

Hyperbasophilic Variant of Acute Promyelocytic Leukemia

Preeti Bajaj^{1*}, Rajyaguru Devangana², B. S. Shah³ and Amrinder Kaur⁴

¹Professor and Head, Department of Pathology, Dr. Vasant Rao Pawar Medical College, Hospital and Research Centre, Nashik - 422003, India; dr.prbajaj@gmail.com

²Associate Professor, Department of Pathology, Dr. Vasant Rao Pawar Medical College, Hospital and Research Centre, Nashik - 422003, India

³Former Medical Superintendent and Professor, Department of Pathology, Dayanand Medical College and Hospital, Ludhiana - 141001, Punjab, India

⁴Associate Consultant, Max Superspeciality Hospital, Mohali - 160059, Punjab, India

Abstract

Acute Promyelocytic Leukemia (APL) is an extremely rare variant of acute myeloid leukemia. APL constitutes around 10-15 % of acute myeloid leukemia in adults. It is commonly diagnosed around 40 years age. Molecular/genetic studies exhibit chromosomal translocation between chromosome 15 and chromosome 17-t(15;17)(q22;q21) and PML-RAR α rearrangement. Four variants of APL have been identified: The classic form M₃ hypergranular variant, the microgranular variant, the hyperbasophilic form and zinc-finger form-M_{3,r}, identified by a different chromosomal translocation, between chromosome 11 and chromosome 17:t(11,17) (q23, q11-12).

Keywords: Acute Promyelocytic Leukemia, ATRA, PML/RAR α

1. Introduction

Acute Promyelocytic Leukemia (APL) is a haematological emergency in which patients can have haemorrhagic manifestations and life-threatening coagulopathy¹. APL is a subtype of Acute Myeloid Leukemia (AML) with unique morphological, cytogenetic, molecular and clinical features. APL has a bad clinical course owing to serious haemorrhagic complications related to Disseminated Intravascular Coagulation (DIC) and abnormal fibrinolysis². The majority of M₃ cases fall under the category of Classical M₃ or hypergranular subtype; three other subtypes/variants have been described: Microgranular (M_{3,V}), Hyperbasophilic and PML Zinc Finger/Retinoic Acid Receptor- α (M_{3,r}). The hypergranular or Classical M₃ have folded and lobulated nucleus. Cytoplasm has prominent azurophilic granules. Auer rods are frequent with presence of Faggot cells. The M_{3,V} have irregular folded nuclei and fine small cytoplasmic granules giving a “dusky” appearance to the cytoplasm. Auer rods are rare. The hyperbasophilic APL variant has high nucleo-cytoplasmic ratio. The cytoplasm is strongly

basophilic and shows sparse granules with “cytoplasmic budding” resembling micromegakaryocytes. The PML Zinc Finger form has regular round/ovoid nucleus. The chromatin is condensed and Pelger-like cells are seen³. Auer rods are rare. Faggot cells are absent.

The rapid as well as an accurate diagnosis of APL is of utmost significance because of a characteristic therapeutic approach along with the urgency to initiate the treatment because of life-threatening haemorrhage. In the absence of bundles of Auer rods, hyperbasophilic blebbed cytoplasm and bilobed nuclei may offer a clue to the diagnosis.

2. Case Presentation

A 42 year-old man was admitted to a tertiary care hospital with generalized weakness since 1 week, fever since 5 days and petechial rash since 3 days. On examination, patient was febrile. There was no lymphadenopathy or hepatosplenomegaly. Routine full blood count revealed a white blood cell count of 1.4 \times 10⁹/l, haemoglobin

*Author for Correspondence

concentration of 4.2 gm/dl and platelet count of $48 \times 10^9/l$. There was an increase in Prothrombin time and was reported as 30 sec. Coagulation profile was suggestive of overt Disseminated Intravascular Coagulation (DIC). Peripheral blood smear examination showed presence of few atypical cells. Bone marrow aspiration was done. Bone marrow aspirate revealed hyperbasophilic promyelocytes with prominent cytoplasmic blebs (Figure 1 and 2). Numerous small granules were noted. However, no Auer rods were seen in the aspirate examined. Occasional characteristic bilobed nuclei were seen. The possibility of acute promyelocytic leukemia was kept. Cytochemical staining by Myeloperoxidase (MPO) stain showed strong positivity (Figure 3). Confirmation of diagnosis was done by cytogenetic analysis. Translocation t(15;17) was detected. Hence, based on the available data, the diagnosis of acute promyelocytic leukemia (APL)-hyperbasophilic variant was established.

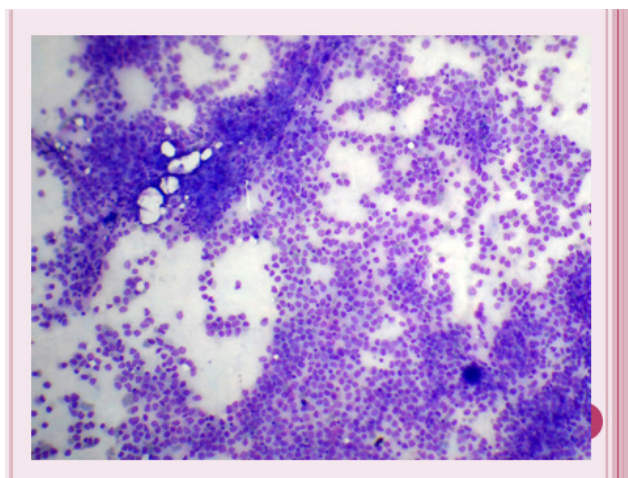


Figure 1. Bone marrow aspirate (10X).

