IMMUNOHISTOCHEMESTRY EXPRESSION OF MICA, MICB AND EPSTEIN- BARR VIRUS IN LYMPH NODE BIOPSY OF PATIENTS WITH DE NOVO NON-HODGKIN LYMPHOMA

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BACKGROUND

NK and Tgd cells are part of the innate immune defense system against neoplasms[1], whose activating receptor NKG2D[2] and its ligands MIC-A and MIC-B have been studied regarding their regulation and function [3,4]. We recently found an increase soluble expression of MICA and MICB in patients with de novo non-Hodgkin's lymphoma, negatively affecting the patient's immune response[5]. Now we want to evaluate the expression of MIC-A and MIC-B ligands directly at the site of injury. On the other hand, EBV is the etiological agent most related to the development of cancers, mainly lymphomas, however, in our country there are still no data that evaluate the presence of EBV infection in neoplastic cells of patients with non-Hodgkin's lymphoma and its possible relationship with the expression of MICA and MICB.

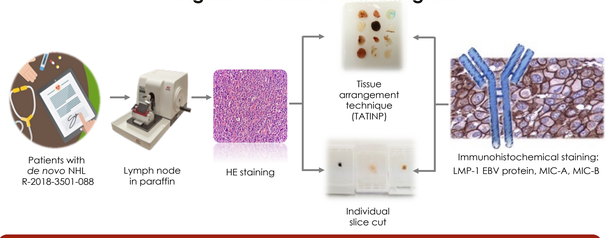
OBJETIVE

To determine the expression of MICA and MICB in the lymph node and whether Epstein Barr virus infection in patients with de novo non-Hodgkin's lymphoma favors the soluble expression of MIC A and MIC B.

MATERIALS & METHODS

Sections were obtained from the paraffin-embedded block of the neoplastic lymph node of each patient to determine the presence of EBV by LMP-1 expression, as well as the expression of MIC-A, MIC-B by immunohistochemistry (figure 1).

Figure 1. General work diagram



RESULTS

A total of 48 patients with a diagnosis confirmed by immunohistochemistry of *de novo* non-Hodgkin's lymphoma were analyzed, from them, 30 paraffin blocks were worked on, 16 were DLBCL, 6 FL, 5 Mycosis fungoides, 1 MCL, 1 NLTCL, and 1 ALCL.

EBV infection was detected by LMP-1 protein expression in 57% (17/30), all cases of mycosis fungoides were positive for EBV and all cases of follicular lymphoma were negative (figure 2, 3).

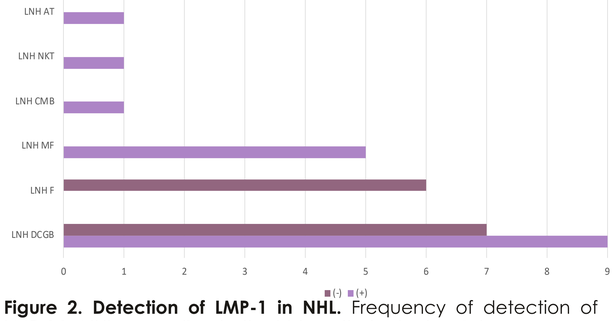


Figure 2. Detection of LMP-1 in NHL. Frequency of detection of LMP-1 in NHL according to the histopathological variety.

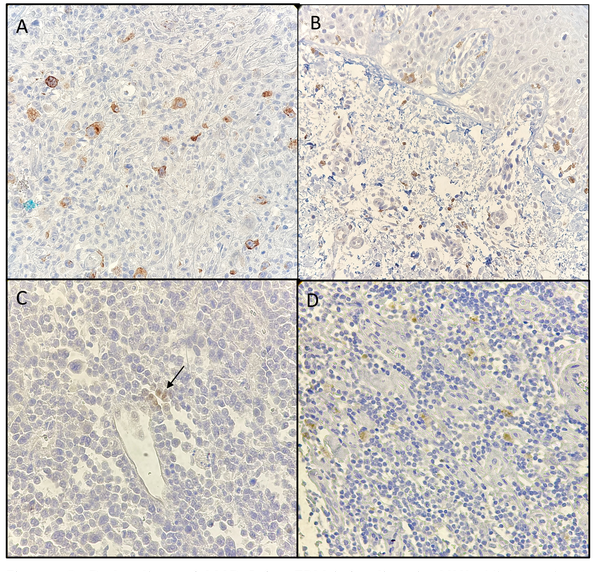


Figure 3. Detection of LMP-1 for EBV infection in NHL. Histological sections of different NHL showing positive cells for the LMP-1 protein: A) Positive control: Classic Hodgkin lymphoma, B) Mycosis fungoides C, D) DLBCL. Peroxidase-conjugated polymer immunohistochemical technique, 40x.

In all the 30 cases analyzed by IHC, the staining was positive for the presence of MIC-A as well as for MIC-B (figure 4), a staining cytoplasmic and extracellular pattern for both markers was revealed.

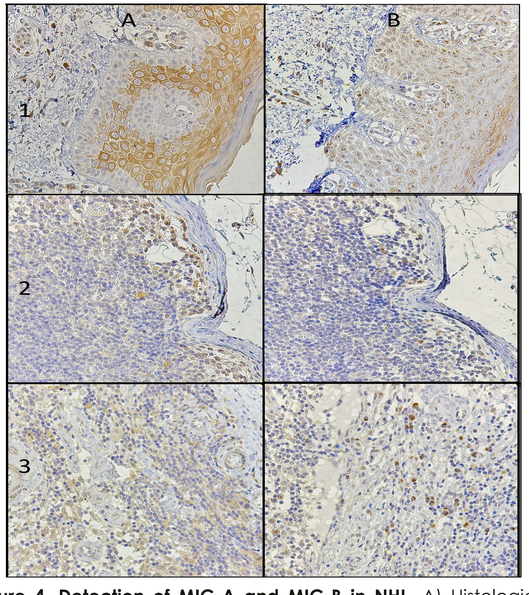


Figure 4. Detection of MIC-A and MIC-B in NHL. A) Histological sections of different NHL showing positive cells for MIC-A, B) MIC-B; 1) MF, 2) FL, 3) DLBCL Peroxidase-conjugated polymer immunohistochemical technique 40x.

CONCLUSIONS

I the staining pattern for MIC-A was stronger and more massive than for MIC-B, which could indicate a greater expression of MIC-A than MIC-B in our patients, which is consistent with what was reported in the serology of these patients in our previous work.

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1)Kunzmann V, Wilhelm M. Anti-lymphoma effect of γδ T cells. Leukemia & Lymphoma. 2009; 46: 5, 671-680; 2) García DA, Pérez P, García L, Cid-Arregui A, Aristizabal F. Gene expression of mica, micb and ulbp (1-6) ligands of the NKG2D receptor of natural killer cells and metalloproteinases adam10, adam17 and mmp14 cells lines of cervical cancer. Rev. Colomb. Biotecnol. 2019; 21, 29-38; 4) Dhar P, Wu J. NKG2D and its ligands in cancer. Curr Opin Immunol. 2018: 51: 55–61; 5) Olivas-Bejarano AC. MIC-A y MIC-B solubles, y expresión de NKG2D en células NK, NKT y linfocitos T gamma-delta en pacientes con Linfoma No Hodgkin de novo y postquimioterapia. Tesis de maestría, ENCB-IPN. 2019.