

## Incidental finding of uterine adenomyosis in a bitch with reproductive disorders: a case report

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**ABSTRACT:** Uterine adenomyosis, a disease not widely addressed in dogs, is characterised by the progressive penetration of endometrial glands and stroma into the myometrium, together with smooth-muscle hyperplasia. This report describes a case of adenomyosis in an 8-year-old German Shepherd bitch with mammary tumours, concomitant with cystic ovarian disease and endometrial cystic hyperplasia. Clinical signs included presence of small nodules and enlargement of mammary glands, and bloody uterine discharge. Ultrasonography confirmed the uterine and ovarian abnormalities, while the diagnosis was later confirmed by histopathological examination. The findings are discussed as possibly related to the reproductive disorders observed, and a hypothetical participation of hormonal factors, as has been described in woman, is suggested. However, further studies must be realized.

**Keywords:** adenomyosis; ovarian cysts; mammary tumour; infertility

Uterine adenomyosis is a non-neoplastic lesion resulting from the abnormal down-growth of the endometrial glands and endometrial stroma into the myometrium (Kennedy et al., 1998). Although it is a rare, sporadic disorder in dogs (Tamada et al., 2005), it is much more common in women.

Uterine adenomyosis results in no symptoms during much of its development, and is usually diagnosed in adult dogs. Since it is generally found as an incidental lesion in pathological changes of the uterus – including endometritis, pyometra and glandular-cystic hyperplasia – it tends to be investigated as a histological finding rather than a clinical disorder. Adenomyosis has recently been associated with infertility in humans (Barrier et al., 2004; Matalliotakis et al., 2005), although little is known of the precise mechanisms involved. Possible causes of adenomyosis in women include defects in the formation of the myometrium (Parrott et al., 2001), an abnormal immune response in the endometrium (Ota et al., 1998), surgery and hormone manipulation (Mori and Nagasawa, 1989; Baskin et al., 2002), and age (Barrier et al., 2004).

Diagnosis of adenomyosis in animals is always post-surgical, since the diagnostic techniques

used in humans, such as the measurement of serum cancer antigen 125 (CA 125) levels (Halila et al., 1987), hysterosalpingography (Marshak and Eliasoph, 1955) and magnetic resonance imaging (Bazot et al., 2001) are not used in canine veterinary practice.

This paper reports a case of adenomyosis diagnosed from a tissue specimen taken from a bitch with cystic endometrial hyperplasia, ovarian cysts and ovarian papillary cystadenoma, together with a previously-diagnosed mammary carcinosarcoma.

### Case history

An 8-year-old nulliparous German Shepherd bitch was admitted to the University of Cordoba, Veterinary Clinic after the owner noticed a number of mammary nodules. Vital signs were normal except for a mild increase in temperature (39.2°C). Blood biochemistry and metabolic tests were normal, with the exception of mild leukocytosis (Table 1). Physical examination revealed bilateral mammary tumours, involving the caudal abdominal (enlarged) and inguinal mammary

Supported by the Consejería de Innovación, Ciencia y Empresa, Junta de Andalucía, Spain (Research Group Project BIO287).

Table 1. Biochemical and haematological parameters

Parameter	Values	Reference values
WBC	$13.8 \times 10^{-3} \mu\text{l}$	$6-12 \times 10^{-3} \mu\text{l}$
RBC	$7.53 \times 10^{-6} \mu\text{l}$	$5.0-8.0 \times 10^{-6} \mu\text{l}$
HGB	18 g/dl	11–17 g/dl
HCT	49%	37–50%
MCV	69.2 fl	60–77 fl
MCH	23.9 pg	20–25 pg
MCHC	34.5 g/dl	32–36 g/dl
PLT	$167 \times 10^{-3} \mu\text{l}$	$200-400 \times 10^{-3} \mu\text{l}$
Urea	32 mg/dl	20–40 mg/dl
Creatinin	1.2 mg/dl	0.5–1.3 mg/dl
Total proteins	7.6 g/dl	6.0–7.5 g/dl
Fibrinogen	200 mg/dl	100–400 mg/dl
Glucose	91 mg/dl	60–115 mg/dl

WBC = white blood cells; RBC = red blood cells; HGB = hemoglobin; HCT = hematocrit; MCV, mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; PLT = platelets

glands of the right chain, and the abdominal and inguinal mammary glands of the left chain (smaller tumour masses). Laterolateral thoracic radiographs revealed no pulmonary metastases and surgical resection of both mammary chains was decided upon as the course of action. Histological examination of the right mammary chain, the first to be removed, confirmed malignant disease; one tumour was diagnosed as a carcinosarcoma (Figure 1 and 2).

