Bovine Cases of Urolithiasis Treated with Traditional Herbal Medicine, P-3

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Bovine renal disorders are common and often serious as indicated in slaughtered cases [2, 4, 6, 7]. Urolithiasis is one of the most important diseases [8] which, from the mid 1960's, has been on the increase in Japan [5, 10]. Since the treatments for urolithiasis are limited, salvage is usually recommended for the bovine cases. Bovine urolithiasis is generally treated according to symptoms [1, 3, 8] with vitamins or ammonium chloride as urinary acidifiers, and occasionally surgery is conducted. In an effort to find means for preventing and treating renal diseases in cattle, herbs that can be given as feed were studied.

In our previous study, the herbal medicine (P-3) was shown to possibly have highly inhibitory effect on renal lesions in mice induced by snake venom [9].

In this study, P-3 was administrated to cattle suffering from urolithiasis with hematuria in farms. P-3 was a blend of 12 herbs [9], one part each: *Achyranthes obtusifolia* Lam., *Clerodendrum camitosum* L., *Desmodium styracifolium* (Osb.) Merr., *Eriobotrya japonica* (Thunb.) Lindl., *Glechoma hederacea* L., *Hypericum japonicum* Thunb., *Ludwigia octovalvis* (Jacq.) Reven, *Pogonatherum crinitum* (Thunb.) Kunth. *Serissa japonica* Thunb., *Solanum surattense sensu act.* Taiwan, and 0.5 each part of hair of *Zea mays* L. and seed of *Nasturtium indicum* (L.) DC. These herbs were dried, powdered, and mixed. Daily doses of 40, 50 or 100 g were administered to diseased cattle once or twice a day per os basically for 6 or 10 days.

Six Holstein cows and 1 heifer, diagnosed as ulolithiasis, were used. Four cows and 1 heifer (Cases 1 to 5) were treated with P-3 and 3 cows (Cases 1, 2 and 5) were subjected to pathological examination. Cases 6 and 7 underwent ordinary therapy, with no administration of P-3.

The clinical and pathological findings are summarized in Tables 1 and 2. All cattle were clinically diagnosed as urolithiasis with bacterial infection, based on the finding of dysuria with gross hematuria and pyuria containing gravel stones. Crystals of magnesium ammonium phosphate and casts were generally seen microscopically in urinary sediment. The urinary sediment of Cases 3 and 7 was examined for bacteria and bacilli or cocci was observed in both cases.

Cases 1, 2, 3 and 5 in the P-3 treated group, which also showed gross hematuria, anorexia, depression, and dysurination, were given ordinary therapeutic agents such as antibiotics, sulfonamides, diuretics, hemostatics, vitamin A and an agent containing ammonium chloride over a period of 1 to 6 months. Following ordinary treatment, P-3 was given. Considerable turbid hematuria was noted soon after the start of treatment and gross hematuria subsequently disappeared (Figs. 1a and 1b). Proteinuria was far less severe at 2 to 7 days and appetite was recovered, generally accompanied by normalized urinary pH.

Case 1 showed uremia with clouding of consciousness and edema on the neck and shoulder before treatment with P-3. Consciousness was recovered the next day and hyperazotemia disappeared within 7 days. Case 2 showed emaciation with loss of appetite and painful urination due to stranguria before treatment. On the 4th day, stranguria and gross hematuria became much less severe and appetite was recovered. Although gross hematuria and anorexia recurred in Cases 1 and 2, the symptoms improved within 2 to 4 days during treatment. In Case 5, hematuria became microscopic within 3 days by treatment with P-3. The cow was further treated with P-3 for 2 weeks and even occult blood disappeared. Cases 1, 2 and 5 were slaughtered 1 to 3 months later. Case 3 showed no gross hematuria for 2 months up to the time the cow was sold.

