Cilostazol-induced Acute Kidney Injury in A Patient With Diabetic Foot Ulcer: A Case Report and Review of Literature

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Introduction. Cilostazol is an antiplatelet agent, that has been recently used as an adjunctive therapy in the management of diabetic foot ulcers. Headache, diarrhea, palpitations, and edema are reported as common side effects.
Case Presentation. A 53-year-old woman was admitted to hospital, with decreased urine output and increased serum creatinine level. She had taken Cilostazol for the first time, for only one day, so the diagnosis of acute kidney injury, probably drug-induced acute interstitial nephritis, due to Cilostazol use, was made. Her kidney function did not improve despite Cilostazol discontinuation and therefore, empirical corticosteroid therapy was initiated. Her urine output increased and her serum creatinine level significantly decreased, on the third day of treatment. She was discharged with acceptable kidney function. Follow-up visits showed gradual normalization of serum creatinine in the next 62 days.
Conclusion. Based on our case, we may draw the conclusion that, Cilostazol may cause nephrotoxicity at any point after ingestion.

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Case Report

INTRODUCTION

Cilostazol is a selective, reversible phosphodiesterase-3 inhibitor, mainly developed for the management of intermittent claudication.[1] Studies have demonstrated its effectiveness, as an adjuvant, for prevention and treatment of diabetic foot ulcers (DFU).[2,3] There are few reports of Cilostazol induced nephrotoxicity.[4,5]

Drug-induced acute interstitial nephritis (DI-AIN) is one of the most frequent cause of unexplained acute kidney injury (AKI) and its diagnosis mainly depends on history of consumption of an offending medication along with skin rash, fever, or eosinophilia. However, kidney biopsy is necessary to confirm its diagnosis.[6] Because of the high morbidity and mortality of DI-AIN, early identification and treatment with glucocorticoids, along with discontinuation of the culprit agent is essential.[7] Here we present a case of Cilostazol-induced AIN which was successfully treated with corticosteroids.

CASE PRESENTATION

A 53-year-old woman was admitted to the hospital with chief complaints of nausea and confusion. She had a history of diabetes mellitus for 12 years. Her baseline serum creatinine was 0.8 mg/dL. She had been hospitalized in a rural hospital for the treatment of DFU in her left foot, before being admitted to our hospital. As the process of wound healing was not remarkable, Cilostazol (100 mg/d) was added to her medications. She had never taken Cilostazol before and reported no history of drug-induced allergic reactions.

One day after consumption of the drug, skin rash, periorbital edema, high-grade fever, and nausea

appeared (Figure 1), and her urine output decreased and hence she was referred to this hospital. On admission, her vital signs were as follows: blood pressure, 118/73 mmHg; pulse rate, 119 /min; respiratory rate, 32 /min and temperature was 103.1 °F. Her laboratory results on admission were serum creatinine, 4.5 mg/dL; blood urea nitrogen (BUN), 70 mg/dL; FBS, 102 mg/dL; Hemoglobin, 9.4 g/dL; RBC, 3.98 million/µL; WBC, 6000 /µL (53.9% neutrophils, 25.6% lymphocyte, 1% monocyte, 7% eosinophil, and 12.5% mixed); platelets 275000 /µL. Urinalysis indicated 2 to 4 RBCs and 8 to 10 WBCs /hpf. Microscopic urine sediment revealed epithelial cells and WBCs. Her urine output decreased during the three days after admission, and she became anuric despite discontinuation of the drug. History and clinical manifestations suggested DI-AIN.

She was prescribed prednisolone at a dose of 50 mg/d on the fourth day of admission and her urine output started to increase to 450 mL, after a day of prednisolone administration. She was observed for more three days, and discharged on the seventh day with 50 mg/d prednisolone with a clinical diagnosis of DI-AIN based on the clinical history and considerable decrease in creatinine level and increase in urine output, in response to oral corticosteroid, together with pronounced facial desquamation (Figure 2), which could be considered as a sign of improvement in drug-induced reactions. She was followed for 62 days, and the dose of prednisolone was tapered. On the last visit, serum creatinine and BUN concentration were 1.4 mg/dL and 30 mg/dL, respectively. Figure 3 summarizes the patient's clinical course.

