SHORT PAPER

Granulomatous Encephalomyelitis and Intestinal Ganglionitis in a Spectacled Amazon Parrot (Amazona albifrons) Infected with Mycobacterium genavense

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Summary

An approximately 30-year-old male spectacled Amazon parrot (Amazona albifrons) was presented with a 2-week history of ataxia, head shaking, weight loss and seizures. Gross findings on necropsy examination included atrophy of the musculature, ruffled feathers and minimal epicardial and abdominal fat. Microscopically, there were perivascular cuffs of macrophages with fewer lymphocytes in the grey and white matter of the brain and spinal cord. These lesions were accompanied by gliosis and mild vacuolation of the white matter. In the small intestine, up to 70% of the intestinal ganglia were effaced by infiltrates of macrophages and fewer lymphocytes. The intestinal lamina propria contained multiple inflammatory aggregates of a similar nature. Ziehl–Neelsen staining revealed the presence of numerous bacilli within the cytoplasm of macrophages in the central nervous system (CNS) and enteric ganglia. Amplification of the DNAJ gene confirmed a mycobacterial infection and subsequent polymerase chain reaction (PCR) using a species-specific primer confirmed the aetiology as Mycobacterium genavense. Infection of the CNS with Mycobacterium spp. is uncommon and has not been previously reported in a parrot. This case is unusual in that the organism exhibited tropism for neural tissue.

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Keywords: central nervous system; encephalomyelitis; enteric nervous system; Mycobacterium genavense; parrot

Mycobacterium genavense is a slow-growing, fastidious, acid-fast bacillus for which a habitat and mode of infection remains to be elucidated (Mendenhall et al., 2000). Since its identification as a human pathogen (Hirschel et al., 1990), M. genavense has been found to cause disease in several animal species, including a cat with feline immunodeficiency virus (FIV) infection, two ferrets, a dog and a variety of avian species (Hoop et al., 1993, 1996; Kiehn et al., 1996; Portaels et al., 1996; Ferrer et al., 1997; Hughes et al., 1999; Lucas et al., 2000; Manarolla et al., 2007). Three previous reports of M. genavense infection in parrots have described generalized infection without nervous system involvement (Hoop et al., 1993; Kiehn et al., 1996; Steiger et al., 2003; Manarolla et al., 2007).

An approximately 30-year-old male spectacled Amazon parrot (Amazona albifrons) was presented to the Texas A&M University Veterinary Medical Teaching Hospital with a 2-week history of ataxia, head shaking and weight loss. Initial physical examination revealed multiple infiltrates of macrophages and fewer lymphocytes. The attending clinician prescribed enrofloxacin, meloxicam and itraconazole. Mild improvement was noted initially; however, during the following 2 weeks, the parrot developed seizures that started at a frequency of 1–2 per night and progressed to seizures that lasted throughout the night, with approximately
15 min intervals between episodes. Additional clinical signs included falling off the perch, vocalizing and wing flapping. The parrot was humanely destroyed and a full necropsy examination was performed.

On necropsy examination, fat deposits and epicardial fat were markedly decreased and the pectoral musculature was severely atrophic. Microscopically, lesions were present in the brain, spinal cord, small intestine, proventriculus, ventriculus, liver and aorta. Lesions in the brain were disseminated throughout the white and grey matter at all levels and consisted of perivascular cuffing with a moderate to large number of macrophages and fewer lymphocytes (Fig. 1). The macrophages had a moderate amount of eosinophilic, granular cytoplasm. The thick perivascular cuffs resulted in occasional and partial occlusion of vascular lumina (Fig. 2). Moderate, diffuse gliosis was present and some astrocytes were swollen and had a glassy nucleus. Mild multifocal white matter vacuolation was present in the cerebrum. Lesions in the spinal cord were similar to those in the cerebrum. They were most prominent in the mid-cervical area and less pronounced in the mid-thoracic area.

The lamina propria of the small intestine contained multiple moderately sized aggregates of macrophages and lymphocytes. The ganglia of the proventriculus, ventriculus and small intestine were partially effaced (up to 70% of their area) by a granulomatous inflammatory reaction (Fig. 3). In the liver, periportal areas contained a mildly increased number of lymphocytes. There was mild atherosclerosis of the aorta. No significant lesions were observed in the lung, spleen, sciatic nerve, heart, kidney and testis.

Ziehl–Neelsen staining revealed large numbers of acid-fast bacilli in the brain, spinal cord and enteric ganglia, but not in the lamina propria of the small intestine (Fig. 4). Bacteria in the brain were primarily located within macrophages, although extension into the surrounding neurophil was occasionally observed (Fig. 4). Acid-fast bacteria in the spinal cord and small intestine were generally restricted to the cytoplasm of the macrophages.

