CANDIDAL RENAL PAPILLARY NECROSIS: REPORT OF A CASE AND REVIEW

Y F Chiew

ABSTRACT

Renal papillary necrosis (RPN) due to* Candida *is a rare disease with only 19 cases reported over the past 37 years. But the diagnosis in 17 of the 19 cases was not made until a necropsy was carried out. The 2 cases that were diagnosed antemortem had radiographic sonography. A Singapore case with candidal RPN was described in detail. Candidal RPN was associated with underlying diseases in all these cases. The disease may be more frequently encountered in the future with the advent of radiographic tools like sonography which was not described prior to 1980. Indeed, patients with underlying diseases who develop persistent candiduria should have radiographic investigation of the urinary tract to detect candidal RPN so that early remedial measures can be carried out.

Keywords: *predisposing factors, candidal renal papillary necrosis, persistent candiduria, sonography*

SINGAPORE MED J 1996; Vol 37: 119-121

INTRODUCTION

The kidney is often involved in disseminated and localised candidiasis but papillary necrosis is an infrequently reported complication of such fungal infections[1-8]. Twenty cases of candidal RPN were studied retrospectively. Pathogenic factors such as corticosteroids, immunosuppressive drugs, antibiotic therapy, neoplastic diseases and indwelling vascular catheters were found in candidal RPN. Radiographic investigation is an important tool in the antemortem diagnosis of candidal RPN[9]. The earliest radiographic tool in the investigation of renal abnormalities was intravenous urogram in the 1930s[10]. Sonography was first used to evaluate RPN in the 1980s[11] and the first computed tomography demonstration of RPN was not reported until 1991[12].

CASE REPORT

The patient is a 67-year-old woman with non-insulin diabetes mellitus. She was admitted to a Singapore hospital in 1991 with complaint of fever and chills of 5 days' duration and abdominal distension.

Initial examination was notable for fever of 38°C, coarse crackles at the base of the left lung and dehydration. The provisional diagnosis was chest infection and faecal impaction and empirical therapy of gentamicin and ceftriazone were prescribed for the chest infection. Peak and trough gentamicin levels were within the therapeutic range.

The results of laboratory investigations were: white blood cell (WBC) count of 16 x 10^3/mm^3, haemoglobin 10.3 g/dl, platelets 61 x 10^9/L. Prothrombin time, thrombin clotting time and partial thromboplastin time were prolonged which suggested disseminated intravascular coagulation. Serum urea, electrolytes and creatinine levels were initially within the normal range.

Department of Medical Microbiology
London Hospital Medical College
Turner Street
London E1 2AD
England

Y F Chiew, MSc (Clin Microbiol), DipRCPath (UK), M Med (Int Med), FAMS
Senior Registrar

Correspondence to: Dr Y F Chiew
Department of Laboratory Medicine
National University Hospital
5 Lower Kent Ridge
Singapore 119074

Blood gases showed metabolic acidosis with incomplete respiratory compensation. Urine microscopy showed more than 100 WBC/hpf but cultures were negative. Two blood cultures grew *Escherichia coli* which were susceptible to the antibiotics prescribed. Ultrasound of the abdomen showed marginal dilatation of the left pelvi-calyceal system.

The patient was treated for *E.coli* urinary tract septicaemia complicated by disseminated intravascular coagulation and she was managed at the intensive care unit. Subclavian venous line insertion was carried out along with urinary catheterisation to monitor urine output. She required blood transfusions, platelets, fresh frozen plasma and albumin infusions. Diabetes mellitus was managed with insulin. Her fever recurred on Day 11 of hospitalisation and it was accompanied by hypotension. She had repeat blood transfusions to correct anaemia of 7.9 g/dL. Blood cultures on Day 19 grew *Enterococcus faecalis* which was susceptible to vancomycin only. Urine grew multiple drug resistant *Klebsiella pneumoniae* which was sensitive to amikacin and imipenem. Two urine cultures also grew *Candida* which were regarded as nosocomial commensals. A course of vancomycin and amikacin was prescribed. Amikacin serum levels were within normal limits. Serum urea rose to 39.1 mmol/L and creatinine was 609 μmol/L. A repeat ultrasound showed grossly swollen left kidney with multiple cystic spaces in the medulla and prominent pelvi-calyceal system and the features were suggestive of papillary necrosis. Left antegrade nephrostomy was carried out and it yielded 600 ml of thick yellow blood-stained pus. Pure cultures of *Candida* were isolated from the pus but speciation was not carried out. Drainage from the nephrostomy became clearer but the tube had to be removed because it became blocked. Ten more cultures obtained from the urinary catheter following the nephrostomy grew *Candida* and API 20C system identified one of these cultures as *C.tropicalis*. Antimicrobial testing of *Candida* was not available which could help determine the appropriate anti-fungal regime to be used in this patient. The last urine culture also grew *Acinetobacter anitratus* which had multiple drug resistance. Bladder irrigation with amphoterin B was carried out and this was followed by a five-week course of oral fluconazole for suspected candidal cystitis. Repeat nephrostomy was carried out but the tube slipped out after insertion. Systemic amphotericin B was considered for possible fluconazole-resistant *Candida* but this was not prescribed in view of the patient's rapid deterioration. She developed fits due to severe hypomagnesaemia of 0.39 mmol/L (0.7 - 0.91) and hypocalcaemia of total calcium 1.6 mmol/L (2.1 - 2.6) and ionised calcium 0.96 mmol/L (1.13 - 1.32). These deficits were corrected

