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SURGICAL AND CLINICOPATHOLOGICAL STUDIES ON EXPERIMENTALLY INDUCED REVERSIBLE HYDRONEPHROSIS IN DOGS. 1: SHORT TERM STUDY

BY

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SUMMARY

The apparently healthy experimental dogs were subjected to surgical induction of unilateral ureteral obstruction. Radiographic and utrasonographic changes of the related kidney was conducted in association with hematological and serum biochemical examinations.

Hydronephrotic changes were observed obviously after one week post operation. Release of ureteral ligation was conducted and attempts were made to follow up the restoration of normal kidney size and function at different time intervals.

INTRODUCTION

Post-renal disease, particularluy urinary obstruction are the most common reversible causes of acute renal failure in dogs (Ulm and Miller 1962, Edward et al., 1989 and Stone and Barsanti 1992). Unilateral hydronephrosis may occur due to obstruction of part of the ureter by a primary ureteric tumor, ureteric stricuture, external pressure on the ureter from abdominal vessels, periureteric fibrosis, external adhesions and or ureteric stone or obstruction of the lower end of the ureter by a primary vesicle tumor. The diagnosis of the cause could be achieved by a consideration of the clinical picture together with haemogram, serum biochemical components, intravenous pyelography, ultrasonography and cystoscopy (Black, 1963, Backlund et al., 1965, Kneller, 1974, Feeney, et al., 1982, Walter, et al, 1987, Sone and Barsanti 1992, Gleadhill, 1994, Thomas et al., 1995 and Wu Yeonghuey, 1995).

The present work was carried out to determine the sequence of events following unilateral ureteral ligation for the development of uni-lateral hydronephrosis. This study was ascertained by clinical, radiological, sonographical and clinocopathological investigations to establish an experimental model of unilateral hydronephrotic kindey for the accurate assesment of the renal parameters. Moreover, the present work investigated the effect of release of uretral obstruction on the altered kidney parameters.

MATERIAL AND METHODS

1- Experimantal animals:

Ten apparently healthy mongrel dogs, (6 males and 4 females) were used. The age of the animals ranged from 1-2 years and their weights ranged between 20 to 25 kg. The animals were kept in separate kennels and put under observations and examinations, one week before the experiment. The urinary system was proved to be normal according to blood and urine analysis as well as radiological and sonographic examinations.

II- Surgical intervention:

The animals were prepared for aseptic surgery as usual. They were premedicated with atropine sulphate in a dose of 0.04 mg/kg subcutaneous and sparine* in a dose of 2-3 mg/kg intramuscular. Anaesthesia was induced and maintained by intravenous injection of sodium thiopental in a dose of 20 - 30 mg/kg. 2.5 %.

Each animal was laparotomized through a ca. 7 cm prepubic incision paramedian in males and median in females. The right ureter was exposed and acutely obstructed by ligating close to the wall of the bladder at its distal third using 2/0 vicryl. The abdominal incision was closed in a routine manner and penicillin streptomycin was injected intramuscular for 3 days in a dose of 10000 IU/kg and 10 mg/kg respectively.

after 7 days, the animals were relaparotomized using the same steps as before. The ureteral ligation was removed and the patent distal ureteral end was implanted in the wall of the bladder and the abdominal wound was reclosed and antibiotics were injected for 3 days. The wall of the bladder and the abdominal wound was reclosed and antibiotics were injected for 3 days. The duration of the experiment was 8 weeks.

III- Radiographic examination:

Plain and intravenous contrast urography were done for each animal before being used in the experiment and weekly post operation to follow up the size and function of the kidney. For contrast I/V urography, urographin 78% in a dose of 600 mg lodine / kg body weight was used. Ventrodorsal and lateral radiographs were taken at potential of 65 kvp, 25 mAs and 100 cm ffs.

IV- Sonographic examination:

The sonographic examination was undertaken by using B-Mode real time (Philips ultrasonographic apparatus)**. all animals were subjected to examination before operation to determine the healthy condition of urinary system.

