Mycobacterium xenopi pulmonary infection resulting in self-limited immune reconstitution inflammatory syndrome in an HIV-1 infected patient

Sebastiano Leone[1,2], Sergio Giglio[1,2], Patrizia Maio[1], Piero Capasso[3], Giuseppina dell'Aquila[1], Mario Magliocca[1], Francesco Saverio Nigro[1], Piera Pacifico[1], Nicola Acone[1]

[1]Infectious Diseases Division;
[2]AIDS service;
[3]Radiology Service, A.O.R.N. San G. Moscati, Avellino, Italy

SUMMARY

Highly active antiretroviral therapy (HAART) has been shown to induce a major and durable viral load reduction accompanied by a stable CD4 increase. This process may evolve with adverse clinical phenomena, known as the immune reconstitution inflammatory syndrome (IRIS). In the HIV population, non-tuberculous mycobacteria are a common cause of IRIS. However, only a few cases of *Mycobacterium xenopi* associated IRIS have been described. This paper concerns a case of *M. xenopi* pulmonary infection resulting in self-limited immune reconstitution inflammatory syndrome in an HIV-1 infected patient.

KEY WORDS: Mycobacterium xenopi, HIV, HAART, Immune reconstitution inflammatory syndrome

Received April 01, 2009 *Accepted* June 13, 2009

The prognosis for patients infected with human immunodeficiency virus (HIV) type 1 has improved dramatically since the advent of Highly Active Antiretroviral Therapy (HAART), which allows sustained suppression of HIV replication and recovery of CD4 T cell counts (Lazzarin, 2004). In some patients receiving HAART, immune reconstitution is associated with a pathological inflammatory response leading to substantial short-term morbidity and even mortality (Shelburne *et al*., 2006).

This report concerns a case of *Mycobacterium xenopi* pulmonary infection resulting in self-limited immune reconstitution inflammatory syndrome (IRIS) in an HIV-1 infected patient starting HAART.

Corresponding author
Sebastiano Leone, MD
Infectious Diseases Division
A.O.R.N. San G. Moscati
Contrada Amoretta - 83100 Avellino, Italy
E-mail: sebastianoleone@yahoo.it

A 39-year-old man with advanced HIV infection (CD4 lymphocyte count of 28 cells/mm^3, HIV-RNA of 55200 copies/ml) was admitted to our clinic. There was no history of prior infection with mycobacteria, Mantoux test was negative, and the chest X-ray was normal. Treatment with tenofovir (TDF), emtricitabine (FTC) and efavirenz (EFV) was started.

Co-trimoxazole was started for *Pneumocystis jiroveci* prophylaxis. One month later he presented with productive cough and a fever of 37.5°C. Blood investigations revealed C-reactive protein of 58 mg/L, erythrocyte sedimentation rate of 67 mm/h, lactate dehydrogenase of 600 U/L, white blood cell count of 4850 cells/mm^3 with 65.4% neutrophils. The other examinations showed no abnormalities. Multiple blood cultures were sterile. At this time the CD4 lymphocyte count had increased to 65 cells/mm^3 and the HIV plasma viral load was undetectable. A High Resolution Computer Tomography (HRCT) scan demonstrated ground-glass opacities (Fig. 1). *M. xenopi* isolate was obtained from multiple sputum sam-

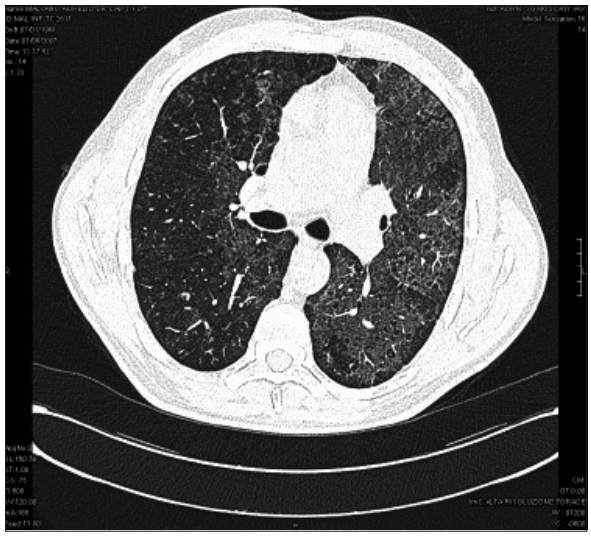

FIGURE 1 - *HRTC at iris onset.*

ples. Testing for *Pneumocystis jiroveci* was negative. Serological tests for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila*, *Cryptococcus neoformans,* and Cytomegalovirus were negative. However, a spontaneous improvement in clinical symptoms was observed within two weeks. During follow-up, sputum cultures for *M. xenopi* were persistently negative. Two months later, the HRTC control was negative (Fig. 2).

