Association of Avian Veterinarians Australasian Committee Ltd.
Annual Conference 2016 pp 28-31

T-cell Lymphosarcoma in a Six-months old Indian Ringneck Parrot

Corrie Pinkster,
Melbourne Bird Veterinary Clinic,
1 George St,
Scoresby, Victoria, Australia
corriepinkster@gmail.com

Case Study

A six-month-old, female Indian Ringneck Parrot (*Psittacula krameri*) presented following four days of lethargy. The bird had been hand reared, owned for approximately three months, was the only pet in the household, and had been fed a diet of seeds, parrot pellets, vegetables, fruit, nuts and dried fruit. On initial examination the bird was found to be slightly underweight with a body condition score (BCS) of 2/5, was quiet and had ruffled feathers. Microscopic examination of her droppings revealed no abnormalities. Conscious lateral and ventro-dorsal radiographs were obtained which showed a markedly enlarged hepatic silhouette with a general increase in size of abdominal viscera and loss of the abdominal air sac shadow. The bird was admitted to a heated cage at 30̊C, given doxycycline by intramuscular injection and crop fed a hand rearing formula. A blood sample was collected prior to commencing of treatment. An ImmunoComb® Avian *Chlamydophila psittaci* antibody test was negative.

On day two the bird was brighter and passing normal droppings. It was elected to continue with supportive care, with the view to run blood tests after 48 hours if there was no further improvement. Over the next two days, the bird stayed in the clinic in a heated cage with twice daily crop feeding and oral administration of a naturopathic liver tonic of echinacea, milk thistle and dandelion in a lactulose base. The bird was eating by day three and had improved significantly so was discharged to the owners care on day four, continuing with the liver tonic.

On day eight, the bird re-presented as the owners were concerned that it had lost vision. It had been eating well and was “fairly bright”, but it had become obvious that in the last 24 hours its eyesight had deteriorated. On examination the bird was now BCS 1.5/5 , despite having gained 5g in body weight, and the liver was now palpable and markedly enlarged. The bird showed no response to approaching objects but had bilaterally normal pupillary light reflexes.

The bird was once again admitted to a heated cage for supportive cage while awaiting biochemistry and haematology results from an external laboratory. Abnormal results are summarised in Table 1.

These results were consistent with severe hepatopathy and associated metabolic decompensation. Treatment with clindamycin was commenced, while the liver tonic continued. The bird was bright and eating well and, despite a very poor prognosis, was discharged to spend some quality time with the owners over the weekend while they contemplated whether to pursue a liver biopsy.

The bird remained bright with a good appetite but became quiet on day 11 and died with the owner the following day. The owners consented to a cosmetic necropsy (brain not examined). Grossly, there was white-yellow opaque fluid within the hepatic capsule and the liver was markedly enlarged, with diffuse changes including generalised pallor, increased visualisation of architecture and mild petechial haemorrhage. The spleen and kidneys were also diffusely and markedly enlarged and pale in colour. Sections from each of these organs and ovary were submitted in formalin to the University of Sydney for histopathology. Massively diffuse infiltration of small lymphocytes was seen in the liver, spleen, ovary and kidney. Immunohistochemistry was performed with CD3 stain which showed massive infiltration of T-cell lymphocytes in all tissues on cytology. The diagnosis was multicentric T-cell lymphosarcoma.

Value	Result	Reference range
PCV	0.32	0.45-0.54
WBC	19.7 x 109/L	8-14 x 109/L
Lymphocytes	14.8 x 109/L	no ref provided
Glucose	6.5 mmol/L	12.2-19.7 mmol/L
Urea	3.0 mmol/L	no ref provided
Total Protein	11 g/L	no ref provided
Cholesterol	29.4 mmol/L	no ref provided
Aspartate aminotransferase (AST)	3659 IU/L	152-386 IU/L
Creatine kinase (CK)	2178 IU/L	no ref provided
Glutamate dehydrogenase (GLDH)	16 IU/L	<3 IU/L
Uric acid	0.09 mmol/L	0.19-0.70 mmol/L

