WILDLIFE

Bilaterally symmetrical lesions of the caudate nucleus in a northern fur seal pup (Callorhinus ursinus)

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SUMMARY

A northern fur seal (Callorhinus ursinus) pup was stranded and brought to The Marine Mammal Center (TMMC) in Sausalito, California, USA, for rehabilitation. Upon admission, the animal was lethargic, underweight and ataxic. Clinical diagnostics, including complete blood cell count (CBC), serum chemistry, protozoal antibody titres, radiographs and cisterna magna ultrasonography, were completed and considered within normal limits. MRI of the brain revealed bilaterally symmetrical focal lesions of the rostrolateral caudate nucleus. Treatment for thiamine deficiency and immune-mediated disease was initiated, but the pup did not improve. The pup was euthanased and postmortem examination revealed no gross lesions. Histopathology revealed bilateral regions of oedema, and areas of early malacia, within the caudate nucleus. Although the aetiology is not identified, the distribution of the lesions suggests a toxic insult or could be related to a developmental neurodegenerative disease. This case also gives an insight into the potential role of the caudate nucleus in fur seals.

BACKGROUND

This is a report on an unusual neurological case in a northern fur seal (Callorhinus ursinus). This case gives an insight into the role of the caudate nucleus and describes a potential toxin-induced encephalopathy involving the caudate nucleus, which has not been reported in northern fur seals, thus increasing the literature on brain disease in this species.

CASE PRESENTATION

A 7.4 kg northern fur seal pup stranded at Cayucos Beach, San Luis Obispo, California, USA, on November 19, 2010, and was transported to The Marine Mammal Center (TMMC) for treatment. On admission, the animal was noted to be underweight, lethargic, ataxic and had a head tremor.

After admission to TMMC, the patient was restrained and anaesthesia was induced with isoﬂurane (isoflurane; Halocarbon Products Corporation) via mask. It was then intubated and maintained on 1.5–2.5 per cent isoflurane. Dorsoventral and lateral projection radiographs of the skull, neck, thorax and abdomen were taken and were within normal limits. Ultrasonography of the cisterna magna using a micro convex transducer at 10 MHz frequency demonstrated no evidence of hydrocephalus. An attempt was made to collect cerebrospinal fluid, ultrasound guided, with a 1-inch 20-gauge needle, but blood contamination prevented accurate analysis. Blood was collected and submitted for repeat complete blood cell count (CBC) and protozoal serology. The latter included mean agglutination titre (MAT) to Toxoplasma gondii, Sarcocystis neurona and Neospora caninum, which were all negative (Brown and others 1974, Carlson-Bremer and others 2012). The CBC was unchanged.

After three weeks, the fur seal had not been heard vocalising, would not eat fish voluntarily and was abnormally gentle and calm with the animal care staff. Ataxia and head tremor were unchanged in severity.

One month after stranding, the fur seal was taken for MRI of the head with acquisition of T1-weighted image pre- and postgadolinium administration, T2-weighted image, proton density-weighted image, fluid-attenuated inversion recovery (FLAIR) and T2*W sequences and acquisition of images in three planes. The MRI revealed bilaterally symmetrical focal lesions of the rostrolateral caudate nucleus (Fig 1). The remaining structures included within the scan field of view were all within normal limits. The patient recovered uneventfully from anaesthesia.

MRI findings are non-specific, but the combination of observations among sequences was strongly suggestive of inflammation or oedema. The bilaterally symmetrical distribution was most suggestive of toxic or metabolic insult or immune-mediated disease, although other differentials, including developmental neurodegenerative disease, were also considered.

INVESTIGATIONS

Two days after stranding, blood was drawn from the caudal gluteal vein using a 1-inch, 22-gauge needle on a 3 ml syringe. In-house routine haematology and blood biochemistry revealed low iron (20 μg/dl, reference range 31–179 μg/dl) and low total protein (4.8 g/dl; reference range 7.1–8.9 g/dl), which were attributed to malnutrition (Lyons and others 1997, Norberg and others 2009, Spraker and Lander 2010, Norberg and others 2011). A week after stranding, the seal was manually restrained and anaesthesia was induced with five per cent isoflurane (isoflurane; Halocarbon Products Corporation) via mask. It was then intubated and maintained on 1.5–2.5 per cent isoflurane.

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Differential diagnosis

Although a variety of neurological diseases have been reported in marine mammals, the aetiologies reported in northern fur seals (C. ursinus) are...

**TREATMENT**
A consideration for the changes observed on the MRI was thiamine deficiency; therefore, the patient was given a three-day treatment of 1 ml of vitamin B complex given subcutaneously once a day. No improvement was observed. The patient was then treated with prednisone (0.5 mg/kg, prednisone; West-Ward Pharmaceuticals) for a month with no response. Due to the patient’s neurological state and poor prognosis, the animal was euthanased.

**OUTCOME AND FOLLOW-UP**
No gross lesions were detected on postmortem examination. Representative samples of all organs and the entire brain were preserved in 10 per cent neutral buffered formalin for histology. At cut section, the formalin-fixed caudate nucleus had no gross changes. Standard histological evaluation of sections of the brain revealed a bilateral region of oedema (most likely of the cytotoxic type), reactive astrocytes with vesicular nuclei and a few areas of early malacia with neuronal loss within the caudate nucleus (Fig 2). Around this region, there was a lesser degree of oedema throughout the caudate nucleus, into the adjacent cortex, and in the roof nuclei of the cerebellum. There was a notable amount of neovascularisation and a large glial scar suggesting a chronic component. All other tissues were histologically within normal limits.

**DISCUSSION**
Infectious causes for the brain lesions were excluded after the diagnostic work-up because there was no evidence of infectious aetiologies or evidence of exposure to known neurological pathogens on serology. Non-infectious encephalopathies seen in canids, such as granulomatous meningoencephalitis, were excluded because of the bilaterally symmetrical distribution of the lesions. Metabolic causes were considered unlikely given the normal blood work and the involvement of the caudate nucleus, but not the basal nuclei. Domoic acid toxicosis was ruled out as the hippocampus was bilaterally symmetrical without evidence of atrophy, and there were undetectable levels of domoic acid in the faeces and urine. (Lefebvre and others 2010). By exclusion, this meant that the bilaterally symmetrical lesions observed were most suggestive of toxic encephalopathy. Similar appearing lesions have been seen in the thalamus in harbour seals (Phoca vitulina) following inhalation of low-chain hydrocarbons (Spraker and others 1994). The glial scar most likely resulted from chronic insult as it represents healed tissue. One final consideration is a neurodegenerative disease, which has not been seen in marine mammals, but has been documented in Kerry Blue Terriers (Montgomery and Storts 1984).

The clinical and behavioural observations of this northern fur seal are similar to findings described in other species with specific caudate nucleus pathology. In dogs receiving haloperidol, diminished dopamine levels specific to the caudate nucleus resulted in head bobbing (Himwich and Glisson 1967). In the fur seal described here, a head tremor was noted. Domestic cats that had their caudate nucleus surgically removed exhibited marked docility, a friendly disposition and persistent purring (Villablanca 2010). Humans with select damage to the caudate nucleus do not show neurological abnormalities, but do show abnormal behaviour, including apathy and/or disinhibition (Villablanca 2010). Fur seals in the rehabilitation setting are typically very aggressive and vocalise frequently. However, in this case, this fur seal was gentle with handlers and never showed any aggression.

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**Contributors** VF and WVB managed the case and performed the postmortem examination. SD performed the ultrasound imaging and interpreted the radiographs and MRIs. TS performed the histopathology.

**Competing interests** None declared.

**Patient consent** Obtained.

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