

FELINE INFECTIOUS PERITONITIS AND CENTRAL NERVOUS SYSTEM

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Rita Gonçalves looks at the coronavirus mutation, FIP, and considers how the dry form can be a cause of eye abnormalities and neurological dysfunction

FELINE infectious peritonitis (FIP) is a progressive systemic disease with a wide spectrum of clinical signs, which is ultimately fatal.

It is an immune-mediated condition caused by a mutation of the common pathogen feline coronavirus (FCoV). FCoV has two biotypes – the feline enteric coronavirus (FECV) causing mild enteritis, and the feline infectious peritonitis virus (FIPV) that causes FIP.

The mutation from FECV to FIPV has been reported to occur most probably during primary infection (although it may also happen because of recurrent bouts of virus replication) and in kittens, as in both cases higher levels of FECV replication are present. In the second case, there is also less resistance to mutation once it has occurred.

FIP can occur wherever FECV is present, so it is ubiquitous among most cat populations worldwide, although it is particularly common in catteries and multi-cat households. The infection is spread by the faecal-oral route and viral shedding occurs approximately within a week of exposure. FECV shedding can be transient, recurrent or chronic over months to years. Immunity in recovered animals is weak and re-infections are not uncommon.

Most deaths from FIP occur in young cats under one year of age and are uncommon in older

animals. Intact and purebred cats appear more likely to succumb from FIP and some breeds, such as the Bengal, birman, ragdoll, rex, Abyssinian and the Himalayan, have been reported to be at higher risk. Other factors such as stress and co-infection with feline leukaemia virus also worsen prognosis.

Approximately 30 per cent of cases with clinical FIP involve the central nervous system (CNS). The vast majority of these patients suffer from the dry form of this disease. In young cats from multi-cat environments, presenting with insidious progressive neurological and ocular abnormalities, FIP should be considered as one of the most likely differential diagnoses.

Pathogenesis

The FIPV has a tropism for macrophages, which is an essential step in the transformation from FECV to FIPV and from what is a fairly innocuous and enterocyte localised virus to a highly virulent systemic macrophage pathogen.

The genetic basis for this difference in tropism is not fully understood.

When the FIPV enters the target macrophage it replicates quite slowly for the initial two weeks or so, followed by a significant increase in viral replication and spread with the appearance of virus-specific antibodies.

FIP has two clinical forms: the effusive or wet form and the non-effusive or dry form.

In the wet form, fibrinous peritonitis is present with excessive abdominal fluid and mainly humoral antibody response with very little cellular immunity.

In contrast, the dry form is mainly associated with the formation of perivascular granulomas around blood vessels and there is both humoral immunity and partial cell-mediated immunity. The dry form is typically associated with the development of neurological signs and is thought to result from a state of partial protective immunity.

Immunity to FIPV is mostly cell mediated and involves a change in the way the macrophages respond to the virus, gaining the capacity to destroy the FIPV, rather than incubate and disseminate the virus. If the cellular immunity develops early in the course of infection and is potent enough, virus replication will be halted and clinical signs will not develop.

If humoral immunity occurs, but the cellular response fails to take place, then the wet form of FIP will occur.

However, when an intermediate stage of immunity develops, with strong humoral and weak cellular immunity, the virus is contained to a certain extent, but not eliminated and this results in the dry

form of the disease. The organ distribution of the dry form is somewhat explained by this – in the initial stage of the infection, the virus reaches several tissues, such as the brain and eyes, via infected monocytes; as the immune response has difficulty crossing the blood-brain barrier, the infected monocytes that would have been cleared from other parts of the body remain unharmed. This explains why ocular and CNS lesions predominate in the dry form of FIP.

Clinical signs

Most people are aware of the typical clinical signs associated with the wet form of FIP – insidious and progressive malaise, fluctuating fever, inappetence, weight loss and the characteristic abdominal distension associated with accumulation of a yellow-tinged, cloudy, mucinous fluid. Dyspnoea associated with pleural involvement and thoracic effusions may also be a feature of this form of the disease.

Dry FIP occurs less commonly than the wet form, but the proportion of cats with this presentation has been increasing over past decades.

As the name suggests, abdominal and/or thoracic effusions are not a feature of this form and the most common tissues affected are the CNS and the eyes.

The clinical expression of the CNS involvement is varied, but commonly results in central vestibular signs, such as tetraparesis, ataxia, head tilt, cranial nerve deficits, nystagmus and loss of balance ([Figure 1](#)). This occurs due to compression of the brainstem structures from difficulty of cerebrospinal fluid (CSF) drainage at the level of the cerebellomedullary region. Behavioural changes and seizures may be secondary to the formation of hydrocephalus from disease of the choroid plexus and ependyma.

