Phaeochromocytoma presenting with coexisting acute renal failure, acidosis and in hyperglycaemic emergency

L-Q. GU, L. ZHAO, J-M. LIU, T-W. SU, W-Q. WANG and G. NING
Department of Endocrinology and Metabolic Diseases, Ruijin Hospital, Shanghai Jiao-tong University Medical School; Shanghai Institute of Endocrinology; Shanghai Clinical Center for Endocrine and Metabolic Diseases, Shanghai, P. R. China

Phaeochromocytoma is a relatively uncommon tumour of the adrenal medulla, and its association with sustained or paroxysmal hypertension has also been labelled 'the great mimic', with a variety of typical or non-typical clinical manifestations.[1] Reversible acute renal failure, although rare, can be the presenting symptom of phaeochromocytoma as a consequence of renal ischaemia due to systemic shock, vasoconstriction, tumour compression of the renal artery or hypoperfusion/acute tubular necrosis following hypotension. Hyperglycaemia and ketoacidosis have also been reported.[2] The present study presents a case of phaeochromocytoma with coexisting acute renal failure, hyperglycaemia and acidosis.

In October 2006, a 36-year-old man with no prior history of renal disease or hypertension attended the emergency room complaining of a two-day history of fever, nausea, vomiting, palpitations, sweating and anuria (12 hours). Medical history, social history and family history were non-contributory and the patient was not on medication. Physical examination showed sinus tachycardia of 110 beats/min and blood pressure of 220/120 mmHg. With the exception of liver function, biochemical results of patient's blood tests, kidney function and plasma glucose were all abnormal (Table 1), with arterial pH 7.2 (7.35–7.45), $PaCO_2$ 30.2 (35–35) and SB 13.1 (22–27). He was diagnosed as being in hypertensive crisis, with acute renal failure, haematuria and hyperglycaemia.

The patient was treated promptly with intravenous fluid infusion, antihypertensive drugs and insulin. Five days later, all serum biochemical tests, including serum creatinine (Scr) level and creatinine clearance rate (Ccr) had returned to within their respective normal ranges. The changes in Scr and Ccr are shown in Figure 1. At the same time, abdominal ultrasound examination detected a 3 cm-diameter mass in the right adrenal area. From October 2006 to January 2007, the patient's blood pressure was 115–140/70–85 mmHg without antihypertensive treatment.

In January 2007 the patient was transferred to the authors' department to explore the nature of the adrenal mass. No paroxysmal or persistent hypertension had been noted. The patient's blood pressure was maintained at 120–140/70–85 mmHg and he showed a normal kidney function, but he still had microscopic haematuria. Primary aldosteronism and Cushing's syndrome were excluded. However, even in this normotensive state, his plasma metanephrine (MN) and normetanephrine (NMN) concentrations were very high, reaching 437.7 pg/mL (normal range: 14–90 pg/mL) and 749.4 pg/mL (19–121 pg/mL), respectively. Abdominal computed tomography (CT) scanning revealed a right-sided 3-cm diameter adrenal mass. (Fig. 2). Thus, the diagnosis of phaeochromocytoma was made.

A right adrenalectomy was performed following three weeks' preparation with Cardura (doxazosin mesilate). Pathological examination confirmed the diagnosis of adrenal phaeochromocytoma, and post-operative plasma MN (75.9 pg/mL) and NMN (112.4 pg/mL) levels were normal.

Correspondence to: Dr. Jian-Min Liu
Department of Endocrinology and Metabolic Diseases, Ruijin Hospital, Shanghai Jiaotong University Medical School, 197 Ruijin Er Road, Shanghai 200025, P. R. China
Email: ljmhh@sh163.net

Table 1. Results of serum and urine tests during paroxysmal hypertensive state and normotensive state.

	Normal range	Hypertensive	Normotensive
White cell count (10^9/L)	4.0 - 10.0	44.4	7.1
Hemoglobin (g/L)	120 - 160	177.0	126.0
Hematocrit (%)	35 - 50	53.0	41.0
Platelet count (10^{12}/L)	100 - 300	179.0	151.0
Sodium (mmol/L)	136 - 145	136.0	140.0
Potassium (mmol/L)	3.5 - 5.1	3.9	4.8
Chloride (mmol/L)	96 - 106	95.0	108.0
Carbon dioxide (mmol/L)	22 - 28	11.0	19.0
Urea nitrogen (mmol/L)	3.2 - 7.1	8.3	7.3
Creatinine (μmol/L)	53 - 115	334.0	83.0
Glucose (mmol/L)	3.9 - 6.1	36.8	5.5
Effective osmolarity* (mOsm/L)	280 - 310	308.8	285.5
Glycated haemoglobin (%)	4.0 - 6.1	5.6	–
Urinalysis (erythrocytes)	–	+++	+++
Urinalysis (ketone bodies)	–	–	–
Urinalysis (proteins)	–	–	–

