Bilateral hydronephrosis during pregnancy in a Korean native cow

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SUMMARY

Hydronephrosis in cattle refers to the dilatation of the renal calices and is congenital or acquired by urinary obstruction. It has been a major cause of hydronephrosis due to obstruction of the upper urinary tract by urolithiasis or neoplasm, especially in adult cattle. A 43-month-old Hanwoo cow at 4 months gestation was admitted for anorexia, depression, and urine dribbling. Rectal ultrasonography revealed a large pregnant uterus, absent urinary bladder, and dilated calices observed in the caudal pole of the left kidney. Percutaneous ultrasonographic images showed dilated calices in the right kidney. The serum biochemical profile showed azotemia (blood urea nitrogen, 90.11 mg/dL; creatinine, 7.28 mg/dL). Blood gas analysis indicated electrolyte abnormalities, including hyponatremia, hyperkalemia, hypochloremia, and hyperphosphatemia. Urinalysis showed a urine specific gravity of 1.020, pH of 7.5, leukocyte count of 70 cells/μL, nitrates negative, and protein negative. White blood cells or struvite crystals were not detected on the urine sediment microscopy. To detect *Histophilus somni*, *Escherichia coli*, and *Corynebacterium renale*, polymerase chain reaction was performed. The alpha-hemolysin gene of uropathogenic *E. coli* was detected in the left kidney and urinary bladder. The left kidney measured 20 x 10 cm and was filled with urine, whereas the urinary bladder was small, and the bladder wall was not thickened. No characteristic histopathological findings were noted in the bladder and kidney; however, macrophages were present. Therefore, the cow was diagnosed with bilateral hydronephrosis due to urinary tract obstruction by the pregnant uterus. To the best of our knowledge, this is the first report of hydronephrosis caused by a pregnant uterus in cattle. It was also the first report that severe azotemia and electrolyte abnormalities could be caused by hydronephrosis induced by a pregnant uterus in cattle. This provides the veterinarian with a new differential diagnosis for hydronephrosis in pregnant cows.

KEY WORDS

Hydronephrosis; alpha-hemolysin gene; pregnant uterus; urinary tract obstruction.

INTRODUCTION

The urinary bladder of cattle is located in the pelvic cavity below the uterus and vagina within the broad ligament of the uterus and is anchored to the abdominal cavity by the right lateral, left lateral, and median ligaments. The pubovesical pouch is the space in the abdominal cavity between the uterus and the bladder. In cattle, the ureter originates in the renal calyx, passes into the broad ligament of the uterus, and enters the bladder neck [1].

Hydronephrosis in cattle refers to dilatation of the renal calyx, not the renal pelvis. This is because anatomically, cattle do not have a renal pelvis. The hydronephrosis-induced clinical manifestations and renal lesions can vary depending on the duration and extent of the disease (unilateral/bilateral) [2]. Moreover, hydronephrosis can occur congenitally or acquired by obstruction. Congenital hydronephrosis due to congenital urethral stricture and acquired hydronephrosis due to focal bladder papillary hyperplasia, obstructive urolithiasis, and neoplasm have been reported in calves and cattle, respectively [3-8].

In humans, hydronephrosis during pregnancy is recognized as a physiological change in more than 80% of pregnant women. Hydronephrosis frequently occurs in the second trimester of pregnancy and is known to spontaneously resolve following delivery. Bladder and ureter compression by the pregnant uterus is believed to be the cause [9-10]. Only a small proportion of pregnant women develop clinical symptoms, and renal failure has been reported in rare cases [9-12]. In contrast, hydronephrosis occurring naturally during pregnancy has nev-

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er been reported in other animals, including cattle. This case report presents hydronephrosis due to a pregnant uterus in a 43-month-old pregnant Hanwoo cow to assist large animal clinicians in their practice.

CASE PRESENTATION

A 43-month-old Hanwoo cow at 4 months gestation was admitted for anorexia and depression, and urine dribbling was observed by the owner. The temperature, respiratory rate, and heart rate were 38.7 °C, 26 breaths/min, and 61 beats/min, respectively, which were all normal. The patient was stabilized and monitored; however, no signs of straining or abdominal pain caused by urinary obstruction were observed.

