

Case Report

Long-term allergic dermatitis caused by sevoflurane: a clinical report

J. LLORÉNS HERRERIAS¹, C. DELGADO NAVARRO¹, M. T. BALLESTER LUJÁN² and A. IZQUIERDO PALOMARES¹

¹Anaesthesia and Critical Care Department, Hospital Clínico Universitario de Valencia, Valencia, Spain and ²Anaesthesia and Critical Care Department, Consorcio Hospital General Universitario de Valencia, Valencia, Spain

Background: Allergy to volatile anaesthetics is extremely rare, but capable of damaging the professional career.

Methods: This article presents the case of a 60-year-old surgeon who developed a skin rash on the reverse of hands, which progressively worsened and extended to distant fold areas. Blood tests were normal but for eosinophilia and risen total IgE, with normal specific globulins and skin prick tests for common allergens. After 8 years, a malfunction in the anaesthetic gas scavenging system was found, and symptoms remitted within a week following its replacement. Repeated open application test with sevoflurane led to the appearance of the same lesions in the tested areas and in distant body folds.

Results: We hypothesize that the most probable mechanism for the reaction in our patient is systemic allergic contact dermatitis, which is caused by repeated systemic exposure to a hapten that reaches the skin through haematogenous transport in a sensitized patient.

Conclusions: The report aims to warn about the potential aetiological relationship between exposure to inhaled anaesthetics and allergic manifestations with cutaneous symptoms.

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ALLERGY to volatile anaesthetics is extremely rare but capable of damaging the professional career. We report a case of allergic dermatitis after a long-term exposure to sevoflurane.

Case report

The subject is a 60-year-old surgeon with no relevant medical history or previous allergic reactions, working in the same operating room for an average of 8 h per week. In the last 10 years, he developed a skin rash consisting of elevated pruritic erythematous areas with small vesicles and lichenifications, distributed bilaterally on dorsum of hands, wrists and forearms. Lesions and pruritus worsened progressively, spreading to the antecubital, axilla, back, groin, scrotum and popliteal fossa. These symptoms significantly improved and even disappeared during holiday periods.

Several dermatological examinations did not lead to any diagnosis. The skin prick tests for standard allergens were all negative with skin biopsies

showing spongiotic dermatitis compatible with eczema. The lesions worsened and spread for 8 years, preventing the patient from carrying out his professional activities. Blood tests were performed coinciding with periods of greatest severity. All parameters were normal except for an increase in eosinophil count to 6%, and plasma globulin immunoglobulin E (IgE) concentrations up to 394 IU/ml. Specific IgE for *Ascaris*, *Anisakis*, *Echinococcus*, latex, ethylene oxide and cow's milk proteins were normal. So were the skin prick tests for latex and epicutaneous tests for common allergens from the surgical environment. These allergens included: different plastics, glues, methacrylates and rubber. Available surgical disinfectants were also tested, including iodine povidone, chlorhexidine, ethyl alcohol and hydrogen peroxide. Respiratory function tests were normal as well.

Initially topical steroids and tacrolimus showed a good response, but the lesions continued to spread so that this initial treatment strategy was replaced with oral steroids. As expected, the oral steroids

lead to a significant improvement but after 2 years led to steroid-induced diabetes, from which the patient is still suffering.

The apparent relationship with the workplace and a negative result for all the tests performed led the Labour Risk Management Department of the hospital to carry out a thorough examination of the surgical facilities where the patient worked. A malfunction in the Anaesthetic Gas Scavenging System (AGSS) in the anaesthesia machine (Excel 210, Datex Ohmeda) was found. The equipment was immediately replaced with a new AGSS. Following its replacement, the clinical manifestations quickly improved, with complete remission within a week. Blood tests performed 6 months after the resolution of the problem showed normal IgE concentrations and eosinophil percentage (Table 1).

Consequently, and given the clear cause–effect relationship, a *Repeated Open Application Test* (ROAT) with sevoflurane was performed. Sevoflurane was applied directly to the right arm and the surface covered with a transparent plastic patch. This procedure was intended to be repeated on a daily basis for 5 days, but, on the second day, the previous skin lesions reappeared on the tested zone, as well as generalized erythema and pruritus in body fold areas (Fig. 1), and therefore, the test was stopped. A similar test with desflurane was negative for 5 days. Three healthy volunteers from the same surgical environment were also tested for sevoflurane and desflurane for 5 days with negative results.

Discussion

Long-term exposure to inhaled anaesthetics in surgical personnel has been a subject of interest since their introduction as part of common clinical practice. The importance of keeping the exposure levels of these substances within safety limits has been clearly emphasized.^{1–4} The outstanding potential effects on professionals are carcinogenesis, hepatic and renal toxicities, alterations in immunity and fertility.^{5–7}

Table 1

Patient's evolution of total IgE levels and eosinophil percentage, before and after ceasing exposure to sevoflurane.

	Prior to resolution	Six months after resolution
Total IgE (IU/ml)	190	394
Eosinophil percentage (%)	6	3.9

Isolated allergic reaction to halothane and isoflurane are documented in the literature.^{8–10} In these cases, cutaneous manifestations consisted of raised erythematous and desquamative areas similar to those observed in our patient, with the same pattern of improvement after exposure was ceased.

In our systematic bibliography review, we could only find two cases of hypersensitivity to sevoflurane. In these reports, clinical manifestations did not consist of skin alterations but of bronchial hyperreactivity with significant drops of forced expiratory volume in one second (FEV₁) and positivity to a metacholine provocation test. In one of them, there was an anaphylactic reaction reported.¹¹

In our case report, the patient did not experience any respiratory symptoms, and functional tests were normal. The relationship between exposure and appearance of signs and symptoms were evident. The diagnosis of an allergic reaction was supported by ROAT positivity, systemic lesions and the initial eosinophilia and total IgE increase with their subsequent normalization after the lesions improvement.

