PROGNOSTIC SIGNIFICANCE OF WILMS' TUMOR 1 GENE (WT 1) EXPRESSION IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/objectives

Wilms' tumor 1 gene (WT 1) is an embryonic zinc-finger transcription factor, which was originally identified as a tumor suppressor gene inactivated in Wilms' tumors. In normal tissue, WT1 is expressed during embryogenesis where it plays a pivotal role in the development of the urogenital tract. Alterations of WT1 expression (both under or overexpression) have been described in a number of malignancies and premalignant syndromes. In this study, we focused on evaluation of WT1 expression and its clinical implications in prognosis of childhood ALL, where WT1 has been least studied and its impact remains most controversial.

Materials and Methods

A case-control study was carried out in pediatric oncology unit of Zagazig university children's hospital during the period from January 2011 to June 2013. We examined the expression level of WT1 gene in 44 newly diagnosed children with acute lymphoblastic leukemia and 20 age and sex matched controls (Patients with hematological problems other than hematological malignancies). Fresh peripheral blood samples were collected from all study participants and submitted for RNA extraction, reverse transcription of extracted RNA and real-time quantitative PCR.

Results

We detected a wide range of WT1 gene expression levels among 44 patients of acute lymphoblastic leukemia. Statistically, WT1 gene expression level was significantly higher in T-cell acute lymphoblastic leukemia than in B-cell Precursor acute lymphoblastic leukemia (P< 0.001) and in those with expression of myeloid markers than those without expression of these markers. Analysis of relapsed cases indicated that abnormally increased WT1 gene expression levels were associated with increased risk of relapse.

		Patients	Controls	Mann Whitney	P value
WT1 gene expression (NCN x 104)	Median	50.7	0.121	U= 650	<0.001
	Mean ±SD	265.0±391.5	0.12 ± 0.07		
	Range	0.15-1827.0	0.02-0.23		

		T cell ALL n(5)	BCP ALL with myeloid markers n(3)	BCP ALL n(36)	ANOVA	P value
WT1 gene expression ($NCN \times 10^4$)	Median	895	620	21.3	F=41.2	<0.001
	Mean ± SD	1070±425.6	641±100.2	121.6±203.2		
	Range	785-1827	553-750	0.15-785		

		No Relapse n(41)	Relapse n(3)	Mann Whitney	P value
WT1 gene expression ($NCN \times 10^4$)	Median	28.2	778	U=1900	0.01
	Mean ±SD	220±379.4	706.8±201.0		
	range	0.15-1827	411-860		

Conclusions

We concluded that WT1 gene expression in childhood acute lymphoblastic leukemia was very variable and much more expressed in T cell ALL and relapsed patients indicating a possible prognostic significance in childhood acute lymphoblastic leukemia