Bloody vulvar discharge – which the owner associated with the heat period – was observed one month later, one day prior to the second operation (resection of the left mammary chain). The vaginal smear comprised mainly intermediate and superficial cells showing signs of keratinization with occasional endometrial cells. Vaginal disorders were not considered during the clinical exploration. Subsequent abdominal ultrasonography showed

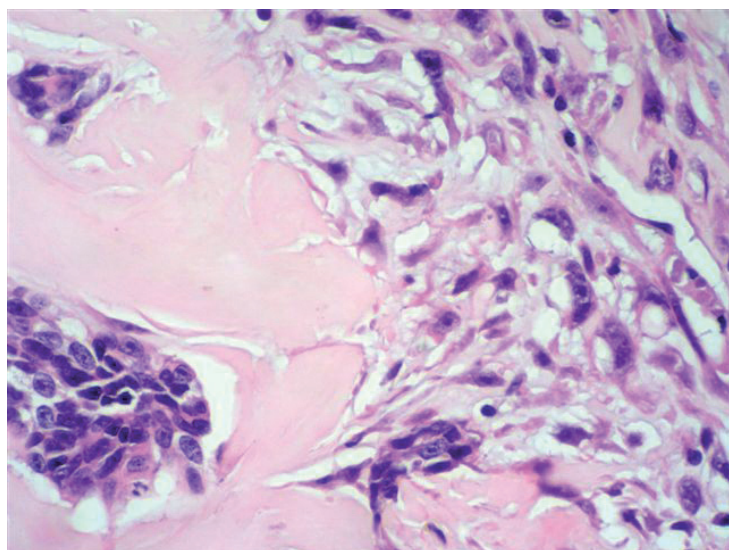


Figure 1. Mammary carcinosarcoma (hematoxylin-eosin, 40×) showing rounded neoplastic epithelial cells with rounded-to-ovoid, vesicular nuclei, marked nucleoli and high-grade atypia. Myoepithelial cells with high-grade atypia

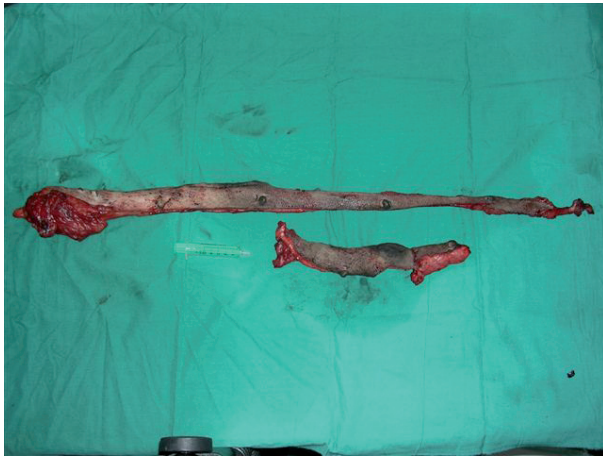


Figure 2. Resected mammary chain

that both ovaries were abnormal in size, with large anechoic structures; ovarian cystic disease was diagnosed (Figure 3). Uterine ultrasonography findings were consistent with endometrial cystic hyperplasia (Figure 4). In the light of these findings, ovariohysterectomy was performed in addition to the programmed mastectomy. At gross examination, numerous cysts were visible on the ovaries. One ovary displayed a brownish-black, morula-like multilobar lesion, measuring  $3.5 \times 2.5 \times 2$  cm and containing solid, chocolate-coloured material (Figure 5). A bleeding cyst was also observed, comprising several thin-walled cavities containing a translucent fluid. A large, thin-walled, multilobar cyst containing amber-coloured material was observed. The cervix was slightly enlarged (approx. 50 mm).

