The Use of Gabapentin to Treat Presumed Neuralgia in a Little Corella (*Cacatua sanguinea*)

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Introduction

Foot and toe mutilation is a common presentation of psittacine patients of all species. It is perhaps more frequently observed in cockatoos, although an "Amazon Foot Mutilation" syndrome has been reported. Affected patients present with clinical signs of intense irritation of the lower extremities – foot shaking, shifting lameness, feather damaging behaviour on the lower leg, and self-mutilation (up to, and including, chewing toes off).

Proposed causes for this behaviour have included: bacterial, mycobacterial or fungal infection of the skin, soft tissues or bone; contact dermatitis e.g. nicotine on the owner's hands; peripheral neuritis due to lead toxicosis, proventricular dilatation disease; malnutrition, especially vitamin deficiencies or excesses; or chronic renal disease.

In human medicine,pain that follows the path of a specific nerve is known as neuralgia. The causes of neuralgia are varied. Chemical irritation, inflammation, trauma (including surgery), compression of nerves by nearby structures (e.g. tumours), and infections may all lead to neuralgia. Diabetes mellitus is another common cause of neuralgia. Diabetes damages the arterial supply to the nerves, resulting in nerve fibre malfunction and sometimes nerve loss. In many cases, however, the cause is unknown. Syndromes associated with neuralgia in people include trigeminal neuralgia, glossopharyngeal neuralgia and post-herpetic neuralgia ('shingles'). Patients report a tingling or burning sensation in the affected area, with intermittent sharp, stabbing pain that can be severe. The symptoms are localised to the affected area.

This paper proposes that one cause of foot mutilation in birds is neuralgia and reports a suspected case.

Case Report

A 7 year old male little corella (*Cacatua sanguinea*) was presented with a history of chewing both legs and feet for approximately 4 weeks. The bird had been obtained from a pet store and was fed on a seed mix as well as various vegetables and legumes. It was housed indoors, with free access outside its cage when the owner was home. The referring veterinarian had administered the antihistamine, diphenhydramine hydrocholoride; the bird showed some initial improvement but the clinical signs resumed while the bird was still on the medication.

On physical examination the bird demonstrated aggressive behaviour and was observed chewing both legs and feet. The left leg was more severely affected; it was bare over the tibiotarsus and the patient was observed shaking the leg and clenching the toes frequently during the physical exam. The bird weighed 486 grams and was moderately obese. No other physical abnormalities were detected.

Blood was drawn for haematological, biochemical and lead analysis (Table 1). Haematology revealed a marked lymphopaenia and monocytosis, and a mild basophilia. Clinical biochemistry showed a mild increase in AST and increased blood cholesterol. Blood lead levels were below those expected to cause clinical signs.

Whole body radiographs showed no evidence of skeletal abnormalities.

A skin biopsy from the affected area was submitted. The epidermis had multifocal perivascular accumulations of lymphocytes, histiocytes, plasma cells and heterophils, accompanied by fibroplasia. Vascular changes, including vasoproliferation, endothelial hypertrophy, mural hypertrophic re-modelling, homogenisation and leucocytic infiltration, were noted. The epidermis had sub-epithelial vesiculation, erosion and ulceration, with a superficial accumulation of a heterophilic crust. The histological diagnosis was immune-mediated vasculitis, complicated by ischaemia and self-trauma.

Analgesia was provided by oral meloxicam 0.5mg/Kg BID (Metacam®, Boehringer Ingelheim). Immune suppression was attempted with oral cyclosporine 5mg/kg BID (Neoral®, Novartis-suspended in vegetable oil). Silver sulfadiazine (Silvazine®, Smith and Nephew) was applied topically to the wounds to encourage healing. The owners were directed to convert the bird to a formulated diet and were advised on behaviour modification.

The owners reported a reduction in leg and foot chewing, as well as an improvement in the bird's behaviour. The bird was maintained on cyclosporine; however, the owners reported a continuing increase in episodes of self-mutilation of the legs for a period of 2 years. The foot shaking was becoming more severe, and the wounds on the left leg were becoming more extensive. The bird was also beginning to chew at the right foot.