*Effective osmolarity = $2[Na^+]$ + plasma glucose (mmol/L)

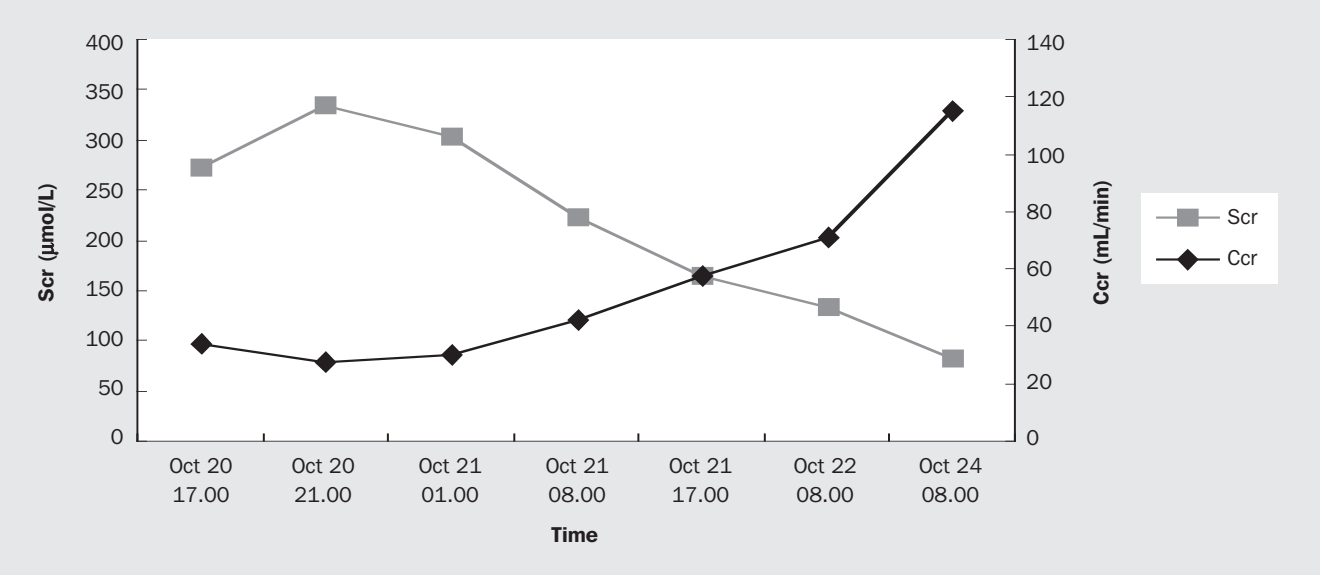
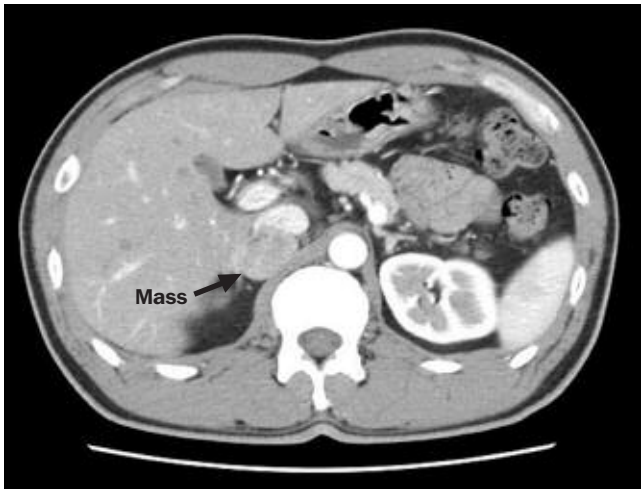


Fig. 1. Changes in Scr and Ccr over time. Ccr is calculated according to the Durate formula: Ccr=109.8/[0.01131 x Scr (µmol/L)]–1.8 (male).

