

CASE REPORT

A RARE CASE OF FATAL EMAMECTIN POISONING

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ABSTRACT

Emamectin is a macrocyclic lactone-ring insecticide widely used on various vegetable crops and fruits. Emamectin acts through high-affinity gamma-aminobutyric acid (GABA) receptors by increasing the chloride permeability, thus causing muscle paralysis in invertebrates. Here we report a fatal case of intentional ingestion of emamectin in an adult. A 53-year-old male presented to the emergency department with an alleged history of suicidal ingestion of emamectin benzoate 5% water soluble granules mixed with around 180ml of ethyl alcohol following which he developed vomiting and was immediately taken to a nearby hospital. Gastric lavage was performed; however, he succumbed to death the following day. The autopsy examination showed evidence of stomach mucosal erosions, alveolar oedema, and hepatic necrosis. Chemical analysis of viscera detected qualitatively the presence of emamectin benzoate in blood and tissues. Toxicological analysis of emamectin and its potential limitations was discussed. Death following emamectin poisoning in humans has been reported very little in the literature due to which its spectrum of clinical features is difficult to comment upon. Future case studies and literature will help better understand the range of clinical and autopsy features to aid the prompt diagnosis.

Keywords: Avermectin; Emamectin benzoate; GABA affinity; neurotoxicity; toxicology.

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INTRODUCTION

Pesticide poisoning-related deaths are prevalent and widely reported in India, mostly in rural areas, and farmers most commonly die from various agricultural poisonings such as organophosphorus, organochlorides, and paraquat. Emamectin benzoate (EB) belongs to the family of avermectins, which is a class of naturally occurring products from soil actinomycetes, named *Streptomyces avermitilis* by a fermentation process¹. Emamectin is a 16-membered macrocyclic lactone ring insecticide which is mostly used in the treatment of pests and parasitic worms due to its inherent anthelmintic and insecticide property². Emamectin is an International Organization for Standardization (ISO) approved name for (4'R)-4"-deoxy-4"-(methylamino)avermectin B1 benzoate³. Eight types of avermectin structures

are identified and divided into four major (A1a, A2a, B1a, and B2a) and minor (A1b, A2b, B1b, and B2b) components². Emamectin is a mixture of B1a and B1b benzoate salts with a ratio of 90:10^{1,3,4}. It has a wide margin of safety reported in animal studies due to its low gamma-aminobutyric acid (GABA) receptor affinities and poor penetration through the blood-brain barrier. Toxicity can occur through various routes, including oral, dermal, inhalation, and intravenous exposure. Additionally, animal studies have indicated the potential for reproductive toxicity, and there is also evidence of skin irritation and sensitisation^{2,5}. This case report discusses a 53-year-old male who died after self-ingestion of emamectin benzoate 5% water soluble granules (SG) pesticide.

CASE HISTORY

A 53-year-old farmer from a rural area was taken to a primary health care facility with an alleged history of ingestion of the pesticide emamectin benzoate 5% SG mixed with around 180ml of ethyl alcohol. The empty container was found at the scene by the relatives. He was referred to the tertiary care center for further management. The deceased had a past medical history of chronic kidney disease (CKD) diagnosed two years back and was on hemodialysis twice a week at the local hospital. Following ingestion, he initially developed vomiting and a burning sensation in his mouth and epigastric region. Within a few hours, he became unconscious, which persisted throughout the treatment course. Decontamination was done with gastric lavage and activated charcoal. His antemortem investigations revealed an elevated blood urea level of 110 mg/dl and a serum creatinine level of 11.9 mg/dl. Despite treatment, he succumbed within 48 hours of ingestion. The body was kept in cold storage, and the autopsy was done after 18 hours as per the request from the investigating officer. The history and the label on the container at the scene confirmed the ingested substance as emamectin. On external examination, the deceased was moderately built and nourished. Nailbeds were cyanosed. On internal examination, the mucosal surface of the stomach showed congestion and mucosal

erosions (Fig. 1A and 1B) along the lesser curvature.

