








CASE REPORT

Clinical and diagnostic approach of male pseudo hermaphroditism with os-clitoris in French bulldog: A case report

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Introduction: Hermaphroditism is less frequently reported in dogs and is often associated with infertility.

Case report: An 8-month-old French bulldog weighing 5 kg with an enlarged structure protruding from the vulva was clinically diagnosed with hermaphroditism. Physical, hormonal assay, computed tomography, and gross and histological studies were done in addition to successfully detailed surgical correction. On physical examination, the dog showed the presence of an os-clitoris protruded from the vulvar labia. Hormonal levels of estradiol, testosterone, and progesterone were 6.39 pg/ml, 0.4 ng/ml, and 8.67 ng/ml, respectively. Surgical removal of internal gonadal tissues and os clirectomy operations were conducted after the exploratory laparotomy. The removed gonadal tissues were identical to that of a female with testicles instead of ovaries, according to a gross examination. Histological examination confirmed gonads as testis, with inactive seminiferous tubules and epididymis attached to uterine horns.

Conclusion: The congenital anomalies in the present case were diagnosed as male pseudohermaphroditism (MPH). Surgical correction was performed, and the owner's satisfaction was achieved.

KEYWORDS

COMPUTED TOMOGRAPHY, French bulldog, hermaphroditism, hormonal assay, surgical correction

1 | INTRODUCTION

Normal sexual development includes three steps: chromosomal sex (XX or XY) determined at fertilization, gonadal development (ovaries or testes), and phenotypic sex development (internal and external genitalia, secondary sex characteristics) (Szczerbal et al., 2019). Thus, disorders occurring at any step can lead to disorders of sex development (DSD) which are an apparent reason for reduced fertility and sterility in dogs (Torad & Hassan, 2016).

Hermaphroditism is a sexual developmental disorder triggered by disturbance during chromosomal, gonadal, and phenotypic sex determination or differentiation, leading to defects in the reproductive tract (Öçal, 2011). There are two types of hermaphroditism: true and pseudohermaphrodites. True hermaphrodites have both ovarian and testicular tissues. However, pseudohermaphrodites have one gonadal kind of tissue with the opposite phenotype and are classified into male or female pseudohermaphrodites based on the type of gonadal tissue (Szczerbal & Switonski, 2016). On the one hand, female

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FIGURE 1 The presence of an os-clitoris protruded from the vulvar labia

pseudohermaphroditism animals have XX chromosomes and ovaries with a masculine appearance of the external genitalia, enlarged clitoris, and even a prostate due to the excess of testosterone hormone during pregnancy. Further, these animals are sterile, and an ovariohysterectomy is recommended (Del Amo et al., 2001).

On the other hand, male pseudohermaphroditism animals have XY chromosomes with an intact and functional SRY gene. The testes are present but may be located within the abdomen, the scrotum, or lateral to the vulva, with the feminine appearance of the external genitalia. In addition, the vestigial oviducts and the uterus may be included (Lyle, 2007; Rossi et al., 2014). Abnormal clitoral development can be visible as clitoral enlargement (clitoral hypertrophy) with a bony structure within the clitoris, referred to as the os-clitoris (Lane & Lofstedt, 1996).

Protrusion of the os-clitoris from the vulvar labia leads to many complications, such as irritation, self-trauma, and vaginal discharge ranging from mucopurulent to serosanguinous and vulvar discharge (Smeak & Turner, 2014). DSD have been detected in more than 40 breeds, with an increased incidence in American Cocker Spaniels, English Cocker Spaniels, Kerry Blue Terriers (Meyers-Wallen et al., 2017), French Bulldogs, and American Staffordshire terriers (Nowacka-Woszuk et al., 2019). French bulldogs' first cases were described in 2011 (Campos et al., 2011; Silversides et al., 2011) with a recent continuous increase, reaching at least 14 cases. The high occurrence of DSD in French bulldogs may be related to the increased popularity in recent years. Records focused on genetic abnormalities in these dogs, with a minimal focus on clinical signs or specifics of surgical management. Therefore, we aim to report clinical, diagnostic, and surgical correction of the male pseudohermaphroditism (MPH) case in a French bulldog.

2 | CASE REPORT

A case of a French bulldog aged 8 months and weighing 5 kg considered by the owner as a female was presented with a complaint of an enlarged clitoris with a continuous licking of the vulva due to dryness and inflammation. The initial examination of the external genital organs revealed that an enlarged clitoris about 5 cm in length and 0.5 cm in width protruded from the vulva with an atypically located urethral orifice (Figure 1).

