Pyometra in a red fox (*Vulpes vulpes*) caused by a *Staphylococcus pseudintermedius* infection

Pyometra bij een vos (Vulpes vulpes) *veroorzaakt door een infectie met* Staphylococcus pseudintermedius

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ABSTRACT

A female adult red fox was found dead in the Flemish countryside (Belgium). At necropsy, a pronounced global distention of the uterus was noted with a prominent dilation of the upper end of the right horn and two dilations of the external wall (myometrium) of the left horn. The uterine lumen was filled with a green to yellowish pasty material. A pure culture of *Staphylococcus pseudintermedius was isolated.* The diagnosis of pyometra caused by *S. pseudintermedius* was made. Pyometra in wild canids has been rarely reported. The cause of death is suggested to be similar to the cause described in dogs, namely septic shock. To the authors' knowledge, this is the first case report of closed pyometra with isolation of *S. pseudintermedius* in a red fox.

SAMENVATTING

Een vrouwelijke volwassen vos die dood werd aangetroffen op een veld in Vlaanderen (België) werd binnengebracht voor autopsie. De uterus was opvallend vergroot met dilatatie van de rechterhoorntop en dilataties van het myometrium van de linkerhoorn. Het lumen van de uterus was gevuld met groengele pasteuze inhoud. Het bacteriologisch onderzoek van deze inhoud resulteerde in een reincultuur van *Staphylococcus pseudintermedius*. De diagnose van pyometra veroorzaakt door *S. pseudintermedius* werd gesteld. Pyometra bij wilde hondachtigen is zelden beschreven. Er wordt aangenomen dat de reden van sterfte gelijkaardig is aan die bij de hond, namelijk septische shock. Volgens de auteurs is dit het eerste beschreven geval van een gesloten pyometra met isolatie van *S. pseudointermedius* bij een volwassen vos.

INTRODUCTION

The red fox (*Vulpes vulpes*) is a highly opportunistic and successful wild canine, having the largest global distribution of any existing terrestrial carnivore. Its dispersal patterns appear related to population density, interspecies competition and habitat changes of the species (Lawler et al., 2017).

In northern Belgium, i.e. Flanders, there has been a spectacular increase in the distribution and density of the red fox population, resulting in the dispersion of the fox over the whole territory of Flanders (Vervaeke et al., 2003).

All canid species studied to date are reported to be monestrous, and most of them have only one seasonal cycle per year in the wild (Valdespino et al., 2002). Cystic endometrial hyperplasia (CEH) in canids can result in pyometra, hematometra or hydrometra, and many features of these uterine diseases can make them difficult to differentiate. Canine pyometra may present clinically with inappetence, depression, polydipsia, lethargy and abdominal distension, with or without vaginal discharge, i.e. closed form. As for pets, in most cases, the owners notice the clinical signs and take appropriate measures. In wild animals however, clinical signs are much more difficult to detect (Kang et al., 2021). Pyometra is a life-threatening condition and, if undetected or untreated, it can result in death (Asa et al., 2014). In fact, if pyometra is not diagnosed and treated in the early stages of infection, the inte-

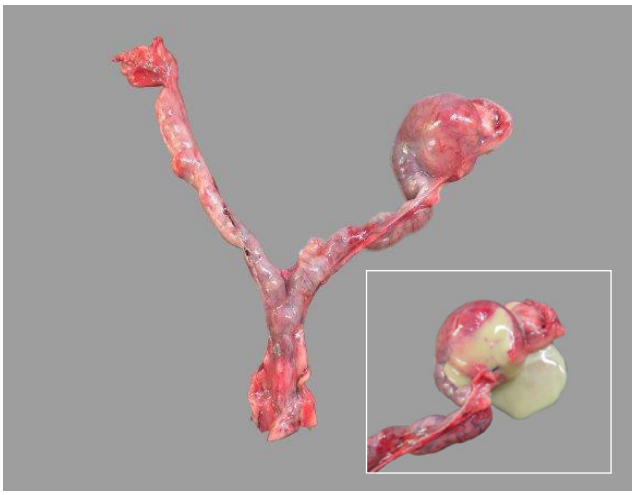

Figure 1. Macroscopical overview of the excised uterus. The uterus is globally enlarged with nodular dilatation of the proximal right uterine horn. Inset: Presence of green yellowish pus in the uterine lumen and macroscopical aspect of the right ovarium (*).

