discuss the disease course and highlight the current literature of HIV vasculopathy, a serious complication of HIV disease associated with increased morbidity and mortality in this vulnerable populations.

Keywords: human immune deficiency virus, vasculopathy, cerebral aneurysm, stroke, anti-retroviral therapy

Cite This Article: Daniela M. Tello, Pramod Theetha Kariyanna, Apoorva Jayarangaiah, and Samy I. McFarlane, "Multiple Cerebrovascular Accidents Associated with Intracranial HIV Vasculopathy: A Case Report." *American Journal of Medical Case Reports*, vol. 7, no. 7 (2019): 145-147. doi: 10.12691/ajmcr-7-7-7.

1. Introduction

Human immunodeficiency virus (HIV) continues to represent a major public health problem with reports from United Nations Programme on HIV and AIDS (UNAIDS) in 2017 indicating that HIV disease affects 36.9 million persons of whom only 21.7 million people had access to antiretroviral therapy (ART) [1]. HIV is an independent risk factor for cardiovascular disease [2]. Various cardiovascular manifestation of HIV include dilated cardiomyopathy, coronary artery disease, pericardial effusion, pulmonary hypertension, cerebral vasculopathy and cerebrovascular accident (CVA). HIV vasculopathy refers to a wide variety of HIV related vascular changes such as vasculitis, stenosis, aneurysms, and accelerated atherosclerosis [2]. Multiple isolated cases of CVA secondary to HIV vasculopathy with cerebral aneurysms have been reported [3,4,5,6,7]. We present a case of 32-year-old African-American female with hypertension, asthma, congenital HIV and blindness secondary to cytomegalovirus infection. She was poorly compliant with ART regimen (abacavir, lamivudine, ritonavir, atazanavir) and had multiple intracranial aneurysms. Patient suffered from multiple cerebrovascular accidents secondary to aneurysmal rupture with the first one discovered 3 years after aneurysms were incidentally found. Subsequently she had two more episodes of strokes at 6 and 10 years after diagnosis and given her history of multiple aneurysms, she had computed tomography angiogram (CT-angiogram) when she presented with sudden

worsening of chronic headaches to the Emergency Department of our institution. CT-angiogram revealed progressive enlargement of multiple intracranial aneurysms in right and left internal carotid artery and left basilar artery when compared to previous imaging and an infarct was also identified. Due to the presence of several aneurysms in multiple arterial territories patient was not a candidate for neurosurgical intervention. ART was continued with emphasis on compliance. While the exact mechanism of aneurysmal formation in HIV patients is largely unknown [8,9,10] multiple etiologies have been proposed such as chronic inflammation, elevated level of elastases, and immune dysregulation as well as the use of protease inhibitors and HIV virus itself [2].

2. Report of the Case

This is a 32 year old African American Woman with congenital HIV disease who was uncontrolled due to ART non-compliance resulting in multiple opportunistic infections including cytomegalovirus retinitis that rendered her blind. Patient was subsequently placed on ART (abacavir, stavudine, aprenavir, ritonavir); medications that are known to increase CVD risk.

She was incidentally diagnosed with multiple intracranial aneurysms during the course of migraine headache workup 3 years prior to presentation. Patient was being monitored closely with serial imaging that revealed fusiform intracerebral aneurysms of bilateral internal carotid arteries, with the right measuring 7.9 mm x 6.2 (Figure 1, blue arrow) and the left measuring 7.9 mm x 4.8

mm (Figure 1, green arrow), basilar 3.6mm x 4.6 mm (Figure 1, yellow arrow) the right MCA cavernous segment has irregularity of narrowing in a beaded pattern very consistent with HIV vasculitis (Figure 1, orange arrow), and MRI showed encephalomalacia involving the right subinsular region consistent with remote infarct. (Figure 2, red arrow)

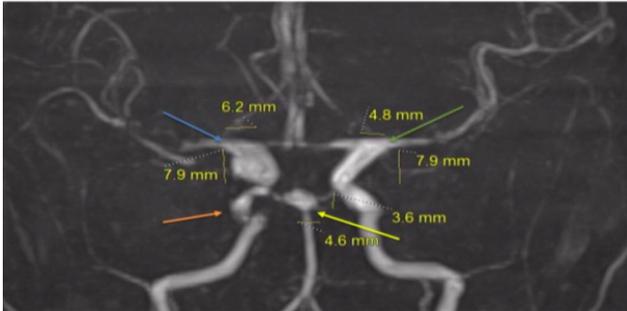


Figure 1. Fusiform aneurysms of bilateral distal internal carotid arteries and basilar tip. This right cavernous artery shows beading

