Expression of ILT 3 in Clonal Lymphoproliferative Disorders

Hasnaa A. Abo- Elwafa, ShereenP.Aziz, Heba A. Ahmed,Sherif A. Sayed, Abdelhady R. Abdel-Gawad,Doaa E.Saber .

Department of clinical and chemical pathology, Sohag Faculty of Medicine, Sohag University.

Abstract

B-cell chronic lymphocytic leukemia (B-CLL), also known as chronic lymphoid leukemia (CLL), is the most common type of leukemia (a type of cancer of the white blood cells) in adults, CLL affects B cell lymphocytes,Immunoglobulin-like transcript-3 (ILT-3), a member of the immunoglobulin superfamily, is a transmembrane inhibitory receptor expressed on antigen-presenting cells (APCs) such as monocytes and dendritic cells (DCs) as well as on endothelial cells The aims of this study was to evaluate the expression of ILT-3 in acute and chronic leukamias and its relation to other diagnostic markers and if it has a role in leukamiogenesis A total of 5 papers were obtained using the mentioned keywords in the research of all internet-based databases

Patients and Methods: Case control study, included 30 patients 15 patients with CLLand 15patients no detectable disease recruited from Sohag university hospital and the mean age of each of them was 32.8 years. There are different method of detection of IL3 in different studies such as PCR, ELISA and (FCM).

Results: The frequency of ILT3 positive CLL B cells was higher in patients with lymphoid tissue involvement, suggesting that ILT3 may have prognostic value in CLL

Introduction

In CLL, B cells grow in an uncontrolled manner and accumulate in the bone marrow and blood, where they crowd out healthy blood cells, CLL is a stage of small lymphocytic lymphoma (SLL), a type of B-cell lymphoma, which presents primarily in the lymph nodes, CLL and SLL are considered the same underlying disease, just with different appearances (**Lichtmanet al,2011).**

Immunoglobulin-like transcript-3 (ILT-3), a member of the immunoglobulin superfamily, is a transmembrane inhibitory receptor expressed on antigen-presenting cells

(APCs) such as monocytes and dendritic cells (DCs) as well as on endothelial cells encoded in the leukocyte receptor cluster on human chromosome 19 (Deng et al , 2014).

They are structurally and functionally related to other leukocyte receptor cluster receptors, such as the killer cell immunoglobulin-like receptors, and have been reported to regulate a broad range of cells involved in the immune response **(Morel and Bello´n, 2011).**

Objectives:

To study the expression of ILT-3 in chronic lymphocytic leukamia and its relation to other diagnostic markers and if it has a role in leukamiogenesis .

Patients and methods:

Patients: This, studyconducted on two groups:Group 1: available number of patientswithchronic,Lymphoblasticleukemia with different both (age, sex).

Group 2: about 15 case ITP subjected to bone marrow aspiration.

All patients,and control cases will be subjected to:

- Full history taking.
- Clinical examination.
- Laboratory investigation include:
- Complete blood count.
- BM examination (BMA, BMB) .
- Routine immunophenotyping panel for diagnosis of acute and chronic leukemia.
- ILT-3 expression of the peripheral blood or BM aspirate using flow cytometer.

Results of the study

This study was carried on 15 cases with leukemia 6 Males , 9 females , their ages ranged from 50 to 74 yearsSamples were collected from oncology clinic of sohag universityData was analyzed using STATA intercooled version 12.1. Quantitative data was represented as mean, standard deviation, median and range. Data was analyzed using student t-test to compare means of two groups and ANOVA for comparison of the means of three groups or more.

Table (1): clinical data of studied population.

Variable	Chronic lymphocytic leukemia (CLL)	Control	*P*
Liver **Normal** **Mild** **Moderate**	**6 (50.00%)** **0** **6 (50.00%)**	**15 (100%)** **0** **0**	**0.002**
Spleen **Normal** **Mild** **Moderate**	**2 (16.67%)** **4 (33.33%)** **6 (50.00%)**	**15 (100%)** **0** **0**	**<0.0001****
LN **No** **Generalized**	**5 (41.67%)** **7 (58.33%)**	**15 (100%)** **0**	**0.001**

***P*compared acute and chronic, p2 compared acute and controls and p3 compared chronic and controls .**

**P-value <0.01 HS.

Table(2):Correlation ILT3 with age and Peripheralhemogram:

Variable	Chronic lymphocytic leukemia (CLL)		Controls	
	Correlation co-efficient (r)	P value	Correlation co-efficient (r)	P value
Age	0.18	0.58	0.19	0.49
TLC	0.32	0.31	0.21	0.44
HB	-0.26	0.41	0.06	0.84
Platelets	0.43	0.16	-0.25	0.38
Blast (peripheral)				
Blast (BM)				

Table (3): Correlation ILT3 with other IPT in CLL:

