Medical Laboratory Journal
Online ISSN: 2538-4449
Golestan University of Medical Sciences

Case Report

Hypoplastic Acute Myeloid Leukemia in a COVID-19 Patient: A Diagnostic Dilemma

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Received: 2022/05/11
Revised: 2022/10/02
Accepted: 2022/10/10

DOI: 10.29252/mlj.16.6.45

ABSTRACT

Hypocellular acute myeloid leukemia (AML) is an infrequent and challenging entity, and superinfection with coronavirus disease 2019 (COVID-19) could further complicate its diagnosis and management. It is characterized by low bone marrow cellularity, prominent cytopenias, and in many cases, clinically simulate aplastic anemia and hypoplastic myelodysplastic syndrome. We report a case of hypocellular AML-M2 in a 65-year-old male who was found to be COVID-19-positive. The cause of hypoplasia of bone marrow in such cases is still ambiguous and could be due to infiltration by blasts or co-infections. The cause of hypoplasia must be determined for proper management, which requires analysis of more such cases.

Keywords: Leukemia, Myeloid, Acute , COVID-19 , Radiation .

INTRODUCTION

Hypoplastic acute myeloid leukemia (AML) is an infrequent entity that constitutes 5-12% of all cases of AML (1). It usually develops secondary to radiation or chemotherapy (2). Hypoplastic AML is a diagnostic and therapeutic challenge as it closely mimics aplastic anemia and at times remains undiagnosed for a long time. Coronavirus disease 2019 (COVID-19) causes immunosuppression and introducing anti-cancer and immunosuppressant drugs for the treatment of acute leukemia can further deteriorate the clinical condition. Thus, proper risk-benefit ratio assessment is a must for the appropriate management of |COVID-19 patients with AML.

Here, we present a case of de novo hypoplastic AML that was incidentally diagnosed with COVID-19. This case report highlights that superinfection with COVID-19 in hematological malignancies further complicates diagnostic and therapeutic management.

CASE PRESENTATION

A 65-year-old male patient presented with complaints of mild to moderate, intermittent fever along with dry cough and generalized weakness for 15 days. He also complained of progressive dyspnea for 15 days. His past medical record was mostly uneventful except for two episodes of blood transfusion done for severe anemia. Pallor and mild hepatosplenomegaly were present on examination. Real-time PCR from nasopharyngeal swab was positive for COVID-19. A complete blood count was performed by using a fully automated hematology analyzer (Siemens Advia 2120i, Germany), and a peripheral blood smear was also prepared and microscopically studied (Table 1).

Table 1- Hematological parameters of the patient

Hematological parameters	Values
Hemoglobin	7.4 gm%
Total leukocyte count	4,230/cumm
Differential leukocyte count	Neutrophil: 62% Lymphocyte: 30% Monocyte: 6% Eosinophil: 2%
Platelet count	65,000/cumm

Peripheral blood smear revealed atypical cells and microcytic hypochromic red blood cells with pencil cells and a few teardrop cells. The COVID-19 severity score was determined as 12/25 per chest computed tomography. Liver function tests including alanine transaminase and aspartate aminotransferase were within normal limits with reversed A:G ratio of 0.7:1. Renal function tests were normal. Serum iron and ferritin were 65 µg/dl and 320 ng/ml, respectively, with a transferrin saturation of 34%. Ultrasound abdomen showed an enlarged liver (14.2 cm) with normal echotexture, and the spleen was also mildly enlarged (12.4 cm). Bone marrow aspiration with biopsy was performed. Bone marrow aspirate showed a hypocellular marrow with suppression of trilineage hematopoiesis along with 16% blasts (Figures 1 and 2).

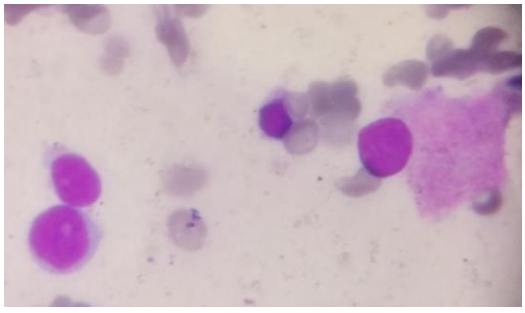

Figure 1- Bone marrow aspirate showing infiltration by blasts (Leishman stain, 100X magnification).

