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Clinical case of ovarian remnant syndrome in a cat

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Abstract

Ovarian remnant syndrome (ORS) has been monitored in a cat, which presents in the form of estrus, 8 months after ovariohysterectomy (OVH). This is an iatrogenic condition as a result of the complexity of the OVH content in 22% of all complications after neutering in small animals. Emphasis is put on the anatomical predispositions for the frequency of occurrence of the ORS in cats compared with dogs. They are described through a detailed observation of the reasons for the presence and localisationlocalization of the residual ovarian tissue, variable clinical manifestations, possibilities for diagnosis and treatment of the ORS in small animals. Almost every time this syndrome is combined with uterine stump pyometra, manifested with vomiting, allotriphagy, severe pain syndrome, leucocytosis and lymphocytosis. Through this clinical case we hope to draw the attention of veterinary surgeons to the possibility of frequent emergence and quick identification and adequate treatment of ORS in cats.

Keywords: ovarian remnant syndrome, uterine stump pyometra, ovariohysterectomy, cat.

Introduction

Ovariohysterectomy (Spaying, OVH) is a radical surgical intervention, in which the ovaries and the uterus are removed by medial or paralumbar incision (Polliari and Bonnett, 1996; Musal and Tuna, 2005; Sontas et al., 2007; Ward, 2009; Bright, 2011; Rumenova et al., 2013; Muraro and White, 2014). It is performed to prevent estrus (heat) and unwanted pregnancies and offspring as well as to decrease the incidence of neoplasia – ovarian and uterine cancer and also breast cancer in the number one type of cancer diagnosed in intact or un-spayed female cats which are influenced by reproductive hormones (Ward, 2009). Spaying is the treatment of choice for the prevention of uterine diseases, including pyometra (uterine infection), metritis, cystic changes of the uterus, rupture of the uterus, etc. Vaginal prolapse, uterine prolapse, and some hormonal (endocrine) problems, such as diabetes mellitus and epilepsy in the cat may benefit from a sterilization procedure. Pregnancy termination is another indication for removal of the ovaries and uterus (Bright, 2011; Ward, 2009). Ovariohysterectomy is one of the most commonly performed surgical procedures in companion animal practice. It is recommended by many animal welfare organisations for canine population control, and is recognized by the World Health Organization as a means of dog population control as a part of rabies control programmes in rabies-endemic areas (Anon, 2004; Muraro and White, 2014). Most cats do well after surgery, with no or minimal complications (Bright, 2011).

Complications were recorded in companion animal practice corresponding to frequency of 1-7.5% (Polliari and Bonnett, 1996; Muraro and White, 2014). Minor complications include licking at the incision, development of inflammation or a small pocket of fluid (seroma) beneath the skin at the incision, and premature loss of external skin sutures (Bright, 2011). Hemorrhage after surgery is more common in larger, obese cats and is more of a concern if it originates from the ovarian artery, uterine vessels, surgical wound and postoperative vaginal state (Bright, 2011; Muraro and White, 2014). As is possible with all abdominal incisions, a breakdown of the abdominal wall with herniation of abdominal contents can occur, albeit rarely. Delayed complications of removing only the ovaries include a return of heat cycles and infection of the uterus (pyometra), especially if removal of ovarian tissue was incomplete - Ovarian Remnant Syndrome (ORS). If the ovaries and the uterus were both removed, the small portion of the uterus left behind may become infected at a later date. This complication is referred to as stump pyometra, and it is sometimes associated with incomplete removal of ovarian tissue at the time of the original sterilization procedure (Bright, 2011). Other complications have been described, including wound healing complications, uterine granuloma formation obstipation, iatrogenic ureteral trauma, vaginoperitoneal fistula formation, enterocutaneous fistula formation, gossypyboma and urinary incontinence (Muraro and White, 2014; Merlo and Lamb, 2000). Anesthetic reaction – any cat can have an unexpected adverse reaction following the administration of any drug or anesthetic (Ward, 2009).

