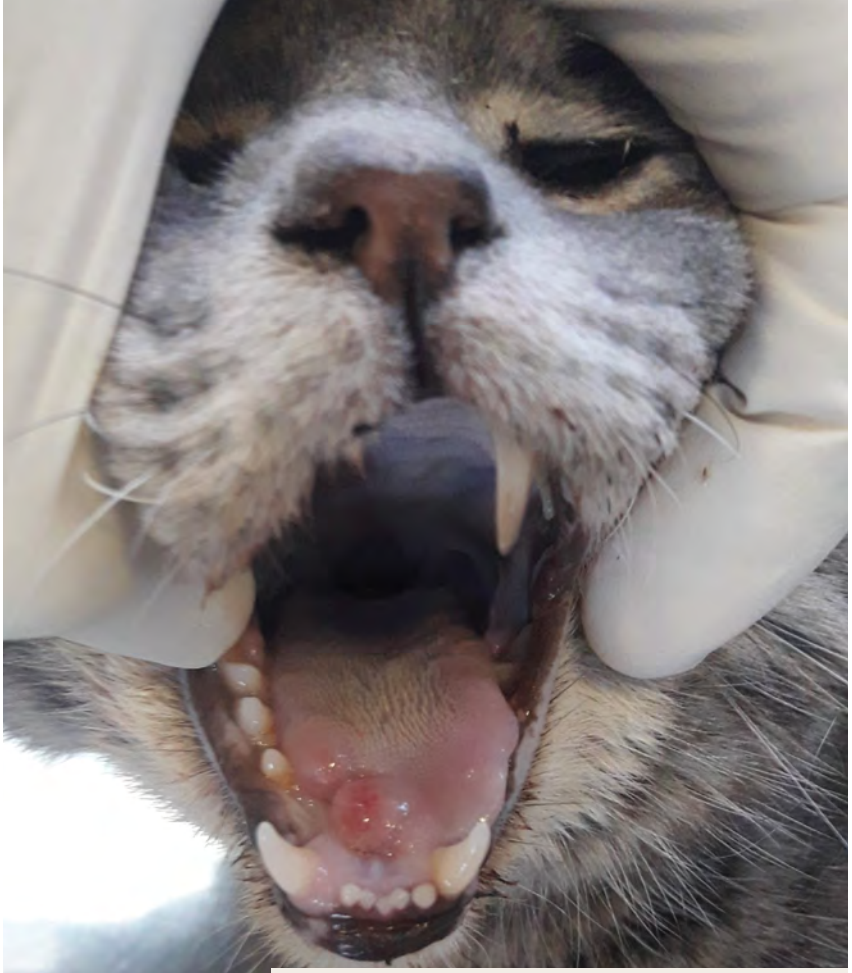

FIGURE 1: Raised nodule on the margin of the tongue.

The search for **the source**

Bernard Vaatstra, from Gribbles Veterinary Palmerston North, and **Vincent Girardot**, from Levin and Horowhenua Veterinary Centre, discuss a case of systemic cryptococcosis presenting as neurological disease in a cat.

CLINICAL HISTORY

A five-year-old desexed, female, domestic, medium-hair cat presented for veterinary attention after being missing for three days. The owner reported the cat was reluctant to eat and move, and was lethargic. On physical examination the cat had a body condition score of 4/9 (3kg) and was moderately dehydrated (approximately 8%). She had a temperature of 38.5°C, elevated heart rate (260 beats/minute), tachypnoea (70 breaths/minute) and normal blood pressure. The most notable finding was evidence of neurological dysfunction characterised by hind-limb ataxia, weakness and photophobia. A blood sample was collected and a complete blood count, basic biochemistry and electrolyte panel run on an in-house analyser. The only abnormality was a mild neutrophilia (11.53 x10^9/L, reference interval 2.3–10.29 x10^9/L) suggesting inflammatory demand.

During the ensuing day the neurological signs progressed to whole-body twitching and falling to the side. Hypersalivation developed, as well as a nasal discharge and wheezes on auscultation. Based on a clinical suspicion of toxoplasmosis, treatment with clindamycin was instituted 16 then 25mg/kg/day. At this point, the owners declined further testing including advanced imaging and serology. Prednisone was added to the treatment protocol (1mg/kg/day). Following two days on fluid therapy, the cat was discharged home on a course of clindamycin and prednisone.

