The significance of cystic adrenal lesions in multiple endocrine neoplasia IIB syndrome

F L S Tan, Y M Tan, D T H Lim

ABSTRACT

Cystic adrenal lesions are common, but cystic pheochromocytomas are rare. In the setting of a cystic adrenal mass in a patient with multiple endocrine neoplasia syndrome (MEN) IIB, the diagnosis of pheochromocytoma must be considered. We report a 29-year-old woman with typical phenotype of MEN IIB (marfanoid habitus, thick blubbery lips, mucosal ganglioneuromas) and a history of medullary thyroid carcinoma. She presented with headaches, palpitations and tremors. Computed tomography revealed a left cystic adrenal mass. The likelihood of the lesion being a pheochromocytoma was thought to be low due to its cystic appearance. However, urine ephinephrine and metanephrine levels were elevated. She underwent a left adrenalectomy and histological examination revealed a cystic pheochromocytoma.

Keywords: adrenal medulla, adrenal gland neoplasms, multiple endocrine neoplasia type IIB, pheochromocytoma

Singapore Med J 2004 Vol 45(10):494-496

INTRODUCTION

The multiple endocrine neoplasia (MEN) IIB syndrome is a rare, familial cancer syndrome inherited in an autosomal dominant fashion. It is characterised by medullary thyroid carcinoma (MTC) in combination with bilateral pheochromocytoma and skeletal deformities. The phenotypic appearance is pathognomonic of this syndrome: marfanoid habitus, thick blubbery lips, and multiple ganglioneuromas on the lips, tongue, face and eyelids. Cystic adrenal lesions on computed tomography (CT) are rare. They usually represent benign adrenal cysts or degenerative lesions, and are often an incidental finding. Pheochromocytomas rarely present as cystic masses and can be easily misdiagnosed. In the context of MEN II syndrome, cystic adrenal lesions have not previously been described. We report a case of a patient with MEN IIB presenting with symptoms of headaches and the CT finding of bilateral cystic adrenal masses. This serves to highlight the significance of cystic adrenal lesions in patients with MEN syndrome.

CASE REPORT

A 20-year-old Malay woman presented with complains of persistent headaches of one month duration. She had a history of MTC for which she underwent a total thyroidectomy and left compartmental nodal clearance eight years ago in another hospital. Post-operatively, she received five cycles of radiotherapy. Metastatic work-up was normal. She also had a history of childhood hip dysplasia for which she had bilateral osteotomies performed. Genetic analysis revealed a mutation in codon 916 on exon 16 of the *ret* proto-oncogene but no pathological mutations were present in her immediate family members.

On physical examination, her blood pressure was 90/60 mmHg without orthostatic changes. She had a marfanoid habitus, thick blubbery lips and multiple ganglioneuromas involving her lips, tongue and eyelids. These features were consistent with MEN IIB (Fig. 1). Rest of the physical examination was otherwise normal. CT of the neck, chest and abdomen showed a left cystic adrenal lesion measuring 4cm in diameter (Fig. 2). The probability of the mass being a pheochromocytoma was thought to be low as it was largely cystic in appearance. The right adrenal gland was normal. However, her 24-hour urine metanephrine was elevated at 10149 nmol/24hr (normal range: 400-1600 nmol/24hr), normetanephrine 5456 nmol/24hr (normal range: 600-1900 nmol/24hr), epinephrine 140 nmol/24hr (normal range: 0-109 nmol/24hr), norepinephrine 76 nmol/24hr (normal range: 89-473 nmol/24hr).

Based on her clinical symptoms and raised urinary metanephrine and normetanephrine levels, the possibility of a cystic pheochormocytoma was now considered. She underwent an open transabdominal left adrenalectomy after a one- week course of phenoxybenzamine. No intraoperative complications

Department of Surgery
Singapore General Hospital
Outram Road
Singapore 169608

F L S Tan, MBBS
Medical Officer

Y M Tan, MBBS, FRCS, FAMS
Associate Consultant

D T H Lim, MBBS, FRCS, FAMS
Senior Consultant

Correspondence to:
Dr Yu-Meng Tan
Tel: (65) 6321 4051
Fax: (65) 6220 9323
Email: gsutym@sgh.com.sg

