

Laboratory divergences in concurrent diagnosis of acute myeloid leukemia relapse and COVID-19: A case report

Dear Editors,

Although acute myeloid leukemias (AML) are well known and are not rarely reported, in time of coronavirus disease 2019 (COVID-19) pandemic, diagnosis, follow-up, and care of patients with AML can become a huge challenge for clinicians and clinical laboratory specialists, due to a lack of experience and the presence of divergences in both clinical examination and laboratory results.

A 61-year-old patient in complete remission for 6 years for an AML with maturation diagnosed with trisomy 8 and treated by allogeneic stem cell transplantation (SCT), was admitted in the emergency department for a flu syndrome with productive cough, headaches, anosmia, and ageusia.

At the admission, physical examination showed only a mild hypoventilation. Chest computed-tomography (CT) scan revealed no abnormalities suggestive of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Nasopharyngeal swab was realized for SARS-CoV-2 polymerase chain reaction (PCR) detection and bone marrow (BM) aspirate was performed due to the patient's AML history.

Laboratory tests indicated an inflammatory syndrome (C-reactive protein 30.5 mg/L), a pancytopenia (hemoglobin 10.9 g/dL, white blood cells count 1.13×10^9 cells/L, and platelets count 66×10^9 cells/L), and the presence of multiple plasma cells (5.5%) and activated lymphocytes (4.5%) in the peripheral blood smear (Figure 1).

The BM aspirate smear revealed a fibrous marrow with a mild lymphocytosis (23%) characterized by the presence of few activated lymphocytes and some plasma cells (approximately 5%), both were also previously noticed in the peripheral blood sample. Otherwise, a large blast population (approximately 24%) was visualized in the BM but was not found in peripheral blood smear (Figure 2). Flow cytometry immunophenotypic analysis identified the presence of 5% myeloblasts, with weak CD45, HLA-DR, CD34, CD117, strong CD33, weak CD11c, weak CD15, and CD13 expression confirming the increased blast population seen in BM aspirate smear and the probable relapse of AML.

SARS-CoV-2 PCR detected the presence of the virus in the nasopharyngeal swab of the patient and confirmed the COVID-19 disease, despite negative chest CT scan and absence of severe respiratory symptoms.

Morphological anomalies of circulating blood cells in COVID-19 patients were already reported and could be caused by cytokine storm and inflammatory syndrome, two pathogenic factors of the SARS-CoV-2 infection.¹⁻³ In this case, presence of plasma cells and activated lymphocytes in both peripheral blood and BM smear samples highlighted the reactive state caused by the SARS-CoV-2 infection while the homogeneous blast population only found in the BM sample showed the probable relapse of AML.

AML relapse of the patient was confirmed by the cytogenetic analysis. Indeed, the majority of mitoses analyzed in the BM sample

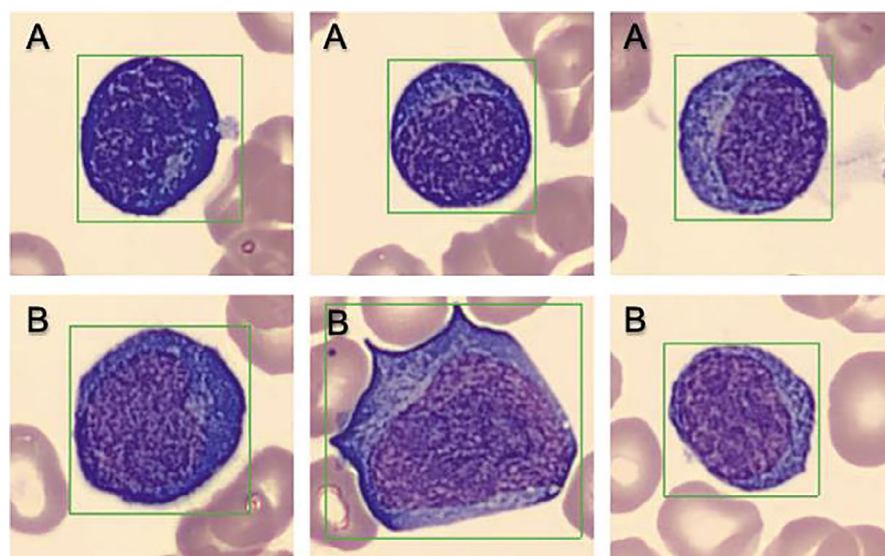


FIGURE 1 Plasma cells (A) and activated lymphocytes (B) found in the peripheral blood smear (50 \times) at the admission of the patient

