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14 15 16	Unusual case of uterine stump pyometra in a cat
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30 Summary

31 This report describes an unusual case of uterine stump pyometra in a cat, in which the main 32 symptom at presentation was abdominal straining. At the time of ovariohysterectomy, the surgeon 33 reported that uterine body had a purulent content. About one month after surgery the cat showed 34 abdominal straining. The enlarged uterine stump, filled with purulent fluid, had caused 35 compression of the rectum and secondary intestinal sub-occlusion. Surgical revision consisted in 36 draining the purulent content of the remnant of the uterine body and ablating as much of it as 37 possible; checking of the ovarian pedicles revealed the presence of a small fragment of whitish tissue on the right side, which was shown to contain, by means of histological observation and 38 39 immunohistochemical staining, ovarian tissue. Four months after surgical revision the cat did not 40 show any pathological sign and he is healthy after one year.

At the end of July 2009 an 8-month-old spayed mixed breed queen, living indoors with free access to the outdoors, was taken to the Veterinary Teaching Hospital of The Faculty of Veterinary Medicine of Turin University because of worsening of abdominal straining, a condition that had appeared about three weeks after ovariohysterectomy. The cat had also shown reduced appetite and activity. Ovariohysterectomy had been performed about 6 weeks earlier and the practitioner had reported that uterus had a purulent content. Two weeks after surgery the queen had shown enlarged mammary glands and milk secretion, and cabergoline (5 μ g/kg) had been administered for 5 days.

48 The cat appeared in quite good condition, alert and not dehydrated. Abdominal palpation was not 49 painful but revealed the presence of a highly distended colon with soft content. The hypothesis of 50 an intestinal sub-occlusion, which was the cause of the straining reported by the owner was 51 confirmed by a radiological exam (Fig. 1). Abdominal ultrasound revealed the presence of a fluid-52 filled structure referable to a uterine stump, measuring 3.7x2.6 cm, compressing the rectum 53 dorsally. Cell blood count, biochemical parameters (aspartate aminotransferase, alanine 54 aminotransferase, creatine kinase, γ -glutamyltransferase, creatinine, urea, glucose, total bilirubin, 55 triglycerides, total cholesterol, alkaline phosphatase, amylase and lipase) and total serum protein were within normal limits. Feline leukaemia virus and feline immunodeficiency virus tests were 56 57 negative. A surgical revision was suggested in order to eliminate the cause of the obstruction. After 58 sedation, anaesthesia was induced with propofol and maintained with isoflurane in oxygen.

59 A median ventral laparotomy revealed the presence of an enlarged uterine stump, with 60 granulomatous tissue and adhesions to the bladder. Grossly, the uterine wall appeared thinned and the uterine lumen showed a conspicuous amount of purulent exudate, which was drained. A sample 61 62 was taken for culture and sensitivity testing. The remnant of uterine tissue was removed as 63 completely as possible. Bilateral exploration of the abdomen, from the caudal pole of each kidney 64 to the uterine stump was performed and an increased vascularisation of the right ovarian pedicle 65 was detected, together with the presence of a small fragment of whitish tissue which was removed 66 for histological examination. At the end of the surgical procedure an enema consisting of warm water and mineral oil was administered. Two more enemas were administered during the following 67 days, and the intestinal functionality was re-established. The cat was treated with amoxicillin-68 69 clavulanic acid (12.5 mg/kg BID), a therapy that was confirmed after culture results and 70 antimicrobials susceptibility tests (β-haemolytic *Streptococcus* sp.). Recovery was uneventful.

Histopathological examination of the fragment of tissue removed from the right ovarian pedicle showed a mild inflammatory process with presence of haemorrhagic areas and scar tissue with fibroblasts. Other areas were characterized by the presence of both small cells with uniform round or oval hyperchromatic nuclei with finely granular chromatin, resembling granulosa cells, and larger cells with *round* or oval nuclei and cytoplasmic vacuolization resembling luteal cells (Fig. 2a).

Histopathological examination of the uterine stump revealed a mild cystic endometrial hyperplasia ,
 meanwhile a diffuse chronic inflammatory infiltrate was present in all layers of uterine wall.

