Pheochromocytoma and haemophilia: an unusual combination

Jebasingh K F, Koshy TG, Paul T V, Paul M J, Abraham D, Viswabandya A

ABSTRACT

We report pheochromocytoma and haemophilia