CASE REPORT

Amitraz: a mimicker of organophosphate poisoning

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SUMMARY

Amitraz is used as an ectoparasiticide for dogs and cattle. Human poisoning due to amitraz may be misdiagnosed as organophosphate/carbamate (OPC) toxicity, since amitraz poisoning shares several clinical features (miosis, bradycardia and hypotension) encountered with OPC poisoning. A 19-year-old man with an alleged history of suicidal ingestion of a pesticide presented with drowsiness and was found to have constricted pupils, hypotension and bradycardia. He was diagnosed as a case of OPC poisoning and was treated with atropine and pralidoxime prior to presentation to our centre. Absence of a hypersecretory state, and the presence of hyperglycaemia and hypothermia along with a normal serum cholinesterase level suggested an alternate possibility. Retrieval of the poison container confirmed the diagnosis of amitraz poisoning. The patient made a rapid recovery with supportive management. Clinician awareness is key to successful management of this poisoning, which carries a good prognosis.

BACKGROUND

Amitraz, a member of the formamidine family of pesticides, is used as a veterinary ectoparasiticide for dogs and livestock.^{1–3} It is supplied as a 12.5–50% solution, generally with xylene as the solvent, and is available for use in many regions in the world.⁴ However, awareness about this compound and its toxicity remains poor among clinicians.⁵ Amitraz poisoning is often misdiagnosed as organophosphate/carbamate (OPC) poisoning, since it manifests with several clinical features (miosis, bradycardia and hypotension) observed with OPC poisoning; organophosphate/carbamates are more widely available compounds and universally known to emergency physicians.^{5–6} We present a case of a young patient who developed amitraz intoxication after suicidal ingestion and was initially misdiagnosed with OPC poisoning.

CASE PRESENTATION

A 19-year-old man presented with an alleged history of suicidal ingestion of 100 mL of a substance used as a pesticide. Within 30 min of intake of the poison, the patient became drowsy. There was no history of fever, headache, vomiting or seizures, and no neurological deficit. There were no symptoms of abdominal pain, diarrhoea, excessive sweating or salivation. There were no urinary problems. The patient was initially rushed to a local hospital where he was found to have pulse rate of 40 bpm, respiratory rate of 28 breaths/min, blood pressure 84/52 mm Hg and a normal body temperature (37.2°C). He was drowsy but followed

verbal commands sluggishly. He also had constricted pupils with sluggish reaction to light. Arterial blood gases showed hypoxaemia and mixed metabolic and respiratory acidosis (table 1). The patient was suspected to have OPC poisoning, and was treated with atropine (cumulative dose 4 mg), pralidoxime (2 g bolus) and dopamine infusion (5 µg/kg/min). His heart rate increased from 40 to 100 bpm and pupils reverted to normal size. However, the patient remained drowsy. He was then brought to our hospital about 4 h after consuming the poison and was admitted to the respiratory intensive care unit. At the time of admission, his heart rate was 105 bpm, respiratory rate was 34 breaths/min and blood pressure was 90/50 mm Hg. There was presence of hypothermia (an axillary temperature of 35°C). He had an altered mental status with a Glasgow Coma Scale score of 8, the pupils were normal sized. Chest auscultation revealed normal breath sounds. There were no abnormal findings on abdominal examination. There was no neck rigidity or focal neurological deficit.

INVESTIGATIONS

Investigations revealed hypernatraemia (serum sodium, 146 mEq/L) and hyperglycaemia (blood sugar, 210 mg/dL), raised alkaline phosphatase (176 U/L), and mildly raised lactate dehydrogenase (504 U/L) with normal levels of aspartate transaminase and alanine transaminase (table 1). Serum cholinesterase levels were normal. Chest radiograph was normal and ECG showed T wave inversion in leads II, III, aVF and V2–V6. Ultrasonography of the abdomen revealed a normal liver and biliary tree.