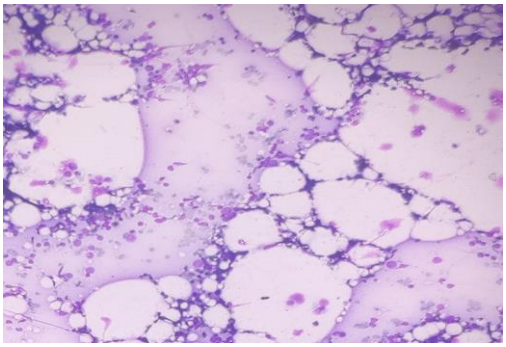

Figure 2- Bone marrow aspirate showing infiltration of blasts in a hypoplastic marrow represented by increased fat spaces (Leishman stain, 40X mganification)

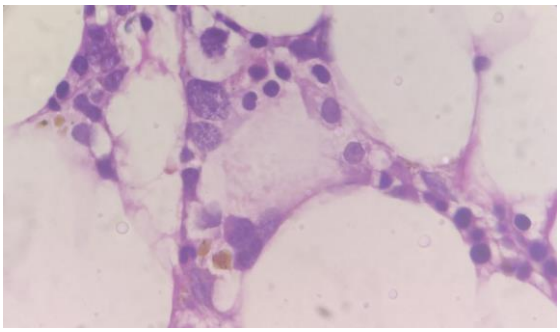

Figure 3- Bone marrow biopsy showing infiltration of blasts in a hypoplastic marrow (hematoxylin and eosin staining, 100X magnification)

Bone marrow imprint and biopsy showed a hypoplastic marrow with infiltration with blasts suggesting acute leukemia (Figure 3). Flow cytometry (BD FACS Canto II) on bone marrow aspirate showed 28% of cells to be expressing dim CD45 with HLA-DR, CD13, CD33, and cytoplasmic MPO expression, favoring AML-M2 subtype (Figures 4 and 5). Treatment for AML was started with a standard chemotherapy regimen, but the patient's condition deteriorated and he succumbed to his illness.

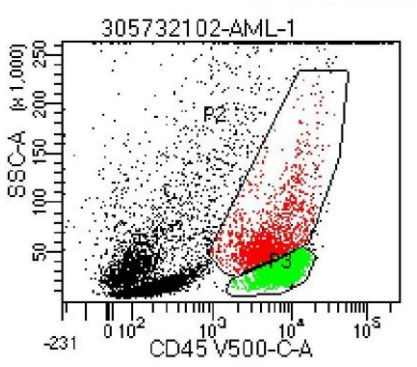

Figure 4- Flow cytometry results with SSC and CD45 showing dim CD45 blasts

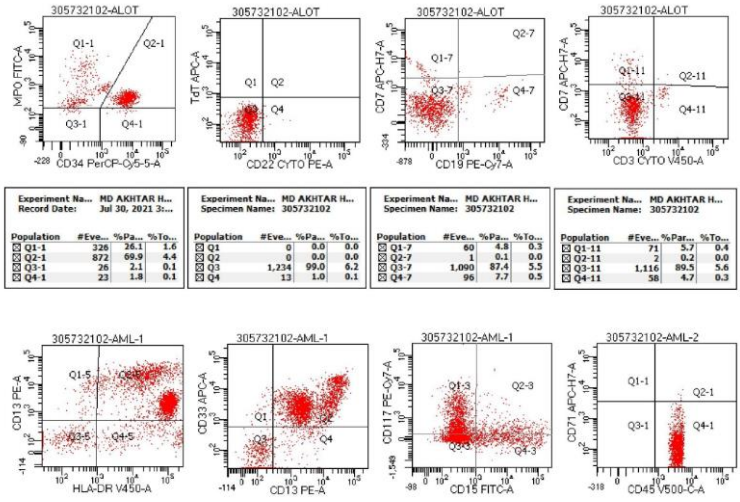

Figure 5- Flow cytometry results showing HLA-DR, CD13, CD33, and c-MPO positive scatter plots

DISCUSSION

Hypoplastic AML is a big challenge both for hematopathologists and treating physicians as it is extremely difficult to differentiate between hypoplastic AML and hypoplastic myelodysplastic syndrome or aplastic anemia(3). The pathogenesis of hypocellularity in acute leukemia is still debatable. It is not clear whether leukemia is secondary to hypocellularity or the primary event. It has been suggested that leukemic cells inhibit myelopoiesis through a humoral mechanism (4). In our case, COVID -19 superinfection added to the ambiguity in the development of hypoplasia.

