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Case Report

CASE REPORT

Leukemic infiltration in the settings of acute respiratory failure

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Abstract

Hematological malignancies need special attention in the intensive care unit (ICU). Leukemia has numerous presentations in the ICU. Most commonly, these patients present with complications of therapy. Infection and neutropenia are major reasons for ICU admission. Pulmonary complications in patients with leukemia are often due to pneumonia, hemorrhage, edema or drug toxicity; however, pulmonary leukemic infiltration is a well-known complication in all types of pneumonia but is not well described in chronic myelomonocytic leukemia. It can contribute to a rapid decline in respiratory status. Distinguishing among infection, pulmonary edema and leukemic infiltrates can be challenging. Characteristic radiological patterns have been described but are still challenging to recognize. Critical care management in these cases can have a large impact, and early intervention could be lifesaving in the appropriate clinical setting.

INTRODUCTION

Pulmonary complications of patients with leukemia are usually caused by infection, hemorrhage or drug toxicity; however, pulmonary leukemic infiltration is an important clinical consideration. Recognizing this complication and applying appropriate interventions may reduce morbidity and mortality.

CASE REPORT

A 62-year-old male with a past medical history of human immunodeficiency virus, who was receiving therapy, had a CD4 count of 641 and had been diagnosed with CMML 2 years ago presented with fatigue and dyspnea on exertion for 1 week. The patient had received different treatment regimens for CMML, including decitabine (5 cycles), ruxolitinib (8-month therapy) and azacitidine (2 cycles). He was recently started on hydroxyurea because of his disease progression and was sent for allogeneic hematopoietic stem cell transplant; however, he was deemed to not be a candidate because of renal dysfunction. The patient was admitted to the hospital for additional work up. He was found to have worsening anemia and thrombocytopenia as well as worsening leukocytosis (62 from 40 K 3 weeks prior to admission). He was diagnosed with autoimmune hemolytic anemia on this admission (positive Coombs test) and was started on prednisone. He received blood products, including several units of packed red blood cell and platelets, to maintain adequate hemoglobin levels and platelet counts. His bone marrow biopsy on admission showed dysmegakaryopoiesis and monoblasts accounting for 14% of the cellularity, which was consistent with CMML.

The patient was started on trimethoprim–sulfamethoxazole for *Pneumocystis jiroveci* pneumonia prophylaxis, hydroxyurea, IV fluids and allopurinol for tumor lysis syndrome prophylaxis. On Day 5 of admission, radiation oncology was consulted for palliative radiation for refractory and symptomatic splenomegaly because all medical therapy had failed. However, during the course of his admission, his respiratory status deteriorated

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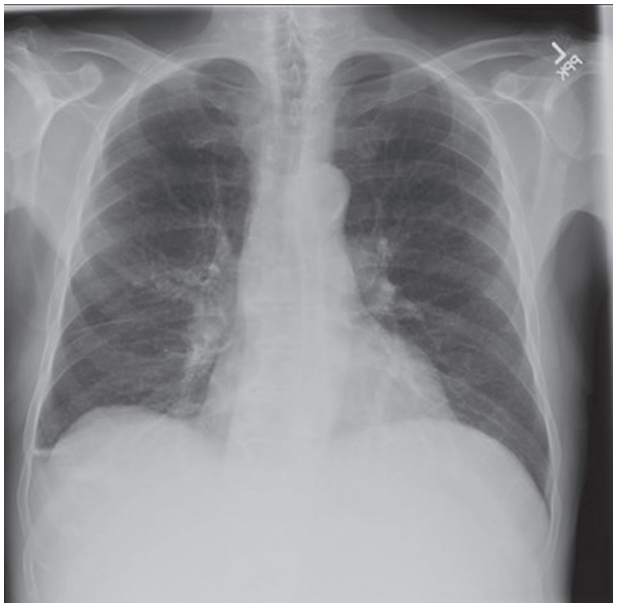

Figure 1: Chest X-ray 1 month prior to admission.

