Hepatitis C virus and Epstein-Barr virus: dual infection or atypical antibody response

José Gutiérrez[1]* and Manuel Rodríguez-Iglesias[2]

[1]Department of Microbiology, School of Medicine, University of Granada, St Cecil Hospital, 12 Av. Madrid, E-18012 Granada, Spain, and [2]Department of Microbiology, University Puerto Real Hospital, University of Cadiz, Cadiz, Spain (*Reprint address)

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Abstract

Positive serological reactions against hepatitis C virus (HCV) appeared in the course of Epstein-Barr virus (EBV) infectious mononucleosis. In 429 consecutive patients with high levels of transaminases, 28 patients with EBV primary infection were found. The presence of anti-HCV antibodies and HCV RNA was studied in these subjects. In seven patients anti-HCV antibodies (C33 and C22c RIBA bands) were detected, but all were polymerase chain reaction (PCR) negative. These results may have been due solely to a HCV infection or were an atypical response to HCV in the course of infectious mononucleosis.

Introduction

In the course of acute infection by Epstein-Barr virus (EBV) immunoglobulin M (IgM) to EBV and other infectious agents can be produced (Fikar *et al.*, 1994; Gutiérrez and Maroto, 1995; Gutiérrez *et al.*, 1997a; Gutiérrez *et al.*, 1997b; Gutiérrez *et al.*, 1999). In patients who are immunosuppressed (transplantations, AIDS, haemodialysis) it is frequently the case that dual infection of EBV and hepatitis C virus (HCV), is diagnosed through the detection of specific antibodies (Lennette, 1995; Wilber, 1995).

This short communication records the appearance of positive serological reactions against HCV in the course of EBV infectious mononucleosis.

Materials and methods

In patients (429 *in toto*) with high levels of transaminases 28 patients with Epstein-Barr virus (EBV) primary infection were found. The infection was defined by (1) the presence of IgM against a pool of antigens comprising Epstein-Barr nuclear antigen (EBNA), membrane antigen (MA), early antigen (EA), and viral capsid antigen (VCA) (ELISA; Enzygnost EBV, DadeBehring Laboratory, Germany); (2) no detection of IgM to cytomegalovirus (ELISA; Enzygnost Cytomegalovirus, DadeBehring Laboratory, Germany) and human herpes virus 6 (ELISA; PanBio Laboratory, Australia); and (3) no immunoglobulin G (IgG) to EBNA present (ELISA; Incstar Laboratory, U.S.A.). The patients were studied in the presence of anti-HCV antibodies for screening (ELISA; Bioelisa HCV, Biokit

Laboratory, Spain) and with confirmatory tests (Immunoblot, RIBA3, Ortho Laboratory, U.S.A.), and the presence of HCV RNA (Amplicor HCV, Roche Diagnostics Laboratories, Switzerland) was investigated.

Briefly, serum samples were tested for HCV RNA by reverse transcription-polymerase chain reaction (PCR), with primers derived from the highly conserved 5'-untranslated region. The specificity of the amplifications was confirmed by hybridization. Negative and positive controls were included in each run (four controls for each set of 20–25 clinical samples). The sensitivity of the assay was 100 RNA copies by 100 µl of serum.

Results and discussion

In seven patients anti-HCV antibodies (C33 and C22c RIBA bands) were detected but all were PCR negative. It is not known whether these results were due to an HCV infection solely or an atypical response to HCV in the course of infectious mononucleosis. We must emphasize that in hepatitis differential diagnoses can result from serological reactions to HCV and EBV. These may be due to (1) superinfection by EBV in a patient with previous infection by HCV, and (2) a false antibody response to HCV by B lymphocyte non-specific clonal stimulation, in a manner analogous to that which has occurred with other viral infections. In the absence of any patient history of antibody response to HCV, the clinical and serological follow-up alone does not permit these two possible causes of infection to be differentiated.

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