CASE REPORT

Acute Kidney Injury with Hemolysis after Glycerin Enema-induced Rectal Injury in a Patient with Type 2 Diabetes

Ryosuke Hayashida, Kyoichiro Tsujiya, Suguru Nakamura, Noriyuki Harima, Masashi Ichijo, Fumihiko Furuya and Kenichiro Kitamura

Abstract:
A 66-year-old man with type 2 diabetes was admitted for glycemic control and weight loss. The rectal mucosa was unfortunately injured during glycerin enema administration in preparation for colonoscopy, after which dark red urine and renal dysfunction were observed. Considering the clinical diagnosis of glycerol-induced hemolysis and acute kidney injury, intravenous hydration and haptoglobin administration were started, which successfully treated the dark red urine and renal dysfunction. This case highlights the importance of appropriate glycerin enema administration and emphasizes the need to recognize glycerol-induced hemolysis and acute kidney injury as complications of glycerin enemas. This case also provides insight into glycerol-induced hemolysis and acute kidney injury as complications of glycerin enemas.

Key words: glycerin, hemolysis, acute kidney injury

BACKGROUND

Glycerin enemas have been widely used in daily clinical practice as well as in home care situations. This medical procedure is generally regarded as safe and is not believed to cause severe complications. However, glycerol has been known to induce hemolysis and acute kidney injury (AKI), given its high osmolality and molecular weight. Since the 1970s, cases of intravascular hemolysis and/or AKI caused by intravenous glycerin infusion have been reported (1). However, intravascular hemolysis and/or AKI after inappropriate glycerin enema administration have rarely been recognized or reported in English publications.

We herein report a case involving AKI in a patient with type 2 diabetes following rectal injury during glycerin enema administration. This case provides insight into glycerol-induced hemolysis and AKI as complications of glycerin enema.

CASE PRESENTATION

A 66-year-old man with type 2 diabetes was admitted to the University of Yamanashi Hospital (Yamanashi, Japan) due to poor glycemic control. The patient unintentionally lost 7 kg of body weight over 3 months, and his HbA1c and blood glucose concentrations on admission were 14.6% and 227 mg/dL, respectively (Table 1). He had maintained normal serum creatinine concentrations for at least the past 1.5 years and had no positive dipstick test for urinary protein or blood. The patient had simple diabetic retinopathy but no history of diabetic neuropathy, nephropathy, macroangiopathy, or hemorrhoids.

The urinary albumin excretion and estimated glomerular filtration rate at admission were 9.6 mg/gCr and 108 mL/min/1.73 m², respectively. After admission, glycemic control was started through multiple daily injections of insulin glargine and lispro, while detailed examinations concerning his body weight reduction were planned. Abdominal ultrasonography and computed tomography (CT) revealed no

Third Department of Internal Medicine, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Japan
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Correspondence to Dr. Kyoichiro Tsujiya, tsuchiyak@yamanashi.ac.jp
DISCUSSION AND CONCLUSIONS

In 1974, the first three human cases of intravascular hemolysis and/or AKI caused by intravenous glycerin infusion were reported (1). Thereafter, reports were published showing that the use of low-concentration (10%) glycerol solutions containing small amounts of fructose could attenuate hemolysis in humans by preventing membrane dehydration of erythrocytes (2, 3). In contrast, glycerin enemas usually contain high (50%) concentrations of glycerol without fructose. Taken together, these previous findings suggest that glycerol-induced hemolysis and/or AKI is more likely to occur through inappropriate glycerin enema administration than through intravenous glycerol agents.

At the onset in the present case, we were unable to check the serum haptoglobin level and did not observe any anemia or schistocytes. Therefore, our findings might not have indicated a definitive diagnosis of hemolysis. However, based on all of the clinical information, including rectal injury by
glycerin enema, we considered hemolysis to be the most likely diagnosis to begin treatment with hydration and haptoglobin. Indeed, the clinical course after treatment was consistent with the diagnosis.

