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Case Study

Anaphylaxis in laboratory workers because of rodent handling: two case reports

Thatchai Kampitak[1] and Stephen D Betschel[1]

[1]Division of Clinical Immunology and Allergy, Department of Medicine, St. Michael's Hospital University of Toronto, Toronto, Ontario, Canada

Abstract: Introduction: Occupational allergy to rodents among laboratory animal workers is common. Most patients generally experience allergic symptoms after the first few years of work. Associated symptoms are usually mild, such as rhinoconjunctivits, urticaria, and asthma. Anaphylaxis, although rare, could be severe and life threatening. **Methods:** We have described in this study two cases of laboratory workers that developed skin and respiratory reactions following laboratory rat and mouse bites, consistent with anaphylaxis. **Results:** Skin testing was found positive for rat epithelium in the patient with anaphylaxis due to rat bite. Elevated levels of specific IgE antibodies against rat and mouse epitheliums were also detected in both the patients. **Conclusion:** These cases illustrate a severe hypersensitivity reaction that could potentially occur in occupational workers that are in close contact with rodents. Reduction of allergen exposure, regular screening, and job modification could be beneficial for affected individuals. Health care workers should be made aware that anaphylaxis could be a serious consequence of laboratory animal bites, particularly in those already sensitized.
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Introduction

Laboratory animal allergy remains an important occupational health problem for personnel whose work is in close contact with animals at their workplace. Rodents, in particular rats and mice, are the most common animals that cause allergic diseases. Some of reported symptoms of these allergies include rhinoconjunctivitis, urticaria, asthma, and anaphylaxis. Although only a few reports of anaphylaxis following laboratory mouse and rat bites have been described previously[1-5], such cases have not been published in any occupational medicine journals, which are more relevant for the target audience. In an attempt to raise awareness about the anaphylactic reactions after laboratory rat and mouse bites, we present here two cases of laboratory animal workers.

Patient 1

In 2010, a 48-year-old female laboratory worker was bitten on her right hand while handling a rat. Within 5 min, she developed a diffuse erythema followed by cough, chest tightness, and shortness of breath. Her symptoms were gradually reduced after several hours by administration of oral antihistamine and bronchodilator. However, epinephrine was not administered in this case. Her past medical history included asthma, overactive bladder, and migraine; requiring oxybutynin, sumatriptan, and salbutamol inhalation. Further, skin prick testing revealed a positive reaction for rat epithelium with a wheal diameter of 7 mm. Radioallergosorbent test (RAST) for specific IgE antibodies against rat epithelium was positive class 2 with a value of 0.99 KU/L. However, she continued to work with complete avoidance of direct exposure to laboratory rats.

Patient 2

In 2015, a 25-year-old female laboratory technician developed a systemic reaction, approximately 30 min, after being bitten on her finger by a laboratory mouse. The allergic reaction included facial erythema and swelling,

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Correspondence to: T. Kampitak, MD, Division of Clinical Immunology and Allergy, Department of Medicine, St. Michael's Hospital University of Toronto, 4th floor Cardinal Carter Wing 30 Bond Street, Toronto, Ontario M5B 1W8, Canada (e-mail: thatchai_k@yahoo.com)

cough, and chest tightness. However, her previous laboratory mouse bites had resulted in only self-remitting local reactions. During the same time, she was on oral contraceptives and antihistamine for allergic rhinitis. She initially took antihistamine with little benefits and later received additional antihistamine, corticosteroid, and bronchodilator at the emergency room. In this case, also no epinephrine was administered. Her symptoms eventually resolved within an hour after receiving the aforementioned treatments. RAST for specific IgE antibodies against mouse and rat epithelium were found positive class 4 with a value of 42.40 KU/L and positive class 3 with 10.50 KU/L, respectively. This patient was not skin tested because of the fact that she had severe systemic reaction from breach to cutaneous barrier. She later resumed laboratory animal handling; however, without any direct contact with laboratory mice and rats.

Discussion

Laboratory animal workers, such as scientists, technicians, physicians, and animal handlers are at an increasing risk of sensitization and allergy to animals in their workplace. Rodents, in particular rats and mice, are the most important laboratory animals that contribute to this problem because of their widespread use in experimental research. Rodent allergy in the workplace has been reported to affect 11%-44% of the exposed personnel[6]. Moreover, it is also considered to be a significant concern for general population in non-occupational settings[7].

