Disseminated Xanthomatosis in a Female Green Water Dragon, *Physignathus cocincinus*

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Abstract: An adult, reproductively active, female, green water dragon, *Physignathus cocincinus*, developed corneal opacities and neurologic signs as a result of xanthomatous changes in the corneas and brain. Similar pathology was noted in the ovaries.

Key Words: Water dragon, *Physignathus cocincinus*, xanthoma, xanthomatosis, eye, cornea, brain, ovary.

CASE REPORT

Beginning in the last quarter of 1998, a 4-yr-old, female, green water dragon, *Physignathus cocincinus*, became reproductively active and began exhibiting stereotypical escape behavior including digging and rubbing of the head and rostrum against the glass walls of the enclosure. At that time the lizard was kept singly in a glass-sided 122 x 46 x 46 cm enclosure with 1 plastic pan for water (10cm deep) and 1 for potting soil (10cm deep). A natural plant, *Dieffenbachia* sp., and wooden branches were used as cage accessories, and newspaper was placed on the bottom of the enclosure. The water was changed twice weekly (or when feces were noted), and the soil was changed monthly. Distilled water was misted into the enclosure daily, and the plant was watered weekly. Humidity ranged from 40-80% RH. A 36-watt full-spectrum fluorescent lamp (Vita-Lite, Duro-Test Corporation, Fairfield, NJ) and an incandescent bulb (various brands, 60-100 watt – changed seasonally to adjust for varying ambient temperature) were illuminated above the screen cover for 14hr daily. Daytime temperature ranged from 23-32°C (74-90°F) during the day with the entire enclosure dropping to 21°C (70°F) at night. The diet consisted of 2 thawed neonatal mice 3 times a week with live insect prey offered occasionally. Eleven fully shelled eggs were found in the potting soil in December 1998.

The lizard presented for anorexia in January 1999, several weeks after oviposition. The physical examination revealed no abnormalities other than mild, multifocal, pale yellow, nonreflective opacifications in the left cornea that did not take up fluorescein dye; it weighed 247g. A diagnosis of traumatic corneal degeneration was made, and neomycin-polymixin-bacitracin ophthalmic ointment (Neobacimyx, Shering-Plough, Kenilworth, NJ, USA) OU q24hr x 30d was prescribed to protect the corneas from continued trauma. The client refused diagnostics including fecal examination, coelomic ultrasound, whole body radiographs, complete blood cell count, and plasma biochemistry analysis. Recommended changes in husbandry included: 1) increasing the misting to twice daily; 2) daily tepid water soaking; and 3) application of brown paper 15cm high along the inside bottom of the enclosure walls to obscure the line of sight and reduce escape behavior.

In December 1999, the lizard re-presented for anorexia of 30d duration after oviposition of 10 more eggs. At that time, a mild right-sided head tilt was evident. Corneal opacification had progressed to include approximately 30% of the cornea in the left eye and was now present in the right. The left globe was smaller than the right (phthisical). Both corneas were negative for fluorescein dye uptake. It weighed 238g. The client again refused diagnostic testing and decided to hand-feed 1 neonatal mouse 3 times weekly for 30d.

The lizard presented in January, 2000 for enucleation of the left globe due to the possibility that the anorexia could be associated with ocular pain. Preoperative plasma biochemistry and CBC were refused. Two hours preoperatively, a 1:1 mixture of balanced electrolyte solution (Normosol-R, Abbott Laboratories, Abbott Park, IL, USA) with 5% dextrose (Abbott Laboratories, Abbott Park, IL, USA) 20ml/kg IL, and ceftazidime (Fortaz, Glaxo Wellcome, Research Triangle Park, NC, USA) 20mg/kg IM were administered. Anesthesia was induced with propofol (PropoFlo, 10mg/ml, Abbott Laboratories, Abbott Park, IL, USA) 10mg/kg IV in the ventral caudal vein. Isoflurane (IsoFlo, Abbott Laboratories, Abbott Park, IL, USA) 3.5-5% in oxygen 1.5L/min was administered with intermittent positive pressure ventilation to maintain anesthesia via endotracheal intubation with a 1.5mm ID Coles tube. Butorphanol tartrate (Torbugesic-SA, 2 mg/ml, Fort Dodge Laboratories, Fort Dodge, IA, USA) 0.5mg/kg IM was administered at the onset of anesthetic maintenance. Enucleation of the globe was performed using the transpalpebral method. The eyelid margins were apposed and sutured with polyglactin 910 (Vicryl, Ethicon, Incorporated, Somerville, NJ, UA) using a simple continuous suture pattern. The site was prepared for aseptic surgery, and incisions were made 1mm from the eyelid margins connecting just beyond the canthi and encircling the palpebral fissure. A combination of sharp and blunt dissection were used on the musculature and supporting structures of the globe in a circumferential pattern until the optic nerve was identified. Curved mosquito forceps were applied at the optic vessel-nerve bundle and curved iris scissors were used to cut it against the scleral surface. The nerves and vessels were ligated in one stump with polyglactin 910, and absorbable gelatin sponge sections (Gelfoam, Pharmacia and Upjohn Company, Kalamazoo, MI, USA) were packed into the orbit to control seeping hemorrhage. Skin was closed with polyglactin 910 in a simple continuous pattern. Postoperative instructions included force-feeding 1 neonatal mouse every other day, daily tepid water soaking (beginning 5d postoperatively), and ceftazidime 20mg/kg IM q72hr x 14d.

