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CASE REPORT

Fatal Amitraz Poisoning: A Case Report

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Abstract

Amitraz is insecticide and acaricide derived from formamidine which is commonly used in veterinary and agricultural practice, which has a significant risk of accidental, occupational, or intentional exposure. Even though, Amitraz poisoning is very rare clinical presentation, it can mimic organophosphate poisoning due to overlapping features such as bradycardia, hypotension, and respiratory depression, increasing the risk of misdiagnosis. In this article, we report a fatal case of Amitraz poisoning in a 25-year-old female who ingested the compound with suicidal intent. She developed severe toxic symptoms and died approximately 36 hours post-ingestion. Autopsy revealed 100 ml of greenish-brown, pungent gastric contents, congestion of the gastric mucosa and internal organs, and chemical analysis confirmed Amitraz in viscera. Histopathology showed focal sinusoidal dilation, mild steatohepatitis, zone-3 necrosis, and inflammatory infiltrates in the liver; acute tubular necrosis and degenerative changes in the kidneys; and diffuse alveolar hemorrhages, pulmonary oedema, and thickened alveolar septa in the lungs. To distinguish Amitraz poisoning from organophosphate poisoning, clinicians should note the absence of a hypersecretory state, the presence of hypothermia, frequent hyperglycaemia, and normal serum cholinesterase levels in Amitraz poisoning. Early recognition of these differences is essential to ensure correct diagnosis and prompt, appropriate treatment.

Keywords: Amitraz, Acaricide, Suicide, Autopsy

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Introduction

Amitraz (CAS No: 33089-61-1) is an formamidine pesticide (1,5 di(2,4-dimethylphenyl)/3-methyl-1,3,5 triazapenta-1,4-diene) that acts on α-2 adrenergic receptors as α-2 agonist and is used worldwide to control ticks in animals [1]. The clinical toxidrome seen in amitraz poisoning cases is somewhat similar to that of cholinesterase inhibitor poisoning and sometimes had been misdiagnosed as poisoning due to organophosphates (OP) and clonidine. As a result, many patients receive an incorrect treatment due to an erroneous diagnosis [2]. This, along with underreporting, further complicates the identification and documentation of such cases in India [3].

From 2014 through 2016 New South Wales Poison Information Centre (NSWPIC, Australia's largest poisons information centre) received 2655 calls regarding exposure to veterinary pharmaceutical products which amounts to 11.72 human exposures to veterinary pharmaceuticals per 1000 PIC (Poison Information Centre) initial contact exposure calls (Confidence Interval, CI: 10.95–12.49) per year. The vast majority of exposures were with products intended for companion animals, particularly of the class "antiparasitic products, insecticides and repellents" [4]. This indicates a global concern about accidental poisoning from veterinary care products.

In India, the National Poisons Information Centre and studies conducted at several tertiary care hospitals have noted a rising trend in pesticide poisonings, with amitraz accounting for a small yet significant fraction of these cases. A 2019 retrospective study from a South Indian tertiary care centre reported that amitraz was responsible for approximately 1.5–2% of all pesticide poisonings over a five-year period. In fact, the true incidence may be higher due to frequent misclassification of this substance under a more commonly used pesticide or unknown poison categories[5]. This case report brings forth a rare but fatal outcome of amitraz ingestion in an adult patient.

Case details

A 25-year-old female was referred to our institute with an alleged history of deliberate ingestion of an insecticide (later confirmed to be Amitraz). Despite continuous treatment, the patient succumbed to poisoning after a survival period of approximately 36 hours. On postmortem examination, no external injuries were noted. Internal examination revealed approximately 100 ml of greenish-brown fluid with a pungent odour in the stomach, with congestion of the gastric mucosa. The internal organs, including the brain, lungs, liver, and kidneys, appeared grossly congested. No other gross pathological findings were observed. Viscera including stomach and its contents, small intestine and its contents, one half of each kidney and liver were preserved and sent for chemical analysis. The forensic science laboratory report confirmed the presence of Amitraz, establishing the diagnosis of Amitraz poisoning. In addition, tissue samples from the lungs, liver, and kidneys were sent for gross and histopathological examination.