Phaeochromocytoma is an uncommon neoplasm that develops from the chromaffin cells of the sympathetic nervous system and is associated with a hyperkinetic, vasoconstrictive, hypovolaemic form of hypertension. The classical clinical manifestations include headache, sweating and palpitations, together with hypertension, as seen in the present case. However, the patient described here also exhibited acute renal failure. The reason for this could be that phaeochromocytoma usually produces large amounts of catecholamines (CA), which generally reduces circulating blood volume and renal glomerular perfusion, and leads to intense intrarenal vasoconstriction.[3–6]

Severe vomiting in the patient precluded oral replacement of the excessive fluid loss, further aggravating acute renal failure. Elevation of the haematocrit usually is associated with a normal red cell mass and therefore reflects the reduced plasma volume. Excess secretion of norepinephrine and stimulated production of renin and angiotensin II due to renal hypoperfusion would be responsible for the appearance of haematuria found in this patient.

Acute renal failure may also result in metabolic acidosis with an increased anion gap due to failure to excrete organic acids (e.g., sulphates or phosphates). However, the anion gap calculated as Na^+–(Cl^-+HCO_3^-) = 30 (136–[95 +11]) (Table 1). The normal anion gap is usually approximately 10 mmol/L and its elevation indicates the presence of increased anion gap acidosis. For this patient, however, the acid retained in the circulation was approximately 20 mmol/L (30–10 = 20), which is higher than that seen usually in renal failure.



ig. 2. Abdominal CT scan showed a 3-cm-diameter mass in the right adrenal area.

Metabolic acidosis with increased anion gap is seen only in patients with advanced renal failure. It is possible that organic acids other than sulphates or phosphates (e.g., keto-acids and lactate) were retained in this hypertensive and hyperglycaemic patient. In severe ketoacidosis, β-hydroxybutyrate rather than acetoacetate is the predominant ketone, but urine tests may not detect β-hydroxybutyrate. Thus, although the patient's urine was negative for ketone bodies it is difficult to dismiss ketoacidosis.

Catecholamine-induced carbohydrate intolerance may lead to hyperglycaemia in 50% of patients.[7] Diabetic ketoacidosis (DKA) had also been associated with phaeochromocytoma in sporadic cases.[2] Diabetic ketoacidosis and hyperosmolar hyperglycaemic non-ketotic state (HHS) are two major hyperglycaemic emergencies. Although the effective serum osmolarity in this case was nearly 310 mOsm/kg (Table 1), it was less than the diagnostic cut-off for HHS (320 mOsm/kg),[8] thus a diagnosis of HHS cannot be made in this case. However, due to a high plasma glucose level (36.8 mmol/L) and the presence of acidosis, the patient was in a hyperglycaemic emergency state.

Elevated fasting plasma glucose concentrations or carbohydrate intolerance may be present in patients with phaeochromocytoma, most commonly during paroxysms. Elevated plasma glucose level is associated with low plasma insulin level, the latter reflecting α-receptor-mediated suppression of insulin release. β-receptor-mediated stimulation of hepatic glucose output may also contribute.

This patient suffered severe vomiting and could not drink sufficient fluid to keep pace with the osmotic diuresis caused

by his hyperglycaemia. Impaired renal function reduces glucose loss via the kidney, further leading to elevation in blood glucose level.

As DKA and HHS can occur in both diagnosed and undiagnosed diabetic patients, it can also be complicated by hypertension and functional renal failure. Therefore, during the treatment of hyperglycaemia, underlying causes other than diabetes should be investigated.

When phaeochromocytoma is considered, appropriate approaches must be used for its diagnosis and localisation. Measurement of plasma metanephrine is the biochemical test of choice. A three- to four-fold elevation of plasma metanephrine is associated with nearly 100% specificity for the diagnosis of phaeochromocytoma in patients without renal failure.[9] When available, the measurement of plasma free metanephrine should be performed. In sporadic phaeochromocytoma, the test has a reported sensitivity of 99% and a specificity of 82%.[10]

Once phaeochromocytoma has been diagnosed, appropriate antihypertensive drugs are used to manage hypertension, control the associated cardiovascular symptoms and prepare the patient for surgery.

In conclusion, although uncommon, the diagnosis of phaeochromocytoma should be considered in patients with severe hypertension complicated by acute renal failure, acidosis and hyperglycaemia. □

References

1 Brouwers FM, Lenders JWM, Gisenhofer G, Pacak K. Pheochromocytoma as an endocrine emergency. *Rev Endocr Metab Disord* 2003; **4** (2): 121–8.