Case 4 had anorexia, high body temperature and turbid hematuria, with swelling of the kidney according to rectal examination. By antibiotics and P-3, gross hematuria disappeared within 4 days, though slight swelling of the kidney with proteinuria and occult blood persisted for 10 days. By repeated treatment, the kidney resumed normal size; urinary occult blood and protein were positive. No recurrence of gross hematuria could be detected during the following 2 years and a calf was born to this cow.

On autopsy, Cases 1 and 2 showed the presence of gravel stones containing in purulent-mucous contents in the calices of several lobes. Changes of the ureter and bladder were less than in ordinary therapy cases. Histopathologically, pyelonephritis was severe in Case 1 (Fig. 2) and moderate in Case 2. Case 5 clinically showing urolithiasis had no calculi. Histopathologic changes were mild in Case 5. All cases showed slight to moderate increase in cells and matrix in the mesangium of the glomeruli.

The renal lesions thus consisted of chronic pyelonephritis with urolithiasis and mesangial proliferative glomerulonephritis.

The other organs in all cases were unremarkable by macroscopic inspection.

In the present study, the main clinical symptoms of all

Table 1. Clinical findings of each case before and after P-3 treatment

Case (age)	Duration of P-3 treatment[a]	Day(d) or months(m) after each treatment	Anorexia[b]	Dysuria[c]	Urine				Blood			
					blood[d]	protein[e]	pH	Calculus[f]	BUN[g]	sCr[h]	TP[i]	Ht[j]
treated with P-3												
1 (15 M)												
	1st 6 d (100 g)	0 d	+++	+	++++	++++	8.5	++	>100	>10	9.0	40.3
		4 d	+	−	+++	+	8.5	++	80	8.0	8.5	38.8
		9 d	−	−	−	+	7.5	+	20	1.8	7.8	29.5
	2nd[k] 6 d (40 g)	0 d (1 m)[l]	+++	±	++++	+	8.0	++	19	1.4	7.4	31.0
		7 d	+	±	+	+	8.0		19	1.0	8.0	
	3rd[k] 6 d (40 g)	0 d (3 m)[l]	++	±	++++	+++	8.0		28	1.5	8.2	30.2
		8 d	−	−	+	++	7.5	+	15	1.2	8.0	31.7
		3 m	−	−	+	+	7.5		24	1.8	7.7	32.5
2 (3 Y)												
	1st 10 d (100 g)	0 d	+++	+	++++	++	8.5	++	14	1.1	7.0	29.5
		4 d	+++	±	++++	+	8.5	++	20	1.0	6.8	
		10 d	+	−	++	+	8.5		11	1.0	7.6	29.0
		21 d	−	−	+	+	7.0	−	15	1.2	7.8	31.6
	2nd[k] 10 d (100 g)	0 d (2 m)[l]	++	±	++++	++	7.5		17	1.0	7.4	
		2 d	++	+	+++	++	8.0					
		5 d	−	±	+++	+	8.0	++	11	1.2	7.9	32.0
		14 d	+	−	+++	+	7.5	+				
		1 m	++	±	+++	+	8.0		14	0.9	7.2	30.8
3 (4 Y)[m]												
	14 d (40 g)	0 d	+	±	++++	++++	8.0	++	22	0.8	7.0	28.5
		4 d	+	−	+++	+++	8.0					
		6 d	−	−	+++	++	7.5		17	1.1	7.2	28.8
		10 d	−	−	+	+	8.0	+				
4 (4 Y)[n]												
	1st 10 d (50 g)	0 d	+++	±	++++	++	8.5	++	20	2.3	9.0	37.8
		4 d	+	±	+++	++	8.5	++				
		10 d	+	−	++	+	8.0		19	1.2	8.7	36.5
	2nd[k] 10 d (50 g)	0 d (21 d)[l]	−	−	++	++	8.5		20	1.5		
		10 d	−	−	+	++	7.0	−	15	1.0	8.5	35.5
5 (6 Y)												
	1st 7 d (100 g)	0 d	+++	+	++++	++++	8.0	++	23	1.8	7.1	28.4
		3 d	+	±	+++	++	8.0	++	19	1.6	8.0	29.7
		7 d	−	−	+	+	7.0	+	19	1.3	7.8	29.9
	2nd[k] 14 d (100 g)	0 d (13 d)[l]	−	−	+	+	7.5	+	13	1.3	7.5	29.2
		15 d	−	−	−	+	7.5	+	16	1.0	7.6	30.7
		2 m	−	−	−	+	7.5		11	1.2	7.6	31.6
treated without p-3												
6 (4 Y)	—	0 d	+++	+	++++	++++	8.5	++	20	1.9	8.5	32.2
		14 d	+	±	++++	+++	8.5	++				
		1 m	++	+	++++	+++	8.5	++				
		3 m	++	+	++++	+++	8.5	++	30	2.0	7.7	29.0
7 (6 Y)[m]	—	0 d	+++	+	++++	++++	8.5	++	15	1.1	7.0	33.5
		10 d	+	±	++++	+++	8.5	++				
		21 d	+	±	++++	++	8.0	++				
		3 m	+++	+	++++	+++	8.5	++	23	1.2	7.3	28.8