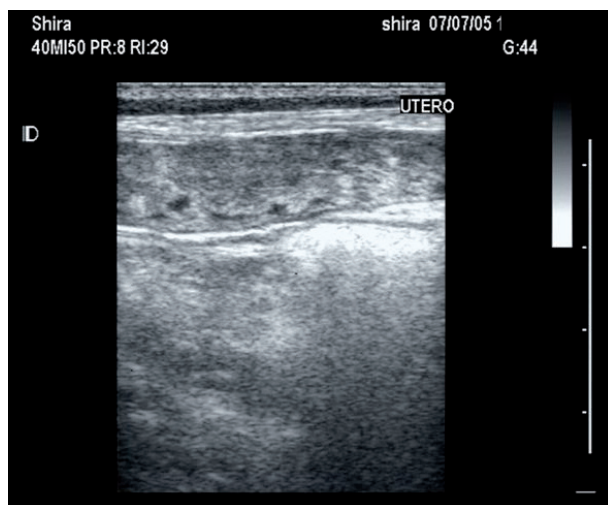


Figure 4. Echoic uterus containing anechoic cysts, indicative of endometrial cystic hyperplasia

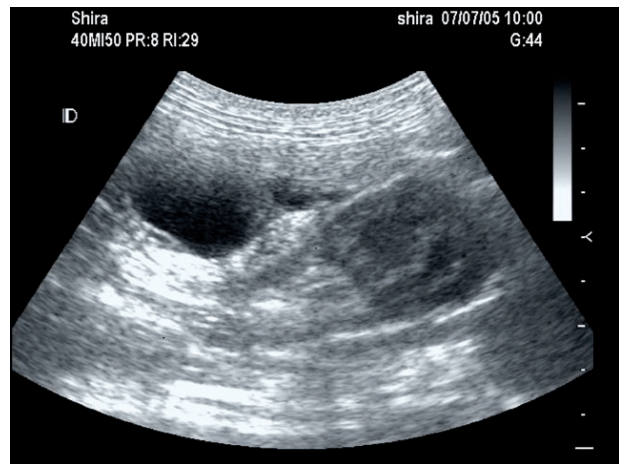


Figure 3. Left: ultrasonograph of cystic ovary (anechoic); right: kidney for purposes of comparison

Microscopic examination disclosed a highly-edematous endometrial mucosa, which hindered interpretation of possible hyperplasia; endometrial cysts with fluid retention were also observed. The cervical mucosa *lamina propria* displayed chronic inflammatory infiltrate and cystic glandular dilation; evidence of fibrosis among muscle-fiber bundles suggested a possible cause of enlargement. Glandular structures surrounded by endometrial stroma were visible in the cornual and cervical myometrium (Figure 6). This finding enabled diagnosis of adenomyosis.

## DISCUSSION

In the present case, uterine adenomyosis was an incidental finding in a bitch with mammary tumours and

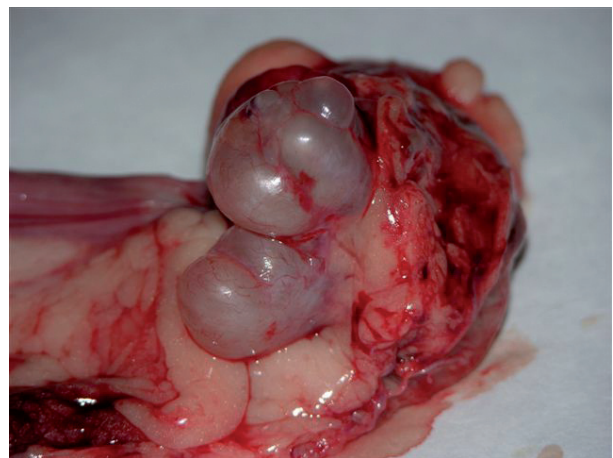


Figure 5. Ovary showing brownish-black multilobar lesion containing solid, chocolate-coloured material, with a thin-walled, bleeding cyst containing translucent fluid



