

Vertebral Carcinoma in a New Zealand Takahe (*Porphyrio hochstetteri*)

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HISTORY

An 18 year old female Takahe (*Porphyrio hochstetteri*) from a nature reserve in Christchurch New Zealand was noticed with acute leg paresis. The bird appeared to be ataxic and was observed falling backwards. Physical examination at a local veterinary clinic revealed no further abnormalities. A faecal examination showed two capillaria eggs per gram, a low number of coccidia and no bacterial growth after bacterial culture for *Salmonella* spp. and *Yersinia* spp. Clinical findings included a cloacal temperature of 40°C and slightly pale oral mucous membranes. A blood sample was taken and biochemistry results showed a normal to mildly elevated creatine kinase (CK) concentration of 1486 u/l (reference range 666.8-1416.9 u/l [Rose, 2000], 388-1632 [Youl, 2009]) and a low plasma phosphorus (Phos) concentration (0.45 mmol/l - reference ranges for non-Takahe avian species (psittacine birds and mallards) vary between 0.90 to 2.1 mmol/L (Harrison and Lightfoot, 2006). Other biochemistry results were within normal limits (AST 198 u/l; BA<35 µmol/l, UA 292.5 mmol/l, total proteins 38 g/l, albumin 24 g/l, globulin 14 g/l, K⁺ 3.1 mEq/l, Na 148 mEq/l). No haematology was done. No further treatment was given.

CLINICAL FINDINGS

The bird was flown to the wildlife hospital at Massey University in Palmerston North, where it arrived three days after the initial clinical signs.

On arrival the bird weighed 2.535 kg. The Takahe was unable to support its body weight, sat on its hocks and fell back in this position during attempts to stand, at the most managing to move two steps forwards with marked ataxia. The bird appeared alert. A menace and palpebral reflex were present, no strabismus or asymmetry between left and right pupil size were seen, and jaw tone appeared normal. Wings were carried in a normal position and muscular wing movements appeared normal and strong on both sides. While the bird's weight was supported, mild proprioceptive deficits were demonstrated. Knuckling of the toes showed a delayed correction on both sides, with the right side being worse. Withdrawal reflexes were present and no crossed extensor reflexes were seen. A vent sphincter reflex was present.

DIAGNOSTIC TESTS

Radiographs and blood samples for haematology, repeat biochemistry, zinc and lead levels were taken under general inhalation anaesthesia with isoflurane. Radiographs showed multiple small particles with suspected metallic density in the intestinal tract. Otherwise no abnormalities were observed. No worms or worm eggs were detected in faeces, but a faecal count of 3150 coccidia

oocysts/gram was found. A blood biochemistry panel was run on an in-house Vetscan biochemistry analyser, which showed an elevated aspartate aminotransferase (AST) concentration of 601 u/l (reference range 211.4-291.8 [Rose, 2000]; 252-388.2 [Youl, 2009]) and a CK concentration outside the Vetscan's detection limits. Other biochemical parameters were within normal limits (BA<35 µmol/l, UA 268 mmol/l, GLU 17.5 mmol/l, Ca⁺⁺ 2.37 mmol/l, Phos 1.02 mmol/l, TP 38 g/l, ALB 25 g/l, GLOB 14 g/l, K⁺ 3.2 mEq/l, Na 143 mEq/l). The packed cell volume (PCV) was 44% and total plasma protein concentration was 38 g/l. Results of a total white blood cell count (WCC) were within normal limits (16.0 x 10⁹ cells/l; reference range 11.6-16.3 x 10⁹ cells/l [Rose, 2000]), but leukocyte differentiation showed a relative heterophilia and lymphopaenia with 88% heterophils (normal range 37.9-47.1%), 9% lymphocytes (normal range 44.9-54.6%), 1% monocytes (normal range 3.8-5.5%) and 2% eosinophils (normal range 1.5-2.7%). Red blood cells showed <5% polychromatosis and thrombocyte numbers were adequate. A blood lead level of 0.013 mg/l was measured on an in house portable blood lead analyser (LeadCareH, ESA Inc., Chelmsford, Massachusetts, USA). This is considered to represent a very low level of lead exposure and is not consistent with lead toxicosis (Stauber et al., 2010).

