Response to immunotherapy in six related horses with urticaria secondary to atopy

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An 8-year-old Arabian stallion (horse 1) was referred to the Texas A&M University College of Veterinary Medicine Veterinary Teaching Hospital for treatment of recurrent urticaria of 5 years' duration. Drug- and food-induced urticaria had been ruled out prior to referral. The urticaria had initially been responsive to treatment with dexamethasone (0.5 mg/kg [0.23 mg/lb] of body weight, IM, q 24 h, tapered to a dose of 0.15 mg/kg [0.07 mg/lb], IM, q 48 h) and hydroxyzine (0.7 mg/kg [0.32 mg/lb], PO, q 12 h). Within the past few months, however, the urticaria could be controlled only by administering dexamethasone at a dosage of 0.25 mg/kg (0.11 mg/lb), IM, every 48 hours. The urticarial lesions had progressed to open wounds that oozed a serous material and crusted over.

The horse was not pruritic. Initially, lesions developed during the spring and fall, but in recent years, the urticaria was a year-round problem. On 4 occasions, serum had been submitted for detection of IgE directed against various allergens, using an ELISA. The first assay had been performed when the horse was 4 years old,^a^ the second was performed when the horse was 5 years old,^a^ and the last 2 were performed on the same day when the horse was 8 years old.^a^ Test results were inconsistent. The horse had been administered immunotherapy, with antigens selected on the basis of results of the first assay, but the response to immunotherapy had been poor.

During the week prior to referral, the horse had been treated topically with an antibacterial shampoo[^2] and a leave-on conditioner[^2] containing 2% chlorhexidine and parenterally with cefotiofur (3 mg/kg [1.36 mg/lb], IM, q 24 h). According to the owner, these medications had been effective in reducing the amount of crusting.

On physical examination, the horse had multifocal areas of alopecia and crusts on the dorsum, legs, and thorax. Skin under the crusts was dry and not ulcerated. Cytologic examination of the skin under the crusts revealed cocci bacteria with a few neutrophils. Ectoparasites were not seen in skin scrapings. Staphylococcus aureus and a coagulase-negative Staphylococcus spp were isolated by means of bacterial culture from underneath a crust; fungal culture did not yield any growth. Bacterial isolates were susceptible to numerous antibiotics, including cefotiofur.

**Intradermal testing (IDT)** was performed, as described.[^1] Briefly, test antigens were injected intradermally in a clipped area on the lateral aspect of the neck. Positive (histamine phosphate; 1:100,000 wt/vol) and negative (sterile saline [0.9% NaCl solution]) control samples were injected intradermally at the beginning and end of the test procedure. The histamine reaction was graded as +, and the saline solution reaction was graded as 0. Reactions for the test antigens were graded by comparing them to reactions for the histamine and saline solutions in regard to wheal diameter, turbidity of the wheal, and severity of erythema. For example, a reaction that had halved the wheal size and turbidity of the histamine control was considered a 2+ reaction.

Reactions were graded 15 minutes, 30 minutes, 4 to 6 hours, and 24 hours after injection of test antigens. Antigens that yielded reactions ≥ 2+ and that were considered important on the basis of the clinical history were primarily weeds (firebush, dock/sorrel, lamb’s quarter, pigweed mix, ragweed mix, Russian thistle, and western ragweed), a grass (alfalfa), a tree (Virginia live oak), cat epithelium, and some grain-related antigens (corn smut and grain mill dust). All of these antigens were included in a vaccine for immunotherapy. Additional antigens that were not included in the vaccine but thought to be important were some insects (horse fly, cockroach, mosquito, and black flies) and sheep wool epithelium. Because immunotherapy against biting insects is of questionable benefit in animals,[^2] a strict insecticidal protocol was recommended instead of adding these antigens to the vaccine. Exposure to sheep wool epithelium can easily be avoided by avoiding products or material that contain wool (eg, wool blankets). Results of IDT correlated poorly with results of serum ELISA performed previously.