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In order to confirm the hypothesis of ovarian remnant, 4μ-thick sections from the tissue fragment were subjected to immunohistochemistry with anti-progesterone receptor (PR) and anti-aromatase antibodies. PR expression is selectively induced in granulosa cells of preovulatory follicles by LH¹⁻³ and persists in the corpus luteum of the ovary.^{4,5} Aromatase is a key enzyme in ovarian steroidogenesis and plays an important role in sexual differentiation, oestrogen biosynthesis, fertility and carcinogenesis. It is highly conserved amongst mammals and it is expressed in granulosa cells and participates in conversion of androgens to oestrogens.⁶

The tissue fragment removed from the right ovarian pedicle showed a positive staining for both PR and aromatase. In particular, nuclei of putative granulosa cells stained strongly positive for PR, while putative luteal cells showed a mild cytoplasmic staining (Fig. 2b). Immunohistochemistry for aromatase showed a diffuse cytoplasmic immunoreactivity in several areas where both granulosa and luteal cells were detected (Fig. 2c). 92 The reported findings suggested the presence of ovarian tissue in the fragment.

Four months after surgical revision, the cat had gained weight and the owner reported that no
pathological signs had occurred since. At ultrasound the uterine stump was appreciable as a small
(1x0.5 cm) hyperechoic area dorsal to the bladder which was interpreted as fibrosis. To this day (i.e.
about one year later) the cat has been healthy.

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99 In cats uterine stump pyometra is reported to occur in neutered queens either in case of ovarian remnants or following administration of progestagens.^{7,8} Ovarian remnant syndrome is usually 100 diagnosed when a previously spayed queen shows recurrent behavioural signs of oestrous.^{9,10} In our 101 102 case, the cat had been in heat for the first time at about 6 months of age, but neither signs of oestrus 103 were present after ovariohysterectomy, nor she had ever received progestagens. The interval between ovariohysterectomy and uterine stump pyometra diagnosis was around 40 days; our 104 105 hypothesis is that uterine stump pyometra was sustained by the presence of functional ovarian luteal 106 tissue. The duration of luteal function is about 40-50 days in the non pregnant queen,¹¹ and, in our 107 case, the luteal tissue localized in the examined fragment could represent the remnant of old corpora 108 lutea. We believe that ovarian luteal tissue maintained the conditions of endometrial hyperplasia and increase of the secretory activity of the endometrial glands,^{7,12} which allowed the 109 persistence/recurrence of the uterine infection. We did not measure serum progesterone 110 concentration at the moment of surgical revision, but, according to our hypothesis, it could have 111 112 been low or around basal. From the history of the queen, we know that she had been treated with 113 cabergoline because of mammary secretion following ovariohisterectomy: the prolactin increase 114 causing milk secretion is likely to have been induced by a sharp decline in progesterone concentration, and this means that the gueen had ovulated and had corpora lutea on ovaries when 115 116 she had undergone ovariohysterectomy. In cats cabergoline has an antiprolactinic action and induces abortion¹³ by means of a slow (3-4 days) reduction in plasma progesterone concentration¹⁴. 117 After the end of cabergoline effect, residual luteal tissue may have regained functionality. However, 118 119 we can not exclude that the observed condition might have developed also in the absence of 120 functional luteal tissue: in fact, although a correlation between pyometra and corpora lutea presence has been observed in cats,⁸ cats with pyometra may also have low serum progesterone concentration 121 122 because the effects of progesterone on uterine mucosa and glands may persist beyond the end of the 123 luteal phase. 124

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- Fig 1. Right lateral radiographic projection showing distended colon and rectum and enlarged uterine stump (open arrow) dorsal to the bladder (closed arrow).

Fig. 2 a: Microphotograph of the fragment of tissue removed from the right ovarian pedicle showing the presence of both small cells with uniform round or oval hyperchromatic nuclei with finely granular chromatin, resembling granulosa cells, and larger cells with round or oval nuclei and cytoplasmic vacuolization resembling luteal cells (H.E. 60x); b: PR immunostaining in the tissue fragment, showing strongly positive nuclei of putative granulosa cells (60x); c: Aromatase immunostaining in the tissue fragment, showing a diffuse cytoplasmic immunoreactivity in both granulosa and luteal putative cells (40x)



