Uremic Changes Induced by Experimental Urinary Retention in Goats

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ABSTRACT. The disease process of urinary retention resulting in uremia reported in cattle was studied clinically, clinico-pathologically and pathologically in 4 male goats with artificial urethra obstruction (UO). The blood urea nitrogen (BUN) and serum creatinine values increased at constant rates (mean rates: 29.1 mg/dl/day and 1.6 mg/dl/day, respectively) from the initial stage. These increased levels were thought to be the most useful indicator for the diagnosis of the uremic stage. The serum sodium and chloride values decreased gradually after UO. The glucose and potassium values increased remarkably later than in the intermediate stage. Rupture of the bladder caused severe dehydration. The animals died between 8 to 13 days post-urinary retention. Unusual respiration and heart beat, and severe nervous signs were seen at moribundity. Gross lesions of the urinary organs were characterized by the pressure of retained urine and hemorrhage and edema in the subcutaneous tissues, skeletal muscles and some other organs. To study the effect of urethrotomy, 3 male goats were relieved from UO 3 or 4 days after UO operation. The animals became capable of urination and recovered from the uremic condition within 4 days.—KEY WORDS: blood analysis, goat, uremia, urethrotomy, urinary retention.


Urolithiasis is known to be the most frequent disease in fattening cattle in Japan [1, 9, 10], causing urinary retention and accumulation of urinal components in the body, resulting in uremia. It is stipulated by law in Japan that uremic animals are not esculent and most of fattening cattle diagnosed as uremic by meat inspection are due to urolithiasis. Uremia in animals is grossly diagnosed based on erosion, hemorrhage or rupture of the urethra or bladder and inflammation of the kidney. Since our knowledge on the clinical signs and pathological changes of uremia induced by urinary retention is limited, the diagnostic criteria still remain inaccurate. Ante mortem diagnosis of uremia is needed to avoid economic loss by disuse of the animal affected with urolithiatic uremia. If the animals recover from the uremic condition before the slaughter, they are possible to be esculent. The most practical treatment of animals affected with urinary retention is urination by urethrotomy [11].

This paper describes clinico-pathological changes in goats with experimentally induced urinary retention and urination.

MATERIALS AND METHODS

Eight healthy male goats (Saanen, weighing from 28 to 41 kg, and ranging in age from 6 to 10 months) were used for the experiment.

Artificial urethra obstruction (UO) was made in 7 of the animals (Nos. 2–8) and sham operation as the control was carried out in an individual (No. 1). UO was performed as follows: The skin of the lower abdomen was incised to expose the penis near the glans, and the urethra was also incised by 3 to 4 mm. Then, a grass stick, about 2.5 cm in length and 3 mm in diameter, which was called "false calculus"
was inserted into the urethra from the incision hole and slid up toward the perineal region. In addition, the urethra was ligated at two following points: 1) between the false calculus and incision hole not so tight as to affect passage of the false calculus, 2) at the middle of the false calculus not affecting urine passage with dilation of the urethra. This technique caused urinary retention without crushing the urethra induced by simple tight ligation. Operation was performed under intravenous general anesthesia with pentobarbital sodium.

Clinical observations were made until the animals died or were moribund in fatal UO goats (Nos. 2–5). In temporary UO goats (Nos. 6–8), UO was relieved by removal of the false calculus to recover from uremic condition 3 or 4 days after UO operation. Clinical observations were made until the 6th to 7th day after being relieved from UO. The control (No. 1) and 2 fatal UO goats (Nos. 4 and 5) were euthanized 5, 8, and 13 days, respectively, after operation.

Blood samples were collected from the jugular vein immediately before operation and every morning after operation. Erythrocytes (RBC) and leukocytes (WBC) were counted by using an automatic blood cell counter, and hematocrit value (Ht) was determined by using a microhematocrit tube. Biochemical serum analysis consisted of determination of blood urea nitrogen (BUN) by the urease indophenol method, creatinine by the method of Folin-Wu, glucose (Glu) by the orthotoluidine blue method, sodium (Na) and potassium (K) by flame photometry, and chloride (Cl) by colorimetric titration. In addition, inorganic phosphate, calcium, glutamic oxaloacetic transaminase (GOT), glutamate dehydrogenase, and ornithine carbamoyltransferase were also determined.

