

Pseudo-placentational Endometrial Hyperplasia (PEH) in a bitch: clinical and hystopathological findings



A healthy female Labrador Retriever was referred to the University's Reproduction Unit for a gynaecological examination and for monitoring of the oestrous cycle in anticipation of breeding. The bitch underwent natural mating and pregnancy was diagnosed on day 35 after breeding. The ultrasound examination revealed a mono gestational pregnancy and the presence of a parenchymatous structure with very scarce fluid content, consistent with the remnant of an empty gestational sac. At the end of pregnancy a caesarean section was performed. The puppy was alive and apparently healthy. After ovariohysterectomy various nodular structures were detected on the endometrium of both uterine horns. The histopathological diagnosis was of Pseudoplacentational Endometrial Hyperplasia (PEH), an uncommon pathological finding often misdiagnosed as Cystic Endometrial Hyperplasia (CEH).

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INTRODUCTION

Cystic lesions that characterise the uterus of many intact bitches may be divided into cysts originating from the endometrium (by far the most common and clinically relevant) and cysts that originate within the myometrium or from the serous surface of the uterus. Cystic uterine lesions include: serous cysts, adenomas, endometrial polyps, cystic remnants of mesonephric ducts and cysts associated with endometrial hyperplasia.¹ Cystic lesions that develop from the endometrium vary greatly in terms of size, number, distribution, histomorphology and clinical importance;² they usually derive from the glandular epithelium, although some may originate from luminal epithelial villi and folds.¹ These endometrial lesions are usually grouped under the

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name of Cystic Endometrial Hyperplasia (CEH); this is a common finding and is often associated - especially in elderly bitches - with the development of pyometra.³⁻⁴⁻⁵⁻⁶⁻⁷ The scientific literature reports that 23-24% of bitches develop pyometra within 10 years of age.² These studies have clarified that CEH associated with endometritis is an event that mostly occurs in the luteal phase of the ovarian cycle;¹ the endometritis appears to be

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caused by the bacteria that enter into the uterus during oestrus. A particular form of CEH takes the name of Pseudo-Placentational Endometrial Hyperplasia; being the condition difficult to recognise, it is little described in the literature compared to the more common endometrial cystic abnormalities; the condition is also known as pseudocystic endometrial hyperplasia,⁸⁻⁹ deciduoma¹⁰ and segmental hyperplasia.¹¹ Although the first cases of deciduoma described in literature date back to about a century ago,¹⁻¹² the genesis of pseudo-placentational endometrial hyperplasia is not yet very clear and is now the object of several studies.¹³⁻¹⁴ This paper describes a case of pseudo-placentational endometrial hyperplasia found

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accidentally during a caesarean section in a pregnant bitch monitored throughout the duration of gestation.

CLINICAL CASE

In the month of October, 2016, a 7-year-old female Labrador dog was brought to the Department of Veterinary Medical Sciences of the Alma Mater Studiorum - University of Bologna - for a gynaecological examination and monitoring of the oestrous cycle in anticipation of breeding.

The general physical examination, in particular of the genital tract, as well as ultrasonography did not detect the presence of any abnormality. During the same clinical examination, the blood test for the quantitative determination of progesterone and colpocytology revealed the presence of a state of anoestrus. The dog was brought back by the owner about a month later, at the first signs of pro-oestrus vaginal discharge. The oestrous cycle was monitored by means of blood progesterone and vaginal cytology; the tests allowed to determine the optimal time for breeding.

Pregnancy was confirmed ultrasonographically on day 35, with the detection of a single vital and normally conformed foetus. In addition, a 3.5 cm diameter ovoid parenchymatous structure was detected at the apex of the left uterine horn. Upon initial evaluation, the nature of this alteration seemed compatible with the presence of an empty gestational sac, in the process of resorption, in the vicinity of the apex of the uterine horn (Figures 1 and 2).