Percutaneous ultrasonography (LOGIQ e R8, GE Healthcare Technologies Inc., Chicago, IL, USA) with a 3-MHz convex probe revealed dilated calices in the right kidney. Additionally, ultrasonography revealed dilated calices in the caudal pole of the left kidney. Rectal ultrasonography with a 7-MHz linear probe revealed a descending uterus and absent urinary bladder at the level of the pelvic inlet (Figure 1). No fluid was observed in the abdominal cavity. Uroperitoneum was excluded from the differential diagnosis. Rectal examination and ultrasonography could not locate the urinary bladder; therefore, a urethral catheter (14 Fr, 50 cm long) was inserted, which passed unobstructed from the urethra to the urinary bladder and confirmed the presence of a small amount of urine in the urinary bladder.

The blood was analyzed for complete blood count (CBC; Procyte DX Hematology Analyzer, IDEXX Laboratories, Westbrook, ME, USA), serum biochemical profile (SBP; Dri-Chem 4000i, Fujifilm, Tokyo, Japan), and blood gas analysis (BGA; i-STAT 1 Analyzer, Abbott Laboratories, Abbott Park, IL, USA). CBC showed only neutrophilia without bands. The SBP showed azotemia with blood urea nitrogen and creatinine levels of 90.11 mg/dL and 7.28 mg/dL, respectively. BGA revealed electrolyte abnormalities, including hyponatremia, hyperkalemia, and hypochloremia (Table 1). Urinalysis showed a urine specific gravity of 1.020, pH of 7.5, leukocyte count of 70 cells/mL, nitrates negative, and protein negative. White blood cells or struvite crystals were not detected on urine sediment microscopy. The owner did not want to continue treatment and decided to slaughter the cow. The bladder and left kidney were sent to the abattoir for detailed examination and pathology.

DNA was extracted from the bladder and kidney samples using the DNeasy Blood & Tissue Kit (Qiagen, Hilden, Germany) following the manufacturer's instructions. To detect *Histophilus somni*, *Escherichia coli*, and *Corynebacterium renale*, polymerase chain reaction was performed. Only the alpha-hemolysis (*hlyA*) gene of uropathogenic *E. coli* (UPEC) was detected in these samples (Figure 2).

Macroscopically, hemorrhages are observed outside the left kidney and pinpoint hemorrhage and slight erosion in the urinary bladder (Figure 3). The left kidney measured 20 x 10 cm and was filled with urine, whereas the urinary bladder was small, and the bladder wall was not thickened. The remaining tissues were fixed in 10% buffered formalin, routinely processed, and embedded in paraffin for hematoxylin and eosin staining for histological examination. Pathologists performed all evaluations (Animal and Plant Quarantine Agency; APQA, ROK) and no histopathologic findings were found in the bladder and kidney.

DISCUSSION

Generally, the ureters enter the bladder wall at an angle. Moreover, the constant ureteral contraction causes urine to flow in one direction. Therefore, urine does not return from the bladder to the ureters even with an increased bladder pressure [1]. In human medicine, it is believed that hormonal effects during pregnancy caused genitourinary system relaxation, which in turn caused urinary tract dilation [9, 12-15]. However, it has

Table 1 - Findings on serum chemistry and blood gas analysis in a Korean native cow with hydronephrosis due to a pregnant uterus.

Analysis	Parameters	Values	Reference range
Serum biochemistry	Total protein (mg/dL)	8.6	6.7-7.5
	Albumin (mg/dL)	3.7	3.0-3.6
	Globulin (mg/dL)	4.8	3.0-3.5
	Total bilirubin (mg/dL)	0.2	0.01-0.5
	Direct bilirubin (mg/dL)	0.1	0.0-0.2
	Alkaline phosphatase (U/L)	101	0-488
	Aspartate transaminase (U/L)	91	78-132
	Blood urea nitrogen (mg/dL)	90.11	20-30
	Creatinine kinase (U/L)	125	44-211
	Creatinine (mg/dL)	7.28	1.0-2.0
	Gamma-glutamyl transferase (U/L)	23	15-39
	Calcium (mg/dL)	12.5	9.7-12.4
	Magnesium (mg/dL)	2.5	1.8-2.3
	Phosphorus (mg/dL)	15.8	5.6-6.5
Blood gas analysis	Chloride (mmol/L)	87	97-111
	Potassium (mmol/L)	7.9	3.9-5.8
	Sodium (mmol/L)	122	132-152
	pCO_2 (mmHg)	43.8	35-44
	pH	7.418	7.31-7.53
	Total CO_2 (mmol/L)	30	21-32
	Anion gap (mmol/L)	15	14-20
	Bicarbonate (mmol/L)	28.3	17-29