ORS which is defined as functional ovarian tissue present in a previously ovariectomized patient, has been reported to represent 22% of spay complications presented to a referral hospital (Pearson, 1973; Wallace, 1991). Three explanations have been suggested for the development of ORS in companion animals (Feldman and Nelson 2004; Sontas et al., 2007). The first and the most accepted explanation is incomplete surgical removal of one or both ovaries as a surgical error. This may be due to a small abdominal wall incision that makes difficult to visualize, reach and carry out the ligature of the ovary or ovaries, or to incorrect ligaturing of ovarian tissues or anatomical location of the right ovary (Wallace, 1991, Miller, 1995, Johnston et al., 2001a, Prats, 2001, Sontas et al., 2007). Anatomically, the right ovary and uterine horn are located in a more cranial position than the left ovary and uterine horn and the

suspensory ligament is shorter, making that ovary more difficult to exteriorize, which predisposes the surgeon to leave the ovary during the surgery (Evans and Christensen, 1993, Sontas et al., 2007). The reports by Pearson 1973, Wallace 1991, England, 1997, Prats 2001, Sontas et al., 2007, and Ball et al., 2010 demonstrated that the right ovary is more frequently found to be the remnant in the dog and cat. However, in a study by Miller 1995 and Sontas et al., 2007, the numbers of right ovary and both ovaries as ramnants were found to be equal.

Dropping of some ovarian tissue into the abdomen during the surgery was suggested as a second cause of ORS (Wallace, 1991, Feldman and Nelson, 2004, Romagnoli, 2004). If a piece of ovarian tissue is accidentally dropped into the abdomen during the surgery, this tissue revascularizes with omentum or the serosa of abdominal viscera and begins to function like a normal ovary (Prats 2001, DeNardo et al., 2001; Feldman and Nelson 2004, Romagnoli 2004; Sontas et al., 2007). This condition has been demonstrated experimentally by Shemwell and Weed (1970) in cats, by Le Roux and Van Der Walt 1977 in dogs and by Minke et al., 1994 in laboratory rats. ORS may account for more dogs than cats being affected in some reports (McEntee, 199; Hedlund, 2002; McEntee, 1990; Ball et al., 2010). Dogs have more adipose tissue surrounding the ovaries that can obscure exposure, and the suspensory ligament of the ovary in dogs is more difficult to rupture to achieve adequate exposure, compared with the situation in cats. In addition, dogs typically have a deeper abdominal cavity, which makes it more challenging to exteriorize each ovary (McEntee, 199; Hedlund, 2002; McEntee, 1990; Ball et al., 2010).

The third and final explanation is the presence of an accessory ovary or of ovarian tissue (ectopic) that is localized in the broad ligament or proper ligament of the ovary (McEntee, 1990; Miller, 1995; Johnston et al., 2001; Feldman and Nelson, 2004; Sontas et al., 2007). An accessory ovary is defined as an extra ovary which is located adjacently and may be connected to the normal gonad (McEntee, 1990; Sontas et al., 2007). An accessory ovary has been reported in queens (Anonymus, 1977; Sontas et al., 2007), cattle and in women (McEntee, 1990, Sontas et al., 2007). It is important to be aware of the fact that an accessory ovary may be activated if normal gonads are removed (McEntee, 1990; Sontas et al., 2007). Accessory ovaries have not been reported in dogs. In the bitch, ectopic tissues have been identified within the ovarian ligament at its junction with the abdominal wall according to Johnston et al., 2001a, Sontas et al., 2007 and in a pregnant queen with functional corpus luteum (Prats 2001; Sontas et al., 2007).

In the above and in another clinical report (Pearson, 1973; Okkens et al., 1981; Musal and Tuna, 2005) it was observed that in 58% and 71% of uterine stump pyometra cases there is also functional ovarian tissue present. This is considered important evidence of hormonal influence, especially progesterone secretion, which is essential in the formation of stump pyometra (Nelson and Feldman, 1986; Johnston et al., 2001a, Musal and Tuna, 2005). Uterine remnants were excised and evaluated histologically and showed evidence of cystic endometrial hyperplasia. Microbial culture from these yielded Escherichia coli and Enterococcus spp, which indicated a uterine stump pyometra (Ball et al., 2010).