The control and fatal UO goats were necropsied immediately after death or euthanasia. Liver and kidney tissues were fixed in 10% formalin for histopathology.

RESULTS

1. Clinical signs

Fig. 1 shows the clinical signs and urinary retention in individual animals. The control (No. 1) revealed no abnormality.

(1) Findings in the fatal UO goats: Complete urinary retention was observed immediately after UO operation in Nos. 2 and 5, in which abdominal swelling was found on 4 days after UO operation. Rupture of the bladder was confirmed by aspiration of urine from the abdominal cavity. No. 2 died 8 days after operation and No. 5 was

<table>
<thead>
<tr>
<th>Goat No.</th>
<th>Days of observation</th>
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<td>1</td>
<td>+ + + + + + b)</td>
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<tr>
<td>2</td>
<td>+ + + + + + c)</td>
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<tr>
<td>3</td>
<td>+ + + + + + c)</td>
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<tr>
<td>4</td>
<td>+ + + + + + b)</td>
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<tr>
<td>5</td>
<td>+ + + + + + b)</td>
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<td>6</td>
<td>+ + + + + + a)</td>
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<tr>
<td>7</td>
<td>+ + + + + + a)</td>
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<tr>
<td>8</td>
<td>+ + + + + + + + +</td>
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</table>

Fig. 1. Clinical signs.
Day 0: Immediately before operation [No. 1, sham operation; Nos. 2–8, urethroobstruction (UO)].
■ Normal urination.
■ Complete urinary retention.
■ Incomplete urinary retention (urine was retained in the subcutaneous tissues or dribbled).
■ Rupture of the bladder (in spite of complete or incomplete urinary retention).
+, ++ and −: physical condition estimated by vigorousness, appetite and water consumption.
a) Relief from UO b) Euthanasia c) Dead Neuropathy at moribundity of the fatal UO goats was as follows: No. 2, unknown; No. 3, nystagmus; No. 4, nystagmus and trismus; No. 5, nystagmus and opisthotonus.
moribund and euthanized 8 days after it. Urinary retention was incomplete in Nos. 3 and 4, in which urine leaked from the urethra and the operation wound and was retained in the subcutaneous tissues. No. 3 showed bladder rupture after 5 days and died 9 days after operation, manifesting moribund neurological symptoms immediately before death. No. 4 had no bladder rupture and was euthanized 13 days after operation because of moribund symptoms.

Clinical signs with urinary retention were as follows; An anxious, tense state appeared 1 day after operation and the animals strained to urinate. They stopped taking concentrated feed and there was decreased in water consumption from the early stage. Thereafter, they stopped either ruminating or taking roughage and became gloomy in the later stage. Tachycardia persisted from the initial stage but abnormalities of the body temperature and respiratory rate were not found until becoming moribund. An ammonia odor of the breath was not noted in all the animals throughout the experiment. Moribund symptoms consisted of an inability to stand up, feeble and irregular heart sound, drop in temperature, Cheyne-Stokes breathing, agony, lethargy and nervous symptoms such as nystagmus, trismus and opisthotonus. (2) Findings in temporary UO goats: Complete urinary retention continued in all the 3 animals until relief from UO. Thereafter, reurination was confirmed in Nos. 6 and 8. In No. 7, however, bladder rupture occurred immediately after relief from UO and reurination started 2 days later. Retained urine in the abdominal cavity was absorbed within 2 days after reurination.

The clinical signs were similar to those in the fatal UO goats until reurination began, but all the animals recovered from the signs within 4 days after reurination.

