Case Series

Changing Practice in Childhood Acute Promyelocytic Leukaemia: A Case Series on Reduced-Intensity ATRA and Arsenic Trioxide Regimens in Bangladesh with Excellent Outcome

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Abstract

Background: *Acute promyelocytic leukaemia (APL) is one of the most curable forms of acute myeloid leukaemia following treatment with all-trans retinoic acid (ATRA) and arsenic trioxide (ATO). Risk-adapted ATRA-ATO regimens with reduced chemotherapy exposure are increasingly used to minimize toxicity and treatment burden. However, experience with reduced-dose ATRA in children remains limited in Bangladesh.*

Objective: *To describe the treatment, toxicity, and molecular outcomes of children with APL treated with risk-adapted ATRA-ATO-based regimens.*

Case Presentation: *Five children with newly diagnosed APL, aged 3.8–12 years, were treated at Khwaja Yunus Ali Medical College & Hospital, Bangladesh, during 2025. Diagnosis was confirmed by bone marrow morphology, immunophenotyping, and PML-RARA RT-PCR. Patients were risk-stratified according to presenting white blood cell count. One standard-risk patient received the Lo-Coco regimen with ATRA 45 mg/m²/day and ATO 0.15 mg/kg/day. Four patients received the COG AAML1331-based regimen with reduced-dose ATRA 25 mg/m²/day and ATO 0.15 mg/kg/day; two high-risk patients also received limited-dose idarubicin.*

Results: *All five patients achieved morphological remission after induction and complete molecular remission after the second consolidation, confirmed by negative PML-RARA RT-PCR. Toxicities were manageable. Differentiation syndrome and leucocytosis responded to dexamethasone and hydroxyurea, respectively. Severe pseudotumor cerebri occurred in the patient receiving ATRA 45 mg/m²/day but was not observed among those receiving 25 mg/m²/day.*

Conclusion: *Risk-adapted ATRA-ATO therapy, including reduced-dose ATRA, appears feasible and effective for childhood APL in a resource-constrained setting. These encouraging findings warrant larger studies with longer follow-up.*

Key words: *Acute promyelocytic leukaemia, Paediatric APL, low-dose ATRA, Arsenic trioxide, PML-RARA, Bangladesh.*

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Introduction

Acute promyelocytic leukaemia (APL) represents a special type of acute myeloid leukaemia comprises 5-10 % of all pediatric Acute Myeloid Leukaemia (AML) cases.[1] It is characterized by the t (15;17) chromosomal translocation, leading to the PML-RARA fusion gene.[2] This mutation obstructs normal myeloid differentiation at promyelocytic stage and promotes abnormal cellular proliferation, contributing to the oncogenic process.[3] While historically associated with a high mortality rate, Acute promyelocytic leukaemia is now considered one of the most curable leukaemia's due to the incredible efficacy of differentiating agents.[4] Specifically, all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) induce leukemic cell differentiation into mature granulocytes, ultimately leading to natural like apoptosis, thus transforming Acute promyelocytic leukaemia treatment paradigms to the cure by this synergistic molecular targeting engineering.[5] This therapeutic shift has notably reduced the reliance on intensive chemotherapy, particularly for standard-risk patients, making treatment less toxic and more accessible.[6] This changing practice towards chemotherapy free regimens, particularly in paediatric cohorts, has demonstrated comparable or superior outcomes to traditional intensive chemotherapy, significantly minimizing long-term sequelae without compromising therapeutic efficacy.[7]

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Recent publications & international trails such as COGAAML 1331 have projected that ATRA dose can be substantially reduced (25 mg/m²) in pediatric Acute promyelocytic leukaemia.[8] Where higher dose of ATRA were associated with higher side effect frequency of ATRA, notably Pseudotumor Cerebri, even required treatment interruption.[9] These optimized regimens not only enhance patient outcomes but also reduce treatment costs and the need for extensive supportive care, addressing critical challenges in resource-constrained environments.[10]

This report details a case series from Bangladesh, illustrating the successful application of reduced-intensity ATRA and ATO protocols in pediatric Acute promyelocytic leukaemia, aligning with global efforts to optimize therapy in resource-limited settings. This case series of five Pediatric Acute promyelocytic leukaemia patients; highlights the successful implementation of these modern protocols at Paediatric Haematology & Oncology department of Khwaja Yunus Ali Medical College & Hospital.

Case Series Presentation

This is a case series of five (Table I) pediatric patients diagnosed with Acute Promyelocytic Leukaemia (APL) at Khwaja Yunus Medical College & Hospital those were admitted during the year of 2025, Diagnostic confirmation relied on bone marrow morphology (Figure 1), Immnuophenotyping, and detection of the PML-RARA fusion transcript via reverse transcriptase-polymerase chain reaction[11] at presentation with evaluation of other investigations like CBC, PT, APTT, D-dimer, renal function tests & liver function tests.