The Lung sections showed diffuse alveolar haemorrhage, pulmonary oedema and infiltration of inflammatory infiltrates with alveolar septal wall thickening (Figures 1 and 2), Liver showed focal sinusoidal dilation, mild steatohepatitis, zone-3 necrosis, lobular and periportal inflammatory infiltrates (Figures 3 and 4), Kidney showed degeneration of tubular

epithelium (Acute tubular necrosis), some tubules show atrophic changes, some show dilatation with granular casts and chronic inflammatory infiltrates (Figures 5 and 6). These findings were supportive of multi-organ toxicity associated with Amitraz ingestion. The cause of death in this case was opined as multi organ dysfunction syndrome as a complication of amitraz poisoning.

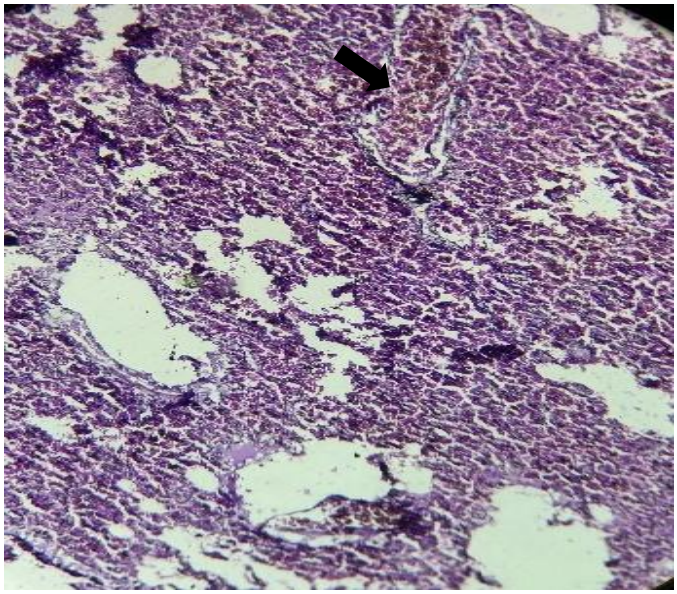

Figure 1. Alveolar haemorrhage (High power 40x, H&E)

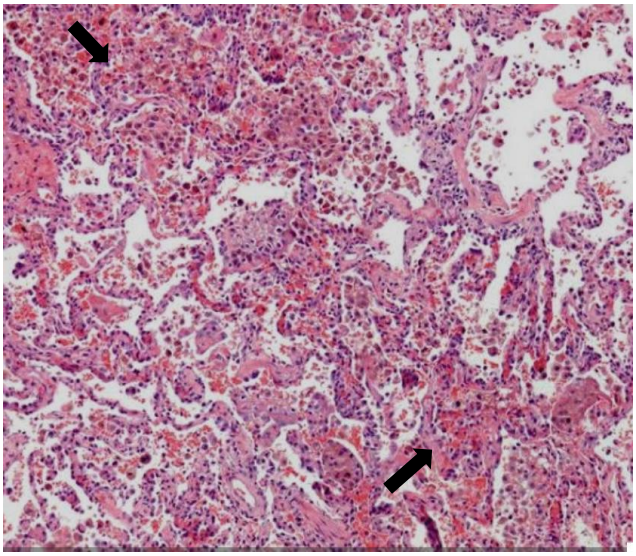

Figure 2. Capillary congestion, diffuse alveolar haemorrhage and pulmonary oedema. Alveolar spaces and interstitium are infiltrated by numerous inflammatory cells. (40x, H&E)

