CASE REPORT

Dual Candida albicans and Cryptococcus neoformans fungaemia in an AIDS presenter: a unique disease association in the highly active antiretroviral therapy (HAART) era

ROBERTO MANFREDI, LEONARDO CALZA and FRANCESCO CHIODO

Department of Clinical and Experimental Medicine, Division of Infectious Diseases, University of Bologna "Alma Mater Studiorum", S. Orsola Hospital, Bologna, Italy

A case report of a patient who discovered his HIV infection concurrently with an advanced immunodeficiency and a dual Candida albicans and Cryptococcus neoformans fungaemia is discussed with reference to the changing epidemiology and clinical features of HIV infection and AIDS in the highly active antiretroviral therapy (HAART) era. The tendency to develop multiple concomitant AIDS-defining illnesses at the time of first hospitalisation seems to be an increasing feature in patients who remain unaware of or neglect their HIV disease and who are still at risk of opportunistic infections even with the availability of HAART.

Introduction

Since 1996, the introduction of potent combination antiretroviral regimens (highly active antiretroviral therapy, HAART) has had a significant impact on the natural history of HIV infection in industrialised countries. HAART led to an early, sharp drop in the absolute frequency of opportunist diseases related to a severe degree of HIV-associated immunodeficiency (as expressed by a CD4+ lymphocyte count <50–100 cells/μl), such as visceral candidosis and cryptococcosis, which represent the most common opportunistic fungal infections in AIDS [1–3]. However, an appreciable number of patients remain unaware of their HIV status, refuse antiretroviral therapy or show a poor adherence to HAART, and so remain at high risk of developing severe opportunistic disorders as a result of their persistently low CD4+ cell count [4, 5]. As a consequence, multiple AIDS-defining disorders may be discovered concurrently only at the time of the first hospitalisation of a patient with an extremely severe immunodeficiency. Thus, 5 of 10 patients notified with AIDS at our tertiary care centre in the first 4 months of 2002 had an unknown or a neglected HIV infection. This led to a diagnosis of full-blown disease at the time of their first admission, when three-to-seven concomitant AIDS-defining illnesses were identified (R. Manfredi, unpublished data). A similar situation encompassing key diagnostic and therapeutic implications occurs in the developing world, but underlying causes and supporting factors appear to be substantially different [6].

The aim of this report is to describe a particular case of concurrent haematogenous Candida-Cryptococcus visceral and disseminated co-infection in a patient with undiagnosed HIV infection.

Case report

A 59-year-old male who reported multiple heterosexual contacts at risk for acquiring HIV infection during the previous years, and who was unaware of his HIV infection, was referred to the Emergency Service and was first hospitalised at the Division of Internal Medicine of the University Hospital as a result of a severely compromised clinical situation. The latter included: an irregular hyperpyrexia of 2 months duration that was resistant to multiple broad-
spectrum empiric antibiotic therapies; pancytopenia; bilateral interstitial-alveolar Pneumocystis carinii and Staphylococcus aureus pneumonia (confirmed by microscopy and culture performed on both sputum and broncho-alveolar lavage); a respiratory infection with a multiresistant Mycobacterium kansasii strain (the isolate was sensitive only to protonamide and cycloserine); and a severe cachexia (wasting syndrome) arising from a long-term dysphagia due to an erosive Candida albicans oesophagitis. This patient came to our attention when HIV infection was confirmed by immuno-enzymic and immunoblotting assays.

From a mycological point of view, this patient suffered from extensive pharyngeal and oesophageal candidosis (ascertained by endoscopy and confirmed by direct microscopy, culture and histopathological assays) and a dual, concurrent septicaemia with C. albicans and Cryptococcus neoformans, confirmed by repeated growth and identification of both these yeasts from multiple consecutive blood cultures subcultured on Saboraud agar. Cerebrospinal fluid examination was negative for cryptococcus by microscopy and culture, as was a polysaccharide antigen test, which excluded meningeal and central nervous system localisation (the patient had no neurological symptoms). Both C. albicans and Cr. neoformans isolates were susceptible to all tested antymycotic agents (polyenes, imidazoles-triazoles and flucytosine), as measured in a microbroth assay according to current NCCLS standards [7]. At the time of admission to our division, the severe HIV-associated immunodeficiency was expressed by a CD4+ lymphocyte count of 44 cells/µl. Plasma HIV viral load was >500 000 copies of HIV-RNA/ml (as assessed by an ultrasensitive branched-DNA technique). The patient did not undergo any invasive therapeutic or diagnostic procedure (including use of central lines), before detection of his multiple opportunistic infections.

As a result of the concomitant dual Candida-Cryptococcus visceral infection, treatment was instituted with high-dose fluconazole (800 mg/day for 10 days, followed by 400 mg/day), concurrent liposomal amphotericin B (3 mg/kg for the first 10 days) and topical nystatin for 8 weeks. This led to the disappearance of clinical signs and symptoms and mycological tests also became negative.

At the time of discharge – which occurred 8 weeks after admission because of a persisting fever, fatigue, sweating and weight loss attributable to the multi-resistant M. kansasii disease – the CD4+ count had risen to 164 cells/µl and HIV viraemia had dropped to 1 and 4.5 log_{10} HIV-RNA copies/ml compared with baseline, with a reduction of viraemia ranging from 1.5 to 3.5 log_{10} HIV-RNA copies/ml compared with baseline, within 3 months of hospitalisation (R. Manfredi, unpublished data).

The present availability of very potent and varied antiretroviral therapeutic regimens has not impacted upon the persistent diagnosis of advanced cases of HIV disease, which continue to occur in patients who were unaware of their infection, in those who refused HAART or in those who had insufficient compliance with the prescribed antiretroviral therapy or antimicrobial prophylaxis [4, 5]. This alarming tendency seems related to epidemiological rather than clinical or therapeutic issues, but the introduction of HAART does not seem to have altered the proportional distribution of the majority of HIV-related opportunistic infections [4, 5]. Meanwhile the limited availability of HAART in the developing world means that AIDS patients are still at risk from opportunistic infections, including those of fungal origin [6].
References

4. Manfredi R, Chiodo F. Features of AIDS and AIDS-defining diseases during the highly active antiretroviral therapy (HAART) era, compared with the pre-HAART period: a case-control study. Sex Transm Infect 2000; 76: 145–146.