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* Wyeth laboratories inc., Philadelphia, USA.
** Philips ultrasonographic apparatus (Donated by the Alexande v. Humboldt Founudation
*** Biomereux Laboratory Reagents products, Marcy L, etoile, France.

Ultrasonographic control of the kidney size ureter, and urinary bladder was made daily for a week postoperation and then weekly after that till the end of experiment .

V- Clinicopathological examinations:

Blood samples for the evaluation of hematological and serum biochemical profiles were obtained from dogs before operation and at the 3rd and 7the day after ureteral ligation. After release of ureteral obstruction, blood somples were also collected at intervals of 3,7,10,21, 30 and 45 days after operation. Each sample was divided into 2 portions, the first portion (1 ml) was anticoagulated with dipotassium EDTA and was used for determination of the hemogram following the standard techniques as described by Jain (1986). The second portion (3ml) was placed in a plain centrifuge tube for serum separation and determination of serum chemistry. Blood serum was analysed for total protein, albumin, glucose, total lipids, cholestrol, blood urea nitrogen (BUN), creatinine, calcium, inorganic phosphorous and chloride. Commercial kits*** were used. Sodium and potassium were estimated by a corning model 41o, England, flame photometer. Serum osmolality was calculated according to Coles (1986). Data obtained from serum biochemistry assays were statistically evaluated after Snedecor and Cochran (1973).

RESULTS

All dogs survived the duration of the experiment without any complications regarding surgery except some intermitent colicy pains which could be relieved by antispasmodics (Novalgin) when necessary. Intravenous pyelography revealed marked unilateral increase in the size of kidney of the ligated ureter without opacification of the renal pelvis and ureter during the first 2 weeks before and after removal of ligation (Fig. 1). after that the renal pelvis and ureteral diltation varied from slight to marked distortion and enlargement was observed (Fig. 2). In one case, a cortical rim of functional renal tissue was visualized with slight opacification of renal pelvis. One and half month after removal of ligation, the kidney size and function appeared approximately normal radiographically (Fig. 3).

Ultrasonographics examination revealed a gradual enlargement of the renal size related to the obstracted ureter reaching the maximum after 7 days post ligation. After removal of ligation, the kidney returned to approximately normal size within 1.5 month (Table 1). The hydronephrotic kidney characterized by dilated pelvic diverticulum and proximal ureter are easily visualized (Fig. 4).

Table 1: The ultrasonogaphic changes during the experiment.

	long. section	cross section	Ureter	Cortical thickness
Control normal	4.4	2.4	-	0.6
2 days after ligation	5.7	3.5	1.0	0.3
3 days after ligation	5.8	3.5	1.1	0.3
7 days after ligation	6.2	3.9	1.5	0.3
1-day after removal of ligation	6	3.8	-	0.3
3 days after removal of ligation	5.6	3.4	-	0.3
10 days after removal of ligation	5.3	3.2	-	0.3
21 days after removal of ligation	5.1	3.0	-	0.4
1 month after removal of ligation	5.0	2.9	-	0.5
1.5 month after removal of ligation	4.7	2.8	-	0.5

