AN ANALYSIS OF ONE HUNDRED AND FIVE RENAL BIOPSIES

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INTRODUCTION

There is no longer disagreement that renal biopsy has provided the physician with a useful tool in the study of renal disease. The clinical value of percutaneous renal biopsy has been discussed in detail (Kark *et al*, 1955). By its use an exact histological diagnosis can be made which provides a sound background for treatment and prognosis. Through repeated renal biopsies the natural history of diseases involving the kidney can be studied. The procedure is also one way of obtaining culture of organisms from infected kidneys. In the field of organ transplantation, renal biopsies have added much light on the process of organ rejection and on the effects of immuno-suppressive drugs to reverse the tissue rejection.

Though renal biopsies during open operations were often done, it was Perez (1950) and Iversen and Brun (1951) who showed that in the right hands renal biopsy was a safe procedure. Iversen and Brun carried out their procedures on 80 patients in the sitting position with the Iversen-Roholm canula. Kark and Meuhrcke (1954) discussed their technique using a modified Vim-Silverman needle; this method has since its introduction gained world wide popularity. Kerr (1964) described a technique employing a modified Menghini needle which, because of its speed, may be a preferred method in children who are unable to co-operate. However, improvement of success rate has been due to better methods of localization of the kidney at the time of biopsy, the most recent being the usage of television-monitored fluoroscopy (Kark and Buenger, 1966).

The purpose of this paper is to confirm the clinical value of percutaneous renal biopsy as a relatively simple and safe procedure in providing an exact histopathological diagnosis of kidney diseases, and to point out the difference in incidence of the histopathological types causing idiopathic nephrotic syndrome in Asians.

PATIENTS STUDIED

The 90 patients studied were 10 years old and above with renal diseases seen in Medical Unit I, Outram Road General Hospital, Singapore, between the period 1966 and 1968. They were made up of 76 Chinese, 12 Malays and 2 Indians and suffered from a wide variety of renal abnormalities. Each patient, in addition to other investigations, had one or more renal biopsies done on him by the first author. In 5 cases, the renal biopsy was performed soon after the patients had died.

A renal biopsy was considered adequate only if 4 or more glomeruli were seen in order to make a histopathological diagnosis. Thus defined there were 82 cases with adequate renal biopsies, of whom 42 had idiopathic nephrotic syndrome, 10 diabetes mellitus, 5 systemic lupus erythematosus, 11 acute nephritis, 4 anaphylactoid purpura, 2 asymptomatic proteinuria, 3 hypertension, 1 amyloidosis, 1 renal tubular acidosis, 2 subacute bacterial endocarditis with urinary abnormalities, 1 thyrotoxicosis with nephrotic syndrome and finally a case of acute rheumatic fever with acute glomerulonephritis (Table I).

RENAL BIOPSY

The method of percutaneous renal biopsy was that popularized by Kark and Muehrcke (1954). Because of its relative safety and simplicity its indications have grown wider and will include any renal disorder provided there are no contraindications. Although Kark *et al* (1958) had listed about a dozen contraindications there appears to be agreement only in 3: haemorrhagic diathesis, uncooperative patient and single kidney. High blood urea is no longer considered a contraindication unless there is a bleeding tendency associated with it (Brun and Raashou, 1958). The theoretical risk of dissemination of underlying infection by renal biopsies in pyelonephritis is without support and it is now agreed that there is no added risk. Renal biopsy in patients with hypertension

