AN UNUSUAL FINDING: AORTIC DISSECTION IN A PATIENT WITH AIDS ON ANTIRETROVIRAL THERAPY. A CASE REPORT AND REVIEW OF LITERATURE

Shut G. Zi[1], Dashan Domshak[1], Amusa G. Adeniyi[1]

Cardiology Unit, Department of Internal Medicine, Jos University Teaching Hospital, P.M.B 2076, Jos, Nigeria.

***Correspondence*: Ganiyu A. Amusa**
E-mail: drganiamusa@gmail.com

ABSTRACT

The aorta is said to be dissecting when there is separation of the layers within the aortic wall. It is caused by a circumferential or less frequently, transverse tear of the intima. Even though aortic dissection is relatively uncommon, it is a catastrophic illness that requires early and accurate diagnosis and treatment for patient survival. Human immunodeficiency virus infection is an increasingly important cause of heart disease. Availability of treatment with highly active antiretroviral drugs has prolonged patient's life expectancy but has also increased the incidence of non-AIDS co-morbid conditions.

Many cardiovascular diseases have been described in HIV infected individuals, among which is aortic involvement which manifest as: aortitis, aneurysms and dissections. HIV infected individuals also suffer from vascular lesions such as large artery vasculopathy secondary to vasculitis and accelerated atherosclerosis of the coronary arteries. Accelerated atherosclerosis has been linked to patients on protease inhibitors used as part of Highly Active Antiretroviral Therapy (HAART) regimen and have also been implicated in a lipodystrophy syndrome. Aortic dissection has a wide range of clinical presentations.

To make the diagnosis of aortic dissection, a high index of suspicion is required, especially in patients with predisposing risk factors, e.g., hypertension, aneurysmal disease of the aorta, or a familial connective tissue disorder. Typically, the patient is a hypertensive male in his 60s, who presented with a history of abrupt onset of chest pain. We present a case of Aortic dissection in HIV patient on ART with background Hypertension.

CASE REPORT A 55-year-old civil servant who is a known RVD patient diagnosed 16 years ago and regular on HAART and diagnosed with hypertension 3 years ago on moduretic presenting with complains of sudden chest pain which was said to be sharp and associated with difficulty in breathing. Symptoms persisted for four days before he was admitted. He is obese with a BMI of 34. He was in respiratory distress, with a regularly irregular pulse and a wide pulse pressure.

Chest X-ray done revealed presence of cardiomegaly and widened mediastinum, ECG findings included sinus tachycardia with features of chamber enlargements and an Echocardiography revealed presence of aortic aneurysm alongside DCM with Pulmonary hypertension. He was initially managed as a case of hypertensive heart disease in failure precipitated by suspected Acute Coronary Syndrome. A CT angiography which was done confirmed a descending aortic aneurysm with presence of dissection. He was reviewed by Cardiothoracic Unit on that account. Unfortunately, surgery could not be done due to unavailability of needed surgical facilities.

He was placed on oral medications and discharged home after adequate counselling to be on regular clinic follow up.

Keywords: Aortic dissection, HIV, ART, Hypertension.

INTRODUCTION

The aorta is said to be dissecting when there is separation of the layers within the aortic wall. Propagation of dissection (proximally and distally) in the intimal layer of the aorta is brought about by tears secondary to blood entering the intima-media space.(1) The aortic wall is made up of the tunica intima, tunica media and tunica adventitia.

The tunica intima, which is the innermost layer, is thin, delicate, lined by the endothelium and is easily traumatized. The tunica media imparts strength to the aorta and consist of laminated but intertwining sheets of elastic tissue.(2) the aorta has its maximum allowable tensile strength because of the arrangement these sheets in a spiral fashion. The adventitia which is the outermost layer consist largely of collagen. The adventitia houses the vasa vasorum which supplies blood to the outer half of the aortic wall.

