

Case Report

An autopsy case of corrosive gastritis caused by calcium polysulfide colloid preparation

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Abstract: Mutouhapu (610 hap) was a calcium polysulfide colloid preparation, which was sold as a bath salt in Japan. Herein, we report on the autopsy of a suicide case as a result of taking 610 hap orally and present histopathological findings with a focus on corrosive changes observed in upper gastrointestinal tract. The subject was a 60-year-old man who was discovered dead 200–300 m from his home. The site smelled of sulfur. Sixty parts per million hydrogen sulfide was detected in the oral cavity of the deceased. He had schizophrenia since junior high school. At autopsy, the oral and nasal cavities had a rotten-egg smell. Adipose tissues had green coloring. There was thickening and sclerosis of the gastric wall, and a green to pale yellow pseudomembrane-like substance was observed adhering to the gastric mucosa. Gastric content was 400 ml of green to pale yellow sludge. The distal portion of the stomach was highly contracted. Qualitative analysis for hydrogen sulfide was positive. Histological changes in the digestive tract were particularly notable in the stomach. Degeneration and necrosis of the mucosa and submucosa, degeneration of the submucosal fat, and dissection-like changes in the blood vessels of the submucosa were discovered. Basophilic lime granules were found on the mucosal surface. There were hypercontracture changes in the proper muscle layer of the pyloric region. The cause of death was hydrogen sulfide poisoning with associated corrosive gastritis. (DOI: 10.1293/tox.2020-0036; J Toxicol Pathol 2020; 33: 287–290)

Key words: calcium polysulfide, corrosive gastritis, hydrogen sulfide

Mutouhapu (610 hap) (Mutosho Pharmaceutical, Nagoya, Japan) was a calcium polysulfide colloid preparation, which was sold as a bath salt in Japan. It was prepared by heating and dissolving 202.5 g sulfur, 67.5 g calcium oxide, 0.12 g casein, and 0.15 g potassium sulfide in 729.73 g water; concentrating the solution so that the specific gravity at room temperature would be approximately 30° on the Baumé scale; and then filtering the concentrated solution. It was widely used as a bath salt and a topical remedy for scabies^{1,2} but, since 2007, many cases of suicide were reported where 610 hap was found mixed with toilet bowl cleaners containing hydrochloric acid to produce hydrogen sulfide³. The social issues that it led to resulted in the discontinuation of its sale in 2008. Herein, we report on the autopsy of a suicide case as a result of taking 610 hap orally and present histopathological findings with a focus on corrosive changes observed in the upper gastrointestinal tract.

The subject was a 60-year-old man who was discovered dead 200–300 m from his home. A passerby walking approximately 50 m away noticed the man collapse suddenly and rushed to his side. The man spewed yellow vomit from his mouth and nose. The passerby then called the ambulance. There were remnants of yellow vomit on the road around the deceased, and a tote bag containing a 350-ml plastic bottle with a yellow liquid was discovered at his side. The site smelled of sulfur. Sixty parts per million hydrogen sulfide was detected in the oral cavity of the deceased. He had a mental disorder since junior high school and was treated for schizophrenia on an outpatient basis for 17 years. On the day of his death, he had consulted his physician with complaints of auditory hallucinations, which he experienced often, and uttered phrases such as, “I want to die. They keep telling me to die.” It was assumed that the deceased was on his way home from the appointment at the psychiatric clinic. An administrative autopsy was conducted by the medical examiner (E.O.) 20 h after the death.

Postmortem lividity was not green, but the face had a mild green tint. The oral and nasal cavities had a rotten-egg smell. Adipose tissue had a green coloring, and the gastric serosa was congested. There was thickening and sclerosis of the gastric wall, and a green to pale yellow pseudomembrane-like substance was observed adhering to a wide area (Fig. 1A). Gastric content was 400 ml of green to pale yellow sludge. The distal portion of the stomach was highly

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contracted, and no material similar to the gastric content was found in the duodenum. The color of the mucous membrane from the pharynx to the esophagus was dark red with a grey tint. It was dark red with a green tint from the lower esophagus to the stomach. The duodenal mucosa had a slightly paler color than the stomach. No penetrating or perforating ulcers were detected in the stomach or small and large intestines. A small amount of material similar to the gastric content was discovered in the respiratory tract. The tracheal and bronchial mucosa were dark red with a grey tint (Fig. 1B). A section of the lung showed bleeding. Bleeding in the pancreatic capsule and fat necrosis were noted. Intracardiac blood was dark red and fluidal with no clots. The myocardium showed patchy fibrosis but no acute ischemic lesions. There was no occlusion or thrombus in the left or right coronary artery. There was no bleeding or infarction in the brain. Neither pleural effusion nor ascites were observed.

