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INTRACRANIAL HEMORRHAGE VS SEVERE NON-INTRACRANIAL HEMORRHAGE IN CHILDHOOD ACUTE LEUKEMIA, EGYPTIAN MULTI-CENTER RETRO & PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION

Hematologic malignancy has the highest rate of intracranial hemorrhage (ICH). Acute leukemia in children may present with silent or symptomatic hyperleukocytosis, a medical emergency that necessitates rapid stabilization of the patient and lowering of the leukocyte count and good metabolic control. Data on patients with ICH associated with T-cell acute lymphoblastic leukemia with hyperleukocytosis, had been reported. Chemotherapy was started at 10% of the usual dose. Brain magnetic resonance (MRI and MRA) are essential part of definitive diagnosis. Intracranial hemorrhage is often fatal in children with acute leukemia whether T-cell acute leukemia or acute promyelocytic Leukemia (M3), potential contributing factors differed by ICH timing, older age, and high white blood cell count (1). Serious non-ICH had been in focus and might attribute to significant morbidity and mortality.

AIM

The door was open

METHOD

We reviewed the database of patients 1-16 years diagnosed with AL during (2017-2022) for a minimum of 2-5 years in 7 tertiary oncology centers treating > 30-100 new cases annually and 9 months follow-up prospectively (September 2022- June 2023). Initially bone marrow aspiration and biopsy were done for all patients, immunophenotyping, cytogenetics, viral markers, electrolytes, serum uric, kidney and liver functions. While brain MRI / MRA in cases of suspected ICH or pulmonary and GIT imaging and or endoscopy for non-ICH were done.

RESULTS

Complete data of 1262 children with AL (ALL (78%), AML 22%) as well as 274 new AL prospectively for 9 months. The median age was 7 years (interquartile range 5-9). Follow-up duration was 3504 patient-years. Severe non-ICH was 71(pulmonary, gastro-intestinal, or urinary hemorrhage) vs 36 children with ICH (three-quarter were early), median age was 4 years (interquartile range 2-7) vs 11 years (interquartile range 9-14) respectively. The incidence rate of ICH was 14 vs 28 per 1000 person-years for severe non-ICH respectively. Fatality frequency of 69.1% in ICH vs 17.1% in severe non-ICH bleed (pulmonary hemorrhage was fatal in one-third of cases mostly associated with disseminated fungal infection). Patients with early ICH had higher white blood cell count range and low PC as shown in table (1), whereas patients with late ICH had more concurrent systemic mixed infections and disseminated intravascular coagulopathy. Most cases of ICH were intraparenchymal, then intraventricular and multi-centric. One-fourth of ICH were reported before the start of chemotherapy, and two-thirds were during induction or intensification. Risk of death from ICH was 4 times higher than that of the severe non-ICH group but double the pulmonary hemorrhage. Risks of ICH were age at diagnosis >12 years, initial WBC count >100,000/mm3, as well as, high bleeding score, T-cell leukemia, M3. Prospective data were comparable with the retrospective with a non-significant better outcome

Parameter	ICH (n=36)	Non-ICH (n=71)	p-value[a]	Overall (N=107)
Age, Years				
Mean ± SD	11.8 ± 2.1	3.7 ± 1.3	<0.001	7.75 ± 1.7
AL =>12 years, n (%)	22 (61.1)	18 (25)	<0.001	40 (37.4)
Sex, n (%)				
Male	25 (69.4)	38 (53.5)	0.113	63 (58.9)
ALL				
T-cell/All	16/24 (66.7)	12/59 (20.3)	<0.001	28/83 (33.7)
AML				
M3/All	10/12 (83.3)	6/12 (50)	0.083	16/24 (66.7)
TLC 10x3/mm PC 10x6/mm	44-1200(88) 2-112 (14)	2-122(8.4) 8-212 (51)	<0.001 <0.001	2-1200(14) 2-212 (37)
Type of bleed Intraparenchymal Pulmonary/ Non-pulm.	20/36 (55.6) 0 (0.0%)	0 (0.0%) 32/71 (45.1)	<0.001 <0.001	20 (18.7%) 32 (29.9%)
Outcome Mortality %	25/36(69.4)	18/71(25.3)	<0.001	43/107(40.2)

Table 1. Children with acute leukemia; ICH and severe non-ICH, the retrospective (2017-2022) characteristics at enrolment.

Parameter	ICH (n=10)	Non-ICH (n=23)	p-value[a]	Overall (N=33)
Age, Years				
Mean ± SD	10.9 ± 1.9	3.9 ± 1.3	<0.001	6.1 ± 2.2
AL =>12 years, n (%)	6 (60)	5 (21.7)	0.032	11 (33.3)
Sex, n (%)				
Male	7 (70)	14 (61)	0.616	21 (60.5)
ALL				
T-cell/All	5/6 (83.4)	6/15 (40)	0.072	11/21 (52.5)
AML				
M3/All	5/5(100)	4/8 (50)	0.057	8/13 (61.7)
TLC 10x3/mm PC 10x6/mm	23-780(78) 3-87 (19)	3-54(9.6) 9-137 (43)	<0.001 <0.001	3-780(13) 3-137 (31)
Type of bleed Intraparenchymal Pulmonary/ Non-pulm.	5/10(50) 0(0.0%)	0(0.0%) 9/23(39)	<0.001 <0.001	5(15.7%) 9(27%)
Outcome Mortality %	5/10 (50)	5/23 (21.8)	0.104	10/33 (30.3)

Table 2. Children with acute leukemia; ICH and severe non-ICH, 9 months prospective (2022-2023) characteristics at enrolment and outcome.

CONCLUSIONS

Major bleeding as ICH and pulmonary hemorrhage were serious problems limiting complication for improving survival. Severe non-ICH had been reported double the ICH. Early form of ICH had more fatal outcome in most enrolled children with AL. Early fatal ICH was associated with age >12 years, hyperleukocytosis, marked thrombocytopenia, liberal platelet transfusion, delayed intervention. Prognosis was guarded in both early ICH (worst) and pulmonary hemorrhage (with fungal infection). Outcome was slightly improved in the prospective series. Improved supportive care has significantly contributed to increased cure rates..

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CONTACT INFORMATION

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