Discussion

This report describes the ultimately unsuccessful management of a very young bird diagnosed at post mortem with lymphosarcoma. The bird showed non specific signs initially, while radiographs, physical examination and biochemistry were all indicative of severe liver disease. Doxycycline treatment was initially started on suspicion of chlamydiosis while tests were pending. Clindamycin was later used in case of toxoplasmosis, knowing this was an unlikely differential but considered, with the combination of hepatopathy and neurological disease. Avian mycobacteriosis was also considered as another important differential. A liver biopsy was not performed, partially due to financial constraints and partially due to concerns about the bird's prognosis regardless, however this would have provided a definitive diagnosis. It is possible that a fine needle aspirate under general anaesthesia may have also provided this information as a less invasive diagnostic method. There was some improvement with supportive care and the bird appeared to be relatively well in itself following initiation of supportive care up until less than one day prior to death. It is unknown whether the apparent blindness was caused by metastatic disease in the central nervous system or secondary to hepatic encephalopathy. A similar case has been reported with lymphosarcoma in an eight month old Blue and Gold Macaw, which also presented with blindness and neurological dysfunction as well as other non specific clinical signs (Coleman and Oliver, 1994). In that case, no lesions were found on histopathological examination of the brain, and it was deduced that the neurological signs were subsequent to hepatic encephalopathy. There were many other parallels with this case including rapid onset and deterioration of disease, young age at presentation and involvement of the spleen, liver and kidneys.

Lymphoid neoplasia has been reported in a large range of avian patients, with lymphosarcoma (aka malignant lymphoma) being the most common in psittacine and passerine birds (Coleman, 1995). The disease develops in primary or secondary lymphoid tissue and spreads via systemic circulation. It can result in diffuse or nodular involvement of target organs and will sometimes result in neoplastic lymphocytes appearing in the circulation. If the disease is found to have originated in the bone marrow, it is classified as lymphoid leukaemia. This form involves diffuse changes, with findings of anaemia, low platelet count and neoplastic lymphocytes in the peripheral circulation. This is not well documented in avian patients, possibly because of dissemination by time of diagnosis and difficulty in defining the site of origin (Coleman, 1995).

There are a number of viral causes of lymphoma that are well documented in poultry. These include Marek's disease, Avian Leukosis virus (ALV) and reticuloendotheliosis. Marek's disease, is caused by an oncogenic herpesvirus that affects chickens, turkeys and quail. Lymphoid leukosis and reticuloendotheli-

osis are caused by retroviruses and between them can affect chickens, geese, Muskovy ducks, pheasants and partridges (Payne and Venugopul, 2000). It is commonly suspected that viral causes of lymphoid neoplasia occur in psittacine and passerine birds, although this has not been proven. ALV antigen has been inconsistently detected in budgerigars with renal tumours, although these are usually adenomas or adenocarcinomas rather than lymphoid neoplasia and the data does not provide conclusive evidence of a causative link (Simova-Curd et al., 2006).

Management challenges of lymphosarcoma in avian patients include presentation with non-specific signs and often advanced progression of disease by time of presentation. Clinical signs, clinical pathology and radiographic changes can be variable depending on which tissues are involved. White cell and lymphocyte counts vary from normal to markedly increased. Leukocytosis with absolute lymphocytosis is suggestive however a higher level of lymphocytes than heterophils can be normal in commonly affected species including amazon parrots, indian ringneck parrots, budgerigars and canaries, as well as in bacterial and viral conditions and stress. A high degree of pseudopodia is an important indicator, although this can also occur with chronic viral and bacterial infections (Coleman, 1995). Biochemistry changes can help to establish which organ(s) may be involved, and hypercalcaemia has been reported in some cases (de Wit et al., 2003). Common radiographic changes include enlargement of the liver, spleen and kidneys. Definitive diagnosis is best achieved with biopsy of affected tissues. Spleen and liver are the most common organs involved. Nodular and diffuse cutaneous lymphosarcoma has been reported in Amazon Parrots (Burgos-Rodriguez et al., 2007). A 12 years old male cockatiel has been reported with lymphosarcoma in the cranial coelomic cavity, with presenting signs of chronic dyspnoea and regurgitation (Wills et al., 2006). The author is also aware of an eight years old cockatiel diagnosed with very similar lesions arising from the cranial proventriculus (Baron, 2016) so perhaps this is an area of predilection in this species. Histopathology changes involve diffuse or nodular infiltration of tissues with lymphocytes of variable morphology. Classification criteria for lymphosarcoma is in dogs and cats is well documented, along with standardized staining and validated immunohistochemistry (IHC) for determining B or T-cell origin. CD3 antigen markers for T-lymphocytes are active in most avian species. However, B-lymphocyte markers have variable reactivity and are not reliable in avian species (Zehnder et al., 2015). IHC determination of cell origin is a useful prognostic tool in dogs and cats. There is currently no known association between tumour classification and behaviour in avian species, but as this is further studied, may become useful in providing prognostic and treatment guidance (Zehnder et al., 2015).