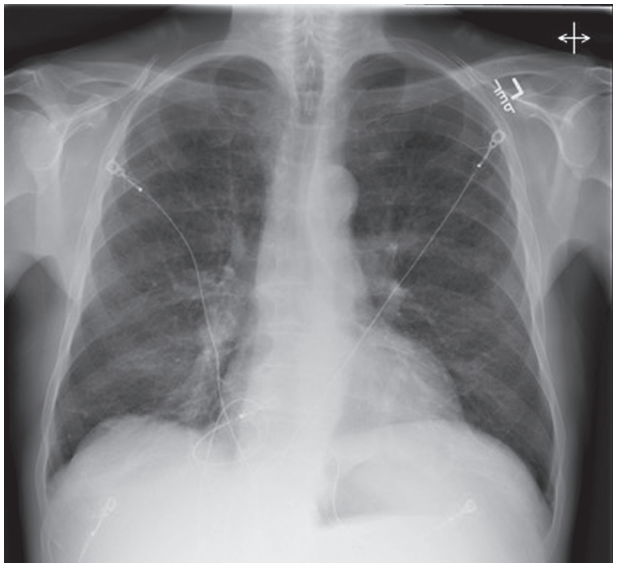

Figure 2: Chest X-ray on the day of admission; no significant change compared to his chest X-ray prior to his admission.

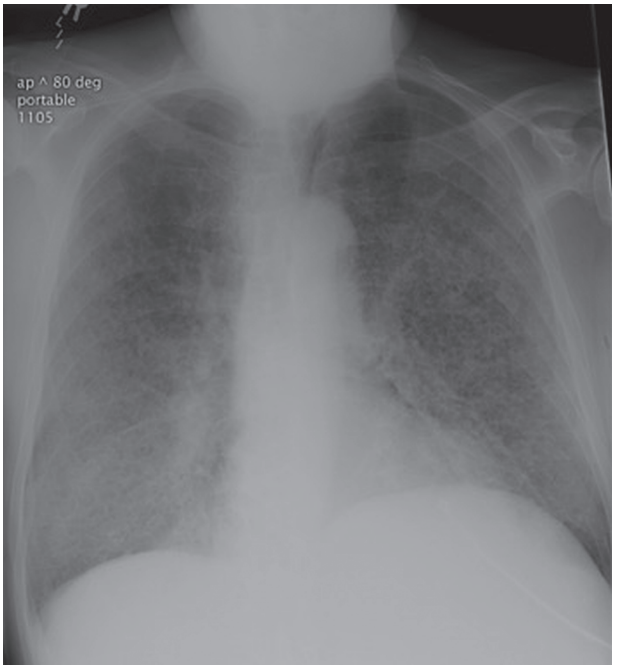

Figure 3: Chest X-ray on Day 8 of admission; there is diffuse interstitial opacity in all lung fields bilaterally.

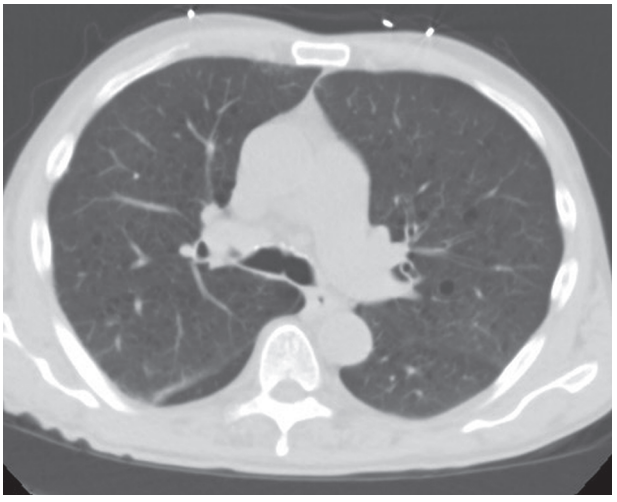

Figure 4: Computed tomography 1 month prior to admission; there is evidence of centrilobular emphysema but no obvious opacity or infiltrates.

