Oviductal and uterine leiomyomata in mares

Leiomyomata van salpinx en baarmoeder bij merries

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ABSTRACT

This paper describes a case of a sessile uterine leiomyoma in a 17-year-old chronic infertile Selle Français mare. The mass was removed by transendoscopic electrocoagulation. In the same period, 725 mares were screened for oviductal and uterine solid masses in a slaughterhouse survey. Two uterine masses and one oviductal mass were detected in three different mares. Histological and immunohistochemical examination revealed leiomyoma in the four masses. To the authors' knowledge, this is the first report of an oviductal leiomyoma in a mare.

SAMENVATTING

In dit artikel wordt een geval beschreven van een baarmoederleiomyoma bij een 17 jarige, chronisch infertiele selle-françaismerrie. De massa werd verwijderd door transendoscopische elektrocoagulatie. In dezelfde periode werden in een slachthuis 725 merries gecontroleerd op solide salpinx- en baarmoedermassa's. Er werd in twee baarmoeders en in één salpinx een massa aangetroffen bij drie verschillende merries. Histologisch en immunohistochemisch onderzoek toonde een leiomyoma aan in de vier bovengenoemde gevallen. Voor zover de auteurs weten, wordt in dit artikel het eerste geval van een leiomyoma in de salpinx van een merrie beschreven.

INTRODUCTION

Neoplasia rarely affects the uterus or oviducts of domestic animals, except in cats (Miller et al., 2003). It is also relatively common in women (Surrey, 2003). Only 0.4 – 1.6% of the tumors diagnosed in horses are of uterine origin (Cotchin, 1977). Leiomyoma, a benign neoplasia arising from the outer smooth muscle of the uterus, seems to be the most frequently occurring uterine tumor in mares (Van Camp, 1993). Several other tumors have sporadically been described affecting either the endometrium: fibroma (Estrada et al., 2008), fibrosarcoma (Govaere et al., 2011), adenocarcinoma (Gunson et al., 1980) and lymphosarcoma (Sweeney et al., 1991) or the myometrium: leiomyosarcoma (Lofstedt et al., 1987), fibroleiomyoma (Broome et al., 1992), and rhabdomyosarcoma (Torbeck et al., 1980). There is only one report on oviductal neoplasia (adenoma) in a mare (McEntee and Nielsen, 1976). Small uterine tumors may be overlooked, whereas larger ones may be palpable per rectum or detected by ultrasonography during a routine breeding soundness examination of the subfertile mare (Hoffsis et al,. 1986). Histopathological examination after biopsy is necessary to identify the origin of the tumor. Benign masses which interfere with fertility may be removed. Malignant neoplasia are usually not treated since the prognosis is generally poor (Neufeld, 1973, Torbeck et al., 1980, Govaere et al., 2011).

CASE REPORT AND SLAUGHTERHOUSE SURVEY

In the same period when the slaughterhouse survey was performed, a clinical case was presented at the hospital (Faculty of Veterinary Medicine (UGhent)). It concerned a 17-year-old Selle Français mare with a complaint of prolonged subfertility. Clinical examination revealed no abnormalities. On transrectal ultrasonography, an echogenic mass was detected in the uterine lumen. Subsequent hysteroscopy revealed a sessile structure of 2.5 cm in diameter located in the middle third of the left uterine horn (Figure 1). The mass was removed using transendoscopic electrocoagulation.

In a slaughterhouse, 725 mares were screened

Figure 1. Uterus in vivo. Hysteroscopic view of a leiomyoma of in the middle third of the left uterine horn of the 17-year-old Selle Français mare.

for the presence of uterine or oviductal solid masses. Pseudotumoral masses such as endometrial cysts and paramesonephric (Müllerian) duct cysts were not taken into account. In only two uteruses and only one oviduct, a tumoral mass was detected. One of the uterine masses originating from a 21-year-old Hanoverian mare, was solid and spherical with a diameter of 13 cm, located in the cranial third of the left uterine horn, originating from the uterine wall and protruding into the uterine lumen. The second uterine mass, found in a 15-year-old Trotter mare was a solid, 1.5 x 2 cm, tear-shaped, subserosal pedunculated mass with a 2 cm stalk, located at the transition of the uterine body to the left horn. The oviductal tumor was detected in a 18-year-old Warmblood mare, and was a solid spherical mass of 1.5 cm in diameter originating from the fimbriae. The cut surfaces of the three masses were uniformly cream colored.

