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Allergic skin disease in a captive Diana monkey (*Cercopithecus diana*): testing, treatment, and training

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ABSTRACT: A 19-year-old female entire Diana monkey (*Cercopithecus diana*) has presented with seasonal scratching and associated alopecia for a duration of 12 years with limited response to oral treatments. Atopic dermatitis was suspected. Intradermal allergy testing and the formulation of allergy-specific immunotherapy is often used in companion animal veterinary practice, however documentation of its use in zoo species and non-human primates is less available. This case report demonstrates the application of allergy testing and immunotherapy in a captive Diana monkey and how the involvement of the veterinary nurse and operant conditioning and positive reinforcement training helped to facilitate this treatment.

Keywords: allergy; allergy testing; atopic dermatitis; Diana monkey; zoo

Introduction

Dermatologic conditions constitute a large proportion of cases in small animal general practice, including in exotic species (Hill et al., 2006), however, dermatological cases are less frequently documented in non-human primates and there is a lack of evidence-based treatment options available for treatment in these species (Bernstein & Didier, 2009). Typically, alopecia in captive primates is assumed to be caused by poor psychological well-being or stressors in their environment, however, there may be a variety of behavioural, environmental and medical causes attributing to these conditions (Bellanca et al., 2014; Luchins et al., 2011). Atopic dermatitis is an allergic, inflammatory skin disease in which the patient reacts and becomes hypersensitive to environmental allergens (Gage et al., 2005; Zur et al., 2002). Scratching, self-trauma and resulting alopecia associated with atopic dermatitis may class as a health problem in primates because their coat functions as a barrier between the animal and the environment and has a role in thermoregulation. Scratching, if interrupting daily functional behaviours and causing secondary bacterial infections, may affect welfare (Luchins et al., 2011; Ovadia et al., 2005; Steinmetz et al., 2005). Even when plans for investigation and treatment are fully understood, the veterinary examination and treatment of zoo housed species can still be challenging, but the implementation of training can help facilitate these processes (Crowell-Davis, 2008).

Case study

Presentation

Mkia, a 19-year-old female entire Diana monkey (*Cercopithecus diana*), has presented with seasonal scratching and associated alopecia, in months February through to September since 2008. Between 2008 to 2013 Mkia had a few enclosure changes but since 2013 has been housed in an enclosure at the Zoological Society London (ZSL), London Zoo, constituting an indoor off show area, and indoor on show area both measuring approximately 47 m^2 in total and an outdoor on show area measuring approximately 57 m^2. The severity of the scratching and self-trauma varied over

the years, ranging from hair thinning and patchy alopecia to severe alopecia and excoriations. Informal observational data indicates that Mkia scratches between 30 to 39 times within an hour which is not too dissimilar to her male companion, however, when comparing 'long' scratching episodes defined as a scratching episode longer than eight seconds duration, Mkia performs nearly four times the amount of these episodes than her male companion, indicating, in association with the damage caused to herself in some years, a potential welfare concern.

Work up, diagnosis and treatment

Initial examinations of Mkia started in March 2008 with visual observations of her scratching. Between this time and 2019 scratching and alopecia reoccurred at varying intensities over the bilateral flanks, inner arms and thighs but never fully resolved until outside of the worst pollen seasons (Figure 1). Treatment to try to relieve the presumed pruritus and treat associated dermatitis are listed in Table 1, but minimal results were observed. During the period between 2008 and 2019 Mkia underwent two general anaesthetics (GA) for skin investigations which included close examination, skin scrapes, swabs of active skin lesions for bacteriology, and biopsies. Biopsy results showed superficial perivascular eosinophilic dermatitis with oedema, epidermal hyperplasia and hyperkeratosis but with no clear aetiology; differentials included ectoparasites and allergies. A prick test by a human allergist under GA in 2010 showed mild reaction to Bethulacea from the Birch tree family only. Bloods show no sign of diabetes or thyroid disease.