At this time it was decided to discount the diagnosis of immune-mediated vasculitis. Gabapentin 10mg/kg PO BID (gabapentin, compounded by a pharmacist as a 10 mg/ml palatable suspension) was administered as an experimental trial with the knowledge of the owners. The drug was administered by the owners twice daily, directly into the bird's mouth using a syringe. The drug was well-tolerated by the bird, and no adverse effects were reported by the owners. The bird showed complete cessation of self-mutilation with improved attitude and behaviour within a few days of starting treatment. Two weeks later the wounds showed marked healing and aloe vera was applied to prevent desiccation and irritation. Drug therapy was continued for approximately 3 months. No recurrence of the presenting clinical signs was noted and therapy was discontinued. Three days later the clinical signs recurred. Treatment was re-instituted and the bird remains clinically normal. No adverse effects from the drug have been noted at this time.

Discussion

Neuralgia is difficult to diagnose in human patients, and even more so in animals. There are no specific tests for neuralgia, and the diagnosis is usually one of exclusion. Nerve conduction studies with electromyography, examining the electrical activity of nerves, may confirm the diagnosis. The clinical signs displayed by this bird were consistent with neuralgia, but there is limited scope for a comprehensive diagnosis in private practice.

Treatment of neuralgia in people is aimed at reversing or controlling the cause of the nerve problem (if identified), as well as providing analgesia. The condition may improve spontaneously or disappear with time, although in many cases it increases in severity and frequency with age.

Non-steroidal anti-inflammatory drugs, such as meloxicam, may be helpful in mild cases. Opioid analgesics may be needed for a short time to control severe pain. However, these analgesics often have disappointing results. Other treatments may include nerve blocks or surgical ablation of the affected nerve using different methods, such as local radiofrequency, heat, balloon compression, and injection of chemicals.

Anti-seizure medications such as gabapentin or lamotrigine have been found to be helpful for pain associated with trigeminal neuralgia.[1] Antidepressant medications such as amitriptyline may also be useful in some cases. The topical application of creams containing capsaicin is also occasionally recommended.

Gabapentin is similar in structure to the neurotransmitter GABA, although it is not believed to act on the same brain receptors; it was initially synthesized to mimic the structure of GABA for the treatment of epilepsy. Its exact mechanism of action is unknown, but its therapeutic action on neuropathic pain is thought to involve voltage-gated N-type calcium ion channels.[2] In human medicine its popularity as an anti-seizure medication has waned in recent years, but is still widely used as a medication to relieve neuropathic pain. Gabapentin is well tolerated in most patients, has a relatively mild side-effect profile, and passes through the body without been metabolised.

There is little documentation of its use in veterinary medicine. It has been used in canine and feline patients for pain management, especially in patients showing signs of allodynia (sensation of pain resulting from a normally non-noxious stimulus) or hyperalgesia (exaggerated response to painful stimuli), and for refractory or complex partial seizures.[3,4,5] Adverse effects are uncommon, but caution should be taken when administering to patients with decreased renal function. In birds (and terrestrial reptiles) any drug that interferes with glutamate/glutamine metabolism potentially interferes with ammonia detoxification and uric acid synthesis, making regular assessment of changes in plasma uric acid, urea and ammonia concentrations advisable. Adverse effects in humans include ataxia, lethargy and diarrhoea. Concurrent use of hydrocodone or morphine may enhance its effects.[6] Gabapentin has also been associated with an increased rate of pancreatic adenocarcinoma in male rats.

Summary

Foot chewing and self-mutilation may be due to pathology of underlying tissues, including bone, skin, muscles, tendons and nerves. Nerve pain, also known as neuralgia, may develop as a result of a variety of conditions. The author proposes that it should be considered as a differential diagnosis for self-mutilation conditions, including foot chewing.

Gabapentin may be a useful drug for treating these conditions. Its apparent efficacy in this case, combined with the lack of adverse effects, suggests that more treatment trials should be conducted to validate its use in avian medicine.

	Result	Reference Intervals
Packed Cell Volume (%)	44	40-55
White Cell Count (x 10^9/L)	3.9	39255
Heterophils (%)	86	45-72
Lymphocytes (%)	0	20-50
Monocytes (%)	11	39113
Eosinophils (%)	1	39083
Basophils (%)	2	39082
Glucose (mmol/L)	13	12.2 – 21
Urea (mmol/L)	0.6	<1
Calcium (mmol/L)	2.4	2.0 – 3.0
AST (IU/L)	440	130-340
CK (IU/L)	106	155-420
Total protein (g/L)	32	26-38
Amylase (IU/L)	1609	<1,500
Bile acids (umol/L)	48	26-96
Uric acid (mmol/L)	0.1	0.2-0.6
Cholesterol (mmol/L)	8.3	4.5-5.8
Blood lead (umol/L)	<0.7	<0.7

Table 1. Haematology and biochemistry results

References

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