# PULMONARY LEUKEMIC INFILTRATION: RADIOLOGIC PATTERNS AND CLINICAL CORRELATION IN MYELOID AND LYMPHOID DISEASE

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## ABSTRACT

Pulmonary leukemic infiltration (PLI) is a rare but significant thoracic manifestation of leukemia. It is often underdiagnosed due to its nonspecific presentation and overlapping features with infection or drug-related lung injury.Differentiating PLI from infectious pneumonia or drug-induced lung injury is crucial for appropriate treatment and prognostication. Awareness of PLI's radiologic patterns, especially in patients with high leukemic burden or relapse, facilitates timely diagnosis and management. PLI presents with diverse imaging features such as ground-glass opacities (GGO), septal thickening, consolidation, and centrilobular nodules. Acute myeloid leukemia (AML) frequently shows GGO - and consolidation-dominant patterns, while lymphoid leukemias may present with nodular infiltrates and pleural effusions. HRCT - pathology correlation studies demonstrate that these patterns reflect direct leukemic cell infiltration.Incorporating HRCT findings into clinical assessment significantly improves diagnostic accuracy.This case-based review synthesizes findings from key radiologic and pathologic studies focusing on CT and high-resolution CT (HRCT) features of PLI with reference to relevant literature and imaging findings across different leukemia subtypes.

**Keywords:** Pulmonary leukemic infiltration; CT; high-resolution CT; leukemia; imaging; myeloid; lymphoid

## Epidemiology and Clinical Relevance

The true incidence of PLI remains underreported due to its frequent misidentification and overlap with other pulmonary pathologies. Estimates suggest that up to 25% of patients with hematologic malignancies may develop pulmonary complications, but only a small fraction of these are confirmed to be PLI.[1] Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) are more commonly associated with this condition. The incidence is believed to be higher in patients with relapsed or refractory disease, and autopsy studies often reveal higher rates of PLI than antemortem diagnosis suggests.[2-6] Furthermore, with the advent of newer immunosuppressive regimens and stem cell transplantation protocols, the susceptibility to PLI may be increasing, particularly in patients who have undergone multiple lines of therapy.[7]

## Case Report

A 47-year-old female presented to the oncology clinicin March 2025 with a 4-week history of persistent fever, generalized weakness, and increased bruising. Initial laboratory investigations revealed a platelet count of 28,000/mm$^3$, haemoglobin of 10.2 g/dL, and a peripheral smear demonstrating 50% blast cells, raising high suspicion for acute leukemia. Subsequent bone marrow

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biopsy and flow cytometry confirmed the diagnosis of acute myeloid leukemia (AML).

A chest radiograph performed at presentation showed mild bilateral pleural effusions. Contrast-enhanced CT of the chest further identified mild left-sided pleural effusion with lower lobe consolidation, as well as small subpleural consolidations, atelectasis, and nodularity in the right lung. These findings were initially reported as consistent with an infectious aetiology.

The patient was treated with broad-spectrum anti-microbials, including multiple courses of antibiotics, antifungals, and antivirals. She was initiated on induction chemotherapy with initial 7 cycles followed by 3 more cycles of (7+3 Cytarabine + Daunorubicin) regimen. However, post-induction bone marrow biopsy demonstrated 32% blast cells, indicating failure of induction therapy.

Xray chest after induction and follow-up chest CT revealed progression of radiologic findings, including multifocal consolidations - predominantly in the right lung - along with bilateral ground-glass opacities and increasing pleural effusions reported as worsening infection. Despite ongoing antimicrobial therapy, the patient continued to have intermittent fever spikes, and repeated laboratory investigations, including cultures and bronchoalveolar lavage (BAL), remained negative for any infectious pathogen.

