

CLINICO-PATHOLOGICAL PROFILE OF THERAPY RELATED ACUTE MYELOID LEUKEMIA

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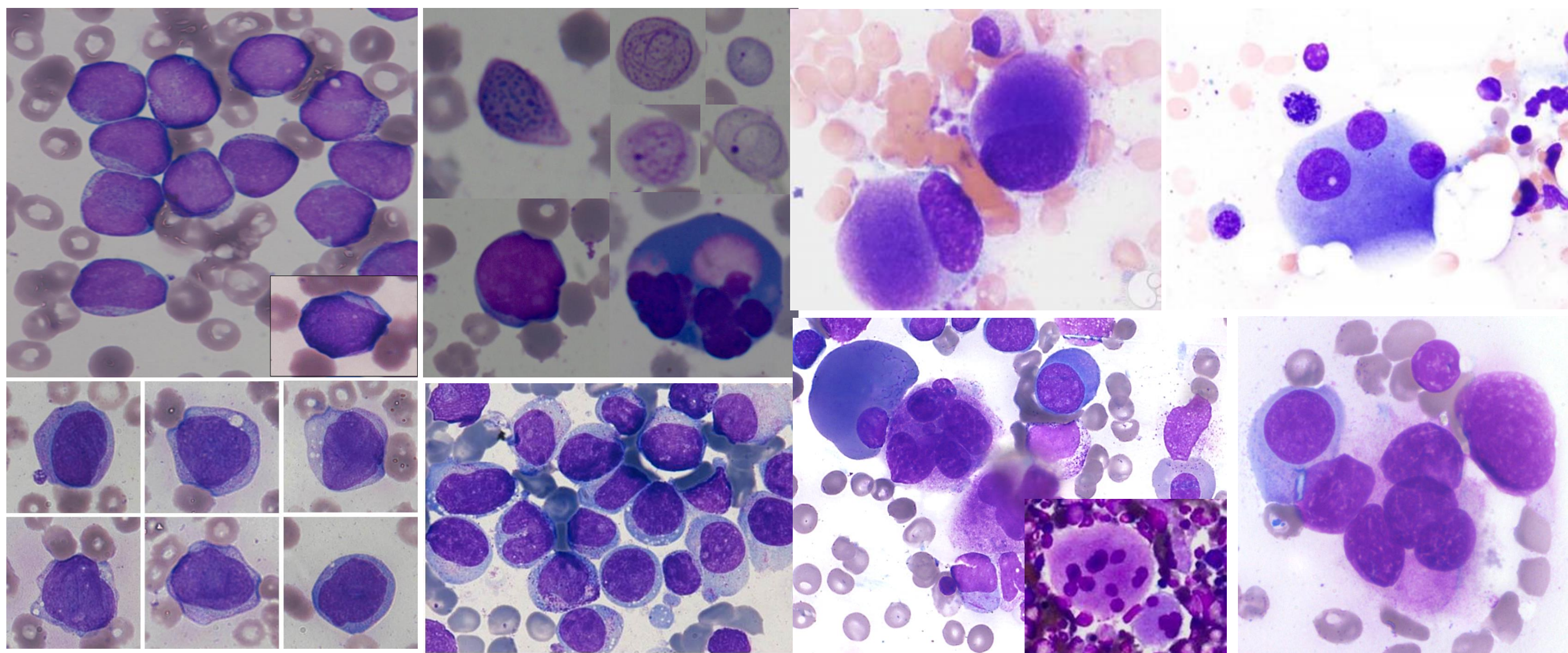
Background

- ❑ Secondary acute myeloid leukemia (sAML) may arise from the previous clonal disorder of hematopoiesis, usually from myelodysplastic syndrome or chronic myeloproliferative neoplasm or as a complication in patients receiving chemotherapy or radiotherapy for a primary malignancy including hematological and non-hematological/ solid malignancies (therapy-related AML (t-AML)).
- ❑ Overall, frequencies of sAML and tAML were 19.8% and 6.6%, respectively.
- ❑ Unfavorable cytogenetics, as complex karyotype or deletion or loss of chromosomes 5 and/or 7 is higher in t-AML.
- ❑ Associated with specific clinical features with uniform poor prognosis with a median survival of 6-12months with higher relapse rate.

