

Rhabdomyolysis after Intentional Acetaminophen and Carbon Monoxide Poisoning

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ABSTRACT

Acetaminophen is one of the most frequent causes of acute liver failure. Rhabdomyolysis is a rare adverse reaction reported with this drug. Carbon monoxide (CO) can also lead to muscle injury but only after severe intoxication. We present a case of rhabdomyolysis associated to Acetaminophen over dosage and mild carbon monoxide exposure. A 38-year-old man was admitted because of acute hepatic injury due to voluntary acetaminophen overdose. He also reported a mild carbon monoxide exposure. He showed a delayed rising of serum creatinine with minimal elevation of other markers of renal damage. Although he was asymptomatic, rhabdomyolysis was suspected and confirmed by blood and urine analysis. The patient recovered spontaneously with conservative management. This is the first report of rhabdomyolysis associated with acetaminophen overdose in which mild CO exposure could play a contributive role.

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Key words: Adverse effect; Overdose; Acetaminophen; Rhabdomyolysis

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INTRODUCTION

Acetaminophen poisoning is the most frequent cause of acute liver failure, accounting for 46% of all cases^[1]. Liver, gastrointestinal tract and kidney injuries are frequently reported in acetaminophen overdose. There are few published reports of the association between rhabdomyolysis and acetaminophen poisoning. Pathogenic mechanisms of acetaminophen-induced rhabdomyolysis are not clearly understood and various potential explanations have been supposed, including hypersensitivity reaction^[2] or ischemic injury in the setting of multiorgan failure^[3]. Carbon monoxide (CO) overdose has also been associated with skeletal^[4,5] and cardiac^[5,6] muscle damage. The final cause of toxicity is tissue hypoxia^[7], and may be followed by reoxygenation injury, because of the production of partially reduced oxygen species^[8]. However the majority of this series refers to intensive care unit (ICU) patients, and rhabdomyolysis occurred mainly in the context of multiorgan failure^[9]. Indeed, the possible implication of hemodynamic or pharmacological factors could not be excluded.

CASE REPORT

A 38-year-old man was admitted to our hospital because of intentional Acetaminophen overdose. He declared daily consumption of cannabinoids and drinking 60 g of ethanol per week. Otherwise his previous medical history was unremarkable. Twelve hours before admission he had ingested 40 g of Paracetamol and thereafter he inhaled car exhaust fumes for almost 3 h. He became slightly confused, with epigastric pain and nausea but remained conscious and he left the car voluntarily. After 6-8 h of gas inhalation he went to the Emergency Department. On admission he was asymptomatic. Physical and neurological examinations were normal. Glasgow scale was 15. Blood pressure was 144/92 mmHg with 91 beats per minute. Arterial oxygen saturation was 97% breathing ambient air. No sign of myocardial ischemia on electro cardiography (ECG) was observed. A complete blood analysis showed increased aminotransferases levels with normal bilirubin, and no other abnormalities (Table 1). Paracetamol levels were 157 mg/ dL 12 h after of Paracetamol ingestion, indicating a probable risk of hepatotoxicity according to Rumack-Matthew normogram^[10]. Carboxyhemoglobin levels were 0.6% 8 h after carbon monoxide inhalation (normal values below 3% in nonsmokers and 10% in smokers).

N - Acetylcysteine (NAC) was administered as a loading dose of 150 mg/kg (13.5 g), followed by a continuous infusion of 50 mg/kg in 4 h and later 100 mg/kg over 16 h. Acute hepatitis A, B and C were excluded by serological tests. An arterial blood gases analysis showed pH 7.39, pO₂ 86 mmHg, pCO₂ 37 mmHg and HCO₃⁻ 23.2 mmol/L. Abdominal and cranial Doppler ultrasound showed no abnormalities.

The clinical course of the hepatitis was favorable, without any signs of encephalopathy or coagulopathy. As shown in Table 1, aminotransferases (AST and ALT) and lactate dehydrogenase (LDH) levels were elevated until day 3 after admission and then progressively decreased. However, from the third day after the admission serum Creatinine levels progressively increased until day 7, with minimal elevation of Urea and spontaneous urine output all the time (Table 1). The same day, the patient had atypical chest pain, with no ECG changes. A complete cardiac panel showed marked elevation of Creatinine phosphokinase (CPK) only (Table 1), so that rhabdomyolysis was suspected and confirmed thereafter by retrospective determination of CPK and Aldolase in stored sera. The patient did not report myalgia at any time during the admission. He remained hemodynamically stable all the time. Only mild kidney tubular damage was present with mild proteinuria. Marked myoglobinuria was observed. N-Acetyl-Glucosaminidase levels were normal, while a slight elevation of cystatin C was detected. Renal function recovered spontaneously, without renal replacement therapy requirement. The patient was discharged fourteen days after the admission. Two months later he was asymptomatic, taking no drugs. Blood analysis showed an almost complete recovery of liver and renal function tests, with a mild elevation on gamma-glutamyl transferase (GGT), Aldolase and Creatinine (Table 1).