A subsequent high-resolution CT scan revealed redemonstration of bilateral multifocal consolidations, most prominent in the peripheral and lower lung zones. Additionally, there were extensive ground-glass opacities more marked in the central and upper zones - along with centrilobular nodules and peribronchial vascular thickening. These features, in the absence of microbiological confirmation and in the clinical context of refractory leukemia, were interpreted as being highly suggestive of pulmonary leukemic infiltration (PLI). (Fig.1)

Given the radiologic progression in the setting of persistently negative cultures, worsening hypoxemia, and relapsed leukemia, the imaging findings were re-evaluated by a multidisciplinary team including hematology, infectious disease, and radiology. The consensus supported the diagnosis of pulmonary leukemic infiltration. The patient was subsequently given another cycle of chemotherapy with Azacitidine + Venetoclax. A repeat bone marrow biopsy was performed on 9th May 2025, which revealed less than 5% blast cells,

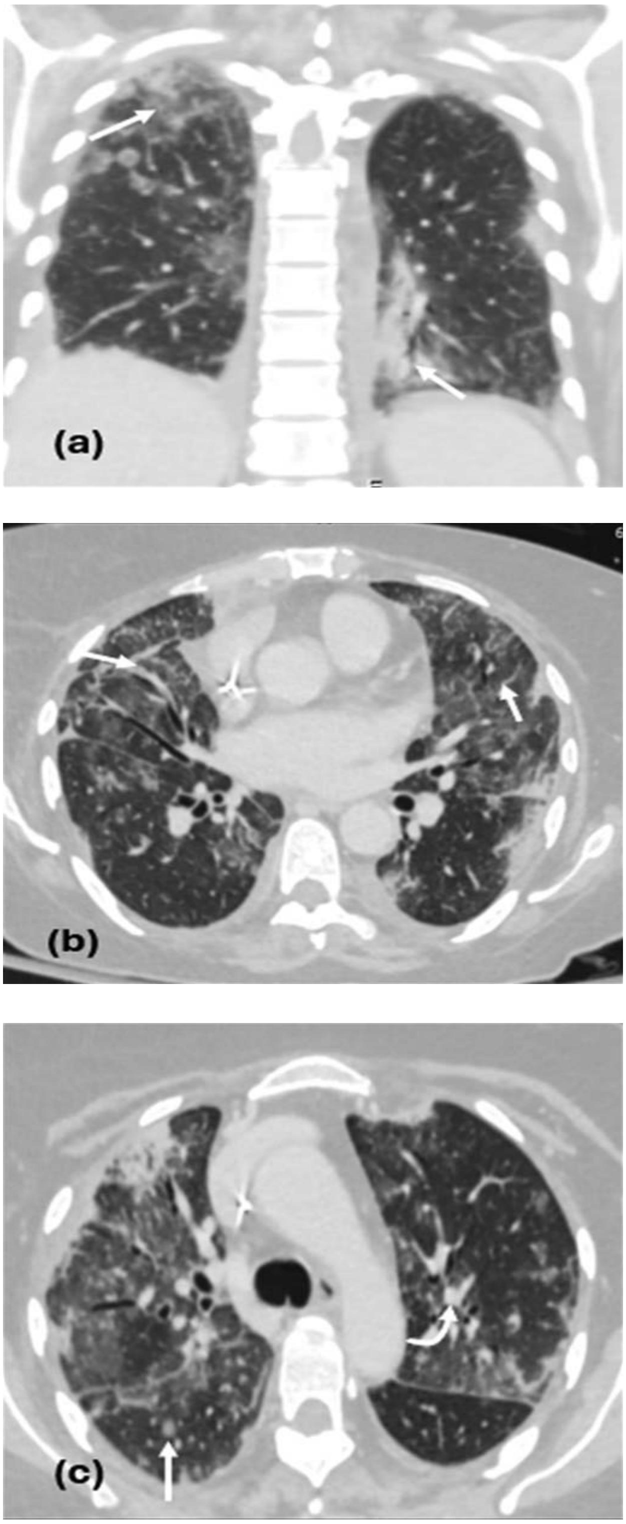



**Figure 1:** A case of a 47-year-old female with AML. **(a):** Bilateral multifocal consolidations, predominantly in peripheral and lower lung zones (straight arrows). **(b):** Ground-glass haziness, most marked in central and upper lung zones (straight arrows). **(c):** Centrilobular nodules (straight arrow) and peribronchial vascular thickening (curved arrow).

indicating remission. Follow-up chest radiograph showed marked improvement in pulmonary opacities. (Fig.2) Clinically, the patient improved and was discharged in stable condition.

