Uterine prolapse with endometrial eversion in association with an unusual diffuse, polypoid, fibrosing perimetritis and parametritis in a cat

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Abstract

Case summary This case describes a young non-pregnant cat that presented with uterine prolapse in association with an unusual diffuse, polypoid, fibrosing perimetritis and parametritis. Following ovariohysterectomy the cat recovered fully. No intra-abdominal complications were seen on ultrasound examination 3 months postsurgery. At the time of writing, the cat remains healthy.

Relevance and novel information Uterine prolapse in the cat is relatively rare and usually associated with the periparturient period. Inflammatory polypoid perimetritis and parametritis have not previously been documented in cats, and in dogs have only been reported in association with the administration of oestrogenic compounds. The polypoid inflammation affecting the uterus and parametrium may have contributed to increased laxity of the uterine ligaments and predisposed to the development of uterine prolapse.

Introduction

Uterine prolapse is rare in the queen, usually occurring after delivery of kittens or abortion.[1] We report uterine prolapse in a non-pregnant queen and in association with an unusual diffuse, polypoid, fibrosis of the perimetrium and parametrium. The perimetrium (syn uterine tunica serosa) is equivalent to the visceral peritoneal lining. It is composed of loose connective tissue containing nerves and smooth muscle cells covered by mesothelium. It blends in with the broad ligaments of the uterus, which is also covered by mesothelium and contains a core of connective tissue, the parametrium.[2] While peritonitis in cats is frequently associated with feline infectious peritonitis, specific lesions unique to the perimetrium have not been documented.

Case description

A stray 6- to 7-month-old domestic shorthair queen, weighing 2.15 kg, was presented to the university veterinary clinic with uterine prolapse after being observed for several days prior to capture. On examination, both uterine horns were prolapsed, everted and swollen, with regions of hyperaemia, particularly towards the

tips of the uterine horns. No evidence of placental zoning or tissue necrosis, in particular gangrene, was noted (Figure 1).

Clinical assessment revealed normal appetite and demeanour. The vital parameters were within normal limits (temperature 37.8°C, respiratory rate 40 breaths/min, heart rate 140 beats/min). There was no mammary tissue development. The cat received hydromorphone hydrochloride injection (Hydromorphone; West-ward Pharmaceutical) at 0.1 mg/kg IV q4h for pain management and to facilitate further examination. Initial haematological and blood biochemical evaluations revealed a markedly regenerative anaemia (packed cell volume 24% [reference interval (RI) 25–45%; erythrocytes

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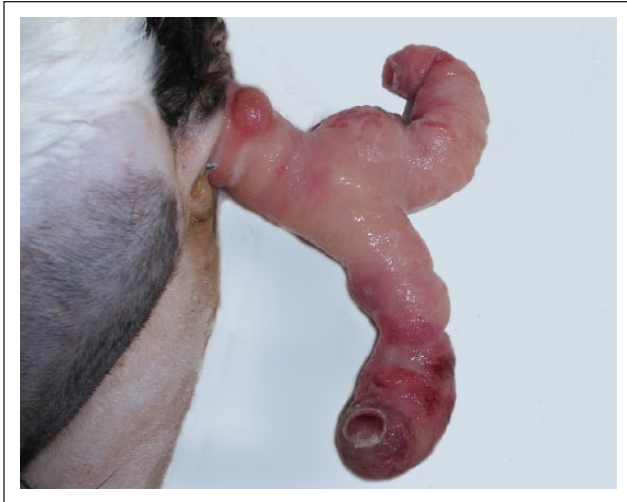Email: mvalentine@rossvet.edu.kn

Figure 1 Prolapsed and everted uterus following lavage which revealed swollen, hyperaemic and viable tissue

Figure 2 Formalin-fixed perimetrial surface of uterine body revealing diffuse-to-coalescing polypoid lesions

4.64×10^{12}/l [RI $5–10 \times 10^{12}$/l], reticulocytes 375.84×10/l [RI $0–40 \times 10^6$/l]) and a neutrophilic leukocytosis with mild toxic changes (leukocytes 37.72×10^9/l [RI $5.5–19.5 \times 10^9$/l]; neutrophils 25.3×10^9/l [RI $2.5–12.5 \times 10^9$/l]). Blood biochemistry showed a mild hyperkalaemia (6.0 mmol/l [RI 3.7–5.8 mmol/l]) and mild hypoglycaemia (66 mg/dl [RI 70–150 mg/dl]). This was attributed to a grossly lipaemic sample. From these samples oestrogen plasma concentrations were retrospectively evaluated at 25.7 pg/ml (RI 15–40 pg/ml). There was insufficient sample to evaluate progesterone concentrations. Intravenous crystalloid fluid solution (Plasmalyte; Travenol Laboratories) was administered to correct an estimated 8% dehydration deficit and maintenance requirement over 12 h. Antibiotic therapy consisting of intravenous cefazolin sodium (Cefazolin for Injection; West-ward Pharmaceutical) at a dose rate of 22 mg/kg IV q8h was also administered.

