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STUDIES ON EXPERIMENTAL COMPLETE UNILATERAL URETERAL OBSTRUCTION IN DOGS (With One Table and 21 Figures)

By

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دراسات على الإنسداد الكامل التجريبي لحالب واحد في الكلاب

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أجري هذا البحث على عدد ١٠ كلاب ضالة بصحة جيدة. تم سد حالب واحد سداً كاملاً في كل حيوانات التجربة وذلك بربطه بالحرير وتم ذلك تحت تأثير التخدير العام. تم تقسيم حيوانات التجربة إلى خمس مجموعات كل مجموعة تحتوي على كلبين وتم إعدام المجموعات دورياً بعد ١٥ يوم وشهر، شهرين، ٤ شهور، ٩ شهور بعد إجراء عملية ربط الحالب. ولمعرفة مدى كفاءة الكلية تم إجراء تصوير إشعاعي بصيغة اليوروجرافين قبل إعدام الحيوانات. تم وصف الكليتين ظاهرياً وأخذت عينات من كل منها للفحص الهستوباثولوجي وقد أظهرت الصور الشعاعية أن الكلية المربوط حاليها قد فقدت وظيفتها بعد ١٥ يوم من الربط ثم عادت جزئياً لوظيفتها حتى ٤ شهور وبعد هذه الفترة فقدت الكلية وظيفتها بالكامل أما الكلية الأخرى فكانت طبيعية ظاهرياً وكانت وظائفها سليمة شعاعياً. وكانت النتيجة النهائية لربط الحالب هو تضخم الكلية خلال شهر من عملية الربط وبعد هذه الفترة بدأت الكلية في الضمور. ظهرت التغيرات المرضية في كبيبات الكلى بعد ١٥ يوم من عملية الإنسداد وحدث تليف كامل في معظم كبيبات الكلى وكذلك تخريب كامل لمعظم الأنابيب الكلوية عند ٤ شهور من عملية ربط الحالب. وحدث زيادة في عدد كبيبات الكلى الشغالة في الكلية السليمة بدون زيادة واضحة في حجم هذه الكلية.

SUMMARY

The present study was carried out on 10 mongrel healthy dogs. Complete unilateral ureteral obstruction was performed in all animals under the effect of general anaesthesia. The studied animals were classified into 5 groups each of two dogs. They were euthanized 15 days, one month, two months, 4 months and 9 months following operation. Before euthanasia excretory urography was performed to evaluate renal function. Gross findings of both

kidneys for each group were recorded and samples were taken for histopathological examination. Excretory urography indicated that, the kidney of the ligated side lost its function at 15 days following ligation, then its function returned partially till 4 months following ligation then lost its function completely. Hydronephrosis was the end result of complete unilateral ureteral obstruction which occurred within the first month following operation then the kidney underwent atrophy. Pathological changes were noted in the glomeruli at 15 days following obstruction. Complete fibrosis of most glomeruli and complete destruction of most collecting tubules occurred at 4 months following obstruction. Contralateral kidney showed compensatory hyperatrophy manifested by increase in the number of functional glomeruli without any significant increase in the gross finding of this kidney.

Key words: Dogs - Ureter - Experimental obstruction

INTRODUCTION

Obstructive uropathy with resultant hydronephrosis is the eventual outcome of most urologic diseases. It is well known that complete ureteral obstruction eventually destroys renal function. The postulated mechanisms are elevated ureteral pressure and decreased renal blood flow which cause cellular atrophy and necrosis. The longer or more severe the obstruction, the more renal damage will result (Gillenwater, 1992). Loss of function in affected kidneys not usually lead to overall renal insufficiency. The elapsed time from occurrence of complete ureteral obstruction till complete renal insufficiency is variable. Return of function may well depend on many factors other than period of obstruction, such as absence of infection, presence of an intrarenal or extrarenal pelvis in the obstructed kidney, or the degree of pyelolymphatic and pyelovenous back flow (Graham, 1962; Lewis and Pierce, 1962 and Reisman *et al.*, 1975).

The aim of the present study is to evaluate the function and structure of the kidney after low experimental unilateral complete ureteral obstruction in dogs as well as the function and structure of the contralateral one.

MATERIAL and METHODS

A total number of 10 mongrel dogs were used in the present study. Before experiment, animals were kept for 2 weeks for klimatization and observation of their healthy conditions.

Complete unilateral ureteral obstruction was performed in all animals under effect of general anaesthesia using thiopental sod.* in a dose rate of 20 mg/Kg B.W. injected I.V. and premedicated with combelen** in a dose rate of 0.2 mg/Kg B.W. I.V. Ventral midline celiotomy was performed and the right ureter was ligated using silk No. 3 One cm above its termination into the bladder. Celiotomy incision was closed as usual and animals were kept for follow up observation.

