Cross Current International Journal of Medical and Biosciences
Abbreviated Key Title: Cross Current Int J Med Biosci
ISSN: 2663-2446 (Print) & Open Access
DOI: https://doi.org/10.36344/ccijmb.2025.v07i02.001

Volume-7 | Issue-2 | Mar-Apr, 2025 |

Case Report

Diagnostic Evaluation and Evolution of Persistent Cytopenias: A Case Report

Laatiris, H[1*], El Faridi, A[1], ELatife, H[2], Baidada, I[1], Zahid, H[1], Essahli, K[1]
[1]Hematology and Immuno-Hematology Laboratory, Mohammed V Military Teaching Hospital, Faculty of Medicine and Pharmacy Mohammed V University of Rabat, Morocco
[2]Clinical Hematology Service, Mohammed V Military Teaching Hospital, Faculty of Medicine and Pharmacy Mohammed V University of Rabat, Morocco

***Corresponding author:** Laatiris, H

| **Received:** 24.01.2025 | **Accepted:** 01.03.2025 | **Published:** 08.03.2025 |

Abstract: Persistent cytopenias, defined by a prolonged decrease in blood cells, are common clinical signs in various malignant hematological disorders, such as myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). Diagnosis relies on a thorough evaluation, including biological tests, notably bone marrow analysis, and sometimes genetic and molecular tests. Treatment of these conditions includes azacitidine and venetoclax, whose combined effectiveness has shown promising results, although side effects such as neutropenia require careful management. This article presents a case of AML treated with this combination, with continuous evaluation of disease progression, genetic mutations, and treatment resistance.

Keywords: Persistent cytopenias, Genetic mutations, immunophenotyping.

INTRODUCTION

Persistent cytopenias, characterized by a prolonged decrease in the number of blood cells (red blood cells, white blood cells, platelets), are common clinical signs in various malignant hematological disorders. The persistence of these abnormalities can indicate underlying severe diseases such as myelodysplastic syndromes (MDS), acute myeloid leukemia (AML), or other malignant bone marrow conditions. The diagnosis of persistent cytopenias relies on a comprehensive evaluation that includes biological tests, bone marrow analysis, and sometimes genetic testing [1].

This article explores the diagnostic evaluation of persistent cytopenias and examines the role of azacitidine and venetoclax in the treatment of these conditions, as well as their impact on disease progression.

OBSERVATION

The patient, aged 68, is followed for several conditions. He has hypertension (HTN) treated for one year and a history of unstable angina in 2016 and 2022, requiring angioplasty and stent placement. He also has idiopathic agranulocytosis and femoral head osteonecrosis. He is currently admitted for febrile neutropenia.

The complete blood count shows hemoglobin at 13.3 g/dl, platelet count of 76 x10³/µL, and leukocytes at 3.1x10³/µL, including 0.84 x10³/µL of neutrophils, 1.12 x10³/µL of lymphocytes, 0.03 x10³/µL of monocytes, and 36% circulating blasts (Figure 1). The blasts are medium to large in size, with a high nuclear-to-cytoplasmic ratio, a round or oval nucleus sometimes indented with loose chromatin, occasionally nucleolated, and basophilic cytoplasm, sometimes granular and rarely vacuolated.

Quick Response Code

Journal homepage:
https://www.easpublisher.com/

Citation: Laatiris, H, El Faridi, A, ELatife, H, Baidada, I, Zahid, H, Essahli, K (2025). Diagnostic Evaluation and Evolution of Persistent Cytopenias: A Case Report. *Cross Current Int J Med Biosci, 7*(2), 5-8.

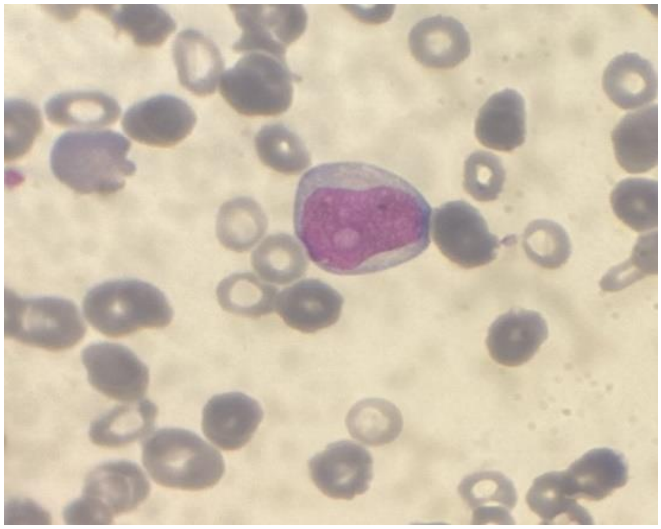

Figure 1: Presence of blasts with loose chromatin, occasionally nucleolated, and basophilic cytoplasm, sometimes granular and rarely vacuolated, in the blood smear (Gx1000)

The hemostasis assessment reveals a prothrombin time (PT) of 78%, an activated partial thromboplastin time (aPTT) ratio of 0.8, and a fibrinogen level of 4.5 g/L. The bone marrow aspirate shows 66% blast cells, strongly resembling the circulating blasts in the blood (Figure 2). Additionally, the eosinophil count is 11%, including precursors and dystrophic mature forms. The myeloperoxidase reaction on bone marrow smears is positive (Figure 3).

