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CASE REPORT

Varicella-Zoster Virus-Induced Rhabdomyolysis: A Case Report and Literature Review

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Infection is a possible cause of rhabdomyolysis. We describe the case of a 63-year-old male with malaise and erythematous papules on the right C5–C7 dermatomes, consistent with herpes zoster. Serum antibody and Tzanck tests of the skin lesion were positive. Increased serum creatine kinase (CK) and myoglobin levels and cola-colored urine indicated the development of rhabdomyolysis. Acute kidney injury was also observed. After excluding other possible predisposing factors, the patient was diagnosed with varicella-zoster virus (VZV)-induced rhabdomyolysis. Extracellular volume with alkalized fluids and topical acyclovir was administered. While CK levels declined to normal by day 13, the renal function was not restored. The skin lesion crusted by day 8 and scaled off gradually by day 13. Our case and literature review highlighted the necessity for systemic antiviral treatment and that poor VZV infection control could lead to irreversible kidney injury. In addition, systemic acyclovir should be administered carefully due to its complication of nephrotoxicity.

Key words: Rhabdomyolysis, varicella-zoster virus, acyclovir, kidney injury

INTRODUCTION

Rhabdomyolysis is not an uncommon syndrome encountered in clinical practice. It can be caused by trauma, excessive exercise, immobilization, drugs, toxins, thermal extremes, grand mal seizures, metabolic and electrolyte disorders, genetic disorders, and infections. The viral infections reported to have caused rhabdomyolysis worldwide include influenza virus, human immunodeficiency virus, cytomegalovirus, herpes simplex virus, Epstein–Barr virus, Coxsackievirus, West Nile virus, and dengue virus.[1,2] A few cases of varicella-zoster virus (VZV)-induced rhabdomyolysis have been reported. Herein, we present the first case of VZV-induced rhabdomyolysis in Taiwan and reviewed VZV-induced rhabdomyolysis. We also discussed subsequent acute kidney injury (AKI) and provided possibly appropriate treatment.

CASE REPORT

A 63-year-old male presented to our hospital with a 1-week history of malaise, decreased appetite, and multiple painful erythematous skin rashes on his left anterior chest and shoulder. Cola-colored urine occurred 2 days after admission. The patient had no underlying disease, current medication treatment, or weight loss in the past year. His vital signs were normal without any signs of fever, tachycardia, or hypotension. Physical examination revealed moist oral mucosa and pustular papules and fluid-full vesicles at different stages of the development on a red base were noted at the right C5, C6, and C7 dermatomes.

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Serum antibody including IgG and IgM of VZV and Tzanck tests of the skin lesion performed by dermatologists revealed positive results. Blood analysis showed elevated creatine kinase (CK) (20,000 U/L), myoglobin (1389 ng/mL), aspartate aminotransferase (474 U/L), alanine transaminase (103 U/L), and lactate dehydrogenase (718 U/L) levels. Urinalysis revealed a positive occult blood reaction in the absence of red blood cells in a high-power field. The patient was diagnosed with rhabdomyolysis. Other blood tests showed the following: white blood cell count, 8570/μL; hemoglobin, 11.9 g/dL; platelet count, 176 × 10^3/μL; C-reactive protein, 13.32 mg/dL; creatinine, 3.0 mg/dL; urea, 35 mg/dL; sodium, 134 mmol/L; potassium, 3.2 mmol/L; pH of the vein, 7.35; and bicarbonate, 24.8 mEq/L. His renal function was in the normal range 3 weeks prior to admission. His glomerular filtration rate on admission was 22 mL/min. The tests for influenza, HIV, cytomegalovirus, and Epstein–Barr virus were negative.

On admission, twice daily topical acyclovir was prescribed for the skin lesion. Extracellular volume with vigorous alkalized fluids was administered to maintain a urine output of up to 2 mL/kg/h. His CK levels slowly declined and returned to normal through day 13, but his renal function was not restored [Figure 1]. The skin lesion crusted by day 8 and scaled off gradually by day 13 [Figure 2]. An episode of hospital-acquired pneumonia with a deterioration of renal function developed after completing the treatment for rhabdomyolysis (day 19). However, the patient refused resuscitation and died several days later.

DISCUSSION

The possible causes of rhabdomyolysis in this patient, including trauma, exhausting exercise, seizure, shock, or electrolyte imbalance, were excluded from the study. VZV infection was the most predisposing factor for rhabdomyolysis. The normalization of CK level was consistent with the convalescent phase of herpes zoster, strengthening the diagnosis of VZV-induced rhabdomyolysis.

