We report a case of acute cytomegalovirus (CMV) infection with positive HEV and Epstein–Barr virus (EBV) serology. No patients have been reported positive for immunoglobulin (Ig)M antibodies to all three viruses. This patient had progressively increasing titres of IgM antibody for CMV, HEV and EBV. Only CMV DNA was detectable before antiviral treatment. After antiviral treatment, the patient recovered completely. At day 180 the CMV IgG test had converted to positive with CMV IgM (+), EBV IgM (-) and HEV IgM (-). Our report indicates that dependence upon serology alone is unreliable in the diagnosis of acute CMV, EBV and HEV infections. The diagnosis of CMV, HEV and EBV should be based on a combination of clinical features, serology and confirmatory PCR testing.

Cytomegalovirus (CMV) is a common virus that can infect almost anyone, but it rarely produces symptoms in immunocompetent people, and is an infrequent cause of viral hepatitis [1]. Detection of specific immunoglobulin (Ig)M antibody (anti-CMV IgM) is widely used for laboratory diagnosis [2]. Herein, we report a case of acute CMV infection with positive HEV and EBV serology. This patient had progressively increasing titres of IgM antibody for CMV, HEV and EBV. Only CMV DNA was detectable before antiviral treatment. After antiviral treatment, the patient recovered completely.

A 28-year-old Chinese woman presented to our hospital with fever and abnormal liver function (alanine aminotransferase [ALT] 74 [reference range 7–40 U/l]). Symptoms that included high fever, malaise, myalgia, sore throat, chills and headache, had developed 2 weeks before. Her temperature could be as high as 40°C at night; no rash was evident. The patient had been treated with several antibiotics, but the symptoms had not improved. She had no history of immunodeficiency or immune-inhibitory drug use. No endocrine, metabolic or autoimmune abnormalities were found. The patient’s partner, who had shared the same food and activities, had not developed any symptoms.

On admission (14 days after onset), physical examination revealed a temperature of 40°C, without skin rash or jaundice. Blood examination revealed normal white blood cell count and absolute lymphocyte count, accompanied by slightly low red blood cell and platelet counts. She had normal proportions of circulating CD3+, CD4+ and CD8+ T-cells. C-reactive protein (CRP) was 28.0 (reference range 0–3.0 mg/l), lactate dehydrogenase 589 (reference range 109–245 U/l), ALT 82 (reference range 7–40 U/l), total bilirubin (Tbil) 5.4 (reference range 0–17 µmol/l) and direct bilirubin (Dbil) 3.3 (reference range 0–5.4 µmol/l). The patient had normal thyroid stimulating hormone (TSH) levels and tests did not reveal anti-DNA, anti-nuclear or anti-thyroglobulin antibodies. The HIV test was negative. Serological testing on admission showed CMV IgM (+), CMV IgG (+), EBV IgM (+), HEV IgM (+), HEV IgG (+; Figure 1). At the same time the test for virus in blood by polymerase chain reaction (PCR) showed detectable CMV load (DNA 2,480; reference range 0–2,000 IU/ml) and negative results for EBV DNA and HEV RNA.
Based on the clinical features and laboratory test results, a diagnosis of CMV acute infection was considered. The patient received ganciclovir at 5 mg/kg of body weight intravenously from day 16. The peak of body temperature had decreased on day 17 and from day 18 the patient had a normal temperature. Serological testing was applied again at day 17. The CMV IgM, EBV IgM and HEV IgM tests were still positive, and the titre of antibodies were increasing. However, the CMV DNA was now below detectable levels. Tests for EBV DNA and HEV RNA were still negative. The patient fully recovered and was discharged from hospital at day 27 after onset. The patient was followed up for more than 6 months, without recurrence of symptoms. The CMV IgM, EBV IgM and HEV IgM tests were still positive at day 47. At day 180 the CMV IgG test had converted to positive with CMV IgM (+), EBV IgM (-) and HEV IgM (-).

Infectious mononucleosis can present as elevated IgM titres to both CMV and EBV [3]. HEV infected patients can show false reactivity to CMV or EBV according to diverse sources of data [4–6]. A high degree of EBV and CMV cross-reactivity was reported, with 33.3% and 24.2% of HEV-IgM-positive samples also testing positive for EBV and CMV IgM [6], respectively. However, no patients have been reported positive for IgM antibodies to all three viruses. Polyclonal stimulation of memory B-cell clones and immunological cross-reactivity might cause problems when IgM tests are positive for all three [6]. Overall, a high level of HEV, EBV and CMV IgM cross-reactivity has been reported, indicating that dependence upon serology alone is unreliable in the diagnosis of acute CMV, EBV and HEV infections. The diagnosis of CMV, HEV and EBV should be based on a combination of clinical features, serology and confirmatory PCR testing.

Acknowledgements

We thank Huijun Mao, Jinhiao Peng and Daihong Chen (Medical Inspection Department, Shanghai Public Health Clinical Center Affiliated to Fudan University, Shanghai, China) for expert technical assistance. This work was supported by grants from SHAPHC (KSF0640 and RCJP19).

Disclosure statement

The authors declare no competing interests.

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