2. Clinico-pathological findings

Fig. 2 shows the results of clinico-pathological findings in the control and fatal UO goats. No significant changes were found in the control. In the fatal UO goats, there were significant changes in WBC, RBC and Ht, especially after rupture of the bladder (shown in bold lines in Ht for Nos. 2, 3 and 5). These parameters were also

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Fig. 2. Results of clinico-pathological analysis of the control and fatal UO goats.
Common remarkable changes (except for BUN and creatinine) in the UO goats are emphasized by bold lines. Arrows indicate the time of bladder rupture.
changed transitorily immediately after UO operation (shown in bold lines in RBC for Nos. 3–5).

BUN and creatinine values continued to increase after urinary retention at constant mean rates of 29.1 mg/dl/day and 1.6 mg/dl/day, respectively. Glu values were elevated from immediately after rupture of the bladder in Nos. 2, 3 and 5, but the increase was delayed in No. 4 (shown in bold lines for Nos. 3–5). Na and Cl values decreased gradually. K value increased markedly close in time to moribundity (shown in bold lines for Nos. 2–4). Obvious changes were present in inorganic phosphorus and calcium values which showed no common patterns (data were not shown). Enzymatic liver function test revealed no changes except a transient increase (GOT activity less than 70 IU/L) immediately after UO operation.

The sera from the late stage of urinary retention frequently were coagulated with fibrin.

Fig. 3 shows the results in the temporary UO goats. The same changes as those in the fatal UO goats were found until relief from UO and then recovered rapidly in Nos. 6 and 8. In No. 7 having bladder rupture, however an increase in BUN and a decrease in Na and Cl values continued until 2 days later. Increased Ht value and RBC were observed while urine was retained in the abdominal cavity. However, these changes also recovered with reurination.

3. Pathological findings

Table 1 shows the necropsy findings of the control and fatal UO goats. No lesions were found in the control. Lesions in the fatal UO

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Goat No.a)</th>
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<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Edema in subcutaneous tissue</td>
<td>–</td>
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<tr>
<td>Systemic petechiae in subcutaneous tissue</td>
<td>–</td>
</tr>
<tr>
<td>Edema in muscular tissues</td>
<td>–</td>
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<tr>
<td>Pulmonary edema</td>
<td>–</td>
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<tr>
<td>Subpericardiac hemorrhage</td>
<td>–</td>
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<tr>
<td>Urine retention in abdominal cavity</td>
<td>–</td>
</tr>
<tr>
<td>Ulcer in abomasum</td>
<td>–</td>
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<tr>
<td>Submucosal hemorrhage in intestine</td>
<td>–</td>
</tr>
<tr>
<td>Focal discoloration of liver</td>
<td>–</td>
</tr>
<tr>
<td>Congestion, hemorrhage and erosion in urethra</td>
<td>–</td>
</tr>
<tr>
<td>Congestion, hemorrhage and erosion in bladder</td>
<td>–</td>
</tr>
<tr>
<td>Rupture of bladder</td>
<td>–</td>
</tr>
<tr>
<td>Perirenal edema</td>
<td>–</td>
</tr>
<tr>
<td>A few scars on kidney surface</td>
<td>–</td>
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<tr>
<td>Swelling of renal pelvis</td>
<td>–</td>
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</tbody>
</table>

a) No. 1 was necropsied 5 days after sham operation.
Nos. 2–5 were necropsied at moribundity or immediately after death.

Fig. 3. Results of clinico-pathological analysis of the temporary UO goats. Arrows indicate the relief from UO.
goats were systemic edema or petechiae in the subcutaneous tissues (Fig. 4) or skeletal muscles, localized pulmonary edema, intraperitoneal urinary retention containing a large amount of jellied clots (there was no evidence of peritonitis), 1 or 2 ulcers in the abomasum (about 0.5–1.0 cm in diameter, occurring near the pyloric region), submucosal hemorrhages in the intestine, and focal discoloration of the liver. Congestion, hemorrhages and erosions were found in the mucous membrane and/or submucosal tissues of the bladder and urethra (more severe at the perineal region). The color of the kidney was normal or slightly pale in all the animals, but a few scars were found on the surface.

Histologically centriflobular fatty degeneration in the liver was found. The renal tubules were mostly dilated with cosinophilic substance and flattened and degenerated epithelial cells (more severe at the distal parts). Some Bowman's spaces were also dilated (Fig. 5). Interstitial edema, fibroelastic proliferation or infiltration of round cells were found in the kidney.