The owner reported a normal pregnancy and then required a follow-up visit 60 days after breeding, not having observed in the animal any preparatory behaviour for parturition. Clinically, the animal was in good health conditions and at ultrasonography the foetus appeared vital, but with a heart rate of 160 bpm. The abnormality at the apex of the left uterine horn, detected during confirmation of the pregnancy, was still present. Being the foetal heart rate indicative of severe distress,¹⁵⁻¹⁶ having 65 days passed from the LH peak (identified based on blood progesterone assays performed during oestrous cycle monitoring in preparation for breeding), having detected a maternal progesteronaemia of 2.6 ng/dl and being in the presence of a mono gestational pregnancy, a surgical intervention with emergency caesarean section was performed. Following the indications of the owner, an ovariohysterectomy was also performed during the same surgery. The foetus was localised in the left ute-



Figure 1 - Dog. Left uterine horn. Transverse section of the normal gestational sac containing the foetus.

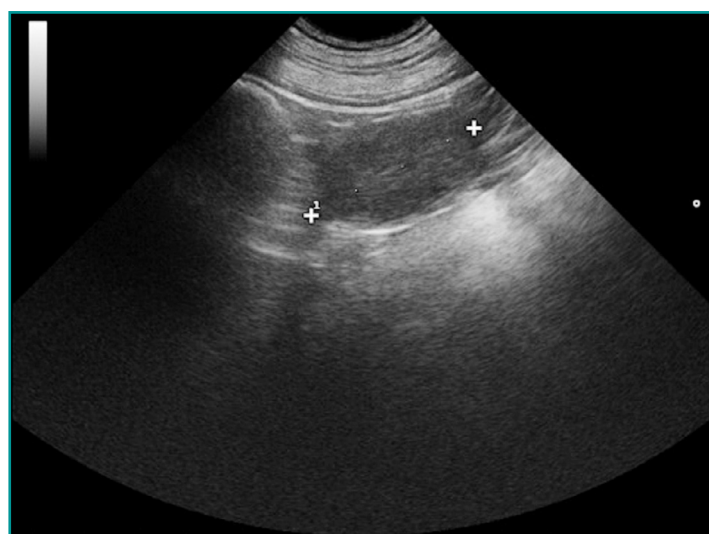


Figure 2 - Dog. Apex of the left uterine horn. Longitudinal section of the gestational sac in the process of resorption. It consists of an ovoid-shaped, parenchymatous structure, with scarce fluid content and a diameter of around 3.5 cm.

rine horn; at the apex of the same uterine horn the remnant of a gestational sac was also detected. On the remaining surface of the endometrium, along both uterine horns, numerous exophytic nodular structures were also detected, of variable diameter (from 0.5 to 1.5 cm), with a broad base of attachment or pedunculated, and covered by the endometrium; in section, they presented either a pale mucous content or whitish soft tissue, containing small (0.5-1 mm) cystic spaces (Figure 3). Two tissue samples (3x2 cm in diameter) were taken from the excised uterus, fixed in formalin and sent to the Pathology Service for histological examination. The histological report described the presence of two demarcated and pseudocapsulated endo-exophytic, multicystic proliferations expanding the endometrial lamina propria and exhibiting expansive growth. In the up-

On the remaining surface of the endometrium, along both uterine horns, numerous exophytic nodular structures were detected.

per (luminal) section the cells were arranged in a single layer, resting on a very thin fibrovascular mesh and forming threadlike villous structures or circumscribing cystic areas replete with basophilic mucus (Figure 4). Each cell was of prismatic shape, with defined edges, intermediate nuclear-cytoplasmic ratio and abundant cytoplasm, which appeared dishomogeneous, vacuolated and eosinophilic. The oval-shaped nuclei appeared variously arranged and nonpolarised, with marginated chromatin and a small round basophilic central nucleolus. The lamina propria was characterised by oedema and hyperaemia. Finally, a layer of dilated endometrial glands (Figure 5) was present, partially containing debris and secretions. The vessels appeared hyperaemic.



Figure 3 - Dog. Uterus. Exophytic nodular structures with broad base attachment or pedunculated, and of variable diameter (0.5 to 1.5 cm).

