

Cloning and Sequencing of Blood Protein LMP1 in Lymphoma NK Patients

Mohamad Adnan Halabi*

*Medical Laboratory Department, Faculty of Health, Holy Family University, Batroun, Lebanon.

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ABSTRACT

Natural killer/T-cell lymphomas are rare and aggressive diseases whose development is rapidly fatal. These lymphomas are associated with Epstein-Barr virus (EBV) in 100% of cases. Recently, a treatment combining L-asparaginase with conventional chemotherapy has increased significantly the survival of patients. Our work consists on characterizing EBV (particularly LMP1 modifications) in the blood of NK lymphoma's patients to see if a particular strain is associated with this disease and/or with the sensitivity to treatment.

We studied samples of 13 patients with NK lymphoma before treatment's initiation and of 9 patients before and during treatment. EBV strain typing was performed on the EBNA2 gene. The entire LMP1 gene of each sample was cloned; 6 clones were sequenced and compared to B95-8 strain for type 1 or to Jijoye strain for type 2. An EMSA was made to test the ability of different strains to activate the NFκB factor.

Type 1 strain was found in most cases. In comparison to B95-8, three different strains regarding the LMP1 gene were found: without deletion, with a deletion of 15 bp or 30 bp. 11 patients harbored a deleted strain before treatment. Deleted strains seemed to be associated with a poor life expectancy and a limited or non-efficacy of treatment. For 4 patients, an association of diverse strains was detected, principally during treatment.

In conclusion, the majority of patients in this series have a type 1 virus, which is found in the general population.

For the vast majority of patients (17/20), cloning, sequencing of six different clones has highlighted one type of virus. Deleted viruses were great majority: they were found in 14/17 patients for type 1, 82.3% and in 100% of case the virus type 2. This finding is important considering that the virus deleted for the LMP1 gene is more aggressive than others, as reported in the literature.

Corresponding author: Mohamad Adnan Halabi, Medical Laboratory Department, Faculty of Health, Holy Family University, Batroun, Lebanon, E-mail: adnan.halaby@gmail.com

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