2 Isotani H, Fujimura Y, Furukawa AK, Morita K. Diabetic ketoacidosis associated with the pheochromocytoma of youth. *Diabetes Res Clin Pract* 1996; **34** (1): 57–60.

3 Takabatake T, Kawabata M, Ohta H *et al*. Acute renal failure and transient, massive proteinuria in a case of pheochromocytoma. *Clin Nephrol* 1985; **24** (1): 47–9.

4 Hamada N, Akamatsu A, Joh T. A case of pheochromocytoma complicated with acute renal failure and cardiomyopathy. *Jpn Circ J* 1993; **57** (1): 84–90.

5 Raman GV. Phaeochromocytoma presenting with cardiogenic shock and acute renal failure. *J Hum Hypertens* 1987; **1** (3): 237–8.

6 Crowe AV, Jones NF, Carr P. Five ways to be fooled by phaeochromocytoma – renal and urological complications. *Nephrol Dial Transplant* 1997; **12** (2): 337–40.

7 Rofougaran R, Mooraki A, Bastani B. Insulin-requiring diabetes mellitus, hyperlipidemia and anginal chest pains as prominent features of pheochromocytoma. *Am J Nephrol* 1997; **17** (5): 474–6.

8 Kitabchi AE, Umpierrez GE, Murphy BE, Kreisberg RA. Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care* 2006; **29** (12): 2739–48.

9 Lenders JWM, Pacak K, Walther MM *et al*. Biochemical diagnosis of pheochromocytoma: which test is best? *JAMA* 2002; **287** (11): 1427–434.

10 Raber W, Raffesberg W, Bischof M *et al*. Diagnostic efficacy of unconjugated plasma metanephrines for the detection of pheochromocytoma. *Arch Intern Med* 2000; **160** (19): 2957–63.

Bovine serum albumin reduces effects of endogenous inhibitors in transport media, facilitating real-time PCR detection of methicillin-resistant *Staphylococcus aureus* from screening swabs

J. P. McKENNA, G. M. HOGG, L. D MAXWELL, T. CURRAN and G. ONG

Belfast Health and Social Care Trust, Department of Microbiology, Grosvenor Road Belfast BT12 6BA, Northern Ireland, UK

Detection of methicillin-resistant *Staphylococcus aureus* (MRSA) carriers by conventional culture techniques requires at least 48 hours to complete, is labour intensive and frequently is a significant drain on laboratory resources. In contrast, real-time polymerase chain reaction (RT-PCR) technology offers 'same day' accurate identification of MRSA, representing a significant improvement in turnaround times.[1–4] Crucial steps for laboratory molecular diagnosis of MRSA include adequate collection and transport of various screening specimens available (e.g., anterior nares, perineum, groin), rapid and efficient release of target DNA, and elimination of potential PCR inhibitors.[5]

The vast majority of screening specimens sent for routine analysis to UK laboratories are collected on cotton-tipped swabs which are placed subsequently in a non-nutritive medium (e.g., Amies) and transported to the laboratory. Such collection systems are simple, cost-effective and easy to use, and it would be advantageous to retain this specimen collection format combined with efficient DNA preparation for rapid RT-PCR testing. However, it is known that swabs containing calcium alginate[6,7] and those with aluminium shafts[7] are inhibitory to PCR. Additionally, agar that survives the DNA preparation stage is known to suppress PCR amplification.[8]

In contrast to commercially available column purification extraction techniques (which theoretically provide samples containing the least amount of PCR inhibitory substances), simple bacterial lysis has the ability to provide bacterial target DNA rapidly for analysis, is cost effective and has high-throughput potential, making it an ideal choice for a busy diagnostic laboratory.[4,9]

During development of an in-house real-time SYBR Green 'dual locus' PCR assay targeting *nuc* and *mecA* genes, it was observed that after lysis of specimens a component of Amies transport medium was inhibiting PCR detection of MRSA, leading to false-negative results. An alternative approach to circumvent PCR inhibition is to enhance or facilitate PCR amplification.[10]

Reports indicate that addition of a suitable PCR facilitator such as non-acetylated bovine serum albumin (BSA) to RT-PCR mixes can relieve the effects of inhibition.[10–15] This study reports the use of non-acetylated BSA as a PCR facilitator, enabling the real-time detection of MRSA directly from clinical screening swabs.

Correspondence to: J. P. McKenna
Email: james.mckenna@belfasttrust.hscni.net