Histopathology

Representative samples of the tumoral masses were taken and fixed in 4% of paraformaldehyde, and a paraffin wax-embedded sample was processed of each mass for histopathology.

The uterine mass of the mare presented in the equine hospital was clearly demarcated, sessile, non-encapsulated, and consisted of well differentiated spindle-shaped cells, strongly suggestive for smooth muscle cells. These cells were arranged in a disorganized, streaming pattern. The mitotic index was low, and there were very few atypical cells. The largest part of the mass was surrounded by endometrium. A small free margin was detected at the level of the stalk. These features are suggestive for a leiomyoma.

The two partly encapsulated uterine tumors of the slaughterhouse survey (Figures 2a and 2b) consisted of densely packed spindle cells organized in randomly orientated bundles (Figures 2a) which often formed a

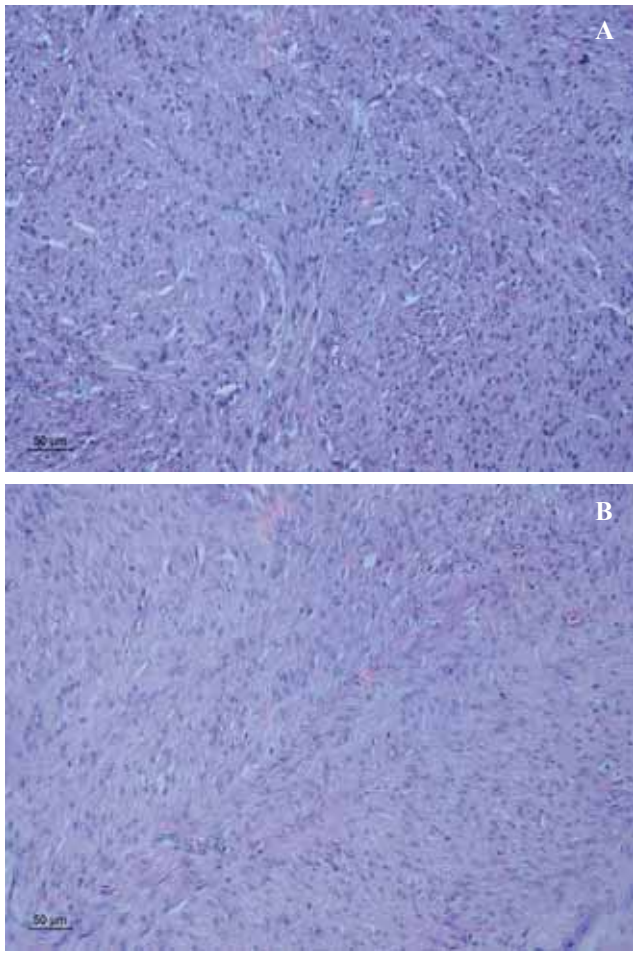

Figure 2. Uterus, slaughterhouse survey (H&E). Detail of the neoplastic cells, demonstrating cells arranged in haphazardly orientated bundles (A), which sometimes form a herringbone pattern (B). Bar = 50 µm

herringbone pattern (Figure 2b). The cells had indistinguishable cytoplasmic borders, a moderate amount of homogenous eosinophilic cytoplasm and a single, elongated, centrally located, cigar-shaped hypochromatic nucleus. Nucleoli were not prominent. There were mild anisocytosis and anisokaryosis, and the mitotic index was less than 1 per 10 high-power fields. The capsule was composed of loosely arranged fibrous tissue with a small number of capillaries.

The well-demarcated, non-encapsulated oviductal mass of the slaughterhouse survey consisted of densely packed spindle cells, also organized in randomly orientated bundles (Figure 3). The cells had a larger amount of homogenous eosinophilic cytoplasm than those in the uterine tumors. The central, elongated, round to cigar-shaped nuclei contained vesicular chromatin and an occasional central nucleolus. Mitoses were rare, and there were limited anisocytosis and anisokaryosis. There were multifocal necrotic areas and a mild infiltration of lymphocytes and plasma cells at the peripheral borders of the mass.

