

Case Report

Terlipressin Induced Severe Symptomatic Reversible Septal Coronary Artery Spasm in Hepato-Renal Syndrome

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Abstract: Terlipressin is a long acting vasopressin analogue used in cirrhosis patients for management of hepatorenal syndrome and variceal bleeding. Terlipressin is not without side effects and sometimes, life threatening complications do occur. Here we present a cirrhotic patient who, after receiving Terlipressin developed reversible cardiac ischemia, documented real time on electrocardiography.

Keywords: Terlipressin, vasopressin, cirrhosis, portal hypertension, ischemic heart disease, electrocardiogram, hepatorenal syndrome.

INTRODUCTION

Terlipressin is a synthetic long-acting analogue of vasopressin, which is widely used in the treatment of cirrhotic patients with variceal bleeding and hepatorenal syndrome. It is a vasoconstrictor with preferential action on the splanchnic circulation, lowering portal venous pressure. The safety profile of terlipressin is better than vasopressin. However, vasoconstrictor effects on the systemic circulation result in ischemic complications in <5% of cases such as bradycardia, cardiac ischemic events, stroke, skin necrosis and bowel gangrene. Here we present a cirrhotic patient who, after receiving Terlipressin developed reversible cardiac ischemia, documented real time on electrocardiography.

CASE REPORT

A 66-year-old obese compensated cirrhotic woman with hypothyroidism presented with history suggestive of acute on chronic liver failure after 4 days of prodromal symptoms in the form of high grade fever, myalgia and diarrhea followed by progressive cholestatic jaundice and abdominal distension since 3 weeks. At admission she was found to be oriented to person, but not to place and time, pale, deeply icteric with asterixis, bilateral pedal edema, multiple ecchymosis over the abdominal wall and the thighs with a difficult to palpate abdomen due to morbid obesity. Investigations revealed serology positive for acute hepatitis E virus infection with liver function tests showing total bilirubin 42.2 mg/dL (normal 0.3 – 1.2), direct bilirubin 28.8 mg/dl (0 – 0.2), alanine transaminase 1022 IU/L (10 – 40), aspartate

transaminase 766 IU/L (5 – 40), serum alkaline phosphatase 128 IU/L (32 – 92), serum gamma glutamyl transferase 493 IU/L (7 – 64), total serum protein 5.2 g/dL (6 – 8), serum albumin 1.6 g/dL (3.5 – 5.2), international normalized ratio 6.1, plasma ammonia 433 µg/dL (12 – 60), blood urea 188 mg/dL (15 – 40), serum creatinine 2.21 mg/dL (0.2 – 1), serum uric acid 5.9 mg/dL (2.5 – 7), serum sodium 122 mmol/L (136 – 145), serum potassium 4.1 mmol/L (3.5 – 5), with normal urine routine and microscopy and urine spot sodium of 8 mmol/L (18 – 214). In view of deranged renal function, the patient was initially administered intravenous 20% human albumin, 30 to 40 g over 36 to 48 hours without improvement in serum creatinine or urine output. She was then started on intravenous Terli pressin infusion for hepato-renal syndrome (HRS) type 1, at a rate of 2 mg per 24 hours with prior confirmation of a normal baseline electrocardiogram (EKG, Figure 1A) and echocardiography. Three hours later, the patient complained of severe left sided precordial pain with a positive Levine sign. An EKG done at the time revealed inversion of T wave in lead V2 (Figure 1B) which was not evident at baseline. Considering coronary vasospasm affecting the left anterior descending arterial region (septal), Terlipressin infusion was stopped immediately and serial EKG's were taken at 5 and 30 minutes. The former EKG showed flattening of T waves in V2 (Figure 1C), followed by normal upright T waves in the latter (Figure 1D), suggestive of dynamic changes towards baseline after Terlipressin stoppage.

The patient was then started on Noradrenaline infusion

as a second line agent for management of HRS.

