RENAL PAPILLARY NECROSIS RETROSPECTIVE RADIOLOGICAL STUDY

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SYNOPSIS

1011 Intravenous Urograms (IVU) done at the Nephrology Unit, General Hospital, Kuala Lumpur from 1968 to 1981 were reviewed for renal papillary necrosis (RPN). It is found that 2.0% of the IVUs have RPN. Contrary to the experience in the West and in Australia, analgesic nephropathy in Malaysia tends to have a male preponderance and occurs even in the younger age groups.

INTRODUCTION

Necrosis of the renal papillae was first described by Von Friedreich in 1877 (1) and the radiological appearances were first described by Praetorius in 1937 (2).

From the early 1950s reports of the condition began appearing with increasing frequency. In 1953 Spuhler and Zollinger suggested that rise in frequency of the condition in Continental Europe was secondary to the increased consumption of compound analgesics containing phenacetin (3). Subsequently analgesic induced renal disease was recognised in Scandinavia, Australia, North America and United Kingdom.

Diagnosis of the condition can be easily missed as these patients tend to deny their analgesic abuse (4) and the radiological changes of analgesic nephropathy can be difficult to distinguish from chronic pyelonephritis. The purpose of this study is to ascertain the prevalence of RPN in Malaysia.

MATERIALS AND METHOD

IVUs done at the Nephrology Unit, General Hospital, Kuala Lumpur from 1968 to 1981 were reviewed retrospectively for RPN. These patients had in addition various investigations relevant to their renal condition performed.

Those patients who had RPN detected in the IVU were called back for review. Patients were questioned as to whether they had consumed analgesics and if so, the type, frequency, amount, duration as well as the reason for intake was ascertained. Ferric chloride test to detect aspirin in the urine was done.

RESULTS

IVUs of 1011 patients were reviewed. There were 412 Malays, 430 Chinese, 162 Indians and 7 others. 586 patients were males and 425 patients were females and they were of all age groups.

TABLE I IVU DONE IN GENERAL HOSPITAL, KUALA LUMPUR, 1968 - 1981

	Malays		Indian		Chinese		Others		Total
	M	F	M	F	M	F	M	F	
10 years	2	-	-	-	-	-	-	-	2
11 - 20 years	33	21	6	5	16	20	-	-	101
21 - 30 years	83	50	25	25	50	65	3	1	302
31 - 40 years	58	36	21	13	42	43	1	-	214
41 - 50 years	47	19	18	13	44	37	-	-	178
51 - 60 years	32	10	18	7	35	28	2	-	132
61 - 70 years	12	4	7	-	20	23	-	-	66
70 years	3	1	3	-	4	1	-	-	12
Age Not Specified	-	1	1	-	-	2	-	-	4
Total	270	142	99	63	211	219	6	1	1011

The indications for IVU are shown in Table II. Indications which are unlikely to cause RPN such as kidney donor, chronic glomerulonephritis and nephrotic syndrome are also included in the review.

TABLE II IVU DONE IN GENERAL HOSPITAL, KUALA LUMPUR, 1968 - 1981

Indication	No.
Haematuria	90
Proteinuria	80
Hypertension	53
Diabetes Mellitus	14
Acute Renal Failure	70
Chronic Renal Failure	110
Nephrotic Syndrome	125
Colic/Calculi	156
UTI/CPN	81
Gout/Hyperuricemia	11
SLE	15
PET	12
Kidney Donor	85
Loin Pain/Low Backache	26
Incontinence of Urine	4
Pain in Loin - PCK	9
MVA with Injury to Kidney	4
Chronic Glomerulonephritis	14
Prostatitis	5
Acute Glomerulonephritis	10
Renal TB	6
Cystitis	6
Hydronephrosis - Acq./Cong.	3
Miscellaneous	21
Total	1,011

Radiological changes of RPN were observed in 20 cases accounting for 2% of all IVU's reviewed. The majority of the patients with RPN were males (15 cases,(Table III).RPN was observed mainly in the older age groups (15 cases were above the ages of 40), but there were 2 cases in the 21-30 year age group and 3 cases in the 31-40 year age groups.