The adventitia of the aorta houses the nervivascularis, which is a bundle of nerve fibers that are involved in the production of pain whenever there is acute stretching of the aortic wall from a dissection.(3) the aorta is particularly prone to injury and disease from mechanical trauma because its wall is exposed to high pulsatile pressure and shear stress as a result of the water hammer effect. With aneurysmal dilatation, the aorta becomes more prone to rupture than any other vessel because of wall tension as governed by the Laplace law is intrinsically high. From results of autopsies conducted, aortic dissection evidence is found in 1-3% (about 1 in 350 cadavers).(4) Bacewicz et al reported a case of HIV and aortic dissection type l which the patient was successfully treated with surgical repair in Detroit Michigan.(5) Aliyu and co-workers reported a case of intramural aortic hematoma in an 11-year-old girl with Marfan's syndrome in Kano, Northwest Nigeria. Sule AZ et al reported a case series of infrarenal abdominal aortic aneurysm (without dissection) in Jos, Nigeria. Two cases of Aortic dissection were reported in Jos University Teaching Hospital in 2007 by Kumtap et al.(6) Aortic dissection is rare in individuals younger than 40years of age.

Ascending aortic dissection occurs most commonly in individuals between the ages of 50 and 60 while descending aortic dissections are more commonly encountered in older individuals with a peak at 60 to 70 years of age. The typical aortic dissection patient is a male in his sixth decade of life. Infection with Human immunodeficiency Virus is characterized by a chronic disease process with systemic multiorgan involvement. In the early years of the Acquired Immune Deficiency Syndrome (AIDS) epidemic, many patients suffered and died from serious opportunistic infection partly because of their compromised immune system.

The use of HAART in HIV patients has significantly reduced HIV-related infectious complications and improved their survival. This improvement, combined with the metabolic effects of antiretroviral treatment, has increased the risk of cardiovascular diseases. HIV patients share many cardiovascular risk factors with the general population, but they also have factors specific to their condition that include the HIV virus itself, HIV replication, chronic inflammation, and exposure to HAART.

In a significant number of patients, the immediate cause of death is cardiovascular complications. Cardiovascular disease spectrum that can be depicted at imaging include; dilated cardiomyopathy, embolism, pericardial effusion, pulmonary hypertension, endocarditis, vasculitis, coronary artery disease, aneurysm, atherosclerotic cardiovascular disease and cardiac tumors related to AIDS. With effective antiretroviral therapy, cardiovascular disease has gained prominence as a cause of mortality and morbidity HIV-infected persons.2

In the elderly population aortic dissection commonly presents with a history of chronic hypertension. When intervention is not rapid, mortality is very high. In HIV infected patients, aortic dissection is a very uncommon cardiovascular complication.

CASE DESCRIPTION

MS, a 55-year-old Ron man who presented with a two-day history of sudden chest pain and difficulty in breathing. Chest pain was retrosternal, sharp and radiates to the back and occasionally to the left shoulder. Difficulty in breathing was initially only present following moderate activity but worsened to occur at rest.

He had Paroxysmal Nocturnal Dyspnoea and orthopnea. There is associated history of diaphoresis. He had cough which also began two days prior to presentation and was productive of whitish sputum. There was no history of leg swelling. He had history of intermittent claudication. He is a known hypertensive diagnosed 3 years ago, on tab moduretic. He was diagnosed to have Retroviral disease 16 years ago and has been regular on his HAART medications and follow up. He was said to have been rushed to a private clinic on account of symptoms where his systolic BP was found to be 80mmHg and DBP could not be ascertained, he was then referred here.

There is history of significant alcohol ingestion for about 20 years, during which he had an average weekly consumption of about 30 units. There is history of smoking within that period which estimated to be 3 pack years. He had no history of consumption of herbal medications. He is married in a monogamous setting with 2 children. There was no family history of hypertension, diabetes, heart disease or sudden death in the young. Physical Examination He was obese (weight: 96.7Kg, height: 1.68m, BMI: 34kg/m2). He was not pale, afebrile, anicteric, not dehydrated, acyanosed, with no significant peripheral lymphadenopathy, no pedal oedema.

His pulse rate was 108/min, regularly irregular and Heart rate was also 108/min with S1, S2, S4 and loud A2 heard. BP was 140/50mmHg, JVP was elevated. The Apex Beat was not localized due to thick anterior chest wall. His respiratory rate was 32 cycles per minute, percussion notes were resonant and breath sounds were vesicular in all lung fields with fine bi-basal crepitations. His abdomen was distended, soft, moves with respiration with no areas of tenderness. There was no palpable organomegaly, intra-abdominal masses or ascites. He was conscious and well oriented in time, place and person. He had no focal body weakness.