slowly, requiring nasal cannula oxygen, and his X-ray showed evidence of bilateral infiltrate suggestive of pulmonary edema (Day 9 of admission). The patient's echocardiogram was normal 2 months prior to his admission, and his current brain natriuretic peptide level was only 71 pg/ml; however, given his clinical and radiological status, he was started on IV Lasix. He continued to deteriorate despite diuresis and required noninvasive positive pressure ventilation. After pan cultures, he was placed on broad spectrum IV antibiotics, specifically vancomycin, piperacillin and tazobactam. He was intubated on Day 10 of admission. His X-ray and chest computed tomography 1 month prior to admission showed no evidence of opacity or acute infiltrate, and the abdominal section showed hepatosplenomegaly (Figs 1, 4 and 5). A chest X-ray on admission (Fig. 2) is shown. The chest X-ray (Fig. 3) and chest computed tomography (Fig. 6) on Day 8 show significant interstitial infiltrate. He continued to deteriorate despite full respiratory support and broad-spectrum antibiotics. His white blood cell (WBC) at the time of admission to the intensive care unit (ICU) was 124 000, and he expired after 6 h of mechanical ventilation. The patient experienced refractory multi-organ failure, and the ICU team was unable to perform bronchoscopy. Limited lung autopsy was requested, and the slides are shown (Figs 7 and 8). The final diagnosis made at autopsy was pulmonary leukemic infiltration associated with marked pulmonary congestion and hemorrhage. No evidence of infection was found in these cultures or on autopsy.

DISCUSSION

CMML is a malignant hematopoietic stem cell disorder with clinical and pathological features of both a myeloproliferative

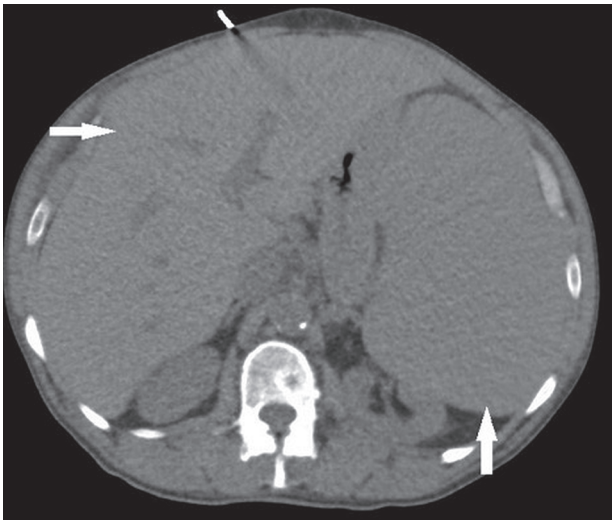

Figure 5: Computed tomography 1 month prior to admission; there is evidence of hepatosplenomegaly (white arrow).

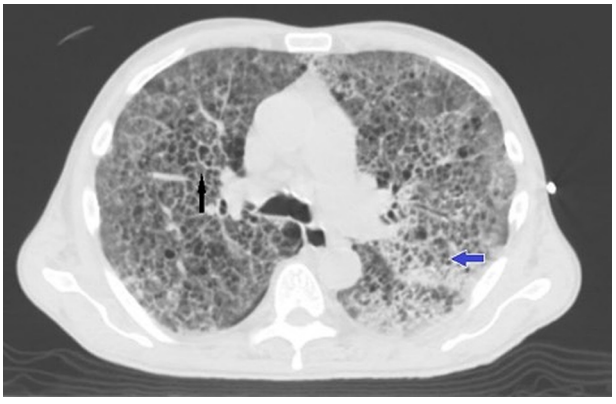

Figure 6: Computed tomography at the time of ICU evaluation; there is new onset of interstitial opacity and ground glass opacity (blue arrow) and interlobular thickening (black arrow).

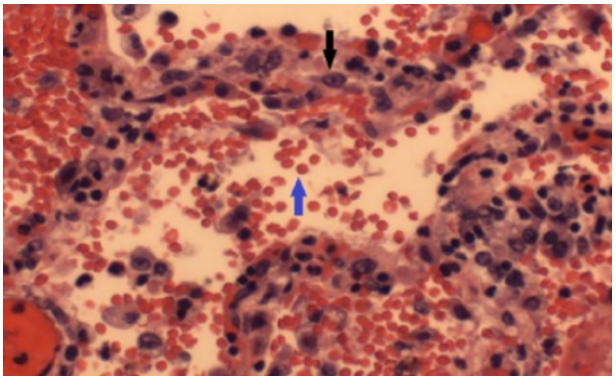

Figure 7: Hematoxylin and eosin slides showed intra-alveolar hemorrhage (blue arrow); the septal capillary blood vessels are distended by a moderately monotonous population of hematolymphoid monocytic cells (black arrow).

neoplasm and a myelodysplastic syndrome. It accounts for <1% of all hematologic malignancies [1]. The disease incidence rate ranges between 3.5 and 4.1/1 000 000 per year in the United States, and the median age at diagnosis is 72 years [2].