TABLE III PATIENTS WITH PAPILLARY NECROSIS - RADIOLOGICAL

	MALAY		INDIAN		CHINESE		TOTAL
	M	F	M	F	M	F	
21 - 30 yrs.	1	1	-	-	-	-	2
31 - 40 yrs.	2	-	-	-	-	1	3
41 - 50 yrs.	2	1	-	-	2	-	5
51 - 60 yrs.	4	1	-	-	1	-	6
61 - 70 yrs.	1	-	1	-	1	1	4
Total	10	3	1	-	4	2	20

2 cases of RPN are due to diabetes mellitus and the rest are due to analgesic abuse. Investigations performed to exclude sickle cell anaemia and tuberculosis were negative in all these patients.

The clinical presentation of these patients are listed on Table IV. 8 patients presented as renal colic or calculi and 1 patient presented as chronic pyelonephritis.

TABLE IV PATIENTS WITH PAPILLARY NECROSIS - RADIOLOGICAL

Initial Diagnosis	
Diabetes mellitus with nephropathy	2
Chronic pyelonephritis	1
Recurrent haematuria (TB?)	1
Renal colic/Calculi	8
Hypertension	6
Asymptomatic albuminuria	1
Chronic renal failure	1
Total	20

Attempts were made to recall all the 20 patients with radiological evidence of RPN but we were only able to review 8 patients.

Of the 8 patients reviewed 5 admitted to taking analgesics regularly, 3 denied taking analgesics. However ferric chloride test to detect the presence of aspirin in urine was positive in 1 (Table V). On the whole, 7 patients admitted taking analgesics regularly, 3 denied analgesic intake and in 10 patients the analgesic intake is not known. The type and estimated quantity of analgesic intake are listed in Table VI. 3 patients had consumed only paracetamol and 3 had consumed Chap Harimau or Chap Kaki Tiga which are local proprietary brands of compound analgesics containing aspirin, phenacetin and caffeine.

TABLE V PATIENTS WITH PAPILLARY NECROSIS - RADIOLOGICAL

	Ferric chloride test		
	+ ve	– ve	Total
Denied analgesic intake	1	2	3
Admitted to analgesic intake	1	4	5

TABLE VI PATIENTS WITH PAPILLARY NECROSIS - RADIOLOGICAL (WITH HISTORY OF ANALGESIC INTAKE)

Paracetamol only	-	3 (rarely, 3960 gm. 1570 gm.)
Chap Harimau	-	1 (130 gm. of ASA)
Chap Kaki Tiga	-	1 (150 gm. of ASA)
Paracetamol/ Chap Kaki Tiga	-	1 (rarely)
Type unknown	-	1

Patients presented at varying stages of renal impairment (Table VII) ranging from normal renal function to end stage renal failure. The majority of patients presented with mild to moderate renal impairment with serum creatinine ranging from 120 to 260 umol/l (16 out of 20 patients).

TABLE VII PATIENTS WITH PAPILLARY NECROSIS - RADIOLOGICAL B.U./CREAT./U.A. AT FIRST VISIT

BLOOD UREA mmol/L	CREAT. umol/L	U. ACID umol/L
	70	
3.8	100	408
5	130	370
	130	610
3.5	130	320
13	120	
6	135	360
8	140	330
10	140	320
6.3	140	451
6	160	640
6	160	760
7.7	160	432
9	170	410
4	190	360
18	210	
10	230	400
30	260	920
	350	1190
52.0	2060	693

The major radiological changes noted were shrinkage and irregularity of the calyces, medullary cavities, swelling of the calyces and ring shadows. Calcification in the necrotic papillae were uncommon (Fig. 1-4).