In 2019, a more thorough diagnostic work up was planned in collaboration with the Royal Veterinary College (RVC) dermatology team. As per recommendations from the dermatologists, all current treatments (Fexofenadine hydrochloride (Fexofenadine hydrochloride, Zentiva) at 4 mg/kg PO q 24 hours and oclacitinib (Apoquel, Zoetis) at 1 mg/kg PO q 24 hours) were discontinued 16 days prior to their visit. For the procedure, Mkia was trained into a squeeze cage and sedated with medetomidine (Sedastart, Animalcare UK) at 0.07 mg/kg and ketamine (Ketaset, Zoetis) at 5 mg/kg intramuscularly. She was transferred to the ZSL veterinary hospital where she was intubated with a 4 mm endotracheal tube and maintained on isofluorane (IsoFlo, Zoetis) and oxygen. Mkia was placed in right lateral recumbency, an intravenous catheter was placed, and Hartmann's fluids (Aqupharm, Animalcare) were administered throughout the procedure. Mkia was monitored closely throughout the anaesthetic with a Burtons Surgivet multi-parameter machine (Smiths Medical ASD, Inc. Minnesota, USA) measuring heart rate, indirect blood pressure,

Table 1. List of treatments and therapies to try to relieve the pruritus and treat associated dermatitis experienced by Mkia, Diana Monkey (*Cercopithecus diana*).

Drug	Dose	Administration route
Amoxicillin (Amoxypen LA, Intervet)	15 mg/kg	SC
Cephalexin (Ceporex, Schering-Plough)	50 mg/kg q 12 hours	PO
Cetirizine hydrochloride (Cetirizine, Almus)	1 mg/kg q 24 hours	PO
Chlorphenamine maleate (Pirirton, GSK)	0.2 mg/kg q 12 hours	PO
Cyclosporine (Sandimmun Neoral, Novartis)	5-7.5 mg/kg q 24 hours	PO
Dexamethasone (Dexamethasone, Almus)	0.1-0.2 mg/kg q 24 hours	PO
Fexofenadine hydrochloride (Fexofenadine hydrochloride, Zentiva)	4 mg/kg q 24 hours	PO
Ivomec (Ivermectin, Merial)	200 mg/kg	SC
Methylprednisolone Acetate (Depo-Medrone, Pfizer)	4 mg/kg	IM
Oclacitinib (Apoquel, Zoetis)	1 mg/kg q 24 hours	PO
Omega 3 and 6 (Yumega Itchy dog, Lintbells)	0.37 mg/kg q 24 hours	PO
Omega 3 and 6 essential fatty acid supplement (Coatex, VetpPlus)	1.2 ml/kg q 24 hours	PO
Omega 3 and 6 essential fatty acid supplement (Efavet, Intervet)	100 mg/kg q 24 hours	PO
Prednisolone (Prednisolone, Millpledge)	0.5-1 mg/kg	PO
Selamectin (Stronghold, Zoetis)	6 mg/kg	Topical

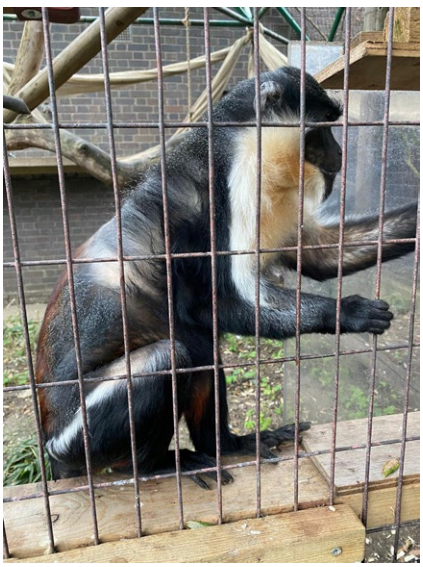

Figure 1. Typical presentation of alopecia on bilateral flanks, inner arms and inner thighs on Mkia the Diana monkey (*Cercopithecus diana*).

Figure 2. Anaesthetic set up for intradermal testing on Mkia the Diana monkey (*Cercopithecus diana*).

Table 2. List of allergens used for Mkia the Diana Monkey's (*Cercopithecus diana*) intradermal testing.

