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Letter to the Editor

Hematogenous Disseminated Pulmonary Tuberculosis in an Elderly Patient with Acute Myeloid Leukemia.

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To the editor.

Patients with acute leukemia often have markedly reduced numbers of functional immune cells due to either the underlying disease or its treatment, making them highly susceptible to infections.[1,2] Mycobacterium tuberculosis (MTB), a facultative intracellular organism, survives and replicates within resting macrophages.[3] Its clearance requires T-cell-mediated activation of macrophages.[3,4] When immune function is impaired, macrophages fail to eliminate MTB, predisposing patients to new infections or reactivation of latent tuberculosis (TB).[4] MTB can also cause lymphocyte depletion and suppress bone marrow function, further worsening immunosuppression, especially in cases of hematogenous spread.[5]

The typical features of TB (prolonged fever, systemic symptoms, and lymphadenopathy) often overlap with those of acute leukemia, leading to frequent diagnostic delays.[6,7] As a result, even in high-burden regions, clinicians may underestimate the possibility of TB reactivation, and imaging findings suggestive of TB are often attributed to fungal or bacterial infections or leukemic infiltration unless confirmed otherwise.[8] Metagenomic next-generation sequencing (mNGS) has emerged as a valuable tool for rapid and accurate TB diagnosis, particularly in immunocompromised hosts.[9,10] In a study of 48 patients with suspected disseminated TB, blood-based mNGS identified 28 cases and showed higher MTB detection rates in patients with elevated procalcitonin, HIV co-infection, and low CD4 counts.[10] Immunosuppression increases the complexity of tuberculosis management. While the WHO recommends that TB patients with HIV should not receive shorter treatment courses than their HIV-negative counterparts, the Infectious Diseases Society of America recommends up to 9 months of anti-tuberculosis therapy (ATT) for those not on antiretroviral therapy (ART) with drug-susceptible TB.[11,12] Both guidelines, however, lack specific recommendations for patients with hematological malignancies. A study of 59 patients with hematological malignancies who received ATT reported a median treatment duration of 9 months (range: 6-20), with no cases of tuberculosis relapse.[13] Evidence remains limited, underscoring the need for further research. Against this background, we report a case of hematogenous disseminated pulmonary TB in a patient with acute myeloid leukemia (AML), diagnosed by mNGS and successfully treated.

An 80-year-old Chinese man was admitted on March 26, 2024, with a recurrent fever for more than two months, accompanied by chills, fatigue, night sweats, weight loss, cough, dyspnea, palpitations, anorexia, and abdominal distention. Laboratory testing showed hemoglobin (HGB) 5.8 g/dL, red blood cells (RBC) 2.35 × 10^{12}/L, white blood cells (WBC) 15.47 × 10^{9}/L, neutrophils (NEUT) 2.59 × 10^{9}/L, monocytes (MONO) 11.34 × 10^{9}/L, and platelets (PLT) 112.4 × 10^{9}/L. CT imaging confirmed pneumonia (**Figure 1 A1, A2**), and elevated procalcitonin, C-reactive protein, and IL-6 prompted empiric piperacillin-tazobactam. Bone marrow morphologic and flow cytometric evaluation confirmed acute myeloid leukemia (AML), M4 subtype (**Figure 2**). The latter revealed 14.33% primitive granulocytes and 45.65% primitive monocytes, which expressed CD13, CD33, cMPO, CD38, CD34, CD117, partial HLA-DR, CD36, CD11b, CD64, and CD14. Next-generation sequencing identified RUNX1, TET2, WT1, and ZRSR2 mutations. Cytogenetics showed a normal karyotype, and no common leukemia fusion genes were detected.

Due to persistent fever (peak temperature, 39.5° C) and unimproved inflammatory markers after a 7-day course of piperacillin-tazobactam, the antimicrobial regimen was escalated to imipenem-cilastatin combined with voriconazole. This change was motivated by concern for uncontrolled bacterial infection and possible fungal co-infection in the context of the patient's immunocompromised state. Continued fever after four

