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A Case of Lung Cancer Mimicking Invasive Pulmonary Aspergillosis in a Patient with Acute Myeloid Leukemia

Akut Miyeloid Lösemiyle Takipli Hastada İnvaziv Pulmoner Aspergillozisi Taklit Eden Akciğer Kanseri Olgusu

Levent Şensoy[1](İD), Aynur Atilla[2](İD), Derya Deniz Kürekçi[3](İD), Yusuf Taha Güllü[4](İD), Engin Kelkitli[5](İD)

[1] Clinic of Clinical Microbiology and Infectious Diseases, Fatsa Government Hospital, Ordu, Türkiye
[2] Department of Clinical Microbiology and Infectious Disease, Ondokuz Mayıs University Faculty of Medicine, Samsun, Türkiye
[3] Division of Hematology, Department of Internal Medicine, Samsun Training and Research Hospital, Samsun, Türkiye
[4] Department of Pulmonary Medicine, Ondokuz Mayıs University Faculty of Medicine, Samsun, Türkiye
[5] Department of Hematology, Ondokuz Mayıs University Faculty of Medicine, Samsun, Türkiye

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ABSTRACT

Infective and non-infective pulmonary lesions, predominantly infective, are commonly observed in patients with hematological malignancies. Secondary malignancies rarely cause non-infective lesions. The presence of undiagnosed pulmonary lesions presents a diagnostic and treatment challenge. As a result, several invasive techniques may be required to diagnose the condition. In this study, we aimed to report a case of a patient being treated for acute myeloid leukemia, initially diagnosed with invasive pulmonary aspergillosis, but later confirmed to have lung adenocarcinoma following a transthoracic lung biopsy.

Key Words: *Invasive pulmonary aspergillosis, acute myeloid leukemia, adenocarcinoma of lung*

ÖZ

Giriş: *Hematolojik maligniteli hastalarda çoğunluğu enfeksiyoz olmak üzere enfeksiyoz ve non-enfeksiyoz pulmoner lezyonlar sıklıkla görülmektedir. Enfeksiyoz olmayan lezyonlara nadiren sekonder maligniteler neden olabilmektedir. Tanısı konmamış pulmoner lezyonlar tanısal ve terapötik bir ikilem oluşturur. Bu sebeple tanıda çeşitli invaziv yöntemlere ihtiyaç duyulabilmektedir. Bu çalışmada akut miyeloid lösemi ile takipli invaziv pulmoner aspergillozis nedeniyle tedavi başlanan ancak transtorasik akciğer biyopsisi sonrası akciğer adenokarsinomu tanısı alan bir olgu sunulmuştur.*

Anahtar Kelimeler: *İnvaziv pulmoner aspergilloz, akut miyeloid lösemi, akciğer adenokarsinomu*

Address for Correspondence/Yazışma Adresi

Levent Şensoy
Clinic of Clinical Microbiology and Infectious Diseases, Fatsa Government Hospital, Ordu, Türkiye
e-mail: dr.leventsensoy@gmail.com

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INTRODUCTION

Acute myeloid leukemia (AML) is a malignancy characterized by myeloid differentiation and leukemic cell proliferation. The disease affects individuals of all age groups, with incidence increasing with age (1). Lung lesions are frequently observed in patients with hematological malignancies, such as AML, mainly due to infectious causes. Non-infectious causes comprise of drug toxicity, vasculitis, bronchiolitis obliterans, leukostasis, hyperleukocytosis, pulmonary alveolar proteinosis, and infrequently, secondary malignancies (1-4).

Among hematological malignancies, it is recognized that secondary lung cancer may develop as a late complication in patients with lymphoma. Additionally, lung cancer has been observed as a late complication of chronic lymphocytic leukemia; however, the reason for this correlation remains unclear (5). The occurrence of solid tumors is rare in association with AML (6).

Our study is presented to emphasize a case in which a patient with AML and active chemotherapy who presented with febrile neutropenia was diagnosed with invasive pulmonary aspergillosis (IPA) but was diagnosed with lung adenocarcinoma after transthoracic lung biopsy.

Definition

European Organization for Research and Treatment of Cancer (EORTC)/Mycosis Study Group (MSG) criteria have been developed by EORTC and MSG to define invasive fungal infections (IFI). According to the fulfilment of the EORTC/MSG criteria, the disease is categorized as “possible”, “probable” and “proven”. For the definition of “proven” IFI, in addition to clinical and host factors, tissue factors must also be present. In the definition of “probable” IFI, in addition to the clinical factor and host factor, there should be a microbiological factor without tissue factor. In the definition of “possible” IFI, there should be a clinical factor or mycological factor in addition to the host factor (7).