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TABLE I

THE CLINICAL AND PATHOLOGICAL DIAGNOSIS OF 82 PATIENTS FROM WHOM ADEQUATE RENAL BIOPSIES WERE OBTAINED

Clinical Diagnosis	No. of Patients	Pathological Diagnosis	No. of Patients
1. Idiopathic Nephrotic Syndrome	39	Minimal change	24
		Proliferative glomerulonephritis	14
		Membranous glomerulonephritis	1
	3*	Proliferative glomerulonephritis	3
2. Diabetic nephropathy	8	Diffuse and/or nodular diabetic nephropathy	7
		Endothelial proliferation	1
	2*	Chronic pyelonephritis and diabetic nephropathy	2
3. Systemic lupus erythematosus (S.L.E.) with nephritis	4	Lupus glomerulonephritis	4
S.L.E. with thrombocytopenic purpura	1	Normal kidney	1
4. Acute glomerulonephritis with no complication	2	Mild endothelial proliferation	2
with minimal urinary change	3	Endothelial proliferation	2
		Minimal change	1
with prolonged haematuria (macroscopic or microscopic)	6	Endothelial proliferation	5
		Endothelial proliferation (with crescents)	1
5. Anaphylactoid purpura with urinary changes (Schonlein-Henoch Syndrome)	4	Endothelial proliferation	2
		Focal nephritis	2
6. Asymptomatic Persistent Proteinuria	2	Endothelial proliferation	2
7. Hypertension	3	Chronic pyelonephritis	2
		Endothelial proliferation	1
8. Amyloidosis	1	Amyloid kidney	1
9. Renal Tubular Acidosis	1	Chronic pyelonephritis	1
10. Subacute Bacterial Endocarditis	2	Endothelial proliferation	2
11. Thyrotoxicosis with Nephrotic Syndrome and Haematuria	1	Endothelial proliferation	1
12. Acute Rheumatic Fever with Carditis and Haematuria	1	Endothelial proliferation	1

* Post-Mortem Renal Biopsies.

should be done only if indications warrant the procedure as the incidence of complications developing is higher.

RESULTS

1. *Analysis of the diagnostic adequacy or inadequacy of renal tissues taken by percutaneous biopsy* (Table II).

One hundred and five renal biopsies were performed in 90 patients. Renal tissue was obtained in 96 instances (91%) but only in 82 instances (78%) was the tissue adequate for a pathologic diagnosis. Non-renal tissues were obtained in six instances and no tissue in three. The success rate of adequate renal tissue was 78% which was only 2% below that of 80% success rate of Kark *et al* (1958).

2. *Complications resulting from renal biopsies* (Table III).

Haematuria

Microscopic haematuria, varying from 100 to 200 red cells per high power field, was usually present in the post-biopsy urinary specimens, and usually cleared up after 24 hours. Frank haematuria was present in 12 patients

(11%), the majority resolving within 24 hours after the renal biopsy. In an Indian obese female (F.B.D.), aged 45, gross haematuria was observed after renal biopsy. She developed severe lower abdominal colic and urine contained frank altered dark blood clots. Later on in the night the patient had urinary retention. On the day following the biopsy her urinary retention was worse and she had to be catheterized and bladder washout was instituted to expel the blood clots. Though there was no obvious drop in blood pressure, her haemoglobin fell from 10 G.% to 7.6 G.%, and she was transfused a litre of fresh blood.

On the second day she was still unable to pass urine because of blood clots and a tidal bladder drainage was instituted and left in situ. In addition she received another 500 ml. fresh blood. The urine was still blood-stained on the third day and this gradually cleared up, and by the fifth day following biopsy she was able to pass urine on her own. Her haemoglobin rose to 11 G.% and the blood urea was 60 mg.%. The slight urinary infection was readily controlled.