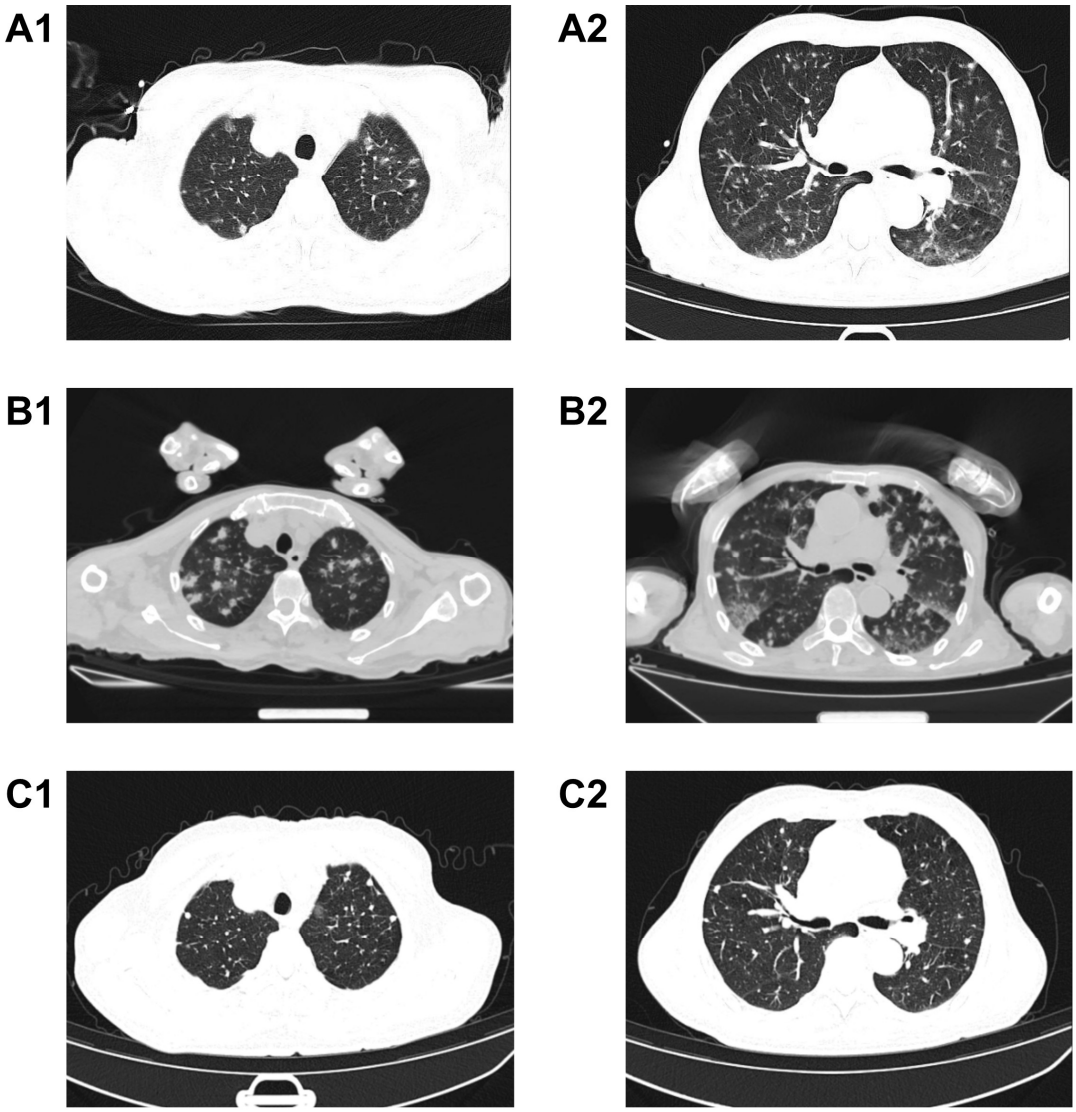

Figure 1. (**A1, A2**) On March 26, 2024, chest CT revealed scattered inflammatory changes in both lungs. (**B1, B2**) On April 9, 2024, chest CT suggested a marked increase in numerous bilateral scattered patchy and nodular opacities. (**C1, C2**) Chest CT (December 11, 2024) showed significant resolution of pulmonary tuberculosis, following 8 months of standardized anti-tuberculosis therapy.

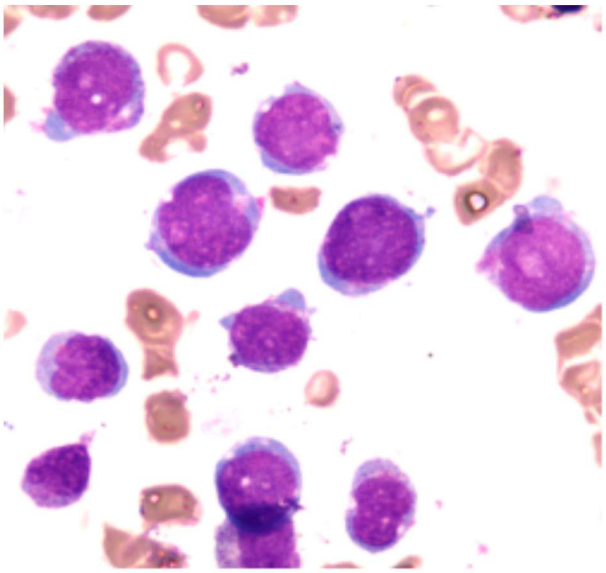

Figure 2. Bone marrow cytomorphology diagnosing AML 4 (Wright-Giemsa staining; magnification, x1,000).