TABLE 1 Hormonal profile of the present case

Hormone	Testosterone	Progesterone	Estradiol
Concentration	0.4 ng/ml	8.67 ng/ml	6.39 pg/ml

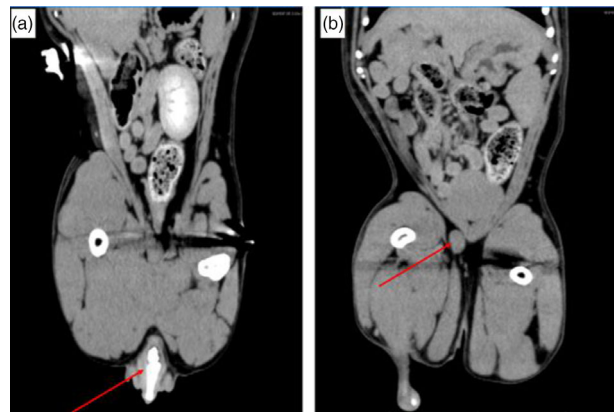


FIGURE 2 (a) Computed tomography revealed an identified os-clitoris protrude from the vulvar labia (red arrow). (b) The presence of the right testicle just under the skin in the subcutaneous tissues in the inguinal area (red arrow)

Complete blood count and serum biochemistry tests revealed no abnormalities in the collected blood samples. Afterwards, a commercial radioimmunoassay (Coat-A-Count; Diagnostic Products Corporation, Los Angeles, CA, USA) was used to determine the concentrations of testosterone, progesterone, and estradiol in the obtained serum. The present case's hormonal profile of testosterone, progesterone, and estradiol is listed in Table 1.

Surgical intervention was decided and performed after determining the precise location of the gonadal tissues for its anatomical relationship to the suspected case of hermaphroditism by computed tomography (CT) under general anaesthesia protocol. Subcutaneous injection with 0.04 mg/kg atropine sulphate (Dormicum; Yamanouchi Pharmaceutical, Tokyo, Japan) 30 min before the surgery and premedication of the animal with 0.3 mg/kg midazolam (Dormicum; Yamanouchi Pharmaceutical) was given intravenously. Induction of anaesthesia was performed with 6 mg/kg propofol (Rapinovel) via IV injection. Following endotracheal intubation, general anaesthesia was maintained with 2% isoflurane (Escain, Mylan Pharmaceutical, Tokyo, Japan). The CT examination revealed an identified os-clitoris protrude from the vulvar labia and the presence of the right testicle in the inguinal area (Figure 2a,b).

The caudal abdominal and inguinal regions were surgically prepared with a 7.5% povidone-iodine surgical scrub. The animal was put in a dorsal recumbent position. A post umbilicus ventral mid-line incision about 2–3 cm in length was done. The internal organs and gonadal tissues were inspected, and the internal gonadal tissues were removed using electrocautery (Figure 3a,b). Additionally, the enlarged clitoris protruded from the vulva was removed by os clitorrectomy operation. The urethral catheter was placed to identify the urethral papilla before transection of the os-clitoris via antegrade cystotomy (Figure 4a,b). The urethral papilla was identified, then the os-clitoris was dissected from the clitoral tissue and removed completely (Figure 5a–d).

