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CASE REPORT

A Nigerian adolescent with Long term Non-progressive HIV-infection: A case report

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Summary

Children infected with the Human Immunodeficiency Virus (HIV) can be rapid progressors or be at the end of the spectrum of the illness as Long-term Non-progressors (LTNPs). Long term non-progressors are patients who never received Highly Active Anti-Retroviral Therapy (HAART) during the first decade of life and are maintaining good CD4⁺ count associated with declining HIV RNA values. The literature on paediatric patients with LTNP infection is sparse.

An adolescent with HIV LTNP and likely vertical transmission of HIV is presented in this report. She presented with chronic cough, severe anaemia and dyspnea. She was wasted with bodyweight less than the 5th centile for age. She was not sexually active and had no history of blood transfusion, scarification, incisions or sharing of sharp grooming objects.

The results of investigations suggested pulmonary tuberculosis and HIV infection. Her CD4 count was 42%. She was commenced on HAART and subsequently, anti-tuberculosis medications according to NTBLCP/DOTS Programme with improvement in symptoms and appreciable weight gain.

Therefore routine voluntary HIV testing is recommended for all paediatric admission after consent or assent is obtained bearing in mind that a small subset of patients may fall into the LTNPs population.

Keywords: Adolescent, Anti-Retroviral Therapy, CD4⁺ count, Highly Active, Long term Non-progressor, Vertical transmission.

Introduction

The scourge of the Human Immunodeficiency Virus infection (HIV) and Acquired Immunodeficiency Syndrome (AIDS) in Nigeria places the country as the second largest in terms of HIV prevalence in the world and one with the highest rate of new infection in Africa. [1] Also, the latest prevalence rate of HIV infection among people aged 15-49 years is 1.4% and viral suppression is at 42.3%. [2] It is a known fact that many people living with HIV in Nigeria are not

aware of their HIV-status and Voluntary Counselling and Testing (VCT) services are not offered or utilized by all hospital clientele who do not know their status. Females are much less likely to use VCT compared to males. [3]

In 2016, 7% of people living with AIDS in Nigeria were adolescents with rising mortality among 10-14 year old occurring only in Nigeria and this reflects poor health outcomes for adolescents. [4] This is not surprising as

only a few adolescents test for HIV regularly according to reports. [5]

HIV-infected persons can be classified into three major groups: (1) Rapid progressors, in whom AIDS develops within three years of infection, (2) Intermediate progressors, in whom AIDS develops slowly over three to ten years after seroconversion and (3) Long Term Non-progressors (LTNPs) where HIV-infected persons maintain high CD4⁺ and CD8⁺ cell counts and are therapy naïve. [6] Long-term non-progressors are further sub-divided into two groups: those with low plasma viraemia (< 5000 HIV-RNA copies/ml) known as long-term non-progressors and those with plasma viraemia persistently < 50 copies/ml known as the “elite” or “natural controllers”. [7]

Infants with vertical infection of HIV have high rates of rapid disease progression with a 50% chance of survival by the age of two years. [7, 8] Based on this observation, survival into adolescence without HAART was considered very rare in Africa. However, newer studies have reported otherwise, with about one-third of HIV-infected infants having a more slowly progressive disease with mean survival rates ranging from eight to sixteen years of age. [10] In Harare, Zimbabwe, a group of untreated adolescents with vertically transmitted HIV infection who were newly diagnosed with no symptoms and normal CD4⁺ count were suggested to be categorised as the Long Term Non-progressors (LTNPs). [11]

Host, genetic and viral factors have all been identified to play specific roles in the response of LTNP patients to HIV infection. The genetic determinants have been suggested to be predicted by the presence of polymorphic Human Leucocyte Antigen (HLA) on chromosome-6 with striking associations reported between HLA alleles and viral control. [12, 13] The genetic factors that influence the rate of progression from HIV to AIDS include: encoding cell- surface receptors,

genes within human leukocyte antigen (HLA) – regulates host immune response to infection and genes responsible for cytokines or immune response. [7] HLA-B81:01 and HLA-B39:10 alleles are associated with viral replication control in HIV-1 infection in Africans, while haplotypes B35 is associated with rapid progression to AIDS. [7, 14] Also, amino acids 25 to 36 in Negative regulatory factor (nef) which are vital in the pathogenesis of HIV-1 are defective and have poor viral infectivity in LTNP. [7] The cellular Antiviral Protein APOBEC3G, which is a cytidine deaminase, has been shown to have various anti-viral effects against HIV-1 infection, including reverse transcription. [15]

This report aims to create awareness about the existence of a subset of paediatric HIV population known as the Long Term Non-Progressors (LTNPs) and to advocate for consented routine voluntary HIV testing for all paediatric admissions for early detection.

