Hematological Profile, Clinical Characteristics, and Post-Induction Remission Status of Mixed Phenotype Acute Leukemia, a Rare and Challenging Entity

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Introduction

Mixed-phenotype acute leukemia (MPAL) is a rare and heterogeneous subtype of acute leukemia, accounting for ≤4% of all cases. Recognized under the WHO classification of hematopoietic tumors, MPAL remains a diagnostic and therapeutic challenge due to variability in immunophenotypic expression and lack of standardized treatment consensus. Updates in WHO diagnostic criteria have influenced the reported frequency and classification of this entity over the years.

Aim

To evaluate the clinical, hematological, immunophenotypic, and cytogenetic characteristics of pediatric MPAL and to assess post-induction remission status, with emphasis on its role in treatment re-stratification.

Objectives

1. To determine the frequency and subtype distribution of pediatric MPAL.
2. To analyze immunophenotypic and cytogenetic profiles.
3. To assess post-induction remission status, including MRD, and its impact on treatment decisions.

Methods

A retrospective study was conducted on newly diagnosed MPAL cases (ages 1–17 years) treated between January 2019 and September 2024. Diagnosis was established using eight-color flow cytometry, conventional cytogenetics, and FISH, in accordance with WHO criteria. Patients were stratified as high-risk and treated with a modified Berlin-Frankfurt-Münster (BFM) protocol. Induction outcomes were assessed on day-35 bone marrow aspirates for morphological remission and flow cytometry–based MRD. Patients failing morphological remission were switched to AML-directed protocols.

- **Patient Selection**
  - Newly diagnosed MPAL
  - Jan 2019 – Sep 2024
- **First Outcome**
  - Two infants with upfront palliations: 1. B/Monocytic lineage, 2. KMT2A
  - 36 with curative intent
- **Protocol**
  - High risk modified BFM
  - Prednisolone response assessment at day-8
- **Induction Course**
  - Induction completed in 24 patients
  - Assessed for BM aspirate remission & MRD by flowcytometry

Results

A total of 38 children (median age 7.5 years; IQR 3–12) were included, with a male predominance and over half presenting with WCC ≥50 × 10⁹/L. The T/Myeloid subtype was slightly more common. Cytogenetic abnormalities were infrequent: BCR-ABL1 (13%), KMT2A (6%), and karyotypic aberrations (23% of 18 tested). The detailed clinical and immunophenotypic details are shown in Table and Figure 1. Despite good prednisone response in most patients, only 53% achieved post-induction morphological remission (Figure 2).

Descriptive Statistics			
Variables	**Category**	**N**	**%**
Age (yrs)	< 10	23	60
	≥ 10	15	40
Sex	Male	27	71
	Female	11	29
White Cell Count (x10E9/L)	< 50	17	45
	≥ 50	21	55
Phenotype	B/Myeloid	18	47
	T/Myeloid	20	53
Pred Prophase Response (n = 19)	Good	17	89
	Poor	2	11
BCR - ABL1 (n = 16)	Negative	14	87
	Positive	2	13
KMT2A (n = 17)	Negative	16	94
	Positive	1	6
ETV6-RUNX1 (n = 16)	Negative	16	100
	Positive	0	0
RUNX1-RUNX1T1 (n = 25)	Negative	24	96
	Positive	1	4
CBFB (n = 25)	Negative	25	100
	Positive	0	0

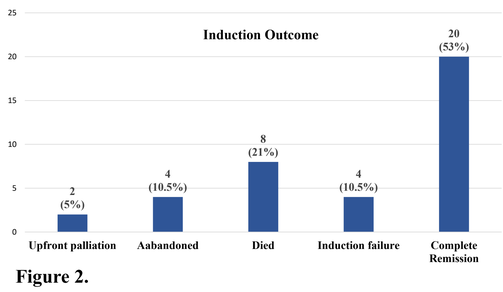


Figure 2.

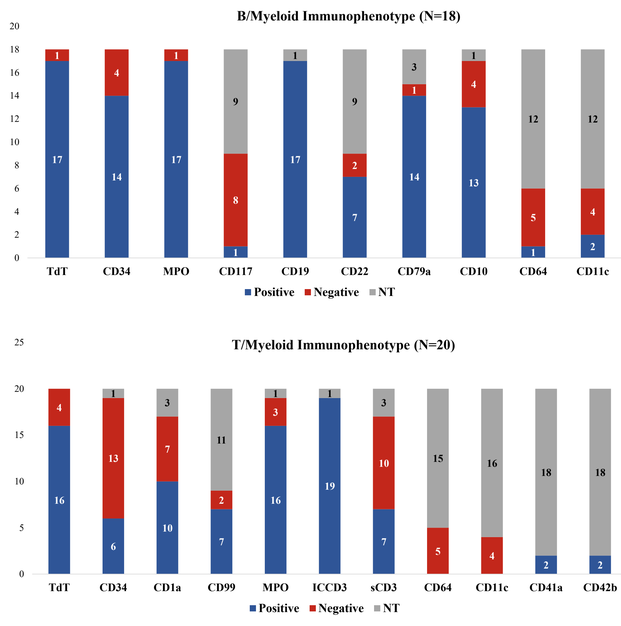


Figure 1.

Summary

We found male predominance, frequent T/myeloid phenotype, and varied cytogenetic profiles. This emphasizes the importance of immunophenotypic and molecular data in treatment decision-making. High induction mortality rate and inadequate post-induction remission response highlight the need for appropriate supportive care and risk-assessed treatment strategies.

Discussion

Our findings highlight that pediatric MPAL carries significant clinical heterogeneity. The clinical characteristics and immunophenotypic profile align with previously reported patterns. Despite a favorable prednisone response in the majority, inadequate post-induction remission response emphasizes the challenges in achieving durable remission. Tailoring therapy, including switching to AML-like regimens in non-responders, appears crucial for improving outcomes.

References

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Conflict of Interest: None
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