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Lipodystrophy in an Immuno-compromised Indian Patient with Pulmonary Tuberculosis and Brain Tuberculoma

KEYWORDS: Lipodystrophy, HIV, Stavudine, Pulmonary tuberculosis, Brain Tuberculoma

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ABSTRACT *HIV-associated lipodystrophy is one of well-known adverse-effect of highly active anti-retroviral therapy (HAART). The authors present a case of an immuno-compromised 35-year old male Indian patient who developed lipodystrophy mainly marked on the face as a result of Stavudine treatment. He was also suffering from pulmonary tuberculosis and had a brain tuberculoma. The patient was treated with anti-tuberculosis and anti-retroviral drugs and responded well. Most of the anti-retroviral therapy can cause lipodystrophy, of which Stavudine is the most notorious one.*

INTRODUCTION

Lipodystrophy is a frequent and disfiguring side effect of anti-retroviral treatment (ART) in immuno-compromised patients. It is characterized by body-fat accumulation (lipohypertrophy) or loss (lipoatrophy) in people living with human immunodeficiency virus (HIV) and can be classified into three groups: lipohypertrophy, lipoatrophy, and mixed syndrome (1). The association between lipodystrophy and anti-retroviral therapy has been reported especially with protease inhibitors (PIs) and nucleoside reverse transcriptase inhibitors (NRTIs). Lipodystrophy has become new physical evidence of HIV infection (2). HIV infection is becoming quite an epidemic worldwide as well as in India. The total numbers of cases worldwide is 35.3 million HIV/AIDS infections and 1.6 million people have died of the disease as per WHO 2012 figures (3). Similarly in India the number of cases is 2.1 million as per National AIDS Control Organization (NACO) 2011 fact sheet (4). Various clinical syndromes and diseases occur as a result of HIV infection. Out of these, brain tuberculoma is a rare complication of tuberculosis arising through hematogenous spread from an extra cranial source, pulmonary tuberculosis is said to be the most common association. In 2011, the figures of tuberculosis worldwide were 8.7 million and 1.3 million TB deaths as per WHO figures whereas India has 2.2 million cases (5). Tuberculosis can present as various manifestations such as pulmonary (PTB) or extra-pulmonary tuberculosis (EPTB) like meningitis or tuberculoma of the brain, abdominal tuberculosis, Pott's disease etc. As per the WHO clinical staging PTB/EPTB is graded as clinical stage III or IV in HIV/AIDS patients. In these situations treatment for tuberculosis as well as anti-retroviral therapy can be started either simultaneously or two to four weeks after initiation of anti-tuberculosis drugs, irrespective of CD_4 counts (6). As per current NACO guidelines ART has to be started if CD_4 counts are less than 350cells/µl (7). In this case report we describe an immuno-compromised Indian male patient who had PTB and EPTB (brain tuberculoma) besides developing lipodystrophy as a result of ART (Stavudine). To the best of our knowledge this is probably the first case report showing lipodystrophy, PTB and EPTB in an immuno-compromised Indian patient.

CASE REPORT

A 35-year old man hailing from Bihar presented to our outpatient ART-clinic in February, 2013 with recurrent loose motions for the past 3 months. His weight was 45Kg. He also had oral candidiasis and was a driver by profession, working in Mumbai, India. He had cough of one month duration with haemoptysis. His wife reported that he had one episode of focal motor seizure proceeding to secondary generalization. He also consented having sex with commercial sex workers. A signed informed consent was obtained from the patient and this study was approved by the Institutional Ethics Committee (IEC). He was subjected to HIV testing by rapid Comb kit, confirmed with enzyme-linked immunosorbent assay (ELISA) and consequently diagnosed as HIV-1. Liver and renal function tests were within normal range.

Chest X-Ray Postero-anterior view showed features of pulmonary tuberculosis (Figure: 1A). Two sputum samples, one spot and one overnight were collected. These were decontaminated by modified Petroff's method and subjected to microbiological examination by Ziehl-Neelsen (Z-N) technique for acid fast bacilli (AFB) along with culture on solid Lowenstein-Jensen (L-J) medium for mycobacterium isolation at 37^0C for 6–8 weeks (8). Niacin accumulation test, growth on para-nitrobenzoic acid and insertion sequence (IS6110) polymerase chain reaction (PCR) was done to confirm the Mycobacterium tuberculosis isolate (9). After isolation of mycobacterium growth, drug susceptibility test was performed by using 1% proportional method of anti-tuberculosis drugs namely Isoniazid (0.2µg/ml), Rifampicin (40µg/ml), Ethambutol (2µg/ml) and Pyrazinamide (200µg/ml) on L-J medium according to WHO–RNTCP guidelines (10–11). The culture was sensitive to above mentioned anti-tuberculosis drugs. A contrast enhanced Computerised Tomography (C-T) of the brain revealed a tuberculoma with oedema (Figure: 1B). CD_4 count was 188/µl and WHO clinical stage IV. The haemoglobin level was 10gm/dL. He was started on directly observed treatment short course (DOTS) for tuberculosis category I with Isoniazid (33mg), Rifampicin (450mg), Ethambutol (1gm) and Pyrazinamide (1.5gm) for 6 months. Phenytoin Sodium was also started in the dose of 300mg once daily at bed time. After 4 weeks Zidovudine (300mg) twice daily, Lamivudine (150mg) twice daily and Efavirenz (600mg) once daily orally at bed time was started.[2] Tablet Fluconazole (200mg) once daily was started for candidiasis. After 8 weeks his haemoglobin level came down to 7.5g/dL. He was given 300ml of blood transfusion and his regime was changed to Stavudine 30mg