There was mild clinical improvement in the following three days and the cat began eating and drinking again. Follow-up neurological exam revealed subtle residual ataxia and positional nystagmus. The prednisone treatment was discontinued.

Eight days later, the cat re-presented very lethargic, anorexic and constipated. Two nodules were found on the tongue (Figure 1). Prednisone was re-started and the cat was sent home after being given subcutaneous fluid. Another nine days later, the owners opted for euthanasia after progression to prostration and syringe feeding.

DIFFERENTIAL DIAGNOSES

Differential diagnoses for central nervous system (CNS) disease affecting the brain in cats include feline infectious peritonitis, toxoplasmosis, cryptococcosis, feline immunodeficiency virus (FIV), *Toxocara* larval migrans, bacterial meningitis, primary or metastatic neoplasia (notably lymphoma and meningioma), lysosomal storage disease, hepatic encephalopathy, feline dysautonomia and idiopathic epilepsy. In the New Zealand diagnostic laboratory setting, feline infectious peritonitis (FIP) and toxoplasmosis are the most common diagnoses pursued. Clinicians should also be aware of diseases exotic to New Zealand, including rabies, spongiform encephalopathy and Borna disease virus.

IMAGERY: SUPPLIED

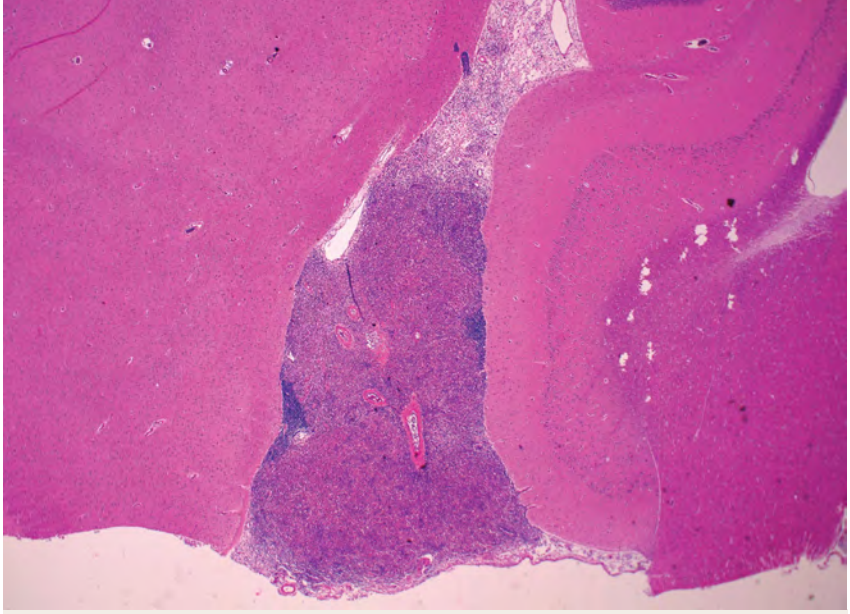

FIGURE 2: Brain with meninges expanded by inflammation. Haematoxylin and eosin stain, 20x magnification.