DIFFERENTIAL DIAGNOSIS

The initial differential diagnoses were spinal injury (contusion, necrosis), bacterial, fungal or neoplastic processes involving the spinal column, heavy metal toxicity, an intra-coelomic processes causing pressure on lumbar or sciatic nerves, exertional myopathy and emboli involving blood vessels of the spinal cord.

Intact spinal reflexes combined with bilateral hind limb paresis and impaired proprioception in both legs, made upper motor neuron disease caused by a pathological process between the brachial and lumbar plexus most likely.

TREATMENT

A single dose of toltrazuril (25 mg/kg PO; Baycox 5% for piglets, Bayer Animal Health New Zealand) was given. Initially a treatment schedule of meloxicam (0.2 mg/kg PO SID; Metacam oral suspension 1.5 mg/ml, Boehringer Ingelheim New Zealand) and Ca-EDTA 20% (40 mg/kg IM q12h; Provet NZ Pty Ltd, Christchurch) was started. The bird was tube fed twice a day with 50 to 60 ml of a mix of Harrison's high potency mash and Jevity (Abott Laboratories B.V, Zwolle, The Netherlands) and 20 ml of Hartmann's solution. After two days in hospital an intravenous catheter was placed in the medial metatarsal vein and Hartmann's solution was given at a constant infusion rate of 3 ml/kg/h for 24 hours, before reducing the rate to 2 ml/kg/h. Antibiotic treatment was started with enrofloxacin (15 mg/kg PO BID; Enrotril, Troy laboratories PTY Ltd., Australia). Ca-EDTA was removed from the treatment schedule subsequent to receiving the blood lead and zinc results.

CASE PROGRESSION AND FURTHER DIAGNOSTICS

After five days of treatment the bird was still paretic and ataxic. Muscle strength in the legs had deteriorated slowly, based on the bird's attempts to stand. Over the next two days a further mild deterioration was noticed. A repeat blood sample was taken and plasma biochemistry values showed a mild continued elevation of AST concentration of 747 IU/l and a CK concentration outside the Vetscan's detection limits. Other biochemical parameters were within normal limits (BA<35 µmol/l, UA 190 mmol/l, GLU 14.1 mmol/l, Ca⁺⁺ 2.45 mmol/l, Phos 1.35 mmol/l, TP 36 g/l, ALB 24 g/l, GLOB 12

g/l, K⁺ 4.5 mEq/l, Na 146 mEq/l). Haematology revealed a mildly elevated white blood cell count of 19.4×10^9 cells/L, with 71% heterophils (13.8×10^9 cells/l), 24% lymphocytes (4.7×10^9 cells/l), 5% monocytes (1.0×10^9 cells/l) and 2% eosinophils (0.4×10^9 cells/l). Red blood cells showed <5% polychromatosis and thrombocyte numbers were adequate.

A computed tomographic scan of the pelvis and spine showed a lytic and proliferative bony reaction involving the cranial edge of the synsacrum and the seventh thoracic vertebra (T7) just cranially of the synsacrum. Abnormal findings included a highly irregular periosteal reaction and punctate osteolysis associated with the entire right aspect of the spinal lamina, pedicle and vertebral body of T7. There was evidence of extension through the pedicle into the vertebral canal. A soft tissue mass was visible in association between the hypaxial musculature and the spine. There were a few nodular thickenings of airsac walls, which could be due to normal variation or small granulomas. The images were suggestive of bacterial or fungal discospondylitis, but a neoplastic process couldn't be ruled out.

A treatment regime was started for a presumptive bacterial or fungal discospondylitis with clindamycin (120 mg/kg PO BID; Antirobe 150 mg capsules, Pfizer New Zealand), amoxicillin/clavulanic acid (120 mg/kg IV BID; Curam powder for injection, 500/100 mg (as amoxicillin/clavulanic acid), Novartis New Zealand Limited, Auckland), enrofloxacin (15 mg/kg PO BID; Enrotril, Troy laboratories PTY Ltd., Australia), itraconazole (10 mg/kg PO BID; Sporonox oral solution, Janssen-Cilag Pty Ltd), meloxicam (0.2 mg/kg PO SID; Metacam oral suspension 1.5 mg/ml, Boehringer Ingelheim New Zealand) and butorphanol (4 mg/kg IM BID; Torbugesic, Ford Dodge Australia). The bird continued on intravenous fluids (Hartmann's solution) at a rate of 2ml/kg/h.

