IMAGES IN HEMATOLOGY
DOI: 10.4274/tjh.galenos.2025.2025.0192

Disseminated Invasive Aspergillosis in a Patient with Chronic Lymphocytic Leukemia

Özbay E. et al.: Disseminated Aspergillosis in CLL

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May 14, 2025
June 11, 2025

A 43-year-old male with relapsed chronic lymphocytic leukemia (CLL) was admitted for hypercalcemia. He had a prior history of B-cell non-Hodgkin lymphoma treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) and rituximab, etoposide, methylprednisolone, cytarabine, and cisplatin (R-ESHAP), followed by autologous stem cell transplantation. Due to disease progression, the patient was diagnosed with CLL and started on rituximab-bendamustine (R-BENDA). On day 3 of chemotherapy, he developed neutropenia (absolute neutrophil count 820/μL). By day 9, he became febrile and hypotensive, and broad-spectrum antibiotics were initiated. Chest CT showed patchy consolidations in the right upper and middle lung zones (Figure 1), raising suspicion for fungal infection. Antifungal therapy with voriconazole was initiated and later switched to liposomal amphotericin B due to QT prolongation.

Initial cranial MRI was unremarkable; however, the patient developed progressive confusion and ataxia, prompting repeat imaging on day 17 demonstrated new ring-enhancing lesions in both cerebellar hemispheres, suggestive of fungal abscesses (Figure 2). Bronchoscopy revealed widespread fungal plaques in the central airways (Figure 3). Bronchoalveolar lavage culture confirmed *Aspergillus fumigatus*, and galactomannan index was markedly elevated (index value 10.4). Despite targeted antifungal therapy, the patient's condition worsened and he succumbed to septic shock in the intensive care unit.

Patients with CLL are prone to neutropenia from marrow infiltration and chemotherapy, increasing susceptibility to invasive aspergillosis. Recent reports also highlight the increased incidence of invasive aspergillosis in CLL patients receiving Bruton tyrosine kinase inhibitors such as ibrutinib. While *Aspergillus* species are harmless in healthy hosts, they can cause severe infections in immunocompromised patients [1, 2].

Keywords: Chronic Lymphocytic Leukemia, Febrile neutropenia, Fungal Infections, Stem Cell Transplantation

Conflict of Interest: The authors declare no conflict of interest.
Financial Disclosure: The authors received no financial support for this work.
Informed Consent: Informed consent for publication was obtained from the patient's next of kin.

Footnotes
Authorship Contributions
Concept: USK, EY, EO, HA, SK
Analysis of Interpratation: USK, EY, HA
Literature Search: EO, EY
Writing: EO, EY, USK, HA, SK
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study received no financial support.

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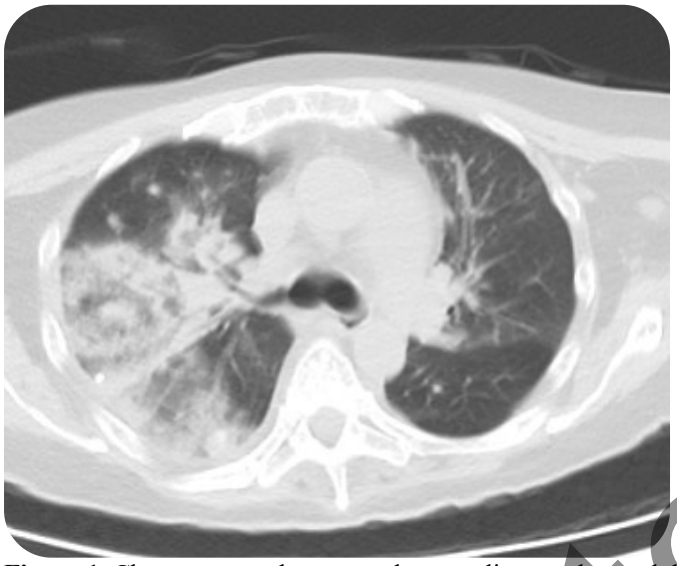

Figure 1. Chest computed tomography revealing patchy, nodular consolidations predominantly in the right upper and middle lung zones, consistent with invasive fungal pneumonia. These findings, in the context of profound neutropenia, raised strong suspicion for pulmonary aspergillosis.