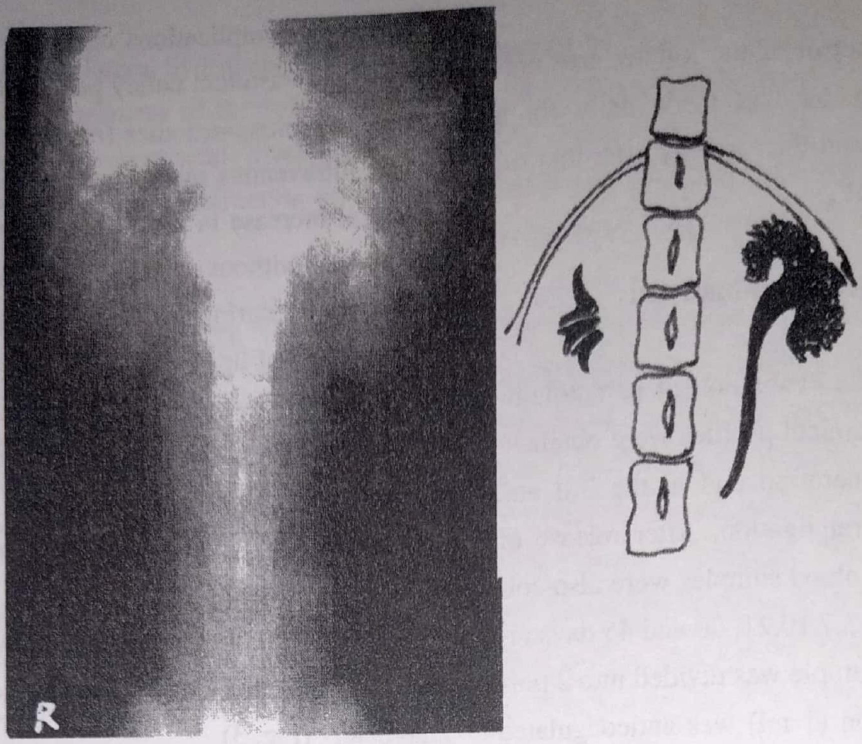

Fig. 1: A ventrodorsal radiographical view showing the excretory pattern of urographine (2 week after removal of the ligation) note, the right kidney is not able to concentrate the dye as the left one. The right ureter is not yet perciptable.

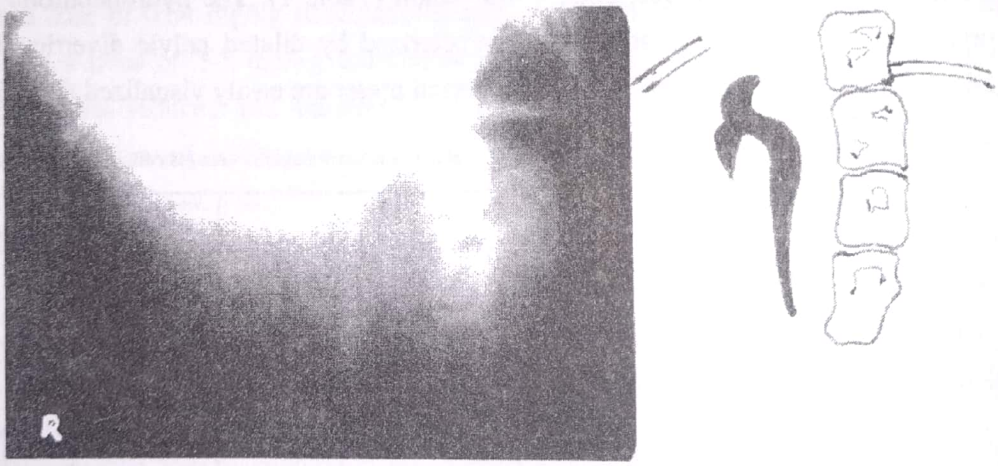

Fig 2: Three weeks after removal of the ligation notice that the kidney regained much of its ability to concentrate the dye and the ureter appeared full field.

