Journal of Clinical and Translational Pathology **2024**
DOI: 10.14218/JCTP.2024.00037

Case Report

Diagnosis of Lung Leishmaniasis by Bronchoalveolar Lavage Cytology in a Human Immunodeficiency Virus-infected Patient: A Case Report

Ahmed A. Ahmed and Y. Helen Zhang*

Department of Pathology and Laboratory Medicine, The University of Texas Health Science Center at Houston, McGovern Medical School, Houston, TX, USA

Received: November 20, 2024 | **Revised:** December 22, 2024 | **Accepted:** December 24, 2024 | **Published online:** January 17, 2025

Abstract

Background: Leishmaniasis is a systemic parasitic disease that can affect unusual sites such as the lungs. ***Case presentation:*** We report a case of a 45-year-old male with human immunodeficiency virus infection who presented with abdominal pain and vomiting. Imaging studies revealed minimal bilateral ground-glass opacities in the lungs, hepatosplenomegaly, and diffuse lymphadenopathy. A bronchoscopy with bronchoalveolar lavage cytology evaluation showed abundant macrophages containing numerous intracellular organisms with characteristic dot-like kinetoplasts, confirming the diagnosis of Leishmaniasis. Special stains for other infections were negative. ***Conclusions:*** This case highlights the value of bronchoalveolar lavage cytology in diagnosing non-neoplastic lung pathologies, including parasitic infections like Leishmaniasis, thereby enabling prompt and targeted treatment.

Citation of this article: Ahmed AA, Zhang YH. Diagnosis of Lung Leishmaniasis by Bronchoalveolar Lavage Cytology in a Human Immunodeficiency Virus-infected Patient: A Case Report. J Clin Transl Pathol 2025. doi: 10.14218/JCTP.2024.00037.

Introduction

Leishmaniasis is a parasitic disease with a wide range of clinical presentations, often affecting patients with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (hereinafter referred to as AIDS) due to the parasite's intracellular nature. As travel to endemic regions increases, leishmaniasis is becoming more common in non-endemic areas, particularly among HIV-infected individuals.[1,2] The parasite can affect unusual sites such as lungs, and its clinical manifestations are frequently atypical. HIV infection can lead to a wide range of lung diseases, including infectious conditions caused by various viral, fungal, and parasitic pathogens, as well as tumors.[3]

Bronchoalveolar lavage (BAL) performed through bronchoscopy is a valuable tool for obtaining specimens from the lower respiratory tract. Since BAL fluid comes directly from the lower respiratory tract, it is less contaminated by microorganisms from the upper respiratory or digestive tracts, providing a more accurate reflection of the lung's physiological and pathophysiological state.[4,5] In immunocompromised patients, who are more susceptible to opportunistic infections, the presentation may not always include classic symptoms or radiographic findings. In such cases, BAL is particularly useful for prompt diagnosis.[6]

Although BAL cytology is commonly used to identify etiologic agents, there is a lack of recent literature on its diagnostic utility for various pulmonary diseases. This case study aimed to assess the effectiveness of BAL cytology in diagnosing visceral leishmaniasis in the lungs.

Case presentation

A 45-year-old Hispanic male, originally from Honduras, presented to the emergency room with a two-week history of left abdominal pain and vomiting, without fever. Additionally, he reported mild shortness of breath and a recent unintentional weight loss of 20 pounds. His medical history was significant for HIV infection. He had been in the U.S. for over 20 years and had no recent travel abroad history. On admission, the physical examination was unremarkable. Laboratory results showed pancytopenia, hyponatremia, elevated creatinine, and hypercalcemia. His CD4/CD8 ratio was 0.82 (reference range: 0.86–2.05), and the CD4 absolute count was 41 cells/μL (reference range: 431–1,623 cells/μL). Blood cultures were not obtained. Imaging studies revealed minimal ground-glass opacities in both lungs, hepatosplenomegaly, and diffuse lymphadenopathy. His current HIV RNA test was negative. Given these findings, the differential diagnosis included hematologic malignancy, tuberculosis, and granulomatous disease.