The most probable mechanism for the reaction in our patient is systemic allergic contact dermatitis, which is caused by repeated systemic exposure to a hapten that reaches the skin through haematogenous transport in a sensitized patient.¹² The clinical picture can be heterogeneous, but the demarcated erythema of the perineal area and the involvement of flexural folds support this diagnosis. Moreover, the fact that the lesions were widespread and



Fig. 1. Result of repeated open application test (ROAT) with sevoflurane, showing reappearance of the skin lesions.

symmetrical tends to lead to the same conclusions, as no other systemic symptoms and signs were found.¹³ Another possible entity could be airborne allergic contact dermatitis, a morphological diagnosis that encompasses acute and chronic lesions observed predominantly on the exposed skin, caused by agents that settle on it.^{14,15} However, in this case, the fact that the lesions can be found in unexposed areas does not support this diagnosis. Another consideration could be fluoroderma – a dose-dependent hypersensitivity reaction to sevoflurane due to its fluoride content, with an extremely low incidence. It consists of exudative plaques with nodules, necrotic ulcers and acneiform eruptions with neutrophil accumulation without vasculitis upon histologic examination.¹⁶ Nevertheless, the macroscopic and microscopic lesions presented by our patient were not compatible with fluoroderma since they were clearly different.

The delay of 8 years in reaching the diagnosis suggests that there is a tendency to ignore the aetiological role played by the inhaled anaesthetics in this type of adverse effects.

The report aims to warn about the potential etiological relationship between exposure to inhaled anaesthetics and allergic manifestations with cutaneous symptoms. This turns out to be especially relevant when exposure is due to environmental factors in the workplace, given the potentially serious impact on the life of exposed personnel and the straightforwardness of the potential solution.

Authors Contributions

Dr Julio Lloréns Herrerías proposed and directed the development of the clinical report and critically revised the contents.

Dr Carlos Delgado Navarro conducted the text redaction and adjusted the final document formatting.

Dr María Teresa Ballester Luján performed the systematic bibliography review and helped with the text redaction.

Dr Ana Izquierdo Palomares gathered the iconographic data and helped with the bibliography review and text redaction.

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References

- Berry AJ. Recommended exposure limits for desflurane and isoflurane. *Anesth Analg* 1999; 88: 1424–5.
- Byhahn C, Wilke HJ, Westphal K. Occupational exposure to volatile anaesthetics: epidemiology and approaches to reducing the problem. *CNS Drugs* 2001; 15: 197–215.
- Byhahn C, Heller K, Lischke V, Westphal K. Surgeon's occupational exposure to nitrous oxide and sevoflurane during pediatric surgery. *World J Surg* 2001; 25: 1109–12.
- Henderson KA, Matthews IP. Staff exposure to anaesthetic gases in theatre and non-theatre areas. *Eur J Anaesthesiol* 2000; 17: 149–51.
- Nilsson R, Björdal C, Andersson M, Björdal J, Nyberg A, Welin B, William A. Health risks and occupational exposure to volatile anaesthetics: a review with a systematic approach. *J Clin Nurs* 2005; 14: 1160–1.
- Burm AG. Occupational hazard of inhalational anaesthetics. *Best Pract Res Clin Anaesthesiol* 2003; 17: 147–61.
- Raj N, Henderson KA, Hall JE, Aquilera IM, Harmer M, Hutchings A, Williams B. Evaluation of personal, environmental and biological exposure of paediatric anaesthetists to nitrous oxide and sevoflurane. *Anaesthesia* 2003; 58: 630–6.
- Bodman R. Skin sensitivity to halotane vapour. *Br J Anaesth* 1979; 51: 1092.
- Caraffini S, Ricci F, Assalve D, Lisi P. Isoflurane: an uncommon cause of occupational airborne contact dermatitis. *Contact Dermatitis* 1998; 38: 286.
- Slegers-Karsmakers S, Stricker BH. Anaphylactic reaction to isoflurane. *Anaesthesia* 1988; 43: 506–7.
- Vellore AD, Drought VJ, Sherwood-Jones D, Tunnicliffe B, Moore VC, Robertson AS, Burge PS. Occupational asthma and allergy to sevoflurane and isoflurane in anaesthetic staff. *Allergy* 2006; 61: 1485–6.
- Thyssen JP, Maibach HI. Drug-elicited systemic allergic (contact) dermatitis – update and possible pathomechanisms. *Contact Dermatitis* 2008; 59: 195–202.
- Häusermann P, Harr T, Bircher AJ. Baboon syndrome resulting from systemic drugs: is there strife between SDRIFE and allergic contact dermatitis syndrome? *Contact Dermatitis* 2004; 51: 297–310.
- Handa S, De D, Mahajan R. Airborne contact dermatitis – current perspectives in etiopathogenesis and management. *Indian J Dermatol* 2011; 56: 700–6.
- Santos R, Goossens A. An update on airborne contact dermatitis: 2001–2006. *Contact Dermatitis* 2007; 57: 353–60.
- Perbet S, Salavert M, Amarger S, Constantin JM, D'Incan M, Bazin JE. Fluoroderma after exposure to sevoflurane. *Br J Anaesth* 2011; 107: 106–7.

Address:

Carlos Delgado Navarro
Hospital Clínico Universitario de Valencia
Anaesthesia and Critical Care Department
Blasco Ibáñez 17
46010 Valencia
Spain
e-mail: cardelna@gmail.com