DISCUSSION

Here we report a suspected case of DI-AIN, due to Cilostazol consumption, based on history, sign and symptoms, and laboratory data, a patients with no previous history of kidney diseases. As the patient refused to undergo kidney biopsy, we could not confirm the diagnosis of DI-AIN. As far as, AIN is supposed to have underlying immune mechanism, corticosteroids administration, in combination with discontinuation of the culprit agent, has been considered its treatment of choice.[6] Although our patient showed a considerable response to corticosteroids, kidney biopsy is necessary to confirm the diagnosis of DI-AIN prior to corticosteroid therapy, due to contraindication of corticosteroids in patients with more than 75% interstitial fibrosis. Hence, in case of unavailability of previous serum creatinine, it may be necessary to confirm the diagnosis and the extent of chronicity before starting the therapy. Otherwise, depending on patient's condition and whether the first diagnosis is AIN, corticosteroids might be

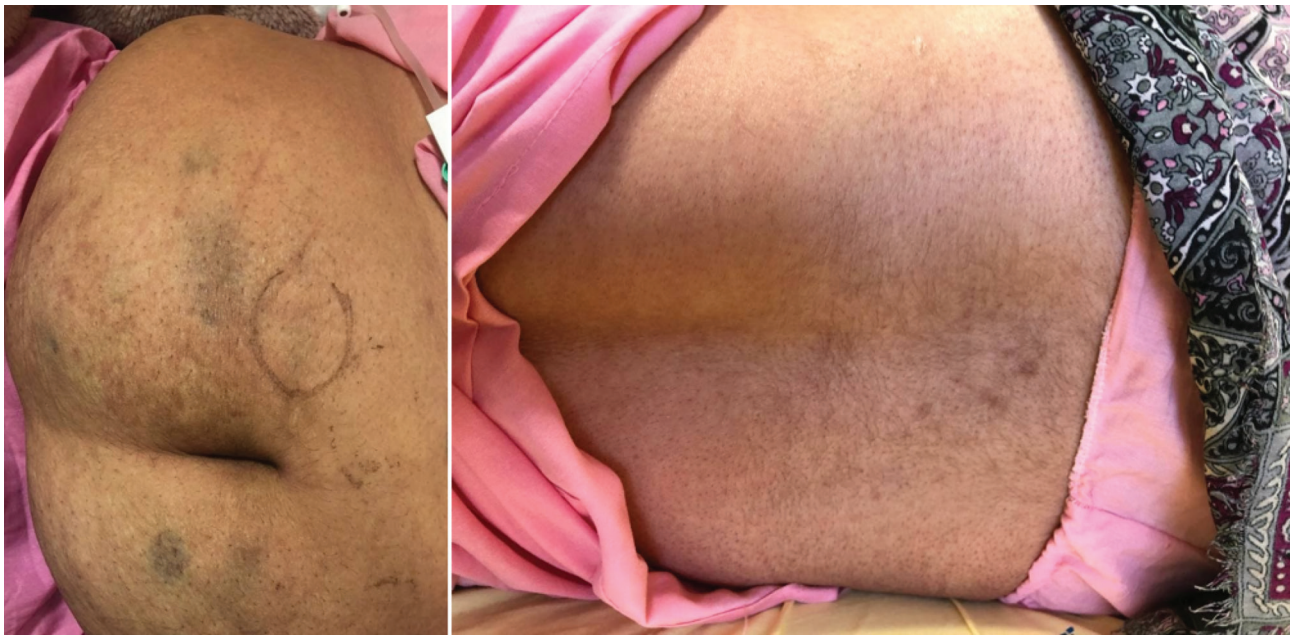

Figure 1. Skin Rash in the Abdomen and Back of the Patient

Figure 2. Desquamation on Face, During Improvement

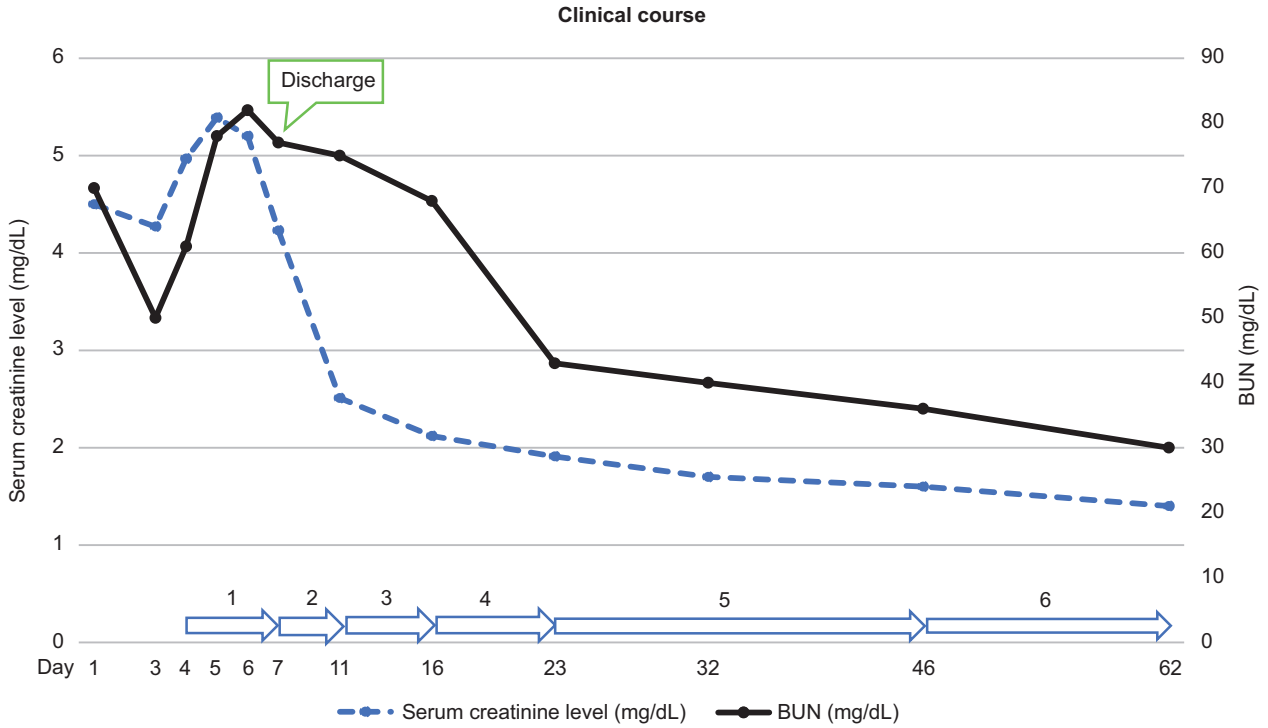