Number	Allergen
1	Histamine – positive control
2	Negative control
3	Flea*
4	*Acarus siro*/Meal mite
5	*Dermatophagoides farina*/Farina mite
6	*Dermatophagoides pteronyssius*/House dust mite
7	*Euroglyphus maynai*
8	*Lepidoglyphus destructor*/Hay mite
9	*Typophagus putrescentia*/Copra mite*
10	*Felis domesticus*/Cat epithelium*
11	*Anas anser*/ Goose feathers*
12	*Pullus gallinaceus*/Chicken feathers
13	Epithelial mix 1 – guinea pig, dog, cat, hamster, rabbit*
14	Grass pollen mixture – Bermuda, Orchard, Sweet Vemal, Timothy, Velvet grasses*
15	*Agrostis gigantean*/Creeping bent/redtop grass
16	*Anthoxanthum odoratum*/Sweet vernal grass
17	*Cynodon dactylon*/Bermuda grass
18	*Dactylis glomerata*/Orchard grass, cocksfoot
19	*Festuca poapratensis*/Meadow grass*
20	*Holcus lantus*/Velvet grass
21	*Lolium perenne*/Rye grass, perennial
22	*Phleum pratense*/Timothy grass
23	*Poa pratensis*/Blue grass, Kentucky*
24	*Avena sativa*/Oat*
25	*Ambrosia elatior*/ Common ragweed
26	*Artemesia vulgaris*/Common mugwort
27	*Chenopodium album*/Lambs quarter
28	*Leucanthemeum vulgare*/Daisy*
29	*Plantage lanceolata*/English plantain*
30	*Rumex acetosella*/Rad or sheep sorrel*
31	*Solidago virgaurea*/Goldenrod*
32	*Triticum aestivum*/Wheat
33	Tree pollen mix 1 – birch, alder, hazel*
34	Tree pollen mix 2 -English Oak, European beech, American Elm
35	*Aesculus hippocastanum*/Buckeye, horse chestnut
36	*Zea mays*/Corn
37	*Parietaria officianalis**
38	*Secale cereal*/Rye*
39	*Brassica napus*/Rape*
40	*Platanus occidentalis*/Eastern sycamore*
41	*Sambacus nigra*/European elder
42	*Tilia cordata*/Linden*
43	Weed pollen mixture - common mugwort, dendelion, stinging nettle, English plantain*
44	Fungus mixture 1*
45	*Malassezia**
46	*Aedes communis*/mosquito
47	*Culex*/mosquito*
48	*Musca domestica*/House fly*
49	*Tabanus*/Horse fly
50	*Culicoides spp*

oxygen saturation and end tidal carbon dioxide (Figure 2). Rectal temperature was measured using a handheld digital thermometer (Kruuse, Langeskov, Denmark) and manual heart rates and respiration rates were measured with a stethoscope (Littman, Minnesota, USA). Blood was drawn from the femoral vein for a complete blood count, a chemistry panel, vitamin D, hormones (oestrogen and progesterone), free T4 and fructosamine. Blood analysis results received the day after the testing were considered within normal limits, with the exception of a mild eosinophilia which was consistent with allergies but not pathological. Abnormal physical findings were limited to a fractured maxillary incisor which was removed, a thin body condition along the dorsal spine, but with good muscle mass and a stiff hind end but with no palpable abnormalities or crepitus; x-rays reveal some spondylosis (early bridging) of the lumbar spine.

To perform the intradermal allergy testing RVC dermatologists clipped an area approximately 10 cm × 8 cm with small portable clippers (Aesculap exacta, Braun, Buchbach, Germany), taking care not to traumatise the skin. No other preparation of the skin was performed. A black indelible marker was used to mark a spot for each of the 50 allergens to be used as part of the intradermal testing (allergens are listed in Table 2). Each site was injected with 0.05 ml of the designated allergen into the superficial dermis with a 31 G 0.5 ml insulin syringe and needle (BD, Plymouth, UK) (Figure 3). A histamine and saline control were also included as sites. During the procedure wheals were evaluated by digital palpation, visualisation and measurement at 15- and 30- minutes post administration (Figure 4) but at the follow up 24 and 48 hour checks only examination through visual exams and photographs were possible. The response to the injected allergen was measured by the degree of erythema, swelling, firmness and diameter. Dermatological testing included hair pluck for assessment of hair growth cycle and dermatophyte test medium culture, hair and scale fluorescence microscopy, acetate tape strip examinations, impression cytology and coat brushing. Results indicated that Mkia responded to many allergens, which are highlighted with an asterisk in Table 2. Immunotherapy using Artuvetrin® (Artuvetrin®, Artuvet Animal Health) was the recommended treatment option; a custom-made formula was made for her based on her results. Until the immunotherapy arrived primate keepers and veterinary nurse began a training programme to facilitate the forthcoming injections.

Training

Mkia's training involves utilising shaping and positive reinforcement to cue a target behaviour in which Mkia holds onto a target with her hands with increasing duration of time (Figure 5). In conjunction with this, desensitisation to a physical touch, with either the trainers finger or a capped needle on a syringe, in an area in which the injection would be administered is gradually built up and desensitisation to the presence of a needle and syringe is also worked on. Positive reinforcement involves an animal experiencing a pleasant consequence for exhibiting a positive, cued for behaviour. Shaping occurs as behaviours asked for are progressively increased until a desired behaviour is achieved. Desensitisation involves gradually exposing an animal to a negative stimulus over time in order to reduce the negative association to the stimulus (Crowell-Davis, 2008).