This case exemplifies the diagnostic challenge posed by PLI in patients with AML, where radiologic patterns may mimic infectious or drug-related complications. The persistence of unexplained pulmonary findings despite negative infectious workup and the context of induction failure highlights the importance of considering PLI in the differential diagnosis. High-resolution CT findings, particularly when demonstrating both peripheral and central ground-glass changes with nodular involvement, can be instrumental in supporting the diagnosis of PLI in such cases.

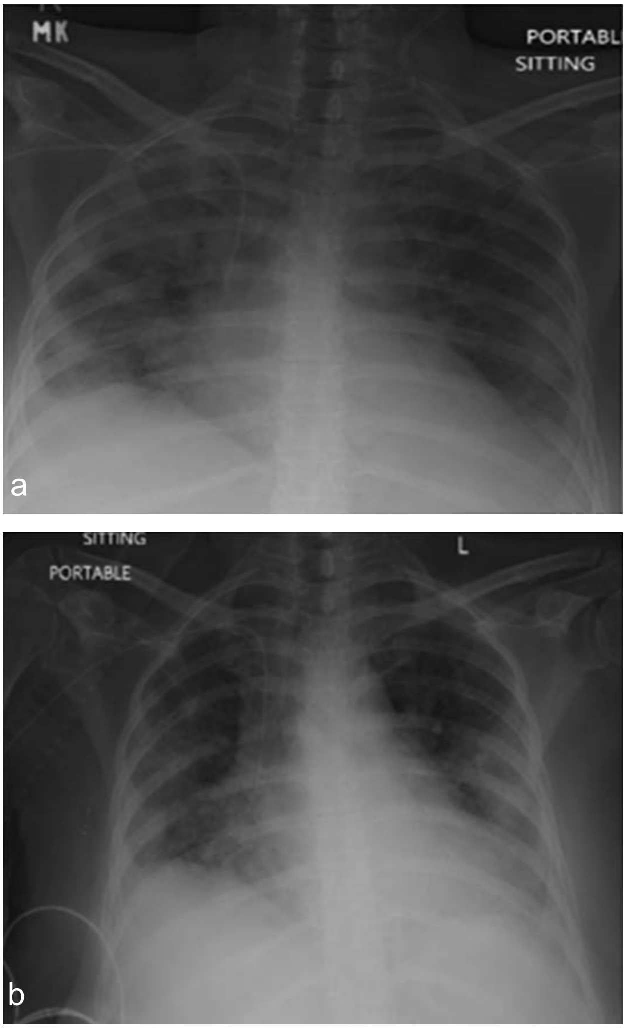
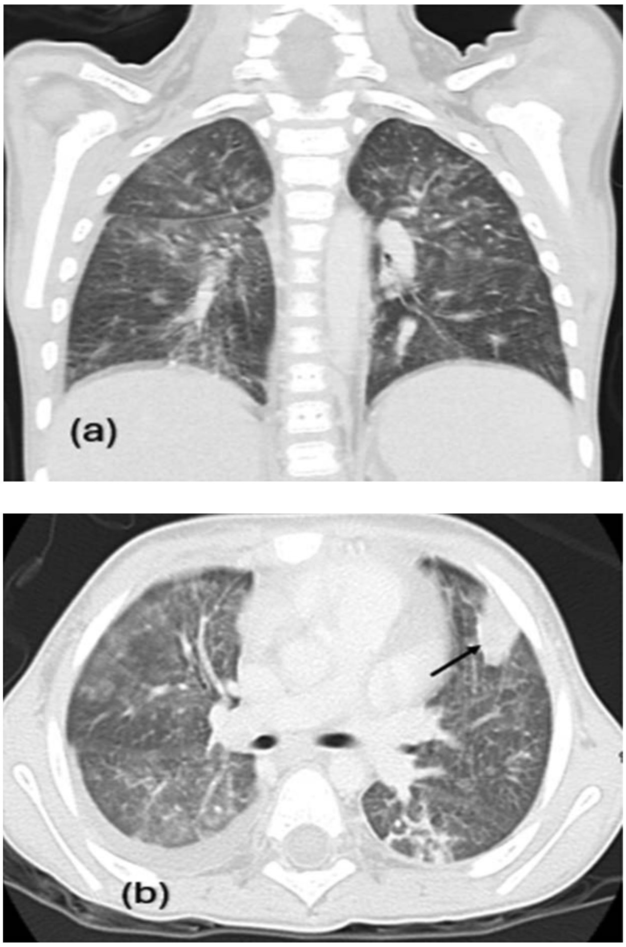



**Figure 2: (a):** Chest X-ray AP view: Multifocal ill-defined air space shadowing in both the lungs, more on the right side after induction chemotherapy. **(b)**: Follow-up chest x-ray after change of regimen reveals interval improvement in bilateral opacities.