Objective

- ❑ To study the frequency of t-AML in a tertiary health care centre in North India.
- ❑ To study patients of t-AML with respect to clinical presentation, laboratory parameters including flowcytometry immunophenotyping, cytogenetic & molecular studies;
- ❑ To assess the cytogenetics in therapy related AMLs and association with complex cytogenetics.
- ❑ To assess the prognosis of therapy related AMLs.

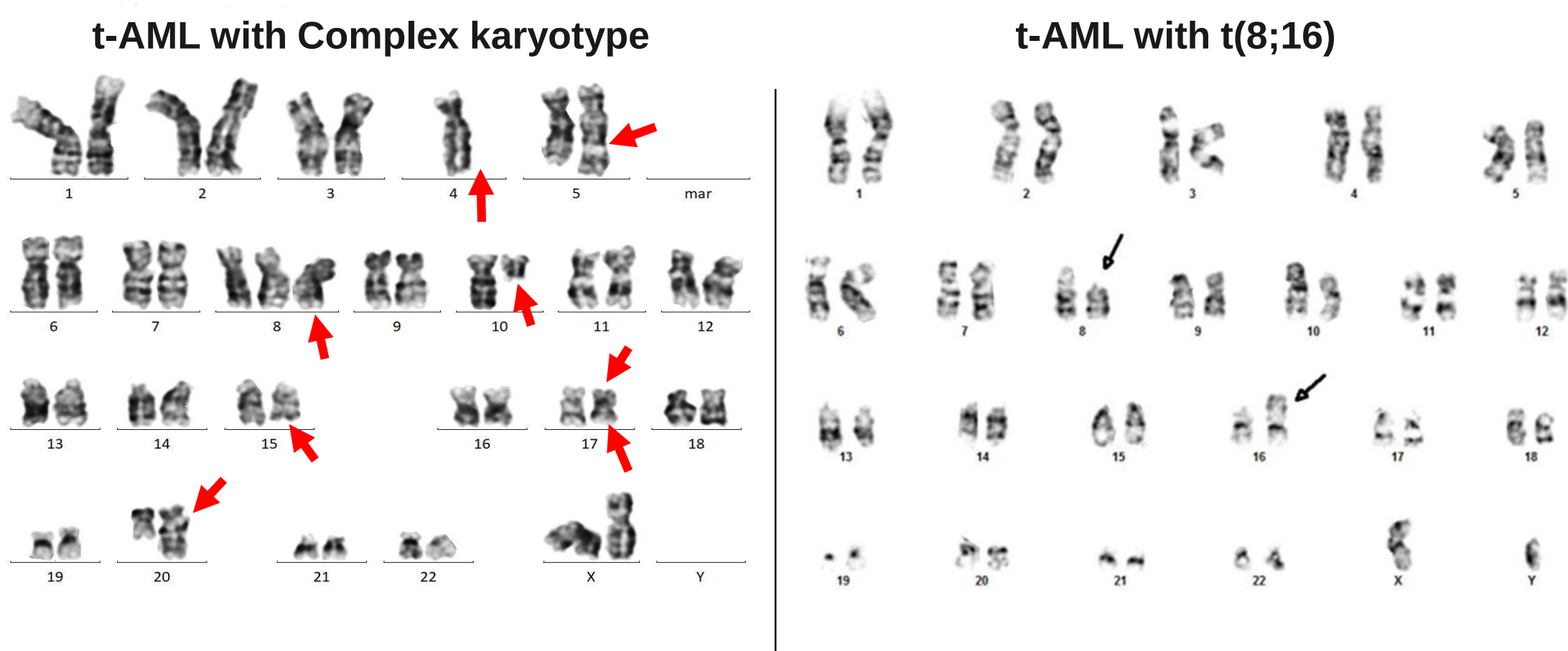
MORPHOLOGY



