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Geriatric human immune deficiency virus (HIV) Infection in Nigeria: A case-series report

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This study involves a case-series of 3 elderly male patients with human immune deficiency virus (HIV) infection managed between 2009 and 2010 at the antiretroviral clinic (ART) University of Ilorin Teaching Hospital, Nigeria. They were all within the age range of 73 to 100 years and had multiple sexual partners. They were also co-managed for hypertension, diabetes mellitus and benign prostatic hyperplasia. Baseline CD4 count was < 350 cell/mm^3 for all of them and their chemistry and haematology results were within normal ranges. Sputum acid fast bacilli (AFB) was also negative. They all had first-line anti retroviral (ARV) therapy and cotrimoxazole prophylaxis. Initially, adherence was perfect in all of them (≥ 95%) especially as their relatives who double as the treatment-partners ensured their regular intake of ARV and clinic attendance but later adherence became poor (< 80%) which was reflected in the fallen CD4 counts. Reasons for this include dementia and polypharmacy. One developed severe anaemia due to zidovudine (ZDV)-induced bone marrow suppression and was appropriately managed. Two of the three cases died < 2 years post-HIV diagnosis. Conclusively, geriatric HIV infection management entails multidisciplinary approach and a sound working knowledge of antiretroviral therapy with all the peculiar charateristics in the elderly.

Key words: Human immune deficiency virus (HIV), geriatric, adherence, highly active antiretroviral therapy (HAART), people living with HIV (PLHIV).

INTRODUCTION

Geriatrics, known as the care of the elderly (≥ 65 years), is fraught with multiple pathologies. These illnesses or disabilities can be categorized into 'age-determined', which are as a result of the inevitable changes associated with the aging process, or'age-related' which result from an accumulation of risk factors such as poor nutrition, cigarette smoking, excessive alcohol intake, lack of exercise and unprotected exposure to multiple sexual partners (Walensky et al., 2006). The latter group can therefore be slowed down or prevented by a healthy lifestyle and adoption of health promotion measures while the former group of morbidities are to a large extent inevitable. Human immune deficiency virus (HIV) infection in the elderly fall into the latter category.

Since the discovery of HIV 30 years ago, there has been a substantial increase in the average age of HIV infected patients worldwide. Much of this increase is because of improved survival of patients on antiretroviral therapy (ART), changes in behavior that have resulted in HIV-1 seroconversion at a more advanced age and a lack of clinical suspicion of HIV-1 infection, which leads to diagnostic delays in older individuals (UK Collaborative HIV Cohort (CHIC) Study Steering Committee, 2007; Centers for Disease Control and Prevention, 1998).

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Because of the low prevalence of recognized infection in older patients and rapid disease progression during the earlier phases of the epidemic, HIV-infected patients are considered to be “elderly” when they were older than 50 years of age (Centers for Disease Control and Prevention, 1998).

Probably due to delayed diagnosis, HIV-infected elderly patients generally have more advanced disease than do younger patients at the time of diagnosis (Centers for Disease Control and Prevention, 1998). Also, mortality rates within 1 year of acquired immune deficiency syndrome (AIDS) diagnosis are substantially greater in older versus younger patients (Centers for Disease Control and Prevention, HIV/AIDS surveillance report, 2006). There are no manifestations of HIV-1 disease that are unique to the elderly. However, some prominent symptom complexes and AIDS-defining illnesses frequently associated with the elderly HIV infection include peripheral neuropathy, weight loss, HIV associated esophageal candidiasis, wasting, and HIV-associated dementia (HAD) (Centers for Disease Control and Prevention, 1998)

Another key distinguishing clinical feature of HIV-1 infection in the elderly is the higher prevalence of comorbidities. To a large extent, personal habits (for example, tobacco, substance, or alcohol use) and the normal consequences of aging contribute to the occurrence of comorbid conditions. Also, various antiretroviral agents are associated with multiple acute and long-term medical complications, and HIV infection itself also contributes to the onset and severity of comorbid conditions (Lodwick et al., 2008; Phillips et al., 2008; Weber et al., 2006). All these factors could make management of HIV infection in the elderly very challenging especially in the low resource settings where necessary medical tools and equipments may not be readily available and these elderly patients are often too poor to afford quality healthcare service in the absence of social benefits.

