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SHORT PAPER

Endometrial Polypoid Adenomyomatosis in a Bitch with Ovarian Granulosa Cell Tumour and Pyometra

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Summary

Endometrial polypoid adenomyomatosis in an 8-year-old German shepherd bitch is described. The lesion was associated with ovarian granulosa cell tumour and pyometra; grossly, it consisted of sessile or pedunculated processes with both epithelial and non-epithelial components, in which smooth muscle cells were predominant. The endometrium was diffusely atrophic and showed multifocal squamous metaplasia. The findings are discussed as possible consequences of the functioning ovarian tumour and pyometra, but an involvement of growth factors is also proposed.

Keywords: dog; endometrial adenomyomatosis; granulosa cell tumour; ovary; tumour

Introduction

Granulosa cell tumour (GCT) is common in the canine ovary. Usually unilateral and benign, it has been reported to produce oestradiol, progesterone and α-inhibin (McCandlish *et al.*, 1979; Pluhar *et al.*, 1995; Marino *et al.*, 2003). Depending on its hormonal production, GCT often induces persistent oestrus, vulval swelling with serosanguineous discharge and alopecia (Johnston *et al.*, 2001). Other GCT effects include cystic endometrial hyperplasia–pyometra complex and inhibin-dependent atrophy of the contralateral ovary (Johnston *et al.*, 2001; Marino *et al.*, 2003). Endometrial squamous metaplasia (SM) may appear as "morules" of immature, stratified squamous cells, replacing the glandular epithelium. It is a fairly common finding in women with various benign uterine diseases (Ronnett and Kurman, 2002). In the dog, focal or diffuse endometrial SM has been reported in association with oestrogen-producing GCTs (Wouda *et al.*, 1978; Zanghì and Gimbo, 1998), oestradiol treatment (McEntee, 1990) and cystic endometrial hyperplasia–pyometra complex (Dow, 1958; McEntee, 1990; De Bosschere *et al.*, 2001). In such cases, abnormalities of the myometrial smooth muscle cells, such as hypertrophy or hyperplasia, have also been observed (Dow, 1958; De Bosschere *et al.*, 2001). Hormone responsiveness of the endometrial and myometrial components in the canine uterus depends on oestrogen and progesterone receptors (Vermeirsch *et al.*, 1999, 2000), which are known to be increased in cases of cystic endometrial hyperplasia–pyometra complex (De Cock *et al.*, 1997; Dhaliwal *et al.*, 1999; De Bosschere *et al.*, 2002). In this paper an endometrial proliferative lesion ascribed to polypoid adenomyomatosis with multifocal endometrial SM is described in a bitch affected by GCT and pyometra.

An 8-year-old nulliparous German shepherd bitch was admitted for clinical evaluation because of an increasing, reddish, vulval discharge. Physical examination revealed a poor general state, with vulval swelling, alopecia and perineal skin hyperpigmentation. Abdominal palpation revealed a large mass caudal to the left kidney and an enlarged uterus. Ultrasound examination revealed a non-homogeneous hypoechoic mass in the left ovarian site, consisting of fluid-filled cysts of various sizes. Segmental enlargements of the uterine horns could be observed, containing hypoechoic fluid and several hyperechoic projections, which

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were predominant in the right horn. Such findings were consistent with an undefined endometrial lesion, together with pyometra and an ovarian neoplasm. As a consequence, the bitch underwent ovariohysterectomy.

The left ovarian tumour (9.5 × 9 × 6.5 cm; weight, 255 g) had irregular, protruding nodules, greyish to bluish in colour. Its cut surface displayed solid and multicystic components. The cysts (2–3 cm in diameter) contained serous reddish fluid and blood clots. The right ovary (1.5 × 1 × 0.4 cm; weight, 1 g) was small and atrophic. The uterine horns, which were enlarged (up to 5 cm in diameter), showed annular constrictions (Fig. 1) and were filled with abundant red–brown purulent exudate. The endometrial surface was roughened by the presence, mainly in the right uterine horn, of irregular and thickened transverse folds, greyish in colour (Fig. 2). Ovarian and uterine samples were fixed in 10% neutral formalin and paraffin wax-embedded. The sections (5 µm) were stained with haematoxylin and eosin (HE) or Masson's trichrome stain. Immunohistochemistry was performed by the avidin-biotin-peroxidase complex (ABC) method (Vectastain Kit elite; Vector Laboratories, Burlingame, CA, USA), with the following antibodies: anti-cytokeratin 34BE12 (Novocastra Laboratories, Newcastle upon Tyne, UK), diluted 1 in 400; anti-α-smooth muscle actin (Novocastra), diluted 1 in 50; anti-α-inhibin (Serotec, Kidlington, Oxon, UK) diluted 1 in 100. The intensity of the immunolabelling was expressed as weak, moderate or strong.

