Skin Necrosis after a Low-Dose Vasopressin Infusion through a Central Venous Catheter for Treating Septic Shock

Eun Hee Kim, M.D., Sae Hwan Lee, M.D., Seung Woon Byun, M.D., Ho Suk Kang, M.D, Dong Hoe Koo, M.D., Hyun-Gu Park, M.D. and Sang Bum Hong, M.D.

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

This is a report on a case of severe skin necrosis in a vasodilatory septic shock patient after the infusion of low-dose vasopressin through a central venous catheter. An 84-year-old male was hospitalized for edema on both legs at Asan Medical Center, Seoul, Korea. On hospital day 8, the patient began to complain of dyspnea and he subsequently developed severe septic shock caused by \textit{E. coli}. After being transferred to the medical intensive care unit, his hypotension, which was refractory to norepinephrine, was controlled by an infusion of low-dose vasopressin (0.02 unit/min) through a central venous catheter into the right subclavian vein. After the infusion of low-dose vasopressin, severe skin necrosis with bullous changes developed, necessitating discontinuation of the low-dose vasopressin infusion. The patient expired from refractory septic shock. Although low-dose vasopressin can control hypotension in septic shock patients, low-dose vasopressin must be used with caution because ischemic complications such as skin necrosis can develop even with administration through a central venous catheter.

Key Words : Arginine vasopressin, Septic shock, Necrosis

INTRODUCTION

Vasopressin is a potent vasopressor that improves organ perfusion during septic shock. Because vasopressin causes arterial smooth muscle cell contraction via the non-catecholamine receptor pathway, it represents an attractive adjunct for the management of septic shock, especially when catecholamines prove to be ineffective\(^3\). Growing evidence has suggested that low-dose vasopressin (0.04 unit/min) is safe and effective for the treatment of vasodilatory septic shock. In a recent prospective randomized controlled study, a combined infusion of vasopressin and norepinephrine proved more effective than norepinephrine alone for the management of catecholamine-resistant vasodilatory shock\(^3\). Vasopressin is recommended as a second-line agent for refractory septic shock\(^3\).

Peripheral administration is often preferred for the treatment of gastrointestinal bleeding such as esophageal varices because of the potential risk of myocardial ischemia that is related to central venous administration of higher doses of vasopressin (0.2~0.5 units/min)\(^4\)~\(^6\). Yet in some settings, peripheral administration of high-dose vasopressin has been reported to cause skin necrosis and gangrene if the drug infiltrates into soft tissue\(^7\)~\(^9\). In addition, peripheral administration of low-dose vasopressin has been reported to cause skin necrosis\(^10\)~\(^11\). However, to the best of our knowledge, skin necrosis has never been reported in connection with low-dose vasopressin administered though a central venous catheter for the treatment of septic shock. Here we report on a patient with septic shock, who developed severe skin necrosis after infusion of low-dose...
An 84-year-old male was admitted to our hospital for edema on both legs that had developed 1 month earlier. Diabetes mellitus had been diagnosed 15 years earlier, and the patient had been controlling his blood sugar levels with insulin. Hypertension had been diagnosed one year earlier, hypertension, and the patient was regularly taking an angiotensin converting enzyme inhibitor and a calcium channel blocker. In addition, 7 years earlier, due to the right hand tremor, idiopathic Parkinsons disease had been diagnosed in this patient due to right hand tremor.

On the day of admission, the abdominal ultrasound examination showed alcoholic liver cirrhosis and small ascites around the liver. The serum albumin concentration was 2.5 g/dL, the serum bilirubin concentration was 2.4 mg/dL and the prothrombin time was 88%: this corresponded to Childs classification B. He had thrombocytopenia (platelets 79,000 /mm³) and diabetic chronic renal failure (creatinine 2.2 mg/dL). The chest radiograph revealed mild cardiomegaly, and the brain natriuretic peptide was 193 pg/mL. The echocardiography showed that the left ventricle ejection fraction was 55%, which was within the normal range.

On hospital day 2, the leg edema was diagnosed as being caused by uncompensated liver cirrhosis combined with diabetic chronic renal failure. After administration of diuretics and albumin, the leg edema improved. However, he complained of a sudden onset of dyspnea on hospital day 8. By that time, he had developed tachycardia (123 beats/min), tachypnea (30 breaths/min) and hypoxemia (SaO₂ 80%). The creatine kinase, CK-MB and troponin-I levels were within the normal range. The electrocardiography showed no significant ST depression or elevation, essentially ruling out the possibility of acute myocardial infarction. The lung perfusion scan also eliminated the possibility of pulmonary embolism. Despite oxygen supplementation (a mask with reservoir bag 10 L/min), the patient failed to maintain a SaO₂ above 90%, and his severe tachypnea (32 breaths/min) was also exacerbated. After the preliminary diagnosis of septic shock and endotracheal intubation, the patient was transferred to the intensive care unit.

On the first day in the intensive care unit, his vital signs were indicative of hypotension (the blood pressure 75/40 mm Hg; the mean arterial pressure 48 mm Hg), exacerbated tachycardia (130 beats/min) and hypothermia (34°C). The laboratory examination results showed that the WBC was 700/mm³, the Hb was 9.7 g/dL, the platelet count was 59,000/mm³, the BUN/Cr was 57/2.2 mg/dL, C-reactive protein was 8.3 mg/dL and the lactic acid concentration was 4.4 mmol/L. The urinalysis showed no evidence of nitrate or pyuria, and the urine culture showed no growth. His chest radiograph showed no evidence of definite pneumonic consolidation. We could not perform a diagnostic ascites tapping because the patient’s ascites was very small.

After the preliminary assessment of hospital-acquired infection and a blood culture examination, the patient was treated with piperacillin/tazobactam, ciprofloxacin and intravenous fluid. The central venous pressure became 12 mmHg, but the systolic blood pressure remained at 80 mmHg. Therefore, we started an infusion of dobutamine (10 ㎍/kg/min), dopamine (25 ㎍/kg/min) and norepinephrine (100 ㎍/min) through the central venous catheter in the right subclavian vein. Due to anuria subsequent to the exacerbated azotemia caused by the septic shock, we began continuous veno-venous hemodialysis (CVVHD).

Although norepinephrine was being infused for about 26 hours, the patients systolic blood pressure remained at 80 mmHg and the mean arterial pressure was also intractably low. The skin necrosis did not develop before vasopressin was administered. We began infusion with vasopressin (40 units mixed with 40 mL of normal saline, and then 0.02 unit/min) through the central venous catheter in the right subclavian vein. The systolic blood pressure increased to 120 mmHg, and the mean arterial pressure increased to 80 mmHg.

After the four hours infusion of low-dose vasopressin, the patient developed multiple purpura on both wrists and both lower legs. In time, the region of skin necrosis expanded to both arms, both thighs and the whole abdomen. At that point, the skin lesions progressed to extensive superficial erosion with variably sized bullous lesions (Figure 1). We assessed the erosion as low-dose vasopressin induced skin necrosis and then after 22 hours we discontinued the infusion of low-dose vasopressin via a central venous catheter.

**CASE REPORT**

Figure 1. Skin necrosis in a vasodilatory septic shock patient treated with low-dose vasopressin. After the infusion, necrosis with variable sized bullous changes developed at both wrists and on both lower legs. In time, the skin lesions expanded to the both arms, both thighs and the abdomen.