SMJ- Sohag Medical Journal, Vol. 28 No(3) 2024

Print ISSN1687-8353 Online ISSN2682-4159

Original Article

The Use Of CD200 As A Diagnostic Marker In Egyptian Patients With Chronic Lymphoproliferative Disorders

Faten Atef Mohamed[1], Ahmed Ahmed Allam[2], Eman H Ali[2], Tamer Abdel-Latef[2]

1. **Akhmim Hospital, Sohag, Egypt**
2. **Department of clinical and chemical pathology, Sohag Faculty of Medicine, Sohag University**

Abstract

Chronic lymphocytic leukemia and non-Hodgkin lymphoma (NHL) are types of Chronic Lymphoproliferative Disorders (CLPDs) that develop from mature B cells. Immunophenotyping and characteristic morphology are used to diagnose chronic lymphocytic leukemia. some people with chronic lymphocytic leukemia have an unusual immunophenotype which increases the probability that they may have mantle cell lymphoma (MCL), a lymphoproliferative disorder unrelated to chronic lymphocytic leukemia. To distinguish between MCL and chronic lymphocytic leukemia, our study was made and involved 70 patients who were attending the clinical pathology department at Sohag University Hospital. These patients were split into 25 cases of MCL, 25 cases of chronic lymphocytic leukemia, and 20 age- and sex-matched controls. Using flow cytometry, the expression of CD200 was assessed in bone marrow aspirate samples obtained from these patients. We found that CD200 helps distinguish between chronic lymphocytic leukemia and MCL since our data demonstrate that 24 cases of chronic lymphocytic leukemia were CD200 positive, whereas 25 cases of MCL and 20 controls were CD200 negative.

Keywords: CD200; flow cytometry; non-Hodgkin lymphoma; chronic lymphocytic leukemia; mantle cell lymphoma.

DOI : 10.21608/smj.2024.281984.1463 **Received:** April 08, 2024 **Accepted:** May 14, 2024

Published: September 01, 2024

Corresponding Author: Faten Atef Mohamed E.mail: fatenatef782@gmail.com

Citation: Faten Atef Mohamed. et al., The Use of CD200 as a diagnostic marker in Egyptian patients with Chronic Lymphoproliferative Disorders. SMJ,2024 Vol. 28 No(3) 2024: 5- 12

Copyright Faten Atef Mohamed , **et al** Instant open access to its content on principle Making research freely available to the public supports greater global exchange of research knowledge. Users have the right to read, download, copy, distribute, print or share the link Full texts

Introduction

Mature B lymphocytes are the source of Chronic Lymphoproliferative Disorders (CLPDs) which affect peripheral blood, bone marrow, and secondary lymphoid organs such as the lymph nodes and spleen. The World Health Organization (WHO) has divided such diseases into two categories: non-Hodgkin lymphoma (NHL) andchronic lymphocytic leukemia (CLL) based on genetics and immunephenotyping. [1-3] Some patients have a normal life span following the diagnosis while others only live for a few years, this indicates that the disease's course varies. Modern laboratory methods such as immunohistochemistry (IHC) and flow cytometry (FCM) have made it possible to distinguish CLL from the majority of mature B cell neoplasms. [4, 5] Unfortunately, there is a chance that mantle cell lymphoma (MCL), which shares morphological characteristics and is CD5 positive, and CLL with an unusual immunophenotype will be misdiagnosed.[6] Among all B cell lymphomas, MCL has one of the worst prognoses due to its aggressive disease course, unlike CLL which can be indolent. Incorrect diagnosis can have hazardous consequences because MCL and CLL not only have distinct prognoses but also vary in their recommended courses of the therapy. [7-9] Cytogenetic analysis or fluorescence in situ hybridization (FISH) can be used to analyze this problem by determining whether the MCL t (11;14) translocation, which results in cyclin D1 expression, is present or not. Unfortunately, not all cases of mature B cell neoplasms undergo FISH due to its high cost. As an alternative, tissue sections can be tested by using immunohistochemistry to determine the expression of cyclin D1 but this test may be false negative for MCL.[10] To distinguish between MCL and CLL with an unusual immunophenotype, additional flow cytometry markers are thus required as CD200. Some hematopoietic and non-hematopoietic cells express CD200, also known as OX-2, which is a membrane glycoprotein belonging to the immunoglobulin superfamily. The purpose of our research is to assess the use of CD200 in the differential diagnosis of MCL and CLL patients, particularly when conventional flow cytometry markers reveal an abnormal immunophenotype.