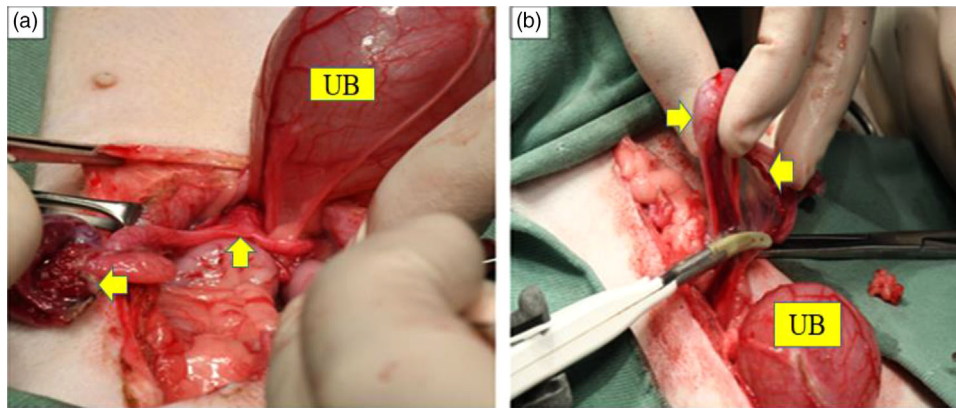


FIGURE 3 Surgical removal of the internal gonadal tissues. (a) An abdominal left testicle-like structure connected to a forked tubular structure (yellow arrows). (b) The right testicle with epididymis-like structures after dissection from the inguinal area (yellow arrows)
Abbreviation: UB, urinary bladder.

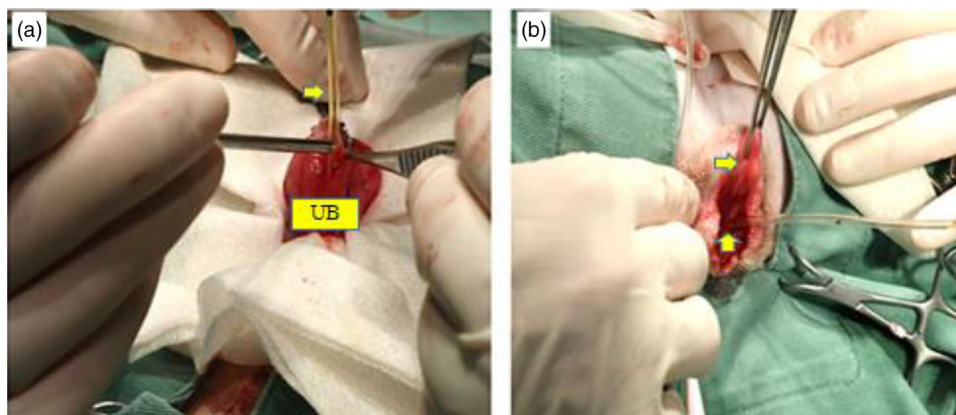


FIGURE 4 (a) The urethral catheter was placed via antegrade cystostomy (yellow arrow). (b) Identification of the urethral papilla before transection of the os-clitoris (yellow arrows)
Abbreviation: UB, urinary bladder

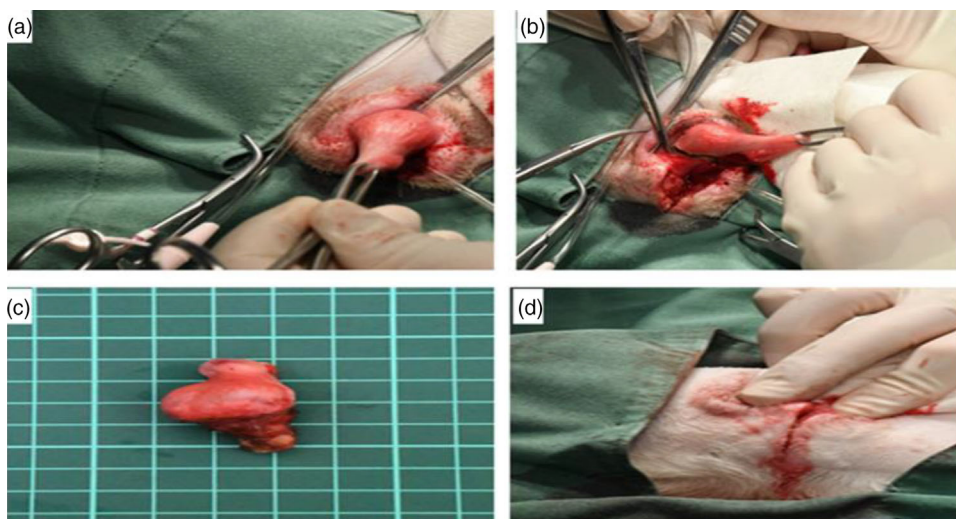


FIGURE 5 (a) The os-clitoris was pulled out from the vulva. (b) An incision was made at the os-clitoris attachment to the ventral aspect of the vulva, followed by blunt dissection of the os-clitoris from the clitoral tissue. (c) Complete removal of the os-clitoris. (d) Suturing the remaining clitoral tissue. The ventral surface of the vagina was reconstructed through suturing of the vaginal floor with a simple continuous suture pattern

