

CASE REPORT

Allergic reaction with angioedema after exposure to e-cigarette liquid: a case report

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ABSTRACT

Background: The use of electronic cigarettes (e-cigarettes) is increasing worldwide. Allergic reactions have been reported from the metal used, and a few cases have been reported of angioedema of the lip, but none were related to the e-cigarette liquid.

Case Presentation: We report a case of allergic reaction with angioedema from e-cigarette liquid, most likely histamine-mediated angioedema, in a healthy 24-year-old Saudi man, who did not have a history of any allergy or atopy. The subject presented complaining of left lower lip swelling 1 hour after smoking an e-cigarette and spilling liquid into the mouth. The case reported no shortness of breath, skin rash, or tongue swelling. On examination, vital signs were normal. The patient had left lower lip swelling and gingival erythema. The patient reported having experienced a similar episode in the past with a different type of e-cigarette liquid on the right lower lip, but it was less severe. The patient was diagnosed with allergic reaction with angioedema from the e-cigarette liquid and was managed with hydrocortisone 200 mg Intravenous and chlorphenamine 10 mg Intramuscular, and was discharged after 3 hours with full recovery.

Conclusion: E-cigarettes are still relatively new and could cause harm. Further studies and reports should be conducted concerning the health effects of e-cigarettes.

Keywords: Hypersensitivity, angioedema, smoking, e-cigarettes, allergy, case report.

Introduction

Recently, the use of e-cigarette has increased worldwide as an alternative to tobacco smoking; hence, companies are manufacturing electronic cigarettes (e-cigarettes) with different shapes and flavors. E-cigarettes usually contain concentrated flavors mixed with propylene glycol (PG) and glycerol (vegetable glycerin), and sometimes a variable nicotine percentage. A number of studies have been conducted previously for the identification of different chemical elements present in aerosols, cartridges, and refill solutions used in e-cigarettes [1,2]. E-cigarettes, instead of burning tobacco, produce aerosols with the help of the metal heating element powered by a battery and a cartridge that contains liquid. The liquid in a cartridge typically consists of concentrated flavors mixed with humectants (PG and glycerol), and sometimes nicotine. Once the power source is activated, a mist is formed due to aerosol production from the liquid, which is then inhaled by the user (often referred to as “vaping”) [1,2]. Liquid and aerosol samples have different analyte profiles, with potential implications for human health, thereby presenting a need of e-cigarette

aerosols testing [2]. The edema of subcutaneous tissues and deep dermis is referred to as angioedema, usually caused by acute mast cell-mediated reaction due to the exposure to any food, pollen, drugs, venom or animal dander allergens. Angioedema could be caused as a result of a hereditary condition, chronic reaction, an acute reaction to the inhibitors of the angiotensin-converting enzyme (ACE), or an acquired disorder due to an abnormal complementary response. The main symptom is swelling, which could be severe. Diagnosis is carried out by examination. Treatment involves eliminating or avoiding the allergen, airway management as needed, and

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administration of drugs to minimize swelling (e.g. H1 blockers) [3]. Reports have showed that there could be an acute allergic reaction to the metal in e-cigarettes and there is limited evidence of the direct adverse effect of or acute allergic reaction to e-cigarette liquid. Some studies reported allergic dermatitis after exposure to e-cigarette liquid components if used topically in some medications, but no reports revealed that e-cigarette liquid could cause an acute allergic reaction. There is considerable evidence that nicotine, in addition to the exposure of toxic substances potentially coming out from e-cigarettes under typical conditions was significantly lower than that emitted from the combustible tobacco cigarettes] 4].

However, the public is slowly deviating from regular smoking to electronic cigarette with the impression that it helps in quitting smoking or less harm or as some thought that electronic cigarette has no harm at all. Few evidences have been published in the comparison between regular smoking and electronic cigarette, especially in regard to smoking cessation; some studies showed that electronic cigarette shows modest cessation rates with benefits of behavioral and sensory gratification. On the other hand, in many studies, where e-cigarettes were introduced as an intervention, participants continued to use them to maintain their habit instead of quitting. A meta-analysis concluded that, as in observational studies, e-cigarettes were not associated with increased smoking cessation in the adult population. In RCTs, the provision of free e-cigarettes as a therapeutic intervention was associated with an increased smoking cessation [5,6].

