Posterior Reversible Encephalopathy Syndrome in Children with Acute Lymphoblastic Leukemia – Risk Factors and Impact on Prognosis

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INTRODUCTION

- Posterior Reversible Encephalopathy Syndrome (PRES) is an increasingly recognized clinicoradiological entity
 It is characterized by seizures, headache, altered mental status,
- visual impairment and typically bilateral subcortical and/or cortical edema on MRI
- Children with hematological malignancies are at increased risk for PRES
- We describe the incidence of PRES in children with ALL, identified its risk factors, and examined its prognostic importance

PATIENTS AND METHODS

- Patients aged 1-17 years old at diagnosis
- Treated according to the Nordic Society of Pediatric Hematology and Oncology (NOPHO) protocols from 1992 to 2008
- Exclusion: Patients with Down syndrome (n = 21) or other cognitive disability syndromes (n = 4) that led to significant modifications in their treatments
- A total of 649 patients fulfilled the eligibility criteria
- Demographic data, clinical characteristics, treatment and outcome was retrieved from the NOPHO-ALL registry
- The medical records were reviewed from diagnosis until the end of treatment or relapse
- If a patient had had any CNS symptoms during the treatment, detailed data was gathered

RESULTS

- PRES occurred in 4,5 % of patients (N=29) and mainly during induction 18 (62%) patients with PRES presented with repeated seizures within the following week
- 9 (31%) PRES patients developed epilepsy
- Hypertension, constipation and long alkalinization were significant risk factors for PRES
 Hyponatremia (serum sodium ≤ 135 mmol/l) occurred in 23 PRES patients
- Relapses occurred significantly more often in those patients with PRES (p=0.001).
- PRES was associated with worse overall survival [p = 0.040, 5-year survival = 75.9%
 - (60.3-91.4%) versus 88.4% (85.8-90.9%)]

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RISK FACTOR	UNIVARIABLE		MULTIVARIABLE		\$ 0.6- 10.4-
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value	0.2-
Age: ≥ 10 years	1.85 (0.82-4.17)	0.14	2.59 (0.91-7.38)	0.075	0.0-
Sex: male	1.21 (0.57-2.58)	0.62	1.35 (0.58-3.16)	0.492	0 5 10 15 20 25 Years from diagnosis
T cell leukemia	3.25 (1.17-9.00)	0.023	2.61 (0.75-9.09)	0.132	6 0.8- 1
CNS leukemia at dx	8.74 (2.19-34.87)	0.002	6.05 (0.78-46.80)	0.085	5 0.6- 5
Hypertension	7.69 (3.24-18.25)	<0.0001	4.10 (1.50-11.25)	0.006	-0.0 tř
Constipation	6.47 (2.59-16.14)	<0.0001	5.60 (2.02-15.52)	0.001	5 0.2-
Alkalinization					0.0-
> 14 days	3.28 (1.35-7.94)	0.009	3.27 (1.23-8.68)	0.017	Years from diagnosis
Missing*	0.22		0.29		CONCLUSIC



- It was associated with an increased risk for relapse and worse prognosis, as well as long-term neurological morbidity
- Our study results suggest that optimizing both alkalinization and hydration, and the treatment of hypertension may be beneficial in preventing the development of PRES



REFERENCES

 Fugate JE, Rabinstein AA: Posterior reversible encephalopathy syndrome: Clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol 14:914-925, 2015
 Hinchey J, Chaves C, Appignani B, et al: A reversible posterior leukoencephalopathy syndrome. N Engl J Med 334:494-500, 1996
 Kim SJ, Im SA, Lee JW, et al: Predisposing factors of posterior reversible encephalopathy syndrome in acute childhood leukemia. Pediatr Neurol 47:436-442, 2012
 Relling MV, Pui CH, Sandlund JT, et al: Adverse affact of anticonvulsants on affaceov

Adverse effect of anticonvulsants on efficacy of chemotherapy for acute lymphoblastic leukemia. Lancet 356:285-290, 2000