

Case Report

Amebic lung abscess with coexisting lung adenocarcinoma: a unusual case of amebiasis

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Abstract: Amebic lung abscess with concurrent lung cancer, but without either a liver abscess or amebic colitis, is extremely uncommon. Here, we report a 70-year-old man presenting with pulmonary amebiasis and coexisting lung adenocarcinoma. During his first-time hospitalization, the diagnosis of lung amebiasis was confirmed by morphological observation and PCR in formalin-fixed and paraffin-embedded sediments of pleural effusion. Almost four months later, the patient was readmitted to hospital for similar complaints. On readmission, lung adenocarcinoma was diagnosed by liquid-based sputum cytology and thought to be delayed because coexisting amebic lung abscess. This case demonstrated that sediments of pleural effusion may be used for further pathological examination after routine cytology has shown negative results. At the same time, we concluded that lung cancer may easily go undetected in the patients with pulmonary amebiasis and repetitive evaluation by cytology and imaging follow-up are useful to find potential cancer.

Keywords: Amebic lung abscess, amebiasis, bacterial infection, immunofluorescence

Introduction

The causative agent of amoebiasis in humans is *Entamoeba histolytica* (*E. histolytica*), a protozoan parasite [1]. *E. histolytica* can cause invasive disease and remains an important cause of morbidity and mortality in developing countries [2]. Amebic liver abscess (ALA) represents the most common manifestation of extraintestinal amebiasis [3]. In contrast, pulmonary amebiasis is the rare form of extraintestinal amebiasis [4]. Amebic lung abscess is usually as the result of the transdiaphragmatic extension of ALA. A amebic lung abscess without either ALA or amebic colitis is extremely rare [5]. In addition, pulmonary amebiasis with concomitant lung cancer is also exceptional. To our knowledge, there is no such amebiasis reported in the medical literature. We herein report a case of amebic lung abscess with coexisting lung adenocarcinoma, but without liver and colon involvement.

Case presentation

A 70-year-old man presented with intermittent chronic cough with expectoration of 30 year'

duration. He had been treated with antibiotics to improve symptoms. In addition, he had a history of *E. histolytica* infections. On May 13, 2013, he was admitted to our hospital for worsen cough with concomitant expectoration and the antibiotic therapy with no clinical improvement. On admission, a physical examination showed a few of rales in the right lung. Except for respiratory, the patient denied any systemic symptoms, weight loss and diarrhea. The routine laboratory examinations demonstrated an increasing eosinophil count 0.59 K/ μ L (9.0%) and a normal liver function. Sputum cultures for bacteria and fungi revealed *Streptococcus Viridans* 3+ and *Neisseria* 2+. In addition, stool sample was normal results. Therefore, a presumptive diagnosis of bacterial infection was confirmed. Subsequently, treatment with antibiotics was administrated. However, the therapeutic efficacy was not ideal. Chest computed tomography (CT) scan were thereafter performed and revealed a mass in right low lung lobe with multiple nodules and pleural effusion (**Figure 1A**). Therefore, the patient complicated with lung cancer or tuberculosis (TB) was suspected. However, all TB sputum smear, serum