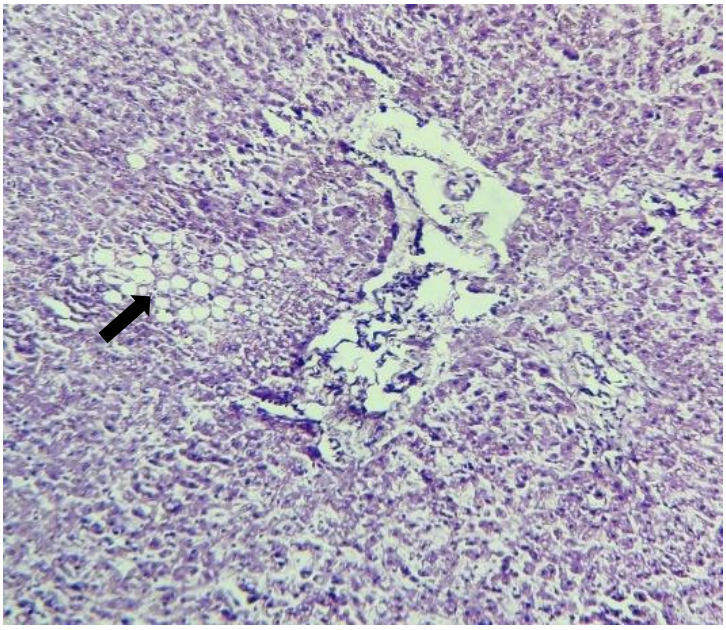

Figure 3. Mild steatohepatitis (H&E staining, 10X)

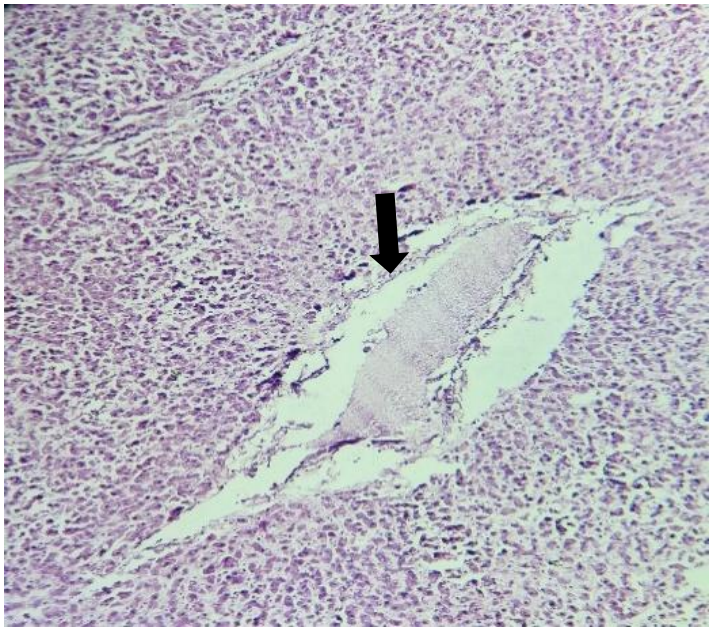

Figure 4. Zone-3 necrosis (H&E staining, 10X)

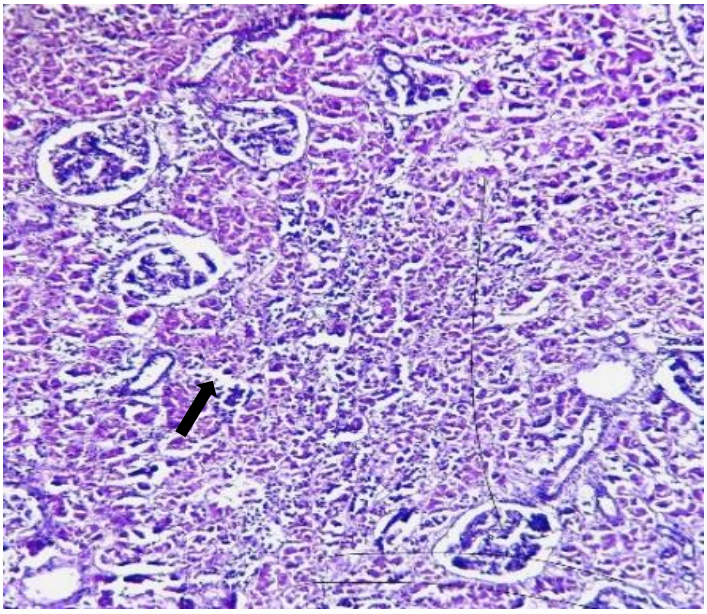

Figure 5. Inflammatory infiltrates and eosinophilic proteinaceous casts in tubules (H&E staining, 10X)