Table I – Summary of cases of candida renal papillary necrosis

Patient No.	Year	Age	Gender	Underlying disease	Approx. duration of illness (days)	Candida cultured antemortem	Disseminate candidiasis	Immuno-suppressive therapy	Prior antibiotic treatment
1	1956[1]	60	?	Diabetes mellitus	NS	-	-	NS	NS
2	1964[2]	41	F	Chronic pyelonephritis, total hysterectomy & bilateral salpingo-oophorectomy	30	mouth, tracheostomy, abdominal, pus	+	steroids	+
3	1968[3]	68	F	Bladder carcinoma	39	colon	-	steroids	+
4	1968[3]	31	F	Chronic pyelonephritis, renal transplant	27	blood, mouth, peritoneal fluid	+	steroids azathioprine	+
5	1971[4]	48	M	Diabetes mellitus	30	urine	-	-	+
6	1977[5]	52	F	Hodgkin's lymphoma	60	-	-	multiple	+
7	1977[6]	3	M	Acute leukaemia	NS	-	+	multiple	NS
8	1977[6]	41	F	Cirrhosis	NS	-	-	-	NS
9	1977[6]	3	M	Extensive burns	NS	-	+	-	NS
10	1981[7]	23d	M	Prematurity	NS	-	+	-	NS
11	1981[7]	23d	F	Prematurity	NS	csf	+	-	NS
12	1981[7]	34d	F	Prematurity	NS	urine, blood	+	-	NS
13	1981[7]	3m	F	Immunodeficiency	NS	blood	+	-	NS
14	1981[7]	56	F	Retroperitoneal sarcoma	NS	-	-	steroids, cyclo-phosphamide	NS
15	1981[7]	71	F	Carcinoma of urethra	NS	nephrostomy	-	-	NS
16	1981[7]	27	F	Lupus nephritis	NS	urine	-	steroids azathioprine	NS
17	1981[7]	65	F	Diabetes mellitus	NS	urine	+	-	-
18	1981[7]	12	M	Hepatitis	NS	-	+	-	-
19	1985[8]	37	M	Diabetes mellitus	98	urine	-	-	-

NS: Not Stated

with parenteral magnesium and calcium. Cerebral CT scan showed right parieto-temporal haemorrhagic infarct. She was discharged three months after admission and was noted to be febrile, non-communicable, bed-ridden and had extensive bedsores towards the end of her hospital stay.

DISCUSSION

A review of the English literature describing candidal renal papillary necrosis revealed 19 such cases from 1956 to 1985[1-8], Table I. All of them had underlying diseases - diabetes mellitus (4 cases), cancers (5 cases), pyelonephritis (3 cases, one co-existing with diabetes mellitus), prematurity (3 cases) and one case each of immunodeficiency, lupus nephritis, hepatitis, cirrhosis and extensive burns. The average duration of illness from the onset of symptoms to patients' demise for Cases 1 to 6 was 47 days. Cases 4 and 5 had concomitant bacterial growth in the urine. The antemortem diagnoses were made in Case 5, who expelled a necrotic renal papilla that was enmeshed in fungal mycelia, and Case 19 who had renal sonogram and retrograde pyelography[8].

There were only three survivors in this review of candidal RPN. Case 5 had received systemic amphotericin B early in the course of the illness and Case 19 was cured with four weeks of oral ketoconazole. The Singapore case had improved after the initial drainage of 600 ml of pus but the candidal pyuria persisted and she deteriorated probably from the combination of candidal sepsis and other complications which were urinary bacterial infections, electrolyte imbalance, bedsores and cerebral haemorrhagic infarct. The *Candida* was most likely resistant to the fluconazole that was prescribed.

