



The importance of elective ovariohysterectomy and progesterone level in African pygmy hedgehogs (*Atelerix albiventris*)

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ABSTRACT

As the number of African pygmy hedgehogs (*Atelerix albiventris*) that suffer from neoplasia grows, so does the need to broaden the knowledge of this species pathology, as well as prevention, diagnostics and treatment options. Uterine tumors are one of the most commonly diagnosed neoplastic changes in these animals, but no recommendations regarding elective ovariohysterectomy have been set. This study aims to examine the possible connection between progesterone level and the presence of neoplastic changes to the female reproductive tract. In this study, females (n=142) were subjected to general and ultrasonographic examination, blood was collected to determine progesterone levels (n=18), and complete ovariohysterectomy was performed (n=18). Following the removal, the reproductive organs were examined pathohistologically. Ultrasonographic changes were observed in 30% of examined individuals. Histopathologically cystic endometrial hyperplasia was present in 33.33% of the examined tissues, endometrial mixed tumors in 22.22%, as well as endometrial stromal sarcoma, endometrial stromal nodules in 5.55% and in 16.6% of tissues no alterations were identified. The progesterone levels ranged from as low as 0.1 ng/mL to 22.83 ng/mL, regardless of the presence of uterine changes. On the basis of the results of this study, as well as the literature review, elective ovariohysterectomy should be performed in African pygmy hedgehogs as a preventative measure. Moreover, progesterone levels cannot be used for diagnostic purposes.

Key words: African pygmy hedgehog; *Atelerix albiventris*; elective ovariohysterectomy; progesterone level; uterine neoplasia

Introduction

African pygmy hedgehogs (*Atelerix albiventris*) are becoming increasingly common household

pets worldwide, and are also often kept in zoological parks ([GARDHOUSE and ESHAR, 2015](#)). Their population is continuously growing, making

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them more frequent patients in veterinary clinics, thus veterinarians need to possess sufficient knowledge about their biological (especially nutritional) needs and pathology, as well as skills to care for their health ([KEEBLE and KOTERWAS, 2020](#)).

Unfortunately, there is insufficient information about pathologies of African pygmy hedgehogs. The available knowledge is far from comprehensive compared to that about other mammalian species and it mostly relies on case reports, most of which have focused on neoplastic diseases ([OKADA et al., 2018](#)). Even the data available in the literature can vary greatly from author to author, and geographic and genetic discrepancies with unequal husbandry may have played a role in these differences ([PEI-CHI et al., 2015](#)). When discussing pathology, hedgehogs are frequently characterized in literature as highly susceptible to neoplastic diseases. The exact cause of this predisposition is not known. It is speculated that it may be due to a longer lifespan in captivity than in the wild, while some authors believe that inadequate husbandry conditions and inbreeding may also contribute to tumor development ([PEI-CHI et al., 2015](#)). The findings of retrospective studies exhibit considerable divergence among different authors' interpretations. When considering those with large sample numbers, the prevalence of neoplastic changes ranges from 29 to 60%, with malignant tumors occurring in approximately 75% of cases ([RAYMOND and WHITE, 1999](#); [OKADA et al., 2018](#)). Furthermore, the occurrence of two types of tumors in one hedgehog is not uncommon ([ANIČIĆ et al., 2023](#)). It is difficult to determine the second most common cause of death in hedgehogs after tumors. Indeed, study results vary greatly, and comparing them with the frequency of clinical symptoms observed in living hedgehogs would further complicate the situation ([HEATLEY et al., 2005](#); [GRAESSER et al., 2006](#); [GARDHOUSE and ESHAR, 2015](#); [PEI-CHI et al., 2015](#); [OKADA et al., 2018](#); [DÍAZ-DELGADO et al., 2018](#); [DEL AGUILA et al., 2019](#); [SILVA et al., 2022](#)).

However, most studies concur that uterine tumors are the most commonly diagnosed neoplastic changes in African pygmy hedgehogs ([OKADA et al., 2018](#)). These tumors can vary in nature, but

are typically diagnosed as incidental findings, except in the case of hematuria, which as a symptom most commonly appears in the later stages of tumor development. It is rarely seen in the initial stages when surgical intervention would be simpler due to the patient's apparently relatively healthy condition. Apart from intermittent hematuria, other symptoms are rarely observed. Also, no reference values for blood progesterone levels have been established in African pygmy hedgehogs, nor is it known whether progesterone levels are associated with the occurrence of tumors in the reproductive organs, as is the case in humans ([DIEP et al., 2015](#)).