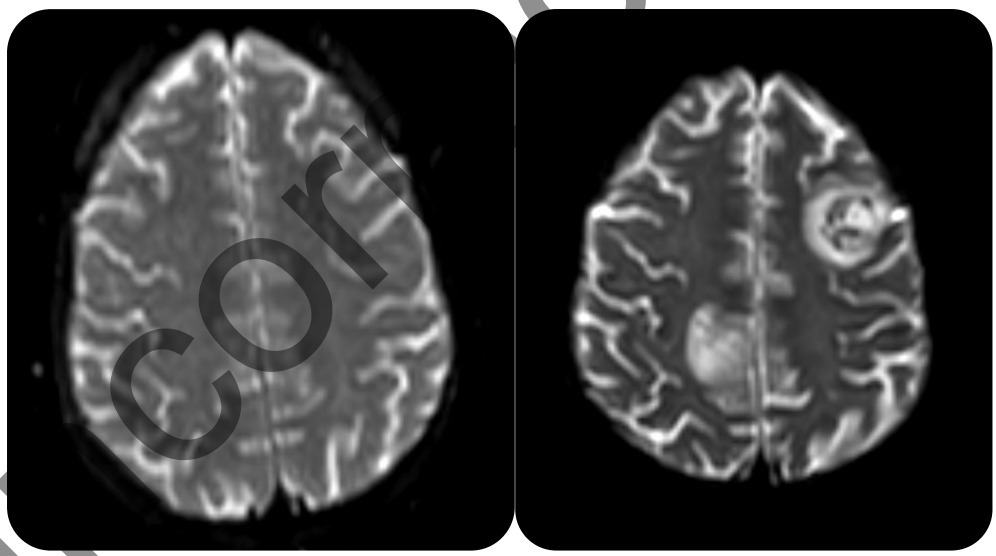

Figure 2. Comparative axial diffusion-weighted MRI images of the brain. (Left) Initial imaging shows no abnormal signal intensity or structural lesions. (Right) Follow-up MRI 17 days later demonstrates new, well-defined ring-enhancing lesions in both cerebral hemispheres, consistent with evolving cerebral fungal abscesses. The interval development of these lesions correlates with the patient's neurological decline and supports the diagnosis of disseminated invasive aspergillosis.

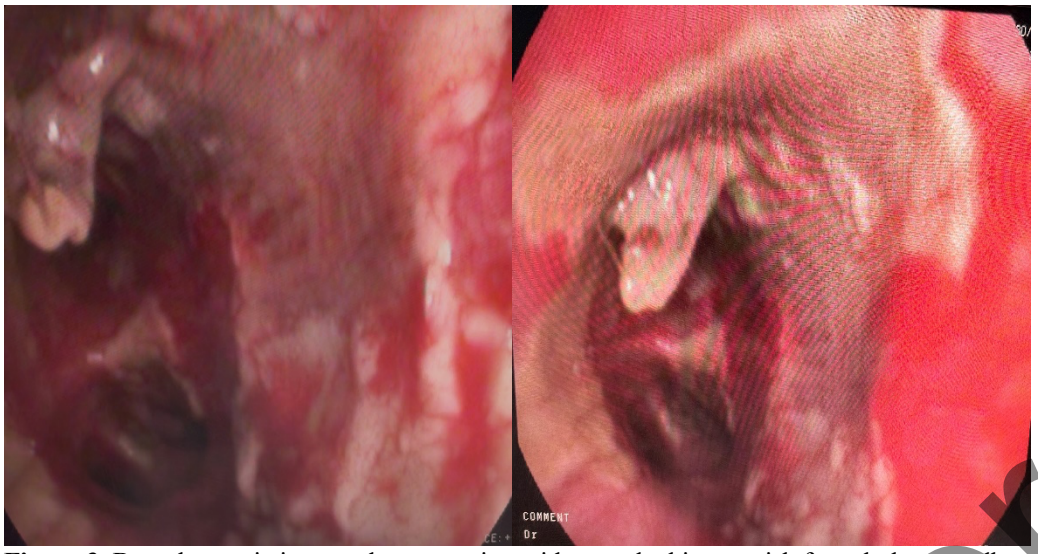

Figure 3. Bronchoscopic images demonstrating widespread white-grayish fungal plaques adherent to the mucosal surface of the main bronchi, more prominent on the left side. These findings are characteristic of invasive tracheobronchial aspergillosis and supported by subsequent *Aspergillus fumigatus* isolation in bronchoalveolar lavage culture.