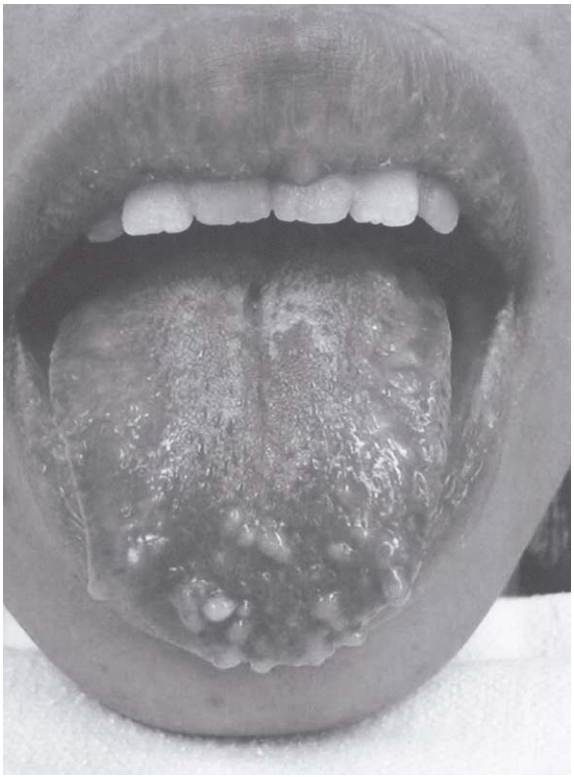

Fig. 1 Typical feature of MEN IIB. Clinical photograph shows multiple ganglioneuromas of the lips, tongue and face.

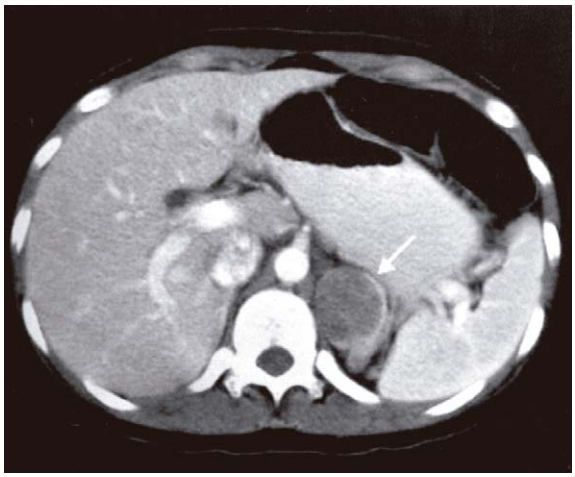

Fig. 2 Enhanced axial CT image shows a left cystic adrenal mass (arrow), proven on histology to be a pheochromocytoma.

were encountered. The histological examination confirmed the diagnosis of a pheochromocytoma with haemorrhage. There were no post-operative complications, and she did not require replacement therapy.

Her symptoms recurred four months after the initial adrenalectomy. A repeat CT of the abdomen now revealed a right adrenal cystic lesion measuring 2.6x2.0cm. 24-hour urine metanephrine and normetanephrine levels were again elevated at 8219 nmol/24hr and 4424 nmol/24hr, respectively. Surgical removal of the right adrenal gland was performed and histology confirmed a right cystic pheochromocytoma. She required replacement therapy (hydrocortisone and fludrocortisone) post-operatively and was well when discharged.

DISCUSSION

This case highlights the significance of cystic adrenal lesions in patients with the MEN syndrome. To our knowledge, this represents the first report in the literature of bilateral cystic pheochromocytomas occurring in the MEN syndrome. Several important lessons can be learnt to add to current knowledge on management of this condition. Firstly, the adrenal mass was largely cystic in appearance, unlike the typical solid, non-homogeneous appearance of pheochromocytomas. Most cystic lesions of adrenal glands represent endothelial cysts or pseudocysts that are benign in nature. Pheochromocytomas usually appear as large (>3cm), non-homogeneous, round or oval solid adrenal lesions, measuring more than 10HU on CT[1]. Cystic pheochromocytomas are unusual variants of adrenal pheochromocytomas. Reports of cystic pheochromocytomas exist[2-6] but none in association with the MEN syndrome. Necrosis or haemorrhage leading to cystic dilatation has been proposed to be the pathogenesis underlying cystic pheochromocytomas[7]. In our patient, histological examination revealed haemorrhage within the tumour.