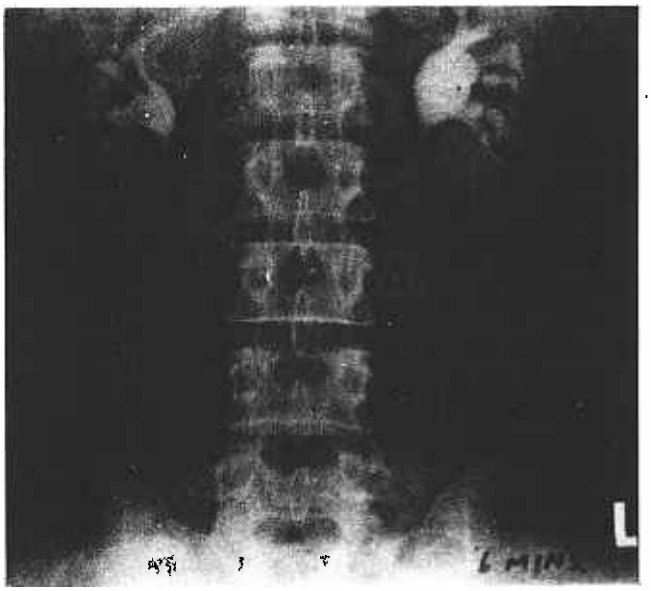

Figure 1
IVU: The precompression film shows blunting and irregularity of the papillae on both sides compatible with papillary necrosis.

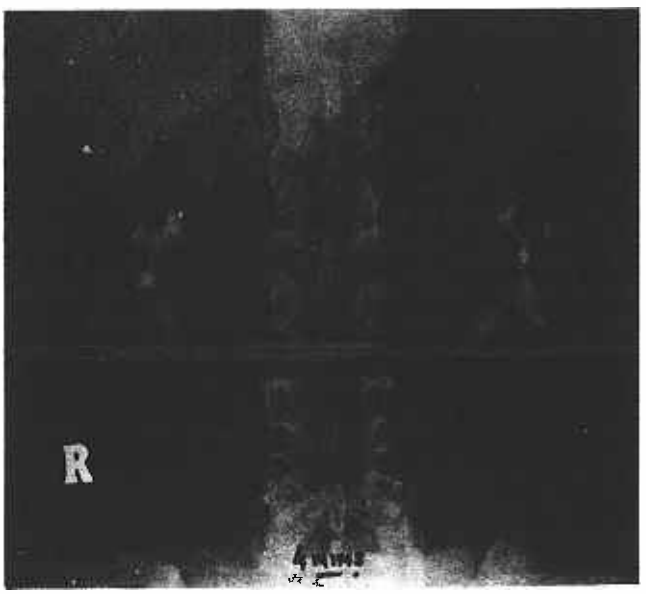

Figure 2
IVU: The precompression film shows blunting of the papillae in the right kidney. There is some cortical loss of this kidney. Findings are compatible with papillary necrosis. The left kidney is normal.

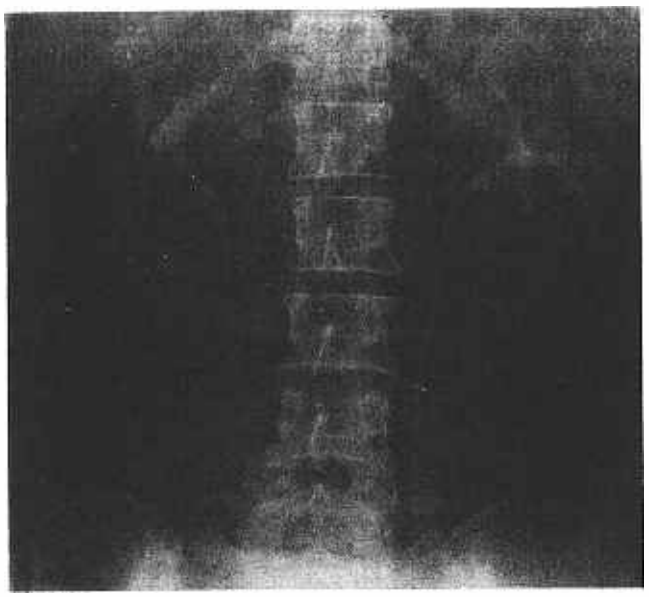

Figure 3
IVU: The precompression film shows erosion of the papillae with clubbing of the calyces on the right side. Clubbing is also noted in the left midpolar calyx. These changes are compatible with papillary necrosis.