DIFFERENTIAL DIAGNOSIS

- ▶ Opioid poisoning
- ▶ Organophosphate poisoning
- ▶ Carbamate poisoning
- ▶ Organochlorine poisoning
- ▶ Amitraz poisoning

The presence of hyperglycaemia and hypothermia, and the absence of a hypersecretory state (salivation, lacrimation, perspiration and diarrhoea) pointed against OPC poisoning. A detailed enquiry about the patient's symptoms revealed that an unusual odour was emanating from his mouth, which was similar to a garlic-like smell. The patient's attendants were requested to retrieve the container of the poison. The container proved to be that of 'RIDD', which contains 12.5% amitraz, which conclusively excluded other causes. The dose of amitraz ingested by the patient was around 12.5 g.

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Table 1 Laboratory findings of the patient

Parameter	Value
Haemoglobin (g/dL)	14.3
Total leucocyte count (cells/mm ³)	12 700
Platelet count (×10 ³ /mm ³)	147
Blood urea (mg/dL)	31
Serum creatinine (mg/dL)	0.5
Serum albumin (g/dL)	4.5
Serum bilirubin (mg/dL)	0.6
Alanine transaminase (U/L)	26
Aspartate transaminase (U/L)	24
Alkaline phosphatase (U/L)	176
Serum calcium (mg/dL)	9.1
Serum LDH (U/L)	504
Serum amylase (U/L)	28
Serum lipase (U/L)	16
Creatine kinase (U/L)	189
Serum sodium (mEq/L)	146
Serum potassium (mEq/L)	4.1
Serum chloride (mEq/L)	112
pH	7.05
PaO ₂ (mm Hg)	40
PaCO ₂ (mm Hg)	95
HCO ₃ ⁻ (mmol/L)	26
FiO ₂	0.21

FiO₂, fractional inspired oxygen; LDH, lactate dehydrogenase; PaCO₂, arterial partial pressure of carbon dioxide; PaO₂, arterial partial pressure of oxygen.

TREATMENT

The patient was intubated and mechanically ventilated. In addition to intravenous fluids (1 L in first hour followed by 100 mL/h for 24 h), norepinephrine infusion (initial dose 0.5 µg/kg/min) was administered for vasopressor support. He was also administered subcutaneous unfractionated heparin (5000 units three times a day) and intravenous pantoprazole (40 mg a day).

OUTCOME AND FOLLOW-UP

The patient's blood gases improved rapidly, hypotension resolved in 6 h and sensorium normalised in 12 h after admission. He was weaned off the ventilator and extubated successfully after 18 h of mechanical ventilation. Blood sugars normalised spontaneously without the need for insulin. The patient was discharged after 48 h of hospital admission. He was in good health without any residual abnormality at 2-month follow-up.

DISCUSSION

This case highlights that amitraz intoxication may get misdiagnosed as OPC poisoning due to similar clinical manifestations. It is important that physicians are aware of this intoxication, especially in regions where this toxin is readily available.

A recent systematic review of 310 patients with amitraz poisoning has summarised the important features of poisoning with this chemical.¹ Toxic exposure to amitraz occurs by ingestion, inhalation or percutaneous exposure. Amitraz is metabolised rapidly in vivo to an active metabolite *N'*-(2,4-dimethylphenyl)-*N*-methyl-formamidine (BTS27271), which acts as an agonist on both presynaptic and postsynaptic α₂-adrenergic receptors.^{7 8} Stimulation of presynaptic receptors inhibits noradrenaline discharge, while postsynaptic receptor stimulation has α₁-agonist effects.^{8 9} These actions are

responsible for most of the clinical manifestations associated with this poisoning. The most commonly reported clinical features of amitraz poisoning include altered sensorium (83%), miosis (50%), bradycardia (47%), vomiting (36%), respiratory failure (34%) and hypotension (31%).¹ Hyperglycaemia (48%) and hypothermia (24%) are distinctive features of this poisoning.¹ Although miosis occurs in about half the patients, higher doses can cause mydriasis (observed in 12%). Seizures are seen only in a minority (6% patients). Arrhythmias such as atrial fibrillation and ventricular arrhythmias may occur uncommonly and generally respond to standard treatment; fatal torsades de pointes is rare.^{10–12}

