Ovarian remnant syndrome – a diagnostic dilemma
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Abstract
Ovarian remnant syndrome is a well-recognized complication of surgical sterilization in dogs and cats. It is characterized by a return of estrus behavior months to years after sterilization. Clinical signs vary widely and may include estrus behavior, vulvar discharge or swelling and attractiveness to males, as well as mammary development and lactation. In some animals, the syndrome is only recognized after the appearance of secondary diseases, such as persistent vaginitis, pyometra and reproductive neoplasia. Differential diagnoses of ovarian remnant syndrome include uterine stump pyometra, exogenous estrogen exposure, vaginitis, urinary tract infections and neoplasia. Suspicion of ovarian remnant syndrome based on clinical signs can be confirmed by several approaches, including vaginal cytologic evaluation, vaginoscopy, hormonal assay, ultrasonographic examination and exploratory laparotomy or laparoscopy.

Keywords: Ovarian remnant syndrome, ovariohysterectomy, GnRH stimulation test

Introduction
Ovarian remnant syndrome is a well-recognized complication of surgical sterilization, accounting for 22-43% of dogs presenting for spay-associated complications.1,2 Two sources suggest that the syndrome may be more common in cats than dogs,3,4 however a recent retrospective study did not support this finding.5 Large breed dogs seem to be over-represented, however no breed predisposition has been documented.2,5 In one study, ovarian tissue was detected bilaterally in most animals,3 while several studies report ovarian remnants more commonly in the location of the right pedicle.1,5,6 Surgical experience has not been documented as a contributing factor to ovarian retention.5 The most common etiology of ovarian remnant syndrome in companion animals appears to be incomplete removal of one or both ovaries, while less common etiologies include revascularization of small pieces of ovarian tissue at sites distant from the ovarian pedicle and the presence of supernumerary ovaries or the presence of ovarian tissue within the pedicle.3,5,7,9 Revascularization of ovarian tissue within omentum or other locations is reported more often in cats than dogs.3,4,10 In a prospective experimental study, eight of nine (88.9%) cats in which ovarian tissue was loosely sutured to the mesentery had functional ovarian tissue six months later.11

The most common presenting complaints of animals with ovarian remnant syndrome were related to a return to estrus, including estrus behavior, vulvar discharge or swelling, persistent vaginitis and attractiveness to males.1,2,4,5,12 Fewer animals presented with reproductive diseases, including pyometra and reproductive neoplasia.1,2,8,9 The interval from time of surgical sterilization to presentation varied from 17 days to ten years.3,5

Diagnostic approach
As with most conditions, the approach to animals presenting for reproductive abnormalities should include a careful history. Most animals with ovarian remnant syndrome have a history of recurrent cyclic clinical signs that are relatively static in severity, whereas occasional animals will have ongoing chronic clinical signs, which may also be consistent with other conditions, such as neoplasia, pyometra or exogenous estrogen exposure. Clinical signs upon presentation vary widely depending on the individual animal, the amount of reproductive tissue remaining in the animal and the stage of the estrous cycle upon presentation. The most common clinical signs observed in reported cases and in our hospital include vulvar swelling, serosanguinous vulvar discharge, estrus behavior (receptiveness to males and flagging in the bitch, vocalization, rolling and lordosis in the queen). Many cases present with more than one clinical sign concurrently,5 while vulvar discharge is not expected in bitches from which the entire uterus was excised. Additional reported clinical signs include purulent vulvar discharge, mammary development and/or lactation. Many cases present without any active clinical signs, but with historical
clinical signs as described above. Differential diagnoses that should be considered for spayed animals presenting with vulvar discharge or a history of vulvar discharge include ovarian remnant syndrome +/- uterine stump pyometra, exogenous estrogen exposure, vaginitis, urinary tract infections and neoplasia (vaginal, ovarian or adrenal).\(^4,5,7,13\) Diagnosis may be achieved by several approaches, including vaginal cytologic evaluation, vaginoscopy, hormonal assay, ultrasonographic examination and exploratory laparotomy or laparoscopy.

Vaginal endoscopic and cytologic examination

Vaginal examination is particularly valuable in bitches with a clinical presentation consistent with proestrus or estrus. Characteristic changes of the vaginal mucosa under the influence of estrogen include vaginal edema (vaginoscopy), increased cellularity and increased numbers of superficial cells, in combination with low numbers of granulocytes (vaginal cytology), while large numbers of erythrocytes will often be seen in proestrus bitches with a uterine stump. Queens resent vaginal sample collection more than bitches and may require sedation to pass a small swab or perform a small volume lavage. Further, interpretation of vaginal smears from queens may be more difficult than those of bitches, as large sheets of anuclear vaginal cells are usually not seen.\(^6,14\)

At the time of vaginoscopy and vaginal cytologic examination, owners should be carefully questioned about potential sources of exogenous estrogen exposure. Estrogenic creams or medications may be available in the household and it is our experience that regular skin-skin exposure or oral exposure to these medications may lead to characteristic signs of heat and vaginal epithelial changes in spayed animals. Likewise animals may be treated with estrogenic compounds for other conditions, such as urinary incontinence.