Diagnosis of ORS can be difficult because the ovarian tissue may be very small. Diagnostic imaging may be used to find residual ovarian tissue, but both ultrasound and CT may miss residual tissue if it is very small, if the patient is in anestrus. So ORS cannot be ruled out if abnormal tissue is not seen (Ball et al., 2007; Sontas et al., 2007). There are several tests to diagnose ovarian remnants in a patient with clinical signs. Vaginal cytology can be obtained during signs of estrus and cornification of the vaginal epithelial cells is consistent with an estrus cycle (Olson et al., 1987; Wallace, 1991). Hormone stimulation tests with human chorionic gonadotropin (HCG) or gonadotropin releasing hormone (GnRH) must be administered

during signs of estrus and can be time consuming and expensive (Pearson, 1973). Levels of two gonadal hormones, oestradiol and progesterone, should be measured to determine the presence of an ovarian tissue. Serum oestradiol levels higher than 10-20 pg/ml or serum progesterone concentrations above 2 ng/ml are indicative of a functional ovarian tissue (Wallace, 1991). One of the most promising tests for determining the presence of ovarian tissue is a hormone assay that measures levels of Anti-Mullerian Hormone (AMH). Because ovaries are the sole source of AMH, a positive test would indicate the presence of ovaries or ovarian tissue (Place et al., 2011, Yilmaz et al., 2015). Differential diagnosis for ORS are the conditions that cause bloody vulvar discharge including vaginal neoplasia, vaginitis, uterine stump pyometra, trauma, exogenous estrogen therapy and coagulopathy (Sontas et al., 2007). One differential diagnosis for a false-positive identification of residual ovarian tissue during ultrasonography is a suture granuloma at the site of ligation of the ovarian pedicle. Suture material can cause a localized immunologic and inflammatory reaction (Rattenbacher et al., 2001; Ball et al., 2007). The timing of the exploratory laparotomy is very important. It will be much easier to detect the ovarian tissue, if the animal is under the influence of oestrogen or if ovulation has occurred. In both cases, the ovary will be enlarged because of the follicles or corpora lutea. However, due to the increased vascularity, intraoperative bleeding could be a complication. Although the intraoperative bleeding will be less in the luteal phase, postoperative false pregnancy may be induced (Perkins and Frazer 1995, Johnston et al., 2001, Prats 2001, Feldman and Nelson 2004, Sontas et al., 2007). Laparotomy is not recommended during an anestrous period, since the remnant tissue might be too small to be detected (Wallace, 1991, Perkins and Frazer 1995, Sontas et al., 2007). Harvey (1998), suggests that the best timing for the surgery would be two weeks after attractiveness has ceased in which oestrogen and prolactin concentrations would be at basal levels. However, Wallace (1991), prolongs the surgery time, until 50 days after oestrous. The abdominal incision should be more cranial than for routine OVH. During the surgery, the caudal poles of both kidneys, the broad ligament, the omentum and the abdominal wall should be examined deeply to identify any ovarian tissue. Moreover, the ligature site at the uterine-cervical junction and proper ovary ligament should be inspected to identify any pathological condition of the uterus as uterine horn or uterine body may be remnant as well (Manfra-Marretta et al., 1989; Sontas et al., 2007). It was demonstrated by Miller, 1995, that in most cases ovarian remnants were located around the ovarian pedicles. If no ovarian tissue can be detected, then granulation tissue at each ovarian pedicle should be excised (Sontas et al., 2007). Histopathology of any resected tissue has a crucial importance in ORS, since granulosa cell tumor has been reported in a 7.5 year old Golden Retriever which had an OVH about 7 years before (Pluhar et al., 1995; Sontas et al., 2007). Animals with neoplastic ovarian tissue, such as granulosa cell tumors, take longer to present with clinical signs with a reported median interval of 96 months. Dogs with ORS have been shown to develop ovarian neoplasms (23.8%) more frequently than intact dogs (6.25%) as reported by Dow, 1960, Ball at al., 2010, Perez-Marin et al., 2014.

The results of study in detail indicate that patient weight is related to the incidence of complications and the odds of a complication occurring increase by a factor of 1.03 for every one kilogram of increase in patient weight. In the same study the absolute weight of the patient therefore appears to be a risk factor for complications, although future studies might focus on differentiating absolute weight from body condition. The period of general anaesthesia also appears to be related to the incidence of complications and the odds of a complication occurring increase by approximately 2% for each additional minute in anaesthesia time (Muraro and White, 2014).