The animals were classified into 5 groups each of two dogs. They were euthanized 15 days, one month, two months, 4 months and 9 months after operation.

Before euthanasia, excretory urography using urografin 76%*** in a dose rate of 3 ml/Kg B.W. I.V. was performed to evaluate the renal function. Animals were fasted 24 hours before radiography. Ventrodorsal abdominal radiographs were obtained immediately, 10 min. and 20 min. after injection. An elastic bandage was applied to the abdomen Just before injection of contrast material to prevent filling of bladder.

Gross findings were recorded including external length, width and weight of both kidneys, then a sagittal section was performed in both kidneys, and thickness of the cortex, thickness of the medulla and width of renal pelvis were recorded.

For histopathological examination, samples were taken from both kidneys. The samples were fixed in neutral buffer formalin. After complete fixation the specimens were dehydrated, infiltrated and embedded in paraffin. The paraffin blocks were sectioned at 7 μ thickness. Tissue slides were stained by the normal Haematoxylin and Eosin stain (Bancroft and Stevens, 1977).

As a control, 5 right & 5 left normal kidneys collected from healthy dogs were measured for the average length, width and weight, then sagittal section was performed and thickness of the cortex, thickness of the medulla and width of renal pelvis were recorded.

RESULTS

Contrast urography: (Fig. 1-4)

Contrast radiography revealed that the kidney of the ligated side lost its function completely 15 days after ligation and the shadowgraph of the

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** : Combelen: Bayer, Liver Kusen, West Germany.

***: SCHERING.

affected kidney was absent, while the contralateral kidney appeared functioning normal.

At two months following ligation, the kidney of the ligated side appeared functioning, the renal pelvis was dilated and filled with contrast media, also the ureter was dilated (hydroureter) and tortuous, while the contralateral kidney appeared normal with slight dilatation of the proximal third of the ureter.

At 4 months following ligation the kidney of the ligated side appeared slightly functioning and the proximal part of the ureter and renal pelvis were dilated and filled with contrast material. The contralateral kidney appeared normal.

At 9 months after ligation the shadowgraph of the kidney of the ligated side disappeared completely while the contralateral kidney appeared normal.

Gross findings: (Fig. 5-13)

Length of the affected kidney increased until it reached 9 cm at one month after ligation, then decreased gradually until reaches 5 cm at 9 months following ligation. Also the width of the kidney of the ligated side increased gradually until it reached 4.5 cm at one month then decreased until reached 2.5 cm at 9 months following ligation. Kidney of the ligated side increased in weight gradually until reaches double weight (100 gm) within a period of one month then after that decreased gradually in weight until reached less than half its normal weight (20 gm) at 9 months. Thickness of the cortex of the kidney at the ligated side decreased gradually from 0.8 cm before ligation to 0.3 cm at 9 months after ligation. Also the thickness of the medulla of the same kidney decreased gradually from 1.6 cm before ligation to 0.3 cm at 9 months after ligation while the width of the renal pelvis increased gradually from 1.3 cm before ligation up to 2.4 cm at 9 months following ligation (Table 1).

The contralateral kidney didn't show any remarkable changes in length, width, weight and in the thickness of its different parts (cortex, medulla & pelvis) (Table 1).

Histopathological changes: (Fig. 14-21).

In the contralateral kidney: Histopathological examination of the unligated kidney showed increase in the number of functioning glomeruli with slight dilatation of some tubules. These changes were not differ at different periods following ligation.

In the kidney of the legated side, the thickening of the kidney capsule began at the 2nd month after legation and became more prominent at the 4th month. The thickening formed of fibrous connective tissue in the form of collagen fiber and fibrocytes.

Decrease in the thickning of the renal cortex was recognized after one month of legation and became more pronounced at the 4th and 9th month.

Slight atrophy of the glomerular tuft with widening of the Bowman's space appeared after 15 days of legation and became more prominent after the 2nd month of legation. At the 4th month, periglomerular fibrosis was observed with evidences of fibrosis of the glomerular tuft. At the 9th month following ligation the glomerular tuft underwent hyalinization and was converted into acid-philic hyalin material. The renal tubules were dilated with atrophy of thier epithelial lining after 15 days of ligation. Some of the tubules were contained acidophilic protenacious material. These changes were progressed by the time of ligation and the tubules were cystically dilated with more pronounced epithelial atrophy at the 2nd month from ligation. After the 4th month from ligation the tubules were disappeared and replaced by connective tissue proliferation and lymphoid cell infiltration. The increase in the amount of interstitial tissue was observed after 15 days from ligation, then progressed with period of ligation till completely replaced the renal tubules. The proliferated interstitial tissue was formed mainly of fibrocytes and collagen fibers. Interstitial lymphoid cell infiltration was observed after the 4th month from ligation and progressed with the time of ligation till the end of the experiment. Hyperatrophy of the tunica media and tunica advenatatia of the interstitial blood vesels were observed at the 4th month and became more pronounced at the end of the experiment. The decrease in the thickining of renal medulla was recognized from the 15th day after legation and was progressed by time till the end of the experiment. The medullary renal tubules were slightly dilated after 15 day following ligation and became cystically dilated after 2 month of ligation with atrophy of their epithelial lining. Complete disappearance of the tubules and replacment by fibrosis were recognized from the 4th month after ligation. Focal lymphoid cells infiltration was observed in the medullary interstitial tissue after 15 day from ligation and became more diffuse and pronounced at the 2th month from ligation. After the 9th month from ligation, the lymphoid cell reaction were subsided from the medullary interstitial tissue. At this time renal medulla was formed mainly from connective tissue with complete obsence of the renal tubules. The epithelium of the renal pelvis underwent pressure

