Pantoprazole-Induced Liver Injury in the Setting of Diabetic Ketoacidosis

Lesão Hepática Induzida por Pantoprazol em Contexto de Cetoacidose Diabética

Keywords: Chemical and Drug Induced Liver Injury; Diabetic Ketoacidosis; Pantoprazole
Palavras-chave: Cetoacidose Diabética; Lesões Hepáticas Induzidas por Produtos Químicos e Medicamentos; Pantoprazol

Dear Editor

Critically ill patients are at higher risk of acquired liver injury, given the multiple coexisting potential causes of injury.[1] They are also at risk of stress ulcers, and prophylaxis with proton pump inhibitors (PPIs) is common in Intensive Care Units (ICUs).

A 54-year-old woman was admitted to the ICU due to diabetic ketoacidosis (DKA). On admission, she was hemodynamically stable, with a Glasgow Coma Scale score of 7 (E2V1M4). Her abdominal examination was normal, without palpable organomegalies, and her liver blood tests were within the normal range. She was intubated for airway protection and started on intravenous fluids, insulin perfusion, and prophylaxis with intravenous pantoprazole 40 mg/day.

A favorable clinical evolution allowed extubation on the second day and her DKA was resolved by the third day.

On the fifth day upon admission, her liver blood tests were markedly abnormal (AST 6189 U/L, ALT 2246 U/L, INR 1.64, total bilirubin 1.3 mg/dL, LDH 4948 U/L). She remained asymptomatic and did not develop hepatic encephalopathy. A careful review of the medical history, Doppler abdominal ultrasound, and viral serologies excluded acute alcoholic and viral hepatitis, vascular causes, and biliary obstruction. Her accumulated fluid balance was neutral in the previous 48 hours. Due to suspected drug-induced liver injury (DILI), pantoprazole was withdrawn, and her liver blood tests quickly recovered (four days after stopping pantoprazole: AST 44 U/L, ALT 430 U/L, INR 0.85, total bilirubin 0.5 mg/dL, LDH 207U/L).

Considering the positive response to withdrawing the potential causative drug, a liver biopsy was not performed.[2] Due to the lower likelihood, hyperacute presentation, and prompt resolution, other causes, such as autoimmune and metabolic hepatic diseases were not investigated. Hypoxic hepatitis had been ruled out, considering the sustained hemodynamic stability throughout the hospitalization.

Although globally very well tolerated, pantoprazole has rarely been reported to cause clinically apparent liver injury with an acute hepatocellular pattern,[3] like the presented case (where the ratio of serum activity of ALT to ALP was ≥ 5 - activity is expressed as a multiple of upper limit of normal). Although no liver biopsy was performed, the pattern of injury and elevation of LDH, after exclusion of hypoperfusion, is consistent with acute hepatic necrosis. Furthermore, according to the Roussel Uclaf Causality Assessment Method (RUCAM) scale,[4] this is a probable case of pantoprazole-associated DILI (RUCAM score 6).

Despite usual prompt resolution after withdrawal of the agent, as it was the case here, acute liver failure with PPIs has been reported. Besides, although there is no information on cross-reactivity among PPIs after pantoprazole hepatotoxicity,[5] caution should be taken in case the patient needs a PPI in the future.

Altogether, this case highlights the importance of a high degree of clinical suspicion for DILI, even with widely prescribed medications such as PPIs, particularly in the critical care setting.

AUTHOR CONTRIBUTIONS

RO: Data acquisition, literature search and writing of the manuscript.

MA: Literature search and critical review of the manuscript.

PL, AB: Critical review of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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