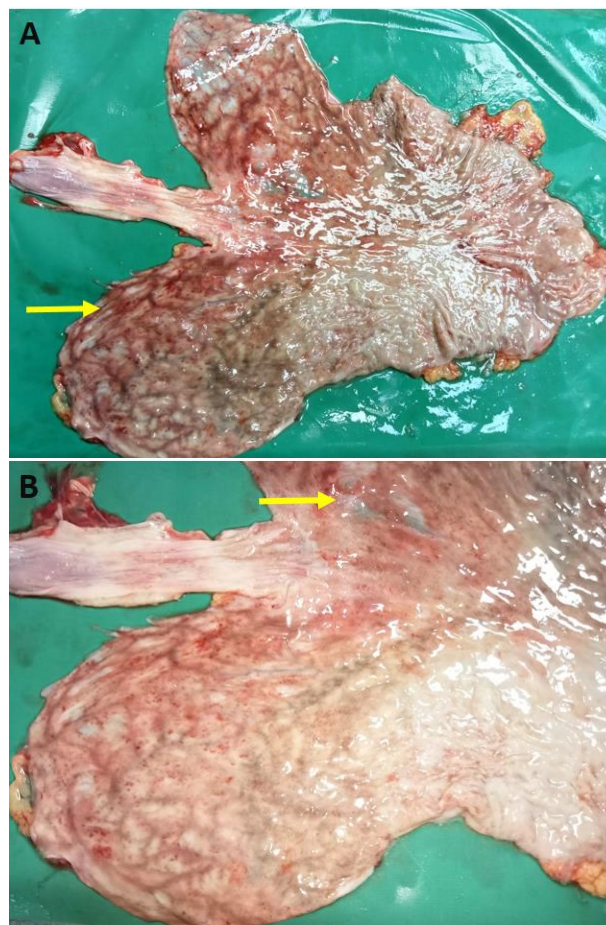
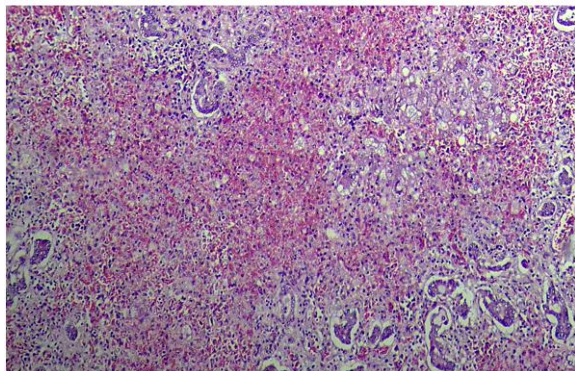


Figure1: Mucosal erosions (arrows) along the lesser curvature of the stomach (A and B)

The brain weighed 1450 g and appeared congested and oedematous. Kidneys were contracted, and the cut surface showed a narrowed renal cortex with multiple cysts at the cortico-medullary junction. The liver weighed 1400 g and showed features of fatty change and, on histology, demonstrated massive hepatic necrosis (Fig. 2A). The right and left lungs measured 720 g and 550 g, respectively, and contained mild to moderate pulmonary oedema. Histology of the lungs showed alveolar oedema (Fig. 2B).

2A



2B

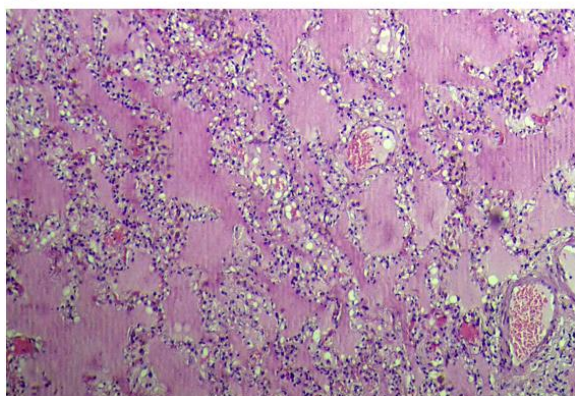


Figure 2: Hepatic necrosis of liver (A) and alveolar edema(B), (H&E, 10x)

Left anterior descending artery and right coronary artery showed 30% and 70% occlusion by atherosclerotic plaques respectively. The stomach with its contents, liver, and kidney preserved in a saturated solution of common salt, and blood preserved in sodium fluoride were sent for chemical analysis. Emamectin was extracted by solid-liquid phase extraction method with chloroform as solvent. The solvent system used was Methanol: Ammonia (100: 1.5v/v). The silica gel plate with ascending technique development and Dragendorff's spray reagent was used. Analysis was done by thin-layer chromatography with the orange spot in the yellow background indicating the presence of the compound emamectin. Ethyl alcohol was detected at a level of 133 mg%(w/v) in blood, 184 mg% in the liver and kidney, and 161 mg% in the stomach. The cause of death was ascertained as hepatic necrosis in a case of emamectin poisoning.

