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HIV/AIDS selective infectivity-report of two peculiar cases

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ABSTRACT

We report two peculiar cases that were observed in two communities of Anambra State, South East Nigeria. The first case was a woman of 44 with a history of blood transfusion from a donor of questionable HIV status. A pint of blood was transfused in a private Hospital on the 15th January, 2000. She has had no form of antiviral therapy until 22nd April, 2008 when she came to the hospital for routine medical check up. Her HIV result came out confirmed positive while that of her husband came out negative. She has had active sexual life with her husband in the previous eight years as they have had some difficulties in getting their desired extra two children having earlier gotten a boy and a girl. The second case involves a family of six. A couple with four children of ages about 6 months, 2 years, 3 years and 5 years. The youngest, a female presented with fever and multiple lymphadenopathy. She tested HIV positive and so was her mother and her second sibling. But her father and two other siblings remained negative at post three and six months intervals from their very first test date with us. These reported cases appear to go contrary to earlier formed opinion on HIV transmission. We support the opinion on a naturally, occurring substance, APOBEC3G which possibly confers permanent immunity against the HIV virus. We recommend clinical trials of the characterized APOBEC3G as a vaccine for non HIV infected persons of all ages and to people living with HIV/AIDS as a therapeutic drug.

1. Introduction

It is now 27 years after the first published report on HIV and the global epidemic continues unabated, with estimates of over 33 million people currently infected, Worldwide[1]. Tropical and developing countries like ours are worse hit by the overwhelming consequences of HIV/AIDS pandemonium.

Development of targeted therapies aimed at perturbing the HIV life cycle can be achieved only with a detailed comprehension of the dynamics of virus-host interactions within the cell. One of such critical virus-host interaction is the recently elucidated interplay between the viral Vif (Virion infectivity factor) protein and innate immune defense molecules APOBEC3G. APOBEC3G potently suppresses HIV replication but, Vif can alleviate this inhibition, rescuing viral infectivity[1].

Vif acts by binding to APOBEC3G, introducing its protein degradation within infected cells and reducing its levels in progeny virions. Interventions that interfere with the Vif-APOBEC3G interaction, raise intracellular or virion associated levels of APOBEC3G or reduce the levels of Vif[2]. It follows logically, that higher levels of APOBEC3G in an individual shall possibly immunize the person against HIV/AIDS. Transmission of HIV to a new host could normally occur via any means that admits or allows blood or some blood products into the vasculature of the new host from an already infected individual. The entry of blood cells is in most cases dependent on chance and volume thus whole blood transfusion remains the most potent means of HIV transmission. HAART reduces the risk of HIV sexual transmission; for individuals with chronically suppressed viral loads, the transmission risk may be negligible in the absence of sexually transmitted infections (STIs). It has been justified that HIV positive individuals with up to 800 CD4 do not transmit HIV to their sexual partners[3].

In Nigeria 80% of HIV infections are transmitted by heterosexual sex. Factors contributing to this include a lack of information about sexual health and HIV, low levels of condom use and high levels of STIs such as chlamydia and gonorrhea, which make it easier for the virus to be transmitted. Blood transfusions are responsible for 10% of

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all HIV infections[4].

There is a high demand for blood because of road traffic accidents, blood loss from surgery and childbirth, and anaemia from malaria. As there is no effective coordinated national blood supply system, blood is not routinely tested for HIV, and a study revealed that 4% of blood donors in Lagos were HIV positive. The remaining 10% of HIV infections are acquired through other routes such as mother-to-child transmission, homosexual sex and injectable drug abuse. The rate of mother-to-child transmission in Nigeria has gone up in recent years as the number of HIV positive women has increased[5].

A recent study has shown that Hepatitis B and C co-infection with HIV might also be a major factor of virulence particularly, among Nigerian inmates in Nasarawa State, Northern Nigeria[6].

Homosexuality other than sharing of injections drugs may be a realistic source of spread, they insinuated. The global prevalence of HIV-1 has stabilized at 0.8%, with 33 million people living with HIV/AIDS, 2.7 million new infections, and 2.0 million AIDS deaths in 2007[7].

Heterosexual spread in the general population is the main mode of transmission in sub-Saharan Africa, which remains the most heavily affected region, with 67% of the global burden. Male-male sex, injection drug use, and sex work are the predominant risk factors in most other regions.

Infection rates are declining in some regions, including some of the most heavily affected countries in Africa, but climbing elsewhere such as in eastern Europe and central Asia[7].

Recent HIV epidemiologic research findings include new insights into the role of HIV viral load, co-infection with sexually transmitted infections, male circumcision, antiretroviral treatment, serosorting, and superinfection in HIV transmission and prevention[7].

These foregoing justifies the pressing need for an urgent means of curbing spread through a clearer understanding of the interplay of the natural defense mechanism and possibly developing drugs that act like these natural defense mechanisms.

2. Cases report 1

Our first case report involves a middle age married woman, a mother of two, a petty-trader and part-time Church Orderly. The husband is unemployed. She presented at our clinic with recurrent fever, anorexia and twitches-kind of skin irritations. She also had secondary infertility of about 8 years standing. She lives with her family.

Blood sample was collected for WIDAL, MP, HB, TPHA, HBSAG and RVD. Urine and HVS samples were also collected for analysis, culture and sensitivity.

