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The Utility of CD200 Expression in the Differentiation of Mantle Cell Lymphoma from B-Cell Chronic Lymphocytic Leukaemia: A Single Centre Experience

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Background

Mature B-cell lymphoproliferative disorders that present with a leukemic phase may have overlapping morphological and immunophenotypic features. Accurate diagnosis is essential to determine prognosis and therapy.

B-cell chronic lymphocytic leukaemia (B-CLL) and mantle cell lymphoma (MCL) both express CD5 but usually have divergent clinical courses. Conventional markers are able to discriminate in many cases but a significant proportion of cases require more detailed analysis.

CD200 is a membrane glycoprotein that has been reported to differentiate between B-CLL and MCL. Rapid assessment of CD200 status of tumours using monoclonal antibodies can be made using flow cytometry.

Objective

We prospectively assessed the utility of this antibody in a single centre, servicing haematology units in North London.

Method

Over a 12 month period we prospectively assessed the expression of CD200 (Clone MRC OX-104, BD Pharmingen) on neoplastic cells of patients presenting with mature B-cell lymphoproliferative disorders (LPD).

EDTA anti-coagulated peripheral blood and bone marrow underwent a lyse/wash technique before being acquired on a BD FACSCanto2 flow cytometer equipped with DIVA 6.1.2 software.

A lymphoid gating strategy was used to analyse the data and expression of more than 20% of nucleated cells referenced to a negative internal control was considered positive.

A diagnosis was made using all available data according to the WHO classification of haematopoietic tumours, including the 5 point CLL score.

The predictive value of CD200 expression was subsequently assessed.

Results

	B-CLL (n= 78)	MCL (n= 7)	CD5 –ve LPD (n=15)
M:F	49:29	3:4	6:9
MEDIAN AGE (years, range)	72 (35-92)	64 (53-72)	64 (29-86)
CD 200 % (mean, median, SD)	65, 67, 18.1	2, 1, 2.2	5.6, 2, 6.2

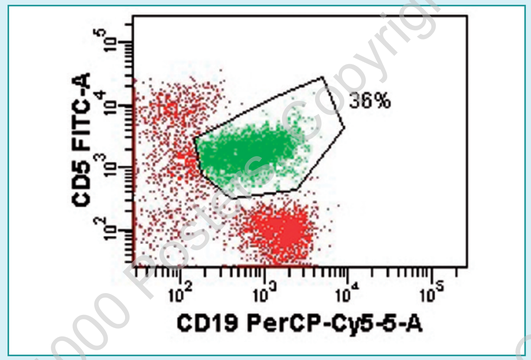
The specificity of CD200 negativity in the setting of a CD5 positive B-cell clone was 100% for MCL *(Figure 1a-b).* Cyclin D1 status was positive in 5/7 patients with MCL and in 2/7 patients this was unavailable.

The sensitivity of CD200 positivity in the setting of a CD5 positive B-cell clone was 98.7% for CLL *(Figure 2a-b)*. One patient with CLL had negative CD200 expression (19%), however this patient was partly treated.

The positive predictive value of CD200 for CLL was 98.7% as one patient with CD5 negative LPD had CD200 expression of 20%.The Pearson's correlation coefficient was 0.99.

Figure 1a,b.

1a: MCL: Staining with CD5 and CD19: double positive cells are marked in green



1b: MCL: Staining with CD22 and CD200 showing CD200 negative cell population

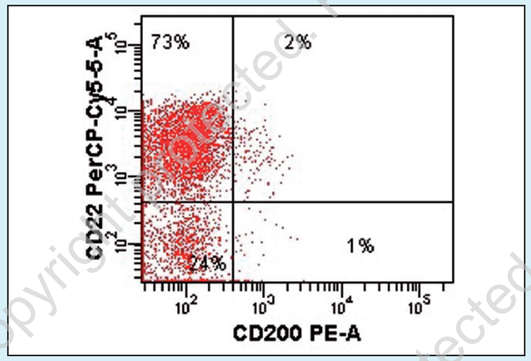
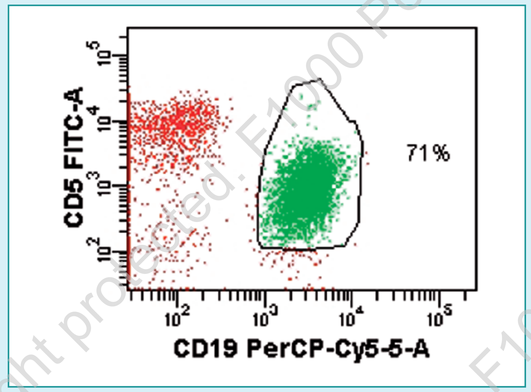
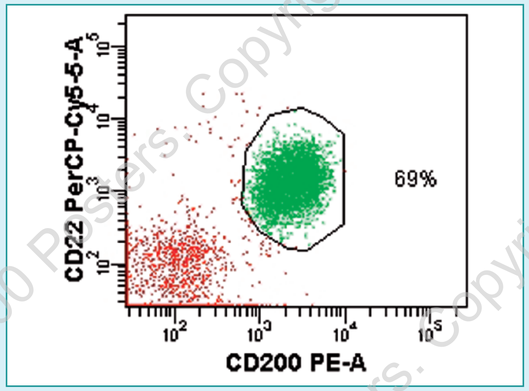


Figure 2a,b.

2a: B-CLL: Staining with CD5 and CD19: double positive cells are marked in green



2b: B-CLL: Staining with CD22 and CD200: double positive cells are marked in green



Conclusions

- Our results confirm CD200 expression in the neoplastic cells of patients with B-CLL but not in MCL with minimal expression in CD5 negative B-cell LPD.
- This antigen may contribute to the accurate differentiation between B-CLL and MCL in patients presenting with the diagnostic problem of a CD5 positive LPD.
- We propose to add CD200 to our diagnostic B-cell lymphoma panel. Further studies are needed to determine whether CD200 could replace other immunophenotypic strategies currently used in this situation, such as CD23, FMC7 and intensity of CD22/CD79b expression.

Conflict of interest: I certify that there is no conflict of interest for any of the authors to disclose.