

## Diffuse heterotopic hair in a canine uterus: case report

[*Heterotopia de pelo difusa no útero de uma cadela: relato de caso*]

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### RESUMO

O presente relato descreve os achados clínicos e patológicos de uma heterotopia de pelos difusa associada com hiperplasia endometrial pseudo-placentacional em um útero de uma cadela. Macroscopicamente, o útero estava intensamente aumentado de volume e espesso, a superfície do endométrio estava irregular e recoberta com pelos pretos semelhantes aos pelos da cadela. Histologicamente, heterotopia de pelos associada com hiperplasia endometrial pseudoplacentacional foi observada.

Palavras-chave: cão, pelo, heterotopia, útero

### ABSTRACT

*The present report describes the clinical and pathological findings related to diffuse heterotopic hairs associated with pseudo-placentational endometrial hyperplasia in a canine uterus. Macroscopically, the uterus was intensely enlarged and thicker, and the endometrial surface was irregular and covered with black hairs similar to the hairs of the bitch. Histologically, heterotopic hairs associated with pseudo-placentational endometrial hyperplasia were observed.*

Keywords: dog, hair, heterotopia, uterus

### INTRODUCTION

Heterotopia is the occurrence of mature tissue in an abnormal location (Sethi *et al.*, 2008). In human medicine, although heterotopic elements, such as bone, cartilage, adipose tissue and squamous epithelium have been reported throughout the female genital tract (Oba, 1975; Tyagi *et al.*, 1979; Grönroos *et al.*, 1983; Taylor *et al.*, 1984; Remmele *et al.*, 1988; Sethi *et al.*, 2008; Szumilo *et al.*, 2009) the appearance of hair in the uterus is rare (Taylor *et al.*, 1984). Few reports of heterotopic hair or skin in the uterus have been reported in women (Tyagi *et al.*, 1979; Taylor *et al.*, 1984; Fichera and Santanocito, 1989). In veterinary practice, there are no reports of heterotopic elements in the uterus. To the best of our knowledge, the present study is the first reported case of heterotopic hairs in a canine uterus. The present report

describes the clinical and pathological findings related to heterotopic hairs associated with pseudo-placentational endometrial hyperplasia in a canine uterus.

### CASUISTRY

A six-year-old intact female mixed-breed dog was presented to the Veterinary Hospital at the *Universidade Federal de Minas Gerais* (UFMG), Brazil, with a history of mating three months prior. She did not develop the external characteristics of gestation but had bloody vaginal secretions. An ultrasound examination demonstrated that the uterus was enlarged, but no fetuses were observed. The serum levels of progesterone and oestrogen were 1.67ng/mL and 21.2pg/mL, respectively, indicating the final stage of diestrus or pregnancy (reference values for the final stage of diestrus or pregnancy: progesterone, 1.00 to 30.00ng/mL; oestrogen,

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15.00 to 50.00pg/mL). On suspicion of pyometra, the animal was submitted to an ovariosalpingohysterectomy.

Macroscopically, the uterus was intensely enlarged and thick, and the endometrial surface

was irregular and covered with black hairs measuring approximately 2cm in length (Figure 1) similar to the hairs of the bitch. In the uterine lumen, a bloody secretion was visualised. Foetuses or foetal remains were not observed. The corpus luteum was observed in both ovaries.

