

CASE REPORT

Life-threatening intraoperative anaphylaxis as a result of chlorhexidine present in Instillagel

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SUMMARY

A 70-year-old man with left lower limb critical ischaemia was admitted to our vascular unit for a femoral-popliteal bypass. He had experienced a skin reaction to chlorhexidine 6 months previously during an angioplasty procedure. After intubation, once in the operating theatre, the patient had a urinary catheter inserted using Instillagel. Around 30 min later the patient had a full-blown anaphylactic reaction that required aggressive medical management and the abandoning of surgery. Postoperative allergy testing confirmed that the suspected primary trigger for the anaphylaxis was indeed chlorhexidine, which was present in Instillagel. The patient was also found to have allergies to atracurium and teicoplanin, which had been given on induction. This case report highlights the importance of recognising that Instillagel contains chlorhexidine, and that indeed intraurethral use during routine urinary catheterisation can be a cause of life-threatening anaphylaxis.

BACKGROUND

Chlorhexidine is commonplace in the healthcare setting, and is widely used both as a topical skin preparation for antisepsis and as a mouthwash. Patients may be exposed to chlorhexidine repeatedly throughout multiple admissions, increasing the risk of developing sensitivity reactions. We report a case of anaphylactic reaction to chlorhexidine found in Instillagel (CliniMed, High Wycombe, UK), used during urinary catheterisation.

CASE PRESENTATION

A 70-year-old man with left femoral artery disease was admitted to our vascular ward on an urgent basis with critical ischaemia. His right limb had previously been treated with a femoral-popliteal bypass graft to good effect. His only other medical history was asthma. He had a known, documented allergy to penicillin and chlorhexidine ('Rash' in notes). This chlorhexidine allergy was discovered 6 months previously when the patient developed a skin rash in the groin after chlorhexidine was used to clean the skin prior to an angiogram procedure.

A left femoral-popliteal bypass planned after an angiogram on this admission confirmed a long superficial femoral artery occlusion.

At 13:15 on the day of the operation, the patient underwent successful induction with propofol and atracurium, and he was intubated with an endotracheal tube without difficulty. He was given intravenous teicoplanin on induction for antibiotic

prophylaxis (due to the documented penicillin allergy). He was then moved from the anaesthetic room to the theatre. A urinary catheter was inserted as a standard procedure in an aseptic manner using Instillagel as a lubricant.

Surgery commenced 15 min later.

At 13:40 as the operation was beginning, the patient was noted to have raised airway pressures with decreasing O₂ saturations (<80%) and end tidal CO₂ measurements. The procedure was abandoned and assistance sought by the anaesthetics consultant. The endotracheal tube was changed.

The patient was noted to have bilateral wheeze on auscultation of the chest and a diffuse skin rash. Intravenous epinephrine, intravenous chlorphenamine, intravenous hydrocortisone and endotracheal salbutamol were given rapidly. Arterial and central lines were inserted and the patient was swiftly moved to the intensive care unit (ICU) for ongoing management.

The patient was found to have an elevated mast cell tryptase (17.9 ng/mL at the time of incident and 23.3 ng/mL that same evening, reference range 2.0–14.0 ng/mL). Following management with intravenous steroids on ICU, the patient was extubated the following day and made a good recovery.

He was discharged home 5 days later with plans for urgent outpatient review by the immunology team prior to the next attempt at revascularisation for his critically ischaemic left leg.

INVESTIGATIONS

Mast cell tryptase—17.9 ng/mL at the time of incident, 23.3 ng/mL that same evening (reference range 2.0–14.0 ng/mL).

DIFFERENTIAL DIAGNOSIS

1. anaphylaxis
 - a. causative agents—chlorhexidine, atracurium, teicoplanin
2. bronchospasm.

TREATMENT

- ▶ intravenous epinephrine
- ▶ intravenous hydrocortisone
- ▶ intravenous chlorphenamine
- ▶ endotracheal salbutamol
- ▶ further consultant anaesthetic support
- ▶ admission to ICU
- ▶ immunology follow-up and patch testing on urgent outpatient basis.



