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CASE REPORT

Fatality following Deliberate Ingestion of a Chemical Hardener: Two Case Reports of Methyl Ethyl Ketone Peroxide Poisoning

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Abstract:

Industrial chemicals and solvents are usually highly toxic and often corrosive. In India, intentional poisoning by industrial chemicals is relatively uncommon. Methyl ethyl ketone peroxide (MEKP), an organic peroxide, is used as a chemical hardener in industries to cross-link polymers. We report two cases of intentional ingestion of this chemical hardener who presented to the Emergency with complaints of severe abdominal pain and multiple episodes of hematemesis. Despite treatment, they succumbed to death within twelve hours and seven days of ingestion, respectively. On autopsy and histopathology, corrosive features were seen in the esophagus and stomach. The pathophysiology is due to the free radicals derived from MEKP causing lipid peroxidation and cell death. Though the MEKP was not detected in the viscera during the chemical analysis, the evidence from the crime scene investigation and other collaborative sources strongly suggests that the poisoning is due to MEKP. This case emphasizes the significance of clinical presentation, autopsy findings, histopathological features, crime scene investigation, and utilizing appropriate preservatives for chemical analysis in uncommon cases like MEKP poisoning. MEKP ingestions are relatively rare in the literature, with only about thirty reported cases associated with increased mortality and morbidity. These cases highlight the role of crime scene visits and emphasize the clinical, post-mortem findings and histopathological features in an uncommon case of MEKP poisoning. In these cases, the workplace being the source of acquiring MEKP, provisions for safe storage and keeping container count prohibit misapplication.

Keywords: Chemical hardener; Methyl ethyl ketone peroxidase; Corrosive; Poisoning.

Background:

Methyl ethyl ketone peroxide (MEKP) is an organic peroxide available as a colorless liquid and industrial solvent which is highly toxic. It has a minimal acetone-like odor and is used as a catalyst due to its substantial oxidizing property.[1] The history of MEKP begins with experimental work in Germany in the late 1900s and was patented in the mid-1930s and introduced to the public in 1949.[2]

It is commonly used as a hardening agent in fiberglass industries,[2] lamination processes, manufacturing hulls of boats, etc. It is also used as an ingredient in acrylic paints[3] and varnishes. Exposure to MEKP can cause chemical burns and lead to the release of free radicals. Since MEKP has an inherent organic peroxide, it possesses an explosive property in its native form, and slight mechanical shock can explode.[3] Hence, it is commercially available as a 40-60% solution with stabilizing agents such as dimethyl phthalate (DMP),[2,4] cyclohexane peroxide or diallyl phthalate to prevent its decomposition and explosion. Inhalation of MEKP or its direct contact with skin and eyes can cause local corrosive effects.[3] Ingestion of any amount can cause death due to its corrosive and systemic effects. Herein, we report two cases of MEKP poisoning.

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Case 1:

A thirty-three-year-old male was taken to a nearby primary health care center after ingesting about 200 ml of an unidentified liquid from an unlabeled bottle at his residence. He was referred to our tertiary care center with a low pulse rate and non-recordable blood pressure. Upon admission, he had about 15 – 20 episodes of blood vomiting and passage of greenish-brown loose stools. Blood investigations revealed a rise in hemoglobin level to 18.7 gm %, red blood cell count 6.55 million/mm,[3] and hematocrit was 58.2%. There was an initial increase in liver parameters, mainly Aspartate transaminase (AST) and Lactate dehydrogenase (LDH), to 226 and 755 U/L, respectively but then began to reduce subsequently. He was intubated due to a non-palpable pulse and severe respiratory distress and died within 12 hours of ingestion. The body was sent for post-mortem examination with an alleged history of consumption of an unknown chemical liquid. Following an inquiry with family members and co-workers, it was found that he had consumed a colorless liquid brought from his workplace.