IRIS has been reported in a limited number of patients with various and previous opportunistic infections and tumours associated with AIDS immunodeficiency despite adequate control of virologic and immunologic parameters.

Paradoxically, patients may experience a progression of symptoms associated with worsening lymphadenopathy, pulmonary infiltrates and pleural effusions after HAART is started. The fall in blood HIV RNA levels and the return of immune function, including an increase in CD4 lymphocytes, restore the ability to mount an inflammatory reaction to infectious antigens (Lazzarin, 2004). Non-tuberculous Mycobacteria (NTM) disease along with its related mortality is a significant pathology as a cause of hospitalization among HIV-infected individuals (Miguez-Burbano *et al*., 2006). In the HIV population, NTM are a common cause of IRIS. However, only a few cases of *M. xenopi*-associated IRIS have been described (Field *et al*., 2006; Lawn *et al*., 2005). *M. xenopi* is usually a non-pathogenic colonizer of the airways. Most of the findings are fortuitous, which raises concerns about their clinical significance, especially for HIV-infected patients in whom concurrent pulmonary diseases are often present (Gazzola *et al*., 2004; Juffermans *et al*., 1998). A literature search via the MEDLINE database using the following MeSH terms 'antiretroviral immune reconstitution syndrome' or 'immune paradoxical reaction' or 'immune reconstitution inflammatory syndrome' or 'immune reconstitution syndrome' or 'paradoxical worsening' or 'immune reconstitution' or 'immune restitution' or 'immunorestitution' and '*Mycobacterium xenopi*' was performed.

Additional references were identified from citations in other published papers. Overall, only four references were identified (Bachmeyer *et al*., 2002; de Boer *et al*., 2003; Buckingham *et al*., 2004; Foudraine *et al*., 1999). The median baseline CD4 lymphocyte count and viral load (VL) were 19±16.7 cells/mm^3 and 575114.5±600878.8 copies/mL, respectively. At the onset of IRIS the CD4 lymphocyte count and VL were 200±63.3 cells/mm^3 and 557±626.5 copies/mL, respectively. All cases were treated with antimybacterial drugs and were resolved without complications. However, the need for routine treatment of *M xenopi* in HIV-infected individuals receiving HAART is doubtful. Recently, Kerbiriou *et al.* reported the outcomes of 20 HIV infected patients

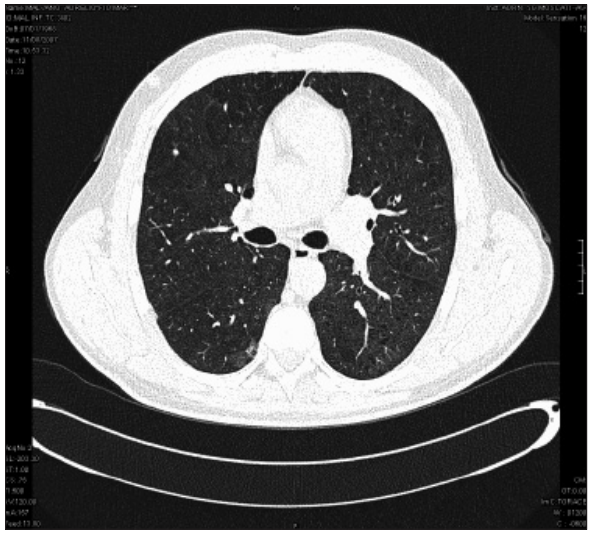

FIGURE 2 - *HRTC at follow-up.*

receiving HAART who had respiratory symptoms and in whom *M. xenopi* was isolated. The median blood CD4+ lymphocyte count was 37/mm^3. Fifteen of 20 patients received no antimycobacterial therapy and remained healthy after a median of ~4 years of follow-up, and two patients required treatment specifically for *M. xenopi* infection, both showed clinical improvement. The authors conclude that pulmonary *M. xenopi* isolation in HIV-1 patients receiving HAART does not usually require specific treatment (Kerbiriou *et al.*, 2003). In conclusion, there is still very little evidence from controlled clinical trials. Future works are needed to clarify both the role of *M. xenopi* in pathogenesis of IRIS and the requirements for routine treatment.