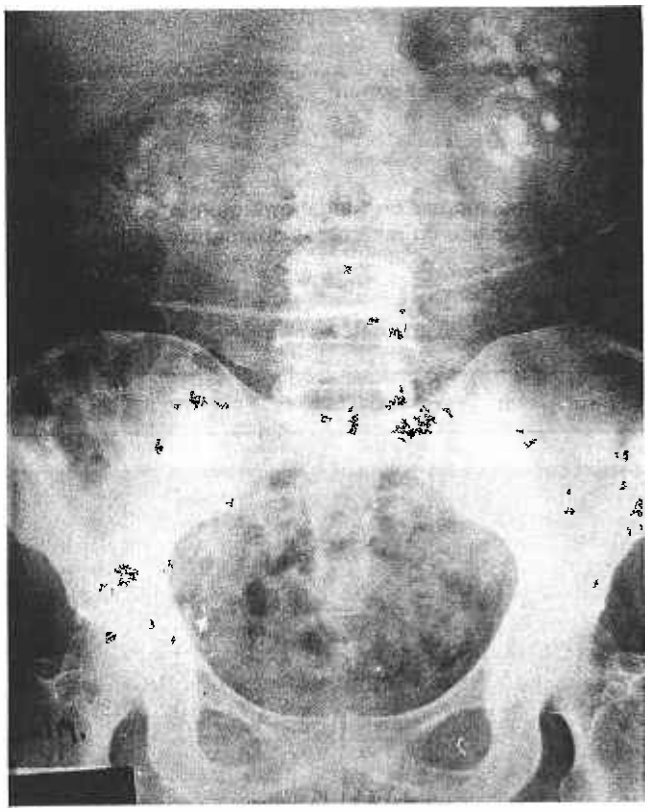

Figure 4
IVU: Radiograph showing marked changes of papillary necrosis involving all calyces of both kidneys. There is significant loss of cortical substance bilaterally.

DISCUSSION

There were 20 cases of RPN (2.0%) of which 2 were due to diabetes mellitus, the remaining 18 (1.8%) can be attributed to analgesic nephropathy. In the latter group other causes for RPN such as diabetes mellitus and sickle cell anaemia had been excluded by laboratory investigations. History of analgesic abuse had been confirmed only in 7 of the cases. Although in 10 cases the analgesic intake is not known and 3 patients denied analgesic abuse, this does not exclude the possibility of analgesic nephropathy as the radiological changes were consistent with RPN and it is well known that many patients with analgesic nephropathy will deny analgesic abuse (4). This is exemplified in one patient who denied analgesic abuse despite the ferric chloride test for aspirin being positive.

Analgesic nephropathy occurs five to six times more frequently in females than in males and rarely occurs under the age of 30 years (5). This study demonstrates a preponderance of males with the male to female ratio being 3 to 1, contrary to the experience of other countries. 2 cases (10%) of RPN occurred below the age of 30 years and 3 cases (15%) of RPN occurred between the ages of 30 to 40 years. It is hence observed that in our population RPN is not uncommon in the younger age groups.

Three patients with RPN had been abusing paracetamol whilst the others had been abusing Chap Harimau and Chap Kaki Tiga. The relevance of the above findings are discussed elsewhere.

Analgesic nephropathy needs to be considered as a differential diagnosis in patients presenting as renal colic or calculus (6). Necrotic papillae can be sloughed and cause symptoms and signs of renal colic such as colicky pain in the loin associated with haematuria. The sloughed papilla could be mistaken for a calculus especially if it is calcified. There is an impaired acidifying capacity in analgesic nephropathy and frank renal tubular acidosis with a minimum urinary pH $>$ 5.7 is seen when renal function is impaired. This functional defect is responsible for medullary calcification and calculus disease. Dystrophic calcification of necrotic tissue and excessive ingestion of milk-alkalis because of gastric disturbances contribute to nephrocalcinosis. The other factors that contribute to stone formation are necrotic papillae, exfoliation of tubular cells by analgesics, urinary tract obstruction and infection by urea-splitting organisms, such as Proteus (7).

