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LETTER TO THE EDITOR

Colchicine Poisoning: An Unusual Cause of Diarrhea with Multiorgan Failure

A 31-year-old obese man (weight 107.5 kg) was admitted to the emergency department with a history of fever, diffuse abdominal pain, vomiting, and watery diarrhea for 1 day. His vital signs were as follows: temperature 39.6°C, heart rate 106 beats/minute, respiration rate 16 breaths/minute, and blood pressure 105/71 mmHg. Physical examination findings were unremarkable, except for hyperactive bowel sounds. Abnormal laboratory studies revealed the following: white blood cell count 20,080/μL, aspartate aminotransferase 153 units/L, alanine aminotransferase 60 units/L, and 4+ occult blood of stool examination (without elevated white blood cells). The initial diagnosis was infectious diarrhea, and the patient received supportive care. Several hours later, he went into shock even after fluid replenishment and disseminated intravascular coagulopathy (a prolonged prothrombin time of 22 seconds, with an international normalized ratio of 2.06 and D-dimer > 35 mg/L). We suspected atypical infection such as leptospirosis or enterovirus; therefore, the patient was admitted to the intensive care unit and treated with empiric antibiotics (meropenem, penicillin G, and ciprofloxacin).

On Hospital Day 2, we further evaluated his detailed history and found that he had ingested 60 tablets of 0.5 mg colchicine in a suicide attempt 24 hours prior to arriving at our emergency department. His condition deteriorated; he went into a state of profound shock and needed ventilator support. Subsequently, he had rhabdomyolysis, oliguria, high anion gap metabolic acidosis, and acute renal failure. The levels of his blood urea nitrogen, creatinine, and creatine kinase were found to be 36 mg/dL, 5.8 mg/dL, and 52,624 units/L, respectively. We administered one course of plasma exchange (PE) to enhance colchicine elimination and performed continuous venovenous hemofiltration. After 5 days, the patient developed pancytopenia, as determined by white blood cell and platelet counts of 660/μL and 16,000/μL, respectively. He continued to have leukopenia in spite of receiving granulocyte colony-stimulating factor (G-CSF; 600 μg/d). He expired on Hospital Day 8 due to multiorgan failure. After receiving consent from his family, we performed postmortem gun biopsies on his left kidney and right thigh skeletal muscle immediately. Pathologic findings were as follows: degeneration of myocytes and myoglobin-associated acute tubular injury induced by an overdose of colchicine (Figure 1).

Colchicine is administered regularly for treating acute gout attacks. However, colchicine overdose can cause a serious sequelae, including gastrointestinal discomfort, hepatic failure, arrhythmias, impaired contractility, rhabdomyolysis, renal failure, seizures, coma, pancytopenia, sepsis, and even death.[1] Its symptoms usually mimic those of major organ disorders, making an accurate diagnosis difficult, especially in patients who attempt suicide without reporting colchicine ingestion. Colchicine poisoning is diagnosed mainly on the basis of the patient's medical history. Tests to determine plasma colchicine concentrations are generally not available and have not been found to correlate with illness severity. Based on the amount of colchicine ingested, poisoning may be mild (<0.5 mg/kg), moderate (0.5–0.8 mg/kg), or severe (>0.8 mg/kg). Mortality due to moderate poisoning is 10%, whereas most patients with severe poisoning die.[1] In this case, the patient was treated for colchicine poisoning, which was diagnosed based on his medical history and clinical presentations. We also performed postmortem gun biopsies, which are performed rarely for patients with a bleeding tendency and thrombocytopenic conditions. Toxic effects of colchicine on the microtubules, which include impairing of endocytosis and trafficking between the endoplasmic reticulum and Golgi compartments, led to the accumulation of various vacuoles.[2] Focal acute tubular necrosis and several myoglobin casts in the renal tubules were consistent with the diagnosis of shock status and rhabdomyolysis. Although vacuolar myopathy, acute tubular necrosis, and myoglobin casts are not specific to colchicine poisoning, these findings supported the clinical diagnosis of colchicine poisoning.

Colchicine-specific Fab fragments were used successfully to treat severe colchicine overdose; however, they are not available commercially.[3] Hemodialysis is not beneficial owing to its large distribution of volume and high protein-binding capacity, even when a high-flux dialyzer is used.[4] By contrast, PE has been reported as beneficial in patients who ingested <0.5 mg/kg of colchicine, but no consensus has yet been reached regarding the total course.[5] Besides, G-CSF was suggested as a supportive care for leukopenia, which may shorten the duration of neutropenia and prevent septicemia.[6] In this case, the patient received PE and G-CSF therapy; nevertheless, he expired even by ingesting only about 0.3 mg/kg of colchicine. A delay in diagnosis by 48 hours and poor response to PE and G-CSF therapy are the possible explanations.