Acute leukemias are usually present with hypercellular bone marrow. However, less than 10% of the cases may have hypocellular bone marrow. Hypocellular acute leukemia is currently defined as acute leukemia with a bone marrow cellularity ≤20%, although in some reports, cellularity less than 40 % is considered to be hypocellular (5). Nagai et al. proposed pancytopenia with a rare appearance of blasts in peripheral blood, <40% bone marrow cellularity, >30% blasts in the bone marrow of all nucleated cells, and myeloid phenotype of leukemic blasts by MPO staining as the diagnostic criteria for hypoplastic AML (6).

Hypocellular AML is more common than hypoplastic acute lymphoblastic leukemia (ALL) (7,8). It mostly occurs in adults and is secondary to radiation or chemotherapy (9). By contrast, hypocellular ALL occurs predominantly in children and constitutes 2-3% of childhood ALL (10). Hypoplastic acute leukemia should be differentiated from hypoplastic myelodysplastic syndrome (MDS) and aplastic anemia, as these also have peripheral cytopenias and bone marrow hypocellularity. In addition, hypoplastic MDS cases may not have very evident dysplastic features because of low cellularity, making its diagnosis extremely challenging. Clinical parameters such as duration of symptoms, history of the antecedent hematologic disorder, or prior chemotherapy or radiotherapy aid the diagnosis (11,12).

No significant difference in the cytogenetic abnormalities between patients with hypocellular AML and those with non-hypocellular AML has been reported. However, molecular studies show a lower frequency of *RAS* and *FLT3* mutations in patients with hypocellular AML similar to patients with MDS (13). Overall survival, remission duration, and event-free survival have been reported to be comparable to that of non-hypocellular AML. Therefore treatment options are similar to that of non-hypocellular AML (14).

Some researchers have tested the serum of patients with hypoplastic acute leukemia and shown the inhibitory role of leukemic blasts on normal hematopoiesis. The inhibitory substances identified include leukemia inhibitor factor, stem cell inhibitor factor, tumor necrosis factor, prostaglandin E, and decreased or aberrant stimulatory factors such as granulocyte colony-stimulating factor

(15,16). Hypoplastic acute leukemia is usually secondary in nature and mostly develops after an antecedent hematologic malignancy, such as MDS, primary myelofibrosis, or radiation or chemotherapy (17,18). In a series of 123 patients, nearly half the cases of hypocellular AML were composed of secondary AML, either with an antecedent hematologic disorder or prior history of chemotherapy or radiotherapy (19-21).

CONCLUSION

To summarize, hypoplastic acute leukemia is a challenging entity characterized by low bone marrow cellularity, prominent cytopenias, and in many cases, clinically simulate AA and hypoplastic MDS. It is important to differentiate these conditions as treatment modalities differ. The disease usually has an indolent course and commonly achieves a good response to remission induction therapy. Despite the low incidence of hypoplastic acute leukemia, it should be considered in the case of hypocellular bone marrows to avoid misdiagnosis and mismanagement. A comprehensive multiparametric diagnostic approach including clinical features, morphology, cytochemistry, immunophenotyping, and genetic analysis is essential for its diagnosis. Our case report also highlights the therapeutic challenge of treating a hematological malignancy during the COVID-19 pandemic. Superinfection with COVID-19 in patients with hematological malignancies further complicates diagnostic and therapeutic management.

ACKNOWLEDGMENTS

None.

DECLARATIONS

FUNDING

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethics approvals and consent to participate

Informed consent was taken from the patient after ensuring him that his personal information will remain confidential.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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How to Cite:
Jamal I, Shuchismita, Choudhary V [Hypoplastic Acute Myeloid Leukemia in a COVID-19 Patient: A Diagnostic Dilemma]. mljgoums. 2022; 16(6): 45-50 DOI: 10.29252/mlj.16.6.45