Immunohistochemical stainings for smooth muscle actin and vimentin (DakoCytomation, Brussels, Belgium) were performed using the Dako

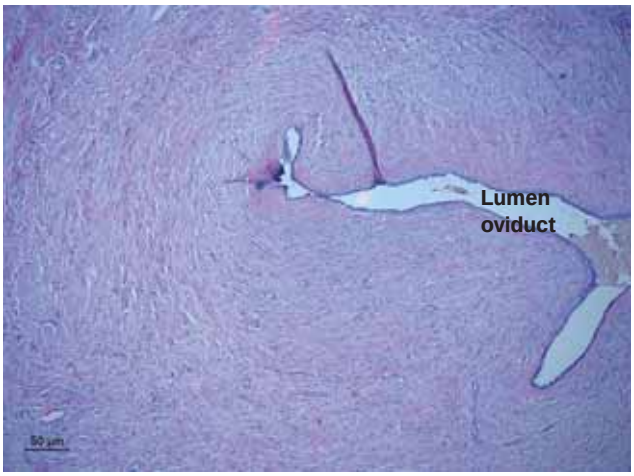

Figure 3. Oviduct, slaughterhouse survey (H&E). Detail of the neoplastic cells, demonstrating densely packed spindle cells organized in haphazardly orientated bundles. Bar = 50 µm.

envision system. The neoplastic cells in all four neoplasms were diffusely labeled for the expression of smooth muscle actin and vimentin, confirming the diagnosis of leiomyoma.

DISCUSSION

Tumors of the oviduct are extremely rare in domesticated mammals. Only a single case of an adenoma attached to the fimbriated part of the oviduct has been reported in the mare (McEntee and Nielsen, 1976). There are no reports of oviductal neoplasms in the cow, ewe, sow and the queen, whereas in the bitch, some cases have been described (Gelberg and McEntee, 1986). In aged laying hens by contrast, a prevalence of oviductal leiomyomas of up to 100% has been reported (Berry et al., 2006). In the slaughterhouse survey discussed in the present case report, the occurrence of oviductal tumors in a mixed population of mares presented for slaughter, ranging in age from 1 to 29 years old, was 0.14 % (1/725). The mass, found in an 18-year-old Warmblood mare, was characterized as being a leiomyoma originating from the fimbriae of the infundibulum.

Whereas in women and cats, uterine tumors frequently occur, in general, it is a rare occurrence in horses (McCue, 1998). A prevalence of uterine neoplasms of 0.4-1.6 % has been reported (Cotchin, 1977). In the slaughterhouse survey of the present case report, the occurrence of uterine neoplasms was 0.27 % (2/725). Comparable to the results of the survey, (fibro)leiomyoma is the most frequent uterine tumor (McCue, 1998). Moreover, (fibro)leiomyomas in mares range in size from 2.5 to 5 cm (Romagnoli et al., 1987). They are solitary or multiple, and may be located submucosally, intramurally or subserosally, and are either exophytic or pedunculated (Kebapci et al., 2002).

Because disease of the oviduct is not easily evaluated, pathology of these structures may be more common than what has been reported in the literature (Miragaya et al., 1997, Bennett et al., 2002). For instance, the clinical incidence of salpingitis has been proven to be higher than assumed (Losinno et al., 1997, Miragaya et al., 1997). Similarly, the occurrence of oviductal tumors is most likely higher than detected in equine veterinary practice.

Although tumors are expected to occur more commonly in older animals (Manothaiudom and Johnston, 1991), some reports are available concerning uterine leiomyomas in fillies (Torbeck et al., 1980, Romagnoli et al., 1987, Broome et al., 1992). Romagnoli et al., (1987) suggested a dominant, sex-chromosome linked or limited form of inheritance for the disease.

