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Case Report

Autoimmune hemolytic anemia as initial presentation of acute myeloid leukemia

Alpika Shukla[1]*, Shailendra Prasad Verma[1], Swasti Sinha[1]

[1] *Dept. of Clinical Haematology & BMT, King George's Medical University, Lucknow, Uttar Pradesh, India*

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ABSTRACT

Hematological malignancies developing in autoimmune disorders have been reported in very few cases. Here, we describe a case where autoimmune hemolytic anemia (AIHA) was the initial manifestation of acute myeloid leukemia (AML). The patient presented with autoimmune hemolytic anemia that was unresponsive to multiple lines of treatments, and an initial bone marrow aspiration and biopsy revealed megaloblastic erythroid hyperplasia. The later emergence of blasts in peripheral blood confirmed the diagnosis of AML. This case underscores that AIHA can be an early presentation of acute myeloid leukemia.

1. Introduction

Autoimmune hemolytic anemia (AIHA) can arise due to several factors, including autoimmune diseases, lymphoproliferative disorders such as chronic lymphocytic leukemia (CLL), and certain medications, though it is most often idiopathic.[1] The clinical presentation of AIHA typically involves reduced hemoglobin, elevated reticulocyte counts, a positive direct Coombs test, and the appearance of spherocytes or red blood cell aggregates on a blood smear.[2] Treatments for AIHA commonly include steroids, intravenous immunoglobulin (IVIG), and anti-CD20 monoclonal antibodies.[2,3] Cases of AIHA have been noted during alpha-interferon treatment in patients with chronic myeloid leukemia (CML) or other blood disorders. Additionally, AIHA is a known but relatively uncommon complication following hematopoietic stem cell transplantation, occurring in approximately 6% of pediatric cases and 3% of adult cases.[1]

While there are limited case reports of AIHA presenting as an early symptom of CML[4] or acute leukemias,[5,6] this report presents an unusual and challenging case of acute myeloid leukemia (AML) initially appearing as AIHA based on clinical and bone marrow findings. AIHA that resists standard treatments may indicate an underlying hematologic malignancy, such as AML, which may become more apparent as treatment progresses.

In this case report we present acute myeloid leukemia debuting as autoimmune hemolytic anemia refractory to treatment.

2. Case Presentation

A sixty four year old male presented with history of marked generalized weakness, lethargy and multiple blood transfusion for last 4 month. Patient had no history of bleeding from any site, chronic pain killer use, oral ulcers, joint pain, joint swelling, stiffness of hands. Complete blood count at presentation showed haemoglobin -5.8g/dl total leucocyte count-29100/cumm and platelet count-65000/cumm.

General blood picture showed marked anisopoikilocytosis with predominant macrocytic cells along with macroovalocytes, 22 nucleated RBC per 100

* *Corresponding author*.
E-mail address: alpika872@gmail.com (A. Shukla).

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WBC, corrected WBC 11400/cumm with no atypical cells. Serum iron-250 ug/dl, Total iron binding capacity (TIBC)-290 ug/dl, Transferrin saturation 86.21%. Serum LDH 1570 U/L, Serum uric acid 6.1mg/dl, Direct coombs test was positive, ANA was found to be negative. He was prescribed tablet prednisolone 1mg/kg body weight but there was no response to treatment and his haemoglobin was 5.5 g/dl after 1 month of treatment .Bone marrow aspirate was hypercellular for age, with no evidence of dysplasia, no atypical cells, corrected retic count 3.68% suggestive of megaloblastic erythroid hyperplasia. Bone marrow biopsy was consistant with finding of megaloblastic erythroid hyperplasia, karyotyping was normal (XY). Patient complete blood count and general blood picture was repeated after ten doses of Injection Vitcofol (Vitamin B12 and folic acid) and it revealed a Hemoglobin of 4.8, Total leucocyte count (TLC) value was 8600 (Differential count N24 L65 M5 E0 B6) and platelet count was 180000cu/mm. Impression was of leucoerythroblastic picture with overwhelming normoblastemia with several giant platelets. Injection Rituximab 375 mg/m2 weekly dosing was started. After four doses of Rituximab in view of decreasing hemoglobin general blood picture was repeated which showed presence of 18% blast with auer rods, following which bone marrow aspiration and biopsy was done which was suggestive of acute myeloid leukemia with myelodysplasia related changes. Flow cytometry was suggestive of following CD markers.