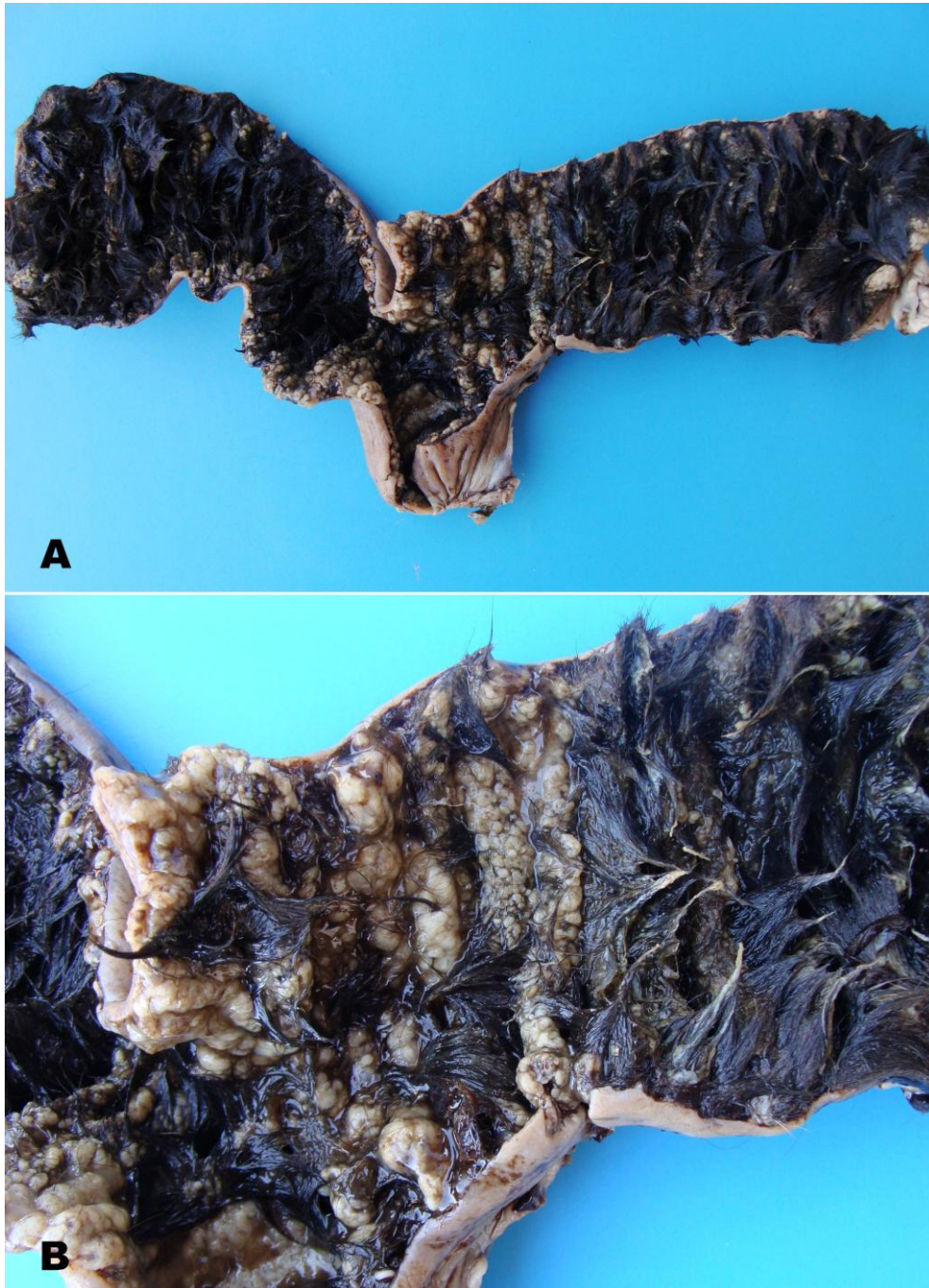


Figure 1. Diffuse heterotopic hair, uterus; female dog. A and B) Intensely enlarged and thicker uterus, and the endometrial surface is irregular and covered with black hairs.

### Diffuse heterotopic hair...

Tissue samples from the uterus and ovaries were fixed in 10% neutral phosphate-buffered formalin, embedded in paraffin and cut into 5- $\mu$ m sections. The sections were stained with the hematoxylin and eosin, periodic acid-Schiff (PAS), and Warthin-Starry stains. Immunohistochemistry for anti-vimentin (Clone V9, Dako, Denmark, CA, USA) and anti-cytokeratin (Clone AE1/AE3, Dako, Denmark, CA, USA) was performed. The streptavidin-biotin-peroxidase complex (LSAB Kit Universal, Dako, Denmark, CA, USA) and 3,3'-diaminobenzidine (DAB, Dako, Denmark, CA, USA) were used as the detection system. Sections were counterstained with Harris hematoxylin. The same tissue incubated with IgG instead of the primary antibodies was used as the negative control. Frozen uterine tissue samples were used to determine the relative expression of genic transcript for trophoblast glycoprotein (TPBG). The expression was evaluated using real-time RT-PCR, and genic transcript expression in the uterus of the present case was compared with genic transcript expression both in a non-pregnant uterus (negative control) and a pregnant uterus (positive control) from different female dogs. Total mRNA was extracted using TRIzol reagent (Invitrogen, Carlsbad, CA, USA) according to the manufacturer's instructions. A total of 1  $\mu$ g of RNA was used for cDNA synthesis using the SuperScript III Platinum Two-Step qPCR kit with SYBR Green (Invitrogen, Carlsbad, CA, USA). The qRT-PCR reactions were conducted in a Smart Cycler II thermocycler (Cepheid Inc., Sunnyvale, CA, USA). Gene expression was calculated using the  $2^{-\Delta\Delta Ct}$  method, where the values from the samples were averaged and calibrated in relation to the  $\beta$ -actin CT values. The primers for the *Canis lupus familiaris* genes (XM\_539020.3) were as follows: sense 5'-CTTCGAGGGCATGGTGGCGG-3', antisense 5'-CCAGGACGTCGCGAGGCAAG-3' for trophoblast glycoprotein; sense 5'-GTACGACGAGTCGGGCCCT-3', antisense

5'-ATGCTACGCATCTGCTCGCAGTC-3' for  $\beta$ -actin.