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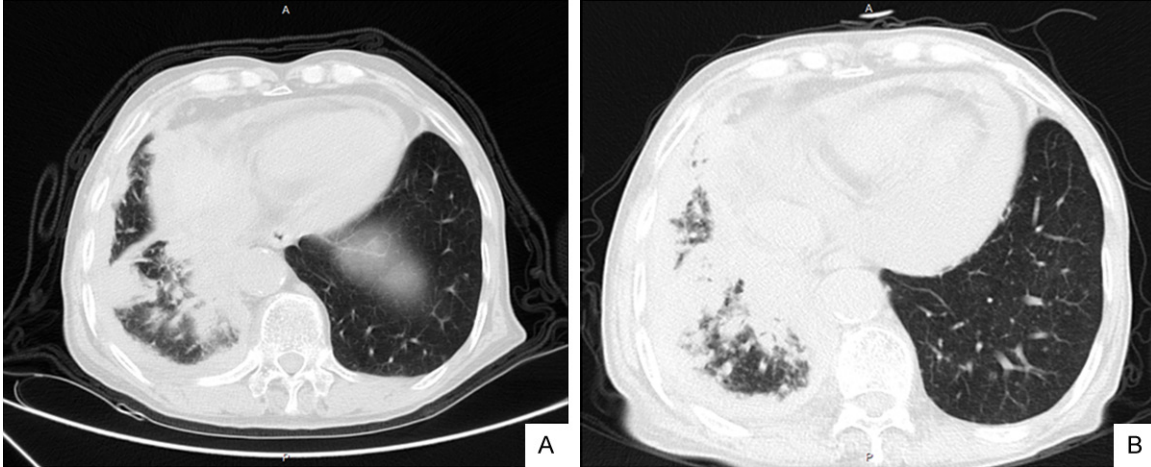


Figure 1. A. CT scan showing a mass in right-low lung lobe with multiple nodules and pleural effusion (2013/5/13). B. CT scan showed a slowly progression on pulmonary mass and nodules (2013/10/10). CT, computed tomography.

antibody to anti-TB and T-SPOT.TB were negative. Radioimmunoassay (RIA) revealed a normal level of tumor biomarker (2.65 $\mu\text{g/L}$ AFP, 0.48 $\mu\text{g/L}$ CEA, 15.47 ng/L NSE, 1.13 $\mu\text{g/mL}$ beta 2-microglobulin, 3.61 ng/mL CYFRA21-1, 2.66 U/mL CA50, 1.15 ng/mL SCCA). In addition, no tumor cells were detected by sputum cytology. CT guided fine needle aspiration reported negative findings. Simultaneously, there were no any parasites in submitted pleural fluid. Further pathological and molecular techniques were then performed, considering the history of *E. histolytica*. The sediments of remaining hydrothorax were fixed with formalin and thereafter embedded in paraffin for morphological observation. The subsequent haematoxylin and eosin (H&E) staining demonstrated scattered amebic trophozoites (**Figure 2A**). At the same time, the PCR was done on the sediments of pleural effusion following deparaffinization and DNA extraction for amplification. The primers and PCR conditions for *E. histolytica* were based on previously described procedures, and produced an amplicon of 100 bp used to detect for the occurrence of *E. histolytica* DNA [6]. The resultant band was matched to *E. histolytica* DNA. The above findings suggested invasive infection due to *E. histolytica*.

A diagnosis of amebic lung abscess was thus established. The diagnosis led to a prompt start of treatment of metronidazole with a daily dosage of 1.8 g for 21 days. The patient showed remarkable clinical improvement on anti-ame-

bic treatment. Almost four months later, the patient was readmitted to our hospital for similar symptoms on October 9, 2013. On readmission, CT scan showed a slowly progression on pulmonary mass and nodules (**Figure 1B**). Adenocarcinoma cells were detected by liquid-based sputum cytology (**Figure 2B**). Subsequently, the serum anti-amebic antibody by indirect immunofluorescence assay (IFA) was $\times 64$ the positive which also supported amebic infection. Therefore, we made a diagnosis of pulmonary amebiasis and concurrent lung adenocarcinoma on October 14, 2013. The families of patient thereafter decided to discharge from our hospital and return to the local hospital for treatment.

