CASE REPORT

Zidovudine-induced nail hyper-pigmentation in 45-year-old women prescribed for HIV/tuberculosis co-infection

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ABSTRACT

Zidovudine is an important component of first-line antiretroviral treatment regimens used to manage HIV and tuberculosis (TB) co-infection. Nail pigmentation is documented both in adult as well as pediatric HIV patients, but to the best of our knowledge, it has not been reported in 45-year-old women of HIV/TB co-infection. Such an adverse drugs reactions (ADR), although is harmless and reversible, psychological aspects of such ADR may be immense to the extent that it can negatively affect the compliance and result in therapeutic failure. Thus, it is worth reporting.

Key Words: Adverse drugs reactions, HIV and tuberculosis co-infection, nail hyper-pigmentation, Zidovudine

INTRODUCTION

More than half of the persons living with HIV infection in the United States will be ≥50 years of age by 2020, including postmenopausal women.[1] A "Cursed Duo," i.e., TB/HIV co-infection is a major public health problem. Globally, one-third of the HIV patients are co-infected with tuberculosis (TB).[2] In India, NACO recommends a regimen containing zidovudine or stavudine along with lamivudine and efavirenz for such patients.[3]

Adverse drugs reactions (ADRs) are a great challenge to national anti-TB and HIV programme. Concomitant administration of highly active antiretroviral treatment (HAART) and anti-tubercular treatment possess significant challenge in the form of cumulative drug toxicities, drug-drug interactions at the pharmacokinetic and pharmacodynamic level leading to complexity of regimens and high pill burden. Advanced immunosuppression in HIV/TB co-infection is likely to increase the incidence of ADRs furthermore complicating the treatment outcomes and the natural history of TB/HIV co-infection. The ADRs can often negatively affect the compliance and can result in therapeutic failure.

Zidovudine is an important component of first-line antiretroviral treatment regimens used to manage HIV and TB co-infection. Nail pigmentation is documented both in adult as well as pediatric HIV patients.[4,5]

However, to the best of our knowledge, it has not been reported in 45-year-old women. Such an ADR, although is harmless and reversible, psychological aspects of such ADR may be immense to negatively affect the compliance. Furthermore, to better understand and create awareness regarding the health concerns of mature women living

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Access this article online

Quick Response Code:

Website: www.jmidlifehealth.org

DOI: 10.4103/0976-7800.179176

How to cite this article: Tandon VR, Sadiq S, Khajuria V, Mahajan A, Sharma S, Gillani Z. Zidovudine-induced nail hyper-pigmentation in 45-year-old women prescribed for HIV/tuberculosis co-infection. J Mid-life Health 2016;7:38-40.

with HIV/TB co-infection as well as to formulate optimal treatment strategies for menopausal women living with HIV infection, the case is worth reporting.

CASE REPORT

A 45-year-old woman with 65 kg weight was a case of recently diagnosed TB/HIV co-infection. She was prescribed zidovudine (300 mg) + lamivudine (150 mg) + efavirenz (600 mg) and Category 2 DOTS Regimen: 2 (HRZES)3/1 (HRZE)/5 (HRE)3. She presented with nail pigmentation after 6 weeks of ingestion of above-mentioned therapy. It first appeared in greater toe nail, gradually increased in intensity over 2 weeks' time. Local examination revealed diffuse bluish-brown discoloration of thumbnails. It did not disappear on compression of nail plate. Nails were brittle and the pattern of nail pigmentation was diffuse in nature and there was no evidence of skin and mucus membranes being involved.

She had no previous history of any such ADR, hypertension, diabetes mellitus, any other chronic organic diseases, smoking or alcohol intake. The patient had even no history of any regular or long-term use of any drug. ELISA for HIV was positive. Polymerase chain reaction for RNA was positive. CD4+ count was 138 cells/mm^3. Erythrocyte sedimentation rate — 47 mm (1 h), Mantoux test, and sputum samples for acid fast bacilli for three consecutive days were positive. A chest radiograph showed bilateral hilar opacities in both the lungs. A computed tomography scan of chest disclosed mediastinal lymphadenopathy.