Histologically, the uterine wall appeared thick with moderate congestion and oedema characterised by the dilation of blood and lymph vessels and foci of dissociated muscle fibres. The endometrium was hyperplastic and formed papillary projections into the lumen. At the tip of some of the papillary projections, one or more layers of voluminous cells with ovoid nuclei, loose chromatin and foamy cytoplasm (pseudo-placentational endometrial hyperplasia), were observed (Figure 2A and 2B). Trophoblastic cells were not observed. The pseudo-placentational reaction was associated with a large amount of abnormal and abortive forms of hair (Figure 2C and 2D) surrounded by a layer of spindle cells that were vimentin positive. The abortive hair forms were also visualised between the fibres of the myometrium. The endometrial glands were dilated and lined by cuboidal epithelium composed of cells with ovoid nuclei, loose chromatin and eosinophilic or vacuolised cytoplasm with PAS-positive contents. At the junction between the endometrial and myometrial foci of inflammatory infiltrate, predominantly neutrophilic and haemorrhagic foci were observed. There were no histological features of neoplasia. There were no histological changes in the fallopian tubes, and the ovaries showed normal histology with follicles in different stages of development, including mature follicles, and corpus luteum regression.

The relative expression of genic transcription for trophoblast glycoprotein in the uterus in this case was significantly higher when compared to the non-pregnant uterus and significantly lower when compared to the pregnant uterus (Figure 3). Based on the gross and histopathological findings, the diagnosis of diffuse heterotopic hairs associated with pseudo-placentational endometrial hyperplasia was confirmed.