On histopathologic examination the eye contained a cholesterol granuloma comprised of cholesterol clefts surrounded by macrophages and multinucleate giant cells. The cornea had numerous cholesterol clefts and infiltrates of moderate numbers of histiocytes and fewer mononuclear cells. The diagnosis was severe xanthomatous iridocyclitis and keratitis.

Although the surgical site healed well, the CNS disease signs progressed to severe right-sided head tilt and circling to the right. In light of the histopathologic findings and progressive clinical signs, the client elected euthanasia in March, 2000. Blood was collected from the ventral caudal vein after administration of high dose tiletamine hydrochloride–zolazepam hydrochloride (Telazol, 100mg/ml, Fort Dodge Laboratories, Fort Dodge, IA, USA) 30mg/kg IM. Findings from a complete blood cell count and plasma biochemical profile were within normal limits except for a monocytosis (5,600 cells/µl; reference range 0-500 cells/µl). Of note, although no reference ranges are available for *Physignathus* spp. for cholesterol or triglycerides, the values were 11.28mmol/L (436.3mg/dl) and 1.52 mmol/L (134.3mg/dl) respectively. Once the lizard was deeply anesthetized, euthanasia was completed with KCl (2mEq/ml) 10ml/kg IV in the ventral caudal vein. Abnormal gross necropsy findings included opacification of the right cornea, multifocal, small (2-3mm), tan plaques on the serosal surfaces of most of the intracoelomic organs, and a gray-brown center of the coagulum in the enucleated (left) orbit. Selected tissues were fixed in 10% formalin and submitted for histopathology. Heart, lung, adipose, trachea, esophagus, greater vessels, intestine, kidney, spleen,

pancreas, stomach, skin, and skeletal muscle were histologically within normal limits. The remaining eye had severe xanthomatous change and mineralization in the cornea. The brain had numerous xanthomas within the lateral and third ventricles extending into the neuropile of the cerebrum in one section. In the ovary, numerous xanthomas replaced the follicles with only a few remaining follicles within normal limits. The interrenal cells of the adrenal gland were hypertrophied. Diffusely, hepatocytes contain small lipid vacuoles, and the enucleated orbit was replaced by fibrous connective tissue and granulomatous inflammation.

The final diagnoses were disseminated xanthomatosis of the ovary, cornea, and brain; interrenal cell hypertrophy (adrenal); fibrosis and granuloma formation of the enucleated orbit; and hepatic lipidosis. Xanthomas in the ventricles and cerebrum of this water dragon were responsible for the progressive neurologic signs. The corneal lesions (i.e., mineralization and xanthomatous change) were consistent with chronic degenerative keratopathy, possibly secondary to trauma induced during escape behavior. Ovarian changes were consistent with follicular resorption with concurrent hypercholesterolemia. Interrenal cell hypertrophy is a stress response, possibly due to postoperative stressors. Hepatic lipidosis was due to a combination of anorexia and fat mobilization associated with reproductive activity.

Xanthomatosis has been reported in humans, dogs, cats, birds, frogs, geckoes, and lizards (Chastain and Graham 1978; Garner and others 1999; Grieshaber and others 1991; Latimer 1994; McNutt and others 1996; Russell and others 1990). In lizards, it is primarily a disease of reproductively active females, and is likely associated with a combination of high fat diet and resorption of ovarian follicles (Garner and others 1999). Clinical presentation varies from mild corneal opacification to severe central nervous system disease signs. Histologically, xanthomas are nodular tissue accumulations of lipid-laden macrophages and cholesterol clefts (McNutt and others 1996). Xanthomas (cholesteatomas) are frequently detected in the third and fourth ventricles of horses but are rare in other species. (Summers and others 1995). These lesions are usually innocuous, except when they occur in the lateral ventricle where they may cause hydrocephalus and brain atrophy associated with impaired flow of cerebrospinal fluid. In horses, the lesions are confined to the ventricle of the brain and are thought to be associated with previous episodes of meningeal or ependymal congestion and hemorrhage. Because cholesterol is a constituent of cell membranes, cholesterol clefts may be observed in foci of chronic hemorrhage due to catabolism of inflammatory, parenchymal, and erythroid cells in these lesions. The lesions in this lizard cannot be attributed solely to this sequence of events because there was no evidence of acute or chronic hemorrhage and the lesions were not confined to the ventricles. Xanthomatosis has also been reported in female geckos with hypercholesterolemia during follicular resorption (Garner and others 1999). Although the plasma cholesterol levels in this lizard were only mildly elevated over those reported for green iguanas, *Iguana iguana* (Stein 1996), they could have been higher during a previous period when being fed up to 6 neonatal mice per week. Neonatal mice contain high levels of fat and cholesterol and could have contributed to chronic hypercholesterolemia in this case. The severe, progressive clinical presentation of this water dragon emphasizes the importance of nutrition during folliculogenesis and follicular degeneration in female lizards.

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