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Case Report

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Chlorhexidine Allergy: Mild Allergic Reactions Can Precede Anaphylaxis in the Healthcare Setting

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Abstract

Chlorhexidine can cause severe immediate-type allergic reactions such as urticaria, anaphylactic shock or, even, cardiac arrest. We report the case of a patient who developed perioperative anaphylactic shock caused by chlorhexidine 1 year after a postoperative urticarial reaction, which was assumed not to be significant at the time. This case highlights the importance of identifying mild allergy symptoms after exposure to chlorhexidine at the pre-anaesthetic assessment to prevent more severe allergic reactions in future.

Keywords: Allergy, anaphylaxis, chlorhexidine, drug allergy, perioperative

Introduction

Chlorhexidine is an effective antiseptic agent. It prevents many infections and is widely used in hospitals, particularly in the perioperative setting (1, 2). However, in rare cases, chlorhexidine can cause severe immediate-type allergic reactions such as urticaria, anaphylactic shock or, even, cardiac arrest (3). During surgery and anaesthesia, several chlorhexidine-containing products are used at different sites of the body, e.g., for skin disinfection at the surgical site, in the swabs used before venous puncture and in the urethral gel used before urinary catheterisation (1). Due to these multiple simultaneous exposures, patients allergic to chlorhexidine are at a risk for developing an anaphylactic reaction on perioperative exposure to this agent. In UK, Belgium and Denmark, chlorhexidine is part of routine testing in patients with suspected perioperative allergy, and it has been identified as the culprit drug in 9%, 9% and 10% of cases, respectively (4-6). Here we report the case of a patient who developed perioperative anaphylactic shock caused by chlorhexidine 1 year after a postoperative urticarial reaction, which was not assumed to be significant at the time. The patient has provided written consent for publishing this case report.

Case Presentation

In March 2015, a 62-year-old man with hypertension, hypercholesterolemia and type II diabetes presented with sudden onset of low back pain and haematuria. Kidney stone was suspected and later verified using computed tomography imaging. Ureteroscopic stone removal was planned for the following day. At the pre-anaesthetic assessment, the patient reported no known allergies and uneventful previous surgeries for phimosis in 2014, lipomas in 2000, and kidney stones in 1995.

General anaesthesia was induced with propofol, remifentanil and sufentanil. Antibiotic prophylaxis with tobramycin was administered 15 min after anaesthetic induction. Within few minutes, his blood pressure dropped

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to 70/40 mmHg, pulse rate increased to 140 bpm and the oxygen saturation dropped to 88%. Moreover, generalised flushing was noted. Anaphylactic shock was suspected, following which intramuscular adrenaline and intravenous ephedrine, glucocorticoid and antihistamine were administered. The patient was stabilised on this treatment, but surgery was terminated with the stone left in situ, and a ureteral stent was placed to provide drainage from the kidney to the bladder. The postoperative course was uneventful, and the patient had no sequelae. Serum tryptase was found to be elevated (27.7 µg L^{-1}) 1 h after the reaction, whereas baseline tryptase measured a few months later was found to be normal (7.1 µg L^{-1}). Due to the timing of the reaction, tobramycin was suspected as the cause and a warning against tobramycin was entered in the notes.

Postoperatively, on again asking the patient about previous allergic reactions, he recalled having urticaria in the neck, chest and abdominal regions after phimosis surgery the previous year, and he even provided a photograph (Figure 1). There had been no localised reaction on the penis.

Surgery was rescheduled 8 days later, avoiding all drugs and substances used prior to the reaction, and was performed uneventfully.

The patient was referred to the Danish Anaesthesia Allergy Centre for investigation 2 months later. Using skin test concentrations recommended by the European Network for Drug Allergy (7), testing was performed with all drugs and substances used during surgery and prior to the reaction: tobramycin, propofol, remifentanil, sufentanil, chlorhexidine, ethylene oxide, methylcellulose, macrogol and latex. Drug provocation was performed for all skin test-negative drugs.

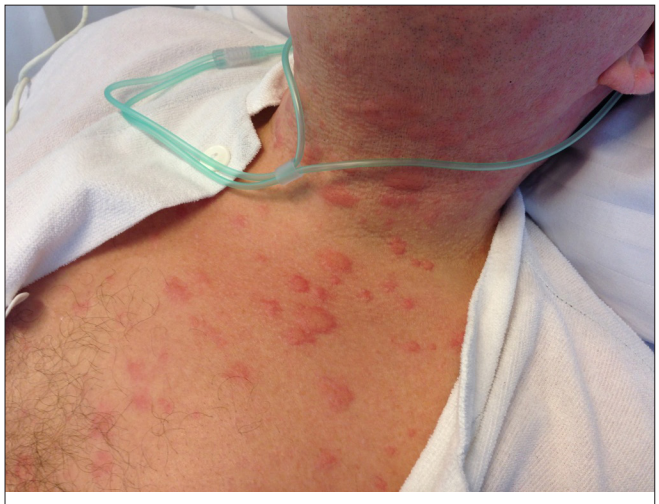

Figure 1. Postoperative urticaria 1 year before the present surgery

All test results for chlorhexidine were positive including skin prick testing and intradermal testing, specific IgE to chlorhexidine (ImmunoCAP®, Thermo Fisher Scientific, Uppsala, Sweden) and histamine-release test (Reflab Aps, Copenhagen, Denmark). Testing for all other drugs and substances including tobramycin gave negative results.

It was concluded that the patient was allergic to chlorhexidine; he was given a warning card and advised to avoid all exposures to chlorhexidine. He has since uneventfully undergone several operations and procedures without the use of chlorhexidine.

Discussion

Perioperative anaphylaxis is a very rare but potentially life-threatening occurrence. In the present case, serum tryptase levels were increased at the time of reaction compared with baseline levels measured a few months later, supporting the clinical suspicion of an anaphylactic reaction. Tobramycin was primarily suspected as the culprit drug by the attending anaesthetist based on the timing between administration and onset of symptoms. However, during allergy investigations, tobramycin was found to be well tolerated and chlorhexidine was identified as the culprit drug. It has been shown that assuming the culprit drug based on timing alone is imprecise, emphasising the need for systematic investigation of suspected perioperative allergic reactions (8).

Notably, many patients allergic to chlorhexidine report previous mild allergic reactions occurring after exposure in the health care setting. This has been described in many case reports, where patients have reported symptoms such as a mild irritant local reaction, an unspecific rash (9-12) or urticaria (13-15) after previous exposure to chlorhexidine. In many cases, like the present one, the patients have reported a mild reaction only after experiencing a more serious reaction on subsequent exposure. This highlights the importance of direct questioning on previous allergic reactions during the pre-anaesthetic assessment for identifying such mild reactions. Questions may include symptoms such as itching, swelling and urticarial rash in health care settings.

Conclusion

This case highlights the fact that chlorhexidine is a common cause of perioperative anaphylaxis. It also brings focus on the importance of identifying mild allergy symptoms after exposure to chlorhexidine at the pre-anaesthetic assessment to prevent potentially more severe allergic reactions in future.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

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