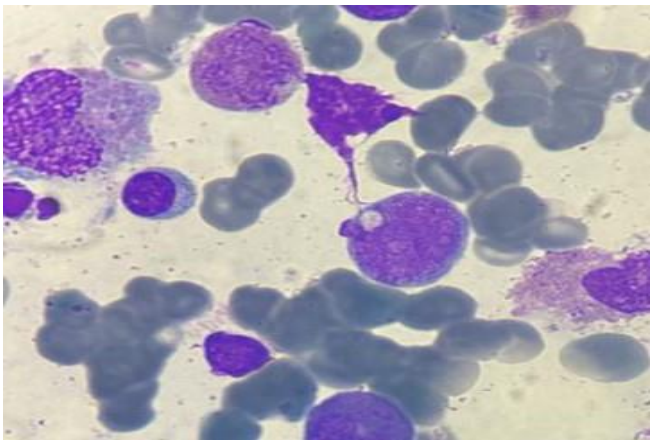

Figure 2: Presence of blasts with loose chromatin, occasionally nucleolated, and basophilic cytoplasm, sometimes granular and rarely vacuolated, in the bone marrow aspirate (Gx1000)

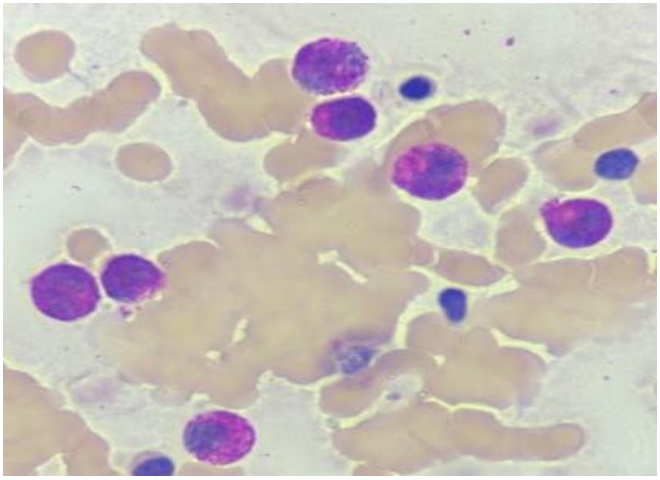

Figure 3: Bone Marrow Aspirate + Myeloperoxidase Reaction: Positive on bone marrow blasts (Gx1000)

The bone marrow immunophenotyping shows an immature myeloid population representing 32% of the cells, expressing the markers CD45, MPO+, CD34+, Tdt+, CD117+, CD13+, CD33+, HLA- and DR-. The lymphocytic (B and T) and monocytic markers are negative. This immunological profile is consistent with AML1. The bone marrow karyotype is normal, which is favorable for prognosis.

The investigation led to the diagnosis of acute myeloblastic leukemia (AML), non-hyperleukocytic and non-tumoral, without signs of Disseminated Intravascular Coagulation (DIC) or tumor lysis syndrome. Genetic sequencing of the WT1 gene reveals intermediate-risk AML.

The patient is undergoing combined AZA-VEN therapy (Azacitidine and Venetoclax). After the first cycle, an evaluation shows grade IV neutropenia, managed with GCSF (Granulocyte Colony-Stimulating Factor), as well as dysuria and diarrhea. The patient is stable hemodynamically and respiratorily, afebrile, with no signs of hemorrhagic syndrome.

Upon re-evaluation of the therapeutic response, hemoglobin is 10.4 g/dl, platelet count is 35 x10³/µL, and leukocytes are 1.5 x10³/µL, including 0.12 x10³/µL neutrophils, 1.33 x10³/µL lymphocytes, 0.01 x10³/µL eosinophils, and 1% (0.01 x10³/µL) circulating blasts. The bone marrow aspirate shows 24% blast cells. Additionally, the eosinophil count has risen to 48%, composed of precursors and mature forms. The bone marrow karyotype shows an inv16, a genetic abnormality frequently associated with relapse risk in certain types of AML. The patient is currently in relapse after his 7th cycle of AZA-Venetoclax.