Materials & Methods

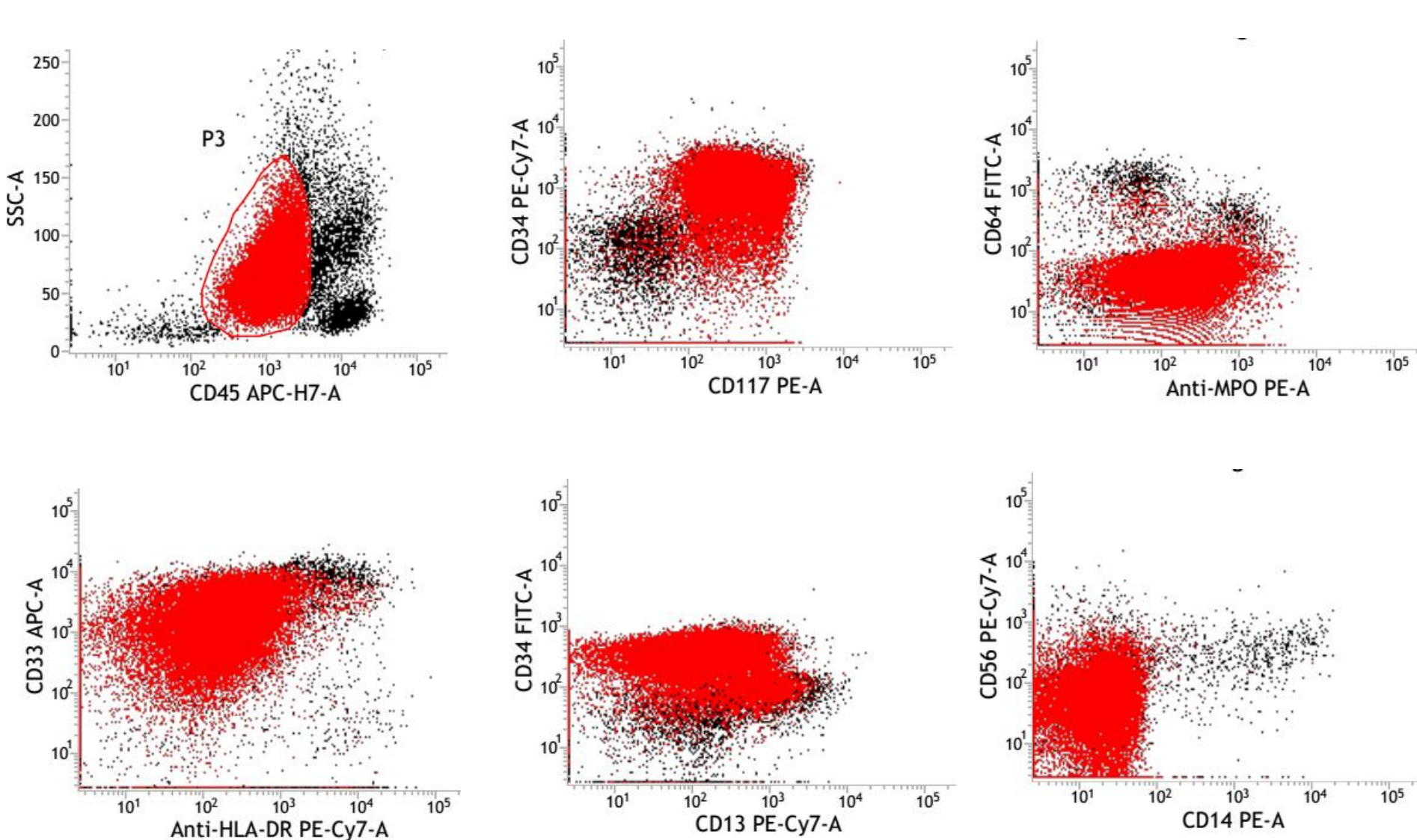
- ❑ This was study a retrospective analysis of patients of t-AML from January 2011 to December 2019 (9 years).
- ❑ The patients underwent detailed hematological work up as peripheral blood smear, bone marrow examination along with flowcytometric immunophenotyping, karyotyping and molecular studies (NPM1, FLT3ITD/TKD, BCR/ABL, PML/RARA, INV16, AML-ETO).
- ❑ Outcome of the patients were also reviewed.