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twice daily along with Lamivudine (150mg) twice daily and Efavirenz (600mg) once daily. This regimen was continued for 6 months. He reported wasting of facial muscles which was mainly of cosmetic significance (figure: 1C). The CD_4 counts had increased to 205/µl (WHO clinical stage III). His regime has now been changed to Tenofovir (300mg) along with Lamivudine (300mg) and Efavirenz (600mg) once daily. He is seizure free and chest lesion has healed. Phenytoin Sodium is still being continued. Lipodystrophy can be due to ART a drug of which Stavudine is the most important one. The lesion in the chest healed after six months with disappearance of the cough and haemoptysis. Anti-tuberculosis drugs were continued for three more months with complete disappearance of the lesion in the brain, as per WHO–RNTCP guidelines.

DISCUSSION

The diagnosis and management of complex syndromes associated with HIV is a very tough proposition as there is no set guideline for lipodystrophy worldwide. PTB diagnosis in a case of HIV is quite challenging as in about 43–51% of the cases sputum AFB examination can be unrewarding (6,8). Hence more sophisticated and expensive tests like GeneXpert, PCR and line probe assay (LPA) are required to arrive at a definitive conclusion. These can prove quite challenging in a developing country like India (12). Besides this, dual-energy X–Ray absorptiometry (DEXA), C-T and Magnetic Resonance Imaging (MRI) are needed to confirm lesions in the chest as well as other parts of the body like brain (13). These investigations are also not available in the public health set–up.

Moreover, as regards management, drug-drug interactions have to be taken in to account and addressed properly. A few points have to be taken in to consideration and these include timing and drug combination of ART, immune-reconstitution and adverse events due to combination of drugs. Nevirapine, which is the first line non-nucleoside reverse transcriptase inhibitors (NNRTIs) used at the ART centre as the best combination can not be administered as it is incompatible with Rifampicin. As a result Efavirenz which is less potent has to be substituted in its place. Similarly Zidovudine which is most effective NRTI can lead to bone marrow depression leading to anemia. So it has to be substituted with stavudine when haemoglobin level is less than 9gm/dL. Stavudine can lead to lipodystrophy and lactic-acidosis, the first one being more of cosmetic significance whereas second one potentially life threatening. A rapid and easy method to diagnose lipodystrophy will help to prevent or diminish further evolution of this disorder and to evaluate any possible intervention. For further evaluation fat mass ratio (FMR) can be used as an objective method for the definition of lipodystrophy in HIV-positive patients (14). Finally the management and investigations of this constellation of syndromes is a must for proper control of HIV, in order to prevent morbidity and mortality.

CONCLUSION

HIV epidemic is on the rise in a developing country like India. The main focus of the disease is on poor labourers and drivers who go to metropolitan cities like Kolkata, Delhi, Mumbai and Chennai to earn their livelihood. They leave their wives in the villages and visit commercial sex workers thereby getting infected. They then infect their wives thus leading to a vicious cycle. Thus proper sex hygiene, proper nutrition for immunity, counselling, avoiding of multiple sex partners, avoidance of alcohol and other drugs are needed to stop the chain of events. Finally the management and investigations of this constellation of syndromes is a must for proper control of HIV, in order to prevent morbidity and mortality.

Conflict of Interest:
All the authors declare no conflict of interest.

