



Clinical Communications

ANAPHYLAXIS AFTER LABORATORY RAT BITE: AN OCCUPATIONAL HAZARD

Jessica D. Hesford, BA,* Thomas A. E. Platts-Mills, MD, PhD,† and Richard F. Edlich, MD, PhD*

Departments of *Plastic Surgery and †Internal Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
 Reprint Address: Richard F. Edlich, MD, PhD, Department of Plastic Surgery, University of Virginia School of Medicine, Box 332,
 Charlottesville, VA 22908

Abstract—Workers exposed to laboratory animals are at risk of developing asthma, rhinitis, angioedema, conjunctivitis, and urticaria. Approximately one in five scientists and technicians handling small animals will develop laboratory animal allergy symptoms within three years of employment, many of whom will have severe symptoms requiring a change of occupation. Individuals suffering from allergy to environmental allergens, such as pollen and ragweed, are more likely to develop allergic reactions to animals, and are more likely to develop asthma. We report a case of life-threatening anaphylaxis secondary to a rat bite in a laboratory research director with known allergies to rat urinary protein. While rodent bites are common in research settings, such severe reactions are extremely rare.

Keywords—anaphylaxis; animal bite; laboratory animal allergy; occupational disease; animal laboratory work

INTRODUCTION

Allergic symptoms caused by laboratory animal allergens, particularly those of rats and mice, pose an important occupational health hazard for scientists and animal husbandry personnel. Most surveys have described prevalence rates of laboratory animal allergy (LAA) of 11–30% (1–8). In the United Kingdom, asthma resulting from workplace exposure to animals has been designated “Occupational Asthma” by the government, thereby according it the status of a “prescribed disease,” that is, a compensable sickness (9). Despite an increased awareness and concern for occupational health in the U.S., there is no recog-

nizable policy dealing with the problem of laboratory animal allergy (10).

Reports addressing risk factors have demonstrated that atopic individuals, for example, those experiencing seasonal hayfever or other allergies, are more likely to develop symptoms, particularly asthma, than individuals with no history of atopy (3,5,7,8,11,12). These atopic individuals are also likely to develop symptoms sooner after beginning animal-related work than nonatopic individuals (12). A significant proportion of workers will experience symptoms within the first year of exposure, although onset of symptoms may be as late as 22 years after beginning employment (2,13). The constellation of clinical symptoms may include rhinitis, conjunctivitis, urticaria, angioedema, and asthma, and there is a wide variation in the severity of symptoms seen in individuals affected by this occupational disease. The most common symptom is rhinitis, while the most common severe symptom is asthma (2,3,12,13). Initial symptoms are mild and usually do not include asthma; however, continued occupational exposure to allergen increases the likelihood of developing asthma and enhances the severity of existing asthma symptoms (13,14). In other situations, for example, reactions to bee venom and food allergens, it has been reported that anaphylactic reactions are markedly more severe in patients with asthma (15,16). Our report presents the case of an asthmatic woman who experienced life-threatening anaphylaxis after receiving a bite from a laboratory rat.

CASE REPORT

A 35-year-old female research director at the University of Virginia School of Medicine sustained a rat bite while supervising a research experiment in her laboratory. The site of the bite was the palmar aspect of the distal phalanx of her left index finger. Approximately two minutes after the bite, she noted facial erythema and periorbital swelling, after which she had shortness of breath. While she was walking to the medical center, which was located approximately 200 yards from her laboratory, she experienced increasing difficulty breathing. Upon arrival in the emergency department 5 min after the bite, she was dyspneic and cyanotic and exhibited stridorous respirations. When she lost consciousness, she had no palpable pulse. Cardiopulmonary resuscitation was started immediately, and her airway was maintained by endotracheal intubation. Aqueous epinephrine 1 : 1000 (0.5 mg) was administered subcutaneously. Ten minutes later, she was given a rapid intravenous infusion of 100 mcg of epinephrine at a rate of 4 mcg/min. Hydrocortisone (100 mg) was then administered intravenously. Within 10 min, this regimen restored normal cardiorespiratory function as well as a normal level of consciousness, allowing her to be safely transferred to the intensive care unit.