Aim

The case is of a two-year-old female non-thoroughbred cat, weighing 3 kg. In May 2016 an ovariohysterectomy was carried out, through ventral median laparotomy. In January 2017, 8 months after castration, the hosts of the cat monitored behavioral signs typical for maturing estrus, lordosis, licking, effluent and slight redness of vulva, which was repeated twice within one month. A clinical examination was carried out at which no changes in the general condition were detected - normal body temperature, without special features on auscultation , percussion and blood analysis. Medroxyprogesteron Acetate (Depo-promone®) and remedial diet (Royal canin® Fibre response) were prescribed. Meanwhile, two days after this the condition of the cat deteriorated, the owner observed pain syndrome in the abdominal area as well as kyphosis, vomiting, allotriophagy, constipation and infirmity. A new examination was carried out because the owner doubted for swollen dry decorative plants. That directed us to a possible diagnosis for foreign body or gastrointestinal inflammation. Therefore an additional examination was done as diagnostic imaging research by ultrasonography of the abdomen, as well as lateral and ventro-dorsal radiography (fig. 1). No pathological changes or presence of a foreign body were detected. Subsequently a strong pain syndrome appeared again in the field of the abdomen, but this time with severe amount of seromucosal streaming from the vulva. Another blood analysis was done, which, this time, showed leukocytosis – 22.9 x109/L and lymphocytosis - 41% and 9.6 x109/L (fig. 2). The increase over the rate of these blood indicators gave grounds to doubt for uterine stump pyometra, which is why a diagnostic laparotomy was made.

Fig. 1. Radiology in ventro-dorsal view – without visual pathologic changes

Fig. 2. Results from the second blood analysis.

July Vet Clinic

Results of laboratory tests

Animal	cat
Breed	mix
Age	2 years
Sex	female
Name	Mishka
Owner	Kalina Karneva

Data: 14.03.2017

Signs	rezults		Reference boundaries dogs	cats
WBC	22.9	$x10^9/L$	6-17	5.5-19.5
LY%	9.6	$x10^9/L$	1-4.8	1.5-7.0
MO	0.8	$x10^9/L$	0.15-1.35	0.1-0.75
GR%	12.5	$x\ 10^9/L$	3-11.5	2.5-12.5
LY%	41.8	%	16.67-28.24	27.27-35.9
MO%	3.5	%	2.5-7.94	1.82-4.36
GR%	54.7	%	50-67.65	45.45-64.1
RBC	9.87	$x\ 10^{12}/L$	5.5-8.5	5.0-10.0
Hgb	135	g/L	120-180	80-150
Hct	46.5	%	37-55	24-45
MCV	47.2	fL	60-77	39-55
MCH	13.6	pg	19.5-24.5	13-19
MCHC	290	g/L	310-360	300-360
RDW	17.3	%	0-90	0.0-90.0
Plt	240	$x\ 10^9/L$	164-510	230-800
MPV	6.6	fL	7.60-8.30	12-16
PDW	17.6	%	0.0-90	0.0-90
PCT	0.158	%	0.150-0.410	0.360-1.000
DBP				
Neo (Sg)		%	60-70	35-75
Neo (St)		%	0-3	0-3
Eo		%	2-10	2-12
Ba		%	0-1	0-1
Ly		%	12-30	15-38
Mo		%	3-10	1-4

Anesthetic protocol: Premedication consisted of a subcutaneos injection of atropine sulfas 0.02 mg/kg (Atropin® Sopharma Bulgaria) and 15min. later intramuscular injection of Xylazine HCl 1 mg/kg (Xylazin® Bioveta). Induction – Ketamine HCl 5mg/kg.m. i.v. (Ketaminol®Intervet – Holand) (Mehandzhiyski et al., 2007). Maitenance with i.v. bolus of propofol 1mg/kg (Norofol® Norbrook, Northern Ireland)