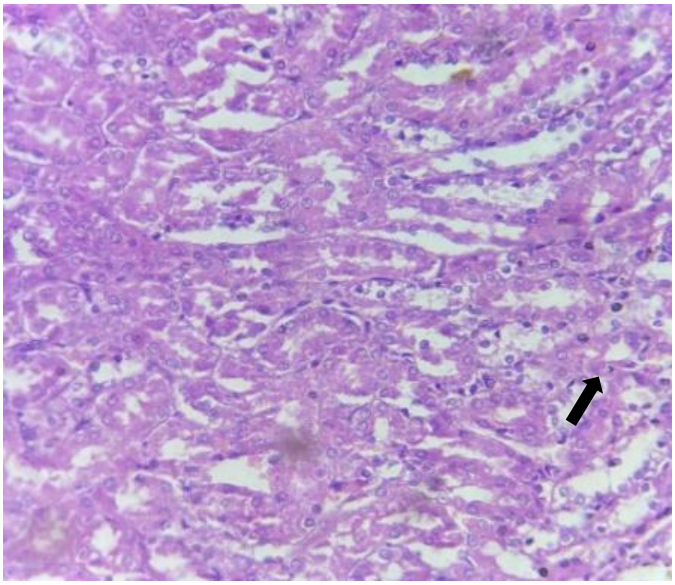

Figure 6. Acute tubular necrosis, (H&E staining, 40X)

Discussion

Amitraz is a commonly used insecticide, veterinary medicine, and antiparasitic agent used in the agricultural practices and pet management. Amitraz belongs to the formamidine class of pesticides and is chemically known as 1,5-di-(2,4-dimethylphenyl)-3-methyl-1,3,5-triaza-penta-1,4-diene [2].

Amitraz can be absorbed through oral, dermal, and inhalational routes. Oral ingestion is more common in suicidal cases, while dermal exposure can occur in veterinary and agricultural settings during spraying and topical application to animals. Absorption is rapid and depends on the solvent used. Amitraz is lipophilic and is well distributed in fatty tissues. It can cross

the blood–brain barrier, causing CNS effects. Amitraz is metabolized in the liver by microsomal enzymes, undergoing hydrolysis into its active metabolite, N-2,4-dimethylphenyl-N′-methylformamidine, and 2,4-dimethylaniline (2,4-DMA). It is excreted mainly in urine, with a small portion excreted in bile and faeces [2,3].

Amitraz has been banned for agricultural use in the European Union; for example, countries like Germany, Austria, and Switzerland do not authorize any pesticide products containing this compound [6]. In the United States, the Environmental Protection Agency (EPA) classifies Amitraz as slightly toxic when ingested (Class III) and lists it as a Group C; 'possible' human carcinogen. As a result, it is not approved for use on crops there but continues to be permitted for certain veterinary treatments [7]. In Canada, agricultural uses of Amitraz have been discontinued, and its use in veterinary products is currently under re-evaluation [8]. Even though amitraz has multiple uses in several aspects in agriculture and veterinary field, there are many alternatives such as synthetic pyrethroids, isoxazolines and organophosphates which are relatively safer [9]. It is always advisable to shift to less toxic alternatives wherever possible.