### Radiologic Features and HRCT Patterns

Recent literature provides critical insights into the imaging characteristics of PLI, with HRCT features including ground-glass opacities, consolidation, interlobular septal thickening, centrilobular nodules, and peribronchovascular thickening.[3,4] These imaging patterns are not pathognomonic but, in the right clinical setting, can support a presumptive diagnosis of PLI. For instance, Yoshifuji et al. categorized pulmonary infiltrates in patients with AML into three radiological subtypes: ground-glass opacity dominant, consolidation dominant, and nodular dominant.[2] These subtypes not only reflect the distribution and density of leukemic cell infiltration but also provide clues for differentiating PLI from its mimics. Moreover, studies by Tanaka and Franquet have revealed a close correlation between HRCT patterns and histopathological findings.[4,5] Ground-glass opacities often correspond to alveolar septal infiltration by leukemic cells (Fig.3), while nodular and consolidative changes are typically indicative of more extensive parenchymal involvement.(Fig.4)



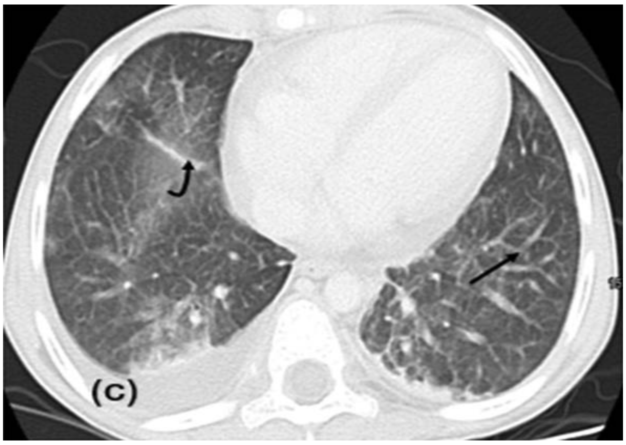



**Figure 3:** A case of a 4-year-old girl with AML. **(a):** Diffuse ground glass attenuation is noted in both lungs. **(b):** Area of consolidation in left upper lung lobe (straight arrow) and mild right sided pleural effusion. **(c):** Smooth interlobular septal thickening (straight arrow) and peribronchial vascular thickening (curved arrow) is noted in both lungs.

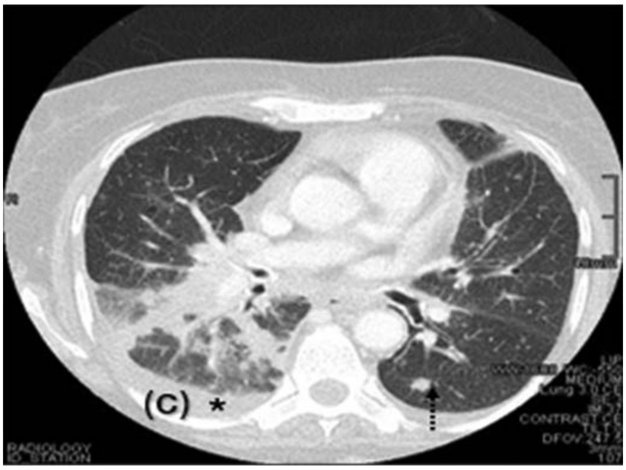




**Figure 4:** A case of 62-year-old female with AML. **(a,b):** Shows patches of dense consolidation (straight arrows) and significant ground glass opacification (curved arrows) in both lungs. **(c):** Show multiple soft tissue nodules in both lungs (dotted arrow) and mild right sided pleural effusion (asterisk).

