Exocrine Pancreatic Insufficiency in a Sulphur-Crested Cockatoo (*Cacatua galerita galerita*)

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INTRODUCTION

Disorders of the pancreas are common in mammals and are likely to occur in avian species with more frequency that has been previously reported. Diagnosis of pancreatic disease can be challenging in avian patients and determination of the primary aetiology can be even more difficult. Clinical signs associated with inflammation of pancreatic tissue are often vague and associated with the endocrine or exocrine components. Inflammation of the pancreas a result of infectious, neoplastic, dietary, traumatic and toxic insults may lead to a destructive cycle of pancreatic tissue loss, inflammation and eventual fibrosis. This paper reports the diagnosis and successful management of exocrine pancreatic insufficiency (EPI) in a sulphur-crested cockatoo (*Cacatua galerita galerita*) with supplemental pancreatic extract.

CASE REPORT

A 16 year old female sulphur-crested cockatoo was presented for weight loss and abnormal droppings. The bird was kept in an outdoor dirt-floored aviary with a short-billed corella (C *sanguine)*. Both birds were fed mainly small seed diet, occasionally some formulated diet, vegetables (carrot, corn, silverbeet, pumpkin, peas, and chilli) and fruit (apple, passionfruit, grapes, and cherries). An egg and biscuit mix was given in winter, with added cuttlefish and vitamins. The bird had never laid an egg.

The bird had been given a health examination almost two years prior, at that time weighing 1166g, with convex pectoral muscle mass; she was deemed obese. Diagnostic testing had been recommended at that time, but had been declined by the owner. A change in diet was recommended, from a predominantly seed diet to a formulated diet.

At this presentation, the cockatoo was in thin body condition, weighing 771g, with droppings consisting of normal urates and a voluminous, pale beige-coloured faecal component (Fig. 1). The bird was bright, alert and reactive with no evidence of weakness or lethargy. The owner reported normal activity levels, appetite and behaviour at home. Faecal and oropharyngeal cytology were normal. Haematology showed a marked heterophilia with normal heterophil morphology (see Table 1). On biochemical examination there was mild hyperglycaemia, hypercholesterolaemia, hyperproteinaemia, and a mild elevation in glutamate dehydrogenase (GLDH) (see Table 2). Long acting doxycycline was administered intramuscularly at 75mg/kg based on a suspicion of a bacterial hepatitis. On repeat examination one week later, the bird had gained weight to 808g and was reported to be brighter in

demeanour at home. Haematology at this time showed resolution of the heterophilia (see Table 3).

Figure 1: Droppings showing normal urates and voluminous, pale beige-coloured faecal component.

The bird's appetite remained normal and droppings continued to be voluminous, with large amounts of sand in the faecal portion. The intramuscular doxycycline injection was repeated. The following week, at re-examination, there was a 24g weight gain to 835g, with no change to the droppings. The owner removed the bird from the aviary in order to monitor its droppings and assess the significance of the sand present in the gastrointestinal tract. Further diagnostics, including radiography were recommended but continued to be declined by the owner at this stage. Concerns regarding malabsorptive intestinal or pancreatic disease were expressed to the owner, along with differential diagnoses including exocrine pancreatic insufficiency, infectious diseases such as mycobacteria, and processes such as neoplasia.

The following week, with no change in the bird's droppings and a weight loss to 820g, the owner consented to radiographs; these showed hepatomegaly, an accumulation of sand in the gizzard and loss of intestinal serosal detail. Exploratory laparotomy was declined and it was elected to pursue removal of the sand present within the gizzard. Lactulose was administered once PO as a cathartic, with no improvement in clinical signs. The bird's weight continued to decline to 771g. Once again, further diagnostics were advised and declined by the owner.

The owner was referred for a second opinion in the hope that consent to further testing to consolidate a diagnosis might be obtained.

On the second opinion examination the bird was vocal, alert and responsive. It was in moderately thin condition, with a bodyweight of 740g (normal 850-950g). Coelomic palpation and auscultation of heart and lungs were normal. The remainder of the physical examination was unremarkable. The faeces were formed but very large and pale brown in colour. Blood was collected for haematology and biochemistry evaluation (see Table 4). Haematology was essentially normal; aspartate transaminase (AST) was elevated while creatine kinase (CK) and bile acids remained normal,

suggesting hepatocellular rupture without significant loss of liver function. Uric acid was slightly elevated, as was total protein, suggesting mild dehydration.