Hemoglobin, 10.8 g%; total leukocyte count, 10,400/cumm; platelet count, 2.4 lac/cumm; blood urea, 19 mg/dl; serum creatinine, 0.8 mg/dl; blood sugar, 98 mg%; serum cholesterol, 180 mg%; triglycerides, 155 mg%; clotting and bleeding time was normal; serum uric acid, 6.6 mg/dl; bilirubin, 1 mg/dl; serum glutamic-oxaloacetic transaminase, 45 U/L; and serum glutamic pyruvic transaminase, 36 U/L. Thyroid profile was normal. Electrocardiogram and ultra-sonography were normal.

Temporal association between starting zidovudine HAART regimen and subsequent development of this ADR and appearance of such ADR could not be explained by any concurrent drug, disease, and chemical. Thus, a possible diagnosis of zidovudine-induced nail pigmentation was established. The de-challenge and re-challenge could not be done due to ethical and clinical constraint. No dose-related study was done in the current case because of similar reasons. The Naranjo's score was 7 and WHO causality assessment showed probable correlation with the current adverse event.[6,7] Severity of the reaction was assessed using Hartwig ADR severity assessment scale[8] which classified

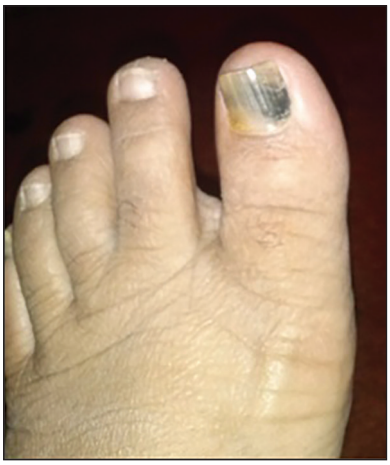

Figure 1: Showing nail hyper pigmentation in advancing age female patient due to zidovudine

the said ADR into nonserious. Due to nonserious nature of the reaction, no change in the treatment was done in the current case except counseling.

DISCUSSION

Zidovudine-induced anemia, fatigue, malaise, myalgia, nausea, anorexia, headache, and insomnia are most common reported ADRs. In advanced HIV disease, bone marrow suppression, mainly anemia and granulocytopenia may also be encountered. However, chronic zidovudine administration has been relatively less documented to be associated with nail hyper-pigmentation [Figure 1].[9]

0.95% and 1.95% of the incidence has been reported for hyper-pigmentation of skin and hyper-pigmentation of nail, respectively, among the patients receiving zidovudine.[10]

Drugs that are well-known to produce nail manifestations are cancer chemotherapeutic agents, psoralens, retinoids, tetracycline, antimalarials, and zidovudine.[11] Zidovudine is an important component of first-line antiretroviral treatment regimens used to manage HIV and TB co-infection. Nail pigmentation is documented both in adult as well as pediatric HIV.[4,5] Nail pigmentation occurs primarily in black patients. Unlike this, the current case was seen in Indian 45-year-old women. It appears to be reversible and relatively dose-dependent.[12] However, this was not studied in our case.

The underlying mechanism of nail pigmentation is not clear. Animal studies have shown that there are increased numbers of melanosomes within epidermal keratinocytes. Histopathologic findings of nail biopsy show deposits of brown pigmented granules containing melanin throughout the epidermis.[13]

Such an ADR although is harmless and reversible, psychological aspects of such ADR may be immense to hamper adherence to therapy and may lead to unnecessary investigations and treatment for misdiagnosis for such ADR as cyanosis or melanoma.

Thus, the current case report highlights and tries to draw attention and create awareness among prescribers regarding nonserious ADR of zidovudine-induced nail pigmentation in advancing age women of HIV/TB co-infection.

Financial support and sponsorship

PvPI, IPC- Ghaziabad, and NACO India.

Conflicts of interest

There are no conflicts of interest.

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