A bronchoscopy with BAL was performed. The BAL cytospin slides showed abundant alveolar macrophages, rare bronchial cells, and mixed inflammatory cells. Numerous oval organisms with gray or clear cytoplasm, dark nuclei, and dot/rod-like kinetoplasts were observed within the macrophages and were rarely present extracellularly (Fig.

Keywords: *Leishmania*; Lung; Bronchoalveolar lavage; Cytology; Human immunodeficiency virus; Parasite.
***Correspondence to:** Y. Helen Zhang, Department of Pathology and Laboratory Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, 6431 Fannin St, Houston, TX 77030, USA. ORCID: https://orcid.org/0009-0008-6963-5115. Tel: +1-713-566-5918, Fax: +1-713-566-5285, E-mail: Yu.H.Zhang@uth.tmc.edu

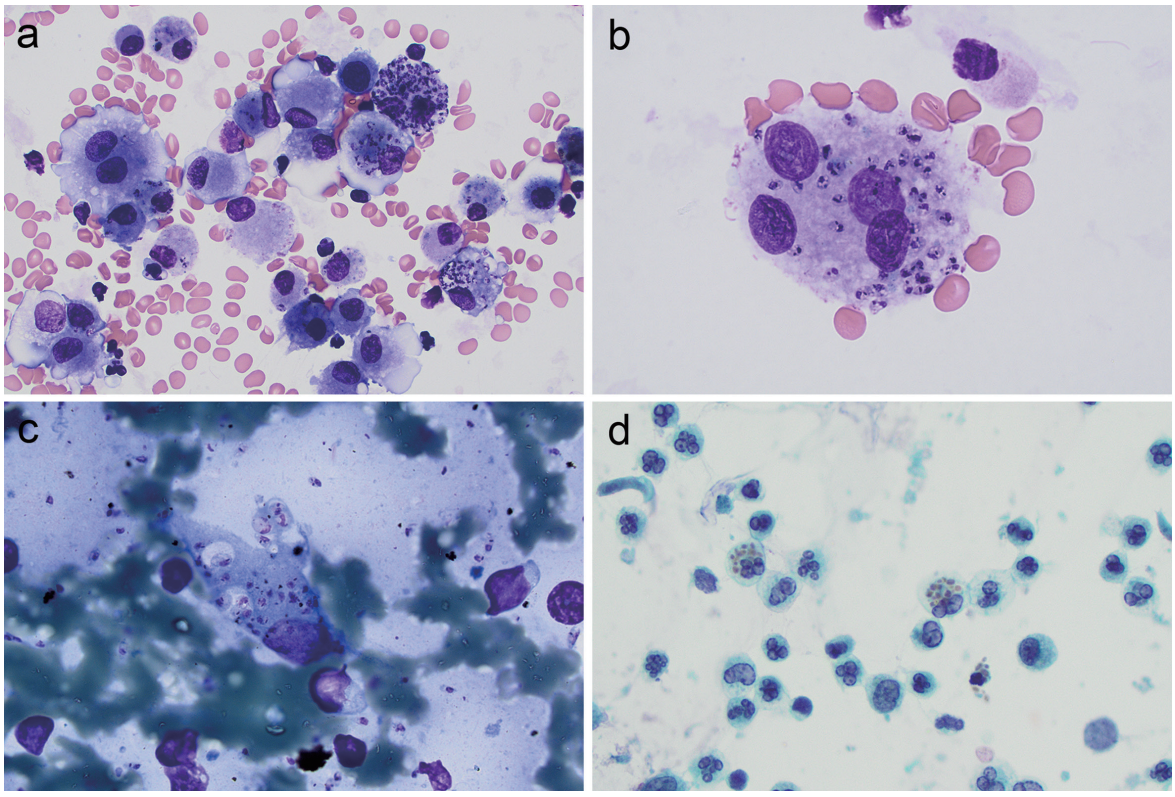

Fig. 1. Numerous intra/extracellular Leishmania amastigotes in bronchoalveolar lavage (BAL) and lymph node fine needle aspiration (FNA) specimens (BAL, Giemsa-Wright stain, a: 500×, b: 1,000×; lymph node FNA, c: 1,000×), and intra/extracellular spores of histoplasmosis in BAL from a different teaching case (Papanicolaou stain, d: 400×).

1a, b). These organisms were negative for Gomori methenamine silver, periodic acid-Schiff, and acid-fast bacilli stains. The overall findings were consistent with lung involvement by *Leishmania*. Concurrent fine needle aspiration of a station 7 mediastinal lymph node revealed similar cytomorphological features (Fig. 1c). No additional tests were performed on these two specimens. However, further history was uncovered after the cytologic diagnosis. The patient had a remote history of cutaneous Leishmania and was confirmed to have *Leishmania infantum* by polymerase chain reaction (PCR) and DNA sequencing at Centers for Disease Control and Prevention (CDC). The serology test was negative at that time.