CASE REPORT

A 67-year-old male patient commenced cytarabine and idarubicin chemotherapy for induction-remission chemotherapy due to recurrent AML in June 2021. Initially, the patient was administered a loading dose of 2 x 300 mg, followed by a maintenance dose of 300 mg/day of posaconazole oral tablets for primary antifungal prophylaxis. On the fourth day after chemotherapy, the patient encountered neutropenia. On the 5th day, the patient developed a dry cough and a new fever of 38.7 °C. Empirical treatment for febrile neutropenia included piperacillin-tazobactam at a dose of 4 x 4.5 g/day, levofloxacin at a dose of 1 x 750 mg/day, and teicoplanin at a loading dose of 3 x 6 mg/kg every 12 hours, followed by a maintenance dose of 6 mg/kg/day. Additionally, blood and catheter cultures, a urine culture, a serum galactomannan test, and a COVID-19 PCR test were requested. Thoracic computed tomography revealed “irregularly circumscribed nodular lesions with a diameter of 16 x 32 mm located in the right lower lobe paramediastinal region, located in the pleura, the largest of which were scattered in both lungs” (Figure 1). Posaconazole was discontinued as 2 x 6 mg/kg loading, and 2 x 4 mg/kg maintenance voriconazole IV (intravenous) was added to the treatment with a prediagnosis of invasive pulmonary aspergillosis. Urine culture yielded 10^5 CFU/ml *Enterococcus faecalis*, and blood and catheter cultures yielded 10^5 CFU/ml methicillin-resistant *Staphylococcus epidermidis*. Galactomannan tests sent every other day resulted as 0.087 and 0.068 ng/ml, respectively. On the second day of treatment, the patient underwent bronchoscopy, with bronchoalveolar lavage (BAL) fluid being subjected to gram staining and bacterial culture, microscopic examination and culture for fungi, galactomannan testing, tuberculosis culture, and bronchial lavage cytology. No acid-resistant bacteria were observed in BAL Ziehl-Neelsen staining, and there was no growth in Mycobacterium tuberculosis culture. The BAL GM test revealed a value of 0.261 ng/ml. The biopsy result was “insufficient for evaluation”. The patient’s neutropenia improved, and the teicoplanin and levofloxacin antibiotics were discontinued on day 10 of the treatment, while piperacillin-tazobactam was stopped on day 14. The patient was considered to have “possible” IPA according to the EORTC/MSG criteria, and treatment with voriconazole was continued. The patient underwent transthoracic lung biopsy (TTBx) of the right upper lobe lesion due to an increase in the size and number of parenchymal nodules and additional mediastinal lymph nodes on control serial chest computed tomography (Figure 1). The patient’s pathology was concluded to be lung adenocarcinoma. The diagnosis of IPA was excluded, and voriconazole treatment was stopped on day 52. Nivolumab treatment was planned for the lung adenocarcinoma. The patient died from methicillin-sensitive *Staphylococcus aures* bacteremia, which developed before the planned chemotherapy.