The ovarian neoplasm consisted of follicle-like structures of various sizes, lined by proliferating granulosa cells, with interposed irregular fibrous septa. Solid tumour components had necrotic and haemorrhagic areas and occasional mitotic figures (0–3 per 10 high-power fields). Moderate immunolabelling for α-inhibin was seen in neoplastic granulosa cells. A left ovarian GCT was diagnosed, while the contralateral ovary presented atresic follicles only. In the uterus, diffuse chronic endometritis with marked atrophy of the endometrium was observed. A lymphoplasmacytic infiltrate with neutrophils and mononuclear phagocytes extended into the uterine wall up to the subserosal layer. The macroscopical transverse folds consisted of sessile or pedunculated polypoid processes of closely admixed epithelial and non-epithelial components (Fig. 3). The latter included varying amounts of smooth muscle bundles (Fig. 4). Multifocal non-keratogenic squamous metaplasia of the endometrial epithelium was observed, including focal morular changes (Fig. 4). Strong α-smooth muscle actin immunolabelling occurred in the non-epithelial component of the polypoid processes (Fig. 5). The metaplastic squamous cells of the endometrium showed diffuse moderate labelling for cytokeratin 34BE12.

Follow-up information from the owner and subsequent clinical examinations showed good post-operative healing. The general health status of the dog promptly improved and the alopecia, vulval swelling

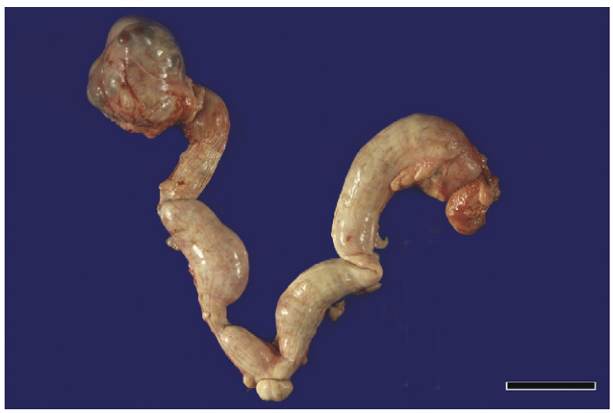

Fig. 1. Reproductive tract of the bitch, showing enlargement of uterine horns and a left ovarian tumour. Note the annular constrictions of the uterus. Bar, 6 cm.

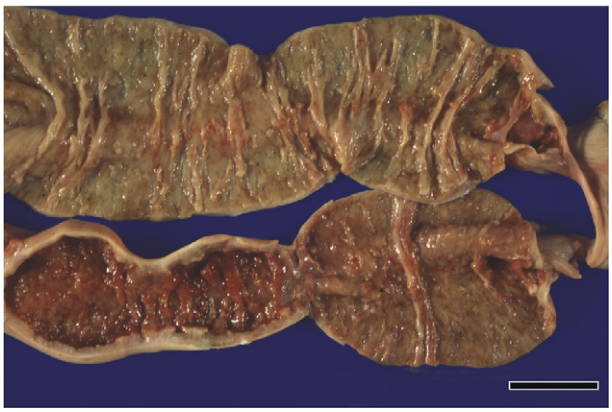

Fig. 2. Endometrial surface, showing transverse folds. Bar, 3.2 cm.

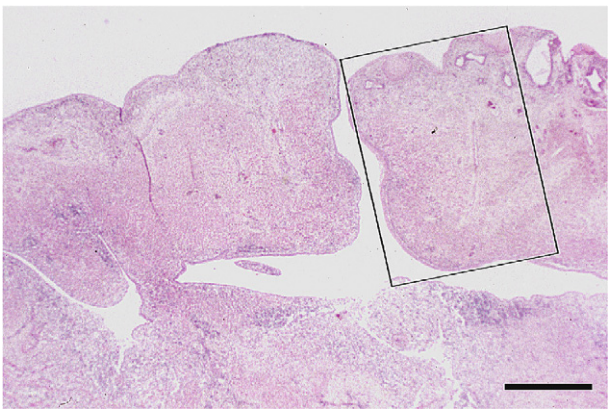

Fig. 3. Histologically, the transverse folds consist of pedunculated polypoid processes arising from the endometrial layer. HE. Bar, 800 µm.

