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Histoplasmosis in HIV-Infected Persons, Yaoundé, Cameroon

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To the Editor: In HIV-infected persons in Cameroon (Central Africa), histoplasmosis is still misdiagnosed as tuberculosis because of clinical similarities (1,2). These patients are automatically given presumptive antituberculous therapy, although tuberculosis is not confirmed. The patients subsequently die of probable disseminated histoplasmosis (DH), and the fungal infection might finally be detected in postmortem tissue samples (3). In this context, 3 cases of DH were detected in HIV-infected patients within a 1-year period (2007–2008) in Yaoundé, Cameroon. We initiated this study to investigate the occurrence of histoplasmosis in HIV-infected patients in 4 medical centers for AIDS treatment in Yaoundé from December 2008 through December 2011.

We recruited patients with known HIV status who agreed to participate in the study. Inclusion criteria were CD4 cells <200/mm³, fever and cough of ≥2 weeks’
duration, weight loss, asthenia, and histoplasmosis-like skin manifestations (i.e., ulcerative lesions and/or umbilicated papules or nodules and/or pustules). Patients under effective antituberculous therapy or antimicrobial drugs for any skin or pulmonary infectious disease were excluded from the study. CD4 cell counts were performed in all patients. Histoplasmosis was diagnosed in sputum, bronchoalveolar fluid (BALF), and bronchial and skin biopsies by direct staining with Gomori’s methenamine silver and periodic acid Schiff stains and by culture of sputum and BALF samples on Sabouraud medium. Tuberculosis and bacterial infections were detected in sputum and BALF by using Ziehl-Neelsen and Gram staining and culture on Lowenstein-Jensen and Streptococcus pyogenes media. All laboratory examinations were performed at the Centre Pasteur du Cameroun in Yaoundé. Data were collected on an anonymous questionnaire. Means (and SDs) were calculated for quantitative variables, and frequencies were calculated for qualitative variables. The National Ethics Committee, the Ministry of Health of Cameroon, and the medical centers where the study took place approved the study. Patients approved and signed the informed consent form at the time of recruitment.

Our study comprised 56 patients. Histoplasma capsulatum was detected in 7 (13%) patients on 6 of 7 skin biopsies and 1 of 3 bronchial biopsies. The median CD4 cell count of H. capsulatum–positive patients was 40 cells/mm³. Similarly, some authors have reported diagnosis of severe DH by using direct staining of skin samples (4); in low-income countries, skin involvement is the main presentation of DH because of limited laboratory facilities and/or late diagnosis. In Cameroon until recently, all DH cases in HIV-infected persons were diagnosed by skin biopsy or by chance on peripheral blood smear, thus revealing AIDS at the terminal stage (3,5). We did not detect H. capsulatum infection in sputum or BALF. These results are congruent with findings in Abidjan, Côte d’Ivoire, in 1999 (6). African histoplasmosis was not detected in any sample; although this type is endemic to areas with high rates of HIV infection, it is infrequently associated with AIDS patients (7).

We detected Mycobacterium tuberculosis in 18 (32%) patients and Candida albicans in 14 (25%) patients; 3 (0.5%) patients were co-infected with M. tuberculosis and C. albicans. M. tuberculosis was detected in sputum of 9 (21%) of 42 patients and in BALF of 9 (53%) of 17 patients; we detected C. albicans in sputum of 13 (31%) patients. Our detection of M. tuberculosis in 32% of patients confirms tuberculosis as the main AIDS-defining illness in Cameroon. We did not find tuberculosis and histoplasmosis co-infection, even though it occurs frequently in low-income countries (1,8).

The limitation in our study was the unavailability of validated sensitive and specific tools for diagnosing histoplasmosis in Cameroon (e.g., detection of the H. capsulatum circulating antigen in body fluid using an enzyme immunoassay) (9). Thus, using direct staining methods and culture of biopsies and body fluid samples could possibly lead to false-negative results.