DISCUSSION

Cytopenias are frequently found in geriatrics, particularly anemia, which may or may not be associated with neutropenia and/or thrombocytopenia. Given the aging population in Western countries, the prevalence of blood cytopenias is steadily increasing, affecting the myeloid lineages (anemia, neutropenia, thrombocytopenia), as well as the lymphoid lineages (lymphopenia). In particular, the prevalence of anemia, the most common cytopenia, rapidly increases in patients over the age of 75, exacerbated by institutionalization and low socio-economic status. The clinical impact of cytopenias largely depends on whether they are isolated or not, their progressive or sudden onset, their severity, and the many comorbidities present in elderly patients. It is well established that anemia has a recognized impact on quality of life, increasing mortality and morbidity risks [2, 3], making it a true public health issue. Poorly tolerated anemia can be a life-threatening emergency requiring immediate red blood cell transfusions. Although the diagnostic approach for elderly patients is not fundamentally different from that applied to younger individuals for each type of cytopenia [4], the frequency of etiologies and certain alert thresholds differ, which medical biologists must be well aware of [5].

When cytopenias persist despite supportive treatment or the absence of an obvious cause, a bone marrow aspiration and biopsy are necessary. This examination assesses bone marrow function and searches for potential specific abnormalities, such as immature blasts in leukemia or dysplasias in MDS. Additionally, molecular biology tests (such as testing for JAK2 mutations) are essential for refining the diagnosis and adapting treatment [6].

These non-intensive therapies have allowed for temporary disease control with an acceptable quality of life, but the outlook remains poor, with an expected overall survival (OS) of ≤ 12 months. Routine biological tests, such as complete blood count (CBC), allow assessment of the severity of cytopenias and help guide the diagnosis toward specific causes such as nutritional deficiencies, autoimmune disorders, or malignant bone marrow diseases. Complementary tests, such as the search for autoantibodies or viral infections, can be conducted to evaluate other potential etiologies [4-7].

It is essential to monitor the evolution of genetic mutations, particularly treatment resistance. For instance, the TP53 mutation is associated with a weaker response to azacitidine and rapid progression to acute myeloid leukemia [3]. However, genetic testing is costly, and its systematic use to assess mutations in response to treatment is still under development. This can make biological monitoring difficult, as the presence of residual malignant cells may be low or difficult to detect with standard tests, making early detection of disease progression problematic. The use of flow cytometry techniques and molecular biology tests such as next-generation sequencing (NGS) panels on bone marrow or blood samples can help track mutation evolution during treatment. This approach allows for rapid detection of signs of progression or resistance to azacitidine and venetoclax [8].

The diagnostic biological challenges associated with persistent cytopenias are numerous and complex. They include difficulties in establishing an accurate diagnosis, identifying the underlying cause of cytopenias, and differentiating between various bone marrow disorders (such as myelodysplastic syndromes and acute myeloid leukemias). These challenges are amplified by the treatments administered, such as azacitidine and venetoclax, which can alter biological results and make diagnosis more difficult.

CONCLUSION

The treatment of persistent cytopenias, particularly in the context of acute myeloid leukemia and myelodysplastic syndromes, requires rigorous diagnostic and therapeutic management. Monitoring genetic mutations remains a major challenge. Disease

progression, especially in cases of treatment resistance, must be closely followed using advanced techniques such as flow cytometry and genetic sequencing to ensure optimal therapeutic response and early detection of relapses.

REFERENCES

1. Steensma, D. P., & Stone, R. M. (2020). Myelodysplastic Syndromes. In Abeloff's Clinical Oncology 2020 Jan 1 (pp. 1798-1820). Elsevier.
2. Culleton, B. F., Manns, B. J., Zhang, J., Tonelli, M., Klarenbach, S., & Hemmelgarn, B. R. (2006). Impact of anemia on hospitalization and mortality in older adults. *Blood*, *107*(10), 3841-3846.
3. Steensma, P., & Tefferi, A. (2007). Anemia in the elderly: how should we define it, when does it matter, and what can be done? *Mayo Clin Proc*, 82, 958-966.
4. Société Française d'Hématologie. In Hématologie, 2e ed., Coll. Les référentiels des Collèges, Elsevier-Masson, Issy-les-Moulineaux, 2014.
5. Guralnik, J. M., Ershler, W. B., Schrier, S. L., & Picozzi, V. J. (2005). Anemia in the elderly: a public health crisis. In American Society of Hematology Education program book, 2005, Berliner N, Lee SJ, Linenberger M, Vogelsang GB, Ed., Washington DC, 528-532.
6. Urabe, A., Chi, S., & Minami, Y. (2023). The Immuno-Oncology and Genomic Aspects of DNA-Hypomethylating Therapeutics in Acute Myeloid Leukemia. *International Journal of Molecular Sciences*, *24*(4), 3727.
7. Chaves, P. H., Xue, Q. L., Guralnik, J. M., Ferrucci, L., Volpato, S., & Fried, L. P. (2004). What constitutes normal hemoglobin concentration in community-dwelling disabled older women?. *Journal of the American Geriatrics Society*, *52*(11), 1811-1816.
8. DiNardo, C. D., Jonas, B. A., Pullarkat, V., Thirman, M. J., Garcia, J. S., Wei, A. H., ... & Pratz, K. W. (2020). Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *New England journal of medicine*, *383*(7), 617-629.