In conclusion, colchicine poisoning is life threatening and difficult to diagnose accurately at the initial stage. A detailed medical history of the patient with the aforementioned symptoms is the cornerstone of correct diagnosis. Early diagnosis of such patients and timely initiation of treatment may improve the prognosis.

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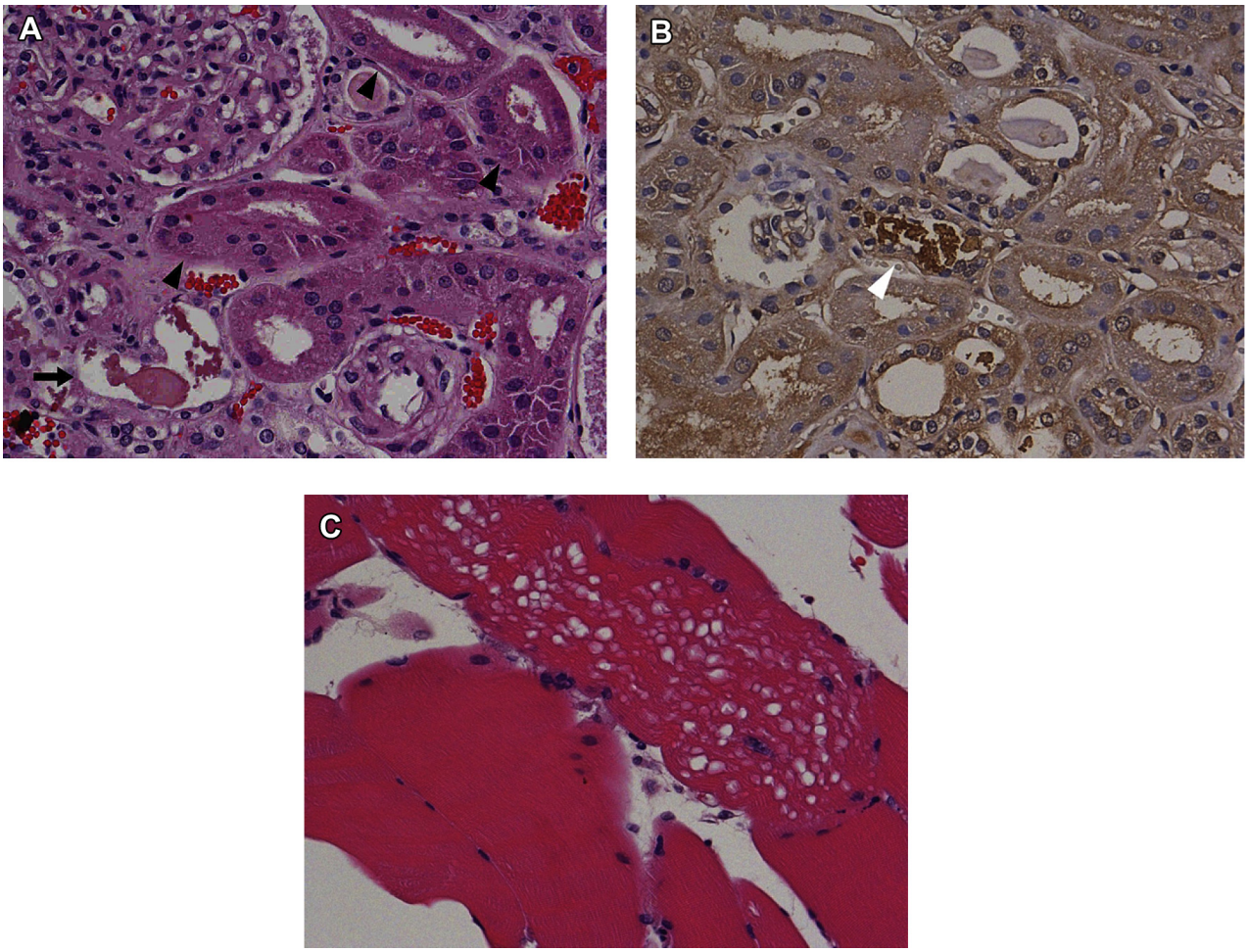

Figure 1 Postmortem gun biopsies of a case of colchicine overdose. (A) Left kidney revealed focal acute tubular injuries (hematoxylin and eosin stain, 100×) characterized by dilated proximal renal tubules (arrow), focal sloughed epithelial cells, and regenerative atypia of the renal tubular epithelium (black arrowheads). (B) Myoglobin casts (myoglobin immunostain, 100×) were noted in the left renal tubules (white arrowhead). (C) Right thigh skeletal muscle with focal vacuolar degeneration (hematoxylin and eosin stain, 200×).

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