Histologically, various pathological changes in hedgehog uteri have been encountered: endometrial hyperplasia, endometrial polyps, endometrial mixed tumors, endometrial stromal nodules, endometrial stromal sarcoma, dysgerminoma, granulosa cell tumor, adenocarcinoma and morbidly adherent placenta ([HEATLEY et al., 2005](#); [OKADA et al., 2018](#)). Additionally, it has been described that two uterine tumors of different origin can be found in one hedgehog ([MIKAELIAN and REAVILL, 2004](#)).

Unlike rabbits and other small mammalian species, where clear recommendations exist regarding the necessity of elective ovariectomy, no such recommendations have been provided for African pygmy hedgehogs. The present study aimed to evaluate the medical justification for elective ovariectomy in African pygmy hedgehogs, utilizing data from the examination of 18 individuals, focusing on the presence of uterine pathology symptoms, progesterone levels, and histopathological analysis of the uterus.

Materials and methods

During a two-year period, a total of 279 African pygmy hedgehogs were examined at the Small Animal Teaching Hospital of the Faculty of Veterinary Medicine, University of Belgrade. The individuals were aged from three months to 7 years, weighing between 150 and 890 grams. All hedgehogs underwent a clinical examination and subsequently abdominal ultrasonography was performed. If indicated, the further protocol implied blood sampling

for hematological and biochemical analyses, with measurement of progesterone concentration, unless the condition of the individual did not permit it. In the case of the need for surgical intervention, the hedgehogs underwent preoperative premedication with meloxicam (Movalis, Boehringer Ingelheim, Ingelheim am Rhein, Germany) (0.5 mg/kg SC). Anesthesia was induced using a combination of ketamine (Ketamidol, Richter Pharma AG, Wels, Austria) (5 mg/kg SC) and medetomidine (Domitor, Orion Pharma, Espoo, Finland) (0.1 mg/kg SC), and maintained with 3% sevoflurane administered via a face mask.

After the preoperative preparation, the surgical intervention began by making an initial incision along the medial line (*linea alba*) to avoid significant bleeding and facilitate the exteriorization of the uterine horns and ovaries. One ligature (3.0 PGA) was placed above the ovary to allow the assistant to provide the surgeon with the position and placement of a single “lower” ligature on the ovario-renal ligament (*lig. ovario-renal*), which is extremely short in female African pygmy hedgehogs and requires exceptional skill from the surgeon. Ligation of the cervix at the bifurcation with two ligatures (3.0 PGA) is necessary to prevent bleeding and intra- or postoperative complications. After the operation, the abdominal cavity was checked to visualize possible bleeding. If no bleeding was present, the abdominal wall could be closed. The muscle layer was closed with sutures (3.0 or 4.0 PGA or PDS). It is imperative to place an intradermal suture (4.0 PGA or PDS) when suturing the skin.

Postoperatively, the hedgehogs received enrofloxacin (Enroxil 5%, Krka, Krka, Slovenia) (5 mg/kg SC q12hr) and meloxicam (0.5 mg/kg SC q24hr) for the subsequent 10 days. The protocol was adjusted as necessary depending on the unique requirements of each case. Over the subsequent weeks, the hedgehogs that underwent ovariectomy exhibited complete recovery.

Out of the 18 individuals used as a sample for this research, 14 were further monitored through regular check-ups conducted by their owners. For these 14 hedgehogs, we diagnosed and treated various illnesses, while in others, autopsies were per-

formed. It is noteworthy that a commonality among all these individuals is that they survived the ovariectomy but eventually passed away due to unrelated causes. Unfortunately, we were unable to continue monitoring the remaining 4 hedgehogs as their owners did not bring them in for follow-up examinations after the surgery.

This study includes the results of examination and analysis of 18 African pygmy hedgehogs, in which ultrasound examination, measurement of progesterone concentration, ovariectomy, and histopathological analysis of uterine tissue were performed. Tissue samples were put in 10% neutral buffered formalin, processed in an automated tissue processor, embedded in paraffin blocks, and 4 µm thick tissue sections were stained with hematoxylin and eosin. Histopathological changes were diagnosed as described by [CHAMBERS et al. \(2018\)](#).