During the autopsy, no external injuries were present. Conjunctiva was found congested, with bluish discoloration of the nail beds. On opening the abdominal cavity, about 500ml of blood-tinged fluid was present. Multiple petechial hemorrhages along the inter-lobar fissures of both lungs were present. On the cut section, hemorrhagic spots were present in the left lung. Upon

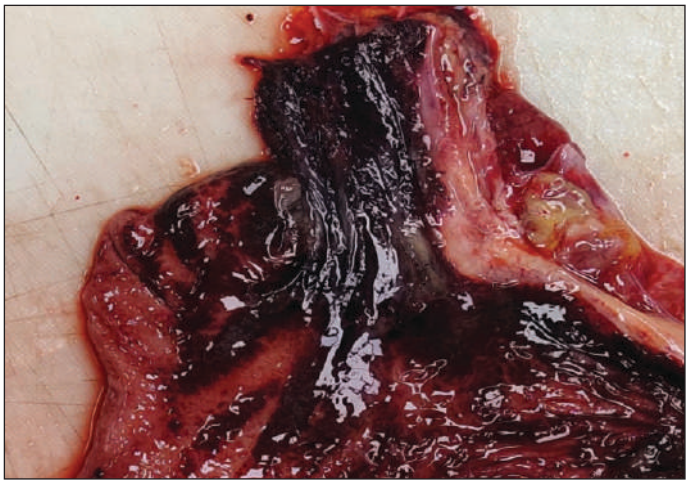

Fig.1a – Shows blackish eroded and hemorrhagic esophageal mucosa.

opening the esophagus, the inner surface was blackish with eroded and hemorrhagic mucosa (Fig.1a). The stomach contained around 500 ml of dark reddish brown colored fluid. The mucosa was eroded and hemorrhagic, with the thickening of the pyloric antrum extending along the rugae (Fig.1b). Other organs were mainly unremarkable.

Histopathology revealed features of loss of mucosal architecture and extensive hemorrhage in mucosa with corrosive ischemic necrosis of the esophagus (Fig.2a). The stomach had focal hemorrhages with lymphocytic aggregates, extensive mucosal hemorrhage with ulceration, and ischemic mucosal necrosis (Fig.2b). Small Intestine had extensive mucosal hemorrhage with ulceration and ischemic mucosal necrosis (Fig.2c). Lungs had alveolar edema and hemorrhage (Fig.3). The liver had micro and macro-vesicular steatosis with mild peri-portal inflammation. Routine viscera were preserved in a saturated salt solution and sent for chemical analysis, which did not detect any poison, toxins, or alcohol. The opinion as to the cause of death was due to alveolar edema and pulmonary hemorrhage.

Case 2:

A twenty-five-year-old male worker in a small boat manufacturing company deliberately ingested 100 ml of MEKP at his residence, which he brought from the workplace. He presented to our tertiary care center with complaints of a burning throat sensation, multiple episodes of bloody vomiting, and abdominal pain. Initially, the physicians managed symptomatically, but his condition progressively worsened. Urea and creatinine levels increased from 16 mg/dl and 0.9 mg/dl on day 1 to 85mg/dl and 2.6mg/dl on day 7, respectively. Hemoglobin levels reduced to 6.3mg/dl. He succumbed on the seventh day. During the autopsy, mucosa of the laryngopharynx, esophagus, and gastric mucosa were found eroded and hemorrhagic. Near the pyloric end of the stomach, mucosa had greenish-black discoloration and thickening with leather-like consistency. Other organs were unremarkable. Viscera were preserved for chemical analysis in rectified spirit. On histopathological examination, the laryngopharynx showed ulcerated mucosa and submucosal tissue congested with inflammatory cells (Fig.4). Stomach and esophagus showed

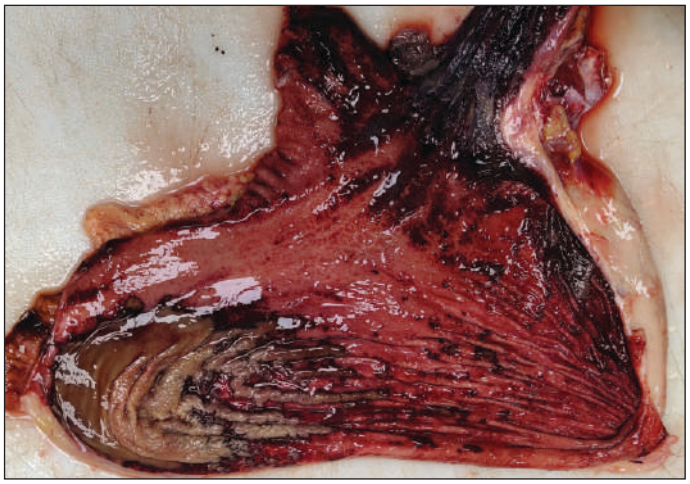

Fig.1b– Shows eroded and hemorrhagic stomach mucosa with thickening.