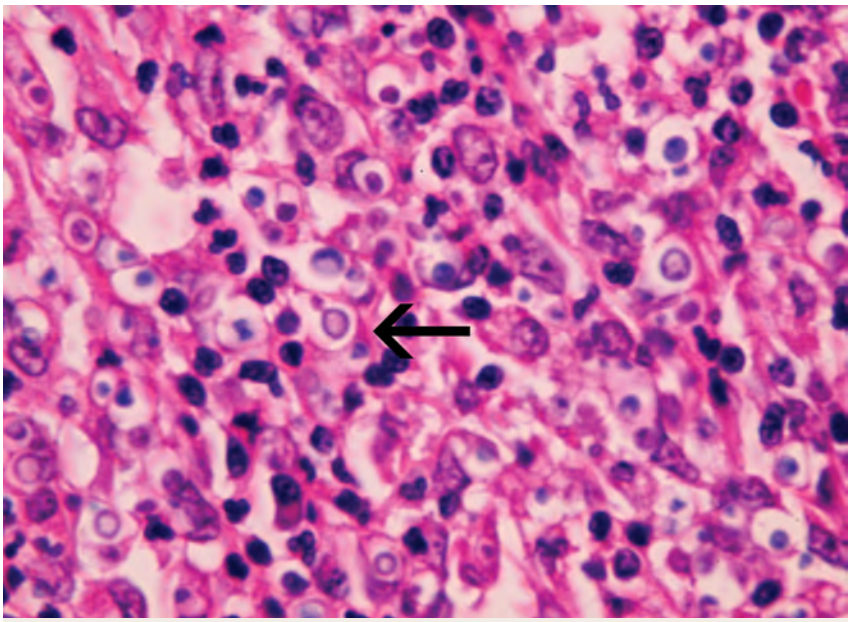

FIGURE 3: Brain with inflammatory infiltrate including many spherical to ovoid yeasts surrounded by clear capsules. One yeast showing budding (arrow). Haematoxylin and eosin stain, 1,000x magnification.

PATHOLOGY

At gross postmortem the cat was in poor body condition, weighing 2.31kg. A 3mm-diameter ulcer was noted on the left cornea. The meninges appeared reddened and congested. Both kidneys had multiple irregular nodules bulging from the cortical surface. A 5mm-diameter mass protruded from the right side of the tip of the tongue. Tissue samples were collected into 10% formalin for histological examination.

Microscopy of the brain sections revealed widespread expansion and disruption of the meninges, ventricles and adjacent neuropil by dense aggregates of epithelioid macrophages, moderate numbers of neutrophils and fewer plasma cells and lymphocytes (Figure 2). Myriad 5–10µm-diameter, round-oval yeasts displaying occasional narrow-based budding were distributed among the inflammatory cells. The yeasts were surrounded by a thick, clear capsule creating a 'soap bubble' appearance (Figure 3).

The tongue lesion was composed of nodular aggregates of inflammatory cells admixed with yeasts similar to those in the brain (Figure 4).

The kidneys and pancreas were disrupted by similar lesions to those in the brain and tongue (Figure 5).

DIAGNOSIS

The morphological diagnosis was granulomatous meningoencephalitis, glossitis, pancreatitis and interstitial nephritis with intralesional *Cryptococcus* sp.

DISCUSSION

Neurological diseases in cats are classified according to the DAMNIT-V system: degenerative, anomalous, metabolic, neoplastic, inflammatory, idiopathic, traumatic and vascular. A recent survey from Japan reported the following diagnoses in 174 cats with diseases localised to the brain: neoplasia (31.4%), idiopathic (29.1%), inflammatory (including infectious and immune mediated (13%), and the remainder a combination of degenerative, anomalous, vascular, metabolic and traumatic diseases (Nakamoto et al., 2019). An earlier UK survey of 286 cats with neurological disorders reported a somewhat different distribution of diagnoses, the largest category (92 cats) having inflammatory disease and 51% of those having FIP (Bradshaw et al., 2004).

In addition to a detailed neurological exam, advanced imaging and adjunct testing such as serology for toxoplasmosis, FIV, FIP and cryptococcosis, cerebrospinal fluid cytology and fluid analysis, routine biochemistry and haematology may aid antemortem diagnosis. However, even with the range of diagnostics available in referral centres, a specific antemortem diagnosis is only reached in 30–40% of cases. Postmortem histopathology is the gold standard for diagnosis. Even here, 17.8% of cats with neurological disease have no histological lesions (Bradshaw et al., 2004)