Results

During a two-year period, 279 African pygmy hedgehogs were examined at the Small Animal Teaching Hospital of the Faculty of Veterinary Medicine, University of Belgrade. Out of this number, 142 were females, and 137 were males. Among the 142 females, changes in uterine tissue were detected by ultrasound examination in 42 individuals (30%). The ultrasonographic findings exhibited variability in lesion morphology: in some cases, the changes were localized within the body of the uterus; in some cases, in one or both horns; while in some individuals, the changes were present in both the body and the horns; however, consistent with all cases, uterine enlargement was evident on imaging (Fig. 1). Out of these, only 4 individuals (10%) had hematuria, while the uterine mass prolapsed through the vulva in only one case.

In 18 individuals, a clinical examination, ultrasonography, measurement of progesterone concentration, ovariectomy, and further histopathological analysis of sampled tissue were performed. Histopathological analysis of uterine tissue revealed cystic endometrial hyperplasia (CEH) in 6 (33.33%) individuals, endometrial mixed tumors in 4 (22.22%) individuals, endometrial stromal nod-

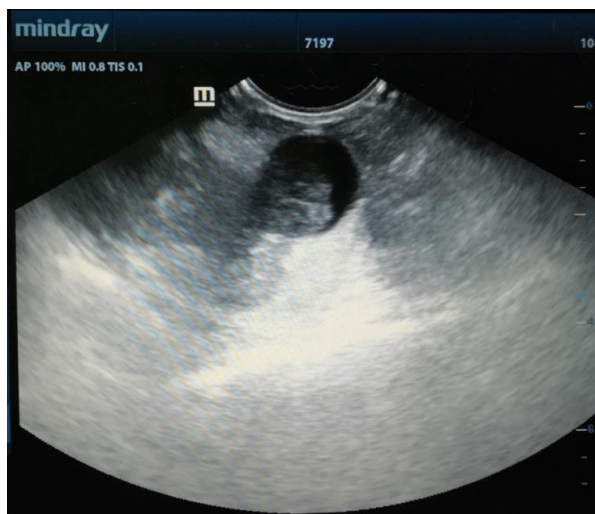


Fig. 1. The ultrasound examination visualizes a portion of the uterine horn lumen filled with a hypo- to hyper-echoic structure consistent with a neoplastic lesion

ule in 1 (5.55%) individual, endometrial stromal sarcoma in 4 (22.22%) individuals, and no pathological findings in 3 (16.6%) individuals.

The results of the analyses are summarized in Table 1.

Discussion

Years of working with hedgehogs, as well as the experiences of other authors, have taught us that the use of medication in the presence of symptoms arising from changes in the uterus does not lead to permanent cure. If symptoms of uterine pathology are present, most commonly hematuria, there may be temporary relief of symptoms after medical therapy, but this improvement is transient, and after a short period (no more than one month), their manifestation will recur. Additionally, what

Table 1. Age, ultrasonographic changes, clinical findings, progesterone levels and histopathological uterine changes

Age	Ultrasound-visible changes	Hematuria	Progesteron (ng/ml)	Histopathological findings
2y	Absent	Absent	2,21	No lesions
1y	Absent	Absent	2,86	No lesions
3y	Absent	Absent	<0,1	No lesions
3y	Present	Absent	1,98	CEH, minimal
2y	Absent	Absent	39,2	CEH
4y	Present	Present	0,49	CEH
5y	Present	Absent	<0,1	CEH, marked with secretory activity
1y	Present	Absent	0,30	CEH
6y	Present	Present	0,32	CEH, with secretory activity
5y	Present	Absent	<0,14	Stromal nodule
5y	Present	Absent	1,52	Mixed tumor CEH, metrorrhagia, hemocysts, calcification
4y	Present	Absent	<0,1	Mixed tumor CEH
4y	Present	Absent	<0,1	Mixed tumor
3y	Present	Absent	<0,1	Mixed tumor
3y	Present	Present	22,83	Stromal sarcoma Stromal nodule, mixed tumor
3y	Absent	Absent	2,11	Stromal sarcoma
3y	Absent	Absent	10,84	Stromal sarcoma CEH, polyp
5y	Present	Absent	25,7	Stromal sarcoma

poses an additional problem is that the individual will then be in poorer condition than at the initial examination. Surgical treatment for uterine pathology is the only medically justified approach.