a) P-3 was orally given and grams in parentheses indicate the daily doses.
b) +++severe, ++moderate, +mild, −normal.
c) +dysuria with painful urination, ±mild, −normal.
d) ++++grossly visible, +++large amount, ++middle amount, +small amount and trace, −negative.
e) ++++>1,000 mg/d*l* ; +++>300 mg/d*l* ; ++>100 mg/d*l* ;+>30 mg/d*l* and trace.
f) ++calculi, +crystals.
g) Blood urea nitrogen (mg/d*l*).
h) Serum creatinine (mg/d*l*).
i) Total protein (mg/d*l*).
j) Hematocrit value (%).
k) Administration for recurrence.
l) Days or months after the first treatment.
m) Bacteria were observed in the urinary sediments.
n) Conceived twice in the next two years without recurrence.

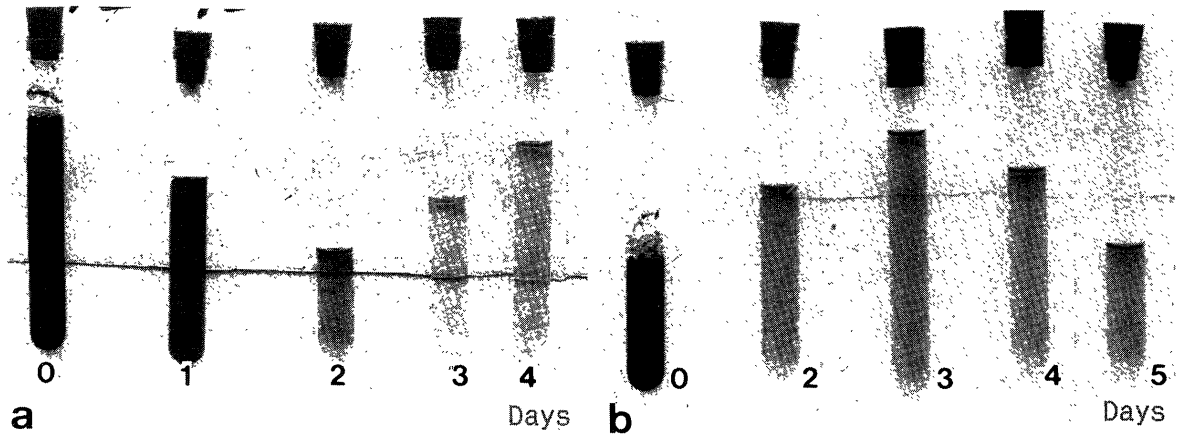

Fig. 1. Change of urine after P-3 administration. Gross hematuria disappeared within 3 days in Case 1 (a) and within 2 days in Case 3 (b).