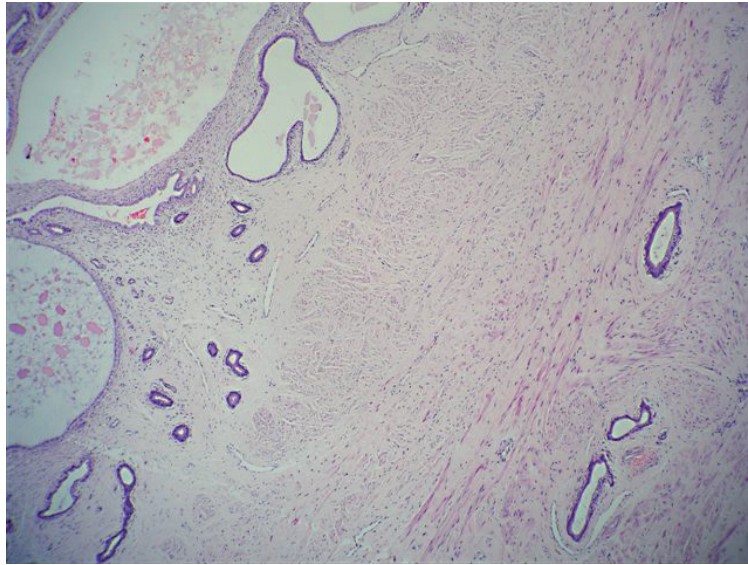


Figure 6. Cervix. Mild chronic inflammatory infiltrate in mucosal lamina propria; cystic glandular dilation; fibrosis among smooth-muscle-fiber bundles (hematoxylin-eosin, 4×)

ovarian cystic disease. In studies with mice, Nagasawa et al. (1987) and Nagasawa and Kusakawa (2001) suggested a possible link between mammary tumours and uterine adenomyosis: the two disorders develop simultaneously pointing to a powerful genetic, as well as environmental, influence. The joint presence of the two disorders here indicates that the clinical signs as a whole may have a hormonal aetiology.

The literature contains three reports of canine adenomyosis, in which clinical signs were only apparent at an advanced stage (Stocklin-Gautschi et al., 2001; Tamada et al., 2005) (Table 2). Although adenomyosis is certainly found in numerous cases of uterine pathology, the present case study suggests a link among adenomyosis, mammary tumour and ovarian cystic disease, perhaps mediated by the influence of oestrogen hormone associated with polycystic ovaries.

Although the mechanism responsible for uterine adenomyosis is not known, research in women has

suggested a link between changes in the endometrium and in ovarian hormones, and increased local production of oestrogen (Leyendecker, 2006). Oestrogen-related hyperperistalsis together with a progesterone-induced increase in intrauterine pressure might result in myometrial dehiscencies that are infiltrated by basal endometrium with the secondary development of peristromal muscular tissue. This would lead to diffuse or focal adenomyosis of varying extent, and local aromatase production would contribute to the proliferation of lesions through local oestrogen synthesis (Ferenczy, 1998; Leyendecker, 2006). This is why adenomyosis may constitute a progressive disease. With regard to the impact of adenomyosis on fertility, the most likely explanation is the impairment of uterine mechanisms of rapid and sustained sperm transport as a consequence of the destruction of normal uterine architecture (Leyendecker, 2006).

Table 2. Findings in the present case study, compared with reports of canine uterine adenomyosis in the literature

Reference	Age	Breed	Weight	Litters	Hormone treatment	Cervix involvement	Other pathologies	Vaginal discharge
Tamada et al., 2005	13	Shiba-inu	5.9	1	no	yes	OCD CEH	purulent
Stocklin-Gautschi et al., 2001	10	Crossbred	41	no	no	yes	OCD cervical enlargement*	bloody, milky, mucosa
Stocklin-Gautschi et al., 2001	12	Toy Poodle	4.5	no	no	yes	no uterine torsion	no, tense abdomen

\*the remainder of the uterus was normal

Here, the joint presentation of endometrial hyperplasia with cysts suggested that adenomyosis may perhaps be due to an endocrine impairment. Ovarian hormones are known to favour the development of mammary tumours; thus, early ovariectomy has been found to limit tumour development (Schneider et al., 1969). However, the aetiology of uterine adenomyosis remains unclear, and the disorder is rarely addressed in the literature. Reported symptoms vary widely, which is suggestive of a multifactorial aetiology.

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Received: 2008–08–13

Accepted: 2008–11–23

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