He had a Chest X-ray done which showed features of cardiomegaly, unfolded aorta, widened mediastinum and bilateral pulmonary infiltrates. He had an ECG done which showed sinus rhythm, rate 100/min, LAD LAE, RAE, LVH and RVH. An Assessment of Ischaemic Heart Disease in failure in a known hypertensive and RVD was made. The following investigations were requested: Echo, cardiac enzymes, troponin T, I, CK MB, Fasting Lipid Profile, E/U/Cr uric acids, LFT. Abdominal USS, Urinalysis, FBC + ESR, HbsAg, Anti-HCV. He was placed on tabs Telmisartan 40mg daily, Tabs spironolactone 25mg daily, Tabs metoprolol 50mg daily, tabs clopidogrel 75mg daily, IV furosemide 80mg am, 40mg pm, tab rosuvastatin 40mg daily.

He was then admitted into the male medical ward; however, patient declined admission on financial grounds despite adequate counselling on the gravity of medical condition and need for admission. He was allowed to go home on tabs furosemide 80mg twice daily and other prescribed medications. He was to return in clinic in a week time with results of requested investigations for review. He presented two days later at the Accident and Emergency due to worsening difficulty in breathing and chest pain and also had two episodes of vomiting. Pulse rate was now 84/min and regular.

He was assessed to have hypertensive disease in failure (NYHA III) precipitated by Acute Coronary Syndrome, chest infection and poor drug compliance with background RVD on HAART. He was admitted and placed on outlined anti-failure and antithrombotic

medications alongside IV Augmentin. Random blood glucose done was 8.9mmol/L other investigations available included PCV 38%. The next day following admission, the cardiology team was invited to review and co-manage the patient. The cardiology unit carried out an Echocardiography which revealed Hypertensive Dilated Cardiomyopathy with pulmonary hypertension and aortic aneurysm.

He was placed on Telmisartan tablets while lisinopril was discontinued.

Two days later, a CT angiography was requested which was carried out and results confirmed presence of a Debakey 1 aortic aneurysm with presence of dissection.

Laboratory Parameter and Reference Range

Parameter	Result	Reference Range
Total Protein	75	62-80g/L
Total Albumin	43	
Total Bilirubin	8.6	3.4-17umol/L
Alkaline Phosphatase	39	21-92 IU/L
Alanine Transaminase	47	Up to 40 IU/L
Aspartate Transaminase	140	Up to 40 IU/L
Packed Cell Volume	40.1	56-54
Total White Blood Cell Count	10	2-8.2 x 10^ 9/L
Neutrophils	70%	
Lymphocytes	20%	
Monocytes	3%	
Eosinophil	7%	
Platelets	180	100-400 x 10 ^9/L
Erythrocyte Sedimentation Rate	40	<27(age/2)mm/hour
HBsAg	Non-reactive	Non-reactive
Anti HCV	Non-reactive	Non-reactive
Fasting Blood Sugar	6.4mmol/L	3.5-5.6mmol/L

Parameter	17/11/19	23/11/19	Reference Range
Na	138	142	134-145 mmol/L
K	3.9	3.1	3.5-5.5 mmol/L
CL		123	96-106 mmol/L
HCO3	27	27	21-31 mmol/L
Urea	11.8	4.1	2.5-6.6 mmol/L
Creatinine	177	84	72-122 mmol/L
Uric Acid	770	552	120-420 mmol/L

Following the diagnosis, oral nitrates were discontinued and patient was now placed on bisoprolol tablets. The Cardiothoracic Unit was invited to review.

After evaluating the patient, they continued the ongoing oral medications and due to unavailability of facilities for a Bentall Procedure, discharged the patient from their point of view. Patient was eventually discharged by Cardiology team on oral medications and placed on routine clinic checkup.

DISCUSSION

With the further spread of AIDS worldwide and a dramatic increase in life expectancy of HIV infected patients treated with effective antiviral regimens, an increasing number of patients live with the illness but more than 10% experience cardiovascular manifestations (7).