Brain tissue was obtained from formalin-fixed, paraffin wax-embedded blocks by dewaxing through xylene and ethanol. DNA was extracted using Puregene® Genomic DNA Purification Kit (Gentra Systems, Minneapolis, Minnesota) and following the manufacturer’s instructions. Polymerase chain reaction (PCR) screening for mycobacterial DNA was performed first using primers T1 [5'-GGGTGACGCG(G/A)CATGGCCCA-3'] and T2 [5'-CGGGTTTCGTCGTACTCCTT-3'] for amplification of the 236 base pair (bp) DNA
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The clinical presentation with *M. genavense* infection varies depending on the species affected and organs involved and ranges from generalized lymphadenopathy in the dog, to conjunctivitis and lymphadenopathy in ferrets, to chronic wasting in man, birds and cats (Bottger et al., 1992; Hoop et al., 1993, 1996; Kiehn et al., 1996; Portaels et al., 1996; Ferrer et al., 1997; Hughes et al., 1999; Lucas et al., 2000; Manarolla et al., 2007). Infection in man and birds tends to be generalized and is characterized by consistent involvement of the intestine, liver and spleen (Bottger et al., 1992; Kiehn et al., 1996). In birds, other manifestations of *M. genavense* infection include pulmonary (Kiehn et al., 1996) and cutaneous (Ferrer et al., 1997) involvement. Microscopical lesions in birds are variable and range from a single focus to sheets of inflammatory cells composed primarily of epithelioid cells. Bacteria and inflammatory cells are most frequently encountered in the intestine and liver and less so in other organs (Hoop et al., 1993).

The neurotropism and prominent perivascular cuffing exhibited in this case have not been previously reported in man or animals. There are numerous reports of mycobacteriosis (largely involving *Mycobacterium avium*) involving the central nervous system (CNS) in human patients with acquired immunodeficiency syndrome (AIDS) (Cegielski and Wallace, 1997), but reports of CNS mycobacteriosis in animals are rare and primarily involve birds with disseminated disease (Hoop et al., 1993). Reports of brain involvement with disseminated *M. avium* infection include a chicken (Odiawo and Mukurira, 1988), a red-tailed hawk (Sykes, 1982) and an experimentally infected Japanese quail (Tell et al., 2001). A single human case with CNS involvement and presenting as a solid mass in the parietal lobe was attributed to *M. genavense* infection (Berman et al., 1994), but reports of *M. genavense* as a cause of encephalitis in immunocompromised people are lacking. In birds, CNS involvement has been reported in generalized *M. genavense* infections in a flycatcher (Hoop et al., 1993), a zebra finch (Hoop et al., 1993) and a European goldfinch with concurrent avian polyomavirus infection (Manarolla et al., 2007). The lesion described in the flycatcher and the zebra finch consisted of epithelioid macrophages laden with acid-fast bacteria in the cerebrum and meninges (Hoop et al., 1993). Perivascular cuffing with macrophages was not noted. In the goldfinch, the lesions included diffuse infiltration of the meninges by macrophages containing mycobacteria. Perivascular aggregates of macrophages were noted, but they apparently did not form the prominent cuffs seen in this case.

Although the source and route of infection with *M. genavense* are yet to be determined, an oral route has been proposed due to significant involvement of the gastrointestinal tract (Kiehn et al., 1996). Recently, an aerosol route was suggested due to an avian case with significant involvement of the respiratory tract with absence of lesions in the gastrointestinal tract (Manarolla et al., 2007). Contaminated water has been considered as the source of *M. genavense*; however, the organism cannot always be isolated from the water of infected avirials (Hoop et al., 1996). Inflammatory lesions in the intestinal lamina propria and ganglia in the present case suggest oral infection and possible neurotropic invasion of the brain via the intestinal tract. However, the perivascular and disseminated...
distribution of the lesions more strongly favours a haematogenous invasion, a route that has been suggested in other CNS mycobacterial infections in cattle and people (Katti, 2004; Oruc, 2005).

In summary, this is the first report of mycobacteriosis in a parrot with prominent involvement of the CNS. The apparent neurotropism in this case is unique. Although rare, M. genavense should be included in the differential diagnosis for parrots exhibiting neurological signs.

Acknowledgments

The authors would like to thank Mrs R. Vollmar for histology support and Drs M. Garner, I. Tizard and D. Phalen for helpful advice.

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Please cite this article in press as: Gomez G et al., Granulomatous Encephalomyelitis and Intestinal Ganglionitis in a Spectacled Amazon Parrot (Amazona albilongis) Infected with Mycobacterium genavense. Journal of Comparative Pathology (2010), doi:10.1016/j.jcpa.2010.08.007