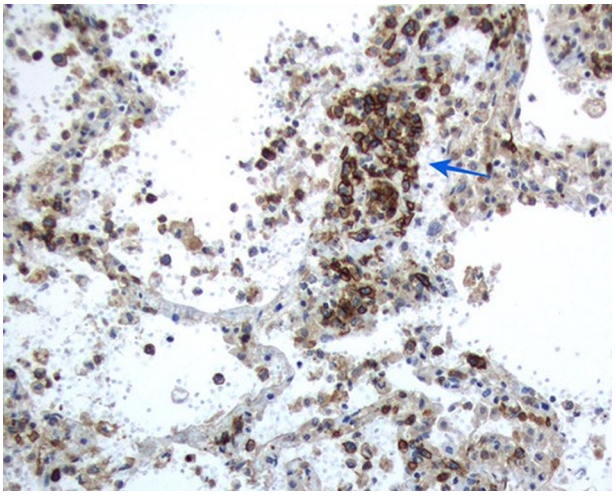

Figure 8: Hematolymphoid monocytic cells; these cells are positive for CD 56 in immunohistochemical stain (blue arrow).

The clinical manifestations of CMML are nonspecific, such as recurrent infection, excessive fatigue, dyspnea, petechiae and hemorrhage. CMML symptoms usually result from bone marrow suppression or disease-related complications. Splenomegaly is present in up to 25% of patients with CMML [3], and symptoms related to splenomegaly can occur (e.g. early satiety and abdominal fullness). The most common intrathoracic leukemic manifestation in all types of leukemia is lymphadenopathy [4]. Leukemia can involve lung tissue, pleura and the heart. Leukemic pulmonary infiltration is defined as extravascular collections of leukemic cells in the lung parenchyma without another apparent cause (e.g. infection, hemorrhage or venous congestion) [5]. It usually occurs in the terminal stage of the disease but can also present in different stages of the disease, especially prior to diagnosis.

Pulmonary manifestations of leukemia should be carefully assessed to distinguish different causes that can impact the management plan [6]. Some autopsy studies have shown leukemic pulmonary infiltration in >25% of patients with leukemia [7]. It manifests as a rapid decline in respiratory status, and the peripheral WBC count is usually >100 000. Distinguishing among infection, pulmonary edema and leukemic infiltrate can be challenging. Reports of computed tomography imaging of leukemic infiltrates have described different radiological patterns, but in general, leukemic cells have the tendency to involve the perilymphatic interstitium, producing smooth or nodular thickening of the bronchovascular bundles and interlobular septa [8]. Other radiological patterns include nodular disease, which can be random, centrilobular or prelymphatic [9]. Additionally, ground-glass opacities and air-space consolidation have been described [8–9].

In addition, computed tomography findings are usually not very specific, but the diagnosis can be made after ruling out other disease processes. Bronchoscopy and bronchoalveolar lavage are usually recommended to rule out bleeding and infection. An accurate diagnosis might require lung biopsy.

The most striking finding in this case was interstitial thickening that involved both the central and peripheral interstitia. In this particular case, the treatment options were limited; however, early intervention with chemotherapy if the condition is diagnosed early can result in a rapid clinical response.

The differential diagnosis of pulmonary infiltrates in leukemia can include pulmonary infections, alveolar hemorrhage, pulmonary edema, induced pneumonitis and leukostasis.

Pulmonary leukemic infiltrate should be considered in all types of leukemia [10] but with stronger consideration during the pretreatment of leukemia or the terminal stage of the disease [6], when there is a progressive decline in respiratory status despite antibiotic therapy, bilateral interstitial infiltrates on imaging and laboratories showing high WBC counts with blasts accounting for >40% of the cells in the peripheral blood.

In conclusion, recognizing the diverse computed tomography patterns of pulmonary leukemic infiltration is paramount for selecting the appropriate therapy. This case represents a characteristic presentation of leukemic infiltrate in CMML that is similar to that in other types of leukemia.

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CONFLICT OF INTEREST STATEMENT

Dr Fayed disclosed no relevant relationships regarding the content of this article. In terms of activities not related to the present article, Dr Fayed is a speaker for Insmed Inc.

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ETHICS APPROVAL

Written consent was obtained from the family of the patient. None of the pictures had any content that could be used to identify the patient.

CONSENT

Written consent for the limited lung autopsy was obtained from the patient's next of kin.

GUARANTOR

Mohamed Fayed is the guarantor of this article.

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