Before the era of HAART, cardiac manifestations in HIV patients mainly included pancreatitis, cardiomyopathy and pulmonary hypertension leading to heart failure, conduction system, abnormalities, and neoplastic infiltration (8). In the post-HAART era, acute coronary events by far outnumber all other cardiovascular complications of HIV (7). Cardiovascular prevention is required in more than one-half of HIV-infected/treated patients for HAART to be reliably effective (7). As the prognosis for HIV patients continues to improve, this rate is likely to increase.

This increase has been attributed to ageing along with a resulting increase in risk factors such as hypertension and diabetes, as well as HAART regimens that include stavudine or protease inhibitors (PIs). All medications in this latter class have a reported association with hyperlipidemia, hyperglycemia, and truncal obesity (9). Atherosclerotic cardiovascular disease has become more frequent with the use of HAART. Studies indicate that new generation PIs such as darunavir/ritonavir (10) and atazanavir/ritonavir (11) are relatively less likely to lead to dyslipidemia.

The integrase inhibitor raltegravir and CCR5 receptor antagonist inhibitor maraviroc have a better lipid and glycemic profile than older PIs and thymidine analogues (12). In addition, HIV has been found to directly affect vascular biology, resulting in an increased risk of cardiovascular disease compared to uninfected persons (13). The current patient had received antiretroviral therapy for 16 years (combination regimen is unknown) he developed hypertension (3years ago). The exact cause in this patient is unknown.

The origins of aortic dissection in the current patient appear to be multi-factorial and related to high blood pressure, HIV infection, as well as to the adverse reactions to antiretroviral drugs. Hypertension prevalence in HIV disease was estimated to be 20-25% before the era of HAART but is now up to 74% in patients with HAART-related metabolic syndrome (14). Lipodystrophy, hypertension and metabolic disorders especially elevated fasting triglycerides are currently thought to be induced by protease inhibitors according to recent reports. (8).

In the current patient, hypertension may have been associated with adverse reactions to antiretroviral therapy and may have been the most significant cause of aortic dissection. Prompt diagnosis and treatment is required in the medical emergency aortic dissection in order to curb morbidity and mortality. A high degree of caution is required for its successful diagnosis as presenting symptoms are so variable that dissection may be overlooked in up to 39% of cases (15).

Because of the advantage of rapid advances in noninvasive imaging technology that has facilitated the early diagnosis of aortic dissection, it should be considered a differential diagnosis of any patient presenting with chest, abdominal and back pain. Aortic dissection may involve the ascending aorta alone, the descending aorta alone, the descending thoracic and abdominal aorta, or the entire aorta. It is serious because it may rupture, causing life-threatening internal bleeding. Death risk in aortic aneurysm depends on the extent of the dissection with the risk highest in those with dissections of the ascending aorta.

Emergency surgery is the best modality for patients with type-A dissection while optimal medical therapy is appropriate for patients with an uncomplicated type B dissection. The medical treatment of an aortic dissection includes aggressive control of heart rate and blood pressure while the aorta heals. An adequate beta blockade is the cornerstone of medical therapy. Selected patients with aortic dissection type l and HIV infection are candidates for surgical repair. One study indicates that perioperative mortality and morbidity rates are high in HIV patients undergoing abdominal aortic surgery (16).

Major cardiac surgeries do not negatively affect the course of HIV infection and HIV infection itself do not seem to increase perioperative mortality and morbidity. (17). Once the acute dissection has healed, adequate control of blood pressure may eliminate the need for surgery. Patients who survive acute aortic dissection need long-term medical therapy with beta-blockers and appropriate serial imaging follow-up. Once aortic dissection is picked, lifelong monitoring is required because a previously dissected aorta may enlarge and rupture.

Because of the nature of the viral infection and the possible mode of viral transmission, many surgeons remain reluctant to perform invasive procedures on patients with HIV infection. Presently, there are no definitive or specific treatment guidelines from different surgical societies regarding surgical treatment of HIV infected patients. The current patient with aortic dissection type l did not undergo emergency surgical repair but he received long-term medical therapy with beta-blockers and follow-up.

As the epidemic progresses and new treatments help increase the long-term survival of AIDS patients, cardiovascular complications will become more common. Even though there is now effective treatment for HIV infection with a combination of antiretroviral medications, cardiovascular diseases are still a challenge for persons infected with HIV.

CONCLUSION

Aortic dissection patients have a high risk of an adverse outcome and need to be managed aggressively in hospital and over the long term with frequent follow-ups (18).