From the analysis of cases processed at our clinic over a two-year period, we found that a significant percentage of individuals (30%) exhibited uterine changes. This percentage is the same or higher than those reported by other authors. For instance, in the study by [OKADA et al. \(2018\)](#), 30% of the examined samples comprised tissue from the female reproductive system organs. One-third of that number consisted of uterine and ovarian tissue. [GARDHOUSE and ESHAR \(2015\)](#) reported this percentage to be only 5.65. A high percentage in a hedgehog population may be a result of inbreeding [PEI-CHI et al., 2015](#)). The hedgehogs examined in our study originate from a small hedgehog population due to the limited influx of new hedgehogs into the breeding program.

The study by [MIKAELIAN and REAVILL \(2004\)](#) indicates that the most common uterine tumors originate from stromal endometrial tissue. In our examined sample of 18 African pygmy hedgehogs, CEH was histopathologically confirmed in 6/18 individuals (30%), mixed type tumors in 4 cases (22%), stromal sarcoma in the same number, and there was one case (5%) of endometrial stromal nodule. No changes were observed in 3 individuals (17%). However, a more extensive study we conducted (unpublished data), focusing solely on the histopathological analysis of uterine pathological changes, revealed a somewhat different distribution. The distribution of observed changes was as follows: CEH was observed in 24% of individuals, polyps in 5%, mixed type tumors in 24%, stromal nodules in 5%, stromal sarcoma in 10%, multiple tumors in 8%, and other changes in 5% of individuals. No changes were observed in the uteri of 4% of the examined subjects. Our results confirm the findings of [MIKAELIAN and REAVILL \(2004\)](#), suggesting that the frequency of uterine changes varies compared to other mammalian species (with the exception of rats and mice) or in humans, and the reasons for these differences are still unknown.

[HEATLEY et al. \(2005\)](#) state that there are studies on tumors of the reproductive system of

hedgehogs that describe the presence of females with more than one type of tumor. In the sample described in this study, that was also the case, and multiple tumors of different origin were identified in 10% of cases. The previously authors state that individuals aged 2 to 5 years are most susceptible to uterine changes. In this research, the youngest hedgehog diagnosed with uterine changes was 1 year old, while the oldest was 6 years old. This refers to the age at the time of examination, but the age at the time of onset of changes is unknown. This indicates that uterine changes in hedgehogs can develop throughout their entire lifespan. Furthermore, as in the cases of [RAYMOND et al. \(1997\)](#) and [MIKAELIAN and REAVILL \(2004\)](#), concurrent neoplasia was present in 6 cases (30%). One animal had a mammary adenocarcinoma, while others had squamous cell carcinoma (4 oral SCC and one cutaneous). Also, from that sample, in 6 cases, autopsy was not performed, so it cannot be confidently stated that there was no parallel neoplasm (lost to follow up).

Furthermore, progesterone levels measured in 18 hedgehogs with and without uterine changes suggest that progesterone concentration cannot be used for early diagnosis of these changes, nor can high progesterone concentrations be the cause of pathological processes or their indicator. On the contrary, [DAI et al. \(2002\)](#) and [YANG et al. \(2011\)](#) asserted that progesterone is the ultimate endometrial tumor suppressor, and observed low progesterone values (<0.2 ng/ml) may indeed be the reason for the appearance of pathological changes in uterine tissue. However, it is also necessary to mention that there are studies indicating that progesterone is essential for maintenance and growth of uterine leiomyoma in humans ([ISHIKAWA et al., 2010](#)). The only type of change in which the level of progesterone was elevated was stromal sarcoma. Information related to animals is not available in the literature, while it is known that in human stromal sarcomas, progesterone receptors are strongly positive ([AMANT et al., 2006](#); [IVY and ESTHER, 2010](#)).

[HEATLEY et al. \(2005\)](#) state that uterine pathology most commonly presents clinically with vaginal bleeding, hematuria, and weight loss.

