Talaromycosis in a Lung Cancer Patient: A Rare Case

Rosario Ching-López¹, Sara Rodríguez Pavón¹

1. Radiation Oncology, Hospital Universitario Virgen de las Nieves, Granada, ESP

Corresponding author: Rosario Ching-López, r.ching.lopez@gmail.com

Abstract

Emergent fungal infections are rare conditions that frequently cause death. Talaromycosis is a fungal infection caused by *Talaromyces* sp. that is predominantly prevalent in patients with acquired immunodeficiency syndrome caused by human immunodeficiency virus infection, but in recent years we have noticed increasing reports of cases in people with other underlying conditions. We report a case of talaromycosis in a Stage IV non-small cell lung cancer female patient undergoing whole brain radiation therapy who presented to us with increasing dyspnea, cough and fever. The diagnosis was based on sputum and blood cultures, and even though our patient received anti-fungal treatment, the outcome was fatal. This case shows that a high index of suspicion could be essential for such a highly lethal but potentially treatable fungal infection.

Categories: Infectious Disease, Oncology, Pulmonology Keywords: non-small cell lung cancer, fungemia, talaromycosis, penicilliosis, emerging infectious diseases

Introduction

Talaromycosis, previously known as penicilliosis, is a fungal infection caused by *Talaromyces* sp. This is a highly opportunistic thermally dimorphic fungal pathogen, and was first isolated in 1956 in Vietnam from the hepatic lesions of a bamboo rat (*Rhizomys sinensis*) [1,2]. We owe its description to Segretain (1959), who was himself the first human case reported as a consequence of an accidental inoculation injury from a contaminated needle [3]. It was not until 1973 when Di Salvo et al. described the first naturally acquired infection in a patient, and it was considered a rarity until the spread of the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) pandemic in Southeast Asia in 1988, a region where this pathogen is now endemic [3,4].

However, over the past years we have noticed increasingly reported cases of infections due to *T. marneffei*, the etiological agent of talaromycosis, in non-HIV-infected patients who were affected with other immunocompromising conditions [3]. There are numerous potential reasons that could have led to this change in the epidemiology of talaromycosis, for example, improved treatment of HIV infection with highly active antiretroviral therapy and control of the HIV/AIDS epidemic, increased use of immune suppressive medications, better diagnostic tests, widened disease recognition, as well as global factors such as migration and travel increase [5]. Regardless of the cause, clinicians should be familiar with the changing epidemiology and clinical management of talaromycosis in potential hosts since an early use of antifungals is critical for improving the prognosis [6-8]. Herein, we report the case of an HIV-negative female patient who presented with talaromycosis coexisting with Stage IV primary non-small cell lung cancer (NSCLC). To the extent of our knowledge and literature review, this hasn't been reported before in Europe.

Case Presentation

Our patient was a 56-year-old woman with a past medical history of chronic obstructive pulmonary disease (COPD), hypertension, and diabetes mellitus, and was diagnosed with NSCLC (initially Stage IIIB) 26 months ago. She underwent a right upper lobectomy followed by adjuvant chemotherapy with cisplatinvinorelbine. After six months, the patient developed a local recurrence for which she underwent another extended resection. Within five months after, she experienced another mediastinal relapse according to the computed tomography (CT) and positron emission tomography (PET)-CT findings, and completed 30 sessions of radiotherapy (60 Gy) with concurrent administration of Taxol/carboplatin for six weeks. Two months later (26 months from diagnosis), she experienced a left-sided sudden hemiparesis and imaging revealed multiple brain metastases (Stage IV), for which she was given high-dose corticosteroids and was scheduled to receive whole brain radiotherapy (WBRT). After her second treatment session, she was admitted to our hospital with complaints of 38.1°C fever, dyspnea, and cough. The patient had an Eastern Cooperative Oncology Group (ECOG) performance status of 2 and was hemodynamically stable. Oxygen saturation was 93% without supplementary oxygen. Physical examination showed diffuse crackles and rhonchi in all lung fields. Analytic studies (biochemistry and blood count) did not present significant findings, whereas the chest X-ray showed enlarged hilar shadow and airspace infiltrates in the right upper and middle lobes without evidence of pleural effusion or pneumothorax (Figure 1).

Review began 09/16/2020 Review ended 09/21/2020 Published 09/23/2020

© Copyright 2020

Ching-López et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



FIGURE 1: Chest X-ray image showing enlarged hilar shadow and interstitial infiltrates in the right upper and middle lobes

We began an antibiotic treatment with intravenous piperacillin-tazobactam (4 g/6 h). However, 24 h after admission, she continued to have fever (38.3°C), and thus linezolid (600 mg/12 h) was added to the empirical treatment. In addition, pneumococcal and *Legionella* urinary antigen tests and bacilloscopy were carried out and the results were inconclusive. Nevertheless, serum galactomannan antigen test was positive and the fungal cultures sent from her sputum and blood yielded *Talaromyces* sp. after four days of incubation. The intravenous treatment was then optimized with liposomal amphotericin B 1800 mg/day while premedicating with normal saline and paracetamol. During the following 72 h, the patient remained afebrile, but her condition worsened and her oxygen saturation dropped to 87% (with supplementary oxygen at 2 lpm), requiring contribution with 40% oxygen to maintain saturation above the threshold of normality (>92%). Additionally, she developed moderate pancytopenia, her lab tests results being significant for hemoglobin of

9 g/dl, a white blood cell count of 800 cells/mm³, a neutrophil cell count of 570 cells/mm³, and thrombocytopenia with 54,000 platelets/µl. Her general status continued to worsen rapidly requiring 60% oxygen to maintain oxygen saturation and, despite targeted treatment, she developed shock and multiorgan failure. She eventually passed away six hours later.