Table 1 Laboratory data.

| Variable (reference range) | On admission | During admission | | | | | | Discharge | Outpatient |
|-----------------------------------|--------------|------------------|-------|--------|-------|-------|------|-----------|------------|
| Days after admission | 0 | 1st | 2nd | 3rd | 4th | 7th | 17th | 45th | |
| Total Bilirubin, mg/dL (0 - 1.2) | 2.10 | 2.58 | 3.23 | 2.18 | 1.86 | - | - | 0.45 | |
| Direct Bilirubin, mg/dL (0 - 0.4) | 0.83 | 1.0 | 1.49 | 1.56 | 1.40 | - | - | 0.11 | |
| AST 1, UI/L (1 - 25) | 503 | 389 | 863 | 6.965 | 741 | 42 | 17 | 11 | |
| ALT 1, UI/L (1 - 29) | 537 | 581 | 1.309 | 9.642 | 4.245 | 1.171 | 92 | 22 | |
| GGT 1, UI/L (0 - 38) | 66 | 59 | 61 | 93 | 153 | 289 | 237 | 44 | |
| LDH 1, UI/L (160 - 320) | 1.071 | 735 | 1.314 | 12.124 | - | - | - | - | |
| CPK 1, UI/L (0 - 130) | 6.700 | 5.273 | 3.014 | 1.812 | - | 179 | 73 | 136 | |
| Aldolase, UI/L (0.1 - 7.6) | 228 | 192 | 300 | 895 | - | 85 | 10 | 6.6 | |
| Urea, g/L (0.08 - 0.55) | 0.26 | 0.26 | 0.11 | 0.21 | 0.50 | 0.77 | - | 0.27 | |
| Creatinine, mg/dL (0.4 - 1.1) | 1.3 | 1.1 | 1.1 | 3.1 | 5.2 | 7.2 | - | 1.6 | |
| Lactic acid, mmol/L (0.6 - 2.44) | 1.29 | 0.84 | 1.13 | 1.39 | - | - | - | - | |
| INR 1 (0.9 - 1.1) | 1.2 | 1.4 | 1.5 | 2.4 | 1.2 | 0.9 | - | - | |
| Factor V (70 - 130 %) | 58 | 65 | 35 | 64 | 93 | - | - | - | |

1 Aspartate transaminase (AST); Alanine transaminase (ALT), Gamma glutamyl transpeptidase (GGT); Lactate dehydrogenase (LDH); Creatine phosphokinase (CPK); International normalized ratio (INR).

DISCUSSION

We report a case of acute hepatic injury secondary to acetaminophen poisoning, without signs of encephalopathy or coagulopathy. No clinical (headache, myalgia, dizziness, or neuropsychological impair-

ment) or analytical (normal carboxyhemoglobin) signs of CO poisoning were seen.

In this report rhabdomyolysis manifested as a rapid increase in plasma Creatinine, CPK and Aldolase. No clinical symptoms developed. Myoglobinuria confirmed the presence of muscle injury because it only occurs in the context of rhabdomyolysis. Muscle injury is initiated by depletion of ATP leading to disintegration of the myocytes. The marked elevation of CPK and Aldolase in this case report indicates a serious muscle injury. However it is noticeable that few symptoms and no acute renal failure developed. In this case, some degree of tissue hypoxia induced by CO might have played a role in myocyte damage, but no other tissue had been affected by this chemical.

Acetaminophen has been supposed to cause rhabdomyolysis in few previous reports. However in almost all cases a clear causal relationship has not been established, because of the interaction of multiple agents (ibuprofen^[2], caffeine, phenazone^[11] and salicylates^[12]) or the simultaneous presence of multiorgan failure. There is only one report of rhabdomyolysis directly related to acetaminophen, where a hypersensitivity reaction has been regarded as the pathogenetic mechanism^[13]. In our case the Naranjo Score^[14] was 5, suggesting that muscle damage was a likely adverse reaction of acetaminophen. On the other hand, rhabdomyolysis has been described as a consequence of severe CO intoxication^[4]. However there is no reported case of mild CO intoxication as cause of rhabdomyolysis.

This is the first case describing the association of rhabdomyolysis as a clinical manifestation of combined acetaminophen and mild CO poisoning. Although in our case CO seems to have played a minor role, the interaction of these two factors could have triggered the muscle damage.

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