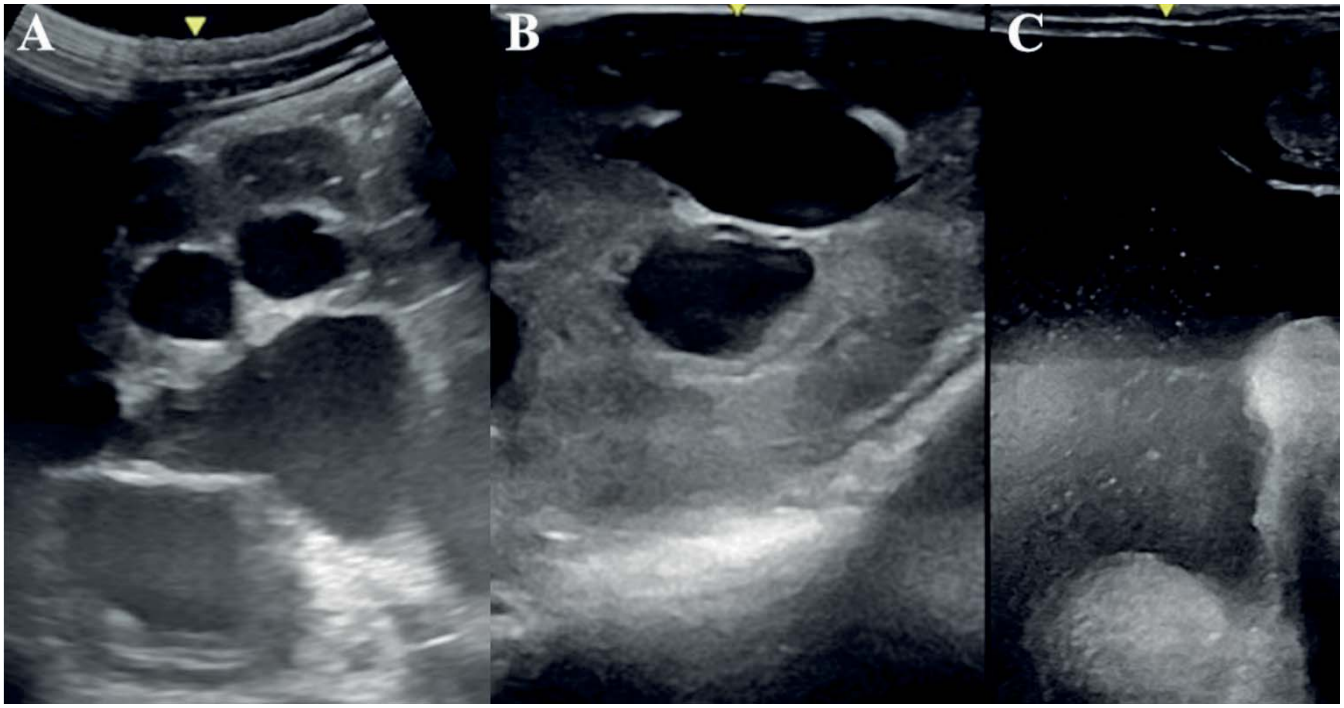

Figure 1 - Rectal and percutaneous ultrasonographic images. Dilated calices in the right kidney (4.06 cm of maximal length) (A). Dilated calices in the caudal pole of the left kidney (1.82 cm of maximal length) (B). The pregnant uterus at the entrance to the pelvic cavity (C).

recently been known that urinary system relaxation could not be caused by hormones; there are also reports that obstruction, not hormones, causes hydronephrosis [9, 16-18]. Hydronephrosis in cattle is caused by obstructions, congenital or acquired, mainly uroliths and tumors [3-8]. In the present case, ureter or urinary bladder compression by the pregnant uterus may have caused the obstruction and resulted in hydronephrosis. In rectal ultrasonography in cattle, the urinary bladder is used as a landmark of the reproductive organ. On rectal examination, the bladder is easily palpable with bladder wall thickening, which is frequently the starting point for the diagnosis of cystitis. In this case, the bladder could not be identified by ultrasonography and rectal examination, and only a small amount of urine was noted when urine was collected using a urethrocatheter. Furthermore, the gross lesion showed a small shrunken bladder with no evidence of bladder wall thickening or inflammation. Ultrasonography and gross lesions revealed enlarged kidneys and hydronephrosis. Only the pregnant uterus was visible where the bladder should be, and no other urinary system mechanical obstruction could be identified. Therefore, bilateral hydronephrosis due to urinary tract obstruction by the pregnant uterus was diagnosed.