Patients and methods

Study layout

In the hematological unit of the clinical pathology department at Sohag University Hospital, fifty newly diagnosed adult CLPD patients and twenty age- and sex-matched controls participated in this study. The investigated patients were chosen based on immunophenotypic criteria for CLPDs as well as clinical, laboratory, and bone marrow aspirate results. The diagnosis was confirmed by the findings of bone marrow trephine biopsy and lymph node biopsy.

Ethical consideration

The research and ethical committee of Sohag University's Faculty of Medicine gave its approval to this study. A signed approval was given from each patient. The patients with CLPDs varied in age from 30 to 75 years old, with a mean age of 52.27 years. There were 33 males and 17 females with a male to female ratio of 1.9: 1.0.

Patients groups

Three groups represented the seventy patients that were part of the study:

There were twenty-five CLL patients in Group 1. The male to female ratio was 1.5:1, with 17 males and 8 females. With a mean age of 44.75 years, their ages varied from 35 to 71.

There were twenty-five MCL patients in Group 2. The male-to-female ratio was 2.3:1, with 16 males and 9 females. With a mean age of 59.8, they were between the ages of 38 and 75.

There were twenty age- and sex-matched controls in **Group 3**.

The following was applied to each patient:

1. Details from the clinical examination and history evaluation are on the clinical sheet.
2. A RUBY cell counter (Coulter, Electronics, USA) was used to perform a complete blood count (CBC), together with the analysis of Leishman-stained peripheral blood smears.
3. Bone marrow aspiration combined with Leishman-stained smear testing was used to determine the morphology and proportion of bone marrow lymphocytes.

4. Using a conventional panel of several chronic lymphoproliferative diseases (CD19, CD5, CD20, CD22, CD23, SIgM, CD79b, FMC7, κ, and l light chains) and CD25 for groups 1 and 2 immunophenotyping was performed on a flow cytometer.
5. For groups 1 and 2, lymph node biopsies were utilized to find cyclin D1 and t [11,14].
6. Using flow cytometry, CD200 was performed on the patient's bone marrow samples. A Coulter Epics XL 3-color flow cytometer (Coulter Electronics) was used for the flow cytometry. When a marker was expressed in cells at a rate of 20% or above, it was considered positive.

2.4 Analyzing data

With a cut-off of greater than 20% over the matching isotypic control the expression was reported as a percentage. Patients were divided into two groups based on CD200 marker expression: those with a value of < 20% expression were considered negative and those with a value of >20% expression were positive.

2.5 Analytical statistics

IBM-SPSS, version 19 (IBM, Chicago, Illinois, USA) was used to analyze the data.

Results

Seventy patients were included in our study, divided into three groups: twenty-five patients with mantle cell lymphoma (group II), twenty-five patients with chronic lymphocytic leukemia (group I), and twenty age- and sex-matched controls (group 3). Every patient was presented to the clinical pathology department's hematological unit at Sohag University Hospital. The Sohag Faculty Committee for Research Ethics gave its approval for this work.
Blood and bone marrow samples from each of the three patient groups that were included in the study were taken to examine the role of CD200 in the differential diagnosis between MCL and CLL. CBC and chemical testing were performed on blood samples. Following that, samples of bone marrow from groups 1 and 2 were submitted to a complete flow cytometric panel assay and a CD200 test for the three groups
According to our findings, 24 patients with chronic lymphocytic leukemia (Group 1) are CD200 positive, all patients with mantle cell lymphoma (Group 2), and the control groups (Group 3) are CD200 negative.

Discussion.

