J Vector Borne Dis 49, September 2012, pp. 193–194

Case Report

Bradycardia in a patient with Crimean-Congo hemorrhagic fever related to ribavirin treatment

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Key words Bradycardia; Crimean-Congo hemorrhagic fever; ribavirin

Crimean-Congo hemorrhagic fever (CCHF) has been reported from more than 30 countries around the world. Ribavirin is the only drug which has *in vitro* effect on CCHF virus. Although there is a debate on the clinical benefit of ribavirin, some experts from the endemic areas strongly recommend ribavirin in patients with CCHF based on *in vitro* activity and rare adverse events with short-term use[1]. Here, we report bradycardia in a patient with CCHF related to high dose ribavirin administration.

Case history

A 57-yr old man was admitted to hospital with fever, fatigue and epistaxis. He was living in an endemic area of CCHF and had history of tick bite four days previously. The physical examination was unremarkable except fever of 38.2°C. Laboratory tests were as follows: White blood cells (WBC) 1.9 x 10^9/l (neutrophils 90%); hemoglobin was 11.3 g/l; thrombocyte count was 128 x 10^9/l. The level of aspartate aminotransferase (AST) was 97 U/l; alanine aminotransferase (ALT) was 55 U/l; lactate dehydrogenase (LDH) was 510 U/l; Gama-glutamyl transferase (GGT) was 20 U/l; total bilirubin was 0.7 mg/dl; prothrombin time was 13 sec; activated partial thromboplastin time was 35 sec; and International Normalized Ratio (INR) was 1.18. The renal function tests and serum electrolytes were in normal range. On third day of follow-up thrombocytes decreased to 43 x 10^9/l and then 18 x 10^9/l. AST and ALT increased to 431 and 189 U/l. Fever continued to spike and ribavirin (2 g loading then 4 g/day maintenance) was started with thrombocyte replacement. After three days of ribavirin treatment bradycardia (heart rate of 30–40/min) developed. Electrocardiograpy was normal except sinusoidal bradycardia. Echocardiography and ambulatuar holter record for 24 h did not reveal any pathologic finding. Serum electrolytes were in normal range. Ribavirin was stopped on fourth day and the heart rate became normal one day later. Clinical diagnosis of CCHF was confirmed by ELISA test that was performed at Refik Saydam National Public Health Agency (RSHM), the reference laboratory for CCHF. On the sixth day of admission fever was resolved and laboratory findings improved as WBC 3.7 x 10^9/l; hemoglobin 13.3 g/l; thrombocytes 166 x 10^9/l; AST: 127 U/l; ALT: 131 U/l; ALP: 89 U/l; GGT: 78 U/l; and LDH: 387 U/l. He was discharged in good condition on the 10th day of hospitalization.

DISCUSSION

Cardiac involvement was reported in patients with CCHF based on echocardiography findings[2]. Two recent studies evaluated the electrocardiography of 49 adult and 23 pediatric patients with CCHF. Although T-wave negativity or bundle branch block was detected in adult patients, rhythm abnormality was not detected in any patient[3, 4]. In our patient, cardiac involvement was ruled out with completely normal echocardiography. The main adverse events related to high dose ribavirin were reversible hemolytic anemia and hypomagnesemia in patients with hemorrhagic fever with renal syndrome (HFRS). Bradycardia was reported in three of 34 patients who received high dose ribavirin. However, bradycardia was also detected as the manifestation of the disease in 19–73% of individuals with HFRS, and in this setting it is very difficult to make a differential diagnosis either bradycardia developed because of the cardiac involvement of HFRS or related to ribavirin treatment[5]. Rhythm abnormality was not detected as an adverse effect in the studies which evaluated the role of oral or intravenous ribavirin in the treatment of CCHF[1, 6, 7]. To the best of our knowladge, this is the first case reporting bradycardia related to ribavirin treatment in a patient with CCHF. It can be concluded that physicians who use ribavirin in the treatment of CCHF should be careful about the rare adverse events related to this drug.

Conflicts of interest: None related to this study for all authors.
Funding source: None

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Received: 5 March 2012 *Accepted in revised form:* 18 July 2012