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OUTCOME AND FOLLOW-UP

The following week the patient went on to have allergen testing via immunology services. He was found to have the following:

- ▶ negative oral challenge to amoxicillin
- ▶ negative skin prick tests to extracts of propofol, pancuronium, vecuronium, suxamethonium, teicoplanin and lignocaine
- ▶ positive skin prick tests to atracurium (5 mm weal) and chlorhexidine (11.5 mm weal)
- ▶ suspected positive intradermal tests to neat teicoplanin
- ▶ positive ImmunoCAP to chlorhexidine.

In summary, he was found to have a significant allergy to chlorhexidine and atracurium, as well as a suspected allergy to teicoplanin. He was given an EpiPen and advised to inform healthcare professionals of his allergy to chlorhexidine. Following allergy testing, the patient underwent successful revascularisation of the affected limb under spinal anaesthesia around a month later with a straightforward postoperative recovery.

DISCUSSION

This patient clearly had an anaphylactic reaction intraoperatively. It was recognised early and managed appropriately. However, the reaction occurred sometime after exposure to any allergens. The likelihood is that this anaphylaxis was precipitated by the intraurethral application of chlorhexidine contained in Instillagel, which may account for the relative delay (30–40 min) between application and the onset of anaphylactic symptoms. This corresponds with the delay reported in a similar case report presented by Khan *et al*,¹ where the identified allergen was also intraurethral chlorhexidine. A case report by Dyer *et al*² presents a very similar situation whereby a patient developed an anaphylactic reaction to intraurethral chlorhexidine in Instillagel postoperatively following cystoscopic laser ablation of a recurrent bladder tumour. In this case the patient suddenly deteriorated as he was about to be discharged following this day-case procedure. Sharp *et al*³ carried out a review of the literature and found that up to 2015, there were 36 articles published on surgical patients suffering anaphylaxis secondary to chlorhexidine. Of these cases, 44% were due to chlorhexidine-containing lubricant for intraurethral catheters. Also, of the 36 articles reviewed, it was found that chlorhexidine-related anaphylaxis was responsible for 40% of patients having their procedures abandoned and unplanned intensive care admissions in 28%. Clearly chlorhexidine allergies, and in particular its presence in lubricants used for routine intraurethral catheterisation, is an important potential cause of morbidity and mortality. When our patient suddenly deteriorated, it was certainly not known at the time by our team

Learning points

- ▶ Chlorhexidine sensitivity is rare but may be fatal if unrecognised.
- ▶ Reports of chlorhexidine sensitivity are increasing.
- ▶ Instillagel contains 0.25% chlorhexidine gluconate. This is often not known or remembered by clinicians and should be borne in mind when performing urinary catheterisation.
- ▶ Delayed anaphylactic reactions may occur through the systemic absorption of chlorhexidine via mucous membranes.
- ▶ If patients have had previous skin reactions to chlorhexidine, the use of Instillagel is contraindicated given the risk of anaphylaxis due to systemic absorption.

that Instillagel contained chlorhexidine and that this could have been the cause of the anaphylaxis.

The Medicines and Healthcare Products Regulatory Authority (MHRA) in the UK issues a *summary of product characteristics* (SPC) for all medical products available in the UK. Interestingly, the SPC for Instillagel lists chlorhexidine as an ingredient (table 1) but does not reference adverse reactions to chlorhexidine,⁴ although there are adverse reactions listed in the SPC for other chlorhexidine-containing products.⁵

The patient was found to have allergies to both atracurium and teicoplanin postoperatively; however, it is the authors' view that these were not the cause of anaphylaxis, as the intravenous administration of these agents would cause an almost instantaneous reaction, not the reaction seen some 45–60 min later.

This case report serves as a warning and a reminder that chlorhexidine is present in Instillagel, and that this route of administration can lead to systemic absorption and delayed anaphylactic reactions. It also serves to remind clinicians to be aware of uncommon allergies to non-medicinal products, both in theatres and ward-based practice, including skin preparations, contrast agents and wound dressings, as well as common allergens such as antibiotics.

Contributors JT was responsible for preparation of the manuscript. JF was responsible for preparation of the manuscript and obtaining consent for publication. AM was the consultant in charge of the patient's care. IC oversaw the preparation of the manuscript. All authors read and approved the final submission.

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Table 1 Qualitative and quantitative composition of Instillagel⁴

Each 100 g gel contains:	
Lidocaine hydrochloride	2.0 g
Chlorhexidine digluconate solution	0.25 g
Methyl hydroxybenzoate	0.06 g
Propyl hydroxybenzoate	0.025 g

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