Epstein-Barr virus: beyond infectious mononucleosis

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Epstein-Barr virus (EBV) is an ubiquitous human herpes virus that has been identified as the etiologic agent of infectious mononucleosis, a self-limited lymphoproliferative disease and, in general, is self-limiting in the immunocompetent host. The disease has a benign course. EBV has also been identified or associated with epithelial and lymphoid malignancies in immunocompetent patients as well as those immunocompromised, such as in the cases of nasopharyngeal carcinoma, AIDS-associated lymphoma, and Hodgkin’s disease, among others.

In recent times and closely linked to technological advances, descriptions of lymphoproliferative diseases (LPD) associated with EBV (LPD-EBV) in posttransplant patients is more frequent.1-4 The overall incidence of LPD-EBV varies from 1-20%, depending on type of organ transplanted, patient’s age, serological status against EBV of the receptor and donor, as well as the type and aggressivity of the immunosuppression provided. It is a rare complication in patients subjected to bone marrow allogenic transplants (1-3%) but usually has a fatal course. LPD-EBV can appear in a variable posttransplant time frame (1 month to years), although the majority of the cases are seen in the first posttransplant year. The greatest risk factor is T-cell depletion due to the use of antithymocyte γ-globulin for disease prophylaxis graft vs. host disease because it originates from an overgrowth of B cells, latently infected because of the absence of a competent immune system. Despite the latter, there are many complications associated with malignant T-cell diseases.3-6

Measurement of EBV DNA load has been used to attempt to characterize the natural history of EBV disease; however, standardization of the various measures to establish the predictive value of viral load in relation to specific clinical situations...
is required. The use of polymerase chain reaction (PCR) techniques for detection and quantification of the virus has the advantage of high sensitivity and reproducibility because there is the possibility of determining the dynamics of viral proliferation, monitor treatment response and seek to differentiate between latent and active infection.

It has recently been suggested that frequent monitoring of EBV DNA load in real-time PCR (RT-PCR) can be used as an early marker in treatment options in cases of active infection, especially when a rapid course of a LPD-EBV is suspected. Some case reports have shown that levels of EBV DNA sometimes do not reach significant values despite the existence of active disease; therefore, close evaluation of the clinical condition should always be carried out.7-9

In addition to problems of interpretation of results of the RT-PCR studies related to the time of infection of the patient clinically, various obstacles must be faced in the laboratory with respect to carrying out the study procedures. Variability exists in the results when laboratory tests already on the market have been evaluated, compared with those done locally in each “home” laboratory, sometimes due to differences in reagents, denaturation temperature, etc. This requires laboratories to verify the reproducibility of the trials with inter- and intra-assay evaluations and with strict controls of the different variables, following established protocols of the laboratory equipment manufacturers.

In this issue of the Boletín Medico del Hospital Infantil de Mexico, Parra-Ortega et al. propose the detection of changes in the denaturation temperature (specifically its reduction) in some samples of patients infected with EBV.10 This finding introduces a series of questions about the clinical significance that a possible mutation may represent. Obviously, this phenomenon must be reproduced and complementary studies must be extended that will be added to the resolution of problems in EBV infection.

For pediatricians, it is a fact that EBV is more than just infectious mononucleosis.

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References