DISCUSSION

Emamectin binds to GABA receptors and glutamate-gated chloride channels and unsettles nerve signals within arthropods. It stimulates the release of neurotransmitters from the synapses and increases GABA's affinity for its receptor on the postsynaptic endings by increasing chloride permeability^{5,6}. The route of elimination is through faeces by the P-Glycoprotein efflux transporter. The clinical features in animal studies include gastrointestinal irritation, tremors, changes in motor activity, hyperactivity, loss of righting reflex, hypothermia, ptosis, bradypnoea, lethargy, ataxia, coma, and death³. Animal studies have documented histopathological features of acute poisoning, including neuronal degeneration and vacuolation of the neuronal cytoplasm associated with cellular debris, macrophages, and pyknotic nuclei⁵. In an animal study, the radio-labeled emamectin was widely distributed to tissues with higher levels in the small intestine, caecum, spleen, liver, lung, and adrenals, and the lowest concentration was seen in the brain and spinal cord^{3,4}. The management of emamectin benzoate poisoning is always supportive and symptomatic because there is no known antidote for it. Drugs like benzodiazepines, barbiturates, and valproic acid which increase GABA activity should be avoided since emamectin has GABA-mimetic activity^{7,8}. In our case, the victim was unconscious throughout the treatment period and his lab investigations showed raised levels of urea and creatinine. Thus, it is essential to ascertain the cause for the clinical manifestations, whether due to the ingested toxin, as a complication of CKD, or due to the combined effects of the two.

Yadav et al. reported a case of a six-year-old girl who developed nausea, vomiting, abdominal pain, and confusion after six hours of accidental ingestion of emamectin 5% SG. On examination, her Glasgow Coma Scale was 13/15. Gastric lavage was done with saline, activated charcoal and coconut oil through a nasogastric tube. Intravenous pantoprazole, hydrocortisone, and ondansetron were administered. Her symptoms improved, and after three days, she was discharged without any neurological deficits. It

was suggested that coconut oil might coat the gastric mucosa to delay the absorption of emamectin and may additionally prevent damage to raw mucosa because of its antiulcer nature⁸. Godhiwala et al. reported a case of a 40-year-old farmer who ingested emamectin benzoate 5% SG 500g under the influence of alcohol. He was drowsy, irritable, and was mechanically ventilated. On the second day, he developed a myoclonic jerk and generalised seizure and was treated symptomatically. On the third day, he developed severe metabolic acidosis, and shock and was on hemodialysis and later succumbed⁵. In our case, the deceased was unconscious throughout the treatment course and succumbed within 48 hours of ingestion. Park et al. reported a 75-year-old male who intentionally ingested emamectin 2.15% mixed with alcohol. He developed severe metabolic acidosis and hypotension and died after 12 hours from ingestion⁶. Yen et al. reported a case of acute poisoning with emamectin benzoate with symptoms of nausea, vomiting and abdominal cramps treated with gastric lavage and activated charcoal. The following day, endoscopy showed gastric erosions and superficial gastritis. Mild central nervous system depression was also observed¹. It was recommended that further case studies and research target the effects of emamectin on target organs like the brain by histological and chemical analysis, which was lacking in the present case.

CONCLUSION

This report highlights an uncommonly reported fatal case of insecticide poisoning by emamectin benzoate. Even though the pathogenesis and clinical spectrum have not been studied extensively in humans, the mainstay of management lies in symptomatic and supportive care. The unavailability of an antidote has posed a significant challenge in managing such cases. In this case, the deceased survived for less than 48 hours following ingestion. The autopsy revealed mucosal erosions of the stomach and hepatic necrosis. Emamectin benzoate was positively detected by thin-layer chromatography in the blood and tissue samples. Additional research is needed to

increase awareness for early detection and to understand the pharmacokinetics of this compound in humans to determine the best course of treatment. Improved awareness of the safe use of hazardous agrochemical compounds should be established, especially among farmers and agricultural communities.

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None.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest.

ETHICAL ISSUES

Not applicable.

SOURCES OF SUPPORT

None.

AUTHOR CONTRIBUTIONS

SV: Conception and design of the work; acquisition, analysis, and interpretation of data for the work; drafting the work; and final approval of the version to be published. **KS:** Conception and design of the work; acquisition, analysis, and interpretation of data for the work; reviewing the work critically for important intellectual content; and final approval of the version to be published.

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