Table 1 shows a list of various factors and how they might influence e-cigarette use behaviors and nicotine yield.

Case Presentation

A healthy 24-year-old Saudi male presented to the emergency department (ED) with lower lip swelling. The

patient gave a history of smoking an e-cigarette and a feeling of spilling e-cigarette liquid into his mouth; 1 hour later, the left side of his lower lip became swollen. The patient reported no history of shortness of breath, tongue swelling, skin rash, palpitation, or altered consciousness. There was no history of allergy or atopy, no family history of allergy or atopy, no dental intervention before the lip swelling, and no insect bites.

The patient had a similar incident with a different type of e-cigarette liquid, which he stopped using previously; however, he developed a similar reaction on the right side of the lower lip, less severe than in the present incident.

On examination, the patient's vitals were normal as blood pressure was 130/76 mmHg, heart rate was 85 beat per minute, respiratory rate was 15 breaths per minute, and temperature was 36.7°C. The patient had a swelling in the left lower lip with gingival erythema (Figure 1), no tongue swelling or wheeze or skin rash was observed, and other systems were also normal.

The patient was diagnosed with an allergic reaction with angioedema (Figure 2).

As the patient was presented to the ED and the diagnosis was most likely to be the allergic reaction with angioedema from the e-cigarette liquid, patch testing was not carried out.

The patient showed the e-cigarette carton, which contained vegetable glycerin, PG, natural or artificial flavoring, and nicotine 5.0%, pink slush flavor. The patient was managed by giving hydrocortisone 200 mg Intravenous and chlorphenamine 10 mg Intramuscular (IM) and was discharged after 3 hours with full recovery. The angioedema was most likely histamine-mediated angioedema as per the clinical presentation and the antihistamine and corticosteroid response in the management, but it was not confirmed by laboratory testing.

Table 1. Overview of the potential mechanisms influencing nicotine delivery from e-cigarettes.

Topic			Facilitate initiation or continued use			Enhance nicotine delivery			Central nicotine effects		Others
Domain	Factor	Paper section	Ap-peal	Per-ceived harm	Nicotine depend-ence	Aerosol volume/ nicotine in aerosol	Respi-ration/ topog-raphy	Nicotine absorption/ bioavaila-bility	Nicotine metabo-lism	Act on nA-ChRs?	Impact toxic-ity
E-liquid	Flavors (general)	3.1	X	X		~					X
	Menthol	3.1.1	X	X	X		X	X	X	X	
	Sweeteners	3.1.2	X								X
	pH	3.2						X			
	PG/VG base	3.3	X			X		X			X
	Alcohol	3.4			~			X		X	
	Nicotyrine	3.5						X	X		
Hard-ware	Nicotine concentration	3.6	X		X	X			X	X	
	E-cigarette generations/ models/types	4.1	X			X					X
	Activation mechanism (airflow, button)	4.2				X	X				
User behavior	Power/heat	4.3	X			X					X
	Puff topography and level of user experience	5.1				X	X	X			X

Adapted from DeVito and Krishnan-Sarin [7].



Figure 1. Left side of the lower lip showing angioedema.



Figure 2. The lip and the mouth showing gingival erythema and angioedema.