Globally, in 2002 there were 605 million old people of which 400 million were living in low-income countries, and It is projected that by 2025, the number of elderly people would have risen to more than 1.2 billion with about 840 million of them in low-income countries (Park, 2007). The increasing number of old people is due to improvement in medical and social services with increase in the standard of living worldwide. In the United States in 2006, persons 50 years of age or older accounted for 14.9% of all new diagnoses of HIV-1 infection and 19.9% of all new diagnoses of AIDS. They make up 25.3% of all individuals living with HIV-1 infection and 36.9% of all deaths of HIV-infected persons (Lodwick et al., 2008) and by 2015, one half of all HIV-infected patients in the United States will be older than 50 years of age (US Department of Health and Human Services, 2009). Figures for low resource settings are unavailable.

The majority of patients enrolled in most HIV clinical trials have generally been too young to provide good insight into the management of older HIV-infected patients. In some studies, participants were younger than 40 years of age. Hopefully, increased attention to elderly (that is, older than 50 years of age) HIV-infected patients will increase their inclusion in clinical trials and provide the data we need to give them better medical care. This case-series obtained from the ART clinic of University of Ilorin teaching hospital, Nigeria therefore aimed to bridge the knowledge gap in geriatric HIV infection, highlight the challenges in managing elderly HIV infected patients and the peculiarities of geriatric HIV presentation in a developing country like Nigeria and the need for multi-disciplinary approach to care.

CASE-SERIES PRESENTATATION

Case 1

Mr. Y. M was a 100 year old, butcher, married to 4 wives and had 15 children, lived in Ilorin, Kwara State, Nigeria. He was diagnosed as HIV seropositive on July 22nd, 2009 while undergoing pre-surgical investigations for herniorrhaphy. At presentation, there was history of chronic weight loss and recurrent genital and perineal rashes. He later developed cough, which was productive of whitish sputum, night sweat and fever. He was screened for pulmonary tuberculosis with sputum acid fast bacilli (AFB) and chest x-ray, both of which came out with negative results. There was no history of previous surgery and blood transfusion but there were remarkable scarification marks on the body and face. These marks and the multiple sexual partners constitute risk factors of HIV infection in this case. Baseline CD4 count was 253 cells/mm^3 with normal haematology and chemistry results. Blood sugar was normal too. He had adherence counselling and was commenced on highly active antiretroviral therapy (HAART) (NVP 200 mg + 3TC 150 mg + D4T 30 mg, 12 hourly) with cotrimoxazole 960 mg daily after a thorough adherence counselling. Concurrent management of the hypertension, diabetes mellitus and the prostatic hyperplasia (BPH) conditions of the patient by the the other medical, endocrinology and the urological teams continued. Adherence to ARV was initially perfect (> 95%) but later became poor and the CD4 count declined to 118 cells/mm^3 over a period of 3 months on ARV therapy. Other causes of declining CD4 count like presence of opportunistic infections and human and mechanical errors in the laboratory were ruled out. He claimed to have disclosed to one of his wives and a son who was his treatment partner and accompanied him to the clinic. HIV status of the other 3 wives was unknown. He defaulted his last clinic appointment; was last seen in the ART clinic in July 2010, and was tracked to his home where it was learnt that he died on October, 2010; 16 months after HIV diagnosis. Cause of death was unknown.

Case 2

Mr. M. S was a 73 year old retiree, married to a second wife after the demise of the first wife in a road traffic accident. He lived in Ilorin, Nigeria. He was diagnosed to be HIV seropositive on 7 August, 2009. At presentation, he complained of generalized body rashes with chronic weight loss, no fever or diarrhea. On examination, nothing was significant except a herpetic rash on the left lower thoracic region with a septic focus on the chest (Herpes Zoster), and for this he was given antibiotics and analgesics. He was a known diabetic and hypertensive patient diagnosed more than a year ago. These conditions were well controlled with oral hypoglycemic and antihypertensive drugs by the endocrinology and the internal medicine units. He was also seen by the chest physician for his bronchial asthma. He later developed productive cough with no fever or night sweat, sputum AFB and microscopy (MCS) done were negative (CXR was not done). He also presented with symptoms of prostatitis and benign prostate enlargement (BPH) confirmed with ultrasound scan of the prostate (PSA was not done), and was referred to the urologist.