With a tentative diagnosis of EPI and a hepatopathy of unknown origin, the owner agreed to further diagnostics. Left flank endoscopy confirmed the presence of a normally active ovary and normal appearing kidneys. The liver was enlarged and pale. A ventral midline coeliotomy was performed and the duodenal loop was exteriorised. There was no obvious pancreas visible; instead small remnants of what appeared to be fibrous tissue occupied the position normally filled by the pancreas. This was not biopsied due to the risk of haemorrhage. The liver was enlarged, pale and mottled. Several biopsies were collected and submitted for histopathology. The results indicated mild to moderate chronic-active cholangitis and hepatitis, although no aetiological or initiating cause could be determined.

Based on these findings a diagnosis of pancreatic atrophy and cholangiohepatitis was made.

Treatment was directed both replacing the loss of exocrine pancreatic function and supporting the liver while it recovered. The necessity for a stable, balanced diet was reinforced to the owner, resulting in a diet of 60% formulated food (Nutriblend®, Vetafarm), 35% mixed vegetables and 5% fruit been offered to the bird. A powdered pancreatic extract containing maltase, protease, and lipase (Enzyplex®, Nature Vet) was added to this diet prior to it been offered to the bird. The bird was also treated with ursodeoxycholic acid (Ursofalk®, Dr Falk Pharma GmbH, Germany) 15mg/kg PO SID; colchicine (Colgout®, Aspen Pharmacare Australia) 0.04mg/kg PO SID; and silibinin (Greenridge Milk Thistle Liver Tonic®) 10mg/kg PO SID.

Within a few days the owner reported that the bird was brighter and vocalising more. Its faeces had become smaller and darker in colour. Over the next few weeks it continued to gain weight, stabilising at 800-810g. Two months after the initial diagnosis plasma biochemistries had returned to normal (Table 5) and all medications other than the pancreatic extract were discontinued. At the time of writing the bird continues to do well.

DISCUSSION

The avian pancreas consists of three lobes. The dorsal and ventral lobes are supported and separated by the pancreatic artery within the duodenal loop, and the splenic lobe runs more laterally up to the spleen, as an extension of the ventral lobe. The pancreas has both endocrine and exocrine functions. While the amount of endocrine tissue is proportionally greater than that of mammals (Hazelwood, 2000), over 99% of the pancreatic mass has an exocrine function (Fudge, 2000). The exocrine pancreas consists of compound tubuloacinar glands divided into lobules. These glands secrete amylase, lipase, proteolytic enzymes and sodium bicarbonate into the ascending duodenum via pancreatic ducts (Denbow, 2000). Pancreatic secretion, which is at a higher rate than that of mammals, is controlled by both neural and hormonal mechanisms. Immediately a bird starts eating, pancreatic secretion begins apparently via a vagal reflex. Distension of the proventriculus stimulates a hormonal response involving vasoactive intestinal polypeptide that results in pancreatic secretion. Diet can also affect the rate of secretion, with diets high in fat and carbohydrates increasing the activity of amylase and lipase (Denbow, 2000).

Pancreatic disease may be more common in birds than is thought (Doneley, 2001). As with mammals, the initiating aetiology is often difficult to pinpoint. Possible aetiological agents and contributing

factors include obesity, often when combined with high fat diets or fatty meals (Pass and Wylie, 1986; Speer, 1998), toxicity, particularly zinc (Doneley, 1992; Hazelwood, 2000), mycotoxins (Balachandran and Patharsarthy, 1995-96) and selenium (Green and Albers, 1997), trauma (Williams, 1996), viral infection (including paramyxovirus type III (Simpson, 1993), adenovirus (Capua et al., 1994; Goodwin et al., 1996), avian influenza A virus (Hooper et al., 1995; Silvano et al., 1997), infectious bronchitis (Montgomery et al., 1997), and herpesvirus (Norton et al., 1991), *Chlamydia* infection (Mirande et al., 1992), bacterial infection (Williams, 1996), egg yolk peritonitis (Speer, 1998; Fudge, 2000), and neoplasia (Abdul-Aziz, 1995; Kennedy et al., 1996; Williams, 1996; Ritchie et al., 1997; Speer, 1998; Fudge, 2000).