Benign oviductal or uterine neoplasia in the mare (Hamir et al., 1989) do not cause any distinctive clinical signs (Hoffsis et al., 1986, Romagnoli et al., 1987, Berezowski, 2002, Janicek et al., 2004, Quinn and Woodford, 2005). Nevertheless, serosanguinous or hemorrhagic vaginal discharge (Torbeck et al., 1980, Romagnoli et al., 1987, Broome et al., 1992, Santschi et al., 1995, Brandstetter et al., 2005, Heijltjes et al., 2009) and colic-like symptoms (Bonfig and Ingenhorst, 1992) have been reported in mares with benign uterine neoplasia, although physical examination revealed no abnormalities. There is one report of anemia, hypoproteinemia and hypoalbuminemia in a filly due to septic metritis caused by torsion of a pedunculated fibroleiomyoma (Broome et al., 1992). Malignant tumors are mostly associated with signs of systemic disease, such as weight loss, depression, anorexia and symptoms dependent on the involvement of abdominal organs and/or thoracic cavity and lungs (Gunson et al., 1980, Torbeck et al., 1980, Chaffin et al., 1990, Freeman et al., 1997). Abdominal pain (Freeman et al., 1997), persistent uterine hemorrhage (Govaere et al., 2011) and protrusion of tumor tissue through the vulva have also been reported (Romagnoli et al., 1987).

Oviductal infundibular masses, such as tumors and fimbrial cysts, are generally not supposed to interfere with fertility, unless they hamper the process of ovulation or oocyte transport into and through the oviduct (Kenney, 1993).

Large uterine tumors are often associated with prolonged infertility due to the impaired gamete transport and interference with embryonic mobility due to the occlusion of the endometrial cavity. The location of a mass at the end of the uterine horn, near the uterine papillae, is thought to potentially reduce fertility, by physically impeding sperm transport to the uterotubal junction. The impairment of blood supply to the endometrium and atrophy and ulceration might be responsible for hampering embryo fixation and maternal recognition of pregnancy (Buttram and Reiter, 1981, Katz et al., 1989).

Uterine neoplasia might possibly play a role in foetal death by disturbing the interdigitation of the allantochorion in the endometrium (Heijltjes et al., 2009). Furthermore, uterine masses may be responsible for the accumulation of intrauterine fluid by

restricting the propagation of uterine contractions, and as a consequence, affecting the clearance of normal uterine fluid resulting in secondary endometritis (Hinojosa et al., 2003). Chronic endometritis can also be caused by the mass passing through the cervix, hence resulting in cervical incompetence (Hamir et al., 1989).

The mare described in this paper was presented for chronic infertility. No abnormalities were observed, neither in behavior nor during clinical examination. Furthermore, endometritis was thought not to be the cause of the infertility, since no uterine free fluid was detected. Possibly, the mass affected the transuterine migration of the embryo in the early stages of pregnancy, since the excision of the tumor resulted in a return to sound reproductive performance.

The etiology of leiomyomas in animals is not fully elucidated, but some studies suggest an influence of oestradiol and progesterone on tumorigenesis (Porter et al., 1995, Walker and Stewart, 2005, Berry et al., 2006). In the mare of the present case, there was no indication of any hormonal imbalance, as evidenced by her normal reproductive cycles.

The diagnosis of oviductal masses may be difficult, whereas uterine tumors are usually detected during rectal palpation or ultrasonography (McCue, 1998; Sokkar et al., 2001; Berezowski, 2002) at a routine breeding soundness evaluation because they seldom cause any noticeable clinical signs. Rectal palpation may reveal a single or a few firm masses within the wall of the uterus. Ultrasonographically, highly echogenic firm structures are detected. Direct visualization of masses is possible with hysteroscopy (Lofstedt et al., 1987).

A presumptive diagnosis of uterine neoplasia can be based on the history and findings of ultrasonographic and hysteroscopic examinations. The differential diagnosis of uterine masses in mares includes a large endometrial cyst (Stanton et al., 2004), abscess, intramural hematoma (Wenzel et al., 1985, Shideler et al., 1990), fibroses (scar tissue) (Knottenbelt, 2003) or neoplasia. Cysts, fluid filled structures, can be ruled out via ultrasonography and hysteroscopy. The persistence and the gradual enlargement of the mass rule out an intramural hematoma, since the size diminishes, and the ultrasonographic appearance of hematoma characteristically changes over a period of a few months (Pycock, 1994). Furthermore, neoplasia is generally a disease of older animals, although, as aforementioned, there are several reports of primary uterine tumors in fillies (Romagnoli et al., 1987, Torbeck et al., 1980, Broome et al., 1992).