Figure 3. Clinical Course of the Patient From Admission (1: Prednisolone 50 mg/d, 2: Prednisolone 40 mg/d, 3: Prednisolone 35 mg/d, 4: Prednisolone 30 mg/d, 5: Prednisolone 25 mg/d, and 6: Prednisolone 20 mg/d)

recommended for its treatment.[6]

Till now, only two cases of DI-AIN due to Cilostazol consumption have been reported. The first case was a 67-year-old male, who was admitted with serum creatinine of 8.28 mg/dL and a baseline creatinine of 0.87 mg/dL, two weeks after taking Cilostazol (200 mg/d). Cilostazol was discontinued and fluid replacement was started. His creatinine level decreased to 0.98 mg/dL, after two weeks.[4] The second case was a 69-year-old female, who was admitted to hospital with a serum creatinine level of 1.41 mg/dL and a history of baseline creatinine of 0.85 mg/dL, after using Cilostazol (100 mg/d) for 13 months. Despite the fact that she had no symptoms, kidney biopsy, gallium-67 scintigraphy, and drug lymphocyte stimulation test demonstrated Cilostazol-related DI-AIN.[5]

CONCLUSION

Based on the aforementioned cases and our case, we may draw the conclusion that, Cilostazol may cause nephrotoxicity at any point after ingestion.

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