The diagnostic laparotomy started with a medial incision of linea alba, then the ovarian pedicles, omentum, abdominal organs and wall were carefully inspected. A remaining piece from ovary tissue or cortex was ascertained in the left side of the abdominal cavity of the cat, which had revascularised with the omentum in proximity to the spleen and the descending colon (fig. 3). During the revision of the cervix, there was enlargement, inflammation, thickening and fluctuation (fig. 4). After the removal of the residual ovarian tissue on the surface of the cortex ovary follicles or follicular cysts were detected, which corresponds to the active reproductive tissue manifested with estrus of the cat (fig.4). The malformation of the uterine cervix was cut, resembling an inflamed bladder with fluid (fig. 4). Outside the abdominal cavity an incision of the malformation was carried out from which pus flew out (fig. 5). After careful revision of the

abdominal cavity, the wall was sewed in a routine manner. The patient was given antibiotic therapy with enrofloxacin for five days. The owner marked an improvement in the general condition of the cat immediately after the effect of the anesthesia – the signs of estrus disappeared, the cat regained its appetite and normal behavior. On the control examination of the blood components, three days after the operation, the leucocyte count of the cat was in norm - 16 x109/L and lymphocytes in their reference limits - 6.0 x109/L. So the cat fully recovered after considering the diagnosis ORS with uterine stump pyometra.

Fig. 3. Left side of the abdominal cavity of the cat.

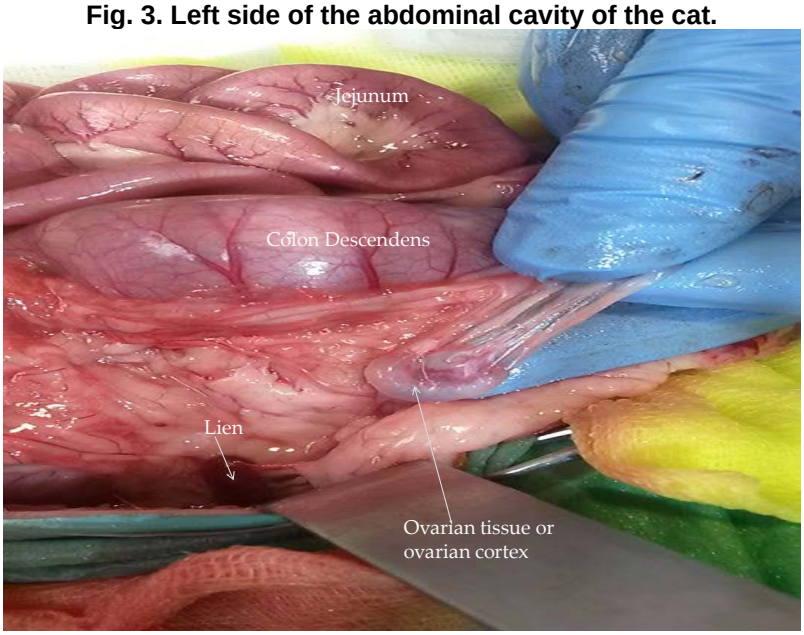
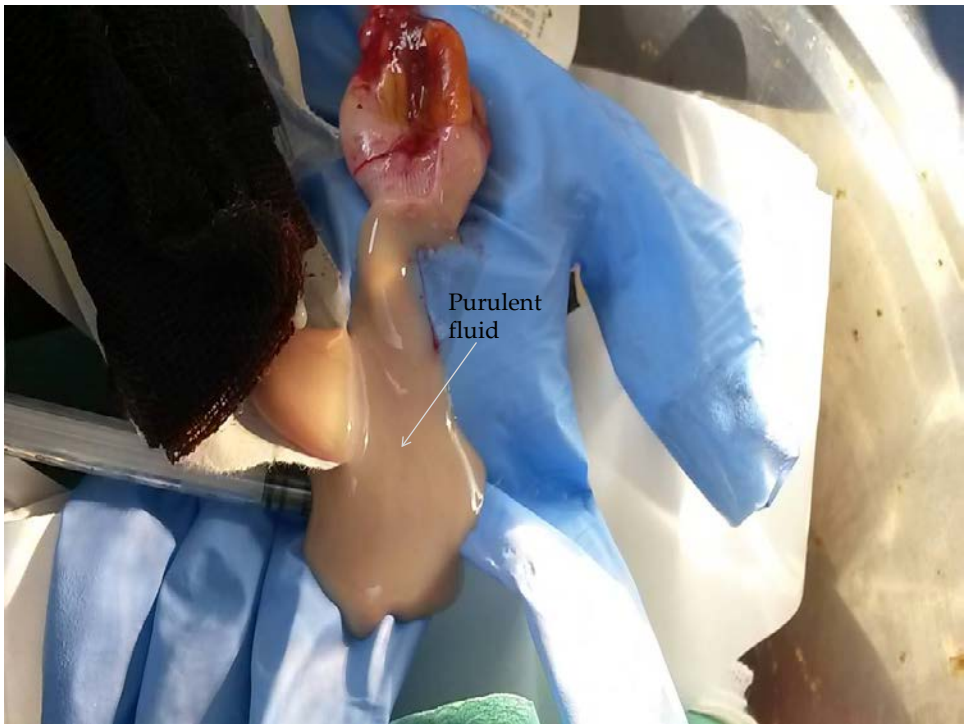