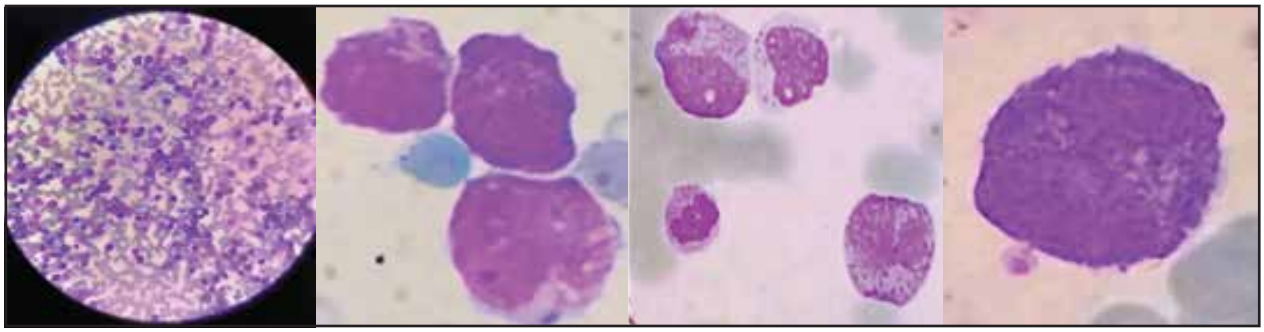

Figure 1: Bone marrow with increased cellularity by abnormal promyelocytes; cell containing numerous azurophilic granules in the cytoplasm & lobulated cerebriform nuclei, pathognomonic cell of APL

Table I : Clinical summaries, regimens, toxicities, and outcomes for the five pediatric Acute Promyelocytic Leukaemia (APL) patients

Case no. Age, Sex	Initial WBC	Risk group	Regimen	Toxicities	Post induction	Follow-up PML-RARA testing	Current status
1. 4.3 Y Male	6500/cmm	Standard Risk (SR)	LoCoco (ATRA 45mg/m²/ day ATO 0.15mg/kg/day)	Differentiation syndrome Leucocytosis Pseudotumor Cerebri Musculoskeleta l pain	Remission	Negative	Treatment Completed (for10m)
2. 7 Y Male	5780/cmm	High Risk (HR)	COG AAML1331 SR (ATRA 25mg/m²/ day ATO 0.15mg/kg/day)	Headache	Remission	Negative	Treatment Completed (for 5m)
3. 12 Y Male	27640/cmm	High Risk (HR)	COG AAML1331 HR (ATRA 25mg/m²/ day ATO 0.15mg/kg/day Ida 12mg/m²/ dose; (day 1,3,5, 7)	Febrile Neutropenia. Headache	Remission	Negative	Treatment Completed (for 4.5m)
4. 6.5 Y Female	3460/cmm	Standard Risk (SR)	COG AAML1331 SR (ATRA 25mg/m²/ day ATO 0.15mg/kg/day)	Headache Musculoskeleta l pain Leucocytosis	Remission	Negative	Treatment Completed (for 2m)
5. 3.8 Y Male	46,740/cmm	High Risk (SR)	COG AAML1331 HR (ATRA 25mg/m²/ day ATO 0.15mg/kg/day Ida 12mg/m²/ dose; day 1,3,5,7)	Neutropenia	Remission	Negative	On consolidation 3

PML = Promyelocytic Leukemia gene, RARA = Retinoic Acid Receptor Alpha gene

Discussion

These treatment strategies are adapted from established international guidelines, specifically the Lo-Coco and COG AAML1331 regimens, tailored according to individual risk stratification based on initial white blood cell counts. These adaptations allowed for a tailored therapeutic approach, can achieve high cure rate while minimizing potential toxicities associated with conventional intensive chemotherapy regimens.[12] This strategy highlights the feasibility and efficacy of implementing reduced-intensity, arsenic-based therapies in resource-limited settings, demonstrating their potential to achieve complete molecular remission with manageable side effects.[13] This is aligning with the current trend of APL management, which emphasizes chemotherapy-free ATRA-ATO strategies as effective and safe.[14] This evolution in treatment has transformed APL from a highly fatal disease to one of the most curable forms of leukaemia, particularly with the reduction or elimination of chemotherapy in standard-risk patients.[15] This approach has shown favourable outcomes, even in high-risk cases when treated with ATO and ATRA, with easily manageable toxicity.[16]

Given these improvements, the current case series examines the feasibility and efficacy of following such reduced-intensity protocols in a pediatric cohort within a resource-constrained setting, specifically Bangladesh. Though robust research is ongoing to incorporate ATRA and ATO, address critical challenges such as treatment accessibility, cost-effectiveness, and toxicity management in contexts where intensive supportive care infrastructure may be limited.[17-20] There are limited study from Bangladesh regarding childhood APL management by chemotherapy free protocol rather some previous report showed the still the practice of traditional chemotherapy containing protocol.[21] While few studies from Bangladesh demonstrating excellent outcome of this chemotherapy free strategies; those study on adult APL case.[14] One of the previous report from the country on pediatric APL treated by ATRA & ATO based protocol showed good survival rate but toxicity rate was also notable 80% had differentiation syndrome.[22] Similar to the 1st case of this case series higher dose of ATRA had more chance of having differentiation syndrome & Pseudotumor Cerebri. Where lower dose of ATRA is recommended in children[23] but no previous data from Bangladesh regarding that lower dose is available. From this context this case series could be important according to the country perspective of treating childhood APL by lower dose ATRA & ATO based protocol like COG AAML 1331. The findings from this case series further support the global paradigm shift towards reduced-intensity, arsenic-based therapies for childhood APL, demonstrating their significant potential for widespread adoption in similar geographical and economic contexts.[24] This approach offers a viable alternative for achieving durable remissions and high cure rates, particularly when long-term follow-up might be challenging in developing countries.[25]

Conclusion

This case series demonstrates that ATRA & ATO combination; particularly the lower dose ATRA protocol is truly effective as well as feasible for treating Paediatric APL to the cure even at LMIC setting like Bangladesh. This approach minimizes immediate as well as long term toxicities associated with drugs while preserving excellent survival rates.

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