Accidental and suicidal poisonings with this substance are more common than homicidal poisoning instances as per available literature. The chances of criminal poisoning with amitraz are less as it has a strong pungent odour, bitter and sharp taste, and strong brown colour that renders it difficult to poison food or drinks with it[7].
Amitraz acts like clonidine by stimulating α-2 adrenergic receptors in the nervous system, which produces effects like bradycardia, miosis, hypotension, and shortness of breath. It can also cause hypothermia and hyperglycaemia. At low doses, it usually causes pupil constriction, but at higher doses, the pupils may dilate. Amitraz can cause hyperglycaemia by reducing insulin in the body. It can affect the liver, though liver function often returns to normal within a couple of days in non-fatal cases. The common solvent used with Amitraz, xylene, can add to its toxicity by causing problems like dizziness, lack of coordination, and even coma[3,7,10]. In the present case, amitraz ingestion caused death with evident multi system involvement. The amount of ingestion remains unknown, and the blood levels of the substance were not evaluated. The most possible cause of the lethal toxicity in the present case could be high-dose ingestion. The primary target organs in Amitraz poisoning are the CNS and CVS. It can cause death due to respiratory failure and cardiac complications such as bradycardia, hypotension, and arrhythmias.

The clinical features associated with amitraz are similar to Organo Phosphorous (OP) poisoning, as a result often can lead to misdiagnosis. Therefore, the point of care physicians should make it a priority to obtain the container of the poison and identify the active ingredient involved if possible. The most frequent symptoms of this poisoning are altered mental status, constricted pupils, and bradycardia. These signs can often cause confusion, leading physicians to mistakenly diagnose it as OP poisoning. Features such as hyperglycaemia, hypothermia, and paralytic ileus are more typical of Amitraz. Patients with Amitraz poisoning may also have a noticeable solvent-like or mothball odour, whereas OP poisoning is more often linked to a characteristic garlic-like smell. Investigations such as RBC and Serum cholinesterase levels estimation can be used to distinguish between the two, normal

levels are seen in amitraz cases whereases low levels are seen in OP poisoning, [3,7].

Gas chromatography–mass spectrometry and gas–liquid chromatography are useful for qualitative and quantitative analysis of Amitraz and its metabolites in serum and urine [7]. There are no specific histo-pathological findings which differentiates amitraz and op poisoning, however the findings which are observed in this case more or less correlate with those findings observed in the OP poisoning or a systemic multi organ failure noticed in poisoning cases.

Symptomatic and supportive care is the mainstay of treatment for Amitraz poisoning. Management includes hemodynamic stabilization, gastric lavage, administration of activated charcoal to limit further absorption, and dialysis if needed. Amitraz has very little mortality rate even though it exerts potent acute toxicity and can cause extended hospitalisation. Correct diagnosis of Amitraz poisoning is crucial, as there have been reported deaths caused by repeated doses of atropine given due to an initial misdiagnosis as organophosphate poisoning [3,10].

Conclusion

Amitraz is widely used in agropastoralism because it serves multiple purposes and is economical. Apart from suicidal ingestion, accidental exposure to amitraz is common, with reported cases of dermal and inhalational poisoning occurring during the spraying of pesticides and insecticides [11]. The majority of deaths due to amitraz poisoning occur as a result of its misdiagnosis as organophosphate poisoning; therefore, immediate identification and prompt treatment are crucial to prevent fatalities. There is an immediate necessity of developing bed side tests to differentiate amitraz poisoning from other common forms of poisoning encountered in practice.

The development of a safer and more effective antidote is one way to help prevent these deaths although the lethality associated with amitraz poisoning is relatively less. The risk of accidental exposure to amitraz can be reduced by providing personal protective equipment (PPE) and educating farmers about the safe use of pesticides and insecticides. Suicidal ingestion of such dangerous pesticides can be curbed only by implementing strict laws and procedures for their purchase. Mandatory purchase licensing for farmers, veterinarians, and people who own pets and livestock should be enforced.

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Not applicable.

Conflict of interest

None to declare.

Ethics approval

Consent for autopsy in this case was obtained from the appropriate law enforcement authorities. All ethical considerations have been duly addressed by the authors.

Acknowledgements

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