REVISTA DO INSTITUTO DE MEDICINA TROPICAL DE SÃO PAULO

JOURNAL OF THE SÃO PAULO INSTITUTE OF TROPICAL MEDICINE

http://doi.org/10.1590/S1678-9946202365004

Human T-lymphotropic virus type 1 and aspergillosis: an invisible co-infection

Sao Paulo, September 23rd, 2022

Dear Editor,

Human T-lymphotropic virus type 1 (HTLV-1) is a retrovirus that causes a lifelong T-cell infection, generalized inflammation, lymphoproliferation, and immune imbalance in humans. HTLV-1 causes high morbidity and mortality diseases, such as HTLV-1-associated myelopathy (HAM) and adult T-cell leukemia/lymphoma (ATLL), among others. However, it is neglected and invisible to most people and healthcare professionals who are from HTLV-1 endemic regions. In Latin America, the same lack of proper diagnosis and attention is observed in relation to endemic/systemic mycoses (paracoccidioidomycosis and histoplasmosis), and aspergillosis[1]. Recently, a scientific review addressed the impact of HTLV-1 on viral, bacterial, helminth, and fungal co-infection outcomes and vice-versa, but the studies did not provide firm conclusions, especially for fungal co-infections[2]; thus, more studies are required. In order to add information on this matter, we conducted a preliminary study about the detection of HTLV-1/2 in 387 serum samples from patients that were positive on a double immunodiffusion (DID) assay for *Paracoccidioides* spp., *Histoplasma capsulatum*, and *Aspergillus* spp. antibodies, and we confirmed the detection of one case of HTLV-1/aspergillosis co-infection in Sao Paulo State, Brazil[1]. Afterwards, we expanded the study and detected another case of HTLV-1/aspergillosis, and curiously, both cases were found to have fungal bulla in the lungs. One patient was a 58-year-old man. He was a former smoker (80 packs/year, stopped 3 years ago), was crack cocaine user for 20 years, HIV negative, with a history of five previous hospitalizations for pulmonary tuberculosis (TB) and three treatment abandons. On August 17th, 2015, he was admitted to the hospital emergency room with respiratory failure, was intubated, and then was referred to the Intensive Care Unit. *M. tuberculosis* was detected in his sputum. The treatment had started, but on September 10th his clinical and laboratory condition worsened. A computed tomography chest scan was carried out, and fungal bulla was detected in the lung; *Aspergillus* was isolated in tracheal secretion, and the serology for fungi was positive for *Aspergillus* spp. (Figures 1A and 1B). Therapy for pulmonary aspergillosis had started with clinical improvement, and he was transferred to another health unit on September 28th, 2015, when he was hemodynamically stabilized, eupneic with nasal O_2 catheter, conscious and oriented. Since then, he has never returned to the hospital, so the outcome of his condition is unknown. It is worth noting that the HTLV-1 infection in these two patients was confirmed by serological western blotting analysis (Figure 1C) in the same serum sample employed in the *Aspergillus spp*. DID diagnosis. In summary, pulmonary aspergillosis has been described as an opportunistic infection in patients with ATL and HAM[3,4], and in HTLV-1-infected pediatric/juvenile patients with bronchiectasis and subpleural bullae[5], and, as shown herein, in a patient with recurrent TB. Recently, a retrospective study on the medical records of 91 patients diagnosed with chronic pulmonary aspergillosis in Sao Paulo State, Brazil, disclosed having pulmonary tuberculosis as the most common underlying factor in such patients, followed by smoking[6]. Although pulmonary tuberculosis was identified as the main cause of chronic

[1]Instituto Adolfo Lutz, Centro de Imunologia, Laboratório de Pesquisa em HTLV, São Paulo, São Paulo, Brazil

[2]Instituto de Infectologia Emílio Ribas, São Paulo, São Paulo, Brazil

[3]Instituto Adolfo Lutz, Centro de Imunologia, Laboratório de Imunodiagnóstico das Micoses, São Paulo, São Paulo, Brazil

Correspondence to: Adele Caterino-de-Araujo
Instituto Adolfo Lutz, Centro de Imunologia, Av. Dr. Arnaldo, 351, 11º andar, CEP 01246-000, Pacaembu, São Paulo, SP, Brazil
Tel: +55 1130682898