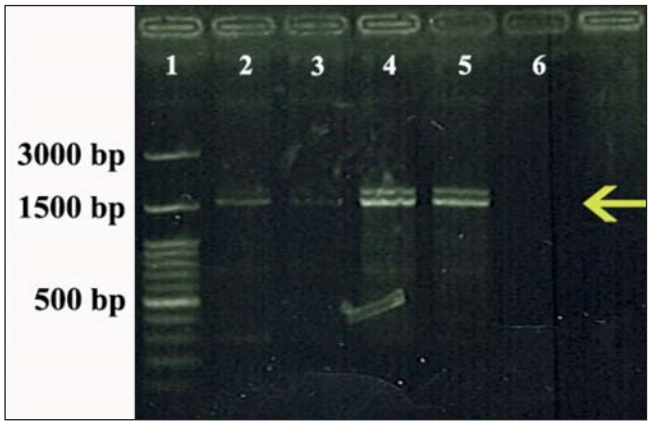

Figure 2 - PCR for the alpha hemolysis (*hlyA*) gene (1,551 bp). Lane 1, ladder (100 - 3,000 bp); lane 2, urinary bladder with lesion; lane 3, urinary bladder without lesion; lane 4, kidney with lesion; lane 5, kidney without lesion; and lane 6, negative control.

Furthermore, urinary tract infections in cattle are primarily ascending infections. *E. coli* and *C. renale* are the most common pathogens; however, *Trueperella pyogenes*, *C. cystitidis*, *C. pilosum*, *Staphylococcus* spp., *Streptococcus* spp., and urea splitting organisms (*Enterococcus* spp., *Klebsiella* spp., and *Pseudomonas* spp.) have also been reported in cattle [19-21]. Reduced urine output, decreased ureteral peristalsis, and reflux from the vesicoureteral junction can lead to urinary retention, thereby making the urine an ideal environment for bacterial growth. Nevertheless, in this case, only the *hlyA* gene of UPEC was detected in the urinary bladder and kidneys, with no other causative organisms. *HlyA* has been reported to induce kidney inflammation and injury [22, 23] and is a significant virulence factor in pyelonephritis. However, on gross and microscopic examinations, neither pyelonephritis nor cystitis caused by *E. coli* was observed, and urine dip stick tests were negative for the bacteria. Histological examination revealed no noticeable lesions in the bladder or kidneys. Although *E. coli* was detected in these tissues, it was highly unlikely that *E. coli* caused this disease. Moreover, the mechanism through which *hlyA* induces kidney injury remains unclear. Consequently, bacteria introduced into the urinary tract are excreted in the urine by host defense mechanisms, including washing; however, the fimbriae or pili of *E. coli* facilitate adhesion to the mucosal surfaces of the urinary tract [24, 25]. At this instant, it is believed that obstructive uropathy appears to accelerate the adhesion of this pathogen to the urinary tract mucosa [19, 26].

In cattle, urethral obstruction is characterized by changes in serum biochemistry with electrolyte abnormalities. Hypona-