Fig. 4. Removed ovarian residual tissue and uterine stump of the cat.

Fig, 5. Incision of fluctuating bladder from uterine stump outside of abdominal cavity.



Discussion

Ovarian remnant syndrome is an iatrogenic disorder, caused by inexperience of the surgeon doing the ovariohysterectomy, as it was in this case. But it can also be caused by an experienced surgeon or as a result of additional ovarian tissue, as some authors report (Anonymus 1977, McEntee 1990; Kustritz, 2001, Sontas et al., 2007; Ball et al., 2010), whose opinion was supported by us. Signs of estrus after OVH within small animals appear between three months and five years, as stated by Miller, 1995 and Sontas et al., 2007; between 4-12 months as defined by Johnston 1991; Miller, 1995 and Sontas et al., 2007 are more concrete in claiming that occurrence of heat as a result of ORS is considered between 3 - 36 months, an average of 8.8 months. This interval is fully confirmed in our case where the estrus excels 8 months after the castration of the cat.

One of the ways for the development of ORS is through dropping of the cortex or part of ovarian tissue in the abdominal cavity by the surgeon, followed by autotransplantation and revascularization of ovarian tissue as reported by a number of authors (Wallace 1991, DeNardo et al., et al., 2001;Feldman and Nelson 2004, Romagnoli 2004, Sontas et al., 2007), as is the case with this patient. This is also demonstrated experimentally for cats by Shemwell and Weed (1970). The attachment of the residual tissue in the case of this cat is on the omentum, but it can also be on the broad ligament, caudal poles of the kidneys, abdominal organs and walls (Manfra-Marretta et al 1989; Sontas et al., 2007) or around the ovarian pedicles (Miller, 1995; Sontas et al., 2007).

According to some authors ORS is observed more frequently on the right because of the small, not sufficient sectional view of the abdominal wall and due to the shorter right ligamentum suspensorum ovarii, which makes the right ovary more difficult to be extracted and resected (Pearson, 1973; England; 1997; Wallace 1991; Miller 1995; Johnston et al 2001; Prats 2001; Sontas et al., 2007; Ball et al., 2010), but according to other authors bilateral ORS is developed in uniform rate (Miller 1995; Sontas et al., 2007; Ball et al., 2010). Because we describe just one case, it is not possible to say clearly which side of attachment of residual ovarian tissue is more frequent, but here it is identified on the left (Fig.3). The ORS is observed more rarely in cats than in dogs because of the deep abdominal cavity, more sturdy ligamentum suspensorum ovarii and obesity in dogs (McEntee, 1990; Hedlund, 2002; Ball et al., 2010).

The signs of the ORS, which we have considered are behavioral changes of heat, lordosis, effluent and seromucinous secretion from the vulva, as similar manifestation is observed Pearson 1973, Johnston 1991, Wallace 1991, Miller, 1995 Johnston et al 2001a, Feldman and Nelson 2004, Romagnoli 2004, Sangster 2005, Sontas et al., 2007; Ball et al., 2010. These signs are quite variable and the secretions can become serosanguineuos and purulent; attracting male animals and copulation; pseudopregnancy can also be monitored; even enlargement and secretion from the mammary glands (Pearson 1973; Johnston 1991; Wallace 1991; Johnston et al 2001; Feldman and Nelson 2004; Romagnoli 2004; Sangster 2005; Sontas et al., 2007; Ball et al., 2010), which we did not witness. Chronic vaginitis in a three-year-old poodle has also been described after OVH (Perkins and Frazer 1995). The most important sign is the estrus after OVH, as it may be variably presented as estrus only with vulvar edema, estrus only with vulvar secretion and estrus with both clinical manifestations (Ball et al., 2010). The last has been reported by us. Sometimes there is a possible heat without any clinical symptoms or only with behavioral changes or even without them, or only with the growth of the mammary glands under the influence of progesterone as described by Ball et al., 2010.