As it is with many cases in primary veterinary care, cost considerations

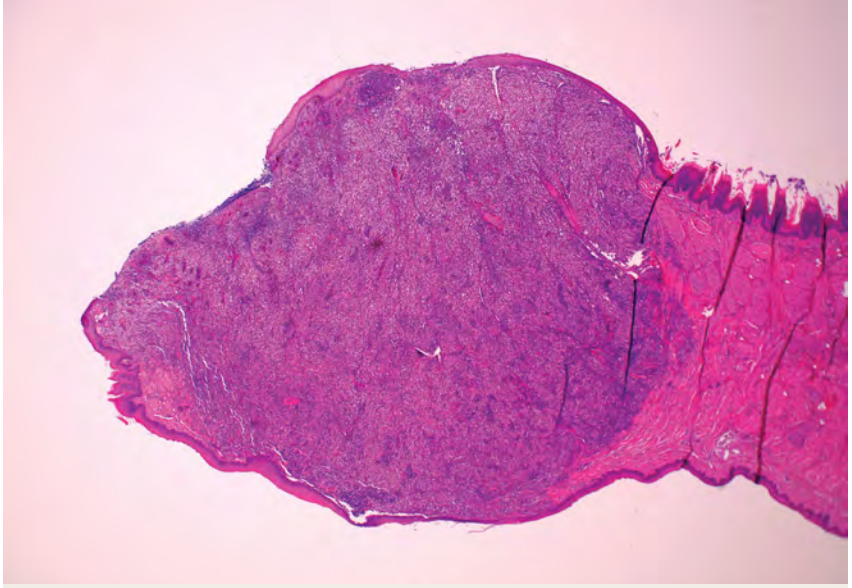

FIGURE 4: Tongue with nodular cryptococcosis lesion at the margin. Haematoxylin and eosin stain, 20x magnification.

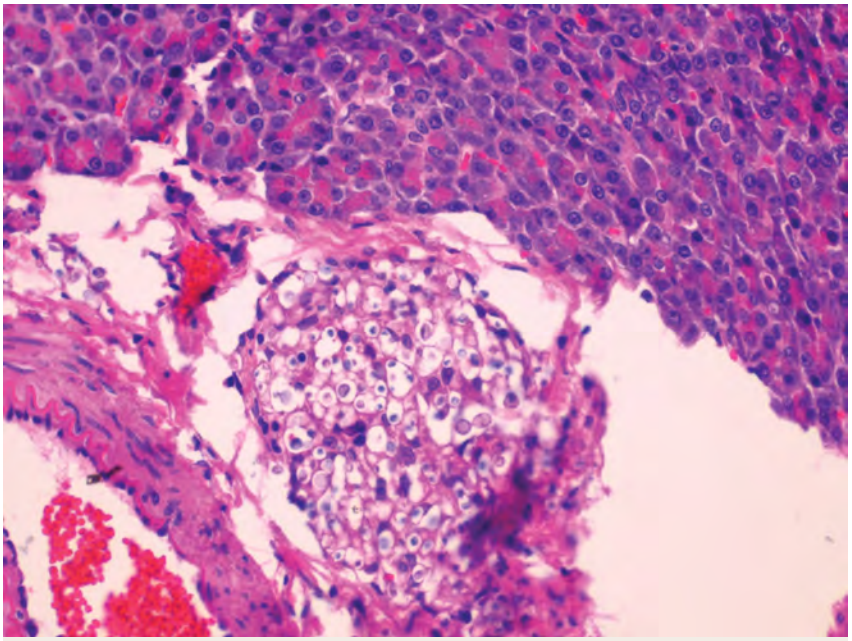

FIGURE 5: Pancreas with interstitial cluster of *Cryptococcus* sp. organisms. Haematoxylin and eosin stain, 400x magnification.

precluded advanced imaging and extensive diagnostics antemortem. However, a definitive diagnosis was possible in this case because Ministry for Primary Industries funded postmortem testing in order to exclude exotic diseases. Since brain disease is difficult to diagnose precisely, even with sophisticated testing, it is not surprising that many companion animal CNS disease cases remain undiagnosed in the primary care setting. The information provided by pathological examination is therefore very helpful in informing clinicians and diagnosticians of the range of possible causes for future consideration.

Cryptococcosis is the most common systemic mycosis of cats. While FIP and toxoplasmosis more frequently cause CNS disease, cryptococcosis should also be considered an important rule-out. Most cases are caused by *Cryptococcus neoformans* or *Cryptococcus gattii*. Infection is typically acquired from the environment, eg, bird droppings (especially pigeons), soil and decaying organic material.

The initial site of infection by basidiospores is usually the nasal cavity. The lungs and gastrointestinal tract may also act as portals of infection. Interestingly in this case no nasal lesion was detected, but there was a focus of infection in the tongue. Hence a penetrating injury to the tongue may have been the initial site of inoculation.

Cryptococcus infections in cats induce less inflammation than they do in dogs, which may reflect differences in infecting strains and/or underlying unrecognised defects in the immune or inflammatory response. An Australian study showed that Siamese, Birman and Ragdoll cats are overrepresented. Immunocompromised cats (eg, FIV, feline leukaemia virus positive) are not necessarily more prone to cryptococcosis, but have more trouble clearing the infection. Amphotericin B, ketoconazole, fluconazole and itraconazole have all been used to treat infected cats. Surgical excisions of any nodules in the skin or mucosa are also advised. It is recommended to continue treatment until a negative antigen test is obtained (Pennisi et al., 2013). VS

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