## Radiologic Mimics of PLI

PLI can mimic a range of other conditions, making diagnosis particularly complex. Common mimics include pneumocystis jirovecii pneumonia, invasive fungal infections like aspergillosis, bacterial pneumonia, drug-induced pneumonitis, diffuse alveolar haemorrhage, and leukostasis.[1,3,6] Each of these has overlapping imaging features, such as ground-glass opacities or consolidations, but subtle differences in distribution and associated findings can aid differentiation. For example, fungal infections may show angio-invasive patterns with halo or reverse halo signs, while drug-induced changes often follow a temporal relationship with the administration of chemotherapeutic agents. Recognizing these patterns in conjunction with clinical context is vital for guiding accurate diagnosis and timely intervention.[7]

## Clinical Subtypes and Imaging Correlation

Subtype-specific differences also play a vital role in the imaging evaluation of PLI. In AML, diffuse ground-glass attenuation and consolidation are commonly observed, often involving lower lung zones and demonstrating a peri bronchial distribution.[2] Lymphoid leukemias, including chronic lymphocytic leukemia and acute lymphoblastic leukemia, may exhibit additional features such as nodularity, peri lymphatic spread, and mediastinal lymphadenopathy.[3,4] Adult T-cell leukemia/lymphoma (ATLL), a rare lymphoproliferative disorder, demonstrates a predilection for pulmonary involvement, with frequent findings of centrilobular nodules, bronchovascular bundle thickening, and pleural effusions.[8] The presence of lymphadenopathy or pleural involvement is more suggestive of lymphoid lineage, aiding in subtype identification.

### Post-treatment Changes and Therapy Response Imaging

Imaging plays a pivotal role not only in the diagnosis but also in the monitoring of treatment response. Following chemotherapy or targeted therapy, resolution of radiologic abnormalities can serve as an early indicator of therapeutic efficacy.[6] However, persistent or progressive findings may reflect refractory disease or transformation. In certain cases, PLI may emerge during therapy as a manifestation of tumor lysis or rapid proliferation, necessitating a dynamic approach to follow-up imaging. Dual-energy CT may help differentiate residual disease from post-treatment fibrosis by analyzing iodine maps, while PET-CT may offer insights into metabolic activity in ambiguous lesions.[9]

### Histopathological Correlation and Challenges

Histopathological confirmation, though ideal, is often impractical in leukemic patients due to risks associated with invasive procedures like lung biopsy. Consequently, radiologic-pathologic correlation studies are invaluable in validating imaging criteria for PLI. Tanaka et al. demonstrated a robust correlation between HRCT findings and autopsy data in leukemic patients, lending further credence to the use of non-invasive imaging as a surrogate diagnostic tool.[4] Their work particularly emphasized the significance of perivascular and interstitial infiltration by leukemic cells as a basis for many of the imaging patterns observed in PLI.

### Future Directions and Research Gaps

Despite growing awareness, there remain significant gaps in our understanding of PLI. Most available studies are retrospective and limited by small sample sizes. There is a pressing need for prospective research and standardized imaging protocols to better classify radiologic findings and correlate them with outcomes.[5,10] The incorporation of artificial intelligence (AI) and machine learning algorithms into chest imaging offers promise in identifying subtle patterns and improving diagnostic accuracy. Radiomics, which involves the extraction of large numbers of quantitative features from medical images, may be particularly useful in risk stratification and longitudinal monitoring.[11]

## Conclusion

PLI is a clinically significant yet frequently under diagnosed condition in patients with leukemia. The nonspecific nature of its clinical and radiologic manifestations necessitates a high degree of suspicion, particularly in the context of unexplained respiratory symptoms or imaging abnormalities unresponsive to conventional therapy. HRCT remains the cornerstone of diagnostic imaging for PLI, offering critical insights into parenchymal patterns that correlate with histopathology. Subtype-specific differences further refine diagnostic accuracy, while careful consideration of differential diagnoses helps avoid misclassification. As non-invasive imaging continues to evolve, its role in the early detection, monitoring, and prognostication of PLI is poised to expand, ultimately contributing to improved patient care and outcomes.

**DISCLAIMER:** None.

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**ETHICAL STATEMENT:** Applied for ERC waiver.

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