Infection with human T-lymphotropic virus type 1 (HTLV-1) can be associated with hematologic malignancy, inflammatory syndromes, or infectious complications. Herein, we bring attention to HTLV-1 infection complications as we discuss a case of disseminated cryptococcosis in a patient with HTLV-1-associated T cell lymphoma.

Keywords. Cryptococcus neoformans; human T lymphotropic virus 1; HTLV-1.

CASE REPORT

An 82-year-old woman, originally from the Caribbean, presented with fever and hemoptysis. She had no known comorbidities and she was not receiving immunosuppressive agents. A computed tomography of her thorax demonstrated extensive right middle lobe consolidation with satellite nodular lesions. She was treated empirically with piperacillin-tazobactam for necrotizing pneumonia with improvement of her symptoms. Ten days later, she was readmitted to the hospital after developing fever and hemoptysis. She had no known comorbidities and she was not receiving immunosuppressive agents. A computed tomography of her thorax demonstrated extensive right middle lobe consolidation with satellite nodular lesions. She was treated empirically with piperacillin-tazobactam for necrotizing pneumonia with improvement of her symptoms. Ten days later, she was readmitted to the hospital after developing fever and hemoptysis.

Careful examination of a peripheral blood smear (Figure 1) showed cells with petal-shaped nuclei, known as flower cells, which are frequently, but not exclusively, seen in human T-lymphotropic virus type 1 (HTLV-1) infection or HTLV-1-associated T cell leukemia/lymphoma [1]. Visualization of round yeasts without pseudohyphae on Gram stain from cerebrospinal fluid suggested cryptococcal infection (Figure 2). Serum and cerebrospinal fluid cryptococcal antigens were detected, at titers higher than 1:64; cerebrospinal fluid and bronchoalveolar lavage fluid cultures yielded Cryptococcus neoformans variant neoformans. Human T-lymphotropic virus type 1 antibodies were detected in blood. Flow cytometry immunophenotyping and T cell receptor rearrangement studies from blood were consistent with adult T cell lymphoma. The above results established the diagnosis of disseminated cryptococcosis in the setting of HTLV-1-associated lymphoma. Despite treatment with amphotericin deoxycholate combined with flucytosine, and aggressive supportive care, she had no neurologic recovery and expired after transition to comfort care. Although the reasons for her clinical deterioration despite treatment remain uncertain, it is possible that overwhelming disseminated infection with multiorgan involvement contributed to rapid decline in this immunocompromised host.

DISCUSSION

Cryptococcal infection may occur in HIV-infected individuals, organ transplant recipients, or otherwise immunocompromised patients. There are only very rare published reports of invasive cryptococcal disease in patients with HTLV-1-associated T cell leukemia/lymphoma [2]. Overall, cryptococcal disease seems to be a rare complication in HTLV-1-associated leukemia/lymphoma, although a potential association between cryptococcosis and HTLV-1 carrier state has been suggested [3, 4]. Cryptococcus neoformans variant neoformans and predominantly Cryptococcus neoformans variant gattii may also infect seemingly immunocompetent hosts [5]. Clinically, infection with either pathogen manifests similarly [6]. Acquisition occurs via the respiratory route, and pulmonary infection and dissemination to the central nervous system is common. Therefore, in case of pulmonary cryptococcosis in immunosuppressed hosts, it is important to exclude meningitis with lumbar puncture, because the presence of central nervous system disease alters...
the dose, duration of therapy, and need for intracranial pressure 
monitoring [7]. In large studies, involving mostly immunocom-
promised individuals, mortality of cryptococcal meningoen-
cephalitis remains high, up to 20%, despite treatment with 
antifungal agents [8].

Although Cryptococcus species have a global distribution, 
HTLV-1 epidemiology has mostly clustered in Japan, sub-
Saharan Africa, the Caribbean, and Latin America [9]. Apart 
from T cell leukemia/lymphoma and inflammatory syndromes, 
HTLV-1 infection has been associated with infectious compli-
cations such as strongyloidiasis, tuberculosis, and leprosy [9]. 
HTLV-1-associated decrease in type 2 helper T cell response 
and HTLV-1-associated malignant transformation of T cells 
are thought to predispose to parasitic infections and abnormal 
cellular immune responses, respectively [9, 10]. Retroviral coin-
fection with HTLV and HIV may also lead to increased freque-
cy of HTLV-1-related neurological complications such as 
myelopathy [11]. Nonetheless, because most HTLV-1-infected 
individuals remain asymptomatic and T cell counts are normal, 
there are no established guidelines in monitoring HTLV-1-in-
fected hosts for opportunistic infections. Serological testing, 
based on epidemiologic suspicion, allows diagnosis and there-
fore can lead to decreased transmission of the virus, which 
takes place sexually, as a blood-borne infection, or from moth-
er-to-child through breastfeeding [9]. In addition, knowledge of 
HTLV-1 infection may raise clinical suspicion for coinfection 
with another pathogen when HTLV-1-infected individuals 
seek care [12].

Note

Potential conflicts of interest. All authors: No reported conflicts. 
All authors have submitted the ICMJE Form for Disclosure of Potential 
Conflicts of Interest.

References

the early diagnosis of acute adult T-cell leukemia/lymphoma with skin 

2. Rhew DC, Gaultier CR, Daar ES, et al. Infections in patients with chron-


esis: Cryptococcus breaks out of the opportunistic box. Nat Rev Micro-

characteristics and epidemiology of cases identified in a South African 

for the management of cryptococcal disease: 2010 update by the 
Infectious Diseases Society of America. Clin Infect Dis 2010; 50: 
291–322.

8. Dromer F, Mathoulin-Pelissier S, Launay O, Lortholary O. Determin-
ants of disease presentation and outcome during cryptococcosis: the 

virus 1: recent knowledge about an ancient infection. Lancet Infect Dis 

10. Porto AF, Neva FA, Bittencourt H, et al. HTLV-1 decreases Th2 type of 
immune response in patients with strongyloidiasis. Parasite Immunol 

progression among patients coinfected with HIV and human T lym-

12. Xavier RJ, Gala MK, Bronzo BK, Kelly PJ. Case records of the 
Massachusetts General Hospital. Case 23-2012. A 59-year-old man with 
367:363–73.

Figure 1. Peripheral blood smear, the arrow is pointing to a flower cell, 
which is a lymphocyte with petal-shaped nucleus. Flower cells may be 
seen in the setting of HTLV-1 infection or HTLV-1-associated T cell leukem-
ia/lymphoma.

Figure 2. Cerebrospinal fluid Gram stain (magnification, x1000). The 
arrows is indicating an encapsulated yeast. Culture subsequently grew Cryp-
tococcus neoformans.