DISCUSSION

Initial clinical signs of the experimental urinary retention are considered to be shown by pain in the urinary organs and restlessness from dysuria, followed by uremic symptoms. The severity of the symptoms in the middle stage and survival days varied in individual animals but moribund symptoms were mostly common.

The lesions of the urinary organs in the fatal UO goats with dysuria seemed to have been caused mainly by the pressure of urine, because the urethrocyctic changes occurred related to the intensity of the anuric condition. Their severity also varied in individual animals and did not indicate uremic disorder. The lesions of organs other than the urinary system were probably induced by uremic metabolic disorder; systemic subcutaneous hemorrhages and intestinal submucosal hemorrhages suggested the involvement of uremic blood coagulation disorder [3, 5]. Fibrin clotting just after separation of the serum in this study may be also correlated with that. Edema of the subcutaneous and muscular tissues may have
been caused by a high osmolality of the interstitial fluid with an increase of urea. Since these systemic changes were not always found in uremic animals, especially in early stages of uremia, they may have occurred in the late or moribund stages.

Clinico-pathologically, BUN and creatinine values increased remarkably from the beginning of UO in straight line pattern. The other blood components changed later. These changes suggest the collapse of homeostasis. Severe dehydration after rupture of the bladder was considered to have been induced by drawing water from the interstitial and intervascular fluid to the peritoneal cavity, because urine has a higher osmolality than these fluids [2]. Diuresis by the same mechanism as post-obstruction diuresis-induced dehydration is also considered [6]. In addition, transient elevation of RBC and Ht level likely caused by splenic contraction under a severe stress [7] was found immediately after operation. The uremic metabolic disturbances became severe after rupture of the bladder. The enzymatic liver function test disclosed no significant changes in correlation to the progression of the uremic condition, although there was fatty degeneration.

On the basis of these findings, we classified the disease process after complete urinary retention as follows (Fig. 6).

1. Initial stage: When ischuria occurs, animals fall into restlessness with pain in the urinary organs.
2. Intermediate stage: Not only the urinary system is involved but latent systemic effects are manifested.
3. Late stage: Homeostasis has collapsed, and lesions such as edema and hemorrhage in the subcutaneous tissues, skeletal muscles or intestinal mucous membrane and hepatic fatty degeneration occur almost simultaneously.
4. Moribund stage: It is impossible for the animals to stand up and they show severe symptoms such as agony or nervous signs, and then die within a few hours.

The intermediate stage is the beginning of uremic condition. However, it is still difficult to judge this stage as uremia by clinical signs or gross lesions, because the symptoms of the initial stage still are persisting indiscriminatively in the intermediate stage and no distinct uremic lesions may be confirmed before the late stage.

After complete urinary retention, BUN and creatinine values increased at constant rates from the initial stage in close correlation with each other, which indicate an accumulation of other urinary components in the body. Furthermore, BUN and creatinine values are the most serious uremic toxins because increased amounts of these substances elevate the osmotic pressure of the body fluid and collapse the water balance or exert an adverse effect on the circulatory system [8]. In addition, these components are closely correlated with production of other uremic toxins including cyanic acid and guanidine compounds [4, 8]. The other blood components examined in
this study demonstrated no conspicuous changes until the late or moribund stage. Therefore, BUN and creatinine values are the most useful indicator in judgment of stages after urinary retention. Standardization of the increased component levels is necessary. Thus, even when uremia can not be estimated from clinical symptoms or necropsy findings, or both, uremia can be diagnosed, by remarkably increased BUN and creatinine values. To avoid the economical loss by disuse of the slaughtered animals suffering from urolithic uremia, uremia judgment by antemortem inspection and suitable treatment in the intermediate stage of urinary retention are needed. Recovery from the uremic condition by reartartation was effective even in cases with rupture of the bladder.

For the standardization of uremia judgment based on clinico-pathological changes, the present authors propose to set a temporary limit of the increased BUN level at 120 mg/dl.

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REFERENCES