However, in this sample, out of 15 African pygmy hedgehogs with uterine changes, only three hedgehog owners observed blood on the hedgehog or in its environment. In the remaining cases, the changes were only detected upon a wellness examination. Additionally, weight loss is a highly nonspecific symptom, often unnoticed by owners (if gradual, as is the case with uterine pathology), or attributed to inadequate nutrition. All of this suggests that uterine pathology is often unnoticed by owners in the early stages, making problem resolution challenging. The therapy for these reproductive system changes in females is questionable. As mentioned earlier, primarily according to the authors' experience and in line with other authors [HEATLEY et al. \(2005\)](#), it is only through surgical intervention (ovariectomy) that a definitive resolution of uterine pathology is achieved. Research from other studies involves the use of estrogen agonists, but in such situations, protocols have proven unsuccessful ([WELLEHAN et al., 2003](#)). The lifespan after ovariectomy can be lengthy – according to literature data, up to 303 days ([DONE et al., 2007](#)), which, considering the relatively short lifespan of hedgehogs, is significant. According to our patient electronic system records, the longest survival post-ovariectomy was seen in a hedgehog who underwent the procedure 19 months previously and had had two additional surgical interventions in the meantime in order to remove subcutaneous masses (apocrine cysts and non-specified cutaneous adenocarcinoma).

Conclusions

From the results of this study and the available literature data, we can conclude that elective ovariectomy in hedgehogs is a medically justified method. This is due to the high prevalence of female reproductive organ pathologies, which exhibit various etiologies and forms, are often undiagnosed in a timely manner, can have malignant potential and potential to metastasize to other organs, are not responsive to medical treatment, and can pose life-threatening risks. Furthermore, it should be noted that the level of progesterone was not prognostically useful.

Ethical statement

The research was approved by the Ministry of Agriculture, Forestry, and Water Management (approval No. 000896071 2023 14841 002 000 323 022), on the basis of the opinion of the Ethics Committee of the Faculty of Veterinary Medicine, University of Belgrade. Additionally, written consent was obtained from the owners for all procedures applied.

Declaration of competing interest

The authors declare no conflicts of interest in relation to the research, authorship or publication of this article.

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Važnost elektivne ovariohisterektomije i razine progesterona kod afričkih patuljastih ježeva (*Atelerix albiventris*).
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SAŽETAK

Kako se povećava broj afričkih patuljastih ježeva (*Atelerix albiventris*) koji pate od neoplazije, tako raste i potreba za širenjem znanja o bolestima ove životinjske vrste, kao i o opcijama njihove prevencije, dijagnostike odnosno liječenja. Tumori maternice su jedna od najčešće dijagnosticiranih neoplastičnih promjena kod afričkih patuljastih ježeva, ali ne postoje preporuke vezane uz elektivnu ovariohisterektomiju. Ova studija ima za cilj ispitati moguću povezanost između razine progesterona i prisutnosti neoplastičnih promjena u reproduktivnom traktu ženki. U studiji su ženke (n=142) podvrgnute općem i ultrazvučnom pregledu, uzeti su uzorci krvi za određivanje razine progesterona (n=18), te je izvedena potpuna ovariohisterektomija (n=18). Nakon uklanjanja, reproduktivni organi su pregledani patohistološki. Ultrazvučne promjene su uočene kod 30% ispitanih jedinki. Histopatološki, cistična hiperplazija endometrija bila je prisutna kod 33,33% ispitanih tkiva, miješani tumori endometrija kod 22,22%, isto kao i endometrijski stromalni sarkom. Endometrijski stromalni čvor bio je prisutan u 5,55%, a u 16,6% tkiva nisu uočene promjene. Razine progesterona su varirale od 0,1 ng/mL do 22,83 ng/mL, bez obzira na prisutnost promjena na maternici. Na temelju rezultata ove studije, kao i pregleda literature, elektivna ovariohisterektomija bi trebala biti izvedena kod afričkih patuljastih ježeva kao preventivna mjera. Pri tome, razine progesterona ne mogu se koristiti u dijagnostičke svrhe.

Ključne riječi: afrički patuljasti jež; *Atelerix albiventris*; elektivna ovariohisterektomija; razina progesterona; neoplazija maternice