The patient was subsequently treated with Ambisome (Amphotericin B), along with a 28-day course of Miltefosine therapy. Miltefosine is the only oral antileishmanial drug effective against all three forms of leishmaniasis: visceral, cutaneous, and mucosal. On the day of discharge, the patient showed significant improvement in hepatosplenomegaly, and hypercalcemia was trending downward. He reported feeling much better compared to admission. Microbial cultures of both the BAL and lymph node aspirate were not contributory. He was discharged in stable condition with appropriate follow-up and medications.

Discussion

Leishmaniasis is a systemic parasitic infection caused by *Leishmania* species and transmitted by sandfly vectors. The parasite has a digenetic lifecycle, existing in two forms: extracellular, flagellated promastigotes and obligate intracellular amastigotes. There are three main forms of leishmaniasis: cutaneous, mucocutaneous, and visceral (also known as kala-azar), which can affect multiple organs. Visceral leishmaniasis primarily affects children and typically presents with fever, anemia, hepatosplenomegaly, lymphadenopathy, hypergammaglobulinemia, and pancytopenia. Atypical presentations are more common in immunocompromised individuals, especially those with HIV infection, as well as in elderly immunocompetent patients. *Leishmania* can cause lung infections in patients with AIDS, significantly increasing morbidity and mortality. It has been rarely demonstrated in BAL, with only a few case reports in the literature.[7–10]

BAL, originally developed to treat conditions like pulmonary alveolar proteinosis, cystic fibrosis, and asthma, is a common and relatively safe procedure for evaluating and diagnosing lung diseases. Compared to traditional methods, such as sputum analysis, BAL allows physicians to obtain targeted samples from the lower respiratory tract with less microbial contamination from the upper respiratory and digestive tracts.[5] BAL plays a crucial role in investigating opportunistic and atypical respiratory infections in immunocompromised patients and exploring unexplained radiographic pulmonary infiltrates or hypoxemia to reach a definitive diagnosis. The aspirated fluid can be evaluated with analytical tests, including cell counts and differential, cytopathologic analysis, cultures, and specific molecular tests.