Vascular diseases affecting the kidneys can lead to papillary necrosis in conditions such as diabetes mellitus. The hyperosmolarity of the renal medulla can also encourage fungal growth. These factors together with the presence of urinary tract obstruction in some of these cases may lead to the development of candidal renal papillary necrosis. Studies on mice[13] had shown that renal candidiasis can result from hematogenous spread but only three of the twenty cases (Cases 4, 12 and 13) presented so far had blood cultures positive for *Candida*. The experiment also showed that fungus balls from masses of necrotic debris and mycelia per se may obstruct the renal pelvis and ureter giving rise to papillary necrosis.

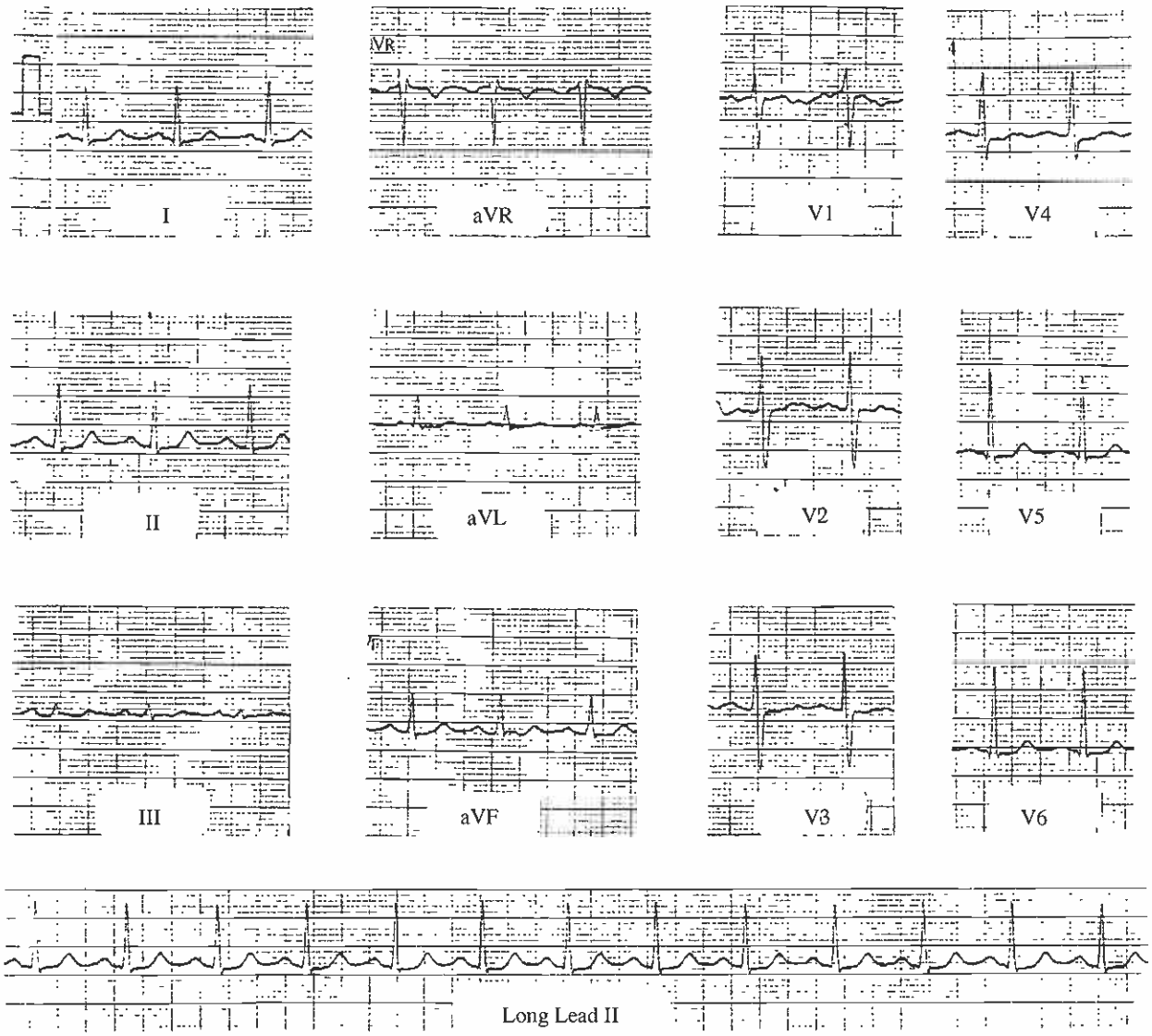
Urinary candidal cultures are by no means specific for papillary necrosis, however, and could indicate cystitis, pyelonephritis, or disseminated candidiasis[14]. But patients with underlying diseases who developed persistent candiduria should have radiographic investigation of the urinary tract to detect candidal RPN so that early remedial measures can be carried out.