Treatment of lymphoma in avian patients with chemotherapy is experimental and few cases of successful treatment have been documented. Doses and treatment regimes are currently extrapolated from mammalian species, which may not be optimal. Limitations in avian patients include limited knowledge of protocols, potential for severe side effects and in small or fractious patients the requirement for general anaesthesia to safely achieve vascular access at each treatment. There have been reports of moderate success with corticosteroid treatment of lymphoma in some birds (Coleman, 1995, Zehnder et al., 2015), however this carries a high risk of complications related to immunosuppression and secondary infections. An umbrella cockatoo with cutaneous B-cell lymphoma was successfully treated with vincristine and chlorambucil (McClearon and Reavill, 2009). Although treatment was ceased at 17 weeks due to severe depression, the bird remained in complete remission at eight years post treatment. Side effects included anaemia, hypoproteinaemia, increased uric acid, AST and CK. These were successfully managed with supportive care with a significant improvement after seven days of ceasing treatment. Hopefully as knowledge of tumour biology and collation of treatment and outcomes progress, optimal chemotherapy protocols can become established for avian patients to provide better outcomes.

Acknowledgments

Thank you to Dr David Phalen for interpretation of the histopathology and to Dr Hamish Baron for interpretation of the immunohistochemistry and sharing of his cockatiel case.

References

Baron, H (2016). Personal communication.

Burgos-Rodriguez AG, Garner M, Ritzman TK and Orcutt CJ (2007). Cutaneous Lymphosarcoma in a Double Yellow-Headed Amazon Parrot (*Amazona ochrocephala oratrix*). Journal of Avian Medicine and Surgery 21, 283-289.

Coleman CW and Oliver R (1994). Lymphosarcoma in a Juvenile Blue and Gold Macaw *(Ara araruana*) and a Mature Canary (*Serinus canarius*). Journal of the Association of Avian Veterinarians 8, 64-68.

Coleman CW (1995). Lymphoid Neoplasia in Pet Birds: A Review. Journal of Avian Medicine and Surgery 9, 3-7.

de Wit M, Shoemaker N J, Kik M J L and Westerhof I (2003). Hypercalcemia in Two Amazon Parrots with Malignant Lymphoma. Avian Diseases 47, 223-228.

Payne LN and Venugopal K (2000). Neoplastic diseases: Marek's disease, avian leukosis and reticuloendotheliosis. Scientific and Technical Review of the Office International des Epizooties (Paris) 19, 544-564.

Rivera S, McClearen J R and Reavill D R (2009). Treatment of Nonepitheliotropic Cutaneous B-Cell Lymphoma in an Umbrella Cockatoo (*Cacatua alba*). Journal of Avian Medicine and Surgery 23, 294-302.

Simova-Curd S, Nitzl D, Mayer J and Hatt JM (2006). Clinical approach to renal neoplasia in budgerigars (*Melopsittacus undulatus*). Journal of Small Animal Practice 47, 504-11.

Wills S, Beaufrere H, DeLay J, Bourque L and Smith D (2006). What is your diagnosis? Lymphosarcoma. Journal of Avian Medicine and Surgery 30, 80-85.

Zehnder A, Graham J, Reavill D and McLaughlin A (2015). Neoplastic diseases in avian species. Current Therapy in Avian Medicine and Surgery, pp 107-141.