Polled Intersex Syndrome with Urethral Atresia in a Goat

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Abstract. A 5-day-old hornless goat was referred with dysuria since birth. The scrotum was absent, and a small penis-like structure was seen below the perineal raphe. On the laparotomy, the testicles were found near the inguinal ring and attached to a uterus-like structure. On histological analysis, the uterus-like structure was blind-end. Germ cells were absent in the testis. The karyotype of this goat was 60, XX and the SRY gene was absent. The goat was homozygous for a DNA deletion responsible for the Polled Intersex Syndrome (PIS). To the authors’ knowledge, this is the first report as the clinical case of the PIS–/– goat with urethral atresia.

Key words: dysuria, hermaphroditism, intersex, PIS, urethral atresia.

A 5-day-old hornless mongrel goat, a breed between Shiba goat and Tokara goat, was presented to our facility with dysuria since birth. The goat was anorexic and debilitated. A fluid-filled bladder was palpable. The testicles were present in each inguinal canal, the scrotum was absent, and a small penis-like structure was seen below the perineal raphe (Fig. 1A). Since it was impossible to pass a catheter through the penile tip, a bladder catheter was inserted through the abdominal wall.

Urine taken from catheter was positive for protein and occult blood, and cytological analysis showed the presence of bacilli. All blood count values were normal, but serum biochemical tests indicated high levels of potassium (7.4 mmol/l), blood urea nitrogen (44.6 mg/dl), and alkaline phosphatase (742 IU/l). Abdominal ultrasonography revealed slight dilatation of the renal pelvis, and intravenous urography revealed a normal urinary tract from the kidneys to the bladder. The goat was diagnosed with urinary tract infection and mild post-renal azotemia. Fluoroquinolones and Cephem antibiotics were prescribed for the urinary tract infection, and intravenous fluid therapy was started for post-renal azotemia; the bladder catheter was maintained. The general health of the goat improved, and urethrostomy and castration were performed at 14 days after birth.

The goat was positioned in dorsal recumbency, the testicles were moved from inguinal region to abdominal cavity. After an incision in the apical part of the bladder, we attempted to pass the catheter, which was inserted from the bladder into the urethral orifice; however we could not do so because urethral orifice was closed at the distal-most position. Hence, a permanent external urethral opening was created, and a urethral catheter was placed. While performing castration, the testicles were found near the inguinal ring and attached to a uterus-like structure, which ran parallel to the ductus deferens. No ovarian structures were noted in the abdomen. For pathological examination, several structures connected with the testicles were extracted (Fig. 1B). The postoperative recovery was good. The urinary catheter was removed 9 days after laparotomy, and the goat was discharged after more than 14 days.

Histopathological examination showed normal ductus deferens and epididymis. The wall of the uterus-like structure was found, and the endometrial glands were absent (Fig. 1C). This uterus-like structure which was assumed to be the Müllerian duct was blind-end near the testis. Although Sertoli cells and Leydig cells were detected in the testis, germ cells were absent (Fig. 1D).

For karyotyping, chromosome preparations were obtained from a peripheral blood lymphocyte culture and stained with Giemsa. Cytogenetic evaluation revealed a normal female chromosome complement, 60, XX. For polymerase chain reaction (PCR) of the sex-determining region Y (SRY), genomic DNA was isolated from the blood samples of the goat and its parents as positive and negative controls. The primers and PCR conditions were identical to that mentioned in a previous report [7]. The SRY product was then separated by agarose gel electrophoresis, stained with ethidium bromide, and photographed in ultraviolet light. SRY (a 660-bp fragment) was not amplified (Fig. 2A), and 60, XX pseudohermaphroditism lacking Y chromosome was concluded.

Using the blood samples used for SRY analysis, PCR was performed to amplify DelE, a part of the region deleted in Polled Intersex Syndrome (PIS) [9]. The primers and PCR conditions were the same as that mentioned in a previous report [7]. Additionally, β-globin (a 113-bp fragment) was also amplified as an internal control, according to previous report [6]. DelE was not detected in the affected goat, whereas the expected 147-bp DNA fragment was obtained in the parents (Fig. 2B). PIS in goats manifests as male pseudohermaphroditism; it occurs in hornless XX females and is caused by the homozygous deletion of the PIS gene.