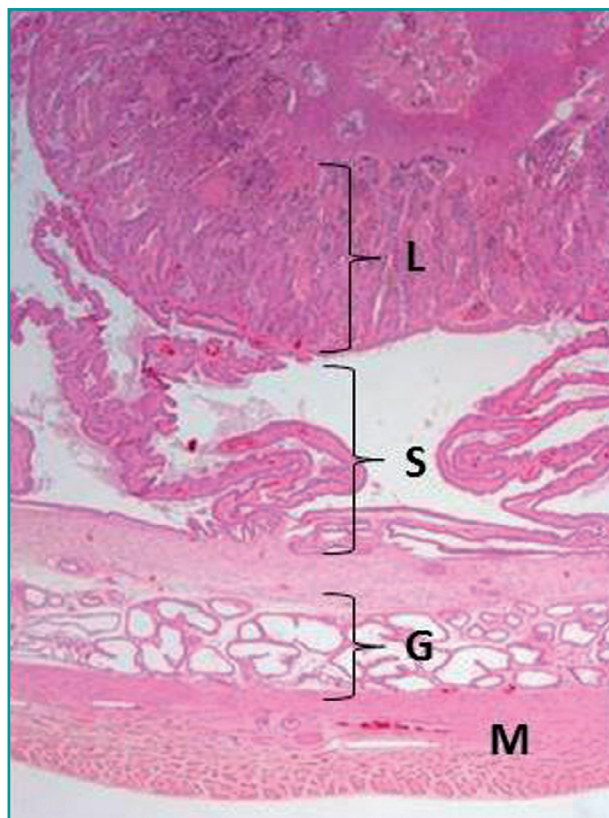


Figure 4 - Dog. Uterus. Normal placenta at the end of pregnancy. The dog's placenta has 3 layers: the labyrinth (L), formed by the trophoblast hosting foetal and maternal vessels and which is in contact with the allantois (allantocorion); the spongy layer (S) and the glandular layer (G), originating respectively from the superficial and deep endometrial glands. M: myometrium. (Steiger et al., 2006). Haematoxylin-eosin (ExE), 2.5x.

This endometrial alteration is poorly recognised by veterinarians; it is consequently not diagnosed much and it is little studied by pathologists.

DISCUSSION

Pseudo-placentational endometrial hyperplasia is an endometrial alteration which is often confused with CEH, but it differs in terms of its macroscopic appearance (focal or multifocal lesions; not diffuse as in CEH), microscopic appearance (tri-laminar structure as in the placenta) and in its aetiology.

In both conditions, the underlying cause is always endometrial stimulation, which can be of different nature (organic or physical) and which occurs during the luteal phase of the ovarian cycle, when progesterone sensitises the endometrium.¹⁷⁻¹⁸⁻¹⁹ In pseudo-placentational endometrial hyperplasia the endometrium reacts with a peculiar, highly-organised proliferative remodelling, very similar to what happens to placentation sites during normal pregnancy. Its presence also in gravid bitches allows to hypothesise that the condition does not