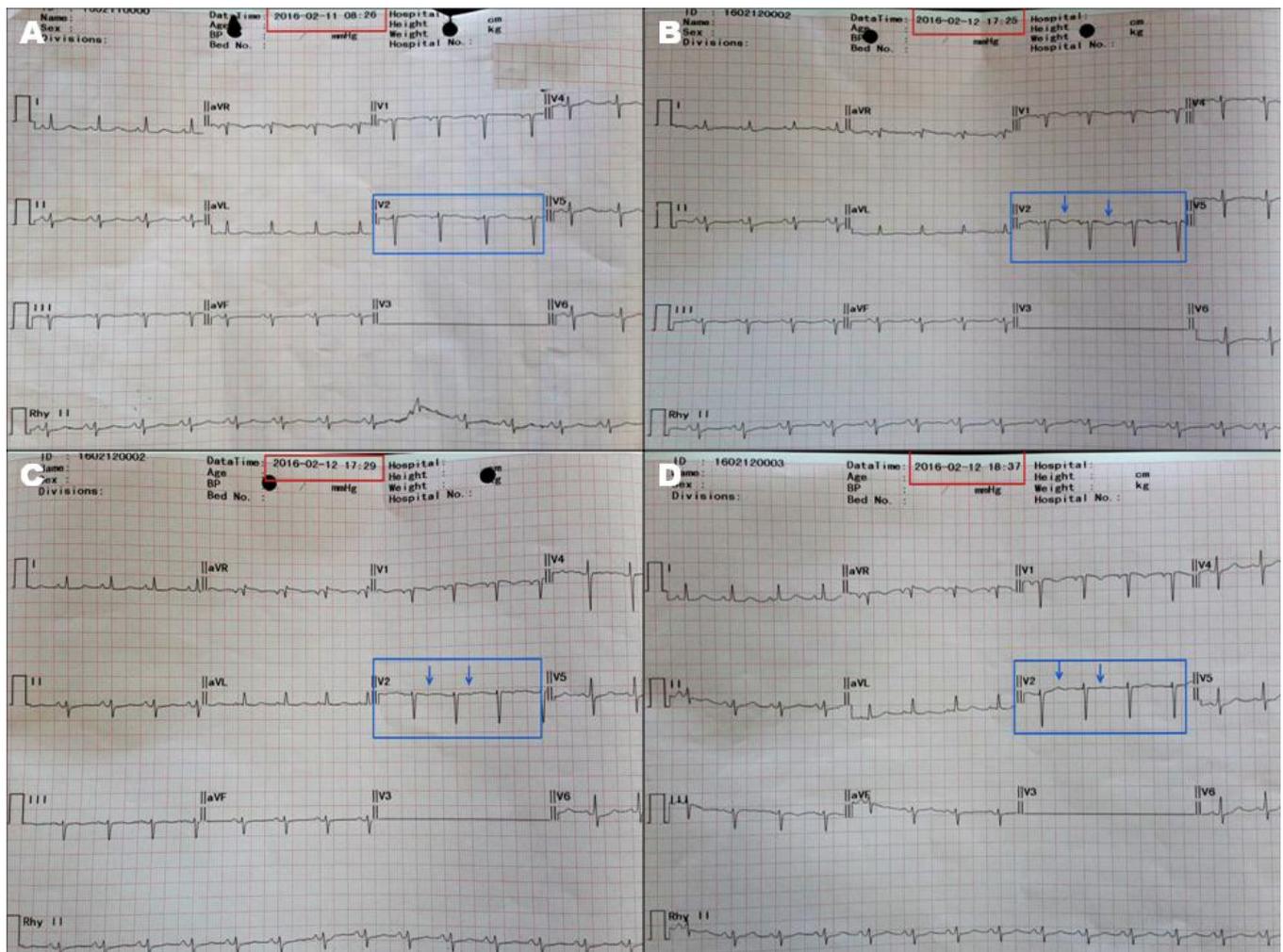


Fig 1: Serial electrocardiogram (EKG) changes of patient on Terlipressin. The timing of EKG is shown in red boxes and the subsequent ischemic changes are shown in blue boxes with arrows

Terli pressin is approved for use in the management of acute variceal bleeding and HRS type 1 in Europe and Asian continents, but not in the United States. It is a tri-glycyl-lysine analogue (prohormone) of vasopressin with longer duration of action and lesser side effects in comparison having affinity for both V1 and V2 receptors, leading to selective splanchnic and extra renal vasoconstriction causing reduction in splanchnic blood flow, increase in mean arterial pressure and systemic vascular resistance and decrement in heart rate, cardiac output and portal pressure [1]. Commonest adverse effects include diarrhea and abdominal pain (20%) but cardiac effects occur over a wider range of selected patients (6 – 40%). Cardiac adverse effects include myocardial ischemia or infarction, left and right ventricular dysfunction, bradycardia and various arrhythmias [2]. Contraindications to Terlipressin use include age more than 70 years, history of chronic obstruction lung disease, peripheral vascular disease, cerebrovascular or ischemic heart disease and prior history of cardiomyopathies [3, 4]. Some authors have also

reported cerebrovascular stroke, life threatening bowel gangrene and gangrenous loss of digits with use of Terli press in [5]. Many of these complications still occurred in well selected patients without known risk factors to Terlipressin as seen with our patient, in whom a life threatening adversity was promptly reversed with identification of the cause at the right time. The use of Terlipressin in selected low risk patients are still not without danger and these patients must be initiated Terlipressin under continuous critical care monitoring and after obtaining informed consent. Further studies are required to rightly identify predictors of adverse effects in patients with low risk, who develop Terlipressin related complications.

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