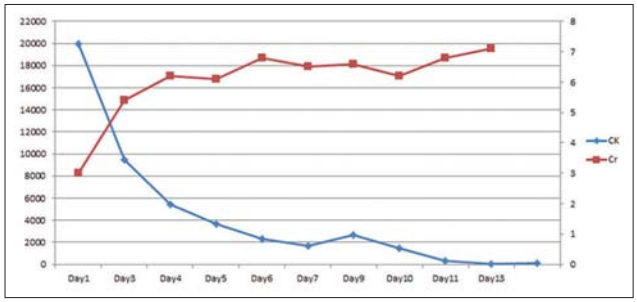

Figure 1: While the plasma creatine kinase (U/L) concentration slowly declined and was within the normal range until day 13, there was no reduction in plasma creatinine levels (Cr, mg/dL)

Rhabdomyolysis caused by VZV is not common, especially when presented with herpes zoster. A review of reported cases of VZV-induced rhabdomyolysis in the English-language literature indicated that most presented with varicella and only one case presented with herpes zoster [Table 1].[3-11] The proposed mechanisms for infection-induced rhabdomyolysis include direct pathogen invasion of muscle, tissue hypoxia, low oxidative and glycolytic enzyme activity, activation of lysosomal enzymes, and mechanisms implicating endotoxins.[1] Seven of ten (70%) cases experienced AKI, which is higher than previous reports.[12] However, all of the reported cases had restored renal function except for our case.

The indications for antiviral treatment in patients with herpes zoster include age ≥50 years, moderate or severe pain, severe rash, involvement of the face or eye, other complications of herpes zoster, and immunocompromised state. Oral or intravenous antiviral treatments are recommended.[13] In other reported cases, systemic acyclovir was administered. However, in our case, only topical acyclovir was applied to the visible skin lesion. Despite vigorous volume supplement with alkalized fluids, irreversible AKI still occurred. This may be attributed to the nature of rhabdomyolysis or inadequate infection control under topical antiviral treatment. Therefore, thorough and timely suppression or eradication of the pathogen may be the crucial strategy for the treatment of VZV-induced rhabdomyolysis. Further, research and evidence are needed to confirm this supposition.

Systemic acyclovir is a well-documented nephrotoxic agent. Aldehyde metabolites and crystal precipitation of acyclovir in renal tubules due to low solubility are factors that can result in acute tubular necrosis.[14] The nephrotoxicity of systemic acyclovir may have contributed to the higher prevalence of AKI in patients with VZV-induced rhabdomyolysis. In the case reported by Lee *et al*.,[4] renal function recovered after replacing acyclovir with antibodies against VZV. Another case with AKI had restored renal function after discontinuation of acyclovir.[6] Famciclovir and brivudine are reported to be safe substitutes for patients with acyclovir-induced nephrotoxicity.[15,16]

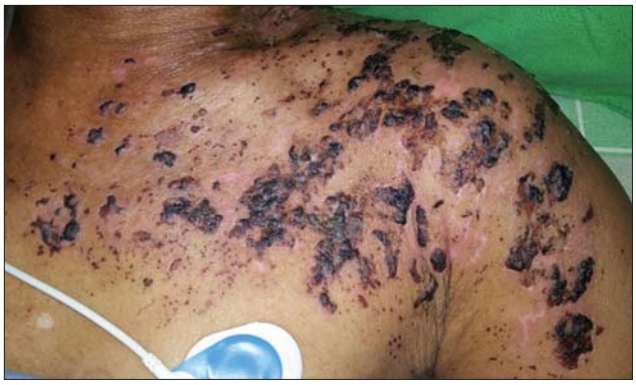

Figure 2: The crusted skin lesion scaled off gradually by day 13

Table 1: Characteristics of reported patients with varicella-zoster virus-induced rhabdomyolysis

Age/sex	Manifestation	Highest CK (IU/L)	Antiviral treatment	AKI	Recovery of AKI	Other VZV-associated complications	Disease duration (days)	Reference
16/male	Varicella	1,977,600	Acyclovir	+	Yes	-	N/A	3
23/male	Varicella	2148	Acyclovir	+	Yes	DIC, ARDS, and pneumonia	21	4
25/male	Varicella	297,000	Acyclovir	+	Yes	-	N/A	5
27/male	Herpes zoster	1899	Acyclovir	+	Yes	Meningoencephalitis	12	6
28/male	Varicella	1079	Acyclovir	+	Yes	DIC, pneumonia, and hepatitis	75	7
29/male	Varicella	11,480	Acyclovir	-		-	7	8
30/female	Varicella	33,200	Acyclovir	-		DIC	15	9
38/male	Varicella	2947	Acyclovir	-		Meningoencephalitis	19	10
70/female	Varicella	N/A	N/A	+	Yes	-	N/A	11
63/male	Herpes zoster	20,000	Acyclovir*	+	No	-	13	Our case

*Our case used topical acyclovir; the others used systemic acyclovir. AKI=Acute kidney injury; ARDS=Acute respiratory distress syndrome; CK=Creatine kinase; DIC=Disseminated intravascular coagulation; N/A=Not available; VZV=Varicella-zoster virus

CONCLUSION

Rhabdomyolysis is considered a possible complication in patients with VZV infection that might be underdiagnosed, because CK levels are not routinely checked in clinical practice. To the best of our knowledge, this is the first case of VZV-induced rhabdomyolysis in Taiwan. The associated literature review highlighted that systemic antiviral treatment was suggested and that poor infection control could lead to irreversible kidney injury. The use of systemic acyclovir should be cautioned due to the complication of nephrotoxicity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

The study was approved by Tri-Service General Hospital, National Defense Medical Center. Approval number: 2-107-05-099 & Approval Date: 2018/7/23.

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Conflicts of interest

There are no conflicts of interest.

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