In the absence of characteristic changes of RPN, the differentiation between analgesic nephropathy and chronic pyelonephritis may be difficult. The radiological features of analgesic nephropathy include RPN, medullary calcification, "clubbed" calyces which are generalised and non-polar, reduction in renal size on serial IVUs and the changes are bilateral. Compensatory hypertrophy and cortical scarring may be present. The ureters are normal and vesico ureteric reflux is absent.

In chronic pyelonephritis the "clubbed" calyces are polar, and the ureter may be dilated at the lower third. Compensatory hypertrophy and cortical scarring are more prominent than in analgesic nephropathy. There is no RPN or medullary calcification. The radiological disease can be unilateral or bilateral. There may be evidence of vesico-ureteric reflux and there is no reduction in renal size on serial IVUs (5). In patients especially males presenting as chronic pyelonephritis in the absence of predisposing factors, analgesic nephropathy needs to be kept in mind.

Both tuberculosis and analgesic nephropathy often

present with sterile pyuria, and early tuberculosis can mimic localised papillary necrosis. However, in such cases renal function will usually be normal. In advanced tuberculosis, there may be extensive calcification, but this usually involves more than the papillae (8).

The 'papillary' cavities of medullary sponge kidneys may also cause confusion, but in analgesic nephropathy, there is seldom more than one cavity per papilla. Splaying of the calyces and accentuation of the tubular blush also helps to distinguish sponge kidneys.

Short-duration severe hypertension with markedly reduced renal function and normal sized kidneys may also mimic analgesic nephropathy, particularly if renal function is so reduced as to prevent an adequate pyelogram being obtained. But, if there is reasonable calyceal detail or if a retrograde pyelogram is performed, then the diagnosis can be made on the basis of the calyceal morphology.

In the differential diagnosis one should also consider post-obstructive renal atrophy. This condition is usually associated with reduced renal function, and may resemble advanced analgesic nephropathy with smooth clubbed calyces. In post-obstructive atrophy the renal outline is usually smooth, but on the rare occasion when the obstruction is bilateral it will be accompanied by anuria.

In conclusion, analgesic nephropathy is rare in Malaysia and can be easily misdiagnosed. With awareness of the condition as well as the common radiological features, it should be possible to diagnose analgesic nephropathy with confidence. It is particularly important to detect such cases, because if analgesic abuse ceases, considerable recovery in renal function may occur.

REFERENCES

1. Von Friedreich N: Ueber Nekrose der Nierenpapillen bei Hydronephrose. Virchows Arch (Pathol Anat) 1877; 69: 308.
2. Praetorius G: Papillitis necroticans bei schwerer chronischer Pyelonephritis. Z Urol Nephrol 1937; 31: 298.
3. Spuhler O, Zollinger HU: Die chronische - interstitielle nephritis. S Klin Med 1953; 151: 1-50.
4. Murray RM:The origins of analgesic nephropathy. Brit J Psychiat 1973; 123: 99-106.
5. Nanra RS: Analgesic nephropathy. Med J Aust 1976; 1: 745-8.
6. Blackman JE, Gibson GR, Lavan JN, Learoyd HM, Posen S: Urinary calculi and the consumption of analgesics. Brit Med J 1967; 2: 800-2.
7. Nanra RS, Stuart-Taylor J, de Leon AH, White KH: Analgesic nephropathy: Etiology, clinical syndrome and clinicopathologic correlations in Australia. Kidney International 1978; 13: 79-92.
8. Adams FG, Murray RM: The radiological diagnosis of analgesic nephropathy. Clin Radiol 1975; 26: 417-27.