Discussion

Amebiasis is the main reasons of parasitic death, especially the developing regions [7]. Colonic amebiasis and ALA represent the most frequent manifestation of intestinal and extraintestinal amebiasis, respectively [3]. AIA is a potentially fatal disease [8]. Which may occur serious complications if not rapidly diagnosed and properly treated [2]. Primary pulmonary amebiasis is far less than ALA and usually as the result of the transdiaphragmatic extension of ALA. Furthermore, pulmonary amebiasis without either ALA or amebic colitis is extremely rare [5]. Pulmonary amebiasis with concomitant lung cancer is also exceptional. With regard to this type of amebic infection, the clinical diagnosis is difficult and the combination of

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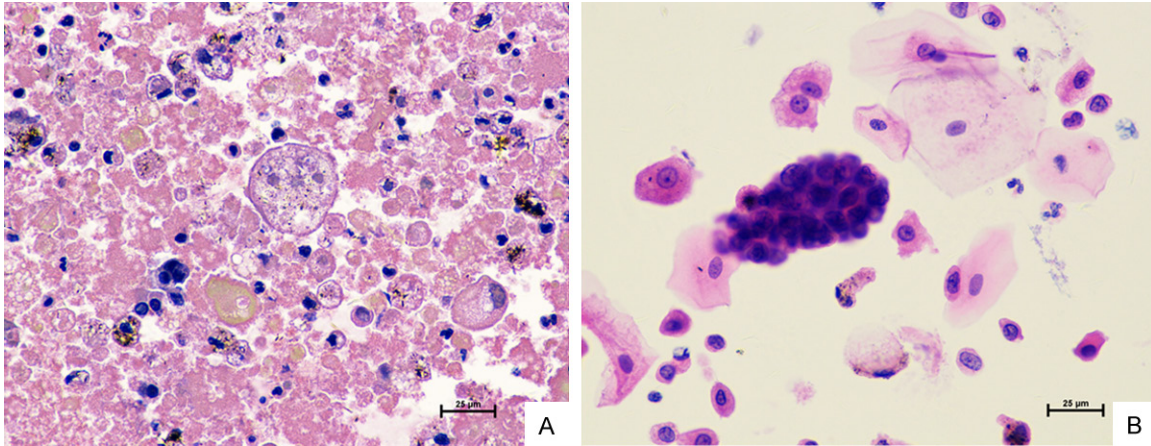


Figure 2. A. Microscopic examination of the sediments section of pleural effusion revealed amebic trophozoites. B. Adenocarcinoma cells were detected by liquid-based sputum cytology. (A and B, hematoxylin and eosin stain, $\times 400$).

microscopic and molecular techniques is the most appropriate way to obtain fully reliable results [9].

In our case, a CT guided fine needle aspiration was performed. Nevertheless, there were not any positive findings of in biopsy tissue besides pleural effusion based cytology. Over the last decade, the significance of sediments of pleural fluid in diagnosis is well recognized, and the diagnosis on tumor cells by formalin-fixed and paraffin-embedded sediments section of hydrothorax has been reported [10]. In order to confirm the clinical diagnosis, pleural effusion in our patient were centrifuged and sediments were fixed with 10% formalin, embedded in paraffin. The subsequent H&E staining showed scattered amebic trophozoites. In clinical practice, the detection by microscopy can be confounded due to overlapping cells, unclear backgrounds with inflammatory exudates and misidentification of macrophages as amebic trophozoites [4]. In our experience, there were two highlight for the identification of amebic trophozoites. First of all, the observer should be familiar with the characteristic morphology of amebic trophozoites and differentiate them from macrophages. The features included large size and the presence of a prominent karyosome and phagocytosed erythrocytes were the utmost useful to distinguish amebic trophozoites from macrophages. Secondly, both PCR and immunofluorescence were quite necessary in the differential diagnosis.

In addition, the diagnosis of lung adenocarcinoma in our patient was delayed. The routine

laboratory examinations and cytology associated with tumor showed negative, possibly explaining this missed diagnosis. Tumor cells in 40% of malignant effusion cases were not detected by the cytological examination of hydrothorax [11], and the normal results of cytology maybe false-negative. Therefore, repetitive evaluation by cytology or combined additional tests such as DNA ploidy analysis in pleural fluid were required if a patient with suspected malignancy. Previous experiences have shown that CT has excellent sensitivity for the detection of amebic abscess, but cannot distinguish amebic abscesses from necrotic tumors which may be another cause of delayed diagnosis [2]. As we known, tumor growth rate such as diameter increase by CT has a clinical significance in the identification of malignancy. In our patient, the number of pulmonary nodules has increased by a comparative appraisal of CT scans on May 13 and October 10, 2013. The results suggested imaging follow-up and comparative evaluation of indeterminate lung nodules were useful to find potential cancer.