The blood from the right side of the heart was positive for hydrogen sulfide based on qualitative testing using lead acetate. No ethanol was detected in the blood or urine. Liquid chromatography with tandem mass spectrometry detected therapeutic concentrations of haloperidol and promethazine.

After completing the autopsy, the systemic organs were fixed in 15% buffered formalin, embedded in paraffin, and sectioned and stained with hematoxylin and eosin. Histological changes in the digestive tract were particularly notable in the stomach. Degeneration and necrosis of the mucosa and submucosa, degeneration of the submucosal fat, dissection-like changes in the blood vessels in the submucosa, and hemagglutination (or thrombus formation) of the submucosa were discovered (Fig. 2A). Basophilic lime granules were found on the mucosal surface, but the von Kossa staining results were negative (Fig. 2B). There was a change in the proper muscle layer in the pyloric region that appeared similar to contraction band necrosis usually seen in the myocardium (Fig. 2C).

Although there was congestion in the esophageal wall, epithelial disorder was not notable (Fig. 2D). Degeneration and necrosis of the duodenal mucosa were mild. In other organs, congestion and bleeding in the lung parenchyma and congestion of respiratory mucosa were confirmed. Myocardial necrosis was not found. Fat necrosis was found in the pancreas. Hepatic congestion was confirmed, and there was no necrosis of hepatocytes. There were no histological abnormalities in the kidneys and central nervous system. From these findings, we concluded that the cause of death was hydrogen sulfide poisoning with associated corrosive gastritis.

Five deaths resulting from 610 hap ingestion have been reported in the past and one of these cases was not autopsied⁴⁻⁷. Although 610 hap was not noted, there were two deaths involving a sulfur-based bathing agent⁸, as well as three deaths from ingestion of a lime-sulfur mixture⁹⁻¹¹. We summarized reports of the histological findings among the autopsied cases in Table 1.

Perforation of the gastric wall caused by a lime-sulfur

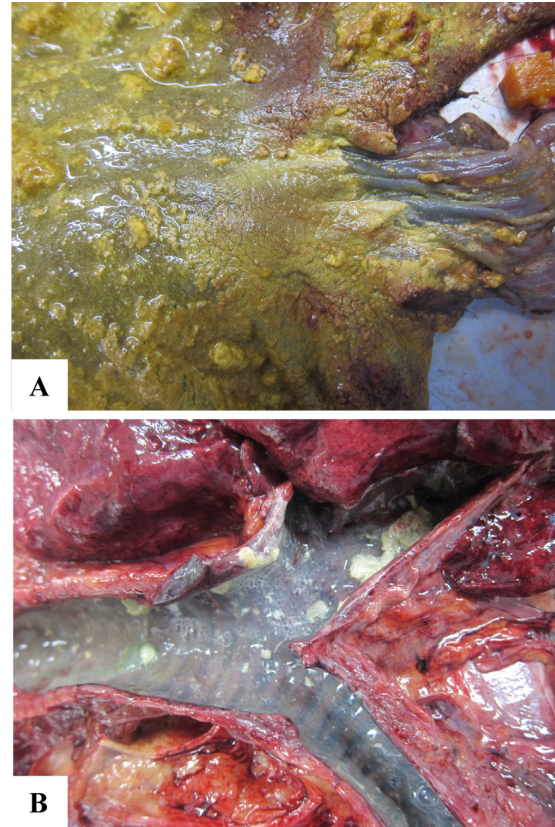


Fig. 1. Macroscopic images. A: Mucosal appearance of the stomach. There was thickening and sclerosis of the gastric wall, and a green to pale yellow pseudomembrane-like substance was observed adhering to a wide area. B: The tracheal and bronchial mucosa were dark red with a grey tint, showing some gastric content.

mixture has been reported^{1, 9}, but was not observed in the present case. The gastric mucosal surface had von Kossa-negative lime granules similar to those reported in the lime-sulfur mixture cases⁹. In such cases, calcium chloride is generated in the following reaction¹: $\text{CaS}_5 + 2\text{HCl} \rightarrow \text{CaCl}_2 + 4\text{S} + \text{H}_2\text{S}\uparrow$. The von Kossa stain only stains for calcium phosphate and calcium carbonate, not calcium chloride.