atrophy which began from the 15 day of ligation and was completely atrophied at the end of the experiment.

Table 1: Showing length, width, weight, cortex thickness, medulla thickness and width of renal pelvis in the normal, ligated side and contralateral kidneys.

Time after ligation	Length (cm)		Width (cm)		Weight (gm)		Cortex thickness (cm)		Medulla thickness (cm)		Renal pelvis wide (cm)	
	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.
Average of normal kidneys	6.9	6.7	3.8	4	43	45	0.8	0.8	1.6	1.6	1.3	1.3
15 days	8	6.0	4.5	3.8	90	50	0.6	0.8	1.3	1.7	2.2	1.3
One month	9.0	5.5	4	3.5	100	49	0.3	0.7	0.8	1.5	4.0	1.0
2 months	6.0	6.0	3	4	50	52	0.6	0.9	0.7	1.5	2.6	1.4
4 months	5	6.5	2.5	4	30	53	0.5	0.8	1.0	1.5	1.5	1.1
9 months	5	7	2.5	4.2	20	50	0.3	0.8	0.3	1.7	2.4	1.4

R= Ligated side = Right kidney

L= Non-ligated side = Left kidney

DISCUSSION

Hydronephrosis or cystic enlargement of the kidney due to ureteral obstruction is a relatively common finding at necropsy but it is seldom detected clinically in farm animals, because it is usually unilateral and the unaffected kidney compensates fully for the loss of function (Skye, 1975). In the present study hydronephrosis was the end results of the unilateral ureteral obstruction in dogs. Dilatation of the renal pelvis, gross enlargement of the kidney and reduction in the renal parenchyma occurred within the first month following obstruction to urine flow (Chandler *et al.*, 1994). Long standing obstruction leads to complete loss of function in the affected kidney and nearly complete destruction of renal parenchyma.

Complete ureteral occlusion caused progressive dilatation of the renal pelvis during the first few weeks. The weight of the kidney increased owing to oedema, even though the renal tissue atrophied. After 4 to 8 weeks, there was a decrease in parenchymal weight because the atrophy of the tissue is greater than the intrarenal oedema (Gillenwater, 1992). The same results were obtained in the present study. The kidney weight first increased to double its weight at one month following obstruction, then the weight of the obstructed kidney reached less than half its normal weight at 9 months following ligation.

The thickness of the cortex and medulla decreased gradually until it reached less than one quarter of the normal thickness at 9 months following obstruction while the renal pelvis dilates gradually until it reached more than double its normal size. The slight increase in the dimensions and weight of the contralateral kidney may be attributed to compensatory hypertrophy.

Preservation of renal function in hydrophrosis (absence of kidney function at 15 day after ligation and its recurrence at one month after ligation) is due to pyelolymphatic backflow. The reabsorption of the renal pelvis urine into the lymphatics allows replacement glomerular filtration to occur. The same results were obtained by Rusznyak *et al.* (1960). The penetration of urine into the interstitial spaces induces liberation of histamine with the resultant increase in capillary permeability and with exudation of protein rich fluid (oedematous fluid) into the interstitial space and into the lymphatics.

Various substances injected into an obstructed renal pelvis appeared in the systemic circulation. Backflow of urine out of the renal pelvis was demonstrated to occur first through rupture of the fornix (Olsson, 1948) while Narath (1940) stated that pyelosinus backflow into sinus renalis and lymphatics occurs without rupture into the venous system.

Histopathological examination of hydronephrotic kidney indicated severe dilatation of the renal tubules and atrophy of them after one month of obstruction. Pathologic changes in the glomeruli was first noted at 15 day of complete ureteral obstruction. Complete fibrosis of most glomeruli occurred at 4 months and hyalinization of the glomeruli took place at 9 months. Complete destruction of most collecting tubules was observed at 4 month of complete ureteral obstruction.

