Case report

High-dose verapamil + trandolapril-induced thrombotic microangiopathy

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Abstract—Thrombotic microangiopathy (TMA) is a syndrome characterized by microangiopathic haemolytic anaemia, thrombocytopenia, and several variable signs of organ damage due to the platelet thrombi in the microcirculation. This article reports a case with TMA which developed after ingestion of a high-dose combination of verapamil and trandolapril. To the authors’ knowledge, no prior cases of TMA induced by trandolapril (an angiotensin-converting enzyme inhibitor) and verapamil (a calcium channel blocker) have been reported in the literature.

Key words: Verapamil; trandolapril; thrombotic microangiopathy.

Thrombotic microangiopathy (TMA) is a syndrome characterized by microangiopathic haemolytic anaemia, thrombocytopenia, and variable signs of organ damage due to the platelet thrombi in the microcirculation [1]. Many causes associated with TMA, such as infection, pregnancy, and organ and bone marrow transplantation, have been identified in adults [1]. TMA has also been associated with drugs such as D-penicillamin [2], piperacillin [3], ticlodipine [4], mitomycin C [5], quinine [6], clopidogrel [7], and alpha-interferon [8]. The early diagnosis of drug-induced abnormalities should be performed in patients undergoing therapy with potentially toxic drugs, and the drug must be discontinued immediately in the case of suspected TMA.

We describe the development of TMA in a patient who had ingested six combined tablets of 180 mg verapamil + 2 mg trandolapril.

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A 19-year-old female patient who had ingested six tablets of 180 mg verapamil + 2 mg trandolapril in a suicide attempt was brought to the Emergency Department approximately 4 h following ingestion. An empty bottle of ‘Tarka’ (Knoll AG 67008) had been found in her room. She stated that she had taken six tablets of ‘Tarka’. She had no history of any medical disorders or surgical intervention. She had not been on any other medication. Initial vital signs were blood pressure of 90/60 mmHg, heart rate of 60 beats/min, respiratory rate of 20 breaths/min, and a temperature of 37°C. The mental status of the patient and head, neck, lung, abdominal, neurological and dermatological examinations were all normal. Heart examination was notable for a regular bradycardia. Intravenous access was initiated and blood was sent for a complete blood count, electrolytes, glucose, BUN, and creatinine. Supplemental oxygen was administered. An orogastric tube was passed and the stomach was lavaged with several litres of 0.9% sodium chloride solution. A slurry containing 60 g of activated charcoal was then instilled into stomach. A second dose of activated charcoal (0.5 g/kg) was administered 4 h after the initial dose and then the orogastric tube was removed. The initial laboratory data revealed a haematocrit of 46.5%, haemoglobin of 14.9 g/dl, an erythrocyte count of $4.91 \times 10^6$ per mm$^3$, MCV of 89.0 fl, WBCs of 20 700 per mm$^3$ with 96% polymorphonuclear cells and 2.5% lymphocytes, and platelets of 150 000 per mm$^3$. The laboratory analysis was as follows: sodium 148 mEq/l, potassium 4.3 mEq/l, chloride 109 mEq/l, BUN 9 mg/dl, creatinine 1.2 mg/dl, glucose 106 mg/dl, lactate dehydrogenase (LDH) 769 U/l, aspartate aminotransferase 16 U/l, unconjugated bilirubin 0.4 mg/dl, and conjugated bilirubin 0.2 mg/dl. Acetominophen, salicylate, and phenobarbital concentrations were undetectable. A urine pregnancy test was negative.

One day after admission, laboratory data revealed a haematocrit of 34%, haemoglobin of 11.3 g/dl; an erythrocyte count of $3.60 \times 10^6$ per mm$^3$, MCV of 90.3 fl, WBCs of 15 500 per mm$^3$ with a normal differential, platelets of 44 000 per mm$^3$, BUN 6 mg/dl, creatinine 1.0 mg/dl, sodium 141 mEq/l, potassium 3.8 mEq/l, unconjugated bilirubin 0.8 mg/dl, and LDH 1665 U/l. Direct Coombs test was negative. Prothrombin time, partial thromboplastin time, thrombin time, and fibrinogen were normal.

Two days after admission, laboratory evaluation revealed hematocrit 29.5%, haemoglobin 10.3 g/dl, erythrocyte count $3.27 \times 10^6$ per mm$^3$, MCV 95.7 fl, WBCs 7700 per mm$^3$ with a normal differential, platelets 34 000 per mm$^3$, BUN 9 mg/dl, creatinine 1.0 mg/dl, unconjugated bilirubin 1.8 mg/dl, conjugated bilirubin 0.2 mg/dl, LDH 1800 U/l, and reticulocyte count 6%. Peripheral blood smear revealed fragmented red blood cells and thrombocytopenia.

Four days after admission, laboratory data were as follows: hematocrit 34.5%, haemoglobin 11.6 g/dl, platelets 78 000 per mm$^3$, and reticulocyte count 4%; BUN and creatinine levels were within normal limits.

Ten days after admission, laboratory examination showed a haematocrit of 40.8%, haemoglobin 14.1 g/dl, erythrocyte count $4.55 \times 10^6$ per mm$^3$, MCV 89.5 fl, WBCs