FOOD/FARmed ANIMALS

Presence of cystic endometrial hyperplasia and uterine tumours in older pet pigs in the UK

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SUMMARY
Experience in farm animal referral centres in the UK has shown an increase in the number of pigs being presented for age-related problems. These include obesity, arthritis, skin disorders, overgrown tusks and overgrown claws. Seven pigs presented over a 7-year period to two university veterinary teaching hospitals in the UK with clinical signs including behavioural change, abnormal vaginal discharge, inappetence and abdominal distension that was found to localise to the reproductive tract. Histology of the reproductive tract found cystic endometrial hyperplasia (n=7) and uterine tumours (n=4) following ovariohysterectomy (n=4) or postmortem examination (n=3). Tumours identified were leiomyoma (n=1), fibroleiomyoma (n=1) and leiomyosarcoma (n=2).

BACKGROUND
In the UK, there has been a gradual rise in the number of pigs being kept as pets or on smallholdings. These are often Vietnamese pot-bellied, kunekune or crosses thereof, but also occasional commercial breed crosses. Although traditionally pig veterinary work has focused on commercial units, and thus has become a specialised area of the profession, increasing numbers of vets in general practice are being asked to treat pigs kept individually or in small groups. In 2017, a survey undertaken by DEFRA 1 found 11 100 registered pig holdings in the UK; of this number, 5000 had registered as keeping 1–9 pigs. Work by Gillespie et al 2 in which a web-based questionnaire was available to members of breed societies and smallholders, as well as advertised in feed merchants and country stores, found that 59% of respondents (total respondents 274) owned kunekunes, 27% Vietnamese pot-bellied pigs and 12% micropigs. Only 84% reported that they were registered with DEFRA, and only 82% with a veterinary practice. Moreover, 66% of owners admitted to feeding their pigs household scraps (this is illegal in the UK) and 17.7% were unaware of legally enforceable movement regulations regarding pigs. This survey highlighted the potentially significant numbers of pigs being kept as pets in the UK and more worryingly the lack of fundamental knowledge that some owners have regarding the legal requirements for these animals.

Pigs kept as pets live longer than their commercially maintained counterparts (as a result of slaughter age) and age-related diseases similar to those observed in other companion animals are reported. 3 These include osteoarthritis, diabetes mellitus, neoplasia and oral disease. 3 In the author’s (PW) experience, particularly while working at UK veterinary schools and farm referral hospitals, there has been an increase in the presentation to clinics of older pigs (up to 20 years old). These patients have demonstrated a range of management and age-related pathologies including obesity, arthritis, overgrown tusks, overgrown feet and various skin disorders.

Overt haemorrhagic vulval discharge is not observed in sows during oestrus, but a clear vulval discharge is common. Lochial discharge is observed after farrowing. Abnormal purulent discharges are seen in commercial systems most commonly 3 weeks after service and are as a result of infections introduced by poor hygiene at breeding. Descriptions can be found in the literature describing the finding of cystic endometrial hyperplasia (CEH) and uterine tumours in different populations of pigs. 4–7

With large numbers of pigs now being kept as pets in the UK, and with the average life expectancy of domestic swine being 15–20 years, veterinarians will be required to treat these animals for age-related diseases. The author’s (PW) experience with pet pigs has shown that CEH and uterine tumours are a common occurrence in these animals. By presenting case information, we hope that practising vets will have more confidence in the diagnosis and treatment of such conditions.

CASE PRESENTATION
Between 2012 and 2019, the author (PW) observed an increase in the number of pet pigs being presented, some referred and some as first opinion, for the following problems: behavioural changes (agression), overt bleeding when in oestrus, purulent vaginal discharge, swollen abdomen, inappetence and recumbency. Seven pigs (median age 6 years, range 4–9 years) were investigated and treated at Cambridge Farm Animal Referral Services (Queen’s Veterinary School Hospital, University of Cambridge, UK) and The Farm Animal Hospital (Royal Dick School of Veterinary Studies, University of Edinburgh, UK). The pigs were all pets and were nulliparous. They were fed on commercially available pig feed and kept in a variety of outside environments. The reported clinical signs included abdominal distension (4/7), behavioural change (5/7) and inappetence (6/7). None of the owners had reported any significant health issues in their...
pigs up to the point of the clinical presentations described. Physical examination findings were varied with the majority of the animals having normal temperatures, heart and respiratory rates. Palpation of the abdomen of the animals revealed some discomfort and in most cases a large degree of distension. At the time of the examinations, there was no sign of vaginal discharge in any of the patients. Through various diagnostic methods these problems were localised to the reproductive tract and, in most cases, led to exploratory coeliotomy, ovariohysterectomy or euthanasia (preoperatively or perioperatively) depending on the severity of clinical signs.

