

Anti-retroviral therapy induced diabetes in a Nigerian

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Abstract

Background: Anti-retroviral therapy (ART) using Highly Active Anti-retroviral Therapy (HAART) has led to considerable reduction in morbidity and mortality associated with human Immune deficiency virus (HIV) infection. This has led to increased life expectancy in HIV infected individuals on one hand, and side effects of chronic administration of these drugs on the other. One of such untoward effects is the association of anti-retroviral drugs especially the protease inhibitors (PI's) with metabolic derangements such as dyslipidaemia, lipodystrophy, insulin resistance and rarely Diabetes mellitus.

Although there is extensive literature on this dysmetabolic syndrome in the Western World; there is to our knowledge no previous report from Nigeria.

Objective: to report a case of diabetes mellitus following the initiation of anti-retroviral therapy.

Methods: a case report of diabetes mellitus induced by anti-retroviral therapy in a 48 year old Nigerian male.

Conclusion: Awareness and high index of suspicion is required to identify the metabolic complications of ART.

Key words. HIV, ART, Proteases inhibitors, Diabetes, Metabolic Complications.

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Introduction

The introduction of anti-retroviral (ARV) drugs has significantly reduced both morbidity and mortality attributable to human Immuno deficiency Virus (HIV) infection¹.

The prolonged administration of these drugs however, has led to new challenges for both physicians and patients. Notable among these challenges are metabolic complications such as peripheral lipodystrophy, Insulin resistance, dyslipidaemia and rarely diabetes mellitus²⁻⁵

Although there is extensive literature on dysmetabolic syndrome especially among HIV infected persons receiving protease inhibitors (PIs) in the Western World²⁻⁶; there is to our knowledge no previous report from Africa.

The aim of this communication is to report a case of diabetes mellitus following the commencement of anti-retroviral therapy (ART) in a Nigerian HIV infected patient.

Case report

A 48 year old male Nigerian presented to us in December

2005 with a three month history of excessive thirst, polydipsia, polyuria, profound weakness and progressive weight loss despite a voracious appetite. He was found five years earlier to be HIV positive antibodies; when he presented then with history of progressive diarrhea, intermittent fever and malaise; at that time his serum was reactive for HIV-1 antibodies. He then opted for non-conventional treatment at that time as there were many claims of cure for the infection in the country then.

A year later however, good sense prevailed and he opted for conventional therapy with Nevirapine and Combivir® in June 2001, at that time, his CD4 cell count was 150 cells per microlitre of blood. Other serum parameters, including blood glucose, liver enzymes and electrolytes were normal at that time (Table 1). He symptomatically improved while on this regimen until three years later, when his symptoms gradually worsened and CD4 count also gradually declined and by February 2005, the count had fallen to less than 30 cells per micro-litre. Resistance to ARV drugs was then suspected. Second line drugs comprising Indinavir 800mg thrice a day, AZT and Nevirapine were commenced in February 2005. Six months after the initiation of the new regimen (August 2005), symptoms of polydipsia, polyuria, profound weight loss despite good appetite developed.

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Table 1 Laboratory results at first commencement of ARV in June 2001.

Investigation.	Result
Random Blood glucose (mmol/L)	7.0
Haematocrit (%)	43
Platelets (X10 ⁹ /L)	230
WBC count (X10 ⁹ /L)	7.8
CD4 count/ micro-litre	150

His father developed type-2 diabetes at middle age, but none of his siblings has so far developed diabetes mellitus. There is no known family history of hypertension, stroke or sudden death. His wife died of complications arising from HIV infection a year before he was diagnosed to have the infection.

Clinical examination in December 2005 revealed a wasted middle aged man who weighed 38 kg and had a BMI of 13.9 KgM².his blood pressure was normal at 120/60 mmHg supine. He was dehydrated and had a lipoma measuring 6 X4 cm below the right shoulder posteriorly. The lipoma developed about 4 months following the introduction of the second line ARV drugs.

His blood sugar was 26.4 mmol\L the lipid profile revealed fasting hypertriglyceridaemia of 4.6 mmol/L and fasting total cholesterol of 5.6mmol/L; but he had normal liver enzymes and electrolytes (Table 2).

Table 2 Laboratory results after symptoms of diabetes developed..

Investigation.	Result
Random Blood glucose (mmol/L)	26.4
Haematocrit (%)	35
Platelets (X10 ⁹ /L)	237
WBC count (X10 ⁹ /L)	4.0
CD4 count/ micro-litre	<30
Total cholesterol(mmol/L)	5.6
HDL cholesterol(mmol/L)	1.2
LDL cholesterol(mmol/L)	2.3
Triglycerides(mmol/L)	4.6
Serum Uric acid (µmol/L)	440

He was commenced on twice daily insulin (30% regular and 70%lente) and is currently controlled on 30 units in a 24 hour period. He now weighs 63 kg with a BMI of 23.1Kg M². He has continued to receive HAART and his latest CD4 count was 164 cells per microlitre.

Discussion

Before the advent of highly active anti-retroviral therapy (HAART), HIV infection on its own was thought to be protective against the development of diabetes mellitus³

With the advent of HAART however, a new dysmetabolic syndrome with substantially increased risk for cardiovascular events emerged.⁵ This syndrome has variable expressibility; and includes insulin resistance, visceral adiposity, peripheral lipodystrophy, dyslipidaemia and glucose intolerance. These components could present independently or in combination, and all are currently classified as the lipodystrophy syndromes⁴. Our patient had an abnormal lipid profile notably hypertriglyceridaemia in addition to diabetes. Furthermore, he also had a lipoma of recent onset, which could be attributed to fat redistribution that could occur in this syndrome.

Several studies have demonstrated an increased risk of diabetes among HIV infected individual on HAART especially when PIs are included in the regimen. Among HIV infected minority patients in the USA for example, the prevalence of diabetes after three years of PI therapy was 12%, compared to none among these not receiving PI's³

However, although PI's are the most frequent agents associated with metabolic complication, there are evidences to suggest that virtually all classes of agents used in ART has the potential to cause metabolic derangements⁴

Although the mechanism by which ART drugs induce these metabolic changes are not fully clear; it has been shown that indinavir, a PI dramatically inhibits glucose uptake in a dose dependent manner in adipocytes by selectively inhibiting the glut 4 transporter function⁶. Furthermore, there is evidence at least in laboratory studies to show that indinavir down regulates the peroxisome proliferator-activated receptor - γ (PPAR γ) receptor in adipocytes⁷. Obviously some genetic predisposition could explain why not all patients on PI's develop diabetes, or any of the other metabolic complications. It seem likely that those who already have other predisposing factors to the development of such metabolic derangements such a positive family history in the case of diabetes, are more likely to have this complication. Our patient had a positive family history of diabetes and could explain his development of diabetes.

Currently there are concerted efforts by governments and multi-national donor agencies to ensure universal availability of ARV including PI's in Nigeria. The likelihood of practitioners coming in contact with more cases of the dysmetabolic syndrome from

ART drugs would certainly increase. There is therefore the need to have a high index of suspicion to identify the metabolic complications of ART.

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