Mega *et al.* described a patient who accidentally ingested 30 ml of 610 hap and developed gastric perforation and pancreatitis with a pseudocyst during the subacute phase¹. In our case, hemorrhage and fat necrosis of the pancreas were found.

In an experiment exploring the effects of lime-sulfur mixtures in animals, histopathological examination showed shedding of the mucosal epithelium and hyperemia and edema in the mucosa and submucosa of dogs¹². Moreover, cloudiness of the gastric mucosa; enlargement, degeneration, and necrosis of the gastric mucosal parietal cells; increased division of hepatocytes; and centrilobular swelling of hepatocytes were noted in rats¹².

In this case, the gastric wall was thickened and sclerotic, and there was severe contraction of the distal side. Ex-

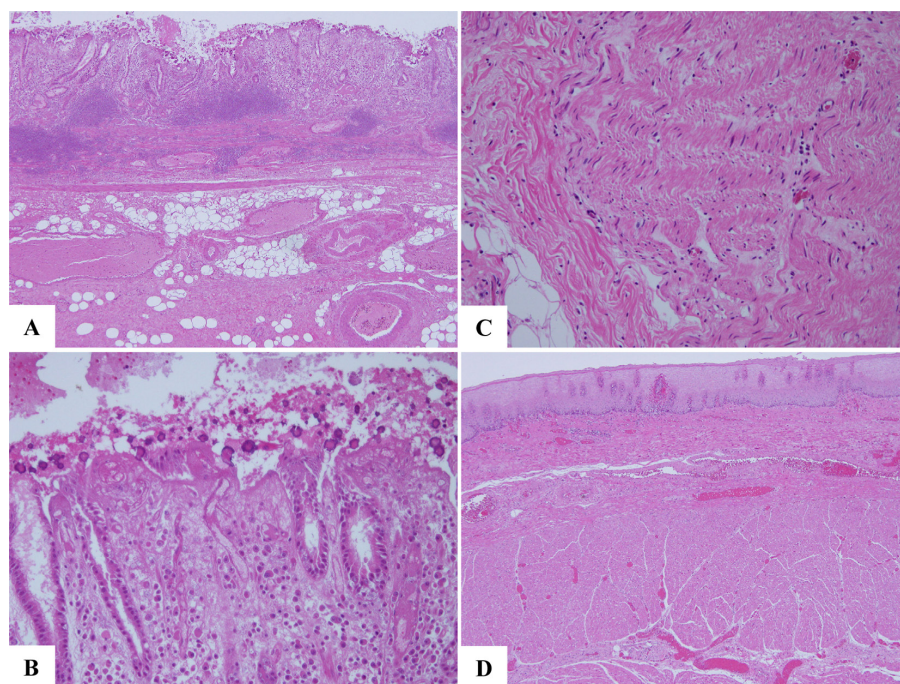


Fig. 2. Histological images of the gastric and esophageal mucosa. A: Degeneration and necrosis of the mucosa and submucosa, degeneration of the submucosal fat, dissection-like changes in the blood vessels in the submucosa, and hemagglutination (or thrombus formation) of the submucosa were observed (HE $\times 40$). B: Basophilic lime granules were found on the mucosal surface (HE $\times 100$). C: Changes in the proper muscle layer in the pyloric region that appeared similar to contraction band necrosis (HE $\times 100$). D: Congestion in the esophageal wall. Epithelial disorder was not notable (HE $\times 40$).

