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LETTER TO THE EDITOR / *LETTRE À L'ÉDITEUR*

Colchicine intoxication mimicking an acute surgical abdomen: report of a pediatric observation

Intoxication à la colchicine mimant un abdomen chirurgical : à propos d'une observation pédiatrique

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To the editor,

Colchicine is an alkaloid extracted from *Colchicum autumnale* and *Gloriosa superba* [1]. It is an antimitotic agent belonging to the family of spindle poisons used in several inflammatory diseases like gout and Behcet's disease. Poisonings have been exceptionally reported in children [2]. Here, we describe an unusual colchicine poisoning in a young girl mimicking an acute surgical abdomen.

A 14 year-old girl, treated for Behcet's disease with colchicine, was referred for acute diarrhea and abdominal pain. She was conscious, afebrile, with the following vital signs: blood pressure: 92/58 mmHg, heart rate: 130 /min, respiratory rate: 22/min, and SpO2: 98% on room air. There was a slight abdominal guarding. Pulmonary and cardiac examinations were unremarkable. Peripheral pulses were symmetrical. Abdominal X-ray did not reveal pneumoperitoneum. Ultrasound examination showed no peritoneal effusion. Despite supportive management and ceftriaxone + metronidazole combination, her abdominal pain worsened and vomiting started. The patient was admitted to the operating room. Midline laparotomy found a few milliliters of peritoneal fluid. Peritoneal lavage with warm isotonic saline was performed. No significant surgical abnormality was observed. The patient was admitted to the pediatric intensive care unit (ICU). Weaning from mechanical ventilator was impossible because of persistent hypoventilation. She developed a progressive paralysis of lower and upper limbs as well as loss of deep tendon reflexes, in the absence of hypokalemia and rhabodmyolysis. Electromyography was normal. Bacteriological cultures were negative. Alopecia appeared on day 2 and pancytopenia was further assessed (platelets: 1 G/L, hemoglobin: 7 g/dl, and white blood cells: 2 G/L) with no abnormal coagulation test. Diagnosis of colchicine poisoning was suspected. Spontaneous neurological recovery was progressive allowing extubation on day 7. The patient disclosed having ingested 24 mg of colchicine (0.6 mg/kg) for a suicidal attempt following an argument with her family. She left the hospital on day 15 after full recovery with a psychiatric follow-up.

Colchicine poisoning is rare in the western countries, representing 0.7% of all intoxications, but more common in the Mediterranean countries because of its wide prescription for periodic disease [2,3]. Colchicine is a soluble alkaloid, absorbed by the ileum, and partially metabolized by the liver cytochrome P450 3A4. Metabolites are excreted in the bile, while one fifth of colchicine is excreted in its active form by the kidneys [3]. Colchicine acts by binding reversibly to tubulin (half life: 20 hours), preventing its polymerization into microtubules, which blocks the mitotic spindle and interrupts cell proliferation [4,5]. Thus, colchicine toxicity mainly involve cells with rapid turnover including the gastro-intestinal (GI) epithelium and bone marrow cells [6].

To our knowledge, the youngest reported colchicine-poisoned patient in the literature was 3-year old [7]. Only one fatal case in children has been reported [8]. Death usually occurs between 36 and 72 hours after ingestion due to respiratory and circulatory failure. Poisoning severity is tightly related to the ingested dose [2,9]: While the therapeutic doses range between 0.015 and 0.03 mg/kg, a dose less than 0.5 mg/kg results in GI disorders. A higher dose between 0.5 and 0.8 mg/kg induces medullary aplasia which causes 10% of deaths. Beyond 0.8 mg/kg, colchicine

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poisoning is fatal [10]. In our case, colchicine poisoning was suspected only after laparotomy and inability to wean the patient from mechanical ventilator along with the progressive neuromuscular paralysis and alopecia. Radioimmunologic assay to measure plasma colchicine concentration is generally helpful to confirm the diagnosis; unfortunately, no measurement was performed in our case.

GI toxicity is variable, ranging from nausea and vomiting to abdominal pain and diarrhea. Symptoms appear in the first hours and lead to dehydration, hypovolemia, and electrolyte disturbances [2]. GI involvement may be more serious with hepatomegaly, elevated liver and pancreatic enzymes [11]. The neuromuscular blockade that markedly occurred in our patient is exceptional and has been described in patients on long-term treatment [12]. Typically there is an ascending flaccid paralysis with loss of deep tendon reflexes [13], like in our patient. Neurological manifestations may also include delirium, stupor, coma, and convulsions, in relation to colchicine-induced acidosis, hypoxia or electrolyte disturbances [14]. Hematologic features are common and include leucopenia leading sometimes to bacterial infections which may contribute to fatality. Platelet consumption secondary to disseminated intravascular coagulation represents the main cause of thrombocytopenia and resulting bleedings [15]. Cardiovascular symptoms are usually related to hypovolemia or sepsis, but cardiac toxicity may occur including cardiac failure and arrhythmias leading to death. Acute respiratory distress syndrome may also occur; however, in our patient, neuromuscular blockade was the cause of respiratory failure. Finally, alopecia is the main dermatologic event of colchicine overdose [2].

Management of colchicine poisoning is supportive and require ICU admission. GI decontamination should follow the current recommendations [2]. Adequate fluid repletion and treatment of GI losses-related electrolyte abnormalities are mandatory [16]. Careful attention should be paid to treat overwhelming infections and overcome hemorrhage secondary to thrombocytopenia [9,17]. Since colchicine has an elevated distribution volume, dialysis is ineffective [11]. Although treatment with glutamate and aspartate was shown beneficial in animals [4], there is no current available antidote. However, after a reported survival following the ingestion of a lethal dose of colchicine [18], immunotherapy with polyclonal anti-colchicine antibody fragments appears promising for the future.

In conclusion, physicians should be aware that colchicine overdose could mimic an acute surgical abdomen and should thus be promptly suspected in case of negative laparotomy in a patient treated with colchicine.

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