Variable	Chronic lymphocytic leukemia (CLL)	
	Correlation co-efficient (r)	P value
CD45	-0.60	0.04
CD5	0.69	0.01
CD19	0.78	0.003
CD22	0.48	0.11
CD3	0.29	0.37
SIGM	-0.27	0.40
CD13	-0.48	0.12
CD7	-0.30	0.35
Kappa	-0.46	0.13
Lambda	-0.19	0.56
CD20	0.02	0.95
CD79b	0.02	0.96
FMC7	0.11	0.74
CD23	0.78	0.003
HLADR	-0.01	0.96

Discussion

Aim of this study was to study the expression of ILT3 in chronic leukamia and its relation to other diagnostic markers and if it has a role in leukamiogenesis.Our study was carried on 42cases classified to 2 groups: CLL and control group. Group I ALL consisted of 15 patients, their ages ranged from 50 to 74 and included 6 males &9 females. ***Also Ghosh et al. (2003)***reported. In this study the hepatosplenomegally was study,hepatosplenomegaly was observed in 50% patients from whole patients, lymphadenopathy was observed in 7 patients from whole patients & was observed more in leukamia group. (***Hoelzer et al. 2000)***said that CLL can be present with hepatic involvement. Pathology of liver shows diffuse infiltration of leukemic cell. Hepatomegaly is a clue for prognostic evaluation. In spite of marked hepatomegaly, liver function tests are mildly abnormal (***Hoelzer et al. 2000)***.

In chronic leukemia group we found that WBCs and PLTsshow elevatedin CLL than control group, but HBwas elevated in control group compared to chronic leukemia group. This was in agreement with ***Qazilbash et al. (2005)***as they observed decreasing in Hb concentration, RBCs number, haematological indicators values and packed cell volume PCV of chronic leukemia in comparison with control groupand chronic leukemia group. Also***Lin et al. (2008)*** reported in their study that the patients with CLL had significantly higher mean values of hemoglobin and platelets in comparison to other leukemic patients.

Delgado et al. (2003)found that CD5, CD23 antigen was expressed with higher frequency in CLL group. ***Dal-Bo et al. (2009)*** reported in their study that CD79b was expressed with lower frequency in CLL group compared to non-CLL groupwhereas CD79b+low expression pattern was detected in the majority of CLL patients compared to non-CLL ones.

In this study The expression of ILT3 isabsent in control group,ILT3 expressed in 6 patients(50%) in CLL groupas by more differentiated CD34-CD117-CD14/- leukemic cells.

Conclusion

The frequency of ILT3 positive CLL B cells was higher in patients with lymphoid tissue involvement, suggesting that ILT3 may have prognostic value in CLL.

References

1. **Byrd and John (2014):** "Chronic Lymphocytic Leukemia".Leukemia & Lymphoma Society. Retrieved 24 March 2014 **.**
2. **Delgado J, Matutes E, Morrila AM, Morilla RM, Owusu-Ankomah KA, Rafig-Mohammed F, et al. (2003):** Diagnostic significance of CD20 and FMC7 expression in B-
3. cell disorders. Am J ClinPathol. 2003;120: 754-9.
4. **Dal-Bo M, Bertoni F, Forconi F, Zucchetto A, Bomben R, Marasca R, et al. (2009):** Intrinsic and extrinsic factors influencing the clinical course of B-cell chronic lymphocytic leukemia: prognostic markers with pathogenetic relevance. J Transl Med. 2009; 7: 76-89.
5. **Ghosh** S, Shinde SC, Kumaran GS, Sapre RS, Dhond SR, Badrinath Y, *et al.* Haematologic and immunophenotypicprofi le of acute myeloid leukemia: An experience of Tata memorial hospital. Indian J Cancer 2003;40: 71-6
6. **Lichtman M, Kaushansky K, Kipps T, Prchal JT and Levi MM (2011):** The clonal lymphoid and plasma cell diseases: The chronic

lymphocytic leukemias. In: Williams Manual of Hematology [(eds.)] 8th edition, Chapter 56, Page 404-427, McGraw-Hill Companies, USA.

7. **Lin TS, Awan FT, and Byrd JC. (2008):** Chronic lymphocytic leukemia. In: Hoffman R, Benz. Jr EJ, Shattil SJ, Furie B, Silberstein LE, McGlave P, et al., editors. Hematology: Basic Principles and Practice. 5th ed. Churchill Livingstone/Elsevier Philadelphia, USA; 2008. ch.83.
8. **Morel E, and Bello´n T. (2011):** HLA class I molecules regulate IFN-gamma production induced in NK cells by target cells, viral products, or immature dendritic cells through the inhibitory receptor ILT2/ CD85j. J. Immunol. 2011; 181: 2368-2381. J. Immunol. 181, 2368–2381.
9. **Nakase K, Bradstock K, Sartor M, Gottlieb D, Byth K, Kita K, et al. (2000):** Geographic heterogeneity of cel-lular characteristics of acute myeloid leukemia: a comparative study of Australia and Japan adult cases. Leukemia 2000; 14: 163-8.
10. **Weinberg OK, Seetharam M, Ren L, Seo K, Ma L, Merker JD, et al. (2009):** Clinical characterization of acute myeloid leukemia with myelodysplasia-related changes as defined by the 2008 WHO classification system. Blood 2009; 113 (9): 1906-8.