Our patient had altered sensorium, miosis, bradycardia, hypotension, hypothermia and respiratory failure, thus exhibiting the classic clinical characteristics of amitraz poisoning. In contrast to a recently reported case, there were no significant ECG abnormalities such as ventricular premature contractions.¹³ Recovery was rapid, similar to previously reported cases.^{13 14} An important learning point from our case is that, due to an overlap of clinical features, amitraz poisoning may be misdiagnosed as OPC toxicity, as seen in the index case. This misdiagnosis may occur in as many as 17–22% of patients.^{5 15} Several clinical features point towards amitraz toxicity as opposed to OPC poisoning. Presence of hyperglycaemia, hypothermia and reduced gastrointestinal motility occurs with amitraz, while OPC leads to increased gastrointestinal motility and hypothermia is rare. Fasciculations and a hypersecretory state (salivation, lacrimation, perspiration and diarrhoea) are absent in amitraz toxicity and point strongly towards OPC poisoning. Although miosis is common to both intoxications, mydriasis, occasionally presenting with amitraz, excludes untreated OPC poisoning. A distinctive 'moth ball-like' odour is encountered with amitraz poisoning, while a garlic-like smell may be noticed in OPC poisoning.¹⁶ Importantly, the serum cholinesterase levels are normal with amitraz poisoning, while they are low in the case of OPC poisoning.⁵ Gas chromatography-mass spectrometry and gas liquid chromatography may be employed to measure the levels of amitraz and its metabolites in the serum and urine, but are not available in day-to-day practice.^{2 10 12}

Clinician awareness is possibly the most important element in the successful diagnosis of the poisoning. In a study reported from a poison information centre, the clinicians were unfamiliar with amitraz in all instances.¹⁵ Thus, knowledge of the clinical manifestations of this poison is vital. Further, physicians should always insist on retrieving the poison container and identifying the active compound in the formulation. If that is not possible, the patient's attendants should be specifically asked about the preparation, whether it is an insecticide or a parasiticide.

Management is supportive as there is no specific antidote for amitraz intoxication. Monitoring of respiratory, cardiovascular and central nervous system functions is vital.¹⁷ Airways should be secured immediately in unconscious patients to avoid the risk of aspiration. Intravenous fluids and vasopressor/inotropic support should be employed in patients with shock. The utility of decontamination methods, namely, gastric lavage and activated charcoal, is unclear. While pralidoxime has no role in management, the use of atropine is controversial. It has been suggested that atropine is useful only in patients with symptomatic bradycardia and is not necessary for those with only asymptomatic bradycardia and/or miosis.¹⁷

Amitraz poisoning carries a good prognosis with a low case fatality rate (2%).¹ Although 33% of patients develop respiratory failure and 20% of patients require mechanical ventilation, most of them were weaned off it in 48 h,¹ as seen in the index case.

Learning points

- ▶ Amitraz intoxication may be misdiagnosed as OPC poisoning due to overlapping clinical manifestations.
- ▶ The presence of a 'mothball-like' odour, hyperglycaemia, hypothermia and/or reduced gastrointestinal motility; absence of fasciculations and hypersecretory state (salivation, lacrimation, perspiration and diarrhoea), supported by a normal serum cholinesterase level, help in distinguishing amitraz toxicity from OPC poisoning.
- ▶ Retrieval of the poison container is extremely important for correct identification.
- ▶ There is no specific antidote; atropine may be used for symptomatic bradycardia.
- ▶ The outcome of amitraz poisoning is excellent with supportive management.

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Competing interests None declared.

Patient consent Obtained.

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