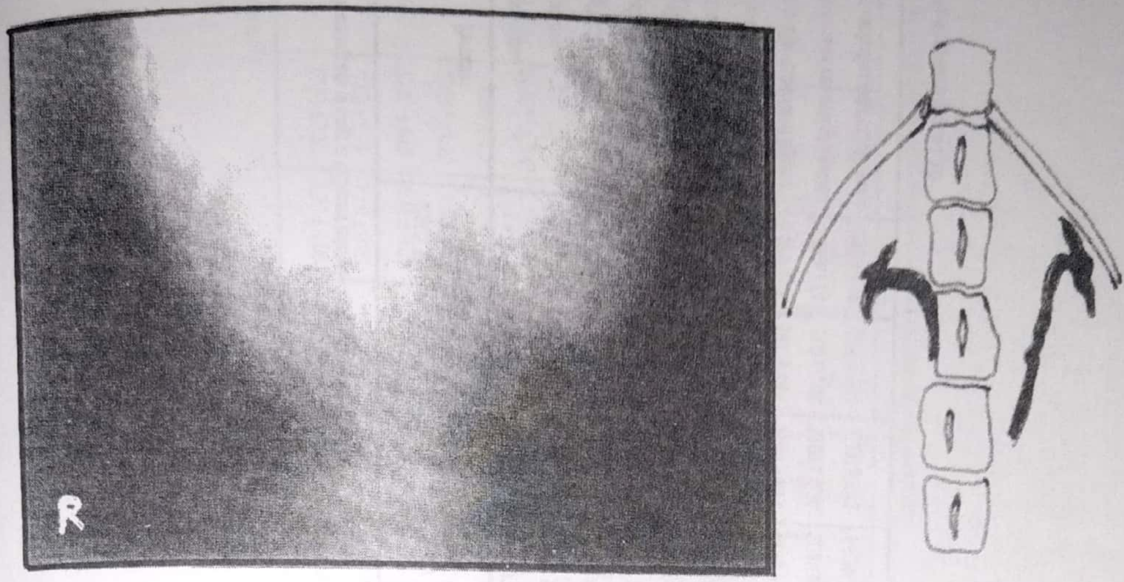

Fig. 3: Vetrodorsal radiographical view after 6 weeks after removal of ligation. Both kidneys and ureters are appeared apparent normal and functioning.

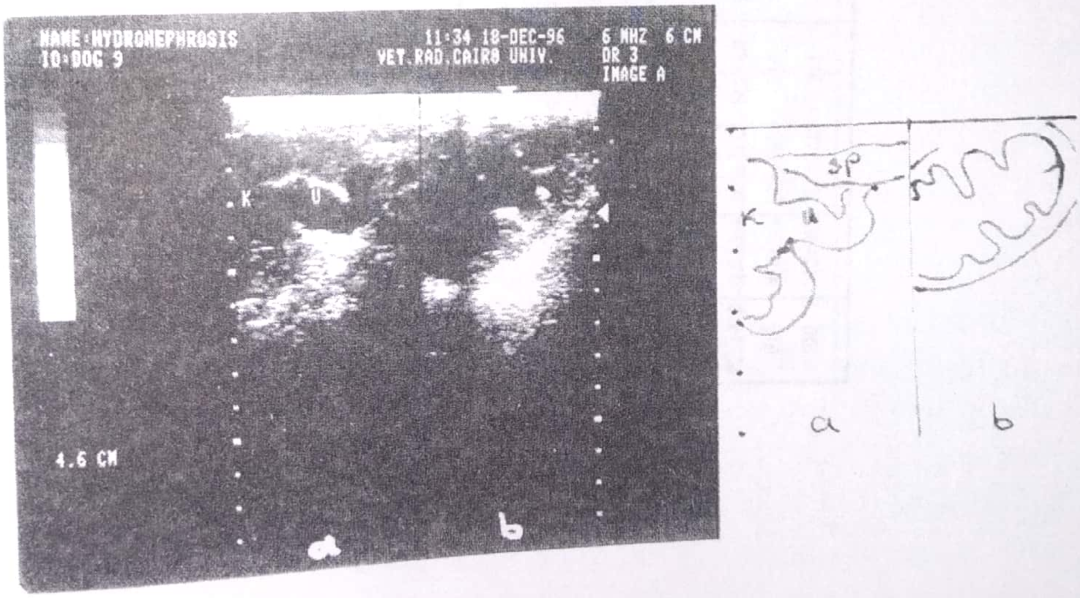

Fig 4: Ultrasonographic image of kidney and ureter by 6 MHz linear array:
a: sagital plane through the right kidney, hydronephrosis and hydroureter are present .
b: sagital plane through the left kidney . Severe hydronephrosis, only a thin rim of functional renal tissue reminants.
Sp= Spleen K= Kidney U= ureter

Table (2): Haemogram of dogs at different intervals of the experiment.