For a diagnostic sample, a minimum of 5 mL (ideally 10–20 mL) is needed for cellular analysis. The specimen should be collected in a sterile container and transported to the laboratory. Total and differential cell counts are performed

by flow cytometry or manually.[11,12] BAL may consist of macrophages, rare neutrophils, lymphocytes, eosinophils, and respiratory epithelial cells. An increase in a specific cell type can be indicative of certain diagnoses. For BAL cytology evaluation, Diff-Quik-stained smears or cytospin preparations are useful for identifying the characteristic morphological features of *Leishmania* amastigotes. Intracellular amastigotes appear oval to round in shape, measuring 2–4 × 1.5–2 μm. They have a single deeply staining nucleus and a paranuclear kinetoplast. Intracellular organisms are typically round, while single extracellular forms tend to be more elongated under the microscope.[1,10] Other possible associated features, such as plasmacytosis, may also be useful indicators of leishmaniasis. Occasionally, aggregates of Leishman-Donovan bodies may appear in irregular, ring, or strap-like shapes, and these forms can sometimes resemble fungal spores or platelet aggregates, which may necessitate consultation with an experienced pathologist who has knowledge of such unique patterns.[13] Other cytopathology specimens, such as splenic aspiration, have been used for diagnosing visceral *Leishmania*, but BAL is less invasive than splenic aspiration, which carries risks like bleeding or infection. It also provides useful samples, especially in cases with lung involvement, making it a safe and effective diagnostic option.

The main differential diagnosis includes histoplasmosis (Fig. 1d). Both leishmaniasis and histoplasmosis on cytology can be seen intracellularly within the macrophages with small, round to oval cytoplasmic structures. The lack of a peri-organism halo, presence of a distinct kinetoplast, absence of budding, and negativity on Gomori methenamine silver, periodic acid-Schiff, and acid-fast bacilli staining are features that help confirm a diagnosis of leishmaniasis. Culture, serology, and molecular studies can provide further confirmation. Another differential is between *Leishmania* and *Trypanosoma cruzi* amastigotes, which can be morphologically indistinguishable. PCR, serologic tests, and clinical context, such as symptoms and geographic location, help differentiate them, as *Leishmania* is typically found in macrophages, while *Trypanosoma cruzi* often involves heart or gastrointestinal tissues.

Our case shared some similar clinical features with previously reported cases, including immunocompromised status, weight loss, and hepatosplenomegaly. *Leishmania* detection methods in those cases included direct visualization of the parasite via microscopy on Giemsa-stained tissue smears or aspirates, microbial culture in Novy-MacNeal-Nicolle medium, and serologic tests, such as rK39 or ELISA. Imaging studies were employed to evaluate organ involvement in visceral cases.[7–9,14] Serology tests are less reliable in immunocompromised patients. Molecular tests are increasingly in use, such as PCR for species-specific DNA, which can be costly and less accessible in certain regions. These challenges can delay diagnosis and treatment, highlighting the need for improved access and affordability.

However, this case report is limited by its focus on a single patient, making it less generalizable. It lacks comparisons with other diagnostic methods and may be influenced by subjective interpretation or misdiagnosis. Additionally, it may not provide sufficient clinical data or apply to regions with different endemic strains.

Conclusions

Opportunistic pulmonary infections pose a significant health risk to immunocompromised patients. BAL cytology can serve as an effective diagnostic tool for identifying specific infections, such as *Leishmania* amastigotes, enabling timely diagnosis and guiding appropriate treatment.

Acknowledgments

None.

Funding

None.

Conflict of interest

The manuscript was submitted during Dr. Y. Helen Zhang's term as an editorial board member of *Journal of Clinical and Translational Pathology*. The authors have no other conflicts of interest to declare.

Author contributions

Study design, data collection, manuscript drafting, and editing (AAA, YHZ). Both authors made significant contributions to this study and have approved the final manuscript.

Ethical statement

The study was performed following the ethical standards of the institutions to which we are affiliated and in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report.

Data sharing statement

As a case report, all data generated or analyzed are included in this article.

