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SHORT PAPER

Orchitis in a Cat Associated with Coronavirus Infection

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Summary

A case of severe, pyogranulomatous and necrotizing orchitis in a cat, which later succumbed to systemic feline infectious peritonitis (FIP), is described. The 3·5-year-old cat, positive for feline immunodeficiency virus infection, presented with a left testicular enlargement. A few months after castration the animal was humanely destroyed due to declining health. Post-mortem examination revealed inflammatory lesions in abdominal organs and in the brain compatible with FIP. Infection was confirmed with a reverse transcriptase–polymerase chain reaction test and by immunohistochemical demonstration of coronavirus antigen in the affected tissues, including the left testicle. FIP is usually a systemic disease. However, lesions and presenting clinical signs in a single organ system such as the brain are not uncommon. The results of this case study indicate that orchitis, although rare, should be on the list of lesions of FIP.

Feline infectious peritonitis (FIP) is an immune-mediated disease of young cats, initiated by a viral infection. The causative virus, feline infectious peritonitis virus (FIPV), is a mutant of feline enteric coronavirus (FECV). Whereas FECV has affinity for enterocytes, FIPV replicates in macrophages and spreads throughout the body in infected monocytes. The course of an infection depends in part upon the type and strength of the immune response (Pedersen, 1995; Foley et al., 1998; Kipar et al., 1998; Paltrinieri et al., 1998). Two major clinico-pathological forms of FIP are recognized. An effusive form, which occurs in the absence of cell-mediated immunity (CMI), is characterized by the accumulation of fluid in body cavities. A non-effusive form, which develops in the presence of weak CMI, is characterized by proliferative inflammatory lesions in parenchymatous organs, the central nervous system, and the eyes (Pedersen, 1995; Foley et al., 1998; Paltrinieri et al., 1998), the clinical manifestations depending upon the organs affected. The histopathological lesions, which are similar in both forms of FIP, are characterized by vasculitis and perivascularitis in serous membranes and in various organs. The inflammatory reaction, which is heterogeneous, includes disseminated granulomatous, pyogranulomatous, fibrinonecrotic and lympho-plasmacytic inflammation (Pedersen, 1995; Foley et al., 1998; Kipar et al., 1998).

A 3·5-year-old male, domestic short-hair cat was presented for examination as the result of decreased appetite, cough and malaise. Clinical examination revealed pyrexia, conjunctivitis, and scrotal swelling caused by an enlarged left testicle. The animal gave a positive test reaction for feline immunodeficiency virus (FIV). Antibiotic treatment led to a temporary improvement of general health but no decrease in testicular size. Further examination 2·5 months later revealed a left testicle that was twice the normal size, firm and tender. The right testicle was small and soft. A tumour was suspected in the left testicle and the cat was castrated. Both testicles were fixed in formalin and submitted to the Section of Pathology, National...
Veterinary Institute, Oslo. The histopathological diagnosis was a unilateral pyogranulomatous and necrotizing orchitis. The cat received further antibiotic treatment, and again some slight but temporary clinical improvement was seen. However, the animal remained lethargic and when antibiotic therapy was discontinued it gradually lost appetite and developed neurological signs. The cat was humanely destroyed 4 1/2 months after castration.

Post-mortem examination was performed at the Section of Pathology, National Veterinary Institute, Oslo. Macroscopic lesions, which were confined to the abdominal organs, were indicative of non-effusive FIP. The renal capsules were thickened and both kidneys were enlarged due to multiple, often coalescing, white lesions within the renal cortices. The spleen was moderately enlarged and cut surfaces showed prominent lymphoid follicles. The abdominal lymph nodes, especially the mesenteric lymph nodes, were enlarged. The carcass showed signs of severe constipation. Tissue samples from the brain, lung, heart, kidneys, renal capsules, mesenteric lymph nodes, liver and spleen were fixed in 10% neutral buffered formalin, processed by routine methods, sectioned at 4 μm and stained with haematoxylin and eosin (HE). The formalin-fixed testicles submitted previously had been subjected to similar procedures; in addition, however, sections of both testicles were stained by the periodic acid-Schiff (PAS), Gram and Ziehl-Neelsen (ZN) methods for fungi, for gram-positive and gram-negative bacteria, and for acid-fast bacteria, respectively.

Histological examination revealed a severe subacute to chronic inflammation in the left testicle (Fig. 1). There was effacement of the normal architecture due to a multifocal to coalescing inflammatory cell infiltration. Many large, necrotic and purulent foci were surrounded by macrophages, lymphocytes and plasma cells. There were also several lymphoid follicles with germinal centres throughout the tissue. Scattered intact but degenerated seminiferous tubules were present. The inflammation involved the mediastinum testis and, multifocally, the testicular capsule. In the epididymis, a mild, mixed inflammatory cell reaction was present, especially around and sometimes involving the walls of veins. A few mononuclear inflammatory cells were seen around one vessel in the mediastinum of the right testicle, and the seminiferous tubules were atrophic. No fungi or bacteria were detected histologically within the lesions of the left testicle. Histopathological lesions compatible with FIP were present in the visceral peritoneum, kidneys, renal capsules, mesenteric lymph nodes, brain and lungs. In addition, occasional protozoal cysts were seen in the brain, giving a positive immunohistochemical reaction with Toxoplasma gondii antiserum. A very mild inflammatory cell reaction was seen around one of these cysts, but the remainder were inert.