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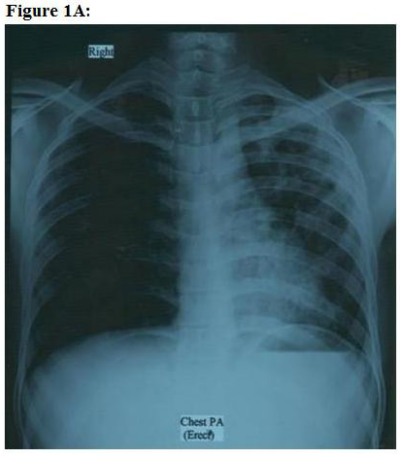
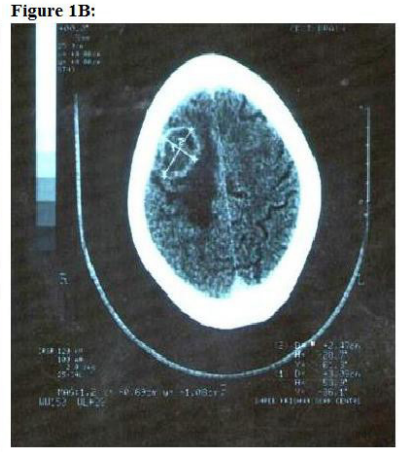
Figure 1A:



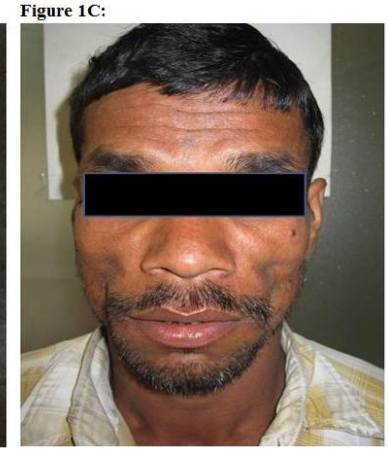
Chest X-Ray Postero Anterior view showing extensive Koch's lesion on the left side.

Figure 1B:



Computerised tomography of the brain showing granuloma (tuberculoma) with surrenounding oedema.

Figure 1C:



The male patient with lipodystrophy of the face.

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REFERENCE

1. Jean-Guy Baril, Patrice Junod, Roger LeBlanc, et al. (2005) HIV-associated lipodystrophy syndrome: A review of clinical aspects. Can J Infect Dis Med Microbiol 16: 233–243. | 2. Kadouch JA, Van Rozelaar L, Karim RB, et al. (2013) Current treatment methods for combination antiretroviral therapy-induced lipoatrophy of the face. Int J STD AIDS 24: 685–694. | 3. UNAIDS (2013) Report on the global AIDS epidemic: www.unaids.org/.../unaids/.../2013/gr2013/UNAIDS. | 4. NACO (2012–13) 'India: Annual Report: www.naco.gov.in/.../Annual%20Report/Annual%20report%202012-13. | 5. TB Statistics for India. (2012) TB Facts. Retrieved 2013; from http://www.tbfacts.org/tb-statistics-india.html. | 6. Swaminathan S, Padmapriyadarsini C, Narendran G. (2010) HIV-associated tuberculosis: clinical update. Clin Infect Dis 50: 1377–1386. | 7. May MT, Gompels M, Delpech V, et al. (2014) Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy: UK cohort study. AIDS 28: 1193–1202. | 8. Katoch VM. (2006) Smear microscopy to diagnose tuberculosis. Indian J Med Res 123: 735–738. | 9. Chauhan DS, Sharma VD, Parashar D, Chauhan A, Singh D, et al. (2007) Molecular typing of Mycobacterium tuberculosis isolates from different parts of India based on IS6110 element polymorphism using RFLP analysis. Indian J Med Res 125: 577–581. | 10. Pandey K, Singh D, Das VR, et al. (2013) Progressive Multifocal Leukoencephalopathy Associated with Pulmonary Tuberculosis in an Immuno-Compromised Indian Patient. J AIDS Clin Res 4:9 http://dx.doi.org/10.4172/2155–6113.1000241. | 11. Katoch VM. (2008) New generation methods for drug susceptibility testing for tuberculosis. Indian J Tuberc 55: 61–63. | 12. Lagrange PH, Thangaraj SK, Dayal R, Despande A, Ganguly NK, Girardi E, Joshi B, Katoch K, Katoch VM, et al. (2012) A toolbox for tuberculosis diagnosis: an Indian multicentric study (2006-2008): microbiological results. PLoS One 7:e43739. doi: 10.1371/journal.pone.0043739. | 13. Scherzer R, Shen W, Bacchetti P, et al. (2008) Study of Fat Redistribution Metabolic Change in HIV Infection.Comparison of dual-energy X-ray absorptiometry and magnetic resonance imaging-measured adipose tissue depots in HIV-infected and control subjects. Am J Clin Nutr 88: 1088–1096. | 14. Guaraldi G, Stentarelli C, Zona S, et al. (2014) The natural history of HIV-associated lipodystrophy in the changing scenario of HIV infection. HIV Med doi: 10.1111/hiv.12159. |