Case Report

Promethazine-induced Tissue Necrosis: A Case Presentation

Urgent message: Due to its versatility, the urgent care clinician will find promethazine an appropriate choice in many situations. Awareness of potentially serious side effects maximizes the chance of good outcomes while minimizing risk.

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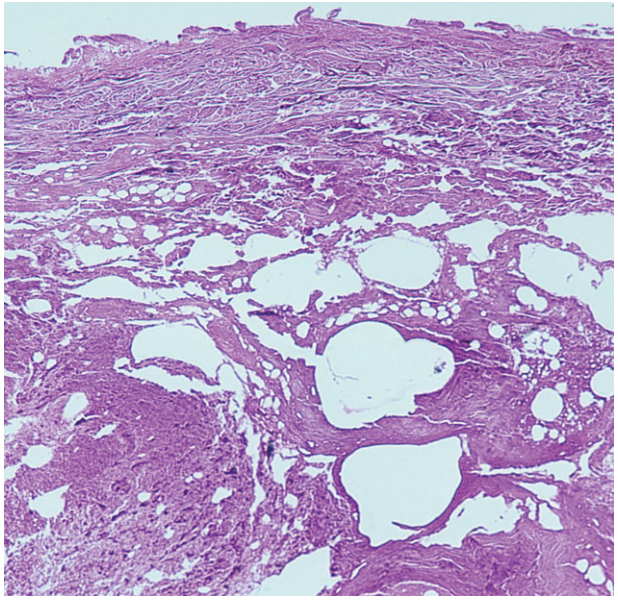
Introduction

Promethazine (Phenergan) is a drug commonly prescribed in emergency departments and urgent care clinics for treatment of a variety of conditions (**Table 1**). Because it possesses antihistamine, sedative, anti-motion sickness, and anti-emetic effects, it is often used for nausea and vomiting.

Physicians may not be fully aware that it is also toxic to the intima of blood vessels and surrounding connective tissue; this can result in severe tissue damage and necrosis.



Although this is not a common side effect of this medicine, the purpose of this article is to bring awareness to and familiarize urgent care physicians with serious complications which *can* happen with this commonly used medication.

Case Presentation

A 48-year-old African-American male presented to the emergency department with an abscess on the right lower abdominal wall and a four-day history of nausea.

The patient underwent incision and drainage (I&D) of the abscess and received 25 mg of promethazine by intramuscular route on the right gluteal area.

Immediately after, he reported a severe burning sensation going down his right thigh. It subsided after an hour, at which time he was discharged home to follow up with his primary care physician.

Two days later, the patient presented to his primary care clinic for the repacking of I&D. He complained that the pain at the injection site was worse—so much so that he was unable to walk.

On physical examination, he had:
temperature: 100.1° F
heart rate: 96 BPM
respiration: 4 RPM
blood pressure: 110/75 mmHg.

His right thigh was warm, tender, and swollen; erythema extended from the right hip down to the knee (**Figure 1**).

Table 1. Common Uses of Promethazine

- *Allergic reactions*
  - hay fever
  - urticaria
  - vasomotor rhinitis
  - skin allergies
  - poison ivy
  - insect bites
- *Relief of pruritus due to various dermatologic conditions*
- *Nausea and vomiting of various etiologies*
  - motion sickness
  - radiation sickness
  - surgery
  - anesthesia and gastroenteritis
  - centrally acting emetics
  - metabolic or endocrine disorders

Figure 1. Cellulitis from right hip to knee.

The patient was immediately admitted to the hospital and had a complete work-up for inpatient treatment of cellulites. He had an elevated white cell count of 14,000, with no bands and a sodium level of 120 mEq.

CT scan of the right thigh demonstrated multiple congruent abscesses extending from the injection site on the right hip to the knee. The surgical team was consulted for possible fasciotomy of the right thigh.

Hospital Course

The patient was admitted for the treatment of cellulites and possible fasciotomy of the right thigh. He was started on intravenous fluids, the broad-spectrum antibiotic piperacillin-tazobactam (Zosyn), and the pain medication hydromorphone (Dilaudid). He had fasciotomy and wound vac placement. The culture grew methicillin-resistant staphylococcus aureus (MRSA), for which IV vancomycin was added in addition to piperacillin-tazobactam.

Subsequently, the patient was taken to the operating room a few more times for wound vac changes. He remained in the hospital for one month and was later transferred to a rehabilitation facility.

Discussion

It is apparent in reviewing the literature that promethazine can cause potentially serious side effects, ranging from mild edema to soft tissue necrosis at the site of injection.