Two days later surgery was performed to collect a biopsy sample of the mass for histology. During a gradual mask induction with oxygen and isoflurane, 2 mg/kg butorphanol was given IM. An endotracheal Cole tube was placed. Intra-operative intravenous fluids (Hartmann's solution with 2.5% glucose) were given at a rate of 10 ml/kg/h. The lumbar muscle covering the cranial ilium and adjoining vertebrae on the right side was reflected from the spinous processes. Biopsy angle and depth were determined by studying the computed tomographic images. Samples from below the cortex of the effected vertebra were taken with a curette and sent to the pathology department of Massey University in Palmerston North for histology and to a commercial laboratory for bacterial culture. A blood sample for bacterial culture was taken from the medial metatarsal vein after surgical preparation of the leg with chlorhexidine scrub solution.

Once daily physiotherapy using a frame with sling was started to stimulate leg movement, maintain muscle tone and reduce muscle necrosis. Midazolam (0.05 mg/kg IM; Midazolam injection, Hospira NZ Ltd, New Zealand) was given 20 minutes prior to each physiotherapy session to minimise stress and aid the bird's compliance while in the sling.

The blood culture showed a heavy growth of *Aeromonas* spp., which were resistant to amoxicillin/clavulanic acid, but sensitive to enrofloxacin. Coagulase negative *Staphylococcus* spp, sensitive to most regular antibiotics, were grown from the biopsy tissue. A gram stain of the biopsy tissue showed gram negative rods. The CT images combined with the bacterial culture results and gram stain suggested bacterial discospondylitis. Amoxicillin/Clavulonic acid and Clindamycin were discontinued. Enrotril, Itraconazol, Meloxicam and Butorphanol were continued, while histology results were pending.

Histology of the biopsy confirmed a diagnosis of a vertebral carcinoma, with no signs of bacterial or

fungal pathogens. In agreement with the Department of Conservation and the management team of the nature reserve, the bird was euthanased and submitted to the Palmerston North Massey University pathology department for a post mortem examination.

POST MORTEM FINDINGS

Gross pathology showed a 15 x 10mm, fairly soft and smooth, pale tan circumscribed mass, projecting from the junction of the cranial part of the synsacrum and the body of T7, causing bone destruction in the cranial edge of the synsacrum and T7.

Histology of the affected vertebra showed extensive replacement of the pneumatic spaces, with destruction of both trabecular and cortical bone and infiltration of the adjacent soft tissues with a population of neoplastic epithelial cells, arranged in dense sheets with many areas of tubule or vague acinar formation. Neoplastic cells were polygonal, with round to oval vesicular nuclei, moderate amounts of pale granular eosinophilic cytoplasm and fairly indistinct cell borders. Many cells also had a single, discrete, clear intracytoplasmic vacuole. Anisokaryosis and anisocytosis were minimal and the mitotic rate was low (less than 5 per/10 high power fields). In the adjacent soft tissue, the neoplasm was fairly well-circumscribed and encapsulated by thick bands of well-organised collagenous tissue. The exact type of neoplasia remained uncertain.

FINAL DIAGNOSIS

The final diagnosis was vertebral carcinoma

DISCUSSION

This report describes the clinical course, diagnostics and pathological findings in a Takahe with a vertebral sarcoma. The bird presented with acute bilateral hind limb paresis. Reported causes of hind limb paresis in birds include space occupying intra-coelomic masses resulting in pressure on the lumbar plexus or sciatic nerve due to egg binding (Crouch, 2009), neoplasias of renal (Freeman et al., 2005; Simova-Curd et al., 2006), adrenal, gonadal (Mickley et al., 2009) or bronchogenic tissue (Baumgartner et al., 2008), renal or ovarian cysts (Rosen, 2012), or proventricular impaction (Lloyd, 2009). Spinal injuries can be caused by a traumatic events (Powers and Bergman, 2005) or infectious neuropathies due to bacterial, fungal, parasitic or viral infectious aetiologies (Jones and Orosz, 1996). Paresis can also be caused by toxic effects of heavy metals such as lead or zink (Degernes, 1995), drug use (Wright, 1992) or exertional myopathy (Smith et al., 2005; Dunne and Miller, 2009).