Treatment included systemic administration of cefotiofur for an additional week and use of a sulfur salicylic antiseborrheic shampoo[^3] twice weekly to help remove excess scales and crusts. Because hydroxyzine was no longer effective, a different antihistamine, diphenhydramine (0.5 mg/kg [0.23 mg/lb], PO, q 12 h), was administered along with a fatty acid supplement[^3] (5 capsules, PO, q 12 h). The horse continued to develop urticaria within a few days after starting treatment with diphenhydramine, so the antihistamine was changed to chlorpheniramine maleate (0.5 mg/kg [0.23 mg/lb], PO, q 12 h), and treatment with the fatty acid supplement was continued.

Immunotherapy was instituted. This horse was given injections of a vaccine containing 200 protein nitrogen units (PNU)/ml on days 1 (0.1 ml), 3 (0.2
A 3-year-old Arabian stallion (horse 2) was referred with a 1-year history of urticaria that developed in the spring and summer. Development of skin lesions could not be correlated with administration of any drug or food. The lesions were mild, and no treatment was given. The horse was not pruritic, and it was noted that other factors, including physical contact (eg, friction), may have been pressing against the horse’s skin. This suggested that other factors, including physical contact (eg, friction) or an immediate reactivity to cotton, may have been involved in the development of urticaria in this horse.3–8

A 3.5-year-old Arabian stallion (horse 3) was referred with the complaint of recurrent urticaria for the past 6 months that was responsive to treatment with dexamethasone and hydroxyzine at dosages similar to those initially used for treatment of horse 1. The horse would develop lesions on its face and flank but was not pruritic. No association was detected between development of skin lesions and administration of any drug or food. Because clinical signs in this horse’s sire (horse 1) and half brother (horse 2) were well-controlled with immunotherapy, the owners of horse 3 requested IDT. Antigens to which the horse reacted included numerous weeds (cocklebur, dock/sorrel, dog fennel, firebush, lamb’s quarter, pigweed, ragweed mix, western ragweed, rough marsh elder, Russian thistle, and sage), several trees (mesquite, pecan, pine, red cedar, and black willow), 3 grasses (alfalfa, timothy grass, and perineal rye grass), molds (corn smut and grass smut), several insects (blackfly, cockroach, horsely, mosquito, black ant, and moth), and grain mill dust. Immunotherapy was instituted, using a vaccine containing antigens selected on the basis of results of IDT, and horse 2 had reportedly not had any problems with urticaria since then.

A 2-year-old Arabian mare (horse 4) that was related to horse 1 was admitted with the complaint of recurrent urticaria for the past 4 months. According to the owner, this horse was only seen scratching once. Development of skin lesions was not known to be associated with administration of any particular drug or food item. Hydroxyzine (0.7 mg/kg [0.32 mg/lb], PO, q 12 h) was used to treat the urticaria with success. Because this horse was related to horse 1, the owner requested IDT.

On physical examination, the horse had hives ≤ 3 cm in diameter distributed diffusely over the body, except the lateral aspect of the neck. Antigens to which the horse reacted included numerous weeds (cocklebur, dock/sorrel, dog fennel, firebush, lamb’s quarter, pigweed, ragweed, rough marsh elder, Russian thistle, sage, and western ragweed), several trees (eastern oak, mesquite, pecan, and red cedar), a grass (alfalfa), food-related antigens (corn smut and oat smut), and several insects (blackfly, moth, and black ant).

Immunotherapy was instituted, and treatment with hydroxyzine was continued at the same dosage for the first month of immunotherapy. The horse has been receiving immunotherapy for 2 years and has not had any recurrences of urticaria.

A 4-year-old Arabian mare (horse 5) was admitted with the complaint of recurrent urticaria that was responsive to treatment with hydroxyzine and dexamethasone at the dosages used in horse 1. Hives would develop primarily on the neck, but at times they would develop all over the body. The problem had started about 1 month previously. Development of urticaria did not appear to be associated with any drug administration or diet change. Because the sire (horse 1) of this horse and several of horse 1’s offspring had urticaria, horse 5 was admitted for IDT.