Table 1. Histological Findings of the Reported Autopsied Cases

substance	age	sex	digestive system	respiratory system	other organ systems	reference
610 hap	20	male		pulmonary congestion and edema	cerebral congestion, minor bleeding, disappearance of Nissl body	4
610 hap	48	male	widespread pseudomembranous pharyngitis, esophagitis, gastroenteritis	tracheitis, bronchitis	moderate adrenal hemorrhage	5
610 hap	45	male	disintegration and exfoliation of the gastrointestinal mucosa	bleeding in a part of the lungs		6
lime-sulfur	60	female	severe liquefactive necrosis and hemorrhage of the gastric wall concentric and layered lime granules (stained blue with hematoxylin)		centrilobular liver necrosis contraction band necrosis and mild tear in the myocardium	9
lime-sulfur	22	male		pulmonary edema and alveolar hemorrhage	vacuolar degeneration of the myocardium, centrilobular fatty degeneration of the liver	10
lime-sulfur	44	male	hemorrhagic gastritis coagulative necrosis of the esophageal and gastrointestinal mucosa	pulmonary edema	centrilobular parenchymal change of the liver degenerative changes in the renal tubular epithelial cells	11

posure to a corrosive material caused sclerosis of the whole wall and irritation by the corrosive agent caused a spasm in the stomach, particularly around the pyloric region, which prevented the leakage of the agent into the duodenum^{13, 14}.

In our case, dissection-like changes in the blood vessels of the submucosa and alterations similar to contraction band necrosis (usually seen in the myocardium) in the

proper muscle layer of the pyloric region were confirmed, suggesting hypercontracture of smooth muscle cells in the blood vessels and proper muscle layer. This smooth muscle hypercontracture was observed in an autopsy case of zinc chloride intoxication¹⁵. The pathophysiology of the smooth muscle cell hypercontracture is thought to include ischemia, spasm, and agonal non-specific changes¹⁵.

In the present case, only congestion was confirmed in the esophagus. Structural changes in the esophagus were reported as mild in cases involving a lime-sulfur mixture¹⁶. Short transit time of the corrosive agent in the esophagus and the toughness of the squamous epithelium may have contributed to this finding¹⁵.

The clinical course of corrosive gastritis is divided into three stages¹⁶. There is degeneration, necrosis, and shedding of tissues during the acute stage (within 1 week of the injury). In some cases, perforation and/or peritonitis may develop. After 2–5 weeks (intermediate phase), tissues begin to repair, and there is localized fibroblastic proliferation, deposition of collagen fibers, and formation of granulation tissues, which leads to stenosis. After 6 weeks, repair is almost complete, and the tissues are in the process of healing and forming scars. A case, where corrosive gastritis caused by lime-sulfur mixture ingestion led to cicatricial stenosis, requiring surgical treatment was reported¹⁶. Pathological examination of the stomach sample from the surgery showed chronic gastritis with atrophied mucosa, lymphocyte infiltration of the submucosa, and fibroblastic proliferation that went beyond the muscle layer and partially reached the serosa¹⁶. In our case, no fibrosis was found in the stomach lesion. The corrosive change was because of first exposure and not repeated exposure, suggesting this suicide was the first attempt.

In the process of death caused by calcium polysulfide ingestion, three mechanisms have been reported: 1) direct corrosive injury, 2) hydrogen sulfide is generated through a reaction with gastric acid and absorbed via the gastric mucosa and lungs, causing hydrogen sulfide poisoning, and 3) metabolic acidosis^{3, 12, 17}. In this case, direct corrosive injury was supposed to be the main mechanism among the three mechanisms. Kobayashi et al. described that the blood sulfide concentration is different between hydrogen sulfide inhalation and oral sulfide intoxication³, suggesting that sulfide concentration is useful for the differential diagnosis. However, we did not measure the sulfide concentration.

From the ethical viewpoint of animal rights protection, histopathological examination of corrosive materials has been restricted in recent years¹⁸. Thus, valuable cases such as the present case need to be evaluated for toxicologic pathology to understand the effects of corrosive substance exposure. This case highlights the need for toxicologic pathologists to perform a complete autopsy to determine the cause of death, including detailed histopathological analysis.

Disclosure of Potential Conflicts of Interest: The authors have no conflicts of interest to report in connection with this paper. We made our best efforts to ensure that readers could not identify the patient in this case report.

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