Case Description

A 12-year old female junior secondary school student was verbally referred to the Olabisi Onabanjo University Teaching Hospital, Sagamu from a private hospital on account of cough and generalized pallor, both of two months duration.

The cough was productive of yellowish, foul-smelling sputum but was not bloodstained. She had a fever in the evenings, loss of weight shown by loosely fitting clothing and loss of appetite but there were no drenching night sweats. She did not consume unpasteurized milk. There was no history of contact with an adult with chronic cough or adults on treatment for tuberculosis. There was no fast breathing or noisy breathing. Generalized pallor was associated with easy fatigability. There was no bleeding from the gums or orifices. She had no history of jaundice, recurrent bone pains, passage of dark coloured

urine, unhygienic hypodermic injections or body swelling.

She was not sexually active with no history of sexual abuse, no scarifications and had never been transfused with blood. She presented at another Teaching Hospital outside Ogun State in the first week of the illness and was treated for febrile illness. She subsequently re-presented at the same facility on account of persistent cough and was treated for possible pneumonia with antibiotics. However, the illness persisted despite antibiotic therapy. Before presentation at our facility, she had earlier been screened positive for HIV at another facility.

The pregnancy was supervised at a Traditional Birth Home and spontaneous vertex delivery took place at the same place at term. She was not breastfed on account of maternal epileptic disorder but she was fully immunized for age according to the National Programme on Immunization schedule. Her haemoglobin phenotype was AA and she had no previous hospital admission until the illness started.

The parents were not married. The father died eleven years prior - the cause of death was unknown. The mother was a thirty-eight-year-old junior secondary school certificate holder and unemployed.

The girl had been residing with a 47-year old married maternal aunt in the last eleven years. The HIV status of the members of the foster family was not known.

Physical examination revealed a chronically ill-looking adolescent, with severe pallor and pyrexia with an axillary temperature of 39.1°C. She was anicteric, acyanosed, not dehydrated with no palpable significant peripheral lymphadenopathy or digital clubbing. There was no oral thrush. She weighed 24.3kg which was < 5th centile for age. The respiratory rate was 40 cycles per minute and pulse oximetry

showed 97% SPO₂ in room air. The chest expansion was reduced on the right hemithorax.

The percussion note was resonant in the upper lobe but dull on the right lower lobe. The quality of breath sounds was also reduced in the right hemithorax.

The pulse rate was 100 beats per minutes, moderate volume and the apex beat was located at the fifth left intercostal space midclavicular line. There was non-tender hepatomegaly of 4cm size with a smooth surface.

The Packed Cell Volume was 14%. She was subsequently transfused with partially packed red blood cells. The initial serum electrolytes panel revealed hypokalemia which was corrected orally with Mist Potassium Citrate and serum potassium was subsequently confirmed normal. The Erythrocyte Sedimentation Rate (ESR) was > 100mmhr⁻¹ (normal value: <15mmhr⁻¹). Mantoux test was non-reactive but the Chest x-ray revealed a thick-walled cavity with an air-fluid level at the right upper lung zone with reticulonodular opacities in the right lower lobe zone. These features were highly suggestive of pulmonary tuberculosis (Figure 1). However, Gene Xpert was negative for MTB. Following counselling and consent and assent, the mother and the child both tested seropositive to HIV and the CD4 count was 42%. The HIV viral load which was determined eight months after the commencement of HAART was 75 copies per ml.

The child was commenced on anti-tuberculosis medications namely: Isoniazid, Ethambutol, Pyrazinamide and Rifampicin according to the National Tuberculosis and Leprosy Control Programme/ Directly Observed Short course Therapy (NTBLCP/DOTS) guidelines.