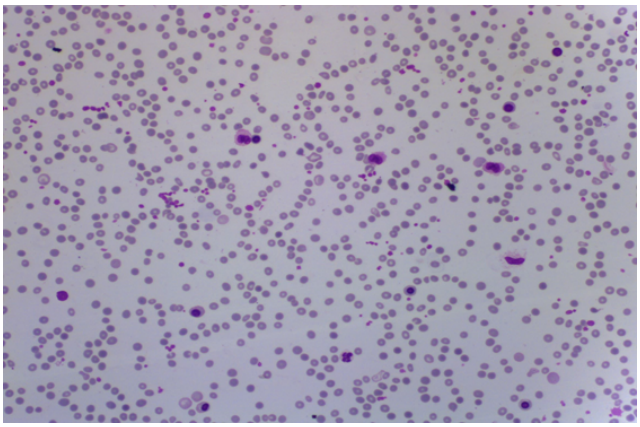

Figure 1: Baseline General blood picture showing marked anisopoikilocytosis with predominant macrocytic cells along with macroovalocytes, with no atypical cells

3. Discussion

We herein present the case of AML developing in a case of autoimmune hemolytic anemia during treatment.[4] Patient was initially treated for hemolytic anemia but despite of therapy there was no improvement. Bone marrow was done which was suggestive of megaloblastic changes and within

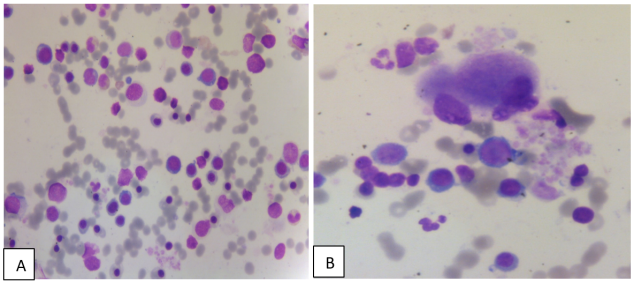

Figure 2: A, B): Bone marrow smears were particulate and hyper cellular. Erythroid precursors are chiefly intermediate and late forms with megaloblastic maturation Lymphocytes are mature in morphology. No atypical cells seen

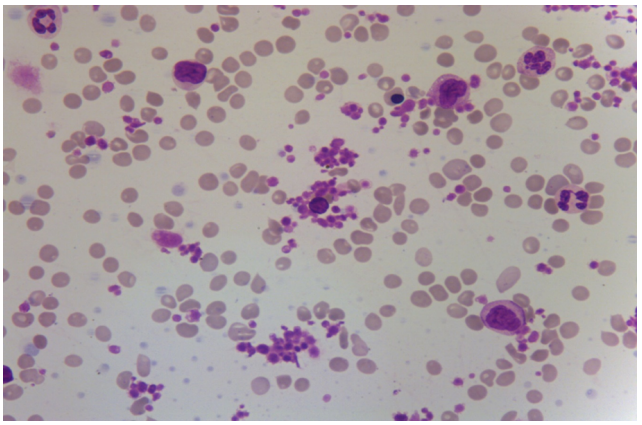

Figure 3: General blood picture after vitamin B12 injection showing leucoerythroblastic picture with overwhelming normoblastemia with several giant platelets

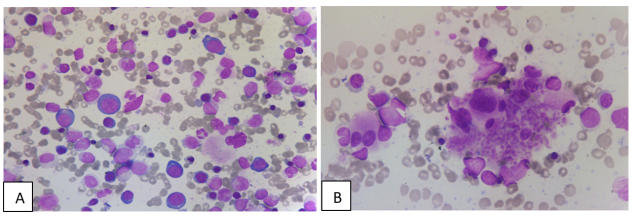

Figure 4: A, B): Bone marrow aspirate showing increased Megakaryocytes with evidence of dysmegakaryopoiesis. Blast cells constitute 30% of all nucleated cells having high nucleocytoplasmic ratio fine chromatin, 1-2 prominent nucleoli and scant amount of basophilic cytoplasm