Future advances in this vein include early detection and optimal treatment of aortic dissection in HIV-infected patients.

REFERENCES

1. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA. 2000 Feb 16. 283 (7):897-903. [Medline]

2. Yinzhong S, Wei S, Hongzhou L. Type I aortic dissection in a patient with human immunodeficiency virus infection. *BioScience Trends*. 2012; 6(3):143-146. DOI: 10.5582/bst.2012.v6.3.143

3. Spiegel EA, Wasserman S. Experimental studien ueber die Entsehung des Aortenschmerzes und seine Leitung zum Zentralnerven system. Ztschr F. d. ges. Exper Med. 1926. 52:180-196

4. Clouse WD, Hallett JW Jr, Schaff HV, Spittell PC, Rowland CM, Ilstrup DM, et al. Acute aortic dissection: population-based incidence compared with degenerative aortic aneurysm rupture. Mayo Clin Proc. 2004 Feb. 79 (2):176-80. [Medline].

5. Baciewicz FA, Jr, MacArthur RD, Crane LR. Repair Type I Aortic Dissection in a Patient With Human Immunodeficiency Virus Infection. *Ann Thorac Surg* 2003;76:917–9

6. Kumtap YC et al. Ascending Aortic Dissection in the developing world; Case report. *Jos Journal of Medicine*, Volume 12(1); 16-21

7. Monsuez JJ, Charniot JC, Escaut L, Teicher E, Wyplosz B, Couzigou C, Vignat N, Vittecoq D. HIV-associated vascular diseases: Structural and functional changes, clinical implications. Int J Cardiol. 2009; 133:293-306.

8. Khunnawat C, Mukerji S, Havlichek D Jr, Touma R, Abela GS. Cardiovascular manifestations in human immunodeficiency virus-infected patients. Am J Cardiol. 2008; 102:635-642.

9. Tsiodras S, Mantzoros C, Hammer S, Samore M. Effects of protease inhibitors on hyperglycemia,

hyperlipidemia, and lipodystrophy: A 5-year cohort study. Arch Intern Med. 2000; 160:2050-2056.

10. Mills AM, Nelson M, Jayaweera D, Ruxrungtham K, Cassetti I, Girard PM, Workman C, Dierynck I, Sekar V, Abeele CV, Lavreys L. Once-daily darunavir/ritonavir vs. lopinavir/ritonavir in treatment-naive, HIV-1-infecte143-146.

11. Molina JM, Andrade-Villanueva J, Echevarria J, Chetchotisakd P, Corral J, David N, Moyle G, Mancini M, Percival L, Yang R, Wirtz V, Lataillade M, Absalon J, McGrath D; CASTLE Study Team. Once-daily atazanavir/ritonavir compared with twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive

HIV-1-infected patients: 96-week efficacy and safety results of the CASTLE study. J Acquir Immune Defic Syndr. 2010; 53:323-332.

12. Blanco F, San Román J, Vispo E, López M, Salto A, Abad V, Soriano V. Management of metabolic complications and cardiovascular risk in HIV-infected patients. AIDS Rev. 2010; 12:231-241.

13. Dau B, Holodniy M. The Relationship between HIV Infection and Cardiovascular Disease. Curr Cardiol Rev. 2008; 4:203-218.

14. Barbaro G. Cardiovascular manifestations of HIV infection. Circulation. 2002; 106:1420-1425.

15. Patel PD, Arora RR. Pathophysiology, diagnosis, and management of aortic dissection. Ther Adv Cardiovasc Dis. 2008; 2:439-468.

16. Lin PH, Bush RL, Yao Q, Lam R, Paladugu R, Zhou W, Chen C, Lumsden AB. Abdominal aortic surgery in patients with human immunodeficiency virus infection. Am J Surg. 2004; 188:690-697.

17. Mestres CA, Chuquiure JE, Claramonte X, Muñoz J, Benito N, Castro MA, Pomar JL, Miró JM. Long-term results after cardiac surgery in patients infected with the human immunodeficiency virus type-1 (HIV-1). Eur J Cardiothorac Surg. 2003; 23:1007-1016; discussion 1016.

18. Mukherjee D, Eagle KA. Aortic dissection – an update. Curr Probl Cardiol. 2005; 30:287-325.