

Hypogonadism and Gynecomastia in 3 Adolescent Boys on ART- 3

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Abstract

Gynecomastia and hypogonadism are not included among the side effects of efavirenz in its drug information even though they had been reported by different authors. Especially they were more common in young adolescent individuals. Here I am reporting a case of Hypogonadism and two cases of gynecomastia among adolescent boys.

Keywords: Efavirenz toxicities; Gynecomastia; Hypogonadism; Adolescent boys

Introduction

Antiretroviral drugs, beyond any doubt, revolutionized the management of people living with HIV/AIDS [1]. At the same time the adverse effects of these ART Drugs incapacitate the individuals in many ways. Especially the wonderful drug Stavudine phased out just because of its adverse effects [2]. Zidovudine lost its place as the first line of drug just because of its side effects as well as the NNRT, Nevirapine.

Still some of the side effects of drugs are yet to be investigated. Drug information on Efavirenz never mentioned about Gynecomastia even though many articles had already been published [3,4]. More than one hundred and twenty HIV positive individuals, who are under my follow up for years, are doing well with Efavirenz combination of ART whereas 2 adolescents who are on long term Efavirenz have developed Gynecomastia and another boy with extreme degree of Hypogonadism. This type toxicity would raise the anxiety to the individual as well as to the parents.

Lipomastia is different from Gynecomastia [5,6]. Lipomastia is common with Stavudine, Didanosine and Zidovudine and sometimes with protease inhibitors, but unheard with Non-Nucleoside Reverse transcriptase Inhibitors.

Case Presentation

Across the long history of human civilization, many discoveries have suggested that deadly viruses to humans are possibly coming from origins outside of human beings. For examples, human plague (black deaths) is proposed to be come from rodents. Rabies virus is widely known to be come from cats or dogs while these animals bite healthy human bodies unexpectedly [1,2]. As a result, the origin of HIV is an important topic in the field of HIV/AIDS studies.

Case 1

18 year old boy was on ART since 4 years. Parents of this boy were nonreactive for HIV infection. History of repeated blood transfusions for neonatal jaundice was there. This boy had pain over joints 4 years back due to multiple osteolytic lesions [7]. Owing to his defective bones he was put on the ART regimen with the combination of Zidovudine, Lamivudine and Efavirenz. He was on this combination for the past 4 years (Figure 1).

Now the parent had the complaints of his genitals are tiny for his age. On examination, this boy's secondary sexual characters were not developed at all with absence of facial, axillary and pubic hairs and small testicular size and micropenis. No obvious gynecomastia. His hormonal analysis revealed a marked low level of Leutinizing hormone, total testosterone and prolactin. FSH and Estradiol were within normal limits [3,4]. His values were: Estradiol: 15.51 pg/mL (Normal for

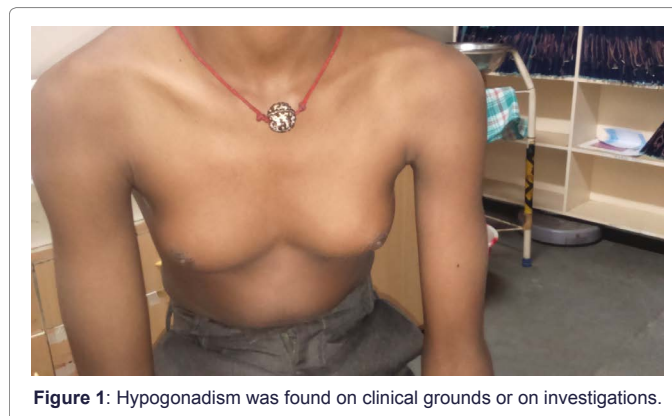


Figure 1: Hypogonadism was found on clinical grounds or on investigations.

males: up to 39.8 pg/mL). FSH: 1.52 (Normal values for adult males: 1.4-18.1 mIU/mL). LH: 0.12 mIU/mL (Normal values for adult males: 1.5-9.3 mIU/mL, above 70 years: 3.1-34.6). Prolactin: 1.69 ng/mL (Normal value for adult males: 2.1-17.7 ng/mL). Testosterone (Total): 68.61 ng/dL (Adult males: 241-827 ng/dL).

Otherwise his general growth and built were normal. His viral load was undetectable and CD4 count was 1094 cells/cubic mm on 27th August, 2016. His CD4 count is progressively improving from 226 cells on 6th August 2013. No other cause for hypogonadism was found on clinical grounds or on investigations.

Case 2

17 year old boy acquired HIV from his parents who were no more. He was on ART at Government ART center since his childhood onwards (more than 14 years). He was on stavudine, Lamivudine, Nevirapine (d4T, 3TC, NVP) combination till his age of 14 year. He was sick then and there. When the regimen switched over to Zidovudine, lamivudine, Nevirapine (AZT+3TC+NVP) due to phasing out of Stavudine [2], he developed marked anemia, so the regimen changed over to Tenofovir, Lamivudine, Nevirapine (TDF+3TC+NVP) on 11-5-2013. Then in the year 2014 his regimen was changed to Tenofovir, Lamivudine, Efavirenz (TDF+5TC+EFV) as per the availability in Government ART center. His CD4 count was fluctuating between 264 in June 2011, 785 in

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December 2011, 470 in June 2014, 585 in December 2014, 412 in May 2015 and 388 in November 2015. He is having marked gynecomastia since 2015 onwards. He was on the Efavirenz combination since 4 years [5-8] (Figure 2).

Case 3

This is also a 16 year old boy acquired HIV through perinatal transmission and presently on the ART regimen of Tenofovir DF, Lamivudine and Efavirenz (TDF+3TC+EFV) combination Government ART centre for the past 3 years. He came to my clinic for an episode of fever with sore throat when he reported the complaint of enlarged breast (Figure 3).

Discussion

Efavirenz is known to cause Gynecomastia [3,4]. But there was no report of hypogonadism so far. Even though 100s of my patients are tolerating well Efavirenz without much of side effects and have a good viral control, this sort of hypogonadism and gynecomastia were obvious manifestations in young adolescent boys on ART with

Efavirenz as the third drug in the ART combination to NRTI backbone. The exact mechanism by which it causes hypogonadism and gynecomastia is yet to be revealed especially when their liver functions were normal and have a good viral control. NRTI drugs are known to cause lipodystrophy and subsequent lipomastia which can be easily differentiated by palpation and consistency (rubbery and firm) of the real breast tissue and exclusive adipose (soft) tissue. Breast tissue (ducts and mammary glands tissue) can well be palpated in case of real Gynecomastia under areola region on palpation [5,6].

Conclusion

Recent guidelines for the management of pediatric HIV as per National Institutes of Health (NIH) of USA has not recommended Efavirenz as a preferred ART in the management of pediatric HIV for both children and adolescents. It comes under either an alternative choice or a preferred drug only for adults.

Efavirenz is well known for its CNS toxicity and mild hepatotoxicity. Gynecomastia and hypogonadism are not focused adequately so far. But it is dreaded complication especially for adolescent boys and prepubertal girls which have to be stressed adequately and physician should be cautious when prescribing Efavirenz for children.

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Figure 2: Developed marked anemia.



Figure 3: Lamivudine and Efavirenz (TDF+3TC+EFV).