CASE REPORT

Bizarre and scary ECG in yew leaves poisoning: Report of successful treatment

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Yew leaves poisoning is a rare life-threatening intoxication, whose diagnosis can be difficult. Initial symptoms are nausea, vomiting, abdominal pain, dizziness, tachycardia, muscle weakness, confusion, beginning within 1 hr from ingestion and followed by bradycardia, ventricular arrhythmias, ventricular fibrillation, severe hypotension, and death. Taxine-derived alkaloids are responsible for the toxicity of the yew leaves, blocking sodium and calcium channels, and causing conduction abnormalities. Because of lack of a specific antidote and limited efficacy of common antiarrhythmic drugs, prompt diagnosis, detoxification measures, and immediate hemodynamic support (also with transvenous cardiac stimulation) are essential.

KEYWORDS

poisoning, taxine, ventricular arrhythmias, yew leaves

1 | INTRODUCTION

The literature reports several cases of yew leaves intoxication in humans, often with fatal outcome (Cummins et al., 1990; Pietsch et al., 2007; Pierog, Kane, Kane, & Donovan, 2009; Thooft et al., 2014; Tranca & Petrisor, 2013; von der Werth & Murphy, 1994; Willaert, Claessens, Vankelecom, & Vanderheyden, 2002). The present report discusses a case of yew leaves poisoning involving a Chinese family (parents and son) who picked up some raw needles from a yew bush in the garden of the railway station of their town and blended them to make an infusion. They were attended and managed simultaneously in our Emergency Department (ED). Unlike most of the previous reports concerning yew poisoning, in the present one the three patients had not suicidal intention: on the contrary, they believed it were a sort of *panacea*, effective in preventing cancer.

2 | CASE REPORT

2.1 | Patient 1

The father, a 66-year-old man, was the first to become symptomatic: after vomiting, he collapsed and, being found in cardiac arrest

due to ventricular fibrillation (VF), was defibrillated at home by the Emergency Medical Service personnel. Once in ED he was conscious and hemodynamically stable. Blood tests were unremarkable, except for a high-lactate metabolic acidosis due to the recent cardiac arrest. The first ECG recorded showed a sinus rhythm with a heart rate of 75 bpm, first-degree atrio-ventricular (AV) block, and enlarged QRS (160 ms), followed by a couple of short-coupled premature ventricular beats (PVC) in bigeminal pattern (Figure 1a). The toxicology service (Laboratory of Clinical & Experimental Toxicology and Poison Control Center, Toxicology Unit, Salvatore Maugeri Foundation, IRCCS, Pavia, Italy) was immediately consulted for the management. Gastric lavage was performed followed by administration of oral charcoal, cathartic, and intravenous magnesium sulfate (2 g) and sodium bicarbonate 1 mmol/kg bolus, followed by infusion of 0.5 mmol kg⁻¹ h⁻¹. In addition, a single bolus of 250 ml 20% lipid emulsion was administered. The patient was admitted in the intensive care unit for 72 hr, with continuous ECG monitoring, without complications. PVCs disappeared within the first 3 hr, while AV block, QRS enlargement, and QT prolongation gradually regressed within 48 hr (Figure 1b).

2.2 | Patient 2

The 36-year-old son complained of general discomfort after the ingestion of the infusion. During monitoring in the ED, he experienced

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FIGURE 1 (a) First ECG of the father, 66-year-old man, recorded on arrival at the Emergency Department. (b) ECG recorded in the same patient after detoxification measures (48 hr later)

cardiac arrest due to the onset of pulseless ventricular tachycardia (VT) degenerating into VF. Cardiopulmonary resuscitation was started and direct current (DC) shock was given, with immediate return of spontaneous circulation. The ECG showed sinus rhythm with normal PR interval, mild QRS enlargement (110 ms), and spread repolarization abnormalities, with coved-type ST segment elevation in III, aVF, aVR, V1-V4 leads, and ascendant ST depression in the other leads (Figure 2a). The same detoxification maneuvers were carried out. The boy had also episodes of vomiting after defibrillation. He remained asymptomatic and ECG gradually normalized (Figure 2b).

2.3 | Patient 3

The 60-year-old mother arrived to the ED in shock, Glasgow coma scale 9, with a slow idioventricular rhythm at ECG, which required immediate temporary external electrical pacing. She was intubated and norepinephrine infusion was started ($0.9 \text{ mcg kg}^{-1} \text{ min}^{-1}$ up to $1.6 \text{ mcg kg}^{-1} \text{ min}^{-1}$). Few minutes later she experienced repetitive episodes of pulseless polymorphic VT, treated with multiple DC shocks (Figure 3a). A temporary transvenous pacemaker was inserted. Amiodarone was not efficient, while lidocaine infusion (0.5 mg/kg) resulted partially effective in preventing relapses of ventricular arrhythmias; the most effective measure was the increase of pacing rate up to 130 bpm. Detoxification maneuvers were promptly carried out in conjunction with alkalization and lipid infusion. Noradrenaline infusion was reduced and discontinued within 36 hr, the pacing rate was gradually slowed and the

temporary pacemaker was removed when stable sinus rhythm was restored (Figure 3b). She was extubated after 72 hr and remained stable and asymptomatic.

