



Centrilobular ground-glass nodule pattern in acute myeloid leukemia patients receiving cytosine arabinoside chemotherapy: an important form of drug-induced lung disease

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Dear Editor,

We read with great interest the pictorial essay titled “Drug-induced lung disease: a brief update for radiologists” by Ufuk et al.¹ in the January 2023 of *Diagnostic and Interventional Radiology* issue. In this article, the authors comprehensively covered the imaging patterns and differential diagnoses of drug-induced lung disease (DILD) with demonstrative case examples.¹ We would like to mention a few points that may contribute to this article, which focuses on this complex issue, a popular topic in radiology.

First, according to the literature, a pulmonary hemorrhage can be classified as a radiological finding of DILD. A pulmonary hemorrhage can be seen as ground-glass opacities (GGO) or consolidations and is known to be associated with drugs such as penicillamine, rituximab, and cocaine.²

Second, Sridhar et al.³ proposed an alternative imaging-based classification system for DILDs consisting of six computed tomography patterns. Although this classification system overlaps with the patterns stated in the article, some differences draw attention.¹ “Organizing pneumonia” and “sarcoid-like” patterns show significant overlap. However, “fibrotic”, “diffuse GGO”, and “centrilobular ground-glass nodule (GGN)” patterns are suggested instead of “non-specific interstitial pneumonia”, “diffuse alveolar damage”, and “hypersensitivity pneumonitis” patterns, respectively.^{1,3} Last, the “linear-septal” pattern indicates the findings of interstitial pulmonary edema.³

As an oncological lung imaging center, we have seen the centrilobular GGN pattern in several acute myeloid leukemia (AML) cases receiving intermediate/high dose cytosine arabinoside (Ara-C) chemotherapy, and it causes a differential diagnosis problem. Therefore, we want to share our experience on this matter through two cases. Although Ara-C pulmonary toxicity mainly presents with non-cardiogenic pulmonary edema, in 2009, Chagnon et al.⁴ described a new pattern characterized by bilateral diffuse/upper lobe-predominant centrilobular nodules in six febrile neutropenic AML patients who had recently received Ara-C (Figure 1).

We believe that awareness of this pattern can assist radiologists in shaping patient management. However, opportunistic infections, especially miliary tuberculosis, should always be considered in febrile neutropenia. Although miliary tuberculosis is generally characterized by randomly distributed uniform micronodules with sharper contours, relying solely on radiological findings might have devastating consequences. Therefore, as emphasized by Ufuk et al.¹, multidisciplinary meetings are vital, especially to establish a diagnosis and determine the best management plan for patients with suspected DILD. Nevertheless, even with a multidisciplinary approach, it is not always possible to make a definitive diagnosis due to various confounders, including radiological mimickers, empirical treatments, limitations of microbiological/serological examinations, comorbidities, and variability in the drug-effect temporal relationship (Figure 2). Thus, it is important to keep in mind that proper patient management is far more crucial than the definitive diagnosis.

KEYWORDS

CT, chemotherapy, lung, pneumonitis, pulmonary toxicity

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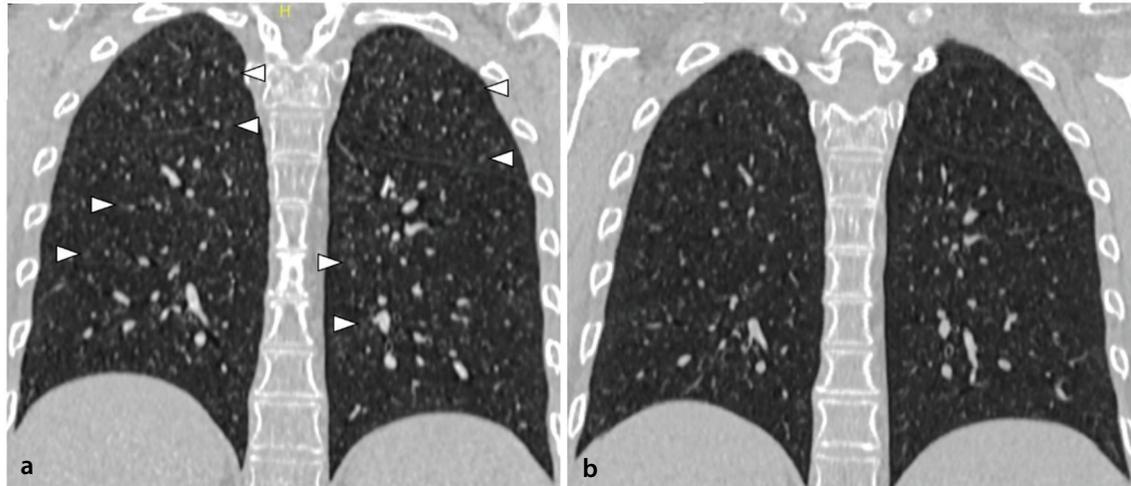