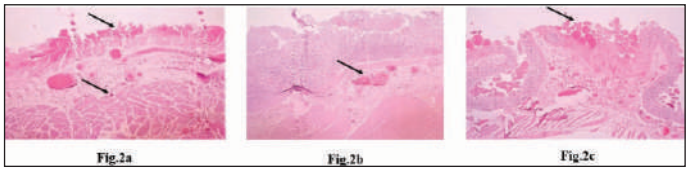

Fig.2a– Esophagus showing loss of mucosal architecture and extensive hemorrhage in mucosa with corrosive ischemic necrosis. H & E 10x.
Fig.2b–Stomach showing focal haemorrhages with lymphocytic aggregates. H & E 20x.
Fig.2c– Intestine showing extensive mucosal haemorrhage with ulceration and ischemic mucosal necrosis. H & E 20x.

ulcerated mucosa and congestion of the wall (Fig.5 and Fig.6). Lungs showed intra-alveolar edema and hemorrhage with acute inflammatory infiltrates and pneumonia-related changes. The chemical analysis of viscera could not detect MEKP or its metabolites. The cause of death was opined multi-organ dysfunction, primarily in the lungs and kidneys.

Discussion:

MEKP is highly hazardous for its highly reactive oxidizing property. It is associated with increased mortality and morbidity. Poisoning through accidental ingestion is more common for its colorless and odorless nature at the workplace than intentional ingestion. However, in both cases, the manner of consumption was suicidal. Chronic exposure and toxicity in unprotected workers in direct contact with this catalyst are expected. MEKP ingestion produces a variety of symptoms, such as airway obstruction due to edema, gastrointestinal bleeding, necrosis and perforation, esophageal stricture, inhalational pneumonitis, optic disc atrophy, severe metabolic acidosis, rapid liver and kidney failure, neurological damage, coagulopathy, and respiratory insufficiency.[3-7] In both cases, the deceased was using MEKP, as it enhances the durability and strength of fiberglass when mixed with polyester resins. The catalytic role of MEKP in the vulcanization process offers more strength and makes it extremely hard.

$$\text{Fiberglass+ Polyester resins} \xrightarrow{\boxed{\text{MEKP}}} \text{Vulcanization} \rightarrow \text{Hardening of ester resins.}^{[8]}$$

(Cross-linking laid across polyester resins)

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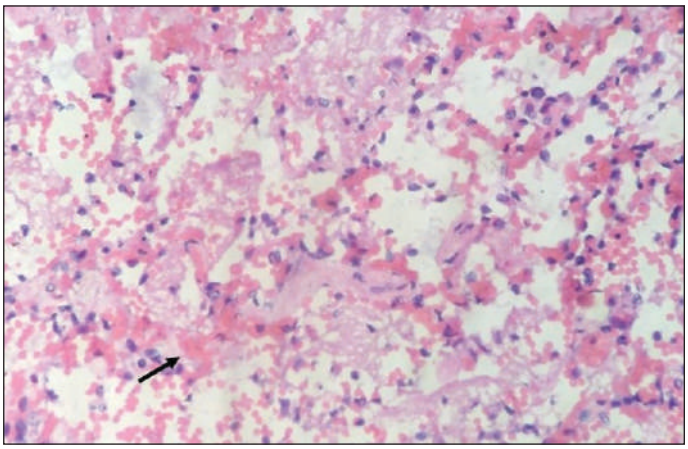

Fig.3– Lung showing alveolar edema and haemorrhage. H & E 40x.