Discussion

Disseminated talaromycosis has been traditionally related to HIV-infected individuals residing in or traveling from endemic areas. However, an increasing number of cases have been reported in patients with other immunosuppressive conditions such as organ transplants or use of immunotherapy [3,9]. In fact, previous studies have proven that the main underlying diseases related to talaromycosis these days are not only hematological but also solid tumors [10-12], which is the case in our patient. This infection is characterized by the fungal invasion of multiple body systems, which may result in fever, cough, skin papules, and thoracalgia. In nonendemic areas, its low incidence and a lack of familiarity with its clinical manifestations can definitely contribute to the diagnostic difficulties [3,13], and given the aggressiveness of this pathogen, it is essential to include this etiology as a differential diagnosis in patients at risk. Based on the sputum and blood cultures, talaromycosis was diagnosed definitely in our patient five days after her admission; our literature review did not show any such previously reported cases in lung cancer patients in Europe.

The recent cycles of chemotherapy and the chronic use of corticosteroids at high doses most likely predisposed our patient to disseminated *T. marneffei* infection, rather than the cancer itself [1].

The lethality of this infection is informed to be 91.3% without early diagnosis and optimal treatment [1], whereas for properly treated non-HIV-infected patients, an estimated mortality rate of 33% can be deduced

from a review of all published reports [3].

Conclusions

In this study, treatment with liposomal amphotericin B was started five days after admission to hospital, but our patient died three days later. With the increasing use of immunosuppressive agents, it is mandatory for the healthcare community to remain vigilant against the reactivation of emerging fungal infections.

Additional Information

Disclosures

Human subjects: Consent was obtained by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

- Wang Y, Cheng J, Ding H, Lin X, Chen GH, Zhou M, Ye SN: Study on the clinical features and prognosis of Penicilliosis marneffei without human immunodeficiency virus infection. Mycopathologia. 2018, 183:551-558. 10.1007/s11046-017-0236-3
- Wong SS, Siau H, Yuen KY: Penicilliosis marneffei—west meets east. J Med Microbiol. 1999, 48:973-975. 10.1099/00222615-48-11-973
- Chan JFW, Lau SKP, Yuen KY, Woo PCY: Talaromyces (Penicillium) marneffei infection in non-HIV-infected patients. Emerg Microbes Infect. 2016, 5:1-9. 10.1038/emi.2016.18
- Di Salvo AF, Fickling AM, Ajello L: Infection caused by Penicillium marneffei: description of first natural infection in man. Am J Clin Pathol. 1973, 60:259-263. 10.1093/ajcp/60.2.259
- Ashraf N, Kubat RC, Poplin V, et al.: Re-drawing the maps for endemic mycosis. (Online ahead of print). Mycopathologia. 2020, 10.1007/s11046-020-00431-2
- Li X, Hu W, Wan Q, Lei Q, Sun C, Hou Z, Shrestha N: Non-HIV talaromycosis: radiological and clinical analysis. Medicine (Baltimore). 2020, 99:e19185. 10.1097/MD.000000000019185
- Lin F, Qiu Y, Zeng W, Liang Y, Zhang J: Talaromyces marneffei infection in a lung cancer patient: a rare case report. BMC Infect Dis. 2019, 19:336. 10.1186/s12879-019-3968-5
- Madgula AS, Covello BR, Singh M, Rao A, Lee JC: Talaromycosis in a patient on nintedanib for interstitial lung disease. Cureus. 2020, 12:e7215. 10.7759/cureus.7215
- Chan JF, Chan TS, Gill H, et al.: Disseminated infections with Talaromyces marneffei in non-AIDS patients given monoclonal antibodies against CD20 and kinase inhibitors. Emerg Infect Dis. 2015, 21:1101-1106. 10.3201/eid2107.150138
- Qiu Y, Liao H, Zhang J, Zhong X, Tan C, Lu D: Differences in clinical characteristics and prognosis of Penicilliosis among HIV-negative patients with or without underlying disease in Southern China: a retrospective study. BMC Infect Dis. 2015, 15:525. 10.1186/s12879-015-1243-y
- Kawila R, Chaiwarith R, Supparatpinyo K: Clinical and laboratory characteristics of penicilliosis marneffei among patients with and without HIV infection in Northern Thailand: a retrospective study. BMC Infect Dis. 2013, 13:464. 10.1186/1471-2334-13-464
- Wang PH, Wang HC, Liao CH: Disseminated Penicillium marneffei mimicking paradoxical response and relapse in a non-HIV patient with pulmonary tuberculosis. J Chin Med Assoc. 2015, 78:258-260. 10.1016/j.jcma.2013.11.009
- Wong SS, Wong KH, Hui WT, Lee SS, Lo JY, Cao L, Yuen KY: Differences in clinical and laboratory diagnostic characteristics of Penicilliosis marneffei in human immunodeficiency virus (HIV)- and non-HIV-infected patients. J Clin Microbiol. 2001, 39:4535-4540. 10.1128/JCM.39.12.4535-4540.2001