The avidin–biotin–peroxidase complex (ABC) method for demonstrating coronavirus antigen was performed on formalin-fixed, paraffin wax-embedded tissue. A monoclonal antibody, 63I, produced by immunizing mice with transmissible gastroenteritis virus (TGEV) capsid protein p56, was used (Tammer et al., 1995). With this method, coronavirus antigen was demonstrated in the left testicle (Fig. 2), choroid plexus of the brain, both kidneys, renal capsules, spleen and a mesenteric
lymph node. Coronavirus antigen was not demonstrated in the right testicle or liver.

A one-tube reverse transcriptase–polymerase chain reaction test for feline coronavirus, based on the amplification of a sequence of the 7b gene common to the known feline coronavirus strains (Gut et al., 1999), was run on formalin-fixed, paraffin wax-embedded tissue from the brain, kidneys, renal capsules and left testicle. All the tissues were positive except brain.

The testicle is an immunologically privileged organ, in which local factors prevent autoimmunity to spermatozoal antigens and protect the tissue from deleterious systemic effects. These protective factors include the blood–testis barrier and immunological regulation. The blood–testis barrier has an epithelial and an endothelial component. The epithelial barrier of Sertoli cells and smooth muscle cells prevents contact between spermatogenic cells and blood constituents (Holash et al., 1993; Mukasa et al., 1995). The endothelial barrier is provided by the testicular capillaries, presumably in conjunction with the Leydig cells. Although not as efficient a barrier as the capillaries of the brain, the testicular capillaries are less permeable than most vascular beds (Holash et al., 1993). In addition to the blood–testis barrier, local immune mechanisms play a role in the “down-regulation” of autoimmunity and inflammatory responses (Mukasa et al., 1995). Disruption of the blood–testis barrier, due for example to local trauma or inflammation, may lead to the breakdown of spermatozoal sequestration. Spermatogenic antigens then become exposed to the immune system, leading to the formation of anti-sperm antibodies. An immune-mediated orchitis, characterized by lympho-plasmacytic infiltration, tubular destruction and foreign body granulomatous reaction to dislodge sperm, may then compound the initial testicular lesion (Ladds, 1993; Mukasa et al., 1995).

Oorchitis is relatively rare in animals, cats being no exception. Bacteria, reaching the testicles via the blood, ductus deferens or wounds of the scrotal skin, are the most common causes of inflammation, together with trauma (Ladds, 1993; Foster et al., 1996). Periorchitis is a recognized clinical manifestation of the effusive form of FIP. The lesion in the tunica vaginalis is an extension along the inguinal canal of the inflammatory reaction in the peritoneal cavity (Ladds, 1993; Pederssen, 1995). A bilateral orchitis in a cat, ascribed to FIP, was recently reported by Foster et al. (1996), but coronavirus infection was not confirmed; the major clinical sign in this cat was testicular enlargement, but gradually other organ systems became affected.

The histomorphological lesions in the testicle of the cat in the present study, together with the demonstration of coronavirus, strongly support the diagnosis of a FIPV-induced orchitis. Two types of hypersensitivity immune responses appear to play a role in the development of FIP lesions, namely types III and IV (Paltrinieri et al., 1998). In type-III hypersensitivity, pathogenic immune-complexes (ICs) are formed and deposited in and around blood vessels. This leads to a cascade of events culminating in vasculitis, disseminated intravascular coagulation, tissue inflammation and necrosis of the Arthus type (Foley et al., 1998; Kipar et al., 1998; Paltrinieri et al., 1998). Since orchitis is not a common feature of FIP, predisposing factors are likely to have played a role in the present case. Inflammation, due for example to trauma, may have disrupted the endothelial blood–testis barrier, promoting the deposition of circulating ICs or ICs production in situ. Disruption of the epithelial blood–testis barrier would further exacerbate the inflammatory cell reaction.

Concurrent infections, especially with feline leukaemia virus (FeLV), are potential predisposing factors for the development of FIP in coronavirus-infected cats (Pederssen, 1995; Kipar et al., 1998). Infection with the FIV may, in the same way as FeLV, adversely affect CMI, thereby predisposing to FIP lesions (Kipar et al., 1998). The cat in the present study was positive for FIV but, other than FIP, had no lesions indicative of an immunosuppressed state. FIV infection was reported by Davidson et al. (1993) to predispose to generalized infection with Toxoplasma gondii. However, the Toxoplasma gondii cysts in the brain of the cat in the present case were presumably of no clinicopathological consequence.

Although lesions of non-effusive FIP may occur in a single organ system such as the brain, eye or the intestine, a systemic disease usually develops gradually (Foley et al., 1998). We propose that the testicles be included on the list of single organ systems affected in FIP. The differential diagnosis of orchitis in cats should include FIP, which would necessitate a guarded prognosis.

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