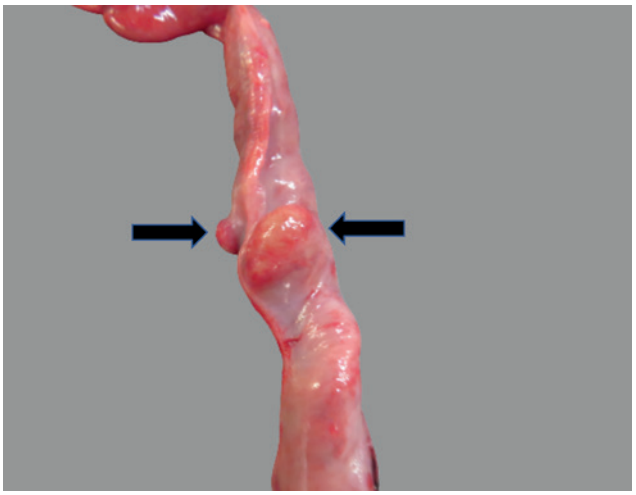

Figure 2. Detail of the myometrial dilatations in the left uterine horn (arrows).

grity of the uterine wall may be affected, resulting in a life-threatening peritonitis. Additionally, the inflammation in the uterus has the potency to result in systemic illness due to endotoxemia and sepsis (Hagman, 2004). In that case, the prognosis is poor, and if not properly and effectively treated within 24 to 48 hours, death may occur. To the authors' knowledge, this is the first report of closed pyometra in an adult vixen (*Vulpes vulpes*) caused by *S. pseudintermedius*.

Case history and necropsy

The animal was found dead in the countryside in February 2023 without evidence of visible lesions or trauma. The animal was submitted to the pathology department of Dierengezondheidszorg Vlaanderen (DGZ), where a full necropsy was performed.

At necropsy, the animal was found to be in rather good body condition and weighed 5.75 kg. The average weight of red foxes is 6-7 kg for males and 5-6 kg for females (www.mammal.org.uk). The heart was dilated (mainly right ventricle) with several petechiae on the level of the epicardium. The stomach showed several small mucosal stress ulcers and a liquid, serohemorraghic content. Liver, spleen and kidneys were congested. The kidneys also showed several small to pinpoint foci of chronic interstitial nephritis. The main lesion was located at the level of the uterus (Figure 1). The whole uterus was enlarged and congested with a focal severe dilation at the tip of the right horn (approximately 3 cm in diameter) and two small myometrial dilatations at the level of the left uterine horn (Figure 2). Upon incision, the uterine lumen was found to be filled with a green yellowish purulent material (Figure 1 (inset)). The cervix was closed, the right ovary was enlarged and contained several large corpora lutea.

Histopathology

Samples of the liver, spleen, kidney, uterine horn and the enlarged right ovary were fixed in 4% neutral buffered formalin solution, routinely processed and embedded in paraffin. Five-µm-thick sections were mounted and stained with hematoxylin and eosin for histological examination.

Histopathologic evaluation of liver and spleen revealed congested vessels but no prominent inflammation. The spleen however, was composed of a diffuse population of activated lymphoid cells (proliferation of white pulp). The kidneys showed multifocal cortical foci of interstitial lymphoplasmacytic inflammation. Several primary follicles and large corpora lutea were seen in the right ovary.

Histopathologic examination of the uterus showed a diffuse endometrial mixed (mainly neutrophils and round cells) infiltrate with different sites of necrotic (cellular) debris infiltrated with bacterial aggregates in the endometrial glands and in the surrounding tissue. The necrosis continued focally in the myometrium with destruction of the wall which sometimes gave rise to the external bulging of the necrotic sites surrounded by thin myometrial tissue (Figure 3). The dilatation of the right uterus horn top was mainly linked to a prominent dilatation of the lumen surrounded by a thinner inflamed endo- and myometrium. The uterine lumen was mainly filled with neutrophils interlaced with necrotic material and coccoid bacteria.

Bacteriology

The purulent material was retracted from the right uterine horn using a sterile syringe and inoculated on an aerobe culture (blood agar); the colonies present were identified using Matrix Assisted Laser Desorption Ionization_Time-Of-Flight Mass Spectrometry (MALDI-TOF MS). This resulted in a pure culture of *Staphylococcus pseudintermedius*.