Laboratory results showed positive to MP and HIV-1 with a yield growth of coliforms. At her next visit, she was given a second degree counseling on HIV/AIDS and was asked to come back on a later date with her husband. The husband obliged and came out negative with a triple-method testing check (Screening a patient's sample with 3standard HIV-kits of different make). His sample was further collected post 3 and 6-months for Western-Blot method (Immuno-Confirm), used for HIV confirmation and he still came out negative. But that of his wife still came out confirmed positive for HIV-1.

On further questioning, the couple could only remember a case of complicated still-birth that resulted in blood transfusion on 15th of January, 2000. Over 8 years from the date of her first clinic visit. There were no observable typical HIV/AIDS observations/symptoms on the woman and she has had no standard anti retro-viral drugs within the said period.

3. Case report 2

The second case involves a family of six. A couple with four children of ages about 6 months, 2 years, 3 years and 5 years. Both parents are petty-traders and the family lives in a Sub-Urban area of the Metropolis. The youngest, a female presented with fever and multiple lymphadenopathy. She was said to be rejecting food and breast milk and showing signs of restlessness. She tested HIV positive to both screening and confirmatory.

In line with our hospital management policy, her entire family was invited and blood samples collected for both screening and confirmatory methods. Her mother and her second sibling age 3 came out confirmed positive. But her father and two other siblings, ages of 2 and 5 remained negative at post three and six months intervals from their very first test date.

3. Discussion

A non published source has demonstrated a case of HIV seropositive of over eleven years standing with no clinical signs and in complete absence or non-usage of any known standard anti retro-viral drugs.

The first major peculiarity of our two cases report is the fact that HIV seropositive cases had remained without clinical signs in complete absence or non usage of any known standard antiretro viral drugs. Could the school of thought that insists on the fact that HIV kills with "know and fear" of the suffer be right? According to NACA[8], most cases of reported HIV infection in Africa, present with clinical signs within the first 1-2 years with most patients dying in the first three years if untreated, globally.

It has been reported that most cases of seropositive HIV manifest clinically, within the first 5 years and maximally before ten years. But, this position was said to only be possible in developed countries and with people on proper diet and highly hygienic life style. In our cases reported, the families are below average Nigerian families thus can not be said to be on proper diet and Nigeria is not yet among the

developed countries. The part of the country where they live is also not part of the high hygienic areas of Nigeria.

The second peculiarity in our cases report is the selective nature of HIV infectivity within people with equal risk of exposure. In the first reported case, the woman has had active faithful sexual life with her husband. The man who has had nothing of economical earnings for over three years could only but, work along the wife's petty-trading and Church orderly job.

Sexual life-style has been documented to be more active among this lower cadre of people as they usually have more ample time to themselves. It follows logically, that this couple has indeed had active sexual life in the past over eight years.The woman most probably may have had a CD4 count of over 800 but, the so called micro-trauma ought to have occurred over the years.

The most astonishing part is the gross disparity of infection in the second family. The children were all delivered in the same hospital and the last child who most possibly has had a safer precautionary delivery, came down with the disease.

According to Ao and colleagues[9], APOBEC3G (A3G), a deoxycytidine deaminase is a potent host antiviral factor that can restrict HIV-1 infection. The A3G is found naturally and its plasma level may be of clinical importance just like that of bcg-antigen/antibody that protects naturally against tuberculosis. HIV-1 synthesizes a viral infectivity factor (Vif) to counter A3G restriction but, it is poorly understood how the human cellular factors regulate the plasma level of A3G[10].

The Vif is found only on HIV-1[11-13] and all of our cases report are those of infliction with HIV -1. Perhaps this is pattern that is helpful in cubing the spread of HIV transmission in this part of the world since HIV-2 is very uncommon in Nigeria.

It is our cock believe from our findings that A3G and Vif are responsible for the selective infectivity and virulence or its delay. Where the interplay between the A3G with Vif remains active with neither overwhelming the other, Virulence will be delayed or suppressed for a long like those of our of typical case mothers. Where A3G completely overwhelms Vif, there may be an outright sero-negative as has been seen in these cases reported and finally where Vif overwhelms A3G, sero-positive case ensues as well the development of an outright virulence. The protective mechanism of A3G centres on apolipoprotein B-mRNA editing enzyme, catalytic polypeptide-Like 3G; a DNA-editing enzyme produced by host cells infected by certain retroviruses that is then incorporated into the virions. The cytidine deaminase activity of A3G aids its mutation of the minus-strand DNA formed during reverse transcription thus A3G particularly, blocks reverse transcription in retro viruses[14] An enzyme linked depletion of A3G comes with the activity of E3 Ligase complex that is recruited by Vif.

Drugs targets on anti-E3 Ligase along with analogs of A3G could possibly put an end to the scourging effect of HIV/AIDS. In our final words, we support the opinion on a naturally, occurring substance, APOBEC3G which possibly confers permanent immunity against the HIV virus. We recommend clinical trials of the characterized APOBEC3G as a vaccine for non HIV infected persons of all ages and to people living with HIV/AIDS as a therapeutic drug.

Conflict of interest statement

We declare that we have no conflict of interest.

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