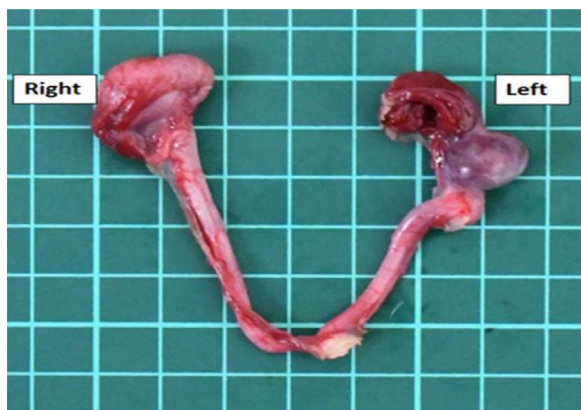


FIGURE 6 Macroscopic view of gonadal tissues, two testicle-like structures attached to tubular blind end Y-form structure similar to uterine horns instead of ovaries

The remaining clitoral tissue was sutured and closed. No complications occurred after monitoring the operation.

Gross examination revealed right and left testicle-like structures attached to uterine horns-like structures (Figure 6). Gonadal tissues were fixed in 10% neutral-buffered formalin, embedded in paraffin wax, sectioned at 5–6 μm , and stained with haematoxylin and eosin (H&E). Histological examination of both external and internal genitalia was critical to obtain a definitive diagnosis. Both right and left testicles were confirmed by histological examination. The microscopic study of both testicles showed numerous degenerative seminiferous tubules with inactive spermatogonia, relatively extensive interstitium, and loosely arranged Sertoli cells in the interstitium. Uterine tissues with endometrial glands were histologically identified. The os-clitoris revealed diffuse vascular and cavernous structures in addition to the osseous tissue (Figures 7a–d).

Cephalexin (Cefex,) 25 mg/kg) was intramuscularly injected daily for 5 days. An Elizabeth collar was advocated with an everyday dressing of the surgical wounds. The patient recovered well, and sutures were removed on 12th day after surgery. The case was followed up for 6 months after surgery. The dog did not develop urinary tract infection or urinary incontinence for 6 months following surgery.

3 | DISCUSSION

Although hermaphroditism is an infrequent congenital case in dogs, the impact is significant, resulting in confusing sexual features and infertility. In addition, hermaphroditism affects dogs' particular breeds, resulting in financial losses for breeders and high medical costs associated with surgical correction of these anomalies for the owners (Albarella et al., 2020; Kai et al., 2003).

Accurate determination of the hermaphroditism type and surgical correction is essential to reduce the risk of malignancy or pyometra formation, prevent the reproduction of animals with hereditary abnormalities, and improve the quality of life (Christensen, 2012). Therefore, the importance of the present report is based on providing a clinical assessment, and surgical correction of MPH with os-clitoris in a French bulldog as this breed showed increased popularity in recent years.

Several mammalian species have shown genital developmental disorders, including humans, pigs, goats, horses, and dogs (K.-S. Kim & Kim, 2006). However, few cases of MPH with os-clitoris have been recorded in dogs (Del Amo et al., 2001; Wernham & Jerram, 2006).

In normal dogs, the blood testosterone concentration ranges between 1 and 5 ng/ml, while in neutered dogs, usually less than 0.2 ng/ml (Roman et al., 2021). The present case showed 0.4 ng/ml testosterone concentration. The progesterone concentration in the present case was 8.67 ng/ml, while the progesterone concentration

