J. Comp. Path. 2016, Vol. 154, 3–8

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INFECTIOUS DISEASE

# Myocarditis caused by Feline Immunodeficiency Virus in Five Cats with Hypertrophic Cardiomyopathy

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## Summary

Viral infections have been implicated as the cause of cardiomyopathy in several mammalian species. This study describes hypertrophic cardiomyopathy (HCM) and myocarditis associated with feline immunodeficiency virus (FIV) infection in five cats aged between 1 and 4 years. Clinical manifestations included dyspnoea in four animals, one of which also exhibited restlessness. One animal showed only lethargy, anorexia and vomiting. Necropsy examination revealed marked cardiomegaly, marked left ventricular hypertrophy and pallor of the myocardium and epicardium in all animals. Microscopical and immunohistochemical examination showed multifocal infiltration of the myocardium with T lymphocytes and fewer macrophages, neutrophils and plasma cells. An intense immunoreaction for FIV antigen in the cytoplasm and nucleus of lymphocytes and the cytoplasm of some macrophages was observed via immunohistochemistry (IHC). IHC did not reveal the presence of antigen from feline calicivirus, coronavirus, feline leukaemia virus, feline parvovirus, *Chlamydia* spp. or *Toxoplasma gondii*. The results demonstrate the occurrence of FIV infection in inflammatory cells in the myocardium of five cats with myocarditis and HCM.



*Keywords:* feline immunodeficiency virus; hypertrophic cardiomyopathy; immunohistochemistry; myocarditis

Viral infections have been suggested to be a possible cause of cardiomyopathy in various mammalian species (Barbaro *et al*., 1998; Badorff *et al*., 1999; Meurs *et al*., 2000; Yearley *et al*., 2006; Sani, 2008). Human immunodeficiency virus (HIV) and simian immunodeficiency virus (SIV) have been detected in myocarditis lesions in man and apes, respectively (Barbaro *et al*., 1998; Yearley *et al*., 2006; Pozzan *et al*., 2009). However, the ability of HIV to infect cardiomyocytes is surrounded by controversy, as the entry pathway of HIV into these cells has not been established, given that they do not express CD4 receptors (Barbaro *et al*., 2001; Currie and Boon, 2003). Moreover, it is likely that other factors also play a role in the aetiopathogenesis of HIV-induced heart lesions, such as opportunistic infections, the immune response to the viral infection, cardiotoxic drugs, malnutrition and prolonged immunosuppression (Sani, 2008).

Myocardial inflammation is often observed in systemic diseases, yet rarely does it manifest as primary changes in the heart. The possible causes of this condition include infection by *Trypanosoma cruzi*, *Toxoplasma gondii*, feline parvovirus (FPV), *Bartonella henselae* and, in some cases, opportunistic fungi (Maxie and Robinson, 2007; Varanat *et al*., 2012).

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0021-9975/$ - see front matter
http://dx.doi.org/10.1016/j.jcpa.2015.10.180

Feline immunodeficiency virus (FIV) is a Lentivirus whose structure, replication cycle and pathogenesis are similar to those of HIV (Hosie *et al.*, 2011). Infected cats are generally presented with lesions associated with immunodeficiency such as gingivostomatitis, chronic rhinitis, lymphadenopathy, immune-mediated glomerulonephritis and dermatitis, although some animals may not exhibit any lesions (Hosie *et al.*, 2009; Hartmann, 2011). Thus far, FIV has not been associated with lesions in the cardiovascular system. This study describes myocarditis associated with FIV infection in five cats with hypertrophic cardiomyopathy (HCM). Virus was detected in cardiac lesions via immunohistochemistry (IHC). The myocarditis associated inflammatory infiltrate was characterized using cell markers for lymphocytes and macrophages.

The five cats were submitted for routine necropsy examination to the Department of Veterinary Pathology, Universidade Federal do Rio Grande do Sul (UFRGS), between 2010 and 2012. The cats had gross and microscopical changes consistent with HCM. Organ and tissue samples were fixed in 10% neutral buffered formalin for 24–48 h, then processed

**Table 1**
**Primary antibodies and immunohistochemical protocols applied in the study**

| *Antibody* | *Antigen retrieval* | *Dilution* | *Detection method* | *Chromogen* |
|---|---|---|---|---|
| **Monoclonal** | | | | |
| Mouse anti-feline immunodeficiency virus, p24 gag (AbD Serotec, Kidlington, UK) | 40 min, 100°C, 0.01 M citrate buffer pH 6.0 | 1 in 100 | LSAB-AP | PR |
| Mouse anti-feline calicivirus, FCV2-16 (Custom Monoclonals, Sacramento, California, USA) | 20 min, 37°C, P-XIV | 1 in 50 | MACH 4 | AEC |
| Mouse anti-coronavirus, FIPV3-70 (Santa Cruz Biotechnology, Dallas, Texas, USA) | 20 min, 100°C, 0.01 M citrate buffer pH 6.0 | 1 in 300 | LSAB-HRP | DAB |
| Mouse anti-feline leukaemia virus, gp 70 (AbD Serotec) | 40 min, 100°C, Tris–EDTA buffer pH 9.0 | 1 in 500 | LSAB-AP | PR |
| Mouse anti-feline/canine parvovirus (AbD Serotec) | 20 min, 37°C, P-XIV | 1 in 1,000 | LSAB-HRP | AEC |
| Mouse anti-*Chlamydia* spp., ACI (Fitzgerald Industries, Acton, Massachusetts, USA) | 5 min, 37°C P-K (ready to use) | 1 in 100 | LSAB-HRP | AEC |
| Mouse anti-CD79αcy, HN57 (Dako, Carpinteria, California, USA) | 20 min, 100°C, Tris–EDTA buffer pH 9.0 | 1 in 100 | LSAB-HRP | DAB |
| **Polyclonal** | | | | |
| Goat anti-*Toxoplasma gondii* (VMRD, Pullman, Washington, USA) | 10 min, 37°C trypsin 0.1% and microwave (700 W), 2 min, 0.01 M citrate buffer, pH 6.0 | 1 in 1,000 | LSAB-HRP | DAB |
| Rabbit anti-human lysozyme, EC 3.2.1.17 (Dako) | 10 min, 37°C P-K | 1 in 200 | LSAB-HRP | DAB |
| Rabbit anti-human CD3 (Dako) | 20 min, 37°C P-XIV | 1 in 500 | LSAB-AP | PR |

P-XIV, protease XIV (Sigma); P-K, proteinase-K (Dako); LSAB-HRP, biotin–peroxidase–streptavidin (Dako); LSAB-AP, streptavidin–biotin–alkaline phosphatase (Dako); MACH 4, universal HRP-polymer (Biocare); AEC, 3-amino-9-ethylcarbazole (Dako); DAB, 3, 3′ diaminobenzidine (Dako); PR, permanent red (Dako).