Parmeter	RBCs X 10^6/ul	Hb gm / dl	CV %	PCV fl	MCHC %	WBCs X10^3/ul	Differential leucocytic count X 10^2/ul				
							S. Neut	Bands	Eosino	Lympho	Mono
Reference Values	5.5 - 8.5	12 - 18	25 - 34	60 - 77	32 - 36	6 - 17	3 - 11.4	0 - 0.3	0.1 - 0.75	1 - 4.8	0.15 - 1.35
Before ligation	5.70 ± 0.96	10.30 ± 2.14	32 ± 6.02	56.14 ± 5.21	32.18 ± 7.30	16.55 ± 10.9	7.94 ± 2.58	0.33 ± 2.10	1.65 ± 0.18	5.29 ± 1.69	1.32 ± 0.18
3 days after ligation	5.20 ± 0.84	9.00 ± 2.56	28.00 ± 5.36	53.84 ± 4.95	32.14 ± 6.21	41.3* ± 11.2*	25.69* ± 3.52*	1.77 ± 2.54*	0.54 ± 0.25	4.43 ± 1.68	0.86 ± 0.25
7 days after ligation	3.98 ± 0.75*	8.00* ± 2.95	23.33* ± 5.85*	57.78 ± 4.81	34.46 ± 6.62	25.5* + 13.55*	18.69* ± 10.70*	2.01* ± 2.84*	0.00	4.71 ± 0.96	0.09 ± 0.15
3 days after removal of ligation	4.6 ± 1.94	8.5 ± 1.73	24.66* ± 8.43*	53.60 ± 4.70	34.46 ± 6.03	26.71* ± 6.60*	21.26* ± 5.72*	1.34* ± 0.68*	0.00	3.90 ± 0.96	0.19 ± 0.29
7 days after removal of ligation	5.70 ± 2.50	9.00 ± 3.53	24.5* ± 6.48*	42.98 ± 4.1**	36.73 ± 5.96	15.05 ± 7.05	9.03 ± 1.56	0.00	0.00	6.03 ± 0.96	0.00
10 days after removal of ligation	6.60 ± 1.08	11.00 ± 1.64	29.00 ± 6.48	43.93 ± 4.0**	37.93 ± 5.41*	11.62 ± 1.83	7.11 ± 0.76	0.00	0.13 ± 0.18	4.17 ± 0.81	0.21 ± 0.29
21 days after removal of ligation	6.50 ± 1.08	10.5 ± 2.82	30.00 ± 9.19	46.15 ± 0.1**	35.00 ± 5.32	18.05 ± 5.42	11.52 ± 2.42	0.2 ± 0.63	0.25 ± 0.36	4.60 ± 0.81	0.16 ± 1.29
1 month after removal of ligation	5.85 ± 1.64	11.0 ± 1.98	30.00 ± 8.74	51.28 ± 4.21*	36.66 ± 5.2*	13..1 ± 5.42	8.29 ± 1.64	0.00	0.62 ± 0.21	4.17 ± 1.06	0.00
1.5 month after removal of ligation	5.50 ± 1.48	11.5 ± 2.64	31.00 ± 3.42	56.36 ± 5.01	37.09 ± 5.01*	13.32 ± 2.65	8.8 ± 0.67	0.00	0.52 ± 0.38	4.19 ± 0.67	0.00

Values represent means ± SD

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Table (3):Serum biochemical parameters in dogs at different intervals of the experiment.

