Original Research Paper

Volume - 14 | Issue - 04 | April - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

A RARE VARIANT OF APML WITH PML_RARA NEGATIVE

Dr. Salahuddin* MD (Postgraduate) *Corresponding Author

Dr. Shaik Miftah Junaid Postgraduate

ABSTRACT **Introduction** Acute promyelocytic leukemia (APL) is a unique subtype of acute myeloid leukemia It is a M3 subtype of AML according to FAB and APL with translocation between chromosomes 15 and 17 {t (15;17)} in WHO According to national cancer SEER registry (from 1992 to 2007), the age adjusted annual incidence of APL was 0.23per 1,00,000 persons

KEYWORDS :

Case Study

A 30 year old male no prior comorbidities presented with easy fatigability, palpitation and bruises for 15 days. On examination he was found to have pallor and bruises over the limbs. Investigation revealed anemia. Peripheral Blood smear showed 25% blast cells promyelocyte. Fibrinogen -83mg/dl. Bone marrow aspirate revealed 78% blast cells promyelocytes. Flow cytometry showed acute promyelocytic anemia (APML)(CD11c, CD13, CD33, MPO, CD117, CD45 positive)

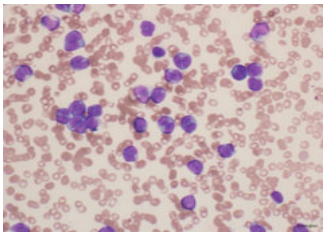
Investigations

PBS - showed 25% Blast + Promyelocytes
PT- 15 sec
INR -1.3
aPTT-36.7
Fibrinogen – 83mg/dl
BM aspirate - s/o 78% blast + promyelocytes.

Flow cytometry consistent with acute promyelocytic leukemia (APML) (CD11c, CD13, CD33, MPO, CD117, CD45 positive)

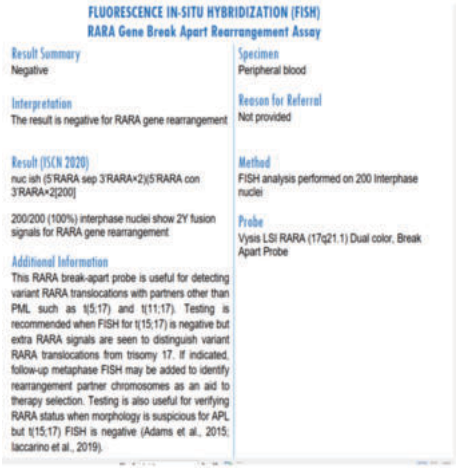
Leukemia genetic profile

AML ETO t(8;21)- Negative
NPM1 gene mutation – Negative
INV16(p13q22)/ t(16;16) (p13;q22)– Negative
BCL-ABL – Negative
FLT3-ITD- Negative
PML-RARA type bcr 1,2,3 – Negative



Faggots Cells

Test Name	Results	Units	Bio. Ref. Interval
LEUKEMIA DIAGNOSTIC PANEL (Flow Cytometry)			
MARKERS	RESULT (%)	INTENSITY	INTERPRETATION
T cell markers			
CD3cyto		Negative	Negative
CD7	0.7	Negative	Negative
B cell markers			
CD19	0.2	Negative	Negative
CD22 cyto	0.1	Negative	Negative
Myeloid markers			
CD15	52.4	Dim pos	Positive
CD13	65.2	Dim to Mod	Positive
CD14	0.7	Negative	Negative
CD33	12.2	Negative	Negative
CD33	98.6	Bright	Positive
CD36	2.3	Negative	Negative
CD41a	0.2	Negative	Negative
CD61	0.6	Negative	Negative
CD64	0.7	Negative	Negative
CD71	2.1	Negative	Negative
MPO	84.5	Dim pos	Positive
Precursor markers			
CD34	0.1	Negative	Negative
CD117	44.2	Dim pos	Positive
Tdt	1.5	Negative	Negative
Other markers			
CD45	99.6	Dim pos	Positive
HLA-DR	0.6	Negative	Negative



FLUORESCENCE IN-SITU HYBRIDIZATION (FISH)
RARA Gene Break Apart Rearrangement Assay

Result Summary
Negative

Specimen
Peripheral blood

Interpretation
The result is negative for RARA gene rearrangement

Reason for Referral
Not provided

Result (ISCN 2020)
nuc ish (5'RARA sep 3'RARA×2)(5'RARA con 3'RARA×2)[200]

200/200 (100%) interphase nuclei show 2Y fusion signals for RARA gene rearrangement

Method
FISH analysis performed on 200 interphase nuclei

Probe
Vysis LSI RARA (17q21.1) Dual color, Break Apart Probe

Additional Information
This RARA break-apart probe is useful for detecting variant RARA translocations with partners other than PML such as t(5;17) and t(11;17). Testing is recommended when FISH for t(15;17) is negative but extra RARA signals are seen to distinguish variant RARA translocations from trisomy 17. If indicated, follow-up metaphase FISH may be added to identify rearrangement partner chromosomes as an aid to therapy selection. Testing is also useful for verifying RARA status when morphology is suspicious for APL but t(15;17) FISH is negative (Adams et al., 2015; Iaccarino et al., 2019).

DISCUSSION

A 30yr old male presented with easy fatiguability, palpitation and bruises of 15days duration. His laboratory evaluation revealed anemia and PBS showed 25% Blast + Promyelocytes. Bone marrow aspirate suggestive of 75% blast + promyelocytes and flow cytometry consistent with APL. However leukemic genetic panel showed negative including PML RARA type bcr 1,2,3.

Treatment

In view of suggestive morphology (faggots cells) and typical clinical and laboratory findings, patient was started on ATRA and Inj ATO. He has shown response to therapy with declining levels of promyelocytes and blasts.

CONCLUSION

Such genetic derangements are usually, but not always, detectable by fluorescence in situ hybridization especially using smaller probes. Diagnosis in such cases established by RT PCR and Translocation-based comparative genomic hybridization. In general, patients with variations identified as ATRA-sensitive are treated with standard ATRA - based therapy. Patients with variants known to be resistant to ATRA are treated with standard AML induction therapy

REFERENCES

1. Grimwade D. The pathogenesis of acute promyelocytic leukaemia: evaluation of the role of molecular diagnosis and monitoring in the management of the disease.
2. Br J Haematol 1999; 106:591 Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016; 127:2391.