KARYOTYPING

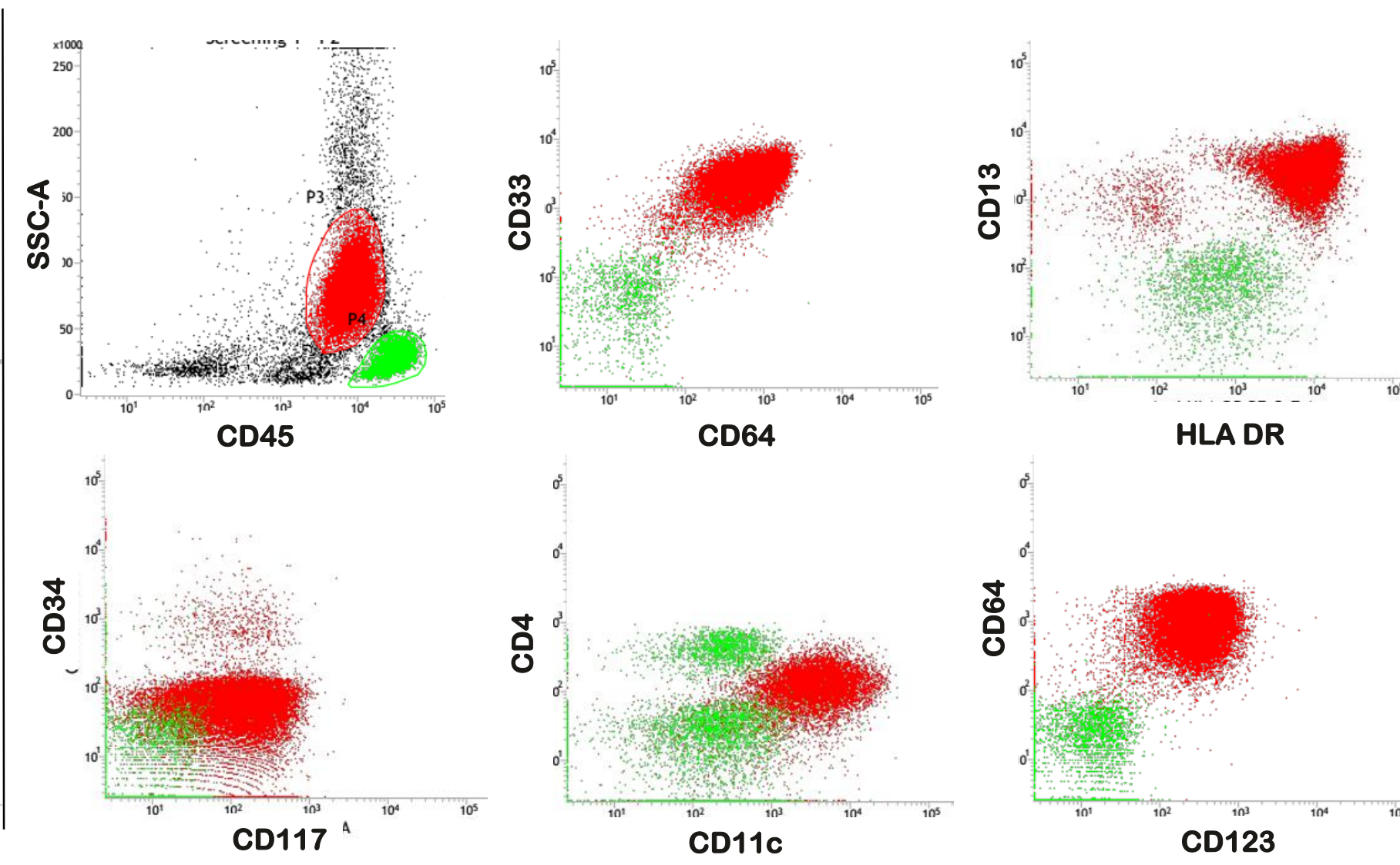


FLOWCYTOMETRIC IMMUNOPHENOTYPING

AML WITH MATURATION



AML WITH MONOCYTIC DIFFERENTIATION



Result

- ❑ Total of 20 cases of t-AML were diagnosed in patients treated for various malignancies.
- ❑ Breast (9 cases), prostate (3 cases), pancreatic (2 cases) and lymphomas (NHL:4 cases and HL:2 cases).
- ❑ There were 7 males and 13 females (M:F: 1:1.85)
- ❑ Median age of 63 years (range 35-82 years).
- ❑ Median latency period to t-AML was 3.5 years (range 0.5-11.0 years).
- ❑ Median haemoglobin was 72.5 g/L (range:61-151 g/L)
- ❑ Median WBC count $3.7 \times 10^9/L$ (range:1.02-169.1 $\times 10^9/L$)
- ❑ Median platelet count $40 \times 10^9/L$ (range:12-257 $\times 10^9/L$)
- ❑ Peripheral blood blast: Median 48% (range: 5-98%)
- ❑ Bone marrow blast: Median 76% (range: 20-98%)
- ❑ AML with monocytic differentiation was the most common morphological and flowcytometric subtype (50% cases) followed by AML with maturation (AML-M2 subtype).
- ❑ Complex karyotype was seen in 50% cases.
- ❑ Molecular studies for NPM, FLT3ITD/TKD, PML/RARA, AML-ETO, and INV16 showed 8 cases with NPM1 positivity and 4 case with FLT3ITD positivity.
- ❑ Only 4 patients (20%) achieved complete remission, however relapsed within one year of duration.
- ❑ Ten patients succumbed to their disease, majority within 1 year of t-AML diagnosis.

Discussion

- ❑ Pathogenesis may involve DNA damage caused by direct oncogenic effects of chemotherapy and radiation as well as decreased immune surveillance.
- ❑ Around 70% of prior malignancy are solid tumor and 30% prior hematological malignancy.
- ❑ PB and BM findings in classical form of t-AML resemble those seen in AML with multilineage dysplasia with mild to marked reticular reticular fibrosis
- ❑ Older median age (>60years).