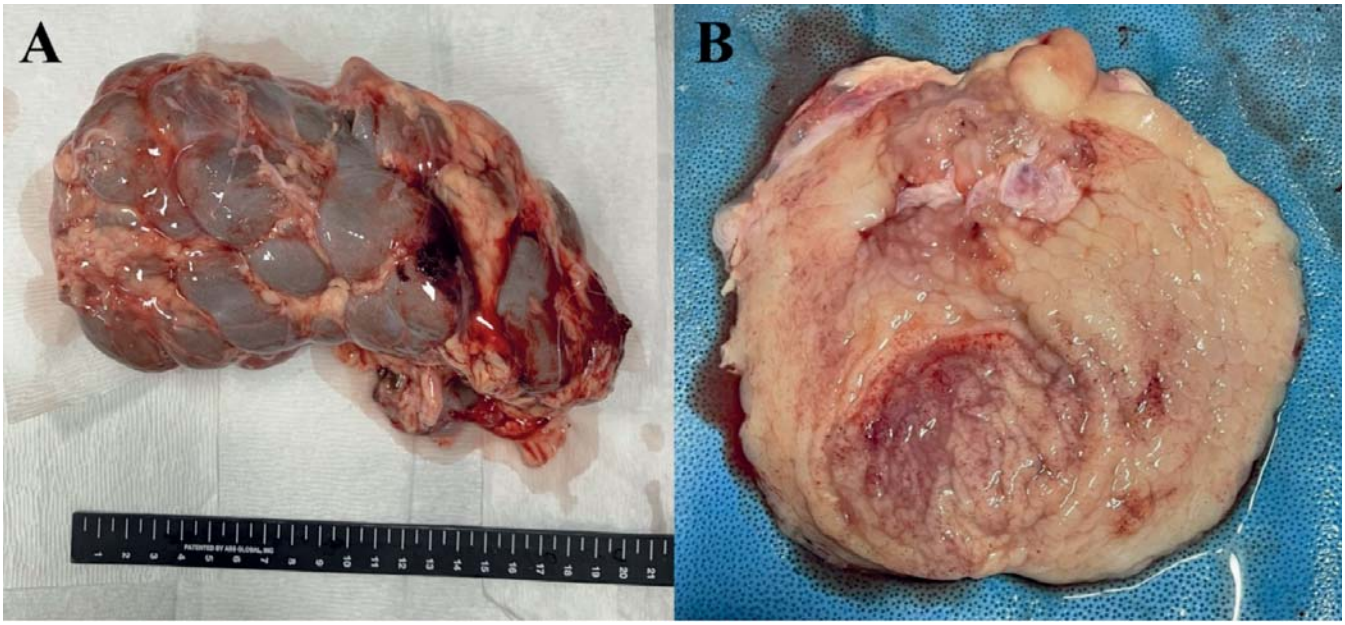

Figure 3 - Gross pathology findings of the left kidney and urinary bladder in a 43-month-old Hanwoo cow with bilateral hydronephrosis. Hemorrhages in the left kidney (A) and urinary bladder (B) are observed. Moreover, pinpoint hemorrhages and slight erosion are observed on the urinary bladder mucosa.

tremia, hypochloremia, hypokalemia, hyperphosphatemia, hyperglycemia, and azotemia are common [8, 27, 28]. However, these changes may vary depending on the location and severity of the obstruction. Hyponatremia, hypochloremia, hyperkalemia, and hyperphosphatemia were observed in the present case but not hyperglycemia. Urethral obstruction is a problem of the lower urinary system; however, in this case, obstruction occurred in the upper urinary system. Therefore, the results shown by glucose may be different. Additionally, the duration and severity of the disease may have influenced the results of SBP and BGA in the obstructive urinary tract disease. Despite bilateral hydronephrosis development, this patient maintained urine concentration with a specific gravity of 1.020, and no proteinuria was detected. According to SBP and BGA analyses, abnormalities were noted in these results; nevertheless, urinalysis showed that some renal function was preserved. In unilateral obstruction, the contralateral kidney may undergo compensatory hypertrophy; however, the kidney may still function properly. Conversely, as hydronephrosis due to the obstruction progresses, renal function declines. If it becomes chronic, irreversible damage will lead to a permanent loss of function [7, 29, 30].

CONCLUSION

In the case of unilateral hydronephrosis due to the pregnant uterus, unilateral nephrectomy may be considered following renal function evaluation on the affected side. However, if there is bilateral hydronephrosis caused by a pregnant uterus and renal function is abnormal based on SBP/BGA results, as in this case, culling the cow as a farm animal would be the first option.

Ethic approval

This study was approved by the Institutional Animal Care and Use Committee of the National Institute of Animal Science, ROK (JBNU IACUC No. NON2023 123). All experimental procedures involving animals were conducted in strict accordance with relevant guidelines and regulations.

Author Contributions

YK: Conceptualization; Investigation; Data Curation; Writing-original draft. MJJ and YJP: Investigation. KL: Histopathological analysis. HCC: Visualization. JP and KSC: Conceptualization; Data Curation; Writing-original draft; Writing-review & editing

Conflict of Interest

The authors declare that there were no conflicts of interest.

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