	BUN mg/dl	Creatinine mg/dl	Cholesterol mg/dl	Total lipid mg/dl	Glucose mg/dl	Total protein g/dl	Albumin g/dl	Calcium mg/dl	Phosphorus mg/dl	Sodium mEq.1	Potassium mEq/1	Chloried meq/1	Chlor meq
Reference value	10 - 56	< 1.5	140 - 210	0.00	71 - 115	5.3 - 7.8	2.3 - 4.3	9.9 - 12	2.5 - 5	141 - 155	3.6 - 5.6	112 - 124	112 -
Before ligation	14.38 ± 3.24	1.69 ± 0.28	156 ± 14.21	6.62 ± 0.38	92.30 ± 1.85	4.90 ± 0.68	2.00 ± 0.21	8.60 ± 0.34	5.22 ± 0.46	145 ± 0.64	4.25 ± 0.08	108 ± 5.69	108 ±
3 day After ligation	21.06* ± 2.21	1.95 ± 0.32	188* ± 13.58	6.79 ± 0.26	82.69 ± 10.51	4.84 ± 0.28	1.97 ± 0.11	8.33 ± 1.21	4.98 ± 0.22	150 ± 11.31	6.25 ± 1.61	103 ± 6.82	103 ±
7 days after operation	33.66** ± 2.3	2.24** ± 0.43	209** ± 15.41	7.87 ± 0.36	133* ± 1.92	5.04 ± 0.65	2.16 ± 0.19	8.05 ± 0.22	6.11 ± 0.36	143 ± 0.51	5.25* ± 0.09	108 ± 7.23	108 ±
3 days after removal of lig.	24.63** ± 3.47	1.53* ± 0.08	206.33** ± 8.23	9.08* ± 1.59	123.24* ± 3.84	5.50 ± 0.4	2.62 ± 0.08	7.68 ± 0.57	5.71 ± 0.6	149 ± 8.24	4.58* ± 0.94	104 ± 3.5	104 ±
7 days after removal of lig.	33.66** ± 2.30	2.24** ± 0.43	209** ± 15.41	7.87 ± 0.36	133* ± 11.92	4.87 ± 0.65	2.00 ± 0.19	8.09 ± 0.22	6.11 ± 0.36	153 ± 0.51	5.25* ± 0.90	108 ± 7.23	108 ±
3 day after removal of lig.	24.63** ± 3.47	1.53 ± 0.08	206.33** ± 8.23	9.08* ± 1.04	106.40 ± 9.59	5.15 ± 0.08	2.43 ± 0.13	7.68 ± 0.57	4.71 ± 0.60	152 ± 8.73	4.58 ± 0.94	109 ± 6.24	109 ±
7 days after	18.20* ± 2.5	1.50 ± 1.12	203.25* ± 9.29*	8.5 ± 2.24	107.69 ± 12.11	5.24 ± 0.98	2.62 ± 0.13	8.05 ± 2.15	5.52 ± 0.1	142 ± 8.5	4.5 ± 0.2	100* ± 6.7	100* ±
10 days after	20.55* ± 6.65	1.5 ± 0.18	203* ± 3.5*	8.84* ± 1.59	104.12 ± 7.64	5.11 ± 0.40	2.21 ± 0.09	8.23 ± 0.42	4.51 ± 0.40	148 ± 5.77	5.43 ± 1.02	104 3.5	104
21 days after	17.01 ± 6.65	1.41 ± 0.05	175 ± 7.88	5.00 ± 1.03	103 ± 3.56	5.46 ± 0.31	2.38 ± 0.1	7.5 ± 1.31	4.03 ± 0.1	143 ± 11.5	5 ± 1.03	1.8 ± 6.33	1.8 ±
1 month after	18.2 ± 5.73	1.39 ± 0.03	194 ± 8.66	5.5 ± 1.98	109.23 ± 6.33	4.46 ± 1.12	2.18 ± 0.08	7.22 ± 1.33	5.19 ± 1.21	140 ± 6.33	4.75 ± 2.11	100 ± 6.53	100 ±
1.5 month	17.50 ± 3.22	1.33 ± 1.08	137 ± 4.66	5.75 ± 2.22	104.30 ± 3.89	4.30 ± 0.53	2.19 ± 1.11	7.66 ± 2.33	5.33 ± 0.5	148 ± 6.11	4.25 ± 2.25	102 ± 9.21	102 ±

Values represent means ± SD
*P 0.05
**P 0.01

Study of the hemogram in dogs suffered from unilateral ureteral obstruction showed a normocytic normochromic anemia which was observed 3 days post ureteral ligation and became prominent after the 7th day. Progressive elevations of the erythrocytic parameters were observed after releasing the ureteral obstruction. Leucocytosis was observed with a peak elevation at the 3rd day after ureteral ligation, This leucocytosis was due to significant elvation of the number of segmented and band neutrophilic cell, then gradual decrease of the total leucocytic count was noticed till reaching a normal pattern at the end of the experiment. (Table 2).

