

Correspondence

***Penicillium marneffe* infection in HIV infected patients in Nagaland & immune reconstitution after treatment**

Sir,

Highly active antiretroviral therapy (HAART) has not only reduced morbidity and mortality in AIDS patients but also improved immune function and decreased viral loads¹. But some patients experience exacerbation of pre-existing subclinical infection known as immune reconstitution inflammatory syndrome (IRIS)².

We describe here a case of HIV associated *Penicillium marneffe* infection who developed IRIS after HAART, the first such case in paediatric age group from India. A 12 yr old HIV positive boy from Nagaland, India presented with history of recurrent fever, cough, weight loss, diarrhoea, and generalised papular, smooth, dome shaped and umbilicated skin lesions of varying size (2-10 mm) of one month duration. The patient had oral thrush and symptoms of oesophageal candidiasis. Differential diagnosis of disseminated *Molluscum contagiosum* and penicillosis with HIV infection was considered on the basis of the skin lesions. His Haemoglobin was 7.5 g/dl, WBC 4300/ μ l of blood and ESR 106 mm at the end of first hour. Mantoux test was negative. Absolute CD4+ count was 11 cells/ μ l. Chest X- ray was normal. Leishman stain of the aspirate from of skin lesions showed intracellular and extracellular septate yeast like cells. Culture of aspirated fluid in Sabouraud's dextrose agar (SDA) showed flat, glabrous, moist, radially folded colonies with diffusible red pigment after 4 days of incubation at 25°C. Microscopic examination revealed septate hyphae with lateral and terminal conidiophores and chains of ovate conidia characteristic of *Penicillium* species. Culture at 37°C showed moist, flat brownish white colonies after 4 days of incubation and under microscope mixture of septate hyphae with yeast like cells divided by septa. Culture from oral swab showed growth of *Candida albicans*. Blood culture was done

in duplicate and did not show any growth till 28 days of incubation. The patient was treated with efavirenz, lamivudine and stavudine along with itraconazole 400 mg/day for two weeks followed by 200 mg/day as maintenance therapy. After 4 wk of therapy, the patient came back with fever, severe arthritis, exacerbation of skin lesions and generalized lymphadenopathy. Blood culture showed growth of *Penicillium marneffe* after 5 days of incubation. His repeat CD4+ count increased to 172 cells/ μ l.

During the first few weeks, after the start of HAART, an increase in memory CD4+ cells type is observed possibly as a result of redistribution from peripheral lymphoid tissue³. The CD4+ lymphocytes are primed to recognize previous antigenic stimuli and thus may be responsible for manifestations of IRIS seen soon after HAART⁴. The various risk factors identified for the development of IRIS include younger age, male sex, short interval between initiating treatment for opportunistic infection (OI) and starting ART, rapid fall in HIV-1 RNA after ART and a very low CD4+ count at the time of starting ART^{2,4,5}. The present patient developed exaggerated skin lesions with disseminated *Penicillium marneffe* infection and clinical manifestation of inflammatory process after 4 wk of HAART. His CD4+ cell count increased >10 times; viral load could not be measured due to operational reasons.

The most frequently reported cases of IRIS are associated with infection due to *Mycobacterium tuberculosis*, genital herpes, *Varicella zoster*, cytomegalovirus and cryptococcal meningitis following initiation of ART⁴⁻⁷. Gupta *et al*⁸ reported the first case of IRIS associated with *Penicillium marneffe* infection in an adult patient hailing from Manipur and perhaps this is the second case of IRIS associated with *Penicillium marneffe* infection from India.

Acknowledgment

Authors thank Dr A.K. Borthakur, Professor and Head, Department of Microbiology, Dr Pragan Saikia, Assistant Professor of Pathology, Dr Mrinalini Das, Assistant Professor of Paediatrics and all the staff of ART Centre and ICTC of Assam Medical College, for their help in making diagnosis.

L. Saikia[‡], R. Nath, P. Biswanath*

D. Hazarika & J. Mahanta[†]**

Departments of Microbiology, *Paediatrics & **Dermatology, Assam Medical College & [†]Regional Medical Research Centre for Northeast (ICMR)

Dibrugarh, Assam, India

[‡]For correspondence:

lahari.saikia@yahoo.com

References

1. Lortholary O, Fontanet A, Memain N, Martin A, Sitbon K, Dromer F; French Cryptococcosis Study Group. Incidence and risk factors of immune reconstitution inflammatory syndrome complicating HIV-associated cryptococcosis in France. *AIDS* 2005; 19 : 1043-9.
2. French MA, Lenzo N, John M, Mallal SA, McKinnon EJ, James IR, *et al.* Immune restoration disease after the treatment of immunodeficient HIV-infected patients with highly active antiretroviral therapy. *HIV Med* 2000; 1 : 107-15.
3. Bucy RP, Hockett RD, Derdeyn CA, Saag MS, Squires K, Sillers M, *et al.* Initial increase in blood CD4+ lymphocytes after HIV antiretroviral therapy reflects redistribution from lymphoid tissues. *J Clin Invest* 1999; 103 : 1391-8.
4. Murdoch DM, Venter WD, Van Rie A, Feldman C. Immune reconstitution inflammatory syndrome (IRIS): review of common infectious manifestations and treatment options. *AIDS Res Ther* 2007; 4 : 9.
5. Ratnam I, Chiu C, Kandala NB, Easterbrook PJ. Incidence and risk factors for immune reconstitution inflammatory syndrome in an ethnically diverse HIV type 1-infected cohort. *Clin Infect Dis* 2006; 42 : 418-27.
6. Puthanakit T, Oberdorfer P, Akarathum N, Wannarit P, Sirisanthana T, Sirisanthana V. Immune reconstitution syndrome after highly active antiretroviral therapy in human immunodeficiency virus-infected thai children. *Pediatr Infect Dis J* 2006; 25 : 53-8.
7. Kumarasamy N, Chaguturu S, Mayer KH, Solomon S, Yepthomi HT, Balakrishnan P, *et al.* Incidence of immune reconstitution syndrome in HIV/tuberculosis-coinfected patients after initiation of generic antiretroviral therapy in India. *J Acquir Immune Defic Syndr* 2004; 37 : 1574-6.
8. Gupta S, Mathur P, Maskey D, Wig N, Singh S. Immune restoration syndrome with disseminated *Penicillium marneffe* and cytomegalovirus co-infections in an AIDS patient. *AIDS Res Ther* 2007; 4 : 21.