One owner had observed similar signs in a related animal without a full investigation undertaken. One owner had been recommended medical treatment for the clinical signs, using oral altrnogest (progestin) (Regumate; MSD Animal Health). This is an off-license use of the product but did result in a reduction in the clinical signs of vaginal bleeding and behavioural aggression while the sow was on treatment.

INVESTIGATIONS
One out of seven pigs had radiography performed (figure 1) which revealed a large soft-tissue mass in the caudal abdomen (figure 2). Abdominal ultrasound was performed in every case (7/7) where fluid filled structures were observed within the uterus. When large uterine masses were detected on ultrasound, these appeared as soft-tissue opacities in close proximity to an enlarged uterus. Haematology was performed on any pigs undergoing surgery (6/7), but in all cases no abnormalities were found. In all cases, the history and presenting clinical signs alongside abdominal ultrasound were suggestive of an abdominal mass and so exploratory coeliotomy was advised (7/7) and performed (6/7) under full general anaesthesia. In one case, the owner requested euthanasia rather than surgery.

TREATMENT
Exploratory coeliotomy was offered in all cases and was performed in six pigs. Exploratory coeliotomy was the treatment of choice as it was the only method of examining and removing the abnormal tissue from the patients. In each case with a more chronic history and more severe clinical signs, the owner was made aware that if the uterus or uterine mass was deemed inoperable, euthanasia while under general anaesthesia would be required.

General anaesthesia
The routine approach to anaesthesia in these cases was premedication with a combination of azaperone (Stresnil; Elanco) 1 mg/kg, ketamine (Anaestamine; Animalcare) 4 mg/kg and xylazine (Rompun 2%; Bayer) 1 mg/kg administered by intramuscular injection into the neck using a 19G 2-inch needle. A 20G catheter was placed in the ear vein and general anaesthesia was induced with ketamine (Anaestamine; Animalcare) 2 mg/kg intravenously. After successful induction, an endotracheal tube was placed using a 9-French canine urinary catheter as a guide. The patients were then maintained on isoflurane (Isoflo; Zoetis) and oxygen at 1.5% and a flow rate of 1 L/min (figure 3). Supportive therapy involved intravenous fluid therapy (Vetivex 11; Dechra) which was administered through the ear vein catheter at a rate of 400 mL/h. Perioperative management included prophylactic antibiosis with 15 mg/kg amoxicillin (Amoxycare LA; Animalcare) intramuscularly and 0.4 mg/kg meloxicam (Metacam; Boehringer Ingelheim), both as a single dose.

Surgical approach
A midline coeliotomy was performed in all surgical patients (6/7) (figure 3). In all cases, the linea alba was subjectively thin and care was taken to ensure no iatrogenic damage to the viscera when entering the abdominal cavity. A full exploratory coeliotomy was performed in all cases, and the uterus was identified as the affected organ. The uterus was exteriorised (figure 4) and packed off using laparotomy swabs. Ovariohysterectomy was subsequently performed. The ovarian pedicles were either ligated and then divided using double encircling ligatures of 1-0 polydioxanone (n=2; PDSII, Ethicon) or cauterised and debrided using a smart bipolar vessel sealing device (n=2; Enseal, Ethicon). The cervical arteries were individually ligated using 1-0 polydioxanone and a transfixing ligature was placed through (and around) the cervix before the uterine body was excised. A routine three-layer closure was performed with 2-0 polydioxanone (PDSII; Ethicon) in a simple continuous pattern in the linea alba, 2-0 poliglecaprone (Monocryl; Ethicon) in a simple continuous pattern in the subcutaneous fat and 2-0 poliglecaprone in a modified Cushing pattern intradermal suture. All uterine masses were sent for histopathological examination.
Following recovery, patients were monitored closely for 48 hours and were then returned home.

In two cases, the uterine mass was considered inoperable (due to size, vascular compromise or adhesions to adjacent organs) and intraoperative euthanasia was performed with owner consent. The cadaver was then submitted for postmortem examination.

OUTCOME AND FOLLOW-UP
Of the seven cases described, one patient was euthanised without surgery, two were euthanised perioperatively, one died on recovery (no cause of death was found on postmortem examination) and three made a full recovery following surgery.