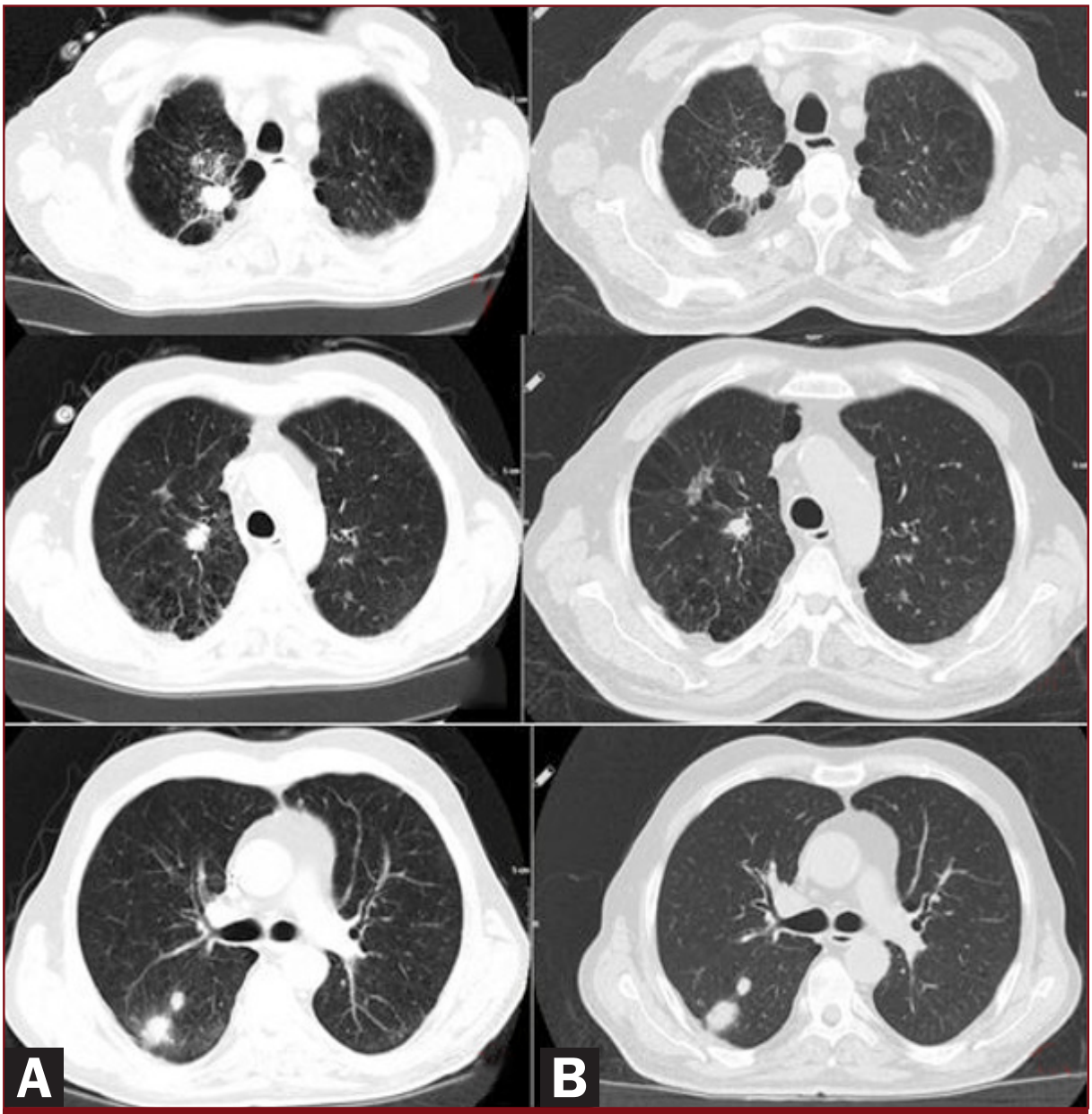

Figure 1. Comparison of lung nodule appearance at baseline and 2 months after treatment (A: baseline, B: After treatment).

DISCUSSION

Pulmonary lesions are a common complication in neutropenic patients with acute leukemia receiving chemotherapy and are usually due to fungal or bacterial infections (3,4). IPA is observed in AML patients at a rate of 8% (8,9). Radiological imaging may vary depending on the time of diagnosis and is not pathognomonic; findings may include dense, well-circumscribed nodules with or without halo sign, air-crescent sign, cavitary and wedge-shaped, segmental or lobar consolidations (9,10). In our case, thoracic computed tomography showed "irregularly circumscribed nodular lesions with multiple scattered nodules in both lungs" and antifungal treatment was initiated with a preliminary diagnosis of IFI, which was the first diagnosis to be considered because the patient had a febrile neutropenic attack, a long history of neutropenia, and AML remission induction chemotherapy. However, despite treatment, radiological progression was observed.

Undiagnosed pulmonary lesions in patients with hematological malignancies present a diagnostic and therapeutic dilemma. Infectious causes include fungal causes such as non-IPA mucormycosis and fusariosis, particularly in patients receiving antifungal prophylaxis (11), while non-infectious causes include alveolar hemorrhage, secondary malignancy, hypersensitivity pneumonitis, radiation damage and leukemic infiltration. Various invasive methods including BAL, transbronchial biopsy, transthoracic biopsy and open lung biopsy can be used to diagnose pulmonary lesions in this patient population (2,3,9). CT-guided lung biopsy has a high diagnostic value in patients with hematological malignancies with unexplained lung lesions and leads to therapeutic changes by providing a specific diagnosis in the majority of these patients. In patients with leukemia, an underlying active malignancy receiving chemotherapy, neutropenia, respiratory symptoms or fever, the biopsy result usually favors infection (2). Despite these findings, our patient was diagnosed with adenocarcinoma. It has been observed that lung biopsy has an important impact on the diagnosis and management of patients with hematological malignancies.

Radiological imaging is the most commonly used method for diagnosing and staging lung cancer. The main radiological findings include lung nodules, irregularly circumscribed masses, lobulation, thick-walled cavities and chest wall invasion. The prevalence of infectious diseases, including bacteria, mycobacteria, fungi and viruses, makes diagnosis difficult (12). As a result, delays in diagnosis, misdiagnosis and treatment may occur, resulting in increased patient mortality and morbidity (12). Cases of aspergillosis mimicking lung malignancy have been reported in the literature (12-14). However, the association of lung adenocarcinoma in an AML patient receiving active chemotherapy is very rare.

As in our case, the presence of nodular lesions on a chest CT taken for neutropenic fever in a patient with risk factors such as prolonged neutropenia, especially in a patient with a hematological malignancy such as AML, is primarily suggestive of IFI, but it should be borne in mind that the differential diagnosis may include non-infectious causes as well as opportunistic pulmonary infections. In such cases, serological tests, bronchoscopy and bronchoalveolar lavage, histopathological examination and, if necessary, image-guided biopsy may be helpful in establishing the diagnosis. Establishing a definitive diagnosis is the first step in initiating appropriate and correct treatment.

INFORMED CONSENT

Informed consent was obtained from the patient for this study.

CONFLICT of INTEREST

No conflict of interest declared.

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AUTHORSHIP CONTRIBUTIONS

Concept and Design: LŞ, AA

Analysis/Interpretation: LŞ, AA, EK

Data Collection or Processing: All of authors

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Review and Correction: AA, DDK, YTG, EK

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