Contralateral kidney showed compensatory hypertrophy manifested by increase in the number of the functional glomeruli and some dilatation of some renal tubules without any significant increase in the gross length, width and thickness of this kidney.

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LEGENDS OF FIGUERS

- Fig. 1:** Excretory urography 15 days following ligation revealed absence of the kidney at the ligated side while the contralateral kidney appears normal.
- Fig. 2:** Excretory urography 2 months following ligation revealed excretion of contrast media through ligated side kidney with dilatation of renal plvis and proximal part of the ureter (hydroureter). The contralateral kidney appears normal.
- Fig. 3:** Excretory urography 4 months following ligation revealed excretion of contrast media through ligated side kidney with dilatation of renal pelvis and proximal part of the ureter while the contralateral kidney appears normal.
- Fig. 4:** Excretory urography 9 months following ligation revealed complete disappearance of the ligated side kidney while the contralateral kidney appears normal.
- Fig. 5:** Kidney specimens 15 days following ligation revealed increase in the size of ligated side kidney with dilatation of its renal palvis and ureter while the contralateral kidney appears normal.

- Fig. 6:** Sagittal section through ligated side kidney and contralateral one 15 days following ligation revealed slight decrease in the thickness of the cortex and medulla with slight increase in the size of renal pelvis of the ligated side kidney while the contralateral kidney appears normal thickness of its different parts.
- Fig. 7:** Kidney specimens one month following ligation revealed increase in the size of the ligated side kidney with marked dilatation of its renal pelvis and ureter while the contralateral kidney shows normal size and shape.
- Fig. 8:** Sagittal section through ligated side kidney and contralateral one one month following ligation revealed marked decrease in the thickness of cortex and medulla with increase in the size of renal pelvis of the ligated side kidney while the contralateral kidney shows normal thickness of its different parts.
- Fig. 9:** Kidney specimens 2 months following ligation revealed decrease in the size of the ligated side kidney with dilatation of its renal pelvis and ureter while the contralateral kidney appears normal.
- Fig. 10:** Sagittal section through the ligated side kidney and contralateral one 2 months following ligation revealed decrease in the thickness of cortex and medulla with increase in the size of renal pelvis while the contralateral kidney shows normal thickness of its different parts.
- Fig. 11:** Kidney specimens 9 months following ligation revealed decrease in the size of the ligated side kidney in spite of dilatation of its renal pelvis and whole ureter while the contralateral kidney appears normal.
- Fig. 12:** Sagittal section through ligated side kidney and contralateral one 9 months following ligation revealed marked decrease in the thickness of the cortex and medulla and marked increase in the size of renal pelvis of the ligated side kidney while the contralateral kidney appears normal in thickness of its different parts.
- Fig. 13:** Sagittal section through ligated side kidney 9 months following ligation revealed marked decrease in the thickness of the cortex and medulla with increase in the size of renal pelvis and proximal part of the ureter.
- Fig. 14:** Renal cortex of the ligated side kidney 15 day following ligation revealed slight atrophy of the glomeruli, dilatation of the renal tubules with atrophy of their epithelium, some tubules contain proteinous material with evidence of fibrosis in the interstatium. (H&E 10x10).

- Fig. 15:** Renal medulla of the ligated side kidney 15 day following ligation revealed an increase in the lymphoid cell reaction with fibrosis and atrophy of the renal tubules. (H&E 10X4).
- Fig. 16:** Renal cortex of the contralateral kidney after 15 days following ligation of the right ureter revealed an increase in the number of the functional glomeruli with slight dilatation of some tubules. (H&E 10X4).
- Fig. 17:** Renal cortex of the ligated side kidney 4 months following ligation revealed chronic interstitial nephritis manifested by atrophy and fibrosis of the glomeruli with periglomerular fibrosis. Fibrocytic and lymphoid cell reaction in the interstitium of the renal cortex were evident (H&E 10X10).
- Fig. 18:** Renal medulla of the ligated side kidney 4 months following ligation revealed chronic interstitial nephritis manifested by diffuse lymphoid cell reaction in the renal medulla in expense of the renal tubules. (H&E 10x10).
- Fig. 19:** Renal cortex and Renal medulla of ligated side kidney 9 months following ligation revealed marked dilatation of the renal pelvis with atrophy of their epithelium, decrease thickening of the paranchyma specially of cortex with evidence of chronic interstitial nephritis and lyalinization of the glomeular tuft. (H&E 10X4).
- Fig. 20:** Ligated side kidney 9 months following ligation revealed marked thickening in the tunica media and adventatia of the blood vessels and hyalinization of the glomerular tuft. (H&E 10X4).
- Fig. 21:** Contralateral kidney 9 months following ligation of the right ureter revealed slight thickening of the sapsule, increase in the number of the functional glomeruli and slight dilatation of some renal tubules. (H&E 10X4).