Gross pathology and histology
All cases (7/7) demonstrated cystic endometrial hyperplasia (CEH), either on postmortem examination or examination of the surgically removed reproductive tract. Three tumour types were also identified, namely leiomyoma (one case; figures 5 and 6), fibroleiomyoma (one case) and leiomyosarcoma (two cases; figures 7 and 8).

DISCUSSION
In this case series, all the pigs were older than 4 years, with the oldest being 9 years old. This is consistent with previous reports where uterine pathologies were only identified in animals over 3 years of age. Pigs previously described in the literature exhibited a range of clinical signs including abdominal distension, inappetence, serosanguinous vaginal discharge, weight loss and tenesmus. All of these clinical signs were observed across the individuals described in this case report.

CEH was diagnosed in all patients described in this report. There are interesting species differences in the pathogenesis of CEH. Studies in humans have shown that cystic endometria demonstrate an increase in progestin receptors but a similar number of oestrogen receptors as non-cystic endometria. It is believed that in humans CEH may be due to periods of hyper-oestrogenism or prolonged exposure to oestrogens and this is
Figure 6 Uterus, pig. The neoplastic mass shown in figure 5 is sparsely cellular and is composed of a population of spindle-shaped neoplastic cells that are supported by an abundant connective tissue stroma, consistent with the diagnosis of leiomyoma.

Figure 7 Uterus, pig. The left uterine horn is expanded by a large, spherical (approximately 50 cm in all dimensions) mass weighing approximately 15 kg.

Figure 8 Uterus, pig. The neoplastic mass shown in figure 7 is composed of interlacing bundles and streams of spindle-shaped cells with six mitoses in 10 high-power fields, consistent with the diagnosis of leiomyosarcoma.

Hypothesised as the cause in sows also. It has been demonstrated that treatment with progestins can lead to the regression of the hyperplastic condition and complete remission. However, recurrence was seen when treatment was stopped. In nulliparous pet pigs, the uterine tract will be more regularly under the influence of oestrogen and therefore potentially more prone to developing CEH than sows experiencing regular pregnancies. Porcine cystic endometrial hyperplasia may also be induced by administration of the zearalenone, an oestrogenic mycotoxin.

Similarly, in ewes, consumption of oestrogenic plants such as subterranean and red clover (Trifolium subterraneum and T pratense, respectively) may lead to development of CEH. In cattle, ovarian lesions such as cystic Graafian follicles and granulosa cell tumours may cause CEH. In dogs, development of CEH is classically considered to be preceded by a period of oestrogen priming followed by progesterone dominance, although this may be an experimental phenomenon rather than a consistent pathophysiological mechanism in the context of natural disease. Importantly, the presence of uterine bacteria is also implicated in the pathogenesis of canine CEH. CEH has also been reported in elephants, where, interestingly, development of the lesion is considered to be unrelated to either exposure to sources of exogenous oestrogen or oestrogen-secreting ovarian lesions.

Three mesenchymal uterine neoplasms were diagnosed in the pet pigs described here. Generally, uterine tumours appear to be more prevalent in the pet pig population when compared with slaughterhouse data from commercial pigs perhaps reflecting the older age attained by the former population. Interestingly, a number of porcine uterine tumours arising from mesenchymal tissue, and specifically smooth muscle, have previously been described.

Taken together, the cases described here illustrate a potential clinical approach to investigation and treatment of uterine pathology in the pet pig. These case descriptions also add to the body of literature suggesting that CEH and neoplasms of smooth muscle origin should be considered when investigating uterine diseases in this species.

For the veterinarian in practice, a nulliparous sow >3 years of age should be considered as a potential CEH case (+/−uterine tumour) if showing a combination of the following clinical signs: abdominal distension, weight loss, inappetence, tenesmus, behavioural changes and overt vaginal bleeding. CEH can easily be identified by abdominal ultrasound in the conscious, sedated or anaesthetised patient by the identification of fluid filled structures within the uterus. Surgical removal of the uterus is relatively straightforward and can be achieved by ovariohysterectomy via a midline approach.

Learning points

► Pet pigs can develop a range of age-related conditions.
► Nulliparous females may be predisposed to cystic endometrial hyperplasia and uterine neoplasia.
► Diagnosis can be made through palpation, ultrasonography or radiography.
► Medical treatments may reduce clinical signs, but ovariohysterectomy is a definitive treatment; however, it can be challenging in advanced cases.
► Prevention of cystic endometrial hyperplasia can be achieved by early neutering of pet pigs.

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