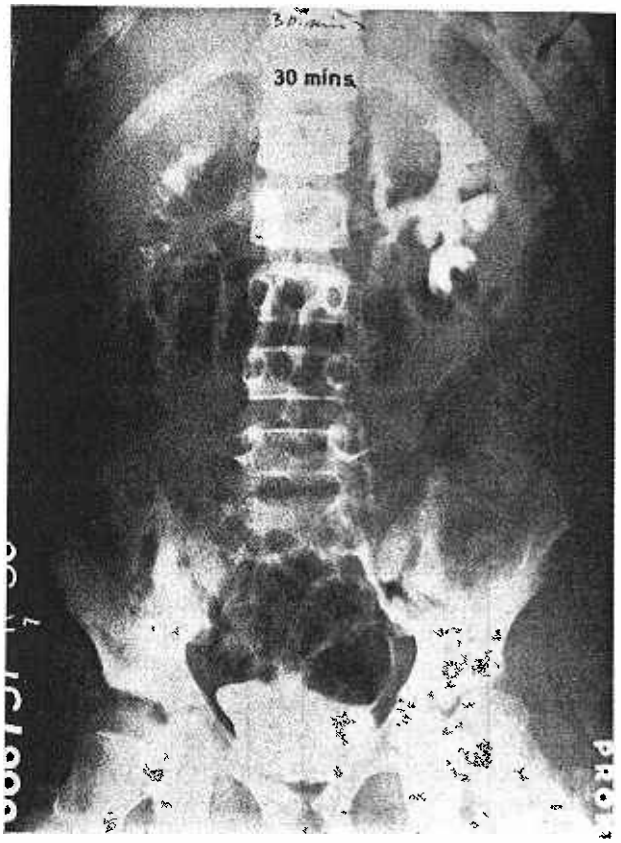

Fig. 1. Extravasation of dye from left pelvis.

Perirenal Swelling

Perirenal swelling with abdominal colic was encountered in 2 cases. One was uneventful whilst the other developed a series of interesting complications. G.K.K., a Chinese 13 year old boy, admitted in a state of relapse of nephrotic syndrome, had a renal biopsy done on his left side in the usual manner. Following the renal biopsy he developed frank haematuria associated with abdominal colic. On the day following the biopsy the haematuria ceased but the colic became worse and the boy vomited twice that day. On the second post-biopsy day in addition to the periodic abdominal colic, transient circinate, confluent, erythema marginatum was observed on the trunk and the limbs which was thought to be related to codiene co. (B.P.C.) given to him for relief of pain. A left perirenal swelling was evident on the third post-biopsy day which was warm and tender. A left pleural effusion was detected clinically and was confirmed by a chest X-ray. An intravenous pyelogram revealed a slight ballooning of the left pelvis with extravasation of dye suggesting traumatization of the renal pelvis with possible extravasation of urine (Fig. 1). That the pelvis was traumatized was confirmed by the finding of transitional epithelium in the biopsy specimen. The left pleural effusion was tapped and 400 ml. of straw coloured fluid was removed.

On the fifth post-biopsy day the left perirenal swelling subsided and the patient gradually recovered. A renal pyelogram 4 months later showed that there was no impairment in excretion of dye on either sides.

Hypotension

A drop of blood pressure below 90 mm. Hg. was observed in 2 patients; in both there had been difficulty in locating and obtaining a piece of renal tissue. Hypotension was observed while the patients were in the prone position. Both were immediately made to lie in the supine position, and the foot of the bed was raised. One improved spontaneously; the other, an obese Chinese female (G.H.E.) aged 50, was given hydrocortisone with dextrose saline intravenously. Though her blood pressure improved, she developed haematuria and oliguria which gradually improved. The hypotension was probably vasovagal in origin.

Pain at Biopsy Site

The majority of the patients were ambulant on the day following the renal biopsy. Pain at biopsy site, if complained of, was easily relieved.

TABLE II

COMPARATIVE ANALYSIS OF THE DIAGNOSTIC OR INADEQUACY OF RENAL TISSUES TAKEN BY BIOPSY

	No.	%	Kark *et al* (1958)	
			No.	%
Patients	90	—	368	—
Biopsies	105	100	500	100
Renal tissues obtained	96	91	465	93
Renal tissues adequate for pathologic diagnosis	82	78	401	80
Renal tissues inadequate for pathologic diagnosis	14	13	—	—
Other tissues*	6	—	—	—
Nothing obtained	3	—	—	—

* Liver 2, muscle 3, blood clots 1.