- ❑ Clonal chromosome abnormalities present in >90% cases, often of a complex nature.
- ❑ Most common abnormality is monosomy 7 followed by del(5q) & monosomy 5.
- ❑ Higher rate of TP53 mutation (50%) and lower CEBPA mutation. Other commonly mutated genes: TET2, PTPN11, IDH1/2, NRAS, FLT3.
- ❑ Overall survival and relapse free survival are worse.

Conclusion

- ❑ The study highlights the development of therapy related AML following chemotherapy and/ radiotherapy as an important therapy related complication.
- ❑ t-AML occurred in a older age group than de-novo AML
- ❑ There is a female predominance due to presence of 9/20 cases of prior breast cancer to t-AML.
- ❑ The latency period and the clinical manifestations may differ depending on the type of cytotoxic drug, cumulative dose, and dose intensity.
- ❑ A close hematological follow up should always be done for an accurate and timely diagnosis.

References

- ❑ Samra B, Richard-Carpentier G, Kadia TM, et al. Characteristics and outcomes of patients with therapy-related acute myeloid leukemia with normal karyotype. Blood Cancer J. 2020 May 4;10(5):47.
- ❑ Elliott K, Devitt K, Gardner JA. Unintended Consequences: Therapy-Related Acute Myeloid Leukemia. J Assoc Genet Technol. 2021;47(2):70-74.
- ❑ Hulegårdh E, Nilsson C, Lazarevic V, et al. Characterization and prognostic features of secondary acute myeloid leukemia in a population-based setting: a report from the Swedish Acute Leukemia Registry. Am J Hematol. 2015 Mar;90(3):208–14
- ❑ Zeichner SB, Arellano ML. Secondary adult acute myeloid leukemia: a review of our evolving understanding of a complex disease process. Curr Treat Options Oncol. 2015 Aug;16(8):37
- ❑ Kayser S, Döhner K, Krauter J, et al. The impact of therapy-related acute myeloid leukemia (AML) on outcome in 2853 adult patients with newly diagnosed AML. Blood. 2011 Feb 17;117(7):2137-45.