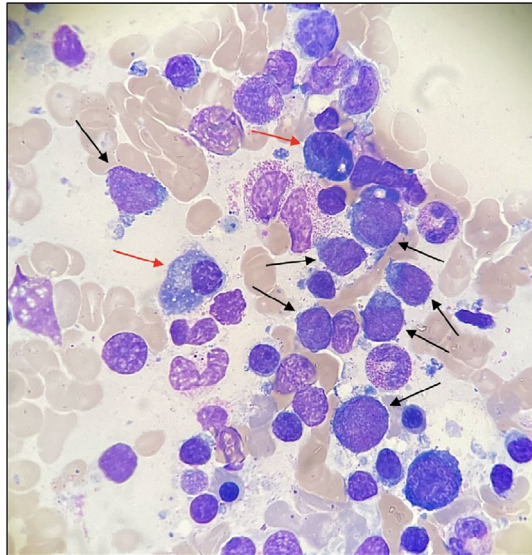


FIGURE 2 Bone marrow aspirate smear (100x) showing the blast population (black arrow) and some plasma cells (red arrow) at the admission of the patient

presented with trisomy 8, identical to the tumor clone present at the time of diagnosis, 6 years earlier.

Concurrent diagnosis of COVID-19 and AML relapse involved an unconventional care by treating two potentially life-threatening diseases at the same time. Recommendations suggested a delayed therapy for the AML in order to provide appropriate care of the SARS-CoV-2 infection and the healing of the disease.⁴ If possible, negative SARS-CoV-2 PCR was required prior to start the induction treatment of AML.⁵⁻⁸ However, the management of COVID-19 leukemia patients must be done case-by-case by the hematologists in collaboration with pneumologists and intensivists.

In this case, the patient was treated by Remdesivir for five days as recommended by the National Institute Health (NIH) USA guidelines and AML therapy was delayed until a negative SARS-CoV-2 PCR. Four weeks later, BM aspirate smear revealed a fibrous and hypocellular marrow with elevated lymphocytosis (40.3%), few plasma cells (2.3%) and an increased blastosis (27%). Flow cytometry immunophenotypic analysis identified 6.5% myeloblasts with weak CD45, HLA-DR, CD34, CD117, strong CD33, and weak CD11c. Peripheral blood smear showed 3% blasts proving the evolution of AML and its blood infiltration. Finally, the patient was treated by a second allogeneic SCT two months after the diagnosis of the AML relapse.

In conclusion, simultaneous diagnosis of COVID-19 and hematological malignancies represent an important and a critical challenge for clinicians and clinical laboratory specialists to provide to the patient a right diagnosis, an appropriate care, and an adequate treatment.

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None.

CONFLICT OF INTEREST

The authors have no competing interests.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

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REFERENCES

1. Zini G, Bellesi S, Ramundo F, D'Onofrio G. Morphological anomalies of circulating blood cells in COVID-19. *Am J Hematol*. 2020;95:870-872. <https://doi.org/10.1002/ajh.25824>
2. Sadigh S, Massoth LR, Christensen BB, Stefely JA, Keefe J, Sohani AR. Peripheral blood morphologic findings in patients with COVID-19. *Int J Lab Hematol*. 2020;42:e248-e251. <https://doi.org/10.1111/ijlh.13300>
3. Foldes D, Hinton R, Arami S, Bain BJ. Plasmacytoid lymphocytes in SARS-CoV-2 infection (Covid-19). *Am J Hematol*. 2020;95:861-862. <https://doi.org/10.1002/ajh.25834>
4. Ljungman P, Mikulska M, de la Camara R, et al. The challenge of COVID-19 and hematopoietic cell transplantation. EBMT recommendations for management of hematopoietic cell transplant recipients, their donors, and patients undergoing CAR T-cell therapy. *Bone Marrow Transplant*. 2020;55:2071-2076. <https://doi.org/10.1038/s41409-020-0919-0>
5. Khan AM, Ajmal Z, Raval M, Tobin E. Concurrent diagnosis of acute myeloid leukemia and COVID-19: a management challenge. *Cureus*. 2020;12:4-5. <https://doi.org/10.7759/cureus.9629>
6. Paul S, Rausch CR, Jain N, et al. Treating leukemia in the time of COVID-19. *Acta Haematol*. 2020;77030. <https://doi.org/10.1159/000508199>
7. Ferrara F, Zappasodi P, Roncoroni E, Borlenghi E, Rossi G. Impact of Covid-19 on the treatment of acute myeloid leukemia. *Leukemia*. 2020;34:2254-2256. <https://doi.org/10.1038/s41375-020-0925-7>
8. Malard F, Genthon A, Brissot E, et al. COVID-19 outcomes in patients with hematologic disease. *Bone Marrow Transplant*. 2020;55:2180-2184. <https://doi.org/10.1038/s41409-020-0931-4>