Nevertheless, histology of a representative biopsy from a suspicious uterine mass is required for a definitive diagnosis (McCue, 1998). However, endoscopic guided biopsy methods or the use of biopsy forceps, turn out to be difficult in practice and of limited value in larger neoplasia (Hoffsis et al., 1986, Lofstedt et al., 1987, Santschi et al., 1995, Berezowski, 2002, Hinojosa et al., 2003).

In this mare, electrocoagulation was chosen due to the location and the size of the tumor. The removal of pedunculated leiomyomas in the uterine lumen has been reported using endoscopic guided electrocoagulation or laser therapy (Blikslager et al., 1993, Bartmann et al., 2003). There is one report on the removal of a chronically bleeding uterine tumor by means of a cerclage wire (Hollerrieder and Toth, 2002). Laparotomy and tumor excision may be considered for larger and/or intramural or serosal-based masses as long as the primary tumor is not metastasized (Torbeck et al., 1980, Hoffsis et al., 1986, Lofstedt et al., 1987, Bonfig and Ingenhorst, 1992). In the past, total hysterectomy was performed (Santschi et al., 1995). Nowadays, hand assisted laparoscopic tumor removal with unilateral ovariectomy and partial hysterectomy is recommended in mares with uterine leiomyomas, especially when the tumor is associated with infertility (Hinojosa et al., 2003, Janicek et al., 2004, Muurlink et al., 2008, Heijltjes et al., 2009). No reports are available on the treatment of oviductal masses. Laparoscopic investigation and confirmation of oviductal patency by flushing and catheterization have been described (Bennett et al., 2002, Allen et al., 2006, Kollmann et al., 2011).

After the removal of the mass, the mare of the present case became pregnant and gave birth to a healthy foal. These findings and the reports of other authors suggest a good prognosis for future breeding after uterine tumor removal, even by means of invasive surgical resection (Hoffsis et al., 1986, Lofstedt et al., 1987, Santschi et al., 1995, Berezowski, 2002).

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EERSTE VROUWELIJKE DIERENARTSEN

De allereerste vrouwelijke dierenarts studeerde af in Zwitserland (Zurich 1889). In diezelfde 19de eeuw nog behaalde een tweede vrouw dat diploma (Alfort, 1896). Hun namen: Stephania Kruzewska (uit Warschau) en Marie Kapcewitsch (uit Oekraïne). In die jaren trokken meerdere jonge Oost-Europese vrouwen naar Zwitserland en Frankrijk om er universitaire studies aan te vatten, vooral in geneeskunde. Van Stephania is geweten dat ze praktijk deed in Odessa. Van Marie ontbreekt elk spoor van enig beroepsleven.

In Nederland was Jeanette Donker-Voet (Utrecht 1930) behoorlijk succesvol in het wetenschappelijk onderzoek, vooral op het vlak van de leptospirosen. Ze tekende voor de eerste isolatie van het *Leptospira* serotype Canicola bij mensen (1934). Het Jeanette Donker-Voetgebouw op de Utrechtse diergeneeskundige campus houdt haar naam levend.

In België kwam de eerste vrouwelijke dierenarts Cristine Cotteleer (Brussel 1951) eveneens in het onderzoek terecht (parasitologie, Ukkel), zij het met iets minder eclatante resultaten. Hilda Wijverkens (Gent, 1954) was eerst twee jaar werkzaam in de kliniek heelkunde van de grote huisdieren bij prof. Bouckaert, waarna ze met haar man naar de toenmalige kolonie Belgisch-Congo trok. In 1999 zette ze een punt achter een welgevuld beroepsleven, met eerst nogal wat rundvee in de praktijk en daarna uitsluitend gezelschapsdieren.

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