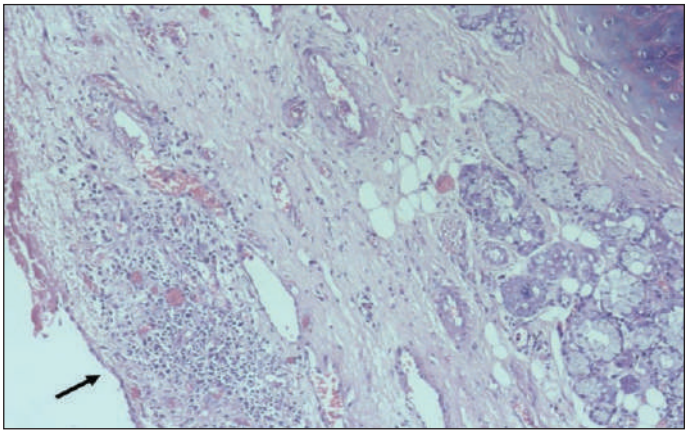

Fig.4 – Laryngopharynx showing ulcerated mucosa and sub-mucosal tissue congested with inflammatory cells. H&E 200x.

Very few cases have been reported of this poisoning since the availability is limited to one's occupation. The toxic oral dose of the commercially available MEKP is 50 to 100 ml.[1,8] On ingestion, it breaks into methyl ethyl ketone (MEK) and peroxide group, which releases free radicals causing peroxidation of lipids leading to cell death. The gastrointestinal damage is due to the direct corrosive effect, while the damage to other organs is due to the absorbed MEKP.[1]

$MEKP = MEK + H_2O_2$

Free radical→ Peroxidation of lipids→ Cell death (GI cells & Hepatocytes)

In the first case, the deceased had multiple episodes of hematemesis and bloody loose stools. The raised hemoglobin and hematocrit were due to the haemo-concentration caused by dehydration and hypovolemia. The initial rise in liver parameters was due to ischemic hepatocyte damage caused by hypovolemia and dehydration. It then subsequently came back to normal limits by blood and fluid resuscitation. The alveolar hemorrhage was attributed due to free radical damage. The esophageal and stomach mucosa was blackish and hemorrhagic due to erosion owing to corrosive action. The antral and pyloric thickening of stomach mucosa was due to coagulative necrosis by the direct effect of the poison. However, the chemical analysis of the viscera couldn't detect the poison. We had to rely on the clinical

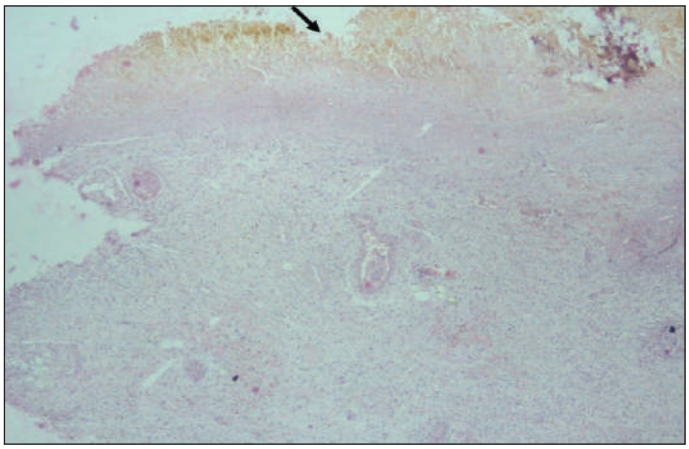

Fig.5 – Stomach and esophagus showing ulcerated mucosa and congestion of wall. H&E 100x.

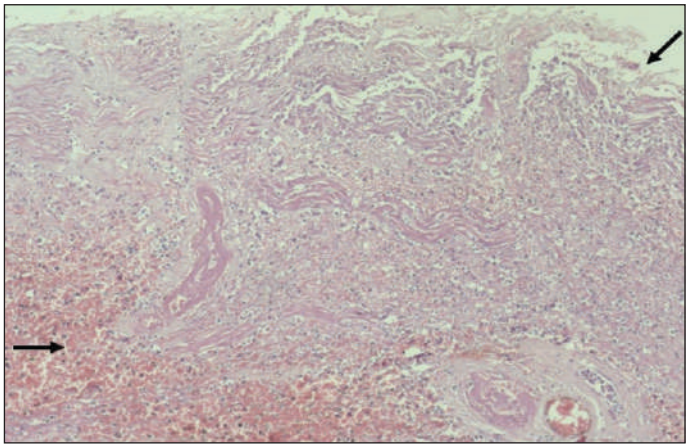

Fig.6 - Esophagus showing ulcerated mucosa and congestion of wall. H&E 200x.