Secondly, the presenting features were atypical and if the index of suspicion is not high, then the diagnosis could be missed or delayed. Our patient presented with headaches, which are non-specific, and there was no documentation of hypertension, but rather hypotension. Pheochromocytomas are adrenal medullary neoplasia that secrete catecholamines responsible for numerous symptoms, the most common of which are headaches, excessive perspirations a nd palpitations. Hypertension, whether paroxysmal or sustained, is characteristic and is present in up to 90%-95% of patients with pheochromocytoma. Our patient did complain of some of the above symptoms but did not have any episodes of hypertension pre-operatively. Cystic degeneration of the tumour could have led to loss of sustained secretive function and hence, the absence of documented pre-operative hypertension.

Finally, the surgical approach to our patient with familial pheochromocytoma needs to be carefully considered. The high incidence of bilateral pheochromocytomas in the natural history of the MEN II syndrome creates a dilemma for the surgeon regarding optimal treatment when a unilateral lesion is detected. The surgical options include:

unilateral adrenalectomy, synchronous bilateral adrenalectomy and subtotal adrenalectomy. These were traditionally approached via an open transabdominal or retroperitoneal incision. We choose to perform a unilateral adrenalectomy as only one gland was abnormal at the initial assessment. This avoids the potential risk of Addisonian crisis and reduces dependence on steroid replacement. After unilateral adrenalectomy, up to 50% of patients experience a long disease-free interval before development of metachronous pheochromocytoma[8]. Close clinical, biochemical and imaging surveillance will allow early detection of metachronous disease[9].

The contrary and more radical approach is to perform prophylactic synchronous bilateral adrenalectomy. This is because of the high incidence of bilateral disease (60%-80%), and risk of recurrence and metastases[10]. In an attempt to preserve adrenal cortical function, some centres perform subtotal adrenalectomy ("adrenal-sparing"), leaving behind the adrenal cortex or autotransplantation of adrenal cortical tissue into an easily accessible site. Lifelong surveillance is also warranted, as in unilateral adrenalectomy, to detect recurrent disease as early as possible. In our patient, we only undertook a unilateral adrenalectomy in the initial surgical resection. The time interval to involvement of the contralateral gland was short and on hindsight, she might have benefited from a bilateral approach. With recent advances in laparoscopic surgery, this approach can be considered in the management of this patient.

In conclusion, there should be a high index of suspicion for pheochromocytoma in patients with MEN syndrome presenting with radiological features of cystic change in the adrenal gland. Biochemical evaluation of urinary or plasma catecholamines and metanephrines, as well as clinical features, are useful in diagnosis.

REFERENCES

1. Lockhart ME, Smith JK, Kenney PJ. Imaging of adrenal masses. Eur J Radiol 2002; 41:95-112.
2. Grissom JR, Yamase HT, Prosser PR. Giant pheochromocytoma with sarcoidosis. South Med J 1979; 72:1605-7.
3. Falappa P, Mirk P, Rossi M, Troncone L, Butti A, Colagrande C. Bilateral pseudocystic pheochromocytoma. J Comput Assist Tomogr 1980; 4:860-2.
4. Bush WH, Elder JS, Crane RE, Wales LR. Cystic pheochromocytoma. Urology 1985; 25:332-4.
5. Munden R, Adams DB, Curry NS. Cystic pheochromocytoma: a radiological diagnosis. South Med J 1993; 86:1302-5.
6. Lembke T, Greenberg H. Cystic pheochromocytoma with inadvertent needle biopsy and glucagons administration. Can Assoc Radiol J 1987; 38:232-3.
7. Medeiros LJ, Lewandrowski KB, Vickery AL Jr. Adrenal pseudocyst: a clinical and pathologic study of eight cases. Human Pathol 1989; 20:660-5.
8. Neumann HPH, Berger DP, Sigmund G. Pheochromocytomas, multiple endocrine neoplasia type 2 and von Hippel-Lindau disease. N Engl J Med 1993; 329:1531-8.
9. Brunt ML, Lairmore TC, Dohety GM. Adrenalectomy for familial pheochromocytoma in the laparoscopic era. Ann Surg 2002; 235:713-20.
10. Proye CA, Nguyen HH. Current perspectives in surgery of MEN. Aust NZ J Surg 1999; 69:106-16.