By the surface of the removed residual ovarian tissue, we can identify follicles or follicular cysts, with even a possible presence of corpora lutea and increased vascularisation (Pearson, 1973; Prats, 2001; Howe, 2006; Ball et al., 2010), which can lead to intrasurgical bleeding as a complication in the operation of the ORS (Sontas et al., 2007), which in our case was avoided. In 71% of cases, together with ORS, an uterine stump pyometra develops under hormonal influence, particularly of progesterone (Okkens et al., 1981; Musal and Tuna, 2005), which is reaffirmed by us with this cat. The uterine residue can develop purulent inflammation and cystic endometriosis.

The best way for treatment is removing the residual ovarian tissue through diagnostic laparotomy or laparoscopic surgery (Naiman, 2014; Phipps, 2015). The ventral median laparotomy is preferable to the paralumbar one (Rumenova, et al., 2012; Kiani et al., 2014), due to a significantly better and easy opportunity for visualization and removal of residual tissue (Perkins and Frazer 1995; Johnston et al 2001; Prats 2001; Feldman and Nelson 2004; Sontas at al., 2007). Therefore this diagnostic laparotomy was selected and carried out by our veterinary team.

The use of Medroxyprogesteron Acetate (Depo-promone®) by us is too contradictory, as it suppresses the condition of estrus and leads the cat in anestrus. Diagnostic laparotomy is not recommended to be carried out in a state of anestrus, because of the difficulty for identification of too small residual ovarian tissue (Wallace 1991, Perkins and Frazer 1995; Sontas et al., 2007), but should be carried out from two weeks to 50 days after attraction of male by female animals (Harvey 1998; Wallace 1991, Sontas et al., 2007). Perhaps Medroxyprogesteron Acetate (Depo-promone®) may have influenced negatively finding the

residual tissue by radiography and ultrasonography in this case because by this medicine the amount of tissue is diminished (Sontas et al., 2007; Ball et al., 2010). On the other hand, there were no great blood vessels on the surface of the found residual tissue, which was favored by the action of the medicine to avoid complications as intrasurgical bleeding (Sontas et al., 2007). The recovery of the cat after the surgery takes several days or 10-14 days, recurrences are not observed (Sontas et al., 2007), which is confirmed in the reported clinical case as well.

Prevention is the best way to avoid ORS. There are two guidelines which must be followed for the limitation of this syndrome, which we fully support. First, sufficient sectional view of the abdominal wall so that the area of the surgery is well visualized, proper ligation of reproductive organs and total removal of the ovaries without admission of residual tissue from them. The second measure is ovariohysterectomy before puberty as ORS has never described in animals castrated younger than 4 months (Sontas et al., 2007).

Because there are no published papers and articles describing the sufficient production of estrogens from the adrenal glands to induce signs of estrus in pets, each dog or cat, which shows proestrus or estrus signs after OVH must be evaluated for ovarian residue (Prats 2001; Sontas et al., 2007), which we can recommend to the veterinary practice.

Conclusion

In conclusion it can be summed up that the ORS is a rare iatrogenic condition, especially in cats, caused not only by inexperience of the surgeon, in which are observed too variable signs of estrus under hormonal influence. They may appear even up to several years after OVH, but an average of about 8 months has been registered, as almost always the syndrome combines with uterina stump pyometra. The most affordable way for treatment of ORS is diagnostic median laparotomy during which all inner organs located close to the reproductive ones should be observed carefully, including the proper ligament of the ovary and the broad ligament of the uterus. This case gives us the opportunity to direct the attention of the veterinary practice to the frequency, the reason for the occurrence, various ways of expression of ORS, the location of the residual ovarian tissue, diagnosis, appropriate treatment and prevention of ORS in cats.

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