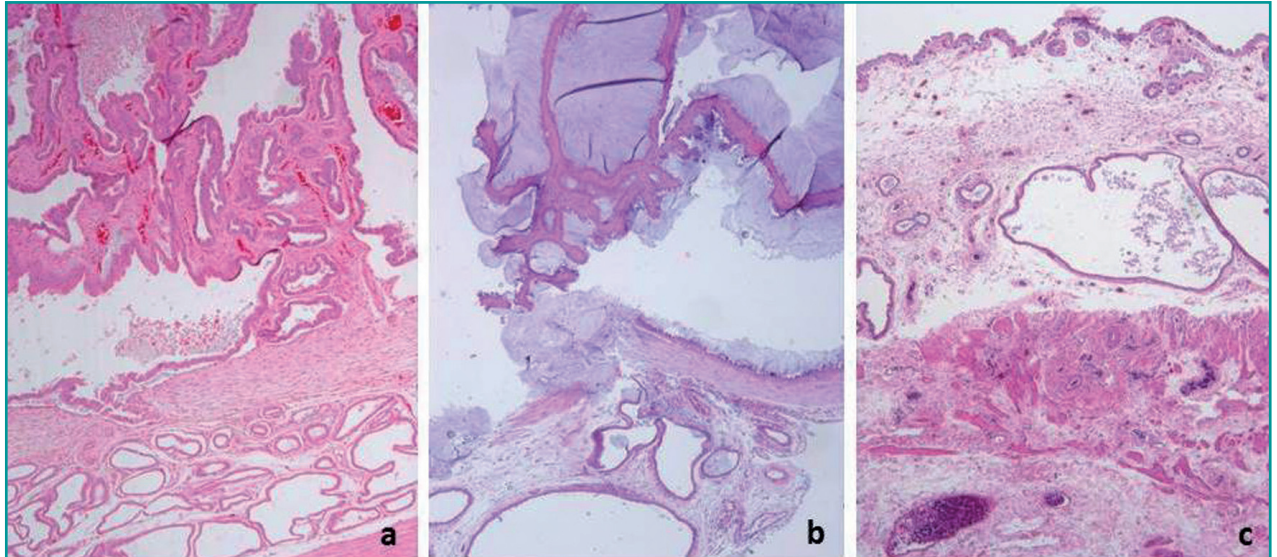


Figure 5 - Dog. Uterus. **a)** Gravid uterus; detail of the spongy and glandular layers, the first characterised by papillary structures with thin stromal support. ExE 5x. **b)** Case being examined. Pseudo-placentational hyperplasia; on the endometrial surface presence of villous proliferations partially delimiting mucus-containing spaces, followed by a thin connectival layer of tissue and ectasia of the endometrial glands. ExE 5x. **c)** Cystic endometriosis. Ectasia of the endometrial glands within the endometrium. Note the structural and stratigraphic similarity of the case examined (pseudo-placentational hyperplasia) with the gravid uterus (spongy and glandular layers) and the divergence with cystic endometriosis, in which the alteration involves only the endometrial glands that remain confined within the endometrium.

affect the subject's fertility. As in CEH, elevated blood progesterone levels are considered a key component. No cases of pseudo-placentational endometrial hyperplasia that have evolved into pyometra have so far been reported in the literature. Deciduoma is a spontaneous alteration which can be reproduced also experimentally;²⁰ the ultrasonographic diagnosis of this condition has not been described as its detection is always accidental, in most cases taking place during surgery or necropsy. The diagnosis is exclusively histological. This endometrial alteration is rarely recognised by veterinarians; it is con-

sequently not diagnosed much and it is little studied by pathologists;¹ it is however clear that even when suspected, based on the macroscopic appearance (focal or multifocal lesions unlike CEH, in which they are diffuse), the final diagnosis can only be histological and is based on the identification of a specific tri-laminar pattern, characterised by: 1) villous endometrial proliferations immersed in mucus or fused so as to delimit mucus-containing lacunar spaces, 2) followed by a thin layer of endometrial stroma, 3) and finally by a layer of ectatic endometrial glands.¹

KEY POINTS

- Cystic uterine lesions include: serous cysts, adenomas, endometrial polyps, cystic remnants of mesonephric ducts and cysts associated with endometrial hyperplasia.¹ Cystic lesions that develop from the endometrium vary greatly in terms of size, number, distribution, histomorphology and clinical importance.²
- A particular form of cystic endometrial hyperplasia takes the name of pseudo-placentational endometrial hyperplasia; being the condition difficult to recognise, it is little described in the literature compared with the more common endometrial cystic abnormalities.
- The foetus was localised in the left uterine horn; at the apex of the same uterine horn the remnant of a gestational sac was also detected. On the remaining surface of the endometrium, along both uterine horns, numerous exophytic nodular structures were also detected.

- The histological report described the presence of two demarcated and pseudo-capsulated endo-exophytic, multicystic proliferations expanding the endometrial lamina propria and exhibiting expansive growth.
- Macroscopically, and in its aetiology, pseudo-placentational endometrial hyperplasia is very similar to CEH. For both conditions, the underlying cause is always endometrial stimulation, which can be of different nature (organic or physical) and which occurs during the luteal phase of the ovarian cycle.
- As in CEH, it has been speculated that the main predisposing factors include the stimulus on the endometrium by the bacteria that enter into the uterus through the vagina during oestrus¹¹ and that increased progesteronaemia is an essential factor.

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