Sensitization to laboratory animals generally occur in 15% of exposed personnel within the first 3 years of work; and approximately 10% may also experience allergic symptoms, such as rhinoconjunctivitis (80%), skin reactions including urticaria or pruritic maculopapular rashes (40%), asthma (20%-30%), and anaphylaxis[7-9]. Anaphylactic reactions in association with laboratory rodent bites have been previously reported in only 6 cases (3 due to rat bite and 3 due to mouse bite)[1-5].

Anaphylaxis is an acute, life threatening systemic reaction resulting due to various mechanisms and different clinical presentations and severities. Such patients developed allergic reactions rapidly with the involvement of skin and respiratory compromise following rat and mouse bites; and fulfilled the clinical criteria for the diagnosis of anaphylaxis[10]. A prompt recognition of the signs and symptoms of anaphylaxis is crucial, as a delay in treatment may result in significant morbidity and mortality. Fortunately, the allergic reactions observed in the patients in our case study were eventually resolved without the requirement for the administration of epinephrine, which would have been the drug of choice for anaphylaxis[10].

Some of the risk factors for the development of rodent allergy include the level of aeroallergen exposure, atopy, genetic susceptibility, working with male rodents, and most importantly, exposure to rodent allergens at the workplace[7-9]. Among the different laboratory animal workers, animal handlers pose the highest risk for sensitization and symptom development due to the higher levels of exposure to animal allergens[7]. Although, anaphylaxis due to rodent bites almost exclusively occurs in the occupational settings; however, surprisingly it has never been reported in any of the occupational medicine-related literature. This might reflect an under-recognized issue of anaphylaxis among health care workers, who themselves carry the highest risk of developing life threatening reactions following laboratory animal bites. We believe that raising the awareness about the potentially severe allergic reactions due to laboratory animal bites may lead to the development of beneficial protective measures as well as appropriate management strategies for laboratory workers who have rodent allergies.

The pathogenesis of laboratory animal allergy involves production of specific IgE against various airborne animal proteins, which can be detected using skin tests or in *in vitro* assays. In rodents, the different sources of allergen include dander, hair, saliva, urine, and serum. Among these, urine represents a major source of allergens in rats and mice. Most of the major mouse and rat allergens are produced in liver under the influence of androgenic hormones. Therefore, working with male rodents is an important risk factor for the development of laboratory animal allergies. The rat and mouse allergens share sequence homology and the IgE cross-reactivity between them has been demonstrated[7-9].

The dose-response relationship has been shown to be non-linear in nature; hence, the relationship between rodent allergen exposure, sensitization, and symptoms appears to be complex. Many studies have demonstrated that workers with highest exposure to rodents were found to have less symptoms or sensitization in comparison to the moderately exposed worker groups. High levels of rat-specific IgG4 antibodies and a high ratio of specific IgG4 to IgE antibodies were observed in the workers with highest allergen exposure; which has been associated with less sensitization and symptoms[7-9]. Although, the mechanism for inducing tolerance to rodent allergies remains unclear, it has been speculated that the intradermal route of exposure and prolonged high levels of allergens in the environment, due to the small particle size of rodent allergens, could be the possible factors involved in inducing tolerance[7].

The best intervention for laboratory animal allergies is the reduction of exposure to the animal allergens in the workplace in order to prevent sensitization and development of symptoms. This may be achieved by various strategies, including substitution, engineering controls, administrative controls, and use of personal protective equipments[11]. Substitution involves using less allergenic species or female animals as opposed to male animals and

utilization of in vitro techniques instead of animal experiments. Engineering controls include improvement in exhaust ventilation, such as the use of filter-top cages, high efficiency particulate air (HEPA) filtered room ventilation, increased room air exchange, and dust-free bedding[11]. The advent of new caging system of individually ventilated cages was found to significantly reduce the animal aeroallergen levels[12]. Administrative controls include modification of working practices, such as handling animals in ventilated cabinets, automated cage cleaning, and use of ventilated tables to minimize animal aeroallergen exposure[9]. Personal protective equipments, such as full-face-fitted mask respirators, eye protectors, gloves, clothing, and footwear; along with thorough hand washing and showering after work completion could also significantly decrease the amount of aeroallergen exposure[11]. However, the supportive evidence of the effects of these interventions on aeroallergen levels for reduction of laboratory animal allergies is limited[9].