Another interesting point is that our patient had had not any hepatic symptom. It is known that amebic lung abscess is usually as the result of the transdiaphragmatic extension of ALA. That may be due to the patient had possessed the resistance to *E.histolytica*, since the history of *E.histolytica* infections. Consistence with that, the patient had low antiamebic antibody titers ($\times 64$) on serological examination.

In this case, a extremely rare amebiasis of amebic lung abscess with coexisting lung cancer,

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but without amebic colitis and ALA was presented. In conclusion, it is recommended that sediments of pleural fluid may be used for morphological observation after routine cytology has shown negative results. In addition, lung cancer may easily go undetected in the patients with pulmonary amebiasis and repetitive evaluation by cytology and imaging follow-up are useful to find potential cancer.

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Disclosure of conflict of interest

None.

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References

- [1] Ralston KS, Petri WA Jr. Tissue destruction and invasion by *Entamoeba histolytica*. *Trends Parasitol* 2011; 27: 254-63.
- [2] Ali IK, Clark CG, Petri WA Jr. Molecular epidemiology of amebiasis. *Infect Genet Evol* 2008; 8: 698-707.
- [3] Ximenez C, Moran P, Rojas L, Valadez A, Gomez A. Reassessment of the epidemiology of amebiasis: state of the art. *Infect Genet Evol* 2009; 9: 1023-32.
- [4] Fotedar R, Stark D, Beebe N, Marriott D, Ellis J, Harkness J. Laboratory diagnostic techniques for *Entamoeba* species. *Clin Microbiol Rev* 2007; 20: 511-32, table of contents.
- [5] Hara A, Hirose Y, Mori H, Iwao H, Kato T, Kusahara Y. Cytopathologic and genetic diagnosis of pulmonary amebiasis: a case report. *Acta Cytol* 2004; 48: 547-50.
- [6] Luo M, Feng M, Min X, Li X, Cai J, Tachibana H, Cheng X. Primary pathogenicity analysis of a Chinese *Entamoeba histolytica* isolate. *Biosci Trends* 2013; 7: 77-81.
- [7] Zermeño V, Ximenez C, Moran P, Valadez A, Valenzuela O, Rascon E, Diaz D, Cerritos R. Worldwide genealogy of *Entamoeba histolytica*: an overview to understand haplotype distribution and infection outcome. *Infect Genet Evol* 2013; 17: 243-52.
- [8] Flores-Franco RA, Carrillo-Miranda JI, Castañeda-Martínez C, Salas-Munoz A. A case of eventrated liver mass presenting as a late outcome of hepatopulmonary amoebiasis. *Trop Gastroenterol* 2009; 30: 104-6.
- [9] Hugard L, Dubrous P, Massoure PL, Theffenne H, Coue JC. Amebic lung abscess: an unexpected diagnosis. *Bull Soc Pathol Exot* 2005; 98: 89-90.
- [10] Guo ZJ, Peng GX, Hu WW, Chen YX, Pan NL, Huang MY. A comparative study of agar-paraffin double-embedded sediments section and routine smear for hydrothorax and hydroperitoneum. *Bull Med Res* 2002; 31: 42-3.
- [11] Carpagnano GE, Costantino E, Palladino GP, Lacedonia D, Martinelli D, Orlando S, Foschino-Barbaro MP. Microsatellite alterations and cell-free DNA analysis: could they increase the cytology sensitivity in the diagnosis of malignant pleural effusion? *Rejuvenation Res* 2012; 15: 265-73.