Activation of the digestive enzymes (trypsin, protease and phospholipase, among others) within the gland, due to any of the aetiological factors described above, can result in pancreatic autodigestion. This leads to further damage to the pancreatic cell walls, allowing the release of these enzymes into the intracellular space and ducts; this in turn causes the production of unopposed free radicals, which cause even more damage. This again releases more enzymes, and the cycle continues. The result is inflammation, cellular destruction, and finally fibrosis (Doneley, 2001).

The cause of EPI in this case could not be determined. The concurrent cholangiohepatitis and the response to doxycycline suggest the possibility of an ascending bacterial infection from the intestinal tract. Obesity and a high fat diet may also have been contributing factors (Speer, 1998; Doneley, 2001).

With the loss of exocrine pancreatic tissue comes maldigestion, particularly of fatty foods and starch. Undigested fats and starch account for steatorrhoea (seen as pale, bulky and often malodourous faeces) and weight loss. In mammals, depletion of body stores of cobalamin occurs rapidly, but this has not been looked at in birds at this time. In mammals, this depletion can lead to a poor coat and general ill-health.

Treatment for EPI is the replacement of lost digestive enzymes. Powdered pancreatic extracts are generally recommended, as their efficacy appears to be greater than tablets. Supplementation with cobalamin is recommended in people, dogs and cats, and this is an area that needs to be looked at more closely in birds.

In summary, EPI in birds may be a consequence of pancreatitis or other pancreatic disease. As in mammals, clinical signs of weight loss and steatorrhoea are seen. Treatment with a powdered pancreatic extract is of benefit. Long term outcomes have yet to be assessed.

Parameter	Value	Reference interval	Units
PCV	50	40-55	%
Leucocytes (total)	13.8	5.2-22	$x10^9$/L
Heterophil	94	45-72	%
Lymphocyte	6	20-50	%
Monocyte	0	0-2	%
Eosinophil	0	0-2	%
Basophil	0	0-1	%

Table 1. Haematology, first visit (Values obtained from in-house haematological analysis, with reference ranges adapted from IDEXX Laboratories and Fudge (2000).

Parameter	Value	Reference range	Units
Glucose	27.2	7.4-22.7	mmol/L
Urea	1.1	0.5-1.1	mmol/L
Calcium (total)	2.0	1.8-2.3	mmol/L
Protein (total)	53	21-39	g/L
AST	222	140-360	IU/L
CK	306	147-418	IU/L
Cholesterol	10.4	3.5-7.3	mmol/L
Amylase	516	170-2170	IU/L
GLDH	5	1-4	IU/L
Uric acid	0.46	0.16-1.04	mmol/L
Triglycerides	4.1	< 5	mmol/L
Bile Acids	20	< 81	umol/L

Table 2. Biochemistry, first visit (values from in-house haematological analysis, with reference ranges adapted from IDEXX Laboratories and Fudge (2000).

Parameter	Value	Reference range	Units
PCV	40	40-55	%
Leucocytes (total)	8.6	5.2-22	$x10^9/L$
Heterophil	65	45-72	%
Lymphocyte	35	20-50	%
Monocyte	0	0-2	%
Eosinophil	0	0-2	%
Basophil	0	0-1	%

Table 3. Haematology, second visit (values from in-house haematological analysis, with reference ranges adapted from IDEXX Laboratories and Fudge (2000).

Parameter	Value	Reference Interval	Units
Glucose	14.9	7.4-22.7	mmol/L
Calcium	2.37	1.8-2.3	mmol/L
Protein	40	21-39	g/L
AST	1043	140-360	IU/L
CK	364	147-418	IU/L
Uric Acid	651	1-4	IU/L
Bile Acids	< 35	< 81	umol/L

Table 4. Biochemistry, second opinion visit (values from in-house analysis, with reference ranges adapted from IDEXX Laboratories and Fudge (2000).

Parameter	Value	Reference Interval	Units
Glucose	20.40	7.4-22.7	mmol/L
Urea	0.60	0.5-1.1	mmol/L
Calcium	2.00	1.8-2.3	mmol/L
Protein	32	21-39	g/L
AST	258	140-360	IU/L
CK	267	147-418	IU/L
Cholesterol	6.30	3.5-7.3	mmol/L
Amylase	438	170-2170	IU/L
Uric Acid	398	1-4	IU/L
Triglycerides	1.40	0.16-1.04	mmol/L
GGT	8	< 5	mmol/L
Bile Acids	43.40	< 81	umol/L

Table 5. Biochemistry, last visit (values from UQ VSDS Laboratory, with reference ranges adapted from IDEXX Laboratories and Fudge (2000).

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