Observation of the pattern of changes in serum biochemical components showed highly significant elevation in the values of blood urea nitrogn, creatinine and cholestrol and significant rise of total lipids and serum osmolality after ureateral ligation . Those parameters returned to normal pattern once the problem is corrected. Other tested biochemical constituents followed rather similar pattern in the blood sera of dogs. (Table. 3).

DISSCUSSION

Obstruction of urinary outflow anywhere along the urinary tract may eventually cause renal failure through obstruction which can result from ureteral stone and neoplasms (Stone and Barsanti 1992). The first consideration of the urologic surgeon should be the preservation of renal function. In the present investigation, the sensitivity of ultrasonographic examination was identical to that pyelographic findings. The assesment hydronephrotic changes through blood picture and serum biochemical profile as well as intravenous pyelography and ultrasonogram in dogs before and after release of ureteral obstruction (hydronephrotic changes were same as mentioned by Kneller, 1974, Cartee et al., 1980, Feeney, 1982, Walter, et al., 1987, Konde (19985 & 1989), Stone and Barsanti. (1992) Gleadhill (1994) and Thomas. et al., (1995).

The concept of renal growth is regulated by protein metabolities called renotrophins, that are normally destroyed or excreted by the kidney. If the renal mass is decreased, circulating renotrophins that stimulate the kidney to hypertrophy are increased until a new equlbium is reached. This compensatory enlargement of the obstructed kidney could be resulted principally from tubular hypertrophy. Aratki, (1962) and Rollason, (1949) recorded that nephrons do not increase in number, but the cells of the tubules, especially in the cortex, undergo mitotic hyperplasia 24 to 48 hours after unilateral nephrectomy. In addition, the glomeruli increase in size and blood vessels increase in caliber. These proceses are essentially complete after 20 days.

In the present work evidence of physiological alteration in renal function as a result of unilateral ureteral ligation was indicated by intravenous pyelography radiological and sonographical finding as well as biochemical inform of normocytic normochromic anemia, mild elevation of the values of cholestrol and glucose (Azotemic pseudodiabetes) was observed as a secondary effectes of alterd renal function. Such observations were previously recorded by Cantarow and Trumper (1955), Coles (1986), Edward et al (1989), Marilyn et al. (1989) by Stone and Barsanti (1992), Gleadhill (1994) and Thomas. et al., (1995).

the involvement of the kidneys in regulation of erythropoiesis by production of erythropoiesis stimulating factor, of fluid and electrolyte balance by formation of renin and prostaglandins, and of hormones degradation including parathormone, insulin and thyrotropic hormone could be the propable contributary factors to the observed changes (Osborne et al 1980).

Restoration of the normal kidney function after relief of the obstruction as indicated by the pattern of intravenous pyelography, ultrasonogram and clinicopathological examination was observed 1.5 month after relief of ureteral ligation. This could be explained by the fact that the destruction of the kidney nephrons still not reaching the critical number (approximately three fourth of the nephrons of both kidneys) before reduction in renal function is severe enough to be associated with an irreversible condition. (Osborne et al 1980, Edward et al., 1989, Gleadhill, 1994 and Behrend et al., 1996).

In conclusion. The model of unilateral hydronephrotic kidney was establised. The clinical, radiological, sonographical and clinicopathological investigations were cleared and corelated. The affected kidney returned to its normal size and function after 1.5 monthes after releasing of the ureteral ligation.

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