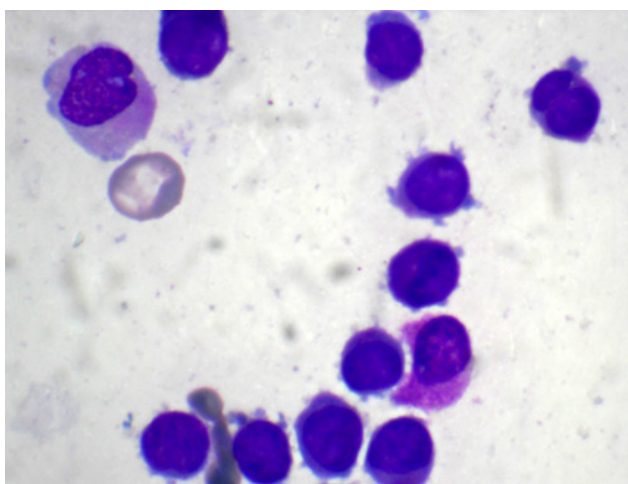


Figure 2. Hyperbasophilic Promyelocytes (100X).

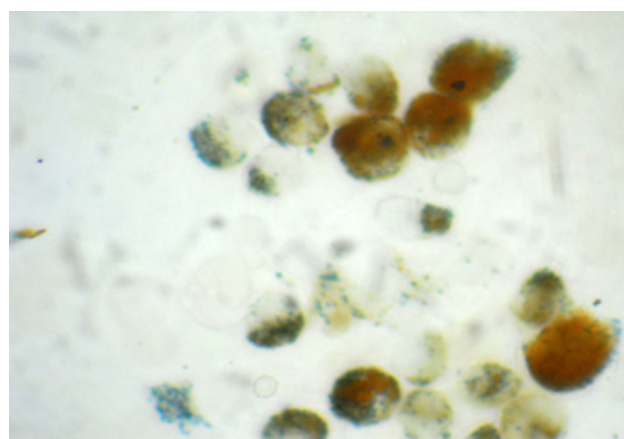


Figure 3. Myeloperoxidase stain (100x).

Cytogenetic studies demonstrated t(15;17) confirming the diagnosis of APL. APL is known for its poor clinical outcome due to serious haemorrhagic syndrome, related to DIC and abnormal fibrinolysis.

3. Discussion

An early and an accurate diagnosis of Acute Promyelocytic Leukaemia (APL) is of extreme importance because of the associated risk of Disseminated Intravascular Coagulation (DIC) that can cause life threatening hemorrhage and the specific response to All-Trans Retinoic Acid (ATRA) therapy. Rapid diagnosis depends mainly on the morphological recognition of this entity². Hyperbasophilic APL is a very rare variant of APL. In the absence of bundles of Auer rods, hyperbasophilic blebbed cytoplasm and bilobed nuclei may be helpful in the diagnosis⁴.

The life threatening bleeding complications, including intracranial hemorrhage, are common during the first two weeks of induction therapy requiring close monitoring and management with products such as fresh frozen plasma and cryoprecipitates⁵.

This case report emphasizes on the significance of morphology and cytogenetic study i.e., chromosomal translocation in the diagnosis of hyperbasophilic variant of APL. Definitive diagnosis of APL can only be established by cytogenetic analysis or molecular genetic studies. But these highly specialized tests take a great deal of time and can be performed in specialized laboratories. Therefore, practically speaking, morphology, cytochemistry and immunophenotyping are still significant tools for diagnosing APL⁶. The t(15;17) chromosomal translocation is the characteristic cytogenetic abnormality in APL. 30-40 % of patients having APL show other chromosomal abnormality; of which trisomy 8 and isochromosome 17

are the most common. There is a negative impact on overall prognosis because of other complex translocations having chromosomal abnormalities. Masked translocations, where pieces of chromosome 15 and 17 are transposed and cannot be detected by routine conventional techniques. The molecular abnormality, either the PML-RAR α or the reciprocal RAR α -PML transcript, can be detected in many of these cases. In the absence of gross chromosomal changes, fusion gene product expression helps in the recognition/diagnosis of APL. Positive results ultimately have an impact on therapy and patient outcome².

4. References

1. Diana C, Vladareanu, et al. Acute promyelocytic leukemia microgranular variant- A clinical and therapeutical approach. *Maedica- A Journal of Clinical Medicine*. 2007; 2(4):327-331.
2. Haslindawani WM, Haslina, et al. A case of hyperbasophilic form of acute promyelocytic leukemia. *Malaysian Journal of Medical Sciences*. 2008 Jan; Supplement:168.
3. Soignet S, Maslak P. Acute promyelocytic leukemia. *Wintrobe's Clinical Hematology*. 12th ed. USA: Lipincot Williams and Wilkins, Wolter- Kluwer Business; 2009. p. 1938-55.
4. Elizabeth J, Amita R, Mamta S, et al. An uncommon morphological variant of acute promyelocytic leukemia. *American Journal of Hematology*. 2011; 87(3):294. Available from: <http://wileyonlinelibrary.com/cgi-bin/jhome/35105>
5. Mohamed M, Dun K, Grabek J. A typical features in a patient with acute promyelocytic leukemia: A potential diagnostic pitfall. *BMJ Case Rep*. 2013. DOI: 101136/bcr-2013-200152.
6. Ibrahim FA, Yassin MA, El-Ayoubi HR, Alhiji IA, Albinali AS, Almansour SM, Qafoud FM. Clinico-pathological profile of acute promyelocytic leukaemia at Al-Amal Oncology-Haematology Centre, Qatar. *East Mediterr Health J*. 2010 Sep; 16(9):958-65. PubMed PMID: 21218723.