Baseline CD4 count was 281 cell/mm^3 with normal haematology and chemistry results. He was started on HAART (NVP 200 mg + 3TC 150 mg + D4T 30 mg, 12 hourly) with cotrimoxazole 960 mg daily. D4T (stavudine) was later substituted with zidovudine 300 mg bd (ZDV) to avoid side effects (peripheral neuropathy). Ongoing adhrerence counseling service was accessed by the patient. There was improvement in the patient's condition as the CD4 count increased from 281cell/mm^3 to 368 and 375 cell/mm^3 at 6th and 12th month follow up visits, respectively. The adherence which was perfect during this period nose-dived later as the patient started denying his HIV serostatus (senile dementia). However, he did not default in his clinic appointment as his wife, who was his treatment partner, brought him regularly to the hospital. The wife was HIV negative. Patient was last seen in January, 2011 but died at home in February, 2011; 17 months after HIV diagnosis. Cause of death is unknown.

CASE 3

Mr Y. A is a 77 year old widower with three children, a civil servant retiree living in Ilorin, Kwara State, Nigeria. He was diagnosed HIV positive in 2010 while attending diabetes mellitus clinic. No prior history of surgery or blood transfusion, no scarification mark. Wife's cause of death was unknown and sexual experience with other women unknown. Baseline CD4 count was 264 cell/mm^3 with normal haematology and chemistry results. He was then commenced on NVP 200 mg + 3TC 150 mg + ZDV 300 mg, 12 hourly but had to be changed to NVP 200 mg + 3TC 150 mg + D4T 30 mg, 12 hourly as the haemoglobin level fell from 14 g/dl (PCV: 42%) at baseline to 3 g/dl (PCV: 9%) over a period of 4 months. Patient had to be transfused with 4 pints of packed cell and placed on haematinics, leading to marked improvement in the haemoglobin level. Other causes of severe anaemia like nutritional deficiency, GIT bleeding etc. were ruled out apart from zidovudine-induced bone marrow suppression. D4T was also replaced with abacavir (ABC) later to avoid side effects of the drug (peripheral neuropaty, lactic acidosis, lipid dystrophy etc). He claimed to have disclosed his status to two of his children, and one of the daughters is his treatment partner who accompanied him to the clinic. At the last clinic visit which was September 7th, 2011, CD4 count was 396 cell/mm^3, weight was 68 kg, had no complaint and was generally looking well.

DISCUSSION

An increasing number of new HIV diagnoses continues to be reported among persons aged 50 years or older. The CDC estimates that there were close to 7,000 new cases in this age group in 2009 in the US alone (US Centers for Disease Control and Prevention, 2009). Many practitioners are beginning to see more of HIV infection in the geriatrics group. Though sexual activity may decline with increasing age, it is still fairly common for many older individuals. Older persons have distinct risks for HIV infection, and therefore needs counseling regarding HIV prevention. Many older adults may find themselves newly single-widowed or divorced, often with little knowledge of the need to protect their sexual health or the skills required to do so. There may be specific age-related barriers to condom use in both men and women. Postmenopausal women, for example, may be less concerned about pregnancy prevention, whereas men may have erectile dysfunction and avoid condom use for this reason. Moreover, lower estrogen levels can lead to vaginal dryness, which is likely to increase the risk of HIV transmission in women. The baseline CD4 count was less than 350 in all the three cases and two of them died less than 2 years after HIV diagnosis despite being placed on HAART. This means they all presented at advanced HIV infection and had a rapid progression of the disease even though the exact time of HIV exposure and seroconversion are not known.

In 2005, 53% of older HIV-infected persons in the United States versus 37% of younger persons developed AIDS within 12 months of their diagnosis of HIV-1 infection (Linley et al., 2007). Similarly, the rates of death within 1 year of AIDS diagnosis are substantially greater in older versus younger patients (Lodwick et al., 2008). The more rapid progression of HIV-1 disease; age-related immune senescence which may be independent of CD4+ T-cell count, the increased prevalence of co-morbidities which may be exacerbated by HIV-1 infection; and decreased rates of immune reconstitution provide a plausible rationale for beginning therapy at higher CD4+ T-cell counts (that is, > 350 cells/mm^3) in older patients than

is generally recommended for younger individuals.