In some cases, spinal cord disease causing signs, such as spinal pain and pelvic limb weakness and incoordination, are the only abnormalities identified. FIP is the most common cause for spinal cord disease in cats under two years of age and one of the most common (along with neoplastic conditions and other inflammatory conditions) in cats of all age.

Ocular abnormalities, such as uveitis and chorioretinitis, are commonly seen in association with the neurological signs, and recognition of abnormalities affecting these two tissues should raise suspicions of FIP (although toxoplasmosis, feline leukaemia virus infection and lymphoma should also remain as differential diagnoses).

Changes in the colour or shape of the iris, as well as keratic precipitates (from accumulation of fibrin macrophages and other inflammatory cells), are also characteristic of dry FIP and should be looked for.

Diagnosis

Antemortem diagnosis is often difficult as definitive diagnosis requires detection of intracellular antigen in macrophages in samples obtained from effusions, or histological examination of organ biopsy samples, which are not often available when the disease is restricted to the CNS. Tentative diagnosis should be based on cumulative odds rather than a single test, and is usually made on the basis of identifying typical haematological and serum biochemical abnormalities, serology on serum and/or CSF, CSF analysis and diagnostic imaging findings. The presence of compatible neurological and ocular signs should raise suspicion and warrant further investigation. Routine haematology analysis often shows non-specific findings, such as lymphopenia and neutrophilia. Non-regenerative anaemia is also common, but occurs in almost any chronic feline disease.

On the biochemistry profile, the most significant abnormality tends to be hyperglobulinaemia, which is found in approximately 50 per cent of cats with effusion and 70 per cent of cats without effusion. The albumin-to-globulin ratio has a higher diagnostic value than either parameter on its own as, if the liver was affected, both albumin and globulin concentrations would be decreased. A cut-off value of 0.8 has been determined, above which FIP is very unlikely. Values of 0.6 or less are, on the other hand, highly suggestive of an inflammatory process, and most commonly of FIP.

Serology testing is also useful, and significant increases in serum titres of FCoV antibodies are suggestive of the disease. Nonetheless, cats with FIP may have low titres and many cats with high titres never develop FIP.

Measurement of anti-coronavirus immunoglobulin G in the CSF is also a useful test to perform, but, unfortunately, it is also not specific for this condition as it often accompanies serum titres. In view of these limitations, FIP diagnosis should never rely on serology alone.

Another test commonly used as an indicator of this disease is measurement of serum alpha-1-acid glycoprotein (AGP), an acute-phase protein that increases significantly in infectious and inflammatory conditions. AGP concentrations greater than 1.5g/L in serum, plasma or effusion samples have been found to be significantly associated with FIP, although high levels may be seen with any inflammatory process.

Analysis of the CSF yields variable results, although most commonly it shows significantly high protein concentration and an increase in the white blood cell count (neutrophils, lymphocytes and macrophages). Occasionally it can be normal in affected cats. Advanced imaging findings (mainly magnetic resonance imaging) are very particular to this condition, usually showing periventricular contrast enhancement, ventricular dilation and hydrocephalus ([Figure 2](#)).

On postmortem examination, pyogranulomatous inflammatory cell infiltration of leptomeninges, choroid plexus, ependyma, and brain and spinal cord parenchyma may be found. A surfacerelated pattern is present and the inflammatory ependymal lesions at the level of the mesencephalic aqueduct and central canal often result in hydrocephalus and hydromyelia (dilation of the central canal of the spinal cord).

Treatment

The prognosis for cats with FIP is poor, with mean survival times after diagnosis of approximately a week. No therapy has proven efficacy, although using corticosteroids may slow disease progression by suppressing the inflammatory and detrimental immune response. The use of feline interferon-omega has also been advocated, as it inhibits FIPV in vitro and in initial uncontrolled studies appeared to be helpful in vivo. However, a larger double-blind study showed that its use did not increase survival times in comparison to a placebo.

If FIP has been diagnosed in a cat that belongs to a multicat household or breeding cattery, reducing contamination and risk of transmission can be achieved by keeping small groups of cats per room, observing strict hygiene, diminishing stressful conditions to a minimum and providing outdoor access so that cats can bury their faeces.

In conclusion, neurological signs in cats with FIP include ataxia and vestibular signs, such as nystagmus and balance problems, seizures, behavioural changes and spinal cord dysfunction. When these are accompanied by ocular signs, for example, uveitis, keratic precipitates and chorioretinitis, FIP should be considered as a likely differential diagnosis.

Definitive diagnosis is difficult as it requires histopathology or identification of FCoV antigen, so it usually relies on a combination of haematological, biochemical, serological and diagnostic imaging findings. Prognosis is poor.

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