DISCUSSION

Pyometra is the most frequently observed reproductive disease in bitches, affecting up to 25% of unspayed females. It is defined as an intrauterine accumulation of pus accompanied by a persistent corpus luteum and failure of oestrus. Despite its clinical relevance, the pathogenesis of this disease remains poorly understood. It is believed that bacterial species may cause pyometra by ascending from the host's intestinal tract, thus causing an opportunistic infection (Xavier et al., 2022). Bacterial genotype examinations have shown that pyometra is most likely caused by *Escherichia coli* clones originating from the normal flora of individual dogs and not by clones spreading between animals (Hagman, 2005; Coggan et al., 2008).

Isolates phenotypically identified as *S. intermedius* can be differentiated into three distinct species: *S. intermedius*, *S. delphini* and *S. pseudintermedius* species, which are together referred to as the *Staphylococcus intermedius* group (SIG). The newly described *S. pseudintermedius* is a known inhabitant of the skin and mucous membranes, and a constituent of the normal microbiota of dogs. It has also been recognized as an opportunistic and zoonotic pathogen that is able to colonize humans and cause severe diseases, especially in immunocompromised hosts. (Iwata et al., 2018; Moses et al. 2023). The natural hosts of *S. delphini* are recognized as Mustelidae, such as minks, ferrets and badgers, those of *S. pseudintermedius* are not only dogs, but also foxes. However, information regarding *S. pseudintermedius* infection in foxes is limited and potentially underdiagnosed (Guardabassi et al., 2012).

Based on the histopathological and bacteriological findings, it can be stated that the present case concerned a closed pyometra caused by *S. pseudintermedius*. Recently, this bacteria has been associated with pyometra in two bitches, which died due to septic shock and peritonitis (Huber et al., 2022). Cases of pyometra in red foxes (especially wild canids) have been rarely described, and most interestingly, to the authors' knowledge, this is the first case in which *Staphylococcus pseudintermedius* could be isolated as a pure culture from the uterus of an adult red fox. In dogs, pyometra can be an acute life-threatening disease. In this case, the fox was found to be in a rather good body condition. Therefore, according to the authors, the animal probably died of septic shock as there was no evidence of peritonitis at the time of necropsy.

Data on the occurrence of uterine pathology in wild canids are scarce and mainly concern captive animals in breeding programs of zoos. Analysis of the data has shown that the longer the period a female produces litters, the lower the risk of CEH or pyometra. Interrupting non-reproductive periods with pregnancy and parturition could help maintain uterine health (Asa et al., 2014).

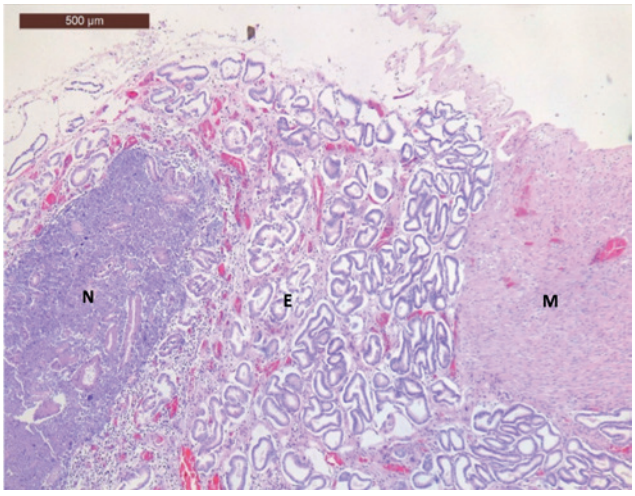

Figure 3. Histology of the myometrial dilatations: E. bulging of the mixed inflamed endometrial, M. tissue through the partially ruptured myometrium, N. the endometrium is pushed into the myometrium due to the large site of necrosis interlaced with bacteria and inflammatory cells.

Evidence on the zoonotic transmission of methicillin-resistant *S. pseudintermedius (*MRSP) from pet dogs to humans, such as dog owners, small animal veterinarians and others in close proximity to dogs is limited, especially due to the misidentification of *S. pseudintermedius* as *S. aureus* (Moses et al., 2023). Given the challenge of canid conservation, it is important that further research is focused on the effect of *S. pseudintermedius* on the reproductive health and fertility of wild canids, as well as on its zoonotic potential.

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Uit: de *Thouroutsche Bode* van 25 juli 1908

Johan De Smet