Surveillance studies to determine the frequency/number of sensitized and symptomatic individuals provide an opportunity to raise awareness among the workers and emphasize the importance of laboratory animal allergies, which might be under-appreciated among the exposed personnel. Screening evaluations might be helpful in identifying the individuals that are at high risk for laboratory animal allergies. All workers should be trained on the correct use of personal protective equipments, proper animal handling and waste disposal, general hygiene, and changing routines for protective clothing for the effective reduction of allergen exposure[13]. Moreover, they should be educated about the recognition of the symptoms of laboratory animal allergies; and should know about the proper management of acute or severe reactions, such as asthmatic attacks or anaphylaxis.

The workers who are known to be sensitized should avoid repeated animal exposure and need to be periodically monitored for the development of symptoms using surveillance programs, such as questionnaires, skin testing, in vitro testing for specific IgE antibodies, pulmonary function test, and methacholine challenge test (if asthma is suspected). A comprehensive program consisting of education and training, various control measures, and medical surveillance for laboratory workers has been demonstrated to prevent the occurrence of laboratory animal allergies[11]. Pharmacologic treatment for symptomatic individuals is generally similar to the treatment of whom with non-occupational allergy. Further, policy changes that would ensure access to an epinephrine autoinjector could be considered in a workplace, where a worker has rodent hypersensitivity even if he/she has not experienced anaphylaxis previously; as their first presentation of anaphylaxis may be due to the first bite, as was the situation with the two cases presented formerly.

However, in some instances, avoidance may not be the only solution for those with severe allergic symptoms and job relocation or a change in the employment might be required. Although, successful treatment of asthma and rhinitis due to laboratory animal allergy using immunotherapy has been reported; however, its clinical value for anaphylaxis due to laboratory animal bites is still unclear[5,8].

In summary, anaphylaxis due to laboratory animal bites, in particular due to rodents, although infrequent but could be severe and life threatening. Health care workers should be made aware that anaphylaxis may be a potentially serious consequence of an animal bite at their workplace and should be prepared to treat it appropriately.

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References

1) Teasdale EL, Davies GE, Slovak A. Anaphylaxis after bites by rodents. Br J Med 1983; 286(6376): 1480.
2) Hesford JD, Platts-Mills TA, Edlich RF. Anaphylaxis after laboratory rat bite: an occupational hazard. J Emerg Med 1995; 13(6): 765-768.
3) Rankin TJ, Hill RJ, Overton D. Anaphylactic reaction after a laboratory rat bite. Am J Emerg Med 2007; 25(8): 985.e1-2.
4) Leng K, Wiedemeyer K, Hartmann M. Anaphylaxis after mouse bite. J Dtsch Dermatol Ges 2008; 6(9): 741-743.
5) Bunyawanich S, Donovan MA, Sherry JM, Diamond DV. Immunotherapy for mouse bite anaphylaxis and allergy. Ann Allergy Asthma Immunol 2013; 111(3): 223-224.
6) Sjostedt L, Willers S, Orbaek P. Laboratory animal allergy — a review. Indoor Environ 1995; 4(2): 67-79.
7) Jeal H, Jones M. Allergy to rodents: an update. Clin Exp Allergy 2010; 40(11): 1593-1601.
8) Bush RK, Wood RA, Eggleston PA. Laboratory aninal allergy. J Allergy Clin Immunol 1998; 102(1): 99-112.
9) Jones M. Laboratory animal allergy in the modern era. Curr Allergy Asthma Rep 2015; 15(12): 73.
10) Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis-a practice parameter update 2015. Ann Allergy Asthma Immunol 2015; 115(6): 341-384.
11) Bush RK, Stave GM. Laboratory animal allergy: an update. ILAR J 2003; 44(1): 28-51.
12) Feary J, Cullinan P. Laboratory animal allergy: a new world. Curr Opin Allergy Clin Immunol 2016; 16(2): 107-712.
13) Gordon S, Preece R. Prevention of laboratory animal allergy. Occup Med (Lond) 2003; 53(6): 371-377.