Discussion

The direct effects of allergic reactions to e-cigarette components are unclear. Some case reports showed that the allergic reaction was to the metal (mainly nickel) used to construct the e-cigarette. Previously, a case report of a 50-year-old man was presented with a history of 2-year intermittent hand and facial dermatitis without known allergy to nickel. Although the patient was using e-cigarettes for past 6 years, clinical examination showed erythematous scaly patches under the chin and nose. Another case report was also reported of a 38-year-old female care assistant, with a history of 3-year pruritic patches on the right hand palm. The patient denied any personal or familial history of atopy [4]. Angioedema could be caused as a result of a hereditary condition, chronic reaction, an acute reaction to the inhibitors of the ACE, or an acquired disorder due to abnormal complement response. Two patients reported increased swelling of tongue and lips after attending the Liverpool University Dental Hospital and were taking ACE inhibitor to treat the angioedema. Furthermore, IM chlorphenamine maleate injection was given to both patients [8]. A 2018 report showed that the use of ACE inhibitors had widespread results in all the EDs for angioedema. It was revealed that angioedema occurred more frequently in smokers, older

individuals, African Americans, women gender, older individuals, seasonal allergies, and those with a history of drug-induced rash and immunosuppressive therapy [9]. There have been no previous reports of an allergic reaction to e-cigarette liquid and only few reported cases regarding angioedema of the lip. There are no reported cases of angioedema from exposure to e-cigarette liquid, as in the presented case, where the cause of the allergic reaction with angioedema was the e-cigarette liquid, causing left lower lip angioedema with gingival erythema, and a history of a previous, similar, incident involving angioedema of the right lower lip. Although studies of components of e-cigarette liquid showed that it had some adverse effects, if applied directly, it has been reported that there could be allergic reactions to PG following repeated dermal applications, mostly irritation as a result of dermal reactions to PG [10-14]. On the other hand, glycerin (glycerol) is non-irritating, stable, and non-toxic, with antibacterial effects and hypoallergenic. Therefore, it is widely used in cosmetics, food, and medicine. Although allergic reactions related to glycerin are rare, it is used as an allergy negative control in scratch tests. Until 2016, only four case reports had been published regarding glycerin allergic reactions. In 2016, Suzuki et al. [15] reported a contact urticarial case. Furthermore, angioedema could be the result of these components as a reaction to allergens that might cause angioedema. Currently, there is limited evidence of allergic reaction and angioedema resulting together from PG and glycerol present in e-cigarette liquid as two major components. It is very important to inform consumers about potential allergens in products such as e-cigarettes. Every individual has a specific immune response to an allergen. Thus, each allergen must be labeled, if present in a product in a certain concentration, as determined by the appropriate regulatory bodies. The same is true for appropriate labeling and listing of the chemicals contained in e-cigarette liquid. Providing a precise ingredient list would facilitate discussion about the cause of allergy. Furthermore, except for nickel, glycerin, and PG, contamination or unproved sensitivity features of some other ingredients should be considered. Another critical point is the risk of developing angioedema, especially on the areas near to the airway like lips, tongue, and vocal cords which can lead to airway obstruction, adding to that the fact that the reaction might lead to bronchospasm and anaphylactic shock. So, observations should be carried out in enough time, and the management should be started as early as the diagnoses made to prevent complications which can lead up to hypoxia, shock, or even death from the asphyxiation due to laryngeal edema as it will be a life-threatening condition, if it involves the airway and if not managed in good time.

Conclusion

Although e-cigarettes are relatively new, the contents of the e-cigarette liquid are not clearly monitored, which could pose health risks. There is limited evidence about the allergic reactions like angioedema caused by exposure to e-cigarette liquid, as in the presented case. Further case reports and studies are needed to assess allergic reactions and other health effects due to the exposure

of e-cigarette liquid to humans. The main purpose of this case report was to raise public awareness regarding the harmful effects that could be caused by e-cigarettes use. Furthermore, provision of appropriate labeling is necessary in terms of the amount of ingredients present in each e-cigarette cartridge based on the standards and regulations established by the European Union.

List of Abbreviations

ACE	Angiotensin-converting enzyme
e-cigarettes	Electronic cigarettes
ED	Emergency department
IM	Intramuscular
PG	Propylene glycol

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this case report.

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Consent for publication

Informed consent was obtained from the patient.

Ethical approval

Ethical approval is not required at our institution for an anonymous case report.

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