Table 1:

Marker	Intensity	Interpretation
CD45	Dim	Positive
CD38	Dim	Positive
CD34	Subset	Positive
CD13	Moderate	Positive
CD33	Moderate	Positive
CD117	Moderate	Positive
CD64	Dim	Positive
Cytoplasmic MPO	Subset	Positive

6 month of treatment blasts with auer rods were reported in general blood picture.

Turpin et al.[7] described a case in which acute myeloid leukemia (AML) appeared five years after autoimmune hemolytic anemia (AIHA) was diagnosed. Identifying the cytological source of the AML was challenging; however, distinct membrane structures and intense acid phosphatase activity pointed to a megakaryocytic origin. It is uncertain whether the conditions developed sequentially due to a preexisting immune deficiency or if AML emerged as a result of the autoimmune anemia itself.

Similarly erythroleukemia is challenging to diagnose in its early stages. It often initially presents as hemolytic anemia and typically becomes apparent only once malignant cells appear in peripheral blood.[8] Supporting this, a large Swedish cohort study by Soderberg et al.[9] reported that patients with autoimmune hemolytic anemia (AIHA) had eight fold increased risk of developing Acute myeloid leukemia as compared to general population.

Autoimmune hemolytic anemia (AIHA) is closely associated with a higher likelihood of developing hematologic cancers, particularly myelodysplastic syndromes (MDS), chronic myeloid leukemia (CML), acute myelomonocytic leukemia,[10] and especially acute myeloid leukemia (AML). Several mechanisms may explain this connection:

1. Genetic predisposition: Some genetic mutations[11] or susceptibilities might predispose individuals to both AIHA and hematologic malignancies. This genetic overlap could involve genes that play a role in immune regulation, hematopoiesis (the formation of blood cellular components), or cellular repair processes. When these genes are altered, they may increase susceptibility to both autoimmunity and malignancy within the hematologic system.
2. Impact of autoimmune disease therapies: Many treatments for autoimmune diseases, including immunosuppressive drugs and certain biologic therapies, can have adverse effects on bone marrow health. These treatments, while beneficial in controlling autoimmune symptoms, may inadvertently contribute to genetic mutations or cellular changes within the marrow. Over time, these changes can impair normal hematopoiesis, potentially increasing the risk of hematologic malignancies such as AML.
3. Direct bone marrow damage from AIHA: In some cases, the autoimmune process itself may damage bone marrow tissues. AIHA is characterized by the immune system mistakenly targeting and destroying red blood cells, and in severe or chronic cases, this hyperactive immune response can extend to the bone marrow. This prolonged autoimmune activity may lead to marrow dysfunction, where abnormal cellular changes accumulate and eventually develop into hematologic cancers.
4. Inflammatory microenvironment: Chronic inflammation, common in autoimmune diseases like AIHA,[12] can create an environment conducive to DNA damage and cellular stress. This inflammatory state may increase the likelihood of mutations in blood-forming stem cells, potentially leading to the clonal expansion of abnormal cells—a precursor to conditions like MDS or AML.

These factors together underscore why patients with AIHA need careful monitoring for signs of hematologic malignancies, particularly if they exhibit signs of refractory AIHA (AIHA that does not respond to standard therapies) or new hematologic symptoms. Early detection of any malignancy may allow for a more effective and targeted therapeutic approach.

4. Conclusion

AIHA not responding to treatment should alert treating physician to repeat bone marrow aspiration and biopsy for emergence of malignant cells as autoimmune hemolytic anemia can be one of the initial presentations of a hematological malignancy.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Author's biography

Alpika Shukla, Senior Resident

Shailendra Prasad Verma, Professor and Head

Swasti Sinha, Assistant Professor

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