Figure 1. A 31-year-old female patient with acute myeloid leukemia. One week after receiving cytosine arabinoside (Ara-C) chemotherapy, a non-enhanced chest computed tomography (CT) was performed with complaints of low-grade fever and mild dyspnea. (a) Coronal plane chest CT shows bilateral upper lobe predominant centrilobular ground-glass nodules (arrowheads). The case was discussed in a multidisciplinary meeting due to the suspicion of miliary tuberculosis. Since all microbiological examinations were negative and clinical presentation was mild, the findings were primarily attributed to the Ara-C effect. After stopping chemotherapy, her symptoms regressed. (b) Follow-up chest CT 1 month later reveals almost complete resolution of radiological findings.

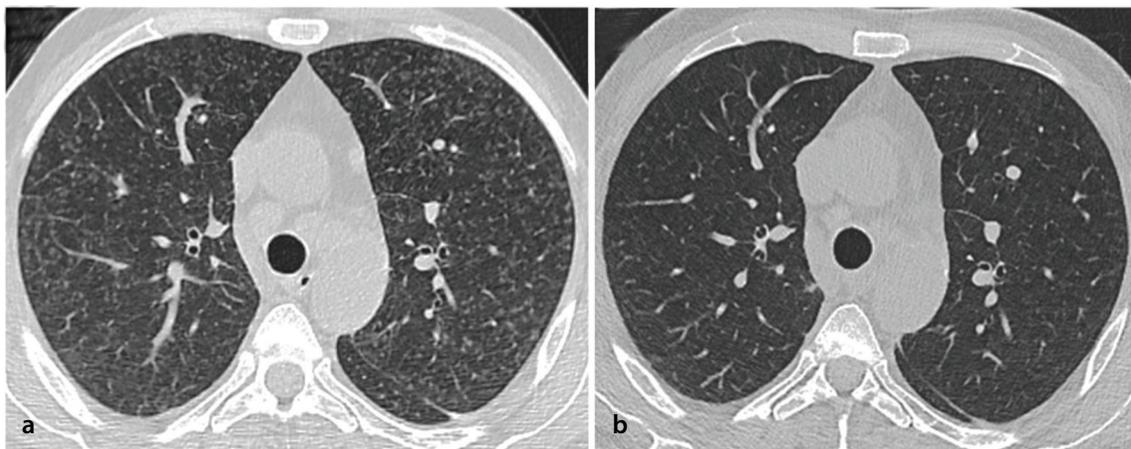


Figure 2. A 53-year-old febrile neutropenic male patient with acute myeloid leukemia. Five days after cytosine arabinoside (Ara-C) chemotherapy, a non-enhanced chest computed tomography (CT) was performed due to new-onset dyspnea and mild hypoxia. (a) Axial plane chest CT shows bilateral diffuse centrilobular ground-glass nodules. The case was discussed in a multidisciplinary meeting due to the suspicion of miliary tuberculosis. Radiologically, it was stated that the Ara-C effect might have caused this pattern. However, despite all negative microbiological examinations, miliary tuberculosis could not be excluded due to severe clinical presentation and previous history of contact with tuberculosis. Therefore, the patient was considered to have miliary tuberculosis. After stopping chemotherapy, an empirical antituberculosis regimen was started in addition to broad-spectrum antibiotics. (b) Follow-up chest CT 2 months later reveals complete resolution of centrilobular nodules. Retrospectively, the radiological findings were thought to be due to drug-induced lung disease, although it was not possible to make a definitive diagnosis in this case due to empirical antituberculosis treatment initiated simultaneously with chemotherapy discontinuation.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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