picture, autopsy, and histopathologic findings to correlate features of corrosive poison. Following an inquiry with family members and co-workers, it was found that he had consumed a colorless liquid brought from his workplace. A visit to the deceased's workplace revealed that the water-like liquid consumed was MEKP, which was transferred into disposable unlabeled water bottles for day-to-day utility. In the second case, features present in the esophagus and stomach were due to the direct corrosive effect of the poison, which on aspiration, caused the mucosal ulceration of the laryngopharynx. The rise in renal parameters was due to free radical damage. Upon survival for a week, pulmonary edema and hemorrhage were complicated by pneumonia. Though the viscera were preserved in rectified spirit, MEKP could not be detected in chemical analysis owing to complete metabolism and excretion. In both cases, the chemical analysis of the viscera did not detect MEKP. In the first case, since we were skeptical of the substance used, saturated salt solution was used as a preservative which was ineffective in detecting MEKP. In the second case, although the samples were preserved in rectified spirit (preferred in corrosives), MEKP was not detected since the patient survived for one week. Further research and reports on MEKP poisoning are essential especially when the patient survived for a shorter duration.

Bates and his associates reported accidental ingestion of

commercially available MEKP by a six-year-old child who initially presented with severe esophageal and gastric burns and coagulopathy.[7] After three months, He subsequently developed a stricture of the gastro-esophageal junction and complete fibrosis of the middle third of the stomach. The pathophysiology of acute intoxication of MEKP has been discussed in four stages.[5,9,10] First, there will be respiratory signs like airway obstruction due to edema, subsequent mucosal damage in airway structures, and associated upper gastrointestinal symptoms like vomiting, hemorrhage, perforation, etc. The second stage is mediated by free radical damage to organs, causing harmful effects to the liver and gastrointestinal tract, and the most commonly targeted cells are the hepatocytes & kidneys. Karhunen et al.[4] reported an acute case where histo-pathological findings of the liver revealed massive periportal hepatic necrosis and atypical pseudo-ductular proliferation. In our first case, a histopathological examination of the liver showed micro and macro-vesicular steatosis and mild periportal inflammation. Thirdly, there will be complications due to organic acids liberated by the disintegration of MEKP. Finally, secondary complications such as renal failure due to rhabdomyolysis, ventilator-associated pneumonia, respiratory distress syndrome, and myocarditis can be seen in the fourth stage.

Zeiger's experimental animal study of topical application of MEKP over mice showed extensive coagulative necrosis of the skin layers and epidermal regeneration and hyperplasia. Secondary to dermal lesions included increased spleen hematopoiesis, increased bone marrow myeloid hyperplasia, and dose-dependent liver hypertrophy at higher doses.[8] MEKP may disintegrate into organic acids such as formic acid leading to a wide range of complications. Van Enckevort et al.[5] reported a case in which MEKP caused severe metabolic acidosis due to formic acid accumulation leading to optic nerve lesions. Long-term exposure to the vapors of this chemical solvent may be categorized into occupational hazards. The workers must follow safety precautions. In the instant cases, chemical analysis of viscera did not detect MEKP due to its property of rapid breakdown.[10] Reasons for not detecting the metabolites of MEKP may be attributed to the following:

a) Inappropriate preservation of viscera in saturated salt solution instead of rectified spirit, leading to the neutralization of MEKP.

b) Unstable nature of the metabolites of MEKP.

c) No proper analytical method was devised.

Conclusions:

The first case highlights the importance of a crime scene visit to the workplace that helps in unveiling the causative agent behind the corrosive features. The second case highlights the clinical features, laboratory investigations, autopsy findings, and other ancillary investigations like histopathological examination in MEKP poisoning. When it comes to detecting the presence of a specific uncommon poison like MEKP, choosing the appropriate preservative is the key. The appropriate preservative can help maintain the stability and integrity of the poison, increasing the chances of its detection during subsequent laboratory analyses. While chemical analysis reports are important in toxicological investigations, a negative result does not definitively exclude the possibility of poisoning. Therefore, ancillary investigations like histopathological examination can assist in reaching a conclusive diagnosis. The need for more data and reports on MEKP toxicity is essential to detect this poisoning in the future.

List of Abbreviations: MEKP – Methyl Ethyl Ketone Peroxide

DMP – Dimethyl phthalate **AST** – Aspartate transaminase

LDH– Lactate dehydrogenase

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