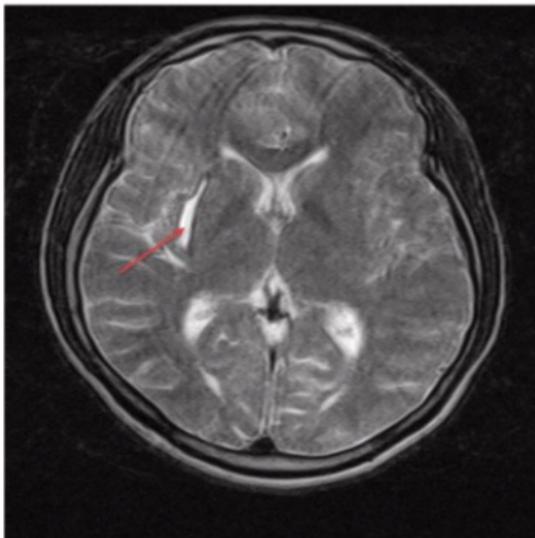


Figure 2. Encephalomalacia involving the right subinsular region consistent with a remote infarct

Patient was evaluated and neurosurgical intervention was not warranted at that time given the multiple nature of the lesions at different arterial territories.

3 years after initial aneurysm diagnosis patient presented with sudden onset of headache that woke her up from sleep, 10/10 associated with photophobia, tinnitus, phonophobia, lightheadedness, and nausea and was found to have a CVA. She subsequently developed 2 more episodes of CVA at 6 and 10 years post diagnosis.

3. Discussion

We presented a case of a young woman with congenital HIV disease with vasculopathy who sustained multiple premature cerebrovascular accidents (CVA). HIV vasculopathy is most commonly associated with fusiform aneurysmal dilatation in intracranial vessels, particularly among young adults, such as our patient [4] In fact most intracranial aneurysms in congenital HIV disease are described in children and adolescents populations [11].

Our case is also consistent with reports correlating severity of HIV disease with the presence of intracerebral aneurysms. Saccular aneurysms are more common among non- HIV infected individuals compared to fusiform aneurysms that are mainly described in the HIV infected patients [4] as demonstrated in this case report.

While the pathophysiologic mechanisms of intracranial aneurysms as demonstrated in children are secondary to immune activation in response to transendothelial migration of HIV strains with tropism for cerebral mononuclear cells [3] and alteration of dynamic vascular flow regulated by circulating cytokines and growth factors leading to vascular remodeling. [12] It is also reported that the repeated opportunistic and other high- risk infections that are specifically associated with HIV/AIDS, may contribute to increased elastases, leading to fragmentation and thinning of the internal elastic lamina, an early histological manifestation in the development of fusiform aneurysms associated with HIV disease [8,13]. Because of this association, opportunistic infections should be promptly be investigated in patients with HIV associated cerebral aneurysms [14]. These mechanisms are the most commonly proposed in the literature, which are thought to contribute to intimal thickening, destruction of internal elastic lamina, loss of muscular layer, and fibrosis of medial arterial layer [12]. Histopathological findings in adults include luminal thrombosis and fibrosis with concentric hyalinization of the intima, atrophy of the media and thickening as well as fragmentation of the elastic lamina. [7] Extracranial aneurysms in patients with HIV are described as being secondary to leukocytoclastic vasculitis in vasa vasorum. [15] There is paucity of data regarding the optimal therapeutic strategies for HIV vasculopathy with cerebral aneurysms [16]. Further research is needed to determine the effects of ARV therapy on the progression of cerebral aneurysms and to elucidate the role of HIV virus itself in the pathogenetic process [17] particularly in light of the recent reports indicating that the use of ART may actually lead to emergence of immune reconstitution inflammatory syndrome (IRIS) which could actually worsen the vasculopathy [14].

4. Conclusion

We presented a case of premature stroke in a 32 year old woman with congenital HIV disease that was initially uncontrolled resulting in multiple opportunistic infections leading to her blindness secondary to Cytomegalovirus infection. HIV disease was subsequently under control for the past few years with ART. Our case presentation illustrates the importance of surveillance and keeping a high index of suspicion of the presence of aneurysms in HIV vasculopathy that could result in strokes that generally occur in young patients leading to increased risk of morbidity and mortality. Our case also highlights the higher burden of cardiovascular risks, independent of the traditional risk factors for cardiovascular disease such as diabetes mellitus/insulin resistance, smoking, central obesity, and advanced age in stroke population. Given the rarity of fusiform aneurysms, and its correlation with HIV infection as highlighted in previous case reports [18],

some authors suggest that in their presence, whether it is found in a child or adult, investigation for HIV infection should be done [19]. Finally, our case report of a young patient with multiple strokes, underscores the need for further research elucidating the mechanisms of aneurysmal formation and the possible preventive and therapeutic options in this vulnerable populations with HIV vasculopathy.

Acknowledgements

This work is supported, in part, by the efforts of Dr. Moro O. Salifu M.D., M.P.H., M.B.A., M.A.C.P., Professor and Chairman of Medicine through NIH Grant number S21MD012474.

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