REFERENCES

1. Keye JD Jr, Magee WE. Fungal diseases in a general hospital. Am J Clin Path 1956; 26:1235-53.

2. Lehner T. Systemic candidiasis and renal involvement. Lancet 1964; 1:1414-6.
3. Knepshield JH, Feller HA, Leb DE. Papillary necrosis due to *Candida albicans* in a renal allograft. Arch Intern Med 1968; 122:441-4.
4. Clark RE, Minagi H, Palubinskas AJ. Renal candidiasis. Radiology 1971; 101:567-72.
5. Hancock BW, Henry L. Renal papillary necrosis asociated with renal candidiasis in a patient with Hodgkin's diseasc. Cancer 1977; 40:2309-11.
6. Salfelder K, Ueda K, Quiroga EL, Schwarz J. Visceral candidosis. Curr Top Pathol 1977; 64:177-224.
7. Tomashefski JF Jr, Abramowsky CR. Candida-associated renal papillary necrosis. Am J Clin Pathol 1981; 75:190-4.
8. Cohen PS, Scheer RL, Bloom MJ, Kolanchik GJ, Tucker JB. *Candida tropicalis* papillary necrosis treated with ketoconazole. NY State J Med 1985; 85:97.
9. Lindvall N. Radiological changes of renal papillary necrosis. Kidney Int 1978; 13:93-106.
10. Praetorius G. Papillitis necroticans bei schwerer chronischer pyelonephritis. Z Urol Nephrol 1937; 31:298.
11. Hoffman JC, Schnur MJ, Koenigsberg M. Demonstration of renal papillary necrosis by sonography. Radiology 1982; 145:785-7.
12. Saifuddin A, Bark M. Case report: computed tomography demonstration of renal papillary necrosis. Clin Radiol 1991; 44:275-6.
13. Hurley R, Winner HI. Experimental renal moniliasis in the mouse. J Path Bact 1963; 86:75-82.
14. Ellis CA, Spivack ML. The significance of candidemia. Ann Intern Med 1967; 67:511-22.

Fig 2 – ECG done preoperatively (on the day of the emergency hysterectomy)



ANSWER TO ELECTROCARDIOGRAPHIC CASE

Diagnosis: Acute pulmonary embolism

DISCUSSION

The 12-lead ECG shows sinus tachycardia of 100/min with an axis of +90°. There is coved ST-segment elevation in leads V1 to V4. There is a prominent S wave in Lead I but no associated pathological Q wave or inverted T wave in Lead III. This ECG pattern was recorded during her chest pain and was completely different from the ECG done pre-operatively (Fig 2). The pre-operative ECG showed sinus rhythm with a normal axis, and without an S wave in Lead I. It also showed normal R wave progression with no ST-segment elevation in the anterior praecordial leads.

Considering the clinical scenario, the diagnosis of acute pulmonary embolism has to be considered although these ECG changes could also indicate an acute transmural anterior myocardial infarction. A bed-side echocardiogram was invaluable in making the correct diagnosis – it showed right ventricular chamber dilatation and good left ventricular systolic function. There was no regional wall motion abnormality in the inferior and right ventricular free wall. The pulmonary artery was dilated but there was no demonstrable thrombi within the pulmonary artery. Right ventricular myocardial infarction is unlikely from the echocardiographic findings. Furthermore, there is no ECG changes of inferior or right ventricular infarct. The above findings would exclude acute myocardial infarction, and is consistent with acute pulmonary embolism, most likely arising from the pelvic veins following gynaecological surgery. The ECG changes in this patient resemble a pseudo infarct pattern ,which is well recognised in acute pulmonary embolism. The diagnosis of acute pulmonary embolism was confirmed from the ventilation-perfusion lung scan. Pseudo infarct patterns in acute pulmonary embolism are due to acute right ventricular dilatation. This can simulate inferior or anterior myocardial infarction[1]. Recognition of these ECG features is essential because of the clinical importance of distinguishing acute pulmonary embolism from acute myocardial infarction. Bedside echocardiography is useful in quickly differentiating these two causes.

ECG changes in acute pulmonary embolism are transient, and depend on the embolus size and time of recording in relation to the onset of the acute event. The morphologic changes of the ECG are secondary to acute dilatation of the right ventricle. This often results in a clockwise rotation of the heart and right ventricular conduction defect. The clockwise rotation of the heart is probably responsible for the S1 Q3 pattern, a classical ECG feature described in acute pulmonary embolism. The ST-segment and T wave changes are probably due to myocardial hypoxaemia

CORRIGENDUM

There is a typographical error in the title of the article "Prolonged treatment with omeprazole does not improve the eradication rate of Helicobacter pylori infection – a short history" which was published in the Sngapore Medical Journal 1995; 36: 619-20. The correct title should be "Prolonged treatment with omeprazole does not improve the eradication rate of Helicobacter pylori infection – a short report".

The Editor of the SMJ sincerely apologises for the inadvertent error.