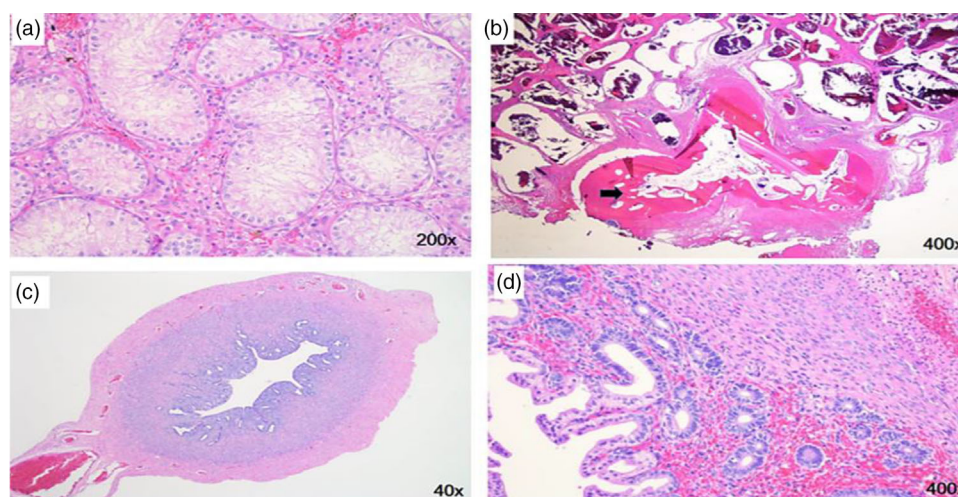


FIGURE 7 Histological result of the gonadal tissues. (a) Both testicles-like structures revealed histologically seminiferous tubules with inactive spermatogonia, relatively extensive interstitium, and loosely arranged Sertoli cells in the interstitium. (b) The enlarged clitoris section showed diffuse vascular and cavernous structures in addition to the osseous tissue (arrowhead). (c) Uterine horn like-structure. (d) Endometrium with endometrial gland, haematoxylin and eosin (H&E) (40 \times , 200 \times , and 400 \times magnification)

in an anestrus or spayed female dog is less than 1.0 ml (Roman et al., 2021). The findings of high progesterone and low testosterone serum concentrations could explain the abdominal location of the left testicle and a mild degree of masculinization of external female genitalia of the present case.

In this case, the dog was presented with the main complaint of protruded structure from the vulva, which is the most commonly reported finding in female pseudo- or true hermaphroditism as described by Meyers-Wallen et al. (1999). Additionally, the French bulldog here had a mild degree of masculinization. Only the clitoris was enlarged and contained a bone, but the vulva was normal in size, shape, and position; these findings are similar to Hubler et al. (1999).

The current dog underwent a CT scan to confirm the anatomical position of the internal genitalia, as both ultrasonographic results and radiographic images were insufficient to pinpoint the specific location of the genitalia. In addition, the exploratory laparotomy permits the examination of the internal gonadal tissues. To verify the diagnosis of gonadal sex, we performed the histological analysis of the gonads. The phenotypic sex was determined by the internal and external genitalia as described by Meyers-Wallen et al. (1999).

Clitorectomy is a simple technique that creates normal female anatomy (Del Amo et al., 2001). We did a clitorectomy operation because the sensibility of the clitoris increases as it becomes hypertrophied, resulting in chronic inflammation and constant licking of the mucosa. A few cases of MPH with surgically corrected urethral anomalies in dogs have previously been identified (K. Kim et al., 2019; Saikia et al., 2017).

Regarding the surgical correction in dogs with MPH, the outcome of the surgical decision usually depends upon the course of the urethra and the position of the external urethral orifice, as explained previously (Torad & Hassan, 2016). Therefore, in the present case, the urethral course has been examined at first. With the presence of an abnormal position of the urethra on the dorsum of the vagina, away from protruded clitoris in this situation, the clitoris and its entire os-clitoridis were safely removed.

Surgical removal of the internal gonadal tissues (testes and uterus) was performed as a part of surgical management of MPH to reduce the risk of severe uterine diseases, overcome the potential risk of neoplasia, as well as allow accurate classification of the type of hermaphroditism (Sacks & Béraud, 2012).

This case represents an excellent and crucial interpretation of the diagnostic and detailed surgical correction of male pseudohermaphroditism with os-clitoridis in a French bulldog, which is less frequently reported in the veterinary literature and is considered an emerging problem in this breed. Most of the prior cases offered a brief overview of the surgical intervention, but this case provides step-by-step surgical guidelines that may be used by inexperienced surgeons as a reference.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. Furthermore, we have informed consent from the animal's owner to use the animal's data to publish this case report.

AUTHOR CONTRIBUTIONS

Conceptualization, investigation, data curation, methodology, and writing-original draft: Hanan Hendawy. *Investigation, resources, and writing-review and editing:* Tomohiko Yoshida. *Methodology and validation:* Danfu Ma, Aki Takeuchi, and Ozai Yusuke. *Investigation and resources:* Lina Hamabe. *Conceptualization, investigation, supervision, validation, and writing-review and editing:* Ryou Tanaka.

DATA AVAILABILITY STATEMENT

As all data are presented within the manuscript, there are no other supplementary data available.

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