On physical examination, the horse had urticaria primarily on the lateral aspect of the right side of the neck, some hives on the trunk, and several hives on the front of the hind limbs. These lesions did not appear to be pruritic, but digital palpation of the lesions did seem to cause some signs of discomfort. Antigens to which the horse reacted included several weeds (dock/sorrel, English plantain, lamb’s quarter, rough marsh elder, sage, and western ragweed), some trees (mesquite and pecan), a grass (Bermuda), a few food-related antigens (corn smut and oat smut), and an insect (black fly). Immunotherapy was instituted, and the horse was treated with hydroxyzine (0.7 mg/kg [0.32 mg/lb], PO, q 12 h) for the first month of immunotherapy. The horse had not had a recurrence of urticaria during the 2 years after immunotherapy was started.

A 3-year-old Arabian stallion (horse 6) that was related to horse 1 was admitted with the complaint of recurrent urticaria for the past 4 months. The urticaria was responsive to treatment with dexamethasone. The horse was not pruritic, and the urticaria was not associated with any drug administration or diet change. The owner had given the horse dexamethasone (0.15 mg/kg [0.07 mg/lb], PO) the morning of the office visit.

On physical examination, the horse did not have any dermatologic lesions. However, the horse was restrained in stocks during IDT, and an urticarial reaction in the shape of a line developed in the area where a rope had been pressing against the horse’s skin. This suggested that other factors, including physical contact (eg, friction) or an immediate reactivity to cotton, may have been involved in the development of urticaria in this horse.9

Intradermal testing was performed 2 days after dexamethasone had been administered. Antigens to which horse 6 reacted included multiple grasses...
Urticaria has been associated with various under-lying causes in horses. The most common cause of urticaria in horses is thought to be drug reactions. Other possible causes include allergies (eg, insect hypersensitivity, atopy, food allergy, and contact allergy) and physical factors (eg, heat, cold, exercise, and friction). History of the horses described in the present report ruled out the possibility that urticaria was a result of drug reactions or food allergies. Because urticaria was seasonal in most of these horses and because insect hypersensitivity is usually associated with papular reactions, it seemed likely that urticaria in these horses was a result of a type-I hypersensitivity reaction in response to inhaled allergens. Results of IDT, in conjunction with the history and response to immunotherapy, suggest that this was the case.

All 6 horses described in the present report were related, suggesting that atopy in these horses was inherit-
ted. Horse 1 was the sire of the other 5, and horses 2 through 6 were related to each other only through horse 1. Because 3 of the offspring were male and 2 were female, the condition was likely not sex-linked. Because 5 of the horses shared a common sire, it is possible that the trait is dominant; however, the mode of inheritance cannot be determined from this small group of horses.

Results of ELISA performed on serum from horse 1 prior to referral were confusing. These assays are designed to measure or estimate the amount of allergen-specific antibody (IgE) in a patient’s serum. No published validation results for the commercially avail-
able ELISA tests for equine allergies exist. Others have reported problems with accuracy and repeatability of these tests. This situation was true in our horse. Results of the first and second assays performed on this horse were contradictory, possibly because the horse had been receiving an immunotherapy vaccine for 9 months before the second assay was performed. On the other hand, results for the third and fourth assays, which were performed on samples collected on the same day and submitted to 2 laboratories, were also contradictory and were different from the results of IDT, suggesting that these assays may themselves be inaccurate. It is possible that results of the ELISA differed from results of IDT because IDT measures reactions of the target organ (skin) to various allergens over time, whereas the ELISA measures reactions of a different target organ (blood) to allergens at a single time (the day of sample collection). However, the response to immunotherapy in this horse was poor when a vaccine containing antigens selected on the basis of results of an ELISA was used but good when a vaccine containing antigens selected on the basis of results of IDT was used.

References