Hormonal assay

Hormonal assay is best performed in conjunction with a stimulation test. Assay of a single sample for serum estrogen, progesterone or luteinizing hormone (LH) concentration has not been reliably diagnostic.\(^4,5,11,15\) Elevated serum estrogen concentrations (>20 pg/mL) are consistent with ovarian remnant syndrome, exogenous estrogen exposure and neoplasia\(^4,13,14\) Conversely, several studies reported cases with behavioral or cytologic signs of estrus which did not have elevated estrogen concentrations.\(^4,5\) Likewise, the absence of elevated serum progesterone concentrations cannot be used to rule out the presence of ovarian tissue. Dogs experience elevated concentrations of serum progesterone (>2 ng/mL or >6 nmol/L) only during diestrus (for 50-80 days after conclusion of proestrus), whereas cats are induced ovulators and will not have elevated serum progesterone concentrations during interestrus or estrus. Thus, increased serum estrogen or progesterone concentrations are consistent with the presence of ovarian tissue, but low serum concentrations of either hormone cannot be utilized to rule out the presence of ovarian tissue. Luteinizing hormone has been reported to be elevated in animals after ovariectomy or ovariohysterectomy compared to intact animals.\(^15,16\) However, serum LH concentrations rise slowly after ovariectomy and may fluctuate widely during the cycle of animals with ovarian tissue.\(^16\)

In contrast, both gonadotropin releasing hormone (GnRH) and human chorionic gonadotropin (hCG) stimulation tests have been shown to have great diagnostic value in dogs and cats.\(^4,6,16-18\) Ovulation can be induced reliably with either GnRH or hCG in cats presenting with clinical signs of heat.\(^4,6,18\) England and coworkers administered 500 IU of hCG to ten cats with suspected ovarian remnants and five fully ovariohysterectomized cats and measured serum progesterone concentrations at the time of drug administration and again seven days later. Serum progesterone concentrations were basal in all samples from ovariohysterectomized cats, while they increased from 0.37±0.2 ng/mL to 10.5±9.2 ng/mL in cats with ovarian tissue.\(^6\)

In dogs, ovulation occurs spontaneously and stimulation of ovulation during estrus is not necessary. To confirm presence of functional ovarian tissue and rule out other sources of estrogen exposure after cytologic examination, serum progesterone concentrations may be measured three to six weeks after cessation of clinical signs.
A stimulation test may further be used to diagnose the presence of ovarian tissue in animals which are currently not experiencing clinical signs of heat. Anestrus animals cannot be clinically or hormonally differentiated from neutered animals. However, a sharp increase in estradiol concentration has been demonstrated in dogs and cats that are intact or have retained ovarian tissue after ovariohysterectomy. Thus, in the absence of behavioral or cytologic signs to support ovarian presence in either a dog or cat, the combination of a single progesterone assay and a GnRH stimulation test with blood collection before and two hours after GnRH administration would reliably serve to diagnose the presence of ovarian tissue.

Ultrasonographic examination

Ultrasonographic diagnosis of ovarian tissue may be difficult due to the small size of the tissue and variable location. However, ultrasonographic confirmation of ovarian tissue may help guide a surgical approach and can be used to evaluate the uterine stump for evidence of inflammation or infection. In a recent retrospective study by Ball and coworkers, ultrasonography correctly identified the presence (or absence) of ovarian tissue in each pedicle in nine of 12 cases (75%). In three animals, tissue was not detected in one or more locations on ultrasonographic examination, but was subsequently confirmed with histology. In two animals, ovarian tissue was suspected, but subsequently not confirmed at that location. In this study, clinical signs of estrus or proestrus did not appear to affect the ultrasonographers’ ability to correctly identify ovarian tissue. However the three dogs that were not in estrus had clinical signs or a history consistent with diestrus. Thus, ovarian tissue may still have been enlarged compared to an anestrus animal, due to the presence of corpora lutea. A granulomatous suture reaction must be considered as a differential for hypoechoic masses in the location of the pedicle and may lead to false positive diagnosis of ovarian tissue.5

Exploratory laparotomy

Due to the invasive nature of this procedure, it is recommended that confirmation of ovarian tissue be achieved prior to surgery, however no diagnostic modality described above can reliably diagnose the number and location of tissues in the animal. Thus, even after abdominal ultrasound, a full exploratory examination of the abdominal contents should be performed. Performing the laparotomy during behavioral estrus or during diestrus may enhance the surgeon’s ability to grossly see ovarian tissue in the pedicles or omentum. However, if ovarian tissue is not detected, excisional biopsies of the pedicles should be performed. Ovarian and other tissues removed during the exploratory laparotomy should be submitted for histopathologic examination. Several cases have documented neoplastic changes in retained ovarian tissue, as well as other reproductive organs of animals with ovarian remnant syndrome. Ball and coworkers further reported increased incidence of neoplastic changes in ovarian remnants (23.8%) compared to sexually intact female dogs (6.25%).5

References