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Immunotherapy for mouse bite anaphylaxis and allergy

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Hypersensitivity to laboratory animal allergens is an occupational hazard for individuals working in research settings. 11-44% of laboratory animal workers develop laboratory animal allergy.¹ With over 1.1 million laboratory animals² and up to 125,000 laboratory animal workers in the United States alone,³ a substantial population is at risk. The majority of individuals with laboratory animal allergy are sensitized to inhalant allergens, experiencing allergic rhinoconjunctivitis and asthma. Treatment for these individuals has focused on avoidance and use of protective gear.⁴ In some cases, however, hypersensitivity reactions may be severe,⁵⁻⁸ and avoidance may not be possible. Here we report a case of a laboratory worker with life-threatening anaphylaxis to mouse bite whom we treated with immunotherapy.

A 55 year-old man with a 22 year history as an animal caretaker was bitten by a laboratory mouse on his right anterior third digit. Ten minutes later, he felt itchy throughout his body and noticed a diffuse erythematous rash, starting on his arms bilaterally. Five minutes following this, his chest felt tight and his throat felt "clogged." His lips became swollen, and he felt dizzy. He was brought to urgent care, where he was pale on presentation with heart rate 85 bpm, BP 94/59, and oxygen saturation 95%. His exam was remarkable for distress, edematous lips, and urticaria. He received intramuscular diphenhydramine, intravenous steroids, ranitidine, and intravenous fluids; no epinephrine was given. His swelling improved within 2 hours, his chest discomfort resolved after 6 hours, and his rash resolved after 7 hours. He was discharged after 8 hours with an epinephrine autoinjector and completed a 5-day course of prednisone and diphenhydramine. He was subsequently referred to our allergy service.

The patient reported one occupational mouse bite 10 years prior that was uneventful. He had not experienced any other animal bites and denied any rodent sightings at home. Over the

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past 11 years, he had been changing cages for laboratory mice daily. He reported runny nose and sneezing at work over the past few years. He wore three layers of surgical masks and latex gloves at work and denied any environmental allergies, food allergy, asthma, atopic dermatitis, or insect bites reactions. His comorbidities included diabetes treated with metformin and psoriasis treated with clobetasol; he had no family history of atopy. As an immigrant of older age and with limited training, he was not able to find an alternative job and was financially dependent on this employment.

Skin testing six weeks after the acute reaction was positive for mouse epithelium (6mm wheal/16mm flare), rat epithelium (11mm/23mm), and cat pelt (8mm/13mm); it was negative for dust mite, dog dander, mold mix, and various tree, weed, and grass pollens. Laboratory results included elevated allergen specific IgE levels for mouse epithelium (6.17 kU/L) and mouse urinary protein (0.41 kU/L), tryptase 7.38 mcg/L, and WBC 8200/mcL with differential within normal limits. We counseled him extensively on avoidance, signs and symptoms of allergy and anaphylaxis, and epinephrine administration. We provided him with a worksite review, workspace modifications, Kevlar gloves and a fit-tested N95 respirator.

As changing employment was not possible, the patient elected for immunotherapy with mouse antigen. Subcutaneous immunotherapy was started at 0.05ml of 1:1000 solution and increased weekly over 28 weeks to reach a maintenance dose of 0.50ml of 1:1 solution. Thereafter, maintenance injections were transitioned to monthly. Stock solutions were made with *Mus musculus* allergenic extract from Greer (0.5 ml epithelium extract in 9.5 ml diluent containing 50% glycerin). The patient experienced occasional local reactions 20mm in diameter with initial injections but no other injection-associated reactions. 14 months after starting immunotherapy, he reported complete resolution of rhinitis symptoms when working with mice. He has not been bitten by a mouse again and continues on his third year of immunotherapy at maintenance doses. We anticipate 5 years of immunotherapy.

The majority of reported mouse allergy describes inhalant reactions, which is consistent with our experience (**Table I**). We found three existing case reports of mouse bite anaphylaxis;⁶⁻⁸ in these cases, the patient was advised to avoid mouse contact and immunotherapy was not attempted. We offered immunotherapy to our patient because alternative employment was not possible, and we sought to provide him with maximal protection given continued daily occupational risk of repeat mouse bite. Fortunately, the patient has not been bitten again. Although we cannot therefore definitely assess the degree of protection against mouse bite afforded by this immunotherapy, we know that his inhalant allergy symptoms resolved with immunotherapy. Our experience providing immunotherapy for workers with mouse allergy is that their allergic rhinitis and/or asthma symptoms improve (**Table I**).

Hypersensitivity reactions to mice have been attributed to three mouse allergens: Mus m 1, Mus m 2, and albumin.⁴ These are variably present in mouse hair, urine, dander, and serum.⁴ No mouse salivary antigens were available to us for testing or immunotherapy. Although immunotherapy with whole pelt allergens for inhalant allergies to laboratory animals has been described,⁹ it is not widely implemented, and we found no reports of immunotherapy for mouse bite anaphylaxis. A previous study examined the clinical and immunologic response of research workers with hayfever and asthma receiving immunotherapy with laboratory animal allergens, including five with mouse allergy.⁹ Hayfever and asthma symptoms improved, and treated patients had significantly higher levels of blocking antibody levels compared to those not treated.

Our patient demonstrated sensitization to rat epithelium in addition to mouse epithelium, despite no history of rat exposure. Cross-sensitization between mouse and rat antigens is possible given commonalities in lipocalin structures.¹ However, examination of immunotherapy responses in individuals allergic to multiple laboratory animals suggests that the blocking antibody response is allergen specific.⁹ Our patient declined rat and cat immunotherapy given no existing or planned contact with these animals.

Our report adds to literature on systemic allergic reaction to mouse bite and describes that immunotherapy in mouse allergic individuals can be well-tolerated and beneficial. Although the focus of clinical guidance for such patients should remain on exposure avoidance, our experience suggests that immunotherapy may be considered for those who cannot avoid continued exposure and remain at high risk.

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Table I

Effect of mouse immunotherapy on laboratory animal workers with mouse allergy.

Patient Age/Sex	Symptoms with mouse exposure	Skin Prick Test (mouse epithelium)	Specific IgE (kU/L)	Change in symptoms with immunotherapy*
55M	Allergic rhinitis Anaphylaxis	Positive	Epithelium: 6.17 Urinary protein: 0.41	AR: TNSS 15 → 1
24F	Allergic rhinitis Asthma	Positive	Not tested	AR: TNSS 13 → 3 Asthma: ACT 10 → 24
27F	Allergic rhinitis	Negative	Epithelium: 0.57 Urinary protein: 2.0	AR: TNSS 14 → 2
28M	Allergic rhinitis Asthma	Positive	Not tested	AR: TNSS 13 → 3 Asthma: ACT 8 → 24
32F	Allergic rhinitis	Positive	Not Tested	AR: TNSS 15 → 0

Abbreviations: ACT: Asthma control test; AR: Allergic rhinitis; TNSS: Total nasal symptom score

* Maintenance dose = 0.50ml of 1:1 solution, as described in text.