Neither electrolyte disorder (except for mild hypokalemia at the arrival to the ED) nor significant blood test abnormalities, including digoxin levels and myocardial markers were found in all the three patients. All of them underwent transthoracic echocardiography, which showed normal contractility of the left ventricle.

3 | DISCUSSION

Yew (*Taxus baccata*) is an ornamental coniferous shrubbery, widespread in Northern Italy. The whole plant is toxic, except for the scarlet aril (von der Werth & Murphy, 1994). The potent effect of the toxin is mainly cardiovascular, resulting in hypotension, rhythm alterations leading to VF within few hours from ingestion. Toxicity is ascribed to taxine alkaloids named A and B. Taxine B is the most cardiotoxic and its properties derive from the inhibition of calcium and sodium channels in myocardial cells, causing an increase in cytoplasmic calcium levels. This interferes with the conduction system, depressing AV conduction in a dose-dependent manner, up to complete cardiac arrest. Moreover, ECG examination reveals prolonged and aberrant QRS intervals and VT, eventually resulting in VF (Willaert et al., 2002). The sodium channel blockade effect of the taxines is similar to that of class I antiarrhythmic drugs such as quinidine, procainamide, and disopyramide, prolonging the QT interval and widening the QRS; the mechanism of calcium channel block is similar to that of class IV

FIGURE 2 (a) First ECG of the son, 36-year-old man, recorded on arrival at the Emergency Department. (b) ECG recorded in the same patient after detoxification measures (48 hr later)

antiarrhythmics, such as diltiazem and verapamil, affecting the phase 2 of the action potential, slowing AV conduction, with prolongation of PR interval up to complete block (Alloatti et al., 1996). Minor manifestations of taxine toxicity (dizziness, pupil dilation, nausea, vomiting, diffuse abdominal pain, muscle weakness, urticarial reactions, and convulsions) can precede bradycardia, bradypnea, diastolic cardiac standstill, and death. Postmortem evaluation of acute poisoning is reportedly unremarkable: macroscopic abnormalities are nonspecific and microscopic lesions are rarely observed (Wilson, Sauer, & Hooser, 2001). Taxines are metabolized by liver enzymes and excreted into the bile; only a small fraction is excreted by the kidney.

Treatment of yew intoxication is mainly based on case reports (Cummins et al., 1990; Pierog et al., 2009; Thooft et al., 2014; Tranca & Petrisor, 2013; von der Werth & Murphy, 1994; Willaert et al., 2002). Since there is no antidote and antiarrhythmic therapy proved to be ineffective, a prompt diagnosis is pivotal as immediate supportive actions are the only valuable alternative. Gastric lavage, oral activated charcoal (to limit further absorption of toxins), administration of intravenous sodium bicarbonate, inotropic support, mechanical ventilation, and temporary cardiac pacing are life-saving measures.

Sodium bicarbonate bolus and infusion have proven to be effective (Pierog et al., 2009), as in the case of our patients, reversing acidosis and increasing sodium conductance through myocardial sodium channels. Hemodynamic support with vasoactive or inotropic amines may be necessary in case of refractory hypotension. Aggressive treatment of concurrent hypokalemia can be important to prevent further arrhythmias (Wilson et al., 2001). There are no data regarding the effectiveness of dialysis in *Taxus* acute intoxication: considering the large volume of distribution of *Taxus* alkaloids and the physicochemical properties of taxines (high molecular weight and relative water insolubility), effective removal of taxines by haemodialysis appears unlikely (Wilson et al., 2001).

Although taxine alkaloids are structurally similar to digitoxin, digoxin-specific antibody fragments resulted ineffective (Cummins et al., 1990; von der Werth & Murphy, 1994; Willaert et al., 2002).

Isotonic lipid emulsion administration was proven effective mainly in local anesthetic intoxication, but clinical improvement has been reported in intoxication from a number of lipophilic and nonlipophilic substances (Cao, Heard, Foran, & Koyfman, 2015). Lipid sink

FIGURE 3 (a) First ECG of the mother, 60 years old woman, recorded in the Intensive Care Unit, after placing temporary transvenous pacemaker. (b) ECG recorded in the same patient after detoxification measures and temporary pacemaker removal (72 hr later)

phenomenon and/or enhancement of cardiac metabolism are the supposed mechanisms of action. Since taxine is a highly hydrophobic molecule, there could be a rationale for lipid emulsion infusion in yew intoxication. Unfortunately, in our experience lipid infusion showed no significant effect.

The favorable outcome of our patients may be due to the prompt diagnosis and treatment. The first and more effective maneuvers were directed to limit further gastrointestinal absorption of taxines, in order to prevent more severe injuries, first of all the development of severe ventricular dysfunction. Moreover, in our case, diagnosis was prompt because the patients wisely brought to the hospital a branch of the plant and a nurse recognized it at a glance, but in most cases diagnosis can be extremely challenging for the physician.

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