Conflict of interest:
No conflict of interest to declare.

REFERENCES

Bachmeyer C., Blum L., Stelianides S., Benchaa B., Gruat N., Danne O. (2002). Mycobacterium xenopi pulmonary infection in an HIV infected patient under highly active antiretroviral treatment. *Sex. Transm. Infect*. **78**, 60-61.

Buckingham S.J., Haddow L.J., Shaw P.J., Miller R.F. (2004). Immune reconstitution inflammatory syndrome in HIV-infected patients with mycobacterial infections starting highly active anti-retroviral therapy. *Clin. Radiol*. **59**, 505-513.

de Boer M.G., Kroon F.P., Kauffmann R.H., Vriesendorp R., Zwinderman K., van Dissel J.T. (2003). Immune restoration disease in HIV-infected individuals receiving highly active antiretroviral therapy: clinical and immunological characteristics. *Neth. J. Med*. **61**, 408-412.

Field S.K., Cowie R.L. (2006). Lung disease due to the more common nontuberculous mycobacteria. *Chest*. **129**, 1653-1672.

Foudraine N.A., Hovenkamp E., Notermans D.W., Meenhorst P.L., Klein M.R., Lange J.M., Miedema F., Reiss P. (1999). Immunopathology as a result of highly active antiretroviral therapy in HIV-1-infected patients. *AIDS*. **13**, 177-184.

Gazzola L., Cesari M., Salerno F., Franzetti F., Gori A. (2004). Clinical and therapeutic management of pulmonary Mycobacterium xenopi infection in HIV-positive patients. *Clin. Infect. Dis*. **38**, 1642-1644.

Juffermans N.P., Verbon A., Danner S.A., Kuijper E.J., Speelman P. (1998). Mycobacterium xenopi in HIV-infected patients: an emerging pathogen. *AIDS*. **12**, 1661-1666.

Kerbiriou L., Ustianowski A., Johnson M.A., Gillespie S.H., Miller R.F., Lipman M.C. (2003). Human immunodeficiency virus type 1-related pulmonary Mycobacterium xenopi infection: a need to treat? *Clin. Infect. Dis*. **37**, 1250-1254.

Lawn SD, Bekker LG, Miller RF. (2005). Immune reconstitution disease associated with mycobacterial infections in HIV-infected individuals receiving antiretrovirals. *Lancet Infect. Dis*. **5**, 361-373.

Lazzarin A. (2004). The role of host immunity in the control of HIV infection: from theory to diagnostic and therapeutic intervention. *New Microbiol*. **27**, 135-139.

Miguez-Burbano M.J., Flores M., Ashkin D., Rodriguez A., Granada A.M., Quintero N., Pitchenik A. (2006). Non-tuberculous mycobacteria disease as a cause of hospitalization in HIV-infected subjects. *Int. J. Infect. Dis*. **10**, 47-55.

Shelburne S.A., Montes M., Hamill R.J. (2006). Immune reconstitution inflammatory syndrome: more answers, more questions. *J. Antimicrob. Chemother*. **57**, 167-170.

ERRATA CORRIGE

The authors' names of the article "Distribution of different carbapenem resistant clones of *Acinetobacter baumannii* in Tehran Hospitals" published in New Microbiol. 2009 July; 32 (3): 265-271

ARE

Morovat Taherikalani, Bahram Fatolahzadeh, Mohammad Emaneini, Setareh Soroush, Mohamad Mehdi Feizabadi

AND NOT

Taherikalani Morovat, Fatolahzadeh Bahram, Emaneini Mohammad, Soroush Setareh, Feizabadi Mohamad Mehdi

We apologize to those concerned for any inconvenience this error may have caused.