Following lavage, uterine replacement was unsuccessful. The following morning the cat was anaesthetised for manual prolapse reduction and ovariohysterectomy. Attempts at reducing the uterus were again unsuccessful so an internal ovariectomy and external hysterectomy were performed. A ventral midline coeliotomy incision was made. The ovarian pedicles were transfixed and ligated prior to transection and before manipulating the uterine body further. The everted uterus was circumferentially ligated distal to the cervix (approximately 5 cm away from the vulva) and transected. The remaining uterus was returned to the abdominal cavity. From within the abdominal cavity, the uterine body was double ligated proximal to the previously placed ligature. Excess uterine stump was removed. During surgery, the serosa of uterine body was noted to be diffusely thickened by multiple-to-coalescing white villous projections (Figure 2). This was sampled for histopathological evaluation.

There was a small amount of mildly flocculent abdominal fluid present. There were no gross signs of peritonitis on abdominal viscera or parietal peritoneum. The cat recovered uneventfully and follow-up examinations in a 6 month period, including ultrasound at 3 months post-surgery, detected no abdominal abnormalities.

Microscopic examination of the uterine body confirmed the presence of multiple nodular perimetrial proliferations of moderately loose connective tissue forming irregular polyps or plaques blending into the myometrium (Figures 3 and 4). Similar polyps extended along the broad uterine ligaments. Most polyps contained multifocal randomly distributed lymphocyte and plasma cell infiltrations, and regions of neovascularisation. Polyps were covered by a combination of normal, attenuated and moderately swollen mesothelial cells. At sites of mesothelial cell loss, there were fibrin formations. The stratum vascularis was moderately oedematous containing both congested medium-to-large size blood vessels and dilated lymphatics. Endometrium and uterine epithelium appeared unremarkable with a low glandular content, intact mucosal epithelium and minimal-to-no inflammatory cell infiltrations. The lesion was characterised as a diffuse, chronic, polypoid, fibrotic perimetritis and parametritis.

Discussion

Uterine prolapse has rarely been documented in cats, with individual case reports citing complete or unilateral
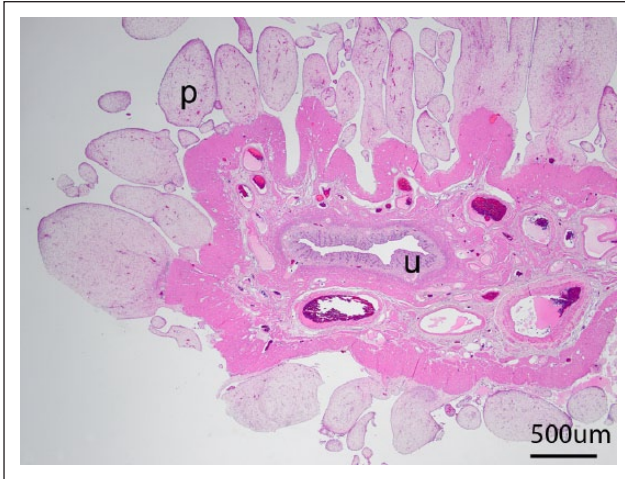
Figure 3 Cross-section of uterine body (u) revealing multiple polypoid perimetrial projections (p) (haematoxylin and eosin)
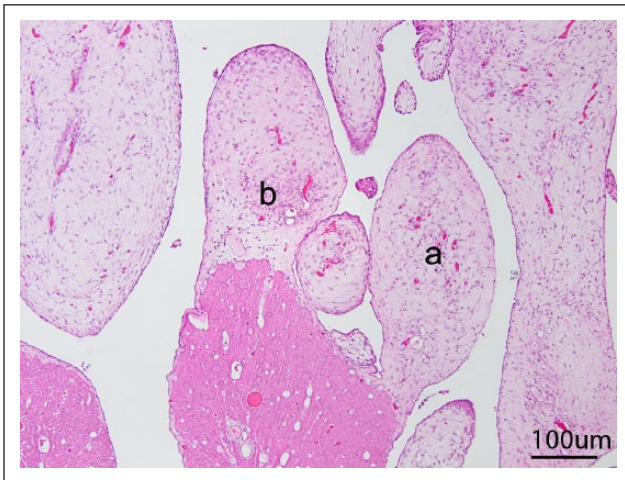

Figure 4 Polypoid structures blending with myometrium and containing (a) foci of angiogenesis and (b) regions of active fibroplasia (haematoxylin and eosin)

uterine prolapse with or without uterine mucosal eversion.[3–10] The majority have occurred in association with the periparturient period, one of which was proposed to be associated with oestrus.[11] The present case was unusual in that the animal was not pregnant. Furthermore, a novel lesion inducing extensive perimetrial fibrosis, not previously reported in cats, was noted and could potentially be implicated as the cause.

