Taiwanese Journal of Obstetrics & Gynecology 55 (2016) 618–619

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Research Letter

Acyclovir-induced nephrotoxicity in a pregnant woman with chickenpox

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ARTICLE INFO

Article history:
Accepted 12 January 2015

Dear Editor,

Acyclovir is a commonly used antiviral agent for the treatment of herpes simplex and herpes zoster infection. According to the Food and Drug Administration, it is classified as a category B drug and is safe for use during pregnancy [1]. Adverse effects of acyclovir include mild symptoms, such as nausea, vomiting, and diarrhea, to more severe symptoms, including neutropenia, hepatitis, and Stevens–Johnson syndrome [2]. Reversible nephrotoxicity can be diagnosed in approximately 5–10% of patients undergoing intravenous (IV) administration. The precipitation of acyclovir crystals results in kidney damage and a rapid rise in serum creatinine [3,4]. However, drug-associated complications during pregnancy have not been documented.

A 33-year-old pregnant woman, G2P1, at 31 weeks' gestation presented at the outpatient department with a 2-day history of generalized tiny vesicles on the erythematous base over her trunk and genital area. She was previously started on oral acyclovir (800 mg 4 times daily) under the impression of chickenpox by a dermatologist. Additionally, she reported abdominal tightness, poor intake, and general weakness. Fetal nonstress test showed uterine contractions. The patient was admitted for management of preterm labor in association with chickenpox. Upon admission, her blood pressure was 118/67 mmHg, dipstick test of urinalysis showed trace proteins, and laboratory findings revealed a hemoglobin level of 10.7 g/dL and a hematocrit of 33.9%. The differential counts of lymphocytes and monocytes were 10.7% and 11.2%, respectively. Other hematological parameters and biochemical data were within the normal range. The obstetrical ultrasound findings were unremarkable, and the results of immunoglobulin G and immunoglobulin M tests for varicella zoster were negative

The patient was started on ritodrine and nifedipine upon hospitalization for treatment of preterm labor, and vital signs and intake/output were monitored. She then received IV acyclovir (750 mg every 8 hours) for progressive skin lesions, with severe vulvar pain and burning. Unfortunately, decreased urine output was noted 3 days after commencing IV acyclovir. Follow-up laboratory data showed elevation of serum creatinine (0.72–3.77 mg/dL). Drug-induced nephropathy was suspected, and acyclovir was stopped immediately. Urinalysis collected after creatinine elevation was negative for granular casts and crystals. Renal sonogram was also normal. The patient was started on aggressive IV fluid hydration. On Hospital day 6, continuous elevation of creatinine (5.5 mg/dL) was still noted. Due to the possible influence of tocolytics on renal and pulmonary function, a chest X-ray was obtained, revealing no evidence of pulmonary edema. However, after discussing and obtaining consent from the patient and her family, cesarean delivery without corticosteroid injection was performed at 32 weeks' gestation for breech presentation and deteriorating renal function. A male baby weighing 1755 g with an Apgar score of 6–8 at 5 minutes was delivered. Patient creatinine levels began to decline to baseline levels over the following 5 days (Figure 1).

To the best of our knowledge, no previous reports on the issue of acyclovir-induced nephrotoxicity during pregnancy have been published. In this particular case, whether concomitant use of the tocolytic agent placed the patient at a higher risk of developing acute renal injury is unknown. Nevertheless, nephrotoxicity is not a common side effect of ritodrine and nifedipine. The diagnosis of acyclovir nephrotoxicity was supported by clinical features and time course of the acyclovir administration. No other cause was identified.

Acute renal failure secondary to acyclovir is a well-described side effect, with the most common mechanism being crystal nephropathy. Other potential mechanisms of injury include acute interstitial nephritis and acute tubular necrosis [5]. Deterioration in renal function may develop within 24–48 hours of acyclovir administration [6]. Risk factors include hypovolemia, rapid IV

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http://dx.doi.org/10.1016/j.tjog.2016.06.012

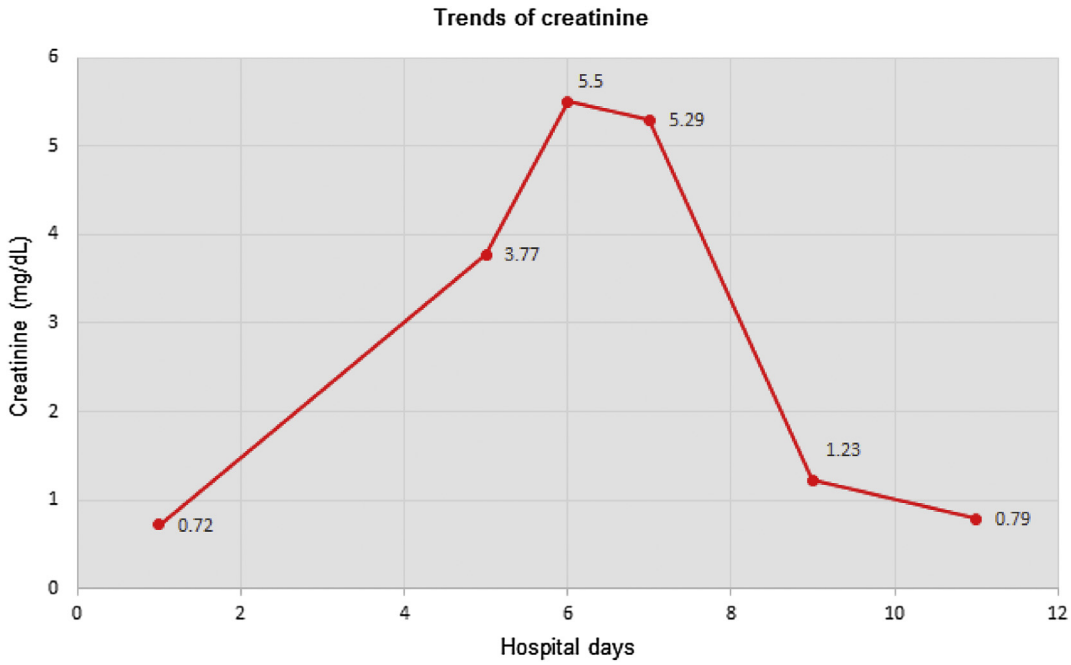

Figure 1. Creatinine levels showing acute renal failure (Day 5) after treatment and after delivery.

infusion, concurrent acute kidney injury before medication administration, and concomitant use of other nephrotoxic agents. Early and immediate detection is necessary to prevent morbidity. Monitoring renal function in hospitalized patients using acyclovir for longer than 48 hours is strongly suggested. The possibility for chronic kidney injury is a strong concern if renal insufficiency is not rapidly corrected [7]. Treatment of acyclovir nephrotoxicity is supportive, with discontinuation or reduction of the drug in addition to maintaining a high urinary flow rate (>150 cc/h) with IV fluids and furosemide [5]. In patients that develop severe renal failure or those who do not respond to treatment, hemodialysis is an option for removal of the offending drug and to support renal function [6]. The risk of acyclovir-induced nephrotoxicity can be minimized with empiric IV fluids to establish euvolemia before drug administration in order to avoid rapid infusion of the drug (infuse slowly over 1–2 hours), with dosage adjustment according to renal function if necessary [7].

Considering the fact that the patient was pregnant at 32 weeks with preterm labor and deteriorating renal function, early delivery was a reasonable alternative to rapidly correct her underlying problems. In conclusion, acyclovir is not uncommonly used in pregnancy; therefore, clinicians should be alerted to avoid failure of early detection of nephrotoxicity.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

Written permission for publication was obtained from the patient.

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