E-mail: adele.caterino@ial.sp.gov.br
caterino@alumni.usp.br

Received: 23 September 2022

Accepted: 16 November 2022

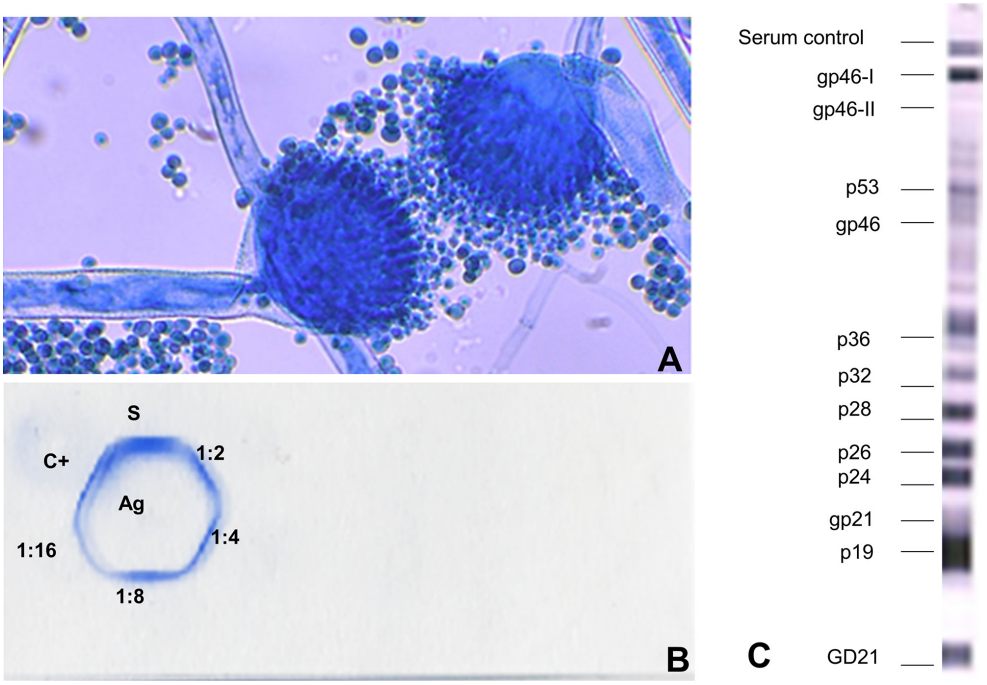

Figure 1 - A) morphological feature of *Aspergillus fumigatus*; B) double immunodiffusion (DID) assay for detection of *Aspergillus* spp.-specific antibodies considered positive up to a serum dilution of 1:16; C) pattern of HTLV-1 seropositive sample by Western blotting analysis.

pulmonary aspergillosis in Brazil[6], the intrinsic risk of immune imbalance caused by HTLV infection could not be excluded. In fact, several studies carried out in Brazil and in other countries have shown a higher prevalence of HTLV-1 in TB patients, and a higher risk of developing TB in patients infected with HTLV-1 compared to control groups[2]. In addition, cases of pulmonary aspergillosis without TB have been described in children infected with HTLV-1[5]. Here, the association of pulmonary tuberculosis, aspergillosis, smoking and crack cocaine use in a patient with HTLV-1 corroborates the studies described above. Unfortunately, we could not know whether HTLV-1 infection represented a greater susceptibility or opportunity to acquire *M. tuberculosis* and *Aspergillus* in this patient, as there were no signs/symptoms associated with HTLV-1 in his medical record. Moreover, even though there is an HTLV outpatient clinic in the hospital where the patient was being attended to between the years 2010 and 2015, HTLV-1 infection was never investigated for this patient. Thus, this correspondence aims to make HTLV-1 infection visible in cases of severe pulmonary diseases[7], such as TB and aspergillosis, in order to better monitor and treat these patients. Compulsory notification of systemic mycoses infection as well as HTLV-1/-2 in Latin America could help governments implement public health policies, such as recommending HTLV serology in patients with systemic fungal diseases.

AUTHORS' CONTRIBUTIONS

ACA: conceptualization, funding acquisition, project administration, investigation, methodology, formal analysis, writing of the original draft, writing review, and editing; MVS: data acquisition, writing review, and editing; APV: data acquisition, methodology, data curation, formal analysis, writing review, and editing.

FUNDING

This study was supported in part by Coordenacao de Aperfeicoamento de Pessoal de Nivel Superior (CAPES), Fundacao de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP grant Nº 2016/03654-0), and Instituto Adolfo Lutz (IAL). The funders had no role in the design of the study, in the collection, analyses or interpretation of data, in the writing of the manuscript, or in the decision to publish the results.

Adele Caterino-de-Araujo [1]
Marcos Vinicius da Silva [2]
Adriana Pardini Vicentini [3]

REFERENCES

1. Caterino-de-Araujo A, Campos KR, Alves IC, Vicentini AP. HTLV-1 and HTLV-2 infections in patients with endemic

mycoses in São Paulo, Brazil: a cross-sectional, observational study. Lancet Reg Health Am. 2022;15:100339.

2. Rosadas C, Taylor GP. HTLV-1 and co-infections. Front Med (Lausanne). 2022;9:812016.
3. Guery R, Suarez F, Lanternier F, Bougnoux ME, Lecuyer H, Avettand-Fenoel V, et al. Poor outcome and high prevalence of invasive fungal infections in patients with adult T-cell leukemia/lymphoma exposed to zidovudine and interferon alfa. Ann Hematol. 2021;100:2813-24.
4. Sugahara K, Yanagihara T, Nakamura Y, Nakayama Y, Hanaoka K, Ohgushi M, et al. A refractory, infected lung bulla and an abscess treated using percutaneous drainage in a patient with human T-lymphotropic virus type 1-associated myelopathy. Cureus. 2021;13:e20333.
5. Mejía-Mertel J, Gómez-Banoy N, Rojas-Hernández JP, Gotuzzo-Herencia E. Clinical profile of human T-lymphotropic virus type I: a forgotten infection in pediatrics. Infectio. 2021;25:28-32.
6. Oliveira VF, Viana JA, Sawamura MV, Magri AS, Benard G, Costa NA, et al. Challenges, characteristics, and outcomes of chronic pulmonary aspergillosis: a 11-year experience in a Middle-income country. Mycopathologia. 2022 In Press.
7. Dias AR, Falcão LF, Falcão AS, Normando VM, Quaresma JA. Human T lymphotropic virus and pulmonary diseases. Front Microbiol. 2018;9:1879.