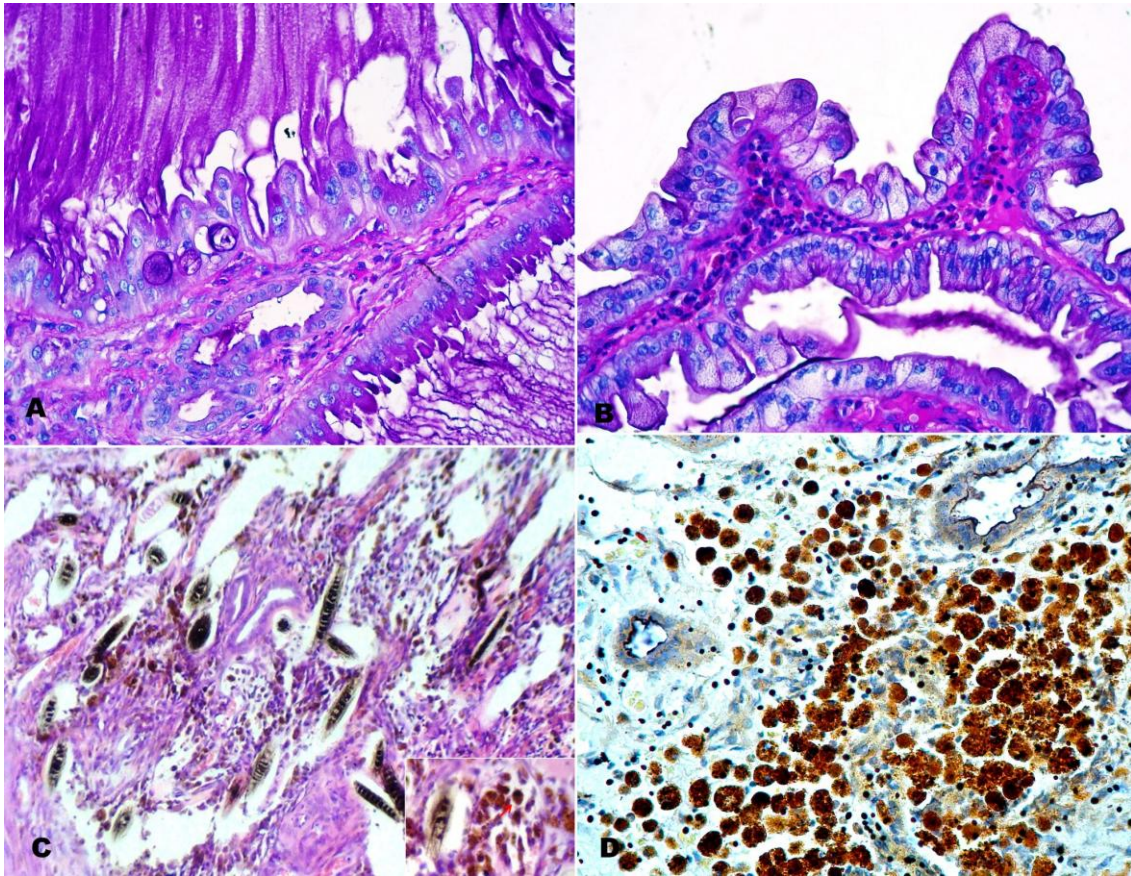


Figure 2. Diffuse heterotopic hair associated with pseudo-placentational endometrial hyperplasia, uterus; female dog. A and B) Endometrial hyperplasia with one or more layers of voluminous cells with ovoid nuclei, loose chromatin, and foamy cytoplasm (pseudo-placentational endometrial hyperplasia) (PAS stain). C) A large amount of abnormal and abortive hair forms in the endometrium. (H&E stain). D) Endometrium with abortive hair forms that stained Warthin-Starry positive (Warthin-Starry stain).

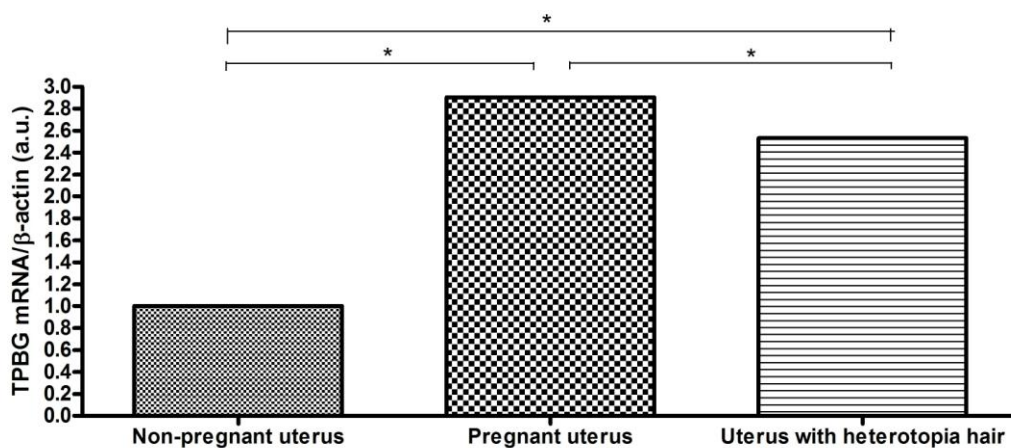


Figure 3. Diffuse heterotopic hair associated with pseudo-placentational endometrial hyperplasia, uterus; female dog. The relative expression (mean  $\pm$  standard deviation) of the transcribed gene for trophoblast glycoprotein (TPBG) by RT-PCR in real time in the uterus of this case compared to non-pregnant and pregnant uteri from different female dogs (\* $p < 0.05$ ).

## DISCUSSION

The aetiology of heterotopic elements in the female genital tract is uncertain. However, hypotheses have been proposed: the iatrogenic implantation of foetal tissue (resulting in adverse conditions or medical treatment); metaplasia of mature; and germ- or embryonic-cell rest neoplasia (Taylor *et al.*, 1984, Sethi *et al.*, 2008). Another hypothesis for the presence of heterotopic elements is the failure of cell migration during embryogenesis originating the choristomas. Choristomas are congenital proliferations defined as a tumor-like mass characterized histologically by normal cells or tissue that develops in an ectopic location (Neville *et al.*, 1995). In the present case, the authors confirmed the diagnosis of heterotopia and not choristoma. This was due to the presence of diffuse hair in utero without the formation of a tumor-like mass. In addition, the bitch in this case had previously normal pregnancies, which would not be possible if the diffuse lesion observed was congenital.

The mating history three months prior to her presentation and the pseudo-placentational reaction observed in the empty uterus (no foetus) associated with high trophoblastic glycoprotein expression for a non-pregnant uterus suggest that the heterotopic hair may have resulted from the implantation of foetal tissue.

Most women with heterotopic elements in the uterus have a discrete bloody vaginal discharge (Grönroos *et al.*, 1983), similar to that observed in this canine during the clinical examination. Interestingly, the heterotopic growths reported in human uteri are described as having a polypoid formation (Tyagi *et al.*, 1979; Grönroos *et al.*, 1983; Taylor *et al.*, 1984; Sethi *et al.*, 2008). However, in the present case, the heterotopic growths were diffusely observed in the endometrium.

According to Grönroos *et al.* (1983), a discrete inflammatory reaction formed by mononuclear cells can be detected around the heterotopic tissue. In the present report, at the junction between the endometrial and the myometrial foci of inflammatory infiltrate, predominantly neutrophilic and haemorrhagic foci were observed, and were characteristic of focal pyometra.

The term pseudo-placentational endometrial hyperplasia was used due to the histological features of the hyperplastic endometrium that were associated with the decidual reaction observed in cases of pregnancy without the presence of trophoblastic cells (Koguchi *et al.*, 1995).

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