Immunotherapy injections were initiated in October 2019 and the first two injections successfully followed the prescribed treatment plan. However, it soon became evident that the increasing volumes recommended were going to be difficult to administer through trained behaviour and hand injection. Mkia's treatment plan was discussed with RVC dermatologists and changed to give smaller volumes but more frequent doses. Between October 2019 and September 2020, up to the time of writing, Mkia has tolerated and participated in 90% of 18 injection attempts, of which 94% have been successful in delivering partial to full doses of the immunotherapy. Mkia still presented with scratching and alopecia on the onset of the pollen season of 2020, however no self-inflicted skin lesions occurred and thus her atopic presentation has been less severe than previous years. This may represent a partial response to the immunotherapy or may be coincidental alongside a milder pollen season and the help of her long term ongoing therapies of Oclacitinib (Apoquel, Zoetis) at 1 mg/kg PO q 24 hours and Fexofenadine hydrochloride (Fexofenadine hydrochloride, Zentiva) at 4 mg/kg PO q 24 hours.

Figure 3. Preparation of 50 allergens for allergy testing in Mkia the Diana monkey (*Cercopithecus diana*).

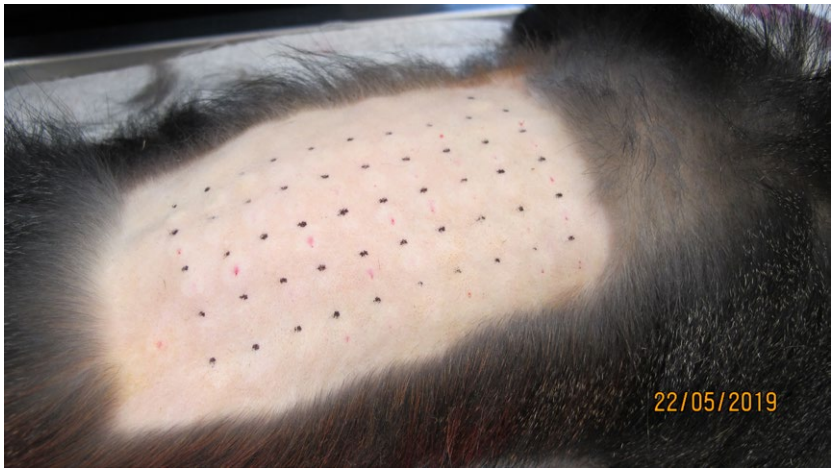

Figure 4. Wheals evaluated by digital palpation, visualisation and measurement following administration of allergens in Mkia the Diana monkey (*Cercopithecus diana*).

Figure 5. Training session with Mkia the Diana monkey (*Cercopithecus diana*) in which Mkia is rewarded for holding onto a target for increasing durations of time and densensitised to the presence of a hand near her right thigh.

Discussion

Many of the animals at the Zoological Society London participate in training programmes which involve using positive forms of operant conditioning in order to facilitate veterinary examination and treatment. Mkia's case entails more frequent and invasive treatment than many other cases, and regular quality of life (QOL) reviews are completed to ensure Mkia's behaviour and welfare are not compromised with regular injections. These QOL reviews also monitor the impact the immunotherapy is having on Mkia's clinical signs. At the time of writing Mkia's clinical signs were improving in association with coming out of the worst allergy season; immunotherapy will continue with the view to review its success in the spring of 2021.

Immunotherapy involves the repeated exposure to doses of allergens to build up an immunological tolerance (Artuvetrin®, n.d.; Warren, 2012). Intradermal skin testing and immunotherapy have been used in many veterinary companion atopic dermatitis cases and immunotherapy results in clinical improvement in 50–80% of those treated (Gage et al., 2005; Warren, 2012; Zur et al., 2002). Atopic dermatitis cases are documented much less frequently in primates and other zoo species (Gage et al., 2005; Johnson-Delaney & Needleman, 2007; Newton et al., 2013), and, where this testing and treatment is described in primates, a conclusive outcome on its success is often lacking (Johnson-Delaney & Needleman, 2007).

It is uncertain whether immunotherapy was the cause for a milder reaction to the pollen season in 2020, but ongoing immunotherapy until the next pollen season is considered a worthy goal given that oral medication options have been exhausted,

making Mkia's welfare and QOL a concern. Further studies and documentation of cases to explore the use and effectiveness of immunotherapy in non-human primates and other zoo housed species are warranted. This case study makes a start at documenting how immunotherapy can be implemented in attempts to improve health, welfare and the QOL of a captive Diana monkey.

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Disclosure statement

No potential conflicts of interest are reported by the author.

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