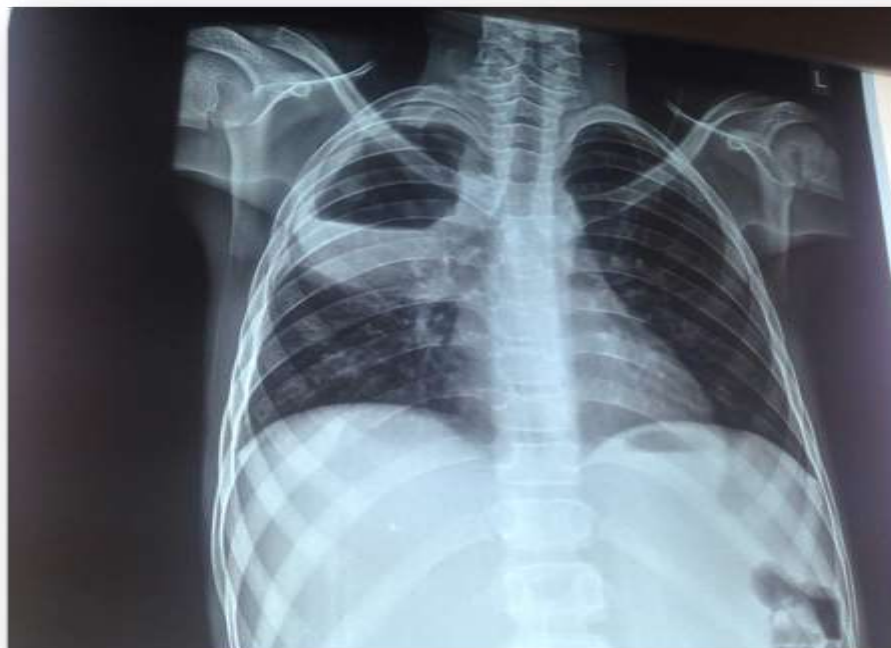


Figure 1: Chest X-Ray showing thick-walled cavity with an air-fluid level at the right upper lung zone and reticulonodular opacities in the right lower lobe zone.

The child was discharged home. The body weight at follow-up visits to the clinic four weeks later was 29.6kg – increase of five (5) kilogram with a significant reduction in cough, resolution of fever and restored appetite. She completed her anti-tuberculosis treatment at our DOTS Unit.

The Highly Active Anti-retroviral medications (Tenofovir, Efavirenz (later changed to Dolutegravir) and Lamivudine) were commenced seven weeks after commencement of anti-tuberculosis treatment. The improvement in the child's clinical state was consistently satisfactory.

Discussion

Paediatric long-term non-progressors (LTNPs) are defined as "HIV-1 infected children who had been observed for at least ten (10) years

who had never received antiretroviral treatment (other than Zidovudine monotherapy), who had never developed symptoms of Centres for Disease Control and Prevention (CDC) clinical category C or B, and for whom the CD4⁺ cell percentage was 25% more than once throughout the follow-up period before they reached ten (10) years of age."^[16] They are also described as a group of patients who never received Highly Active Anti-Retroviral Therapy (HAART) during their first decade of life and will continue to maintain good CD4⁺ count associated with declining HIV RNA values. ^[16] The index patient did not receive HAART in the first ten years of life and the CD4 count at presentation was within normal for her age at 42%, ^[19] though HIV RNA value was not determined.

In a Ugandan study, 9.1% of the children studied were LTNPs, ^[16] while the report from

cohort studies in the USA and Europe approximated the prevalence to 5-8%. [20] Warszaski *et al* found 2% among studied French children, [16] but there is no data on the population of paediatric patients who are LTNPs in Nigeria. This should be researched.

Though the mother's pregnancy was supervised at a traditional birth home with delivery at the same place, the fact that girl was not breastfed could have protected her from perinatal retroviral infection transmission.

She had no history of hospital admission which is an indication that she did not have any major illness before the reported illness. The fact that the foster parents sought medical intervention at a Teaching Hospital in the first week of her illness could suggest that they very likely would have sought medical intervention on her behalf in the past if there was a need.

The opportunistic infection our patient presented with was pulmonary tuberculosis which is common in studied paediatric subjects with LTNPs. [17] It is suspected that the index patient acquired the HIV infection vertically, with the hindsight that her mother was not diagnosed with HIV infection at pre- or perinatal period and she was not on HAART, just as the child never had antiretroviral prophylaxis.

In the biology of HIV infection, after the acquisition of HIV, the virus enters into the cells and attach to the CCR5 and CXCR4 proteins (mostly CCR5). Mutations or deletions of these proteins may explain why an HIV-infected individual rarely progresses to AIDS. [15] Although the CD4⁺ count for the index patient was determined HIV tropism test could not be done.

Some of the factors which may support the tendency for LTNPs to live without taking HAART include gene and receptor mutations, mitochondrial DNA types and different

human leukocyte antigen (HLA) types, specifically, HLA-B81, HLA-B39 (especially in Africans), HLA-B27 and HLA-B57. [14, 21] It was not possible to do HLA antigen typing for the index patient on account of available laboratory facility competence.

However, we are curious to know if the biological father was also HIV-infected. If the father was infected, the girl could have inherited mutated HIV attachment proteins from him.

Conclusion

Though the incidence of LTNPs among children is low from available data in other parts of the world (though no national data is available), as clinicians it is imperative to have a very high index of suspicion and investigate children presenting with AIDS-defining diseases with or without prior history of HIV seropositivity.

Poor laboratory facilities may also contribute to the paucity of data in the population of paediatric HIV patients with Long Term non-progressive disease in Nigeria.

Also, routine voluntary HIV testing is advocated for all paediatric admissions following consent or and assent. This could be of value in identifying paediatric HIV patients with Long Term non-progressive disease in Nigeria.

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