Case Report

An unexpected prolonged coma due to a pharmacobezoar formed from Vegetamine A[®] tablet ingestion

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Case: A 49-year-old man ingested massive quantities of Vegetamine A[®] tablets that contain two anticholinergic agents in addition to phenobarbital. The patient remained in an unexpectedly prolonged coma 4 days post-hospitalization. An acute gastroscopy revealed a pinkish-white pharmacobezoar on the lesser curvature of the stomach, which was extracted using a net. Direct hemoperfusion and treatment with multiple-dose activated charcoal was then initiated. Phenobarbital serum concentrations eventually decreased, resulting in complete recovery of the patient.

Outcome: On day 30, the patient was transferred to the Psychiatric Department.

Conclusion: An intragastric pharmacobezoar should be suspected in patients with promoted and prolonged toxicity or if high serum concentrations of agents indicate their continuous absorption.

Key words: Gastroscopy, pharmacobezoar, phenobarbital, Vegetamine A[®] tablet

INTRODUCTION

IN JAPAN, A pink-colored tablet known as Vegetamine A[®] (Shionogi & CO., LTD. Osaka, Japan) has been commercially available for many years and is commonly prescribed as a hypnotic. The tablet contains three active ingredients: phenobarbital (40 mg), chlorpromazine hydrochloride (25 mg), and promethazine hydrochloride (12.5 mg). In the present report, we describe a patient with a pharmacobezoar formed from massive ingestion of Vegetamine A tablets, resulting in promoted and prolonged toxicity.

CASE REPORT

THE PRESENT CASE involved a 49-year-old man with a history of depersonalization–derealization syndrome who became comatose 45 min after arriving at the Department of Psychiatry. Because a brain stem infarction was suspected, he was immediately intubated and transferred to

the Department of Neurology. A computed tomography (CT) scan and magnetic resonance imaging of the head indicated no acute changes, and laboratory blood and cerebrospinal fluid results showed no abnormal findings. However, an overdose was suspected on day 3 because the patient remained comatose. The patient was screened for tricyclic antidepressants and drugs of abuse (Triage DOA[®], Sysmex & CO., LTD. Hyogo, Japan), and results indicated the presence of barbiturates. Severe phenobarbital poisoning was diagnosed, as serum concentration of the agent was remarkably high (135.6 µg/mL); therefore, activated charcoal (25 g) was given every 4 h through a nasogastric tube. The patient was transferred to the Emergency Center as he remained comatose on day 4 and because serum phenobarbital concentrations had elevated to 145.9 µg/mL.

The patient arrived at the Emergency Center at 09:42 in a coma with a score of 3 (E1V1M1) on the Glasgow Coma Scale. Serum phenobarbital, chlorpromazine hydrochloride, and promethazine hydrochloride concentrations were 99.5, 0.071, and 0.173 µg/mL, respectively. A CT scan revealed a large round mass in the stomach (Fig. 1).

An acute gastroscopy revealed a pinkish-white mass on the lesser curvature of the stomach, which was suspected to be a pharmacobezoar (Fig. 2). A 25-cm overtube was inserted to protect the airway and allow the passage of an endoscope with grasper. Parts of the pharmacobezoar were grasped with a net (Roth Net; Olympus Medical Systems

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Fig. 1. Computed tomography scan of a 49-year-old man who ingested massive quantities of Vegetamine A tablets. The scan, carried out on day 4, shows a large round mass located in the stomach.

Co., Ltd, Tokyo, Japan) (Fig. 2, left-hand image) and extracted from the stomach (Fig. 2, right-hand image). The endoscopic grasper was inserted and removed a total of five times, followed by irrigation of the stomach with water and aspiration of all visible pinkish-white matter. No bleeding or erosion was observed in either the esophagus or stomach. A follow-up CT scan confirmed complete removal of the mass.

After transferring the patient to the Intensive Care Unit, a direct hemoperfusion was carried out for 5 h together with treatment with activated charcoal (25 g) through a nasogastric tube five times every 4 h, resulting in a gradual decrease of serum phenobarbital concentrations (Fig. 3). Mechanical ventilation was stopped on day 6 as the patient began to recover from the coma. The patient confessed to having ingested large quantities of Vegetamine A tablets in his car shortly after arriving at the hospital. However, he denied having taken any other agents.

On day 8, the patient became delirious and exhibited a coarse tremor of his hands. The patient was diagnosed with withdrawal syndrome, and oral administration of phenobarbital (90 mg daily) was initiated. These symptoms subsided with sustained serum phenobarbital concentrations of 10 $\mu\text{g}/\text{mL}$. On day 30, the patient was transferred to the Psychiatric Department.

DISCUSSION

AN INTRAGASTRIC PHARMACOBEOAR is usually suspected in patients with symptoms of promoted and prolonged toxicity. This is routinely diagnosed with an abdominal X-ray, CT scan, or gastroscopy. Removal of the pharmacobezoar by gastroscopy is a common treatment option in clinically stable patients.^{1–4} In a previously published report, an 18-year-old woman ingested

Fig. 2. A pharmacobezoar formed in a 49-year-old man from massive ingestion of Vegetamine A tablets. The pharmacobezoar was grasped with a Roth Net (left) and extracted from the stomach (right).

