Effects of aglepristone, a progesterone receptor antagonist, in a dog with a vaginal fibroma

A 12-year-old, entire, nulliparous crossbreed female dog was presented with a history of vulval bleeding, bulging of the perineum and faecal tenesmus. A firm, non-painful perineal mass, measuring 9.11 × 5.4 cm, with erythema was detected. Abdominal radiography showed compression and elevation of the rectal ampulla. A dose of 10 mg/kg aglepristone was administered subcutaneously on days 1, 2, 8, 15, 28 and 35. An incision biopsy was taken on day 15 and immunohistochemical analysis showed that the majority of neoplastic cells expressed progesterone receptors. Both the cutaneous erythema and the faecal tenesmus had resolved by day 28. A 50 per cent reduction in size was observed by day 60 (surgical excision). This study shows that benign tumours of the vagina of the dog that contain progesterone receptors can be reduced in size in a palliative or neoadjuvant setting using the progesterone receptor antagonist aglepristone.

INTRODUCTION

The most common types of tumours found in the genital tract of bitches are benign, smooth muscle tumours of the vagina and vulva. They are variably referred to as leiomyomas, fibroleiomyomas, fibromas and polyps depending on the amount of connective tissue present (Klein 2001, MacLachlan and Kennedy 2002). The tumours are usually seen in medium-aged, non-spayed, nulliparous dogs and surgery is the treatment of choice (Klein 2001). The majority of canine genital tract leiomyomas have progesterone receptors (Millán and others 2007), a finding that opens up the possibility of using progesterone receptor antagonists as a treatment for these tumours. The clinical and pathological findings of a vaginal fibroma with progesterone receptors that was treated with aglepristone (RU 534 Alizin; Virbac) before surgery to facilitate surgical access is reported here.

CASE HISTORY

A 12-year-old, entire, nulliparous, cross-breed female dog was presented to the referring veterinarian for the investigation of vulval bleeding and faecal tenesmus. The dog had regular oestrus cycles and had not received any previous hormonal treatment. The animal was alert and in good body condition. On physical examination, bulging of the perineum was noticed and on palpation a rounded, firm non-painful mass, measuring 9.1×5.4 cm, was noticed. It was found to compress the overlying, erythematous skin (Fig 1A) and the perianal skin was also found to be erythematous. Vaginal examination showed a firm mass with a smooth surface on palpation occupying its lumen.

A vaginal smear showed 70 per cent superficial keratinised epithelial cells, parabasal epithelial cells, neutrophils and red blood cells. Blood analysis and thoracic radiography (lateral and ventrodorsal) were normal. A lateral abdominal radiograph showed compression and elevation of the rectal ampulla. To reduce the size of the tumour mass and therefore facilitate surgical accessibility, 10 mg/kg aglepristone was applied subcutaneously on days 1, 2, 8, 15, 28 and 35. Blood samples for detecting plasma progesterone concentrations were taken on days 1 (4.56 ng/ml), 28 (28.75 ng/ml), 45 (2.58 ng/ml) and 60 (1.98 ng/ml).

Regular clinical evaluation showed the size of the tumour, measured through the perineal skin with a calliper as it was on day 1, had been reduced by approximately one third, on day 28, and it now measured 6.7 × 5.0 cm. Both cutaneous erythema and faecal tenesmus had resolved by day 28 (Fig 1B). No adverse effects at the site of injection or on the behaviour of the dog were noticed. An incision biopsy was taken on day 15 and submitted for histopathological diagnosis and to determine the presence of hormone receptors. On day 45, the tumour measured 6.4 × 4.7 cm.

Surgery, consisting of tumourectomy and ovariohysterectomy, was performed.

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on day 60. The dog was positioned in external recumbency. The perineal skin was clipped and prepared for surgery, and a standard episiotomy was performed. A median skin incision was made from the level of the caudodorsal aspect of the horizontal vaginal canal to the dorsal commissure of the vulval cleft. Scissors were used to incise the subcutaneous muscle and mucosal layers. Lateral retraction of the edges allowed exposure of the mass, located on the right wall of the vagina. Sharp dissection combined with judicious use of diathermy was used to excise the mass. A clean margin of tissue was obtained and confirmed by the macroscopic appearance of the surrounding tissues. A continuous suture of monofilament glycomer 631 (Byosin 3-0) was used to appose the mucosal edges after the tumour was resected. The episiotomy was closed in layers using standard single interrupted sutures.

Both the excision biopsy and the surgical specimens were fixed in 10 per cent buffered formalin and embedded in paraffin wax. The tumour was classified as a fibroleiomyoma (Kennedy and others 1998) by histological examination of tissue sections stained with haematoxylin and eosin (Fig 3). The ovaries had five highly vascular corpora lutea. In addition, unilocular or multi-locular cysts lined by flat, simple epithelium were identified outside of the right ovary and classified histologically as paraovarian cysts (Kennedy and others 1998). In the uterus, slight cystic endometrial hyperplasia was observed. Cystic endometrial glands surrounded by stroma were located within the myometrium of the right horn of the uterus and were classified histologically as adenomyosis (Kennedy and others 1998). The avidin-biotin-peroxidase complex method was used to evaluate the immunohistochemical expression of vimentin, calponin, Ki67 antigen, oestrogen receptor α and progesterone receptors (Martín de las Mulas and others 2000, Espinosa de los Monteros and others 2002). Immunohistochemically, the tumour cells reacted with the anti-actin antibody, but they did not react with the anticalponin antibody (Fig 4). The majority of tumour cells reacted with both the antioestrogen receptor α and the antiprogestosterone receptor antibodies in the nucleus (Fig 5). The amount of both oestrogen receptor α-positive and...
The findings of the present study indicate that blocking the progesterone receptors with aglepristone may reduce the size of benign genital tract tumours that have progesterone receptors. The use of lineage-specific tumour markers does not confirm the histopathological diagnosis of fibroleiomyoma and the tumour was reclassified as a fibroma on the basis of the exclusive expression of the intermediate filament protein vimentin. The expression of calponin is considered an excellent marker of smooth muscle differentiation. The expression of calponin is considered an excellent marker of smooth muscle differentiation. The expression of calponin is considered an excellent marker of smooth muscle differentiation.

**REFERENCES**

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**Conclusions**

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