TABLE III

COMPARATIVE ANALYSIS OF SYMPTOMS OR COMPLICATIONS WHICH APPEARED DURING OR FOLLOWING RENAL BIOPSIES

Complication or Symptom	No. of Biopsies	Percentage of 105 Biopsies	Kark *et al* (1968) Percentage of 500 Biopsies
1. Death	0	0	0
2. Nephrectomy or Laparotomy	0	0	0
3. Prolonged Gross Haematuria	1	1	0.6
4. Frank Haematuria	12	11	5
5. Perirenal Swelling	2	2	0.6
6. Abdominal Colic	4	4	3
7. Hypoglycemic Coma	2	2	—
8. Vasovagal Hypotension	2	2	—
9. Oliguria	2	2	—

TABLE IV

ANALYSIS OF CAUSES OF NEPHROTIC SYNDROME IN 51 CASES WITH ADEQUATE RENAL BIOPSIES

Diagnosis	No. of Patients	Percentage of 51 cases
1. Idiopathic Nephrotic Syndrome	42	82
2. Diabetic Nephropathy	4	8
3. Systemic Lupus Erythematosus	4	8
4. Amyloidosis	1	2

TABLE V

HISTOLOGICAL PATTERNS OF 42 CASES OF IDIOPATHIC NEPHROTIC SYNDROME

Diagnosis	No. of Patients	Percentage of 42 cases
Minimal change	24	57
Proliferative glomerulonephritis	17	41
(a) diffuse endothelial proliferation	10	
(b) lobular stalk thickening	2	
(c) focal glomerulonephritis	5	
Membranous glomerulonephritis	1	2

Hypoglycaemic Coma

Hypoglycaemic Coma was seen in 2 diabetics, one due to inadvertent starvation prior to renal biopsy and the other because the patient was too sedated to eat after the biopsy.

3. *Analysis of the histopathological diagnosis of 82 patients from whom adequate renal tissues were obtained.*

Details of the renal biopsy appearances and the clinical diagnoses are shown in Table I.

4. *Analysis of causes of nephrotic syndrome in 51 cases with adequate renal biopsies* (Tables IV and V).

In this small selected study on 51 Asians, the causes of nephrotic syndrome were idiopathic nephrotic syndrome in 42 (82%), diabetic nephropathy in 4 (8%), systemic lupus erythematosus in 4 (8%) and amyloidosis in one (2%) (Table IV). The conventional histopathological classification of idiopathic nephrotic syndrome is into three main groups: (1) minimal change, (2) membranous glomerulonephritis, and (3) proliferative glomerulonephritis. Five subgroups are recognised in proliferative glomerulonephritis: (a) diffuse exudative/proliferative, (b) lobular stalk thickening, (c) with crescents, (d) membranoproliferative, and (e) others which include focal and chronic glomerulonephritis (Cameron, 1968). This histopathological classification of 42 patients with idiopathic nephrotic syndrome was minimal change in 24 (57%), proliferative glomerulonephritis in 17 (41%) and membranous thickening in only one (2%) (Table V). Nephrotic syndrome was also observed to be associated with a case of thyrotoxicosis and another with carcinoma of the bronchus.

DISCUSSION

Renal biopsy has been regarded as the greatest recent advance in our understanding of nephritis. Since its popularization by Kark *et al* (1954) its usefulness has been employed so extensively that in 1960 a whole Ciba Foundation symposium was held in London, and the participants had a collective experience of some 500 renal biopsies (Ciba, 1960). In experienced hands it is quite safe and can be done under local anaesthesia on any patient from a few days old to old age. The complications seen include pain at biopsy site, haematuria, perirenal haematoma and biopsy of wrong organs like liver, duodenum and spleen. Appreciable bleeding into the urinary tract or perirenal space occurs in about 1% of patients and may necessitate surgical intervention. Nephrectomy and death from the procedure are rare. The renal biopsy results in this study further confirm the usefulness and safety of this procedure.