Our detection of H. capsulatum in 13% of the HIV-infected patients in this study suggests that histoplasmosis is an unknown public health problem in Cameroon that is misdiagnosed as tuberculosis. Accounting for the endemicity of tuberculosis, which is the main HIV-defining illness in Cameroon, and the fatal outcome of DH in HIV-infected patients, practitioners need a high index of awareness to differentiate between tuberculosis and histoplasmosis. A recent report showed major clinical and biologic factors discriminating between these infections (10). Knowing these factors may lead practitioners to early diagnosis and treatment of histoplasmosis and in turn reduce the death rate among HIV-infected patients.

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References
Divergent Gemycircularvirus in HIV-Positive Blood, France

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To the Editor: Gemycircularviruses are a group of recently discovered single-stranded DNA viruses, found initially in fungi in 2010 (1). These “myco-like” viruses have a genome ranging from 2.1 to 2.3 kb, containing 2 opposite open reading frames that probably code for a capsid protein (CP) and a spliced replication-associated protein (Rep). Related viruses have been subsequently identified in animal blood and fecal matter, raw and treated sewage, and insects and plant material, suggesting that gemycircularviruses may represent a large group of viruses exhibiting considerable genetic diversity (2–8). The presence of these viruses was recently extended to humans after gemycircularvirus sequences were identified in human blood and brain tissue (multiple sclerosis patient), cerebrospinal fluid, and fecal matter (δ,9).

While investigating the virome content of an HIV-positive blood donation, we identified several gemycircularvirus-related sequences. The initial metagenomic approach involved an HIV-1–positive plasma sample (B genotype, ≈530 copies/mL) obtained from the French blood agency national plasma bank in Tours, France. A 4-mL aliquot was prepared for metagenomic analysis after filtration, concentration, and nucleases treatment. Next, particle-protected nucleic acids were recovered and used for the preparation of a next-generation sequencing library and its subsequent analysis (online Technical Appendix, http://wwwnc.cdc.gov/EID/article/21/11/15-0486-Techapp1.pdf). Gemycircularvirus sequences identified among reads (1,680 vs. 82,560 reads total; ≈2%) were assembled into a resulting full-length sequence (Gemyc1c) by using CodonCode Aligner version 5.1 (CodonCode Corporation, Centerville, MA, USA). This sequence was verified by using back-to-back specific primers, and the amplicon was cloned and sequenced according to the Sanger method.

The analysis of the Gemyc1c sequence (2,109 nt, GenBank accession no. KP987887) revealed a genome divergent from those already available in databases, despite a similar genomic organization (Figure, panel A) and assignment to gemycircularviruses after BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi) analysis of putative CP and Rep proteins. This divergence was demonstrated by the phylogenetic analysis of the deduced CP (Figure, panel B), which exhibited ≈72% and ≈44% aa pairwise identity with the 2 closest gemycircularvirus CP sequences available in GenBank (gemycircular virus c from mongoose feces [Conceicao-Neto N., unpub. data] and HCB18.215 from cattle blood, respectively). Moreover, Gemyc1c CP exhibited ≈30% pairwise identity with viral sequences identified previously in humans (BZ1 from feces, SL1 from cerebrospinal fluid, MSS12.225 from blood). The deduced spliced Rep (major Rep1 and minor Rep2), seen in such viruses, contained putative rolling circle motifs I (LFTYS), II (HLHAFVD), and III (YATKD) retrieved from gemycircularviruses (4).

We subsequently investigated the presence of Gemyc1c DNA in 128 HIV-positive plasma samples (French blood agency national plasma bank) along with 256 HIV-negative plasma samples (healthy blood donors, southeastern France; mean donor age 38 years; 136 men; 1 man:1.13 women). Plasma samples were prepared as described previously (10), and extracted nucleic acids were tested for Gemyc1c DNA by using a specific PCR that included negative, positive, and extraction controls (online Technical Appendix).

Application of the above Gemyc1c DNA detection system did not generate any positive signal in the 384 plasma samples in this study, suggesting that the presence...