References

[1] Vicandi B, Jiménez-Heffernan JA, López-Ferrer P, Ortega L, Viguer JM. Cytologic diagnosis of leishmaniasis in HIV infection. A report of eight cases. Acta Cytol 2000;44(5):835–839. doi:10.1159/000328571, PMID:11015989.
[2] Joos L, Chhajed PN, Wallner J, Battegay M, Steiger J, Gratwohl A, *et al*. Pulmonary infections diagnosed by BAL: a 12-year experience in 1066 immunocompromised patients. Respir Med 2007;101(1):93–97. doi:10.1016/j.rmed.2006.04.006, PMID:16740381.
[3] Chen XM, Sun L, Yang K, Chen JM, Zhang L, Han XY, *et al*. Cytopathological analysis of bronchoalveolar lavage fluid in patients with and without HIV infection. BMC Pulm Med 2022;22(1):55. doi:10.1186/s12890-022-01851-0, PMID:35130846.
[4] Zhao Y, Dai X, Ji J, Cheng P. Bronchial lavage under fiberoptic bronchoscopy in the treatment of severe pulmonary infection. Pak J Med Sci 2020;36(3):396–401. doi:10.12669/pjms.36.3.1539, PMID:32292441.
[5] Davidson KR, Ha DM, Schwarz MI, Chan ED. Bronchoalveolar lavage as a diagnostic procedure: a review of known cellular and molecular findings in various lung diseases. J Thorac Dis 2020;12(9):4991–5019. doi:10.21037/jtd-20-651, PMID:33145073.
[6] Kim ES, Kim EC, Lee SM, Yang SC, Yoo CG, Kim YW, *et al*. Bacterial yield from quantitative cultures of bronchoalveolar lavage fluid in patients with pneumonia on antimicrobial therapy. Korean J Intern Med 2012;27(2):156–162. doi:10.3904/kjim.2012.27.2.156, PMID:22707887.
[7] Jokipii L, Salmela K, Saha H, Kyrönseppä H, Eklund B, Evans D, *et al*. Leishmaniasis diagnosed from bronchoalveolar lavage. Scand J Infect Dis 1992;24(5):677–681. doi:10.3109/00365549209054657, PMID:1465589.
[8] Rosenthal E, Marty P, Pesce A. Leishmania in bronchoalveolar lavage. Ann Intern Med 1991;114(12):1064–1065. doi:10.7326/0003-4819-114-12-1064_2, PMID:2029107.
[9] van Griensven J, Diro E. Visceral Leishmaniasis: Recent Advances in Diagnostics and Treatment Regimens. Infect Dis Clin North Am 2019;33(1):79–99. doi:10.1016/j.idc.2018.10.005, PMID:30712769.
[10] Zaidi A, Kaur H, Gupta P, Gupta N, Srinivasan R, Dey P, *et al*. Role of bronchoalveolar lavage in diagnosing pulmonary infections and malignancies: Experience from a tertiary care center. Diagn Cytopathol 2020;48(12):1290–1299. doi:10.1002/dc.24574, PMID:32770787.
[11] Meyer KC, Raghu G, Baughman RP, Brown KK, Costabel U, du Bois RM,

et al. An official American Thoracic Society clinical practice guideline: the clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease. Am J Respir Crit Care Med 2012;185(9):1004–1014. doi:10.1164/rccm.201202-0320ST, PMID:22550210.

[12] Hodge SJ, Hodge GL, Holmes M, Reynolds PN. Flow cytometric characterization of cell populations in bronchoalveolar lavage and bronchial brushings from patients with chronic obstructive pulmonary disease. Cytometry B Clin Cytom 2004;61(1):27–34. doi:10.1002/cyto.b.20020, PMID:15351979.

[13] Chandra H, Chandra S, Kaushik RM. Visceral leishmaniasis with associated common, uncommon, and atypical morphological features on bone marrow aspirate cytology in nonendemic region. J Trop Med 2013;2013:861032. doi:10.1155/2013/861032, PMID:24089618.

[14] Gupta N, Agarwal R, Rajwanshi A. Liquid-based cytology sample showing leishmaniasis in bronchoalveolar lavage fluid. Cytopathology 2015;26(1):59–60. doi:10.1111/cyt.12135, PMID:25830198.