The nephrotic syndrome is one of the groups of the diseases in which kidney biopsy offers the greatest diagnostic support since, on the basis of the clinical criteria alone, one cannot often distinguish with sufficient certainty between various underlying diseases. Kark *et al* (1958) in their extensive study listed 39 causes, more than half of which were due to idiopathic nephrotic syndrome. In another series (Habib *et al*, 1960) idiopathic nephrotic syndrome accounted for 85% of the 127 cases. The main causes of nephrotic syndrome in this study on Asians were comparable with other series (Kark *et al*, 1958, Habib *et al*, 1960, and Blainey *et al*, 1960) in that primary renal "nephritis" was responsible for 82% of the causes.

IDIOPATHIC NEPHROTIC SYNDROME

As mentioned earlier the histopathological classification of idiopathic nephrotic syndrome is into 3 types. "Optically normal" or minimal change group carries a favourable prognosis and the electron-microscopic changes of fusion of foot processes may recover with early prednisolone therapy. It is found in 10% of adults and 40% in children. Prolferative glomerulonephritis occurs in 50% of adults and membranous glomerulonephritis in 25% of adults. In this study on 42 Asians, minimum change accounted for 57%, proliferative glomerulonephritis 41% and membranous glomerulonephritis 2%. Most notable in this series was the marked scarcity of membranous glomerulonephritis (2%) in contrast to the high incidence of either minimal change group (57%) or proliferative glomerulonephritis (41%). In this group of idiopathic nephrotic syndrome, not one case of epithelial proliferation with crescent formation was seen even though some of the patients had been suffering from the disease for more than five years and had recurrent relapses. Further evidence is needed before one can conclude that the Asian pattern is different.

ACUTE GLOMERULONEPHRITIS

The diagnosis of acute glomerulonephritis presents no difficulty if all the following features are present: oedema of sudden onset, oliguria, haematuria and proteinuria. However "partial

syndromes" may appear in the form of minimal or no urinary change, or the patient may present with frank haematuria in the absence of oedema (Tan *et al*, 1968). Whereas previously the diagnosis of acute glomerulonephritis in the absence of haematuria and proteinuria can only be suspected, now the diagnosis can be substantiated by renal biopsy (Hutt *et al*, 1958; Cohen and Levitt, 1963; Berman and Vogelsang, 1963; Albert *et al*, 1966; Tan *et al*, 1968). In the present study 3 out of the 11 patients were noted to have minimal or no haematuria or proteinuria throughout their entire hospital admission. Their diagnoses were confirmed by renal biopsy: 2 showing endothelial proliferative glomerulonephritis and one minimal change.

Six patients had prolonged haematuria which were thoroughly investigated to exclude other local causes of haematuria. Five had severe endothelial proliferative glomerulonephritis and one epithelial proliferative glomerulonephritis with crescents. The cause of haematuria in acute glomerulonephritis remains unclear, although there is some correlation observed between the degrees of endothelial proliferation and degree of haematuria (Jennings and Earle, 1961).

SCHONLEIN-HENOCH SYNDROME

Renal complications frequently complicate the Schonlein-Henoch syndrome and although the majority recover, a few may develop progressive renal failure within a few years (Allen *et al*, 1960). Renal biopsy studies emphasize the focal nature of the lesion whereas post-mortem studies reveal epithelial proliferative glomerulonephritis (Heptinstall, 1966). Of the 4 studied, 2 had endothelial proliferation and 2 focal glomerulonephritis. Endothelial proliferation in Schonlein-Henoch Syndrome is believed to be rare (Vernier *et al*, 1961, Heptinstall, 1966).

SUMMARY

The present study of 105 renal biopsies on 90 Asian patients confirms the clinical value of the relatively simple and safe procedure in providing an exact histopathological diagnosis of kidney diseases which is essential for rational management. The report analyses the results of renal biopsies, the factors that contributed towards renal biopsy failure and discusses the complications that arose during the study. The histological patterns of 82 adequate biopsies are analysed. In the 42 cases of idiopathic nephrotic syndrome, 57% showed minimal changes, 41% revealed proliferative features and only 2% exhibited membranous glomerulonephritis. The scarcity of membranous glomerulonephritis in contrast to the predominance of endothelial proliferative glomerulonephritis in idiopathic nephrotic syndrome in Asians is stressed.

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