Within 4 h, her condition allowed extubation. During the next 20 h, methylprednisolone and diphenhydramine were administered intravenously. Twenty-four hours after admission, she was discharged from the hospital with an epinephrine-containing emergency kit along with instructions for its use. She was referred to the allergy clinic for follow-up evaluation. The University of Virginia industrial hygienist was notified immediately of this work-related injury and was asked to examine her work site. Inspection of the work site identified an improper laboratory ventilation system that could not adequately protect or isolate the patient from exposure to the rat allergens. Because this air handling system does not meet the national consensus standards for laboratory ventilation (17,18), a new system is being designed for the laboratory. During this period, the patient was advised to avoid contact with rats.

As a young child, the patient had experienced rhinitis, conjunctivitis, and mild asthma after exposure to molds and house dust. When she joined the laboratory research program in 1982, it took less than 1 year before she experienced allergic reactions to laboratory animals. She noted increasing symptoms of rhinitis and conjunctivitis after exposure to rats that progressed to the development of bronchospasm. At that time, her respiratory symptoms were

present at work and at home. Her bronchospasm worsened, causing her to be evaluated and treated in the emergency department, after which she was referred to an allergist. Her immediate allergic symptoms responded to antihistamines, a tapering course of prednisone, and avoidance of direct contact with rats. Skin tests demonstrated strong and immediate reactions to a 1 : 10,000 weight-to-volume dilution of rat urine and to a 1 : 1000 dilution of guinea pig dander and horse dander. She also had a 2+ reaction to intradermal cat dander. Skin tests with house dust and dog dander were weakly positive. Skin tests to dust mites, cockroach, a range of fungi, grass pollen, and ragweed were negative. For the next 9 years, her allergic symptoms were reasonably well-controlled by a combination of cromolyn sodium (up to four 20 mg capsules per day), an albuterol inhaler, terfenadine, and pseudoephedrine hydrochloride as needed, although the patient experienced intermittent nighttime bronchospasm.

DISCUSSION

Anaphylaxis secondary to rodent bites is rare. Prior to this report, Teasdale and Davies (19) were the only investigators to document anaphylactic reactions to laboratory animals. In one instance, a nonatopic laboratory worker with an 8-year history of working with rodents was bitten on the hand by a mouse. Within 5 min, he felt a warm flush in his hand, which gradually spread to his arm and body during the next 10 min. Twenty minutes after the bite, his eye and nose began to run profusely, and he developed tightness of the chest. He was given chlorpheniramine intravenously and salbutamol by inhaler. The chest symptoms subsided within 10 min, and the other symptoms disappeared over the next few hours, during which time he complained of a headache. Six hours after the bite, his symptoms had completely subsided. Skin prick tests and serum IgE antibodies measured by standard radioallergosorbent test (RAST) were positive for mouse, rat, and guinea pig allergens. Another worker developed allergic symptoms 5 years after beginning his work with animals. Seventeen months after the onset of the allergic symptoms, he was bitten by a rat. Within a few minutes, he developed tightness of the chest, facial erythema, and eye and nose symptoms. As the acute respiratory distress persisted, he was admitted to a hospital. Within 4 h, his symptoms had subsided. Skin prick tests and radioallergosorbent tests revealed raised antibody concentrations to laboratory animal allergens as well as grass, house dust, and cat and dog dander.

As in the second case report, our patient was atopic. She had experienced allergic symptoms to laboratory animal allergens, rat urine in particular, for at least 9 years prior to her anaphylaxis. Rat urinary protein is known to be an important cause of occupational disease (11,20). The urinary protein molecules present on the hair, dander, and skin of the animal become airborne and remain so for many hours (1,21). For 9 years, the patient's symptoms had been partially controlled by limiting her exposure to rats and by using a combination of oral antihistamines, cromolyn sodium, and an albuterol inhaler. The patient protected herself from allergens using gloves, a respiratory filter device, and clothing barriers on the rare occasions when she was in the room where animal surgical procedures were being conducted. Despite these preventive measures, she noted increasing sensitivity to rats, as well as non-laboratory-associated allergens such as foodstuffs and cats. Because the air handling system in her building was inadequate, the patient was exposed to airborne allergen even when working in her offices located approximately four rooms down the hall from the surgery quarters. The occurrence and severity of atopic diseases are correlated with the amount of antigenic exposure, and constant exposure to antigen appeared to aggravate her bronchial hyperactivity.