Table 2. Pathologic findings

Case	Calculus	Glomerulo-nephritis	Pyelo-nephritis
treated with P-3			
1	+[a)]	mild	severe
2	+	mild	moderate
3	ne[b)]	ne	ne
4	ne	ne	ne
5	−	mild	mild
treated without P-3			
6	++	mild	severe
7	++	mild	severe

a) ++large amount, +small amount, −negative.
b) Not examined.

cases were hematuria, proteinuria, urinary calculi, and poor appetite. Poor appetite and gross turbid hematuria disappeared 3 to 10 days after treatment with P-3. Appetite was recovered immediately after gross hematuria disappeared. In the treated animals, proteinuria improved by increase in urinary output. Appetite, gross hematuria, and urinary volume appeared closely related. BUN and sCr before slaughter in P-3 treated cases were lower than in cases not given P-3. Azotemia was generally slight except in one case (Case 1) in which an anuric episode occurred after dysuria of long duration. Although the present cases were all treated by ordinary therapy for pyelonephritis with antibacterial agents, the clinical course clearly did not improve in animals with urolithiasis until P-3 was given.

Cases without P-3 (Cases 6 and 7) showed anorexia and gross turbid hematuria containing blood clots and gravel stones 2 or 3 months after delivering. Their urination was painful and turbid hematuria and gravel stones were noted for about 3 months. On autopsy, these two cases had a large amount of purulent-mucous exudate and many calculi of varying sizes in the calices of nearly all lobes and

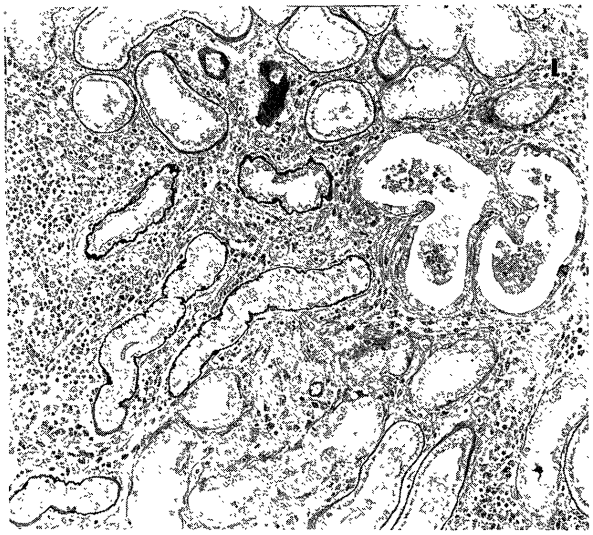

Fig. 2. Renal cortex with older pyelonephritic changes in Case 1. A group of dilated tubules with leukocytes in the lumen adjoin an inflamed area containing a few atrophic tubules. PAS stain; × 120.

in the bladder. The ureters and bladder had thickened walls with mucosal hemorrhaging and erosions.

Histopathologically, there were purulent pyelonephritic, destructive changes. In Case 7 collections of bacilliform bodies were observed among cellular debris in the tubular lumen. P-3 may possibly induce increase in urinary output in cattle, based on the results of additional experiments using rats and humans (unpublished data). Hence, renal calculi may be excreted by diuretic action of this herbal medicine. This would lead to improved appetite and elimination of hematuria due to urolithiasis. Hematuria and proteinuria also appeared to be improved by the hemostatic effects of the herbal medicine, since the symptoms improved promptly by treatment. The previous report [9] showed P-3 to have inhibitory effect on

hemorrhaging in various organs in mice induced by snake venom, a proteolytic enzyme. From the present clinical and pathological findings, P-3 may be concluded to exert diuretic action and possibly hemostatic action. Synergistic effects on pyelonephritis associated with urolithiasis may be expected when P-3 is used in conjunction with antibacterial agents.

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