

Case Series

A case series of efavirenz induced gynaecomastia

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ABSTRACT

The prognosis of HIV infection has significantly changed following the introduction of highly active anti-retroviral therapy by reducing AIDS related morbidity and mortality. At the same time, HAART is documented for its side effects. Gynaecomastia is a less documented side effect of a commonly used ART drug efavirenz. There are only few case reports of HAART-induced gynaecomastia in resource limited settings. Initially gynaecomastia related to HAART in HIV patients was thought due to lipodystrophy and was termed as pseudogynaecomastia. Later, few case reports of efavirenz related gynaecomastia were published after ruling out other causes of gynaecomastia. All other causes of gynaecomastia were ruled out in our patients too. The incidence of gynaecomastia is increasing in men with HIV on HAART therapy, proper identification and management will promote better drug adherence. The present study presented a series of two cases that developed ultrasound confirmed gynaecomastia following efavirenz containing HAART.

Keywords: HIV, HAART, Efavirenz, Gynaecomastia

INTRODUCTION

The prognosis of HIV infection has significantly changed following the introduction of highly active anti-retroviral therapy by reducing AIDS related morbidity and mortality. All guidelines across the world have now accepted the treat all policy, that is, initiation of ART in all HIV positive patients, irrespective of CD4+ count.¹

According to the standard guidelines, first line ART for treatment naive adult should consist of triple drug regimen, nucleoside reverse-transcriptase inhibitors (NRTIs) backbone (2 drugs) and one non-nucleoside reverse-transcriptase inhibitor (NNRTI).² Based on the efficacy and side effects profile, tenofovir+lamivudine+efavirenz (TLE) as a fixed dose combination is preferred. Efavirenz is given in a dose of 600 mg per day in this regimen.³

Side effects profile of anti-retroviral drugs ranges from low grade intolerance which may be self-limiting to life

threatening. Side effects of efavirenz includes most of the adverse effects limited to central nervous system for example drowsiness, dizziness, confusion, vivid dreams.³

Gynaecomastia is one of the lesser known and least reported adverse effects associated with efavirenz based therapy. An imbalance between the sex hormones, that is, oestrogen and androgens leads to benign development of glandular breast tissue in males known as gynaecomastia.⁴

Study done by Piroth et al in males who were on HAART, reported that the incidence of gynaecomastia in the patients on efavirenz was about 0.8/100 patients/year with a prevalence of 2.8% in those treated for longer than 2 years.⁵

Most of the case reports of efavirenz induced gynaecomastia are from resource rich countries, only few case reports are from our country.

The cases who visited the ART center of Bowring and Lady Curzon hospital are taken for the study.

CASE SERIES

Case 1

A 19 year old boy presented to outpatient department with history of bilateral breast swelling since 1 year. He was diagnosed to have retroviral disease 2 years back since then he is on TLE regimen. He noticed the breast swelling 1 year back but did not consult physician regarding the same. There were no signs of infection and no history of discharge from nipple.

Ultrasonography was done which confirmed the diagnosis. Other causes of gynaecomastia are ruled out by asking relevant history and performing the following investigations: CD4 count was 184; LFT and RFT were normal. Endocrinological evaluation done as follows. Serum estradiol (E2)=28 pg/ml; testosterone=470.92 mg/dl; thyroid profile and prolactin levels were within normal limit.

Diagnosis of efavirenz induced gynaecomastia was made after ruling out other causes. Efavirenz was replaced by nevirapine.

Patient underwent surgery due to cosmetic purpose.



Figure 1: Efavirenz induced gynaecomastia.

Case 2

A 46 year old male presented to the outpatient department with history of bilateral breast swelling since 6 months. He was diagnosed to have retroviral disease 1 year back since then he is on TLE regimen. There were no signs of infection and no history of discharge from nipple.

Ultrasonography was done, which confirmed the diagnosis of gynaecomastia.

Other causes of gynaecomastia were ruled out by asking relevant history and performing following investigations: CD4 count was 126; LFT and RFT were normal. Endocrinological evaluation done as follows. Serum estradiol (E2)=32 pg/ml; testosterone=310.12 mg/dl; thyroid profile and prolactin levels were within normal limit.

Diagnosis of efavirenz induced gynaecomastia was made after ruling out other causes. Efavirenz was replaced by nevirapine. Patient started noticing the regression in size within 6 weeks, complete regression within 24 weeks.



Figure 2: Efavirenz induced gynaecomastia.

DISCUSSION

The incidence of gynaecomastia in a HIV positive patients, who was on ART was found to be 0.8/100 patient years, whereas the prevalence was found to be around 2.8%.⁶

Gynaecomastia in a HIV positive patients can be due to direct factors such as hypogonadism, increased production of prolactin and also the presence of HIV associated cirrhosis. Apart from the direct factors, indirect factors are also responsible such as ART consisting of protease inhibitors such as saquinavir, NRTIs such as stavudine, zidovudine and lamivudine and antifungal such as ketoconazole were also contributing to the development of breast masses in HIV patients.⁷ It is found that gynaecomastia is due to interaction between direct and indirect factors.⁸

In this case series, we encountered efavirenz induced gynaecomastia. We noticed that baseline CD4 count in both cases was less than 200. In both cases gynaecomastia were bilateral and developed within 1 year of starting efavirenz containing ART regimen. Regression was within 24 weeks in one patient after replacing efavirenz with nevirapine and one patient undergone surgery.

In our case series patient recovered by replacing efavirenz with nevirapine, which correlates with other previously published articles. Presentation was bilateral and free testosterone level was normal which was in accordance with study conducted by Njuguna et al.

Few studies conducted demonstrated that efavirenz induced gynaecomastia can also be treated with 20 mg of tamoxifen which was widely used for the prophylaxis and management of anti-androgen-induced gynaecomastia. Other than tamoxifen another oestrogen receptor inhibitor raloxifene and anastrozole, an aromatase enzyme inhibitor has also been used in management of gynaecomastia. Tamoxifen was used in the dose of 10-20 mg/day and raloxifene, in the dose of 60 mg/day for 3-9 months were used.⁹

However, if gynaecomastia continues to persists for more than 1-2 years then surgical management will be most effective compared to medical management.¹⁰

CONCLUSION

The incidence of gynaecomastia in HIV positive male patients, who are on ART is increasing. So, it is utmost necessary to identify the patients with increased risk and educate them regarding the same. It is necessary for early identification and change of the ART regimen.

Needs close observation after changing the regimen for regression before directly heading towards surgical line of treatment.

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