The putative causes of uterine prolapse include prolonged parturition and dystocia. However, other factors have been suggested including uterine atony or excessive abdominal contractions, including tenesmus.[3] For the uterus to prolapse there is a requirement for laxity, stretching or rupture of uterine ligaments, and for patency of the cervix. Laxity of the uterine ligaments can occur due to repeated pregnancy,[12] and changes in progesterone,

oestrogen and relaxin concentrations near parturition.[1] Cervical patency occurs at two time points, oestrus (with or without ovulation) and at parturition.[13,14] Based on the absence of any newborn animals, no mammary development and no histopathological features to suggest recent pregnancy, such as placental zoning, recent uterine haemorrhage, inflammation and endometrial regeneration, it is unlikely this animal was in advanced pregnancy or had aborted.[15] It was not possible, however, to establish if this animal had recently been in oestrus as oestrogen levels, which were within normal limits, can vary significantly over short periods of time within the oestrus cycle.[16] While the uterus was large, this reflected oedema and congestion of stratum vascularis within the everted uterus.

The polypoid perimetrial lesions were unusual and also extended along the uterine ligaments. This latter feature could potentially have contributed to uterine prolapse in at least two ways, namely by inducing ligament laxity and/or acting as a caudal abdominal irritant inducing abdominal contractions or tenesmus. While an active lesion, the extent of mature fibrous tissue would suggest the presence of this lesion in advance of the uterine prolapse.

Diseases confined to the perimetrium are unusual in all domestic animal species.[17] Perimetrial inflammation can co-exist as part of peritonitis, and in cats peritonitis is frequently associated with feline infectious peritonitis or primary bacterial septic peritonitis where *Bacteroides* species and *Fusobacterium* species are mainly isolated.[18] However, such lesions do not manifest as polypoid fibrous proliferations. Similar proliferative fibrotic lesions focused on the perimetrium have been described in dogs associated with experimental stilboestrol (synthetic oestrogen) administration.[19] Perimetrial papillae consisting of proliferations of mesothelial cells and subjacent connective tissue were documented in ovariectomised dogs administered stilboestrol over 150–350 days.[19] Similar to the present case, such lesions were confined to genital organ serosal surfaces, including the broad ligament. Such perimetrial lesions were also noted in entire female dogs when administered synthetic oestrogens in association with other lesions, including oestrogen-induced renal fibrosis.[20] Proposed mechanisms of regional fibrous proliferations suggested involvement of stromal oestrogen receptors. While the cat develops oestrogen-associated pathology, similar perimetrial pathology has not been documented in association with oestrogen.[17]

Endogenous hyperoestrogenism is unlikely as the cat lacked behavioural signs of oestrous. The ovaries were not submitted for histopathological evaluation to eliminate ovarian pathology definitively (cystic follicular disease, ovarian neoplasia) as a potential source of hyperoestrogenism. Cats in the tropics are likely to cycle continuously and it is recognised that some unmated cats

may appear to be in persistent oestrous, owing to a relatively short interoestrous period and thus remain in a physiological hyperoestrogenic state.[21] It was also unlikely this cat had access to exogenous oestrogenic compounds.

In humans, more generalised intra-abdominal, fibrosing lesions of peritoneal surfaces (intra-abdominal fibromatosis) are described in mesenteric, retroperitoneal and pelvic locations.[22] Sclerosing peritonitis has been noted after surgery, following long-term continuous peritoneal dialysis and also as a side effect of utilising beta-blockers.[23] The pathogenesis of these lesions is thought to be the result of a delayed healing response due to loss of mesothelial cells or continued serosal irritation.[23] However, the appearance is not described as polypoid and ranges through a spectrum of gross changes in the appearance of the visceral peritoneum, from opacification of the serosa (disorganised collagen fibres and stromal expansion) through to 'tanned peritoneum' (hyalinised collagen, fibrin and vessel sclerosis), which can progress to a stage where the viscera are palpably stiffened (mural fibrosis).

Conclusions

The unique perimetritis and parametritis observed in this case highlights an additional potential cause of uterine prolapse and warrants that, in cases of uterine prolapse in non-pregnant animals, perimetrial and parametrial tissue should be evaluated for varying degrees of inflammation.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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