An essential method for the diagnosis of chronic lymphoproliferative diseases such as CLL is flow cytometry immunophenotyping. The so-called Matutes Score was created more than 20 years ago and is still in use by many laboratories. It is based on the expression of CD5, CD23, FMC7, SmIg, and CD22/CD79b by leukemic cells. [11] Recently, many novel markers that are thought to be produced by CLL cells have been discovered. One of them is CD200, a member of the superfamily of immuneoglobulin receptor membrane proteins, which has been proposed to be selective for CLL.[12, 13]
Our findings confirm the importance of CD200 in the diagnosis of CLL phenotype and are consistent with other studies. Since CD200 is almost absent in MCL and positive in CLL numerous studies have concentrated on its function in the differentiation between the two diseases. [14]
To conclude, CD200 is a sensitive and specific marker that may be used in flow cytometry immunophenotypic analysis to distinguish between CLL and MCL. It is especially helpful in identifying atypical CLL.

References

1. Abramson J. The spectrum of double hit lymphomas:Hematology/Oncology Clinics.2016. 30(6).1239-1249.

2. Hallek M. Chronic lymphocyticleukemia: 2017 updateon diagnosis, risk stratification,and treatment:American journal of hematology.2017. 92(9).946-965.

3. Swerdlow S, Campo E, Pileri S, Harris N, Stein H, Siebert R *et al*. The 2016 revision of the World Health Organization classification of lymphoid neoplasms Journal of Hematology [Blood].2016. 127(20).2375-2390.

4. Craig F, Foon K. Flow cytometric immunophenotyping for hematologic

neoplasms:Journal of Hematology[Blood].2008. 111(8).3941-3967.

5. Hallek M, Cheson B, Catovsky D, Caligaris-Cappio F, Dighiero G, Döhner H *et al*. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute–Working Group 1996 guidelines:Journal of Hematology[Blood].2008. 111(12).5446-5456.

6. Gong J, Lagoo A, Peters D, Horvatinovich J, Benz P, Buckley P. Value ofCD23 determination by flowcytometry indifferentiating mantlecell lymphomafrom chronic lymphocytic leukemia/small lymphocyticlymphoma:American journal of clinical pathology.2001. 116(6).893-897.

7. Hallek M, Fischer K, Fingerle-Rowson G, Fink A M, Busch R, Mayer J *et al*. Addition of rituximab to fludarabineand cyclophosphamide inpatients with chronic lymphocytic leukaemia: arandomised, open-label,phase3 trial The Lancet.2010. 376(9747).1164-1174.

8. Mckay P, Leach M, Jackson R, Cook G, Rule S, Haematology B C F S I. Guidelines for the investigation and management of mantle cell lymphoma Haematology British journal 2012. 159(4).405.

9. Wierda W, Zelenetz A, Gordon L, Abramson J, Advani R, Andreadis B *et al*. NCCN guidelines insights: chronic lymphocytic leukemia/small lymphocytic lymphoma, version 1.2017.Journal of the National Comprehensive Cancer Network:Journal of Hematology[Blood].2017. 15(3).293-311.

10. Remstein E D, Kurtin P, Buno I, Bailey R, Proffitt J, Wyatt W *et al*. Diagnostic utility of fluorescenceinsituhybridization inmantle-cell lymphoma: Haematology British journal 2000. 110(4).856-862.

11. Estella M, Owusu-Ankomah K, Morilla R, Houlihan A, Que T, Catovsky D. The immunological profile of B-celldisorders and proposal of a scoringsystem for the diagnosis of CLL:Leukemia.1994. 8(10).1640.

12. Thomas K, Wittmann V, Bücklein V, Lichtenegger F, Pasalic Z, Hiddemann W *et al*. Diagnosis of CLL revisited: increased specificity by amodified five-markerscoring systemincluding CD 200: Haematology British journal 2017. 179(3).480.

13. Sandes A, De Lourdes Chauffaille M, Oliveira C R M, Maekawa Y, Tamashiro N, Takao T T *et al*. CD200 has an important role in the differential diagnosisof mature B-cellneoplasms by multiparameterflow cytometry:Cytometry Part B: Clinical Cytometry.2014. 86(2).98-105.

14. Starostka D, Kriegova E, Kudelka M, Mikula P, Zehnalova S, Radvansky M *et al*. Quantitative assessment of informative immunophenotypic markersincreases the diagnostic value ofimmunophenotyping in mature CD5-positiveB-cell neoplasms:Cytometry Part B: Clinical Cytometry.2018. 94(4).576-587.