Administering promethazine by intravenous or intra-arterial routes has been found to result in arterial spasm and, in turn, to impaired circulation and gangrene in specific cases.[1] Extravasations of promethazine in the soft tissue are also believed to cause similar effects, as shown in our patient.

In 1999, Malesker, et al reported a similar experience with a 43-year-old woman who was admitted for a hysterectomy and received post-operative promethazine 25 mg every two hours by intravenous route for nausea and vomiting.[2] She developed pain, swelling, and erythema at the site of injection in her right hand.

Patrick J. Marshfied in 2004 described the case of a professional guitar player who was awarded $7.4 million in a lawsuit for pain and suffering following complications associated with the intra-arterial injection of promethazine. The patient was simply treated for migraine headache, initially.[3]

More recently (2009), Grissinger described a case of a 19-year-old woman who received promethazine by intravenous route and developed pain and swelling at the site of injection in her right arm.[4] Her arm and fingers became purple and blotchy; eventually, she underwent amputation of the thumb, index finger, and the top of her middle finger.[4]

Our case report clearly demonstrates the potential for serious complications associated with promethazine.

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symptoms to have inducible myocardial ischemia. Although data on the presence and type of chest pain were recorded before stress testing, they were collected hours after presentation, and we cannot infer if or how they affected decisions about testing and patient disposition.

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Implications of Increasing Battery Ingestions

Key point: Battery ingestions are increasing in frequency and are very high-risk events.

Litovitz T, Whitaker N, Clark L, et al. Emerging battery-ingestion hazard: Clinical implications. *Pediatrics*. 2010;125(6):1168-1177.

Recent cases suggest that severe and fatal button battery ingestions are increasing and that current treatment may be inadequate. The objective of this study was to identify battery ingestion outcome predictors and trends, define the urgency of intervention, and refine treatment guidelines.

Data were analyzed from the National Poison Data System (56,535 cases, 1985-2009); the National Battery Ingestion Hotline (8,648 cases, July 1990-September 2008); and medical literature and National Battery Ingestion Hotline cases (13 deaths and 73 major outcomes) involving esophageal or airway button battery lodgment.

All three data sets signal worsening outcomes, with a 6.7-fold increase in the percentage of button battery ingestions with major or fatal outcomes from 1985 to 2009 (National Poison Data System). Ingestions of 20- to 25 mm diameter cells increased from 1% to 18% of ingested button batteries (1990–2008), paralleling the rise in lithium-cell ingestions (1.3% to 24%).

Outcomes were significantly worse for large-diameter lithium cells (≥20 mm) and in children < 4 years.

The 20 mm lithium cell was implicated in most severe outcomes. Severe burns with sequelae occurred in just two to 2.5 hours. Most fatal (92%) or major outcome (56%) ingestions were not witnessed. At least 27% of major outcome and 54% of fatal cases were misdiagnosed, usually because of nonspecific presentations. Injuries extended after removal, with unanticipated and delayed esophageal perforations, tracheoesophageal fistulas, fistulization into major vessels, and massive hemorrhage.

Revised treatment guidelines promote expedited removal from the esophagus, increase vigilance for delayed complications, and identify patients who require urgent radiographs. ■

In this case, the patient was treated aggressively by the surgical team on board and had significant improvement. However, we believe that to date there have not been any scientific studies to summarize definitive treatment for the catastrophic consequences that may occur with promethazine and other drugs (e.g., phenytoin, thiopental, and propofol).[5-7]

Local anesthetic agents to promote vasodilatation, anticoagulation therapy, sympatholytic therapy (i.e., Stellate ganglion block), and limb elevation have all been described in case studies, with varying results.[8-10] Nevertheless, it is important to point out that in case of inadvertent intra-arterial injection, the catheter should be left in place in order to administer emergency medications. The true extent of the problems associated with promethazine may not be known.

We, along with the manufacturer's recommendations, suggest that the following strategies be considered to prevent or minimize tissue damage:

- As 25 mg/ml is the highest strength of promethazine, try to use this concentration instead of 50 mg/ml.
- The starting dose should be between 6.26 mg/ml and 12.5 mg/ml, especially in elderly patients.
- Dilute 25 mg/ml of promethazine in 10 ml to 20 ml of normal saline (or prepare it in mini bags of normal saline).
- Promethazine should be administered only via a large-bore vein, such as the central venous catheter or deep intramuscular.
- IV promethazine should be administered over 10 to 15 minutes.
- Before administration, advise patients to let the physician know immediately whether pain or burning occur during or after injection. ■

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