Fig. 3. Serial changes in serum phenobarbital concentrations during treatment of a 49-year-old man who formed a pharmacobezoar from massive ingestion of Vegetamine A tablets. DHP, direct hemoperfusion; MDAC, multiple-dose activated charcoal.

large amounts of slow-release theophylline tablets, thereby becoming tremulous and agitated. Gastroscopy showed a 2-cm pharmacobezoar on the greater curvature of the stomach. The mass was removed using a basket extraction method, resulting in immediate improvement of clinical symptoms.¹ Another published report indicated that a 47-year-old woman who massively ingested sustained-release venlafaxine tablets developed acute respiratory distress syndrome, hemodynamic instability, and acute renal failure. A gastroscopy revealed a gelatinous mass of partially dissolved tablets coating the entire greater curvature of the stomach. The pharmacobezoar was removed by multiple gastroscopies using a basket extraction method.² In another report, a 28-year-old woman who massively ingested slow-release clomipramine tablets developed a pharmacobezoar in the stomach that was made evident by an abdominal X-ray, and was subsequently confirmed by gastroscopy and shown to be located in the fundus of the stomach. The pharmacobezoar was crushed with pliers, and the resulting lumps were grasped with a wire basket and extracted.³ Ng *et al.* reported a case of a 45-year-old woman who ingested ferrous sulfate and presented symptoms of nausea, vomiting, and diarrhea. A large mass of radio-opaque tablets was found in the stomach by an abdominal X-ray. A gastroscopy revealed a pinkish friable mass 5 cm in diameter in the fundus of the stomach. A tri-port grasper was used to break up the mass and remove the pieces from the stomach.⁴

Although gastroscopy has many benefits, there is a risk of mucosal injury during the procedure. Lapostolle *et al.* reported three cases where patients ingested large quantities

of clomipramine tablets. Chest X-rays revealed round radio-opaque masses in the stomach. However, gastroscopies were unsuccessful in all three cases and resulted in gastric hemorrhage, thereby requiring subsequent blood transfusion.⁵ Gastroscopy should be carefully carried out and monitored in patients with vomiting or who have an altered mental state. In addition, proper anesthetic control, airway protection, and overtube use should be implemented.

In the present case, a prescribed drug overdose was suspected in a patient given the clinical symptoms of coma, and diagnosis of phenobarbital poisoning was confirmed by toxicological serum analysis. Multiple-dose activated charcoal (MDAC), anticipated to prevent prolonged toxicity due to the enterohepatic circulation of phenobarbital, did not decrease serum phenobarbital concentrations or improve clinical symptoms. A CT scan revealed a large mass in the stomach, which was subsequently confirmed by acute gastroscopy as a pharmacobezoar. After successful removal of the pharmacobezoar by gastroscopy and use of direct hemoperfusion and MDAC, serum phenobarbital concentrations gradually decreased, resulting in complete patient recovery. These results suggest that treatment with activated charcoal in the presence of a pharmacobezoar at the Department of Neurology might have promoted the elevation of the serum phenobarbital concentrations by further suppressing the motility of the stomach.⁶ The overall procedure at the Emergency Center was safe and highly effective in preventing further phenobarbital absorption and toxicity, and also in preventing the manifestation of more severe clinical symptoms.

Risk factors for the formation of intragastric pharmacobezoars include dehydration, anatomical gastrointestinal (GI) abnormalities, diseases, or disorders that cause dysmotility of the GI tract, ingested drugs in a sustained- or slow-release preparation and certain co-ingested drugs such as anticholinergic and opiate drugs.⁷ In the present case, a pharmacobezoar was formed from massive ingestion of Vegetamine A tablets that contain phenobarbital, chlorpromazine hydrochloride, and promethazine hydrochloride. The previous report described a patient with a pharmacobezoar formed from massive ingestion of Vegetamine B tablets that contain the same ingredients and suggested that phenobarbital might have the potential to form a pharmacobezoar.^{6,8} However, phenobarbital does not have any significant effects to suppress the motility of the GI tract. Although Vegetamine A tablets are not present in a sustained- or slow-release preparation, anticholinergic effects from chlorpromazine hydrochloride and promethazine hydrochloride may have partially promoted the formation of the pharmacobezoar by reducing GI motility in the present case.

CONCLUSION

ALTHOUGH VEGETAMINE A tablets are not in a sustained- or slow-release preparation, an intragastric pharmacobezoar should be suspected in patients with promoted and prolonged toxicity or if high serum concentrations of ingredients including phenobarbital indicate continued absorption despite MDAC administration. In stable patients, removal of the pharmacobezoar by gastroscopy may be considered a safe and effective procedure for detoxification.

CONFLICT OF INTEREST

NONE.

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