Despite the rarity of anaphylaxis to laboratory animal bites, there is a high frequency of laboratory workers developing allergic reactions to laboratory animals. The likelihood of developing hypersensitivity is a function of at least three factors: the predisposition of the individual, the allergic potency of the agent, and the nature and intensity of exposure to the agent (3). One of the earliest surveys to identify laboratory animal allergy as an occupational disease was conducted by Lincoln and co-workers (1) in 1974. These investigators reported that of 238 employees with frequent exposure to laboratory animals, 11.3% developed allergic symptoms. Several subjects did not develop seasonal hay fever until they experienced symptoms related to their work with animals, and in some subjects, pollen allergy was made worse by exposure to laboratory animals, suggesting an occupational aggravation of a preexisting condition.

In a survey of some 400 employees of Loyola University of Chicago who had regular contact with laboratory animals, Gross (3) demonstrated a positive correlation between hypersensitivity to laboratory animals and previous allergy to common airborne allergens. Previous allergies were found to be much more common in subjects with LAA than in the general population: 58% as compared to 15%.

Fifty-one percent of those with LAA symptoms experienced asthma, and this investigation established that the use of cromolyn sodium enabled some subjects with asthma due to LAA to continue their employment. One capsule was inhaled before each exposure, and several subjects were able to continue working with tolerable or greatly diminished symptoms.

Employer practices with regard to the recognition, prevention, and treatment of LAA were investigated by Lutsky and co-workers (10). These investigators concluded that in most U.S. animal research facilities, there is no consistent or formal policy for addressing LAA. The survey revealed that, on average, 53% of affected employees were assigned to another job, while 31% were permitted to continue working despite the threat of developing LAA. These investigators argued against hiring individuals for animal-related work if they demonstrated positive skin tests and high specific IgE antibody levels to animal antigens and a positive history of chronic rhinitis and asthma. Such an approach is considered questionable due to the variation seen in the time required to develop symptoms (3), and due to the high prevalence of allergy in the community.

One advance in the study of LAA resulted from the findings of Newman-Taylor and co-workers (20), that a major allergen is found in the urine of rats and mice. It is assumed that patients become sensitized to the proteins following inhalation of airborne dust contaminated with urine. These findings facilitated the subsequent use of specific immunological tests to determine skin reactivity and serum antibody levels to relevant animal allergens. Cockcroft et al. (4) assessed the value of specific immunological tests in the diagnosis of LAA. These investigators used urinary protein extracts of five animal species as diagnostic reagents and correlated positive skin tests to symptoms of LAA. Atopic individuals were found to be no more likely than nonatopics to have animal-related symptoms but were more likely to have asthma.

Platts-Mills and co-workers confirmed that IgE antibody responses to rat urinary protein are an important cause of occupational disease (11). Two-thirds of symptomatic subjects demonstrated positive skin tests to rat urine. This study demonstrated an increased incidence of asthma among atopic individuals. A large proportion of rat-allergic individuals were not previously atopic, and most atopic subjects did not develop allergic symptoms, positive skin tests, or serum IgE antibodies when they worked with laboratory animals. Based on these findings, excluding atopic individuals from employment would be

an inefficient method of reducing the prevalence of asthma or rhinitis among employees.

CONCLUSIONS

The incidence of hypersensitivity symptoms among scientists and technicians handling laboratory animals is significant. In addition to the personal suffering these individuals endure, many may be required to seek new employment. Atopic individuals have been shown to develop symptoms sooner than non-atopics and are more likely to develop asthma. Skin prick tests and serum IgE antibodies to laboratory animal allergens are of questionable predictive value, and further studies are required.

Our report of anaphylaxis in a laboratory researcher secondary to a rat bite should make the emergency physician aware that serious and life-threatening complications such as anaphylaxis may follow rodent bites. Because of the high prevalence

of allergy in the community and the high prevalence of allergic reactions to animal proteins among laboratory workers, it is very difficult to propose screening criteria that are helpful. However, it seems clear that patients with asthma are at risk for increased severity of asthma and should be warned about the risks of working with laboratory animals. Institutions employing personnel for work with laboratory animals should identify atopic individuals by questionnaire. Regular screening would provide an indication as to the severity of the LAA problem within an organization and, in conjunction with occupational histories, would identify particular working areas or practices to be modified. More studies are needed to clearly define the extent of this public health problem.

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