Age-related declines in immune function, including decreased thymic function, as well as deficits of naive and memory CD4+ T-cell function, number, and regeneration contribute to and exacerbate the rate of CD4+ T-cell count decline and disease progression in older HIV-infected patients (Appay and Sauce, 2008; Aw et al., 2007; Haynes et al., 2000; Kovaiou and Grubeck-Loebenstein, 2006). Though not done in these cases due to lack of availability, viral load would have helped In monitoring for virological failure in these patients.

The negative sputum AFB test results seen in these patients despite being TB suspects could mean that they either do not have pulmonary tuberculosis or have negative-smear Koch's disease, which was not surprising too as studies have shown that patients with HIV-related pulmonary TB more often have negative sputum smears (43% versus 24%) (Gupta et al., 2005). There were also adherence problems with two of the 3 cases, even though the use of relatives as treatment partners in the three cases was associated with regular clinic attendance and perfect adherence (> 95%) at the initial stage. Comorbidities necessitating intake of multiple drugs and onset of dementia common in the geriatric population may pose a serious challenge to adherence as seen in one of the cases.

The sudden drastic drop in the haemoglogin level of the 3rd patient due to zidovudine-induced bone marrow suppression should be a source of concern when managing elderly patients irrespective of the baseline haemoglobin. Other ARV adverse reactions common in the elderly include, increased risk of myocardial infarction, cardiovascular disease and/or cerebrovascular event found among patients receiving PI-containing ART, increased rates of cardiovascular toxicity among patients on abacavir and didanosine, especially in patients with previous underlying risk factors for vascular disease (Strategies for Management of Anti-Retroviral Therapy/INSIGHT; DAD Study Groups, 2008; Sabin et al., 2008). Also the rate of development of diabetes has been reported to be more than 3 times higher among HIV-infected men receiving ART (Brown et al., 2005) especially with current use of NRTIs, particularly stavudine, zidovudine, and didanosine agents that cause mitochondrial depletion. Incidence of metabolic syndrome (that is, dyslipidemia, abdominal adiposity, elevated blood pressure, and insulin resistance common in HIV-infected patients increases with age and PI exposure (US Department of Health and Human Services, 2009). The risk of kidney disease associated with HIV infection which is exacerbated by age is worsened with the use of tenofovir.

Careful selection of ARV regimen is important in geriatric patients because of pharmacokinetic interactions between the antiretroviral drugs and other drugs used for other comorbidities for example drugs in classes such as HMGCoA reductase inhibitors (statins), selected antiarrhythmic agents (for example, amiodarone), medications that inhibit gastric acidity, anticonvulsants, warfarin, and selective serotonin uptake inhibitors may be candidates for drug-drug interactions with antiretroviral medications.

HIV infection can cause respiratory disease as a consequence of pneumonia, it is also associated with increased rates of chronic obstructive pulmonary disease and pulmonary hypertension hence it is not surprising that one of the cases developed asthma in the course of management. Regular screening and health maintenance are particularly important in older persons with HIV. In addition to baseline ART evaluations, monitoring of cardiovascular risk, monitoring of fasting lipid and glucose levels, markers of inflammation, renal function, and markers of bone disease, cancer should be undertaken as part of routine medical follow-up to monitor the preexisting age-related comorbidities and laboratory abnormalities, which may be exacerbated by the additive effect of HIV infection itself coupled with adverse effects of ART.

The effects of aging on drug absorption, distribution, and metabolism; the complexities of polypharmacy and drug-drug interactions in patients with concomitant comorbidities; and the increased frequency of pre-existing and emergent laboratory abnormalities with the use of ART warrant special attention in this patient population and often necessitate joint management with other specialties. Also, the geriatric specialists who work with these patients require training in the special issues surrounding HIV infection, and those who work with HIV-infected patients need to be trained in the special issues surrounding aging and these two groups of physicians must communicate.

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ABBREVIATIONS

ART, Antiretroviral therapy; **ARV,** antiretroviral drugs; **CD4-CD4-bearing,** T-lymphocytes; **Sputum AFB,** sputum acid-fast bacilli test; **NVP,** nevirapine; **3TC,** lamivudine; **ZDV,** zidovudine; **D4T,** stavudine; **CXR,** chest x-ray; **MCS,** microscopy, culture and sensitivity; **PSA,** prostate antigen; **PCV,** packed cell volume; **GIT,** gastrointestine; **ABC,** abacavir.

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