days raised concern for tumor-associated fever, and azacitidine plus venetoclax was initiated on April 6, 2024. Daily afternoon fevers persisted, and positive TB serology and T-SPOT.TB prompted reevaluation. A repeat CT on April 9, 2024, showed rapidly progressive bilateral nodular and patchy opacities (**Figure 1 B1, B2**), consistent with hematogenous dissemination. On April 10, 2024, the patient developed agranulocytosis (NEUT 0.28 × 10^9/L) and severe thrombocytopenia (PLT 24 × 10^9/L), requiring cessation of chemotherapy. Peripheral blood mNGS on April 13, 2024, detected MTB complex (13.22% relative abundance; 11 reads), confirming hematogenous disseminated pulmonary TB. Under specialist guidance, ATT was initiated on April 13, 2024, consisting of ethambutol 0.75 g daily, rifapentine 0.45 g twice weekly, isoniazid 0.3 g daily, and moxifloxacin 0.4 g daily. **Table 1** summarizes the patient's clinical course and key laboratory findings. After defervescence on therapy, the patient left the hospital against medical advice on April 15, 2024,

Table 1. Timeline of Key Laboratory Parameters, Diagnostic Findings, and Therapeutic Interventions (2024).

Parameter / Event	26-Mar	28-Mar	01-Apr	02-Apr	06-Apr	09-Apr	10-Apr	13-Apr	14-Apr
Inflammation Biomarkers									
PCT (ng/mL)	0.72			0.986			0.549		0.144
CRP (mg/L)	134.3		130				82.12		39.12
IL-6 (pg/mL)		145.61		4.74					
Hematological Parameters									
WBC (×10⁹/L)	15.47	13.33	10.07				0.76		0.17
NEUT (×10⁹/L)	2.59	3.65	1.88				0.28		0.09
MONO (×10⁹/L)	11.34	8.58	7.27				0.38		0.03
HGB (g/dL)	5.8	5.4	6.1				6.7		6.5
PLT (×10⁹/L)	112	78	72				24		39
Diagnostic Tests and Results									
CD4 T-cell counts		LOW							
Bone marrow		AML-M4							
Acid-fast bacilli (sputum)						negative	negative		
TB-IGRA					positive				
PPD test						negative			
mNGS (peripheral blood)								MTB	
Comprehensive pathogen panel	Serology was negative for IgM antibodies against influenza A/B, parainfluenza, RSV, adenovirus, coxsackievirus, *C. pneumoniae*, *M. pneumoniae*, *L. pneumophila* type 1, rubella, toxoplasma, CMV, and HSV; Bacterial and fungal cultures of blood and sputum were negative; Nucleic acid detection for SARS-CoV-2 and EBV was negative.								
Treatment Regimen									
Antibiotic	PIP-TAZ				IMI/VORI				
Antineoplastic					AZA/VEN				
ATT								EMB+RPT+INH+MFX	

Abbreviations: TB-IGRA, tuberculosis interferon-gamma release assay; PPD, purified protein derivative; RSV, respiratory syncytial virus; *C. pneumoniae*, *Chlamydia pneumoniae*; *M. pneumoniae*, *Mycoplasma pneumoniae*; *L. pneumophila* type 1, *Legionella pneumophila* serum type 1; CMV, cytomegalovirus; HSV, herpes simplex virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; EBV, Epstein-Barr virus; PIP-TAZ, piperacillin-tazobactam; IMI, imipenem-cilastatin; VORI, voriconazole; AZA, azacitidine; VEN, venetoclax; EMB, ethambutol; RPT, rifapentine; INH, isoniazid; MFX, moxifloxacin.

despite severe bone marrow suppression. He remained on oral ATT and reported no recurrence of fever during the following week. After completing a two-month intensive phase, he entered a seven-month continuation phase with isoniazid, rifapentine, and ethambutol. Follow-up CT on December 11, 2024, showed complete resolution of the pulmonary lesions (**Figure 1 C1, C2**).

In conclusion, this case highlights the characteristic imaging features of hematogenous disseminated pulmonary TB in AML and demonstrates the diagnostic value of mNGS in immunocompromised patients. It also provides practical insight into the management of TB co-infection in elderly patients with leukemia.

Ethics approval and consent to participate. The study protocol was approved by the Medical Ethics Committee of the First People's Hospital of Zigong. The patient gave informed consent for the publication of this case report.

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Competing interests: The authors declare no conflict of Interest.

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