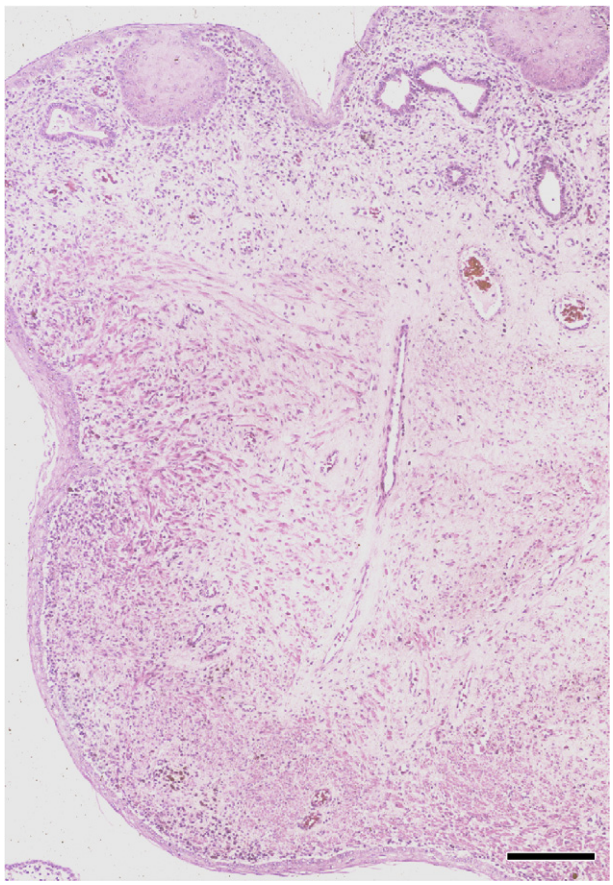

Fig. 4. Detail of the area outlined in Fig. 3, showing the stroma of the polypoid process, including numerous smooth muscle cells. The endometrial epithelium shows extensive squamous metaplasia and morular changes. HE. Bar, 200 µm.

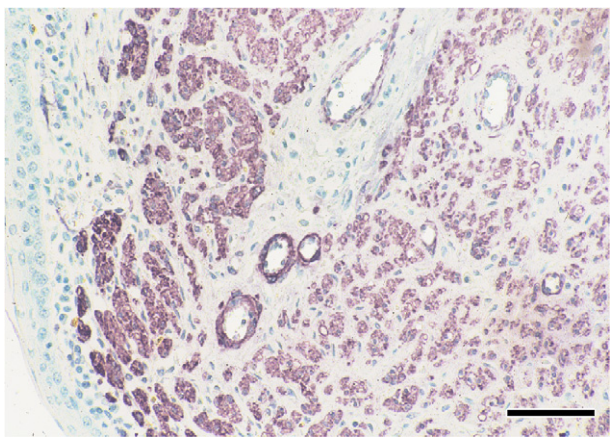

Fig. 5. Strong immunolabelling of α-smooth muscle actin in a polypoid process. ABC. Methyl-green counterstain. Bar, 80 µm.

and skin hyperpigmentation progressively decreased. No complications were noted in the following 2 years.

To our knowledge, this is the first report of endometrial polypoid adenomyomatosis in a dog affected by ovarian GCT and pyometra. The term *polypoid adenomyomatosis* is proposed herein to describe diffuse endometrial projections consisting of admixed epithelial and non-epithelial components with prominent smooth muscle bundles. The endometrial epithelium showed varying degrees of hyperplasia and squamous metaplasia, including morular changes. The less mature and more extensive SM distinguishes such a lesion from that in a previously reported canine case, in which the endometrial SM consisted of focal horn pearls and keratin cysts arising from the deep glandular epithelium (Zanghì and Gimbo, 1998). Single or multiple endometrial polyps have been reported in the bitch (Gelberg and McEntee, 1984), but they have been described as focal hyperplastic growths, generally without smooth muscle involvement or SM. On the basis of its obvious proliferative activity, the endometrial lesion described here more closely resembled the so-called Mazur-type atypical polypoid adenomyoma in women, in whch"extensive squamous or morular metaplasia is a common finding" (McCluggage *et al.*, 2003). In the present case, it would seem probable that the GCT and endometrial exudative inflammation resulted in the uterine polypoid adenomyomatosis. It is known that canine GCTs produce both oestrogen and progesterone (McCandlish *et al.*, 1979; Pluhar *et al.*, 1995), which play a role in the development of cystic endometrial hyperplasia and subsequent mucometra (Feldman and Nelson, 1987; Niskanen and Thrusfield, 1998). Such disorders are often complicated by pyometra, following bacterial colonization of the uterus. The high concentrations of circulating oestrogens and the endometrial inflammation imply the production of different growth factors, such as insulin-like growth factor-1 (De Cock *et al.*, 2002; Moyano and Rotwein, 2004), capable of stimulating endometrial and myometrial proliferative changes. Hormonal imbalance together with local growth factor production may have played a role in the present case of endometrial polypoid adenomyomatosis.

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