The Takahe in this case didn't show an elevated white blood cell count when it arrived at the Massey University Wildlife Hospital, which made infectious causes at that point seem less likely. In case of exertional myopathy or trauma the initial blood sample taken at the local veterinary clinic would likely have shown a much higher CK concentration than the very mild elevation that was seen here. After three days the blood biochemistry results showed a CK concentration outside the Vetscan's detection limits and an elevated AST level, indicating ongoing muscle cell necrosis (Flammer et al., 1990). This second sample was taken after multiple hours of travelling including a flight in a crate and three days of paresis. The ongoing abnormal strain on the bird's soft tissues was a more likely explanation for the elevated CK and AST concentrations than a traumatic insult at the nature reserve.

Radiographic imaging showed multiple particles in the intestinal tract with suspected metallic density.

Field studies have demonstrated that Takahe from various locations in New Zealand are exposed to environmental lead (Youl, 2009). The bird's faeces were well formed and showed no signs of biliverdinuria or undigested particles, as is often the case with heavy metal toxicity. Chelation therapy with Ca-EDTA was started, but discontinued as soon as low zinc and lead blood results ruled out heavy metal toxicity.

The mental state of the bird was bright and alert during her entire stay at the hospital. With bilateral leg paresis being the only abnormal finding a focal process affecting the spinal cord was most likely. Processes involving a kidney or gonad affecting the lumbar plexus or sciatic nerve, most often causing unilateral symptoms (Jones and Orosz, 1996; Harrison and Lightfoot, 2006), were considered less likely.

The decision to perform a CT scan was made based on the suspicion of a pathological process involving the spinal cord. The osteolysis found on the right side of T7 and a small part of the cranial synsacrum was suggestive of a bacterial or fungal discospondylitis, but a neoplastic process couldn't be ruled out. Vertebral and spinal neoplasias are very rare in avian species (Jones and Orosz, 1996) and during a retrospective study of post-mortem examination findings in Takahe from 1992 till 2007 neoplasias of any kind were not reported (McLelland et al., 2011). Treatment was started for bacterial and fungal causes of discospondylitis and pain relief, while further diagnostic procedures involving a surgical biopsy were planned.

Of the antibiotics chosen Clindamycin has the best activity against anaerobic bacteria and shows the best penetration into bone to treat bacterial osteolytic conditions. Recent pharmacokinetic studies have shown a half-life time of Clindamycin in pigeons of 1.25 hours (Lenarduzzi et al., 2011). With Clindamycin being a time dependent antibiotic, its effectiveness is dependent on the percentage of time its serum concentration stays above the minimum inhibitory concentration (MIC). In pigeons dosing four times daily was needed to stay above the MIC for an adequate amount of time. Pharmacokinetic studies in Takahe are not available, but it is likely that administering Clindamycin twice daily is insufficient in this species also. In wildlife patients the negative effects of stress on the patient due to frequent handling have to be taken into account, and treating four times a day is in many cases not feasible. During the last few days of treatment the only antibacterial drug used was Enrotril, to which all cultured bacteria were reported to be sensitive. Enrotril has the advantage of being a concentration dependent drug, which means that its bactericidal effect depends on the ratio between the maximum peak plasma concentration and the MIC. This makes frequent dosing unnecessary as long as a high enough plasma concentration is reached once to twice daily.

Histology of the affected tissues after post mortem confirmed a neoplastic lesion with no sign of bacterial or fungal pathogens, which strongly indicates that the bacteria cultured from blood and biopsy tissue were due to bacterial contamination from the environment.

This report gives clear evidence of the added value of computed tomographic imaging. Compared to conventional radiography computed tomography provides superior soft tissue imaging with no superimposition of structures (Platt, 2006). While no pathological lesions could be seen on plain whole body digital radiographs, the CT scan clearly showed lytic changes in the effected vertebra and the adjoining soft tissue mass. This demonstrates the importance of CT scans for the evaluation of abnormalities in the CNS soft tissue or its protective skeleton.

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<http://muir.massey.ac.nz/bitstream/handle/10179/1031/02whole.pdf?sequence=1>