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(including the DelE sequence) located at Chr1q43 [1, 13]. From the results, the goat was considered homozygous for DNA deletion, which led to PIS.

Since reproductive disorders due to intersexuality are a serious concern for dairy breeders, there are many reports on genital organs abnormalities in goat hermaphrodites [5, 10, 11]. Despite the close association of the development of the genital tract and the urinary systems, there are only few reports on the urinary system of intersex goats and most of these report cases of penile urethral diverticulum, concomi-

Fig. 1. The external appearance and anatomical and histological features of the PIS−/− goat. (A) The urethral orifice (thick arrow) located near the anus (white arrow), flanked by 2 folds representing the scrotum (thin arrows). (B) The male internal genitalia represented by ductus deferens (d), epididymis (e), testis (t), and pampiniform plexus (p). The uterus-like structure (u), which was considered as Müllerian duct is seen, connected to the testis. No ovarian structures are present. (C) The Uterus-like structure (right) is adjacent to the ductus deferens (left), and is blind-end near the testis. Bar=500 μm. (D) Histological section of the testis showing Sertoli cells and Leydig cells. Germ cells are absent. Bar=100 μm.

Fig. 2. Results of the PCR analysis for SRY and DelE in the PIS−/− goat. (A) Ultraviolet photograph of 1.5% agarose electrophoresis gel showing the amplification products for SRY. Lane M: molecular-size marker. Lane 1: Positive control goat sample (from the male parent of the PIS−/− goat) showing the 660-bp SRY band. Lane 2: Negative control goat sample (from the female parent of the PIS−/− goat). Lane 3: The PIS−/− goat showing no SRY amplification. (B) Ultraviolet photograph of 1.5% agarose electrophoresis gel showing the amplification products for β-globin (Lanes 1, 2, and 3; internal controls) and DelE (Lanes 4, 5, and 6). Lane M: molecular-size marker. Lanes 1, 2, and 3: All samples of positive control, negative control, and PIS−/− goat showing the amplification of the 113-bp band, which was presumed to be β-globin. Lanes 4 and 5: The sample from male and female parent of the PIS−/− goat showing the 147-bp band. Lane 6: DelE was not detected in the PIS−/− goat. The goat was thus homozygous for DNA deletion causing PIS.
tatt with urethral dilation, ectopic testis, aplasia of the genitalia, and hermaphroditism without any genetic diagnosis [3, 4]. To the authors’ knowledge, this is the first report as the clinical case of the PIS−/− goat with urethral stricture.

The genitalia of PIS−/− goats were classified typically as follows: the masculine phenotypes characterized by a penis, ductus deferens, epididymis, pampiniform plexus, and no Müller derivatives, and feminine phenotypes characterized by an enlarged clitoris, Wolffian structures, and Müllerian derivatives [11, 14]. It is suggested that the present case goat is a middle phenotype between a male and a female type, because both bilateral Müllerian ducts and male genitalia were present. Although the cause remains unknown, it is notable that the present case exemplifies PIS in a goat with both Müllerian derivatives and masculine genitalia.

We performed castration and urethrostomy in a 14-day-old kid goat. To date, the kid is in good condition. According to previous reports [2, 11, 14], PIS−/− goat foetuses showed genital ambiguity as early as 45 days post-reconstruction, when the testicles were descending. Leydig cells appear to be active in a 3-month-old PIS affected goat, secreting testosterone at an early age. An adult PIS−/− goat diagnosed with advanced Leydig cell tumor probably became hyperandrogenism [7]. Although the mortality of PIS goats remains obscure, the risk of testicular tumors may increase. Early diagnosis and castration in PIS goats may improve the prognosis.

The present case was a mongrel between Shiba and Tokara, which are generally recognized as original Japanese endemic breeds without their horn. It is also estimated that these pure native goats decreased by the introduction of Japanese Saanen which was established by breeding with some European breeds [8, 12]. Therefore, the PIS deletion detected in our case had a potential to be inherited through the reproduction. However, a possibility that the PIS deletion of the case goat was occurred independently at the same time, and its impact on understanding mammalian sex-differentiation may improve.

Further investigation is necessary to identify the gene-carrier goats in Japan.

REFERENCES