Glycerin is rapidly metabolized to carbon dioxide and glycogen by glycolysis, and the elimination half-life of glycerin in serum is consequently about 0.18-0.87 h (4). This suggests that glycerol-induced hemolysis does not last for a long time unless the migration of glycerin continues, and not all typical laboratory findings of hemolysis may be observed. Furthermore, hydration and haptoglobin treatment were immediately started in the present case, which might have partly masked some findings of AKI.

Although the significance and efficacy of haptoglobin treatment for glycerin enema-induced hemolysis remains unclear, it may prevent the progression to hemodialysis; from 1979 to 2017, 15 cases of hemolysis following glycerin enemas were reported in case series and reports in Japanese (5-7). Apparent rectal injury and hemorrhoids were observed in 10 and 6 cases, respectively. While one of seven patients treated with haptoglobin underwent hemodialysis, two of seven patients who did not receive haptoglobin underwent the same treatment. Fortunately, no deaths were observed in any of those cases. Haptoglobin treatment might thus have helped attenuate the progression of AKI in the present case.

Glycerol-induced AKI involves at least two mechanisms: hemolysis and rhabdomyolysis. After hemolysis is induced by increases in intracellular osmolality in erythrocytes, intracellular hemoglobin dissociates into heme and globin. The liberated heme may injure the kidney via tubular obstruction, direct injury of tubular epithelial cells, or vasoconstric-
In conclusion, we reported a case of AKI with hemolysis subsequent increase in the serum CK concentration suggests that myoglobin contributed less to the pathogenesis of AKI than glycerol-induced hemolysis.

The present patient had poorly controlled type 2 diabetes, a proinflammatory state characterized by increased levels of C-reactive protein and proinflammatory cytokines as well as monocyte activation (15). In addition to inflammatory bowel diseases, studies have shown that patients with diabetes exhibit digestive tract inflammation and increased intestinal vulnerability (16, 17). Mucosal vulnerability associated with diabetes may have contributed to the rectal injury following forcible insertion, which then promoted the glycerol-induced hemolysis in the present case.

In conclusion, we reported a case of AKI with hemolysis after glycerin enema-induced rectal injury in a patient with type 2 diabetes. The present case highlights the importance of appropriate glycerin enema administration and emphasizes the need to recognize glycerol-induced hemolysis and AKI as complications of glycerin enemas.

The authors state that they have no Conflict of Interest (COI).

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Figure 2. Clinical course. (A) The clinical course. Days -9 and 0 indicate admission and onset, respectively. (B) Appearance of urine before (left) and 24 h after (right) haptoglobin administration. U-β2-MG: urinary beta-2 microglobulin, U-NAG: urinary N-acetyl-beta-glucosaminidase

Table 2. Serum Haptoglobin, Serum Myoglobin, and Urinary Myoglobin Levels 24 H after Onset.

|                          | Serum haptoglobin | Serum myoglobin | Urinary myoglobin |
|--------------------------|-------------------|-----------------|-------------------|
|                          | 78.0 ng/mL        | 228.8 ng/mL     | 62.0 ng/mL        |
| Normal range             | (15-116)          | (54.9)          | (≤10)             |

Normal range shown in parentheses.

Hemolysis in a 50 kg human (14). Although the exact volume of migrated glycerol in the present patient remains unknown, a sufficient volume was likely to have migrated into the bloodstream and induced hemolysis. The relatively mild subsequent increase in the serum CK concentration suggests that myoglobin contributed less to the pathogenesis of AKI than glycerol-induced hemolysis.

In the present case, increased serum and urinary myoglobin levels, despite being assessed 24 h after the onset, may have contributed to the pathogenesis of AKI, at least in part. However, glycerol migration into the bloodstream was considered the main cause of the hemolysis. Despite using animal data for calculations, a previous report found that only 1.2 mL of intravenous 50% glycerin was sufficient to cause hemolysis in a 50 kg human (14). Although the exact volunee of migrated glycerol in the present patient remains unknown, a sufficient volume was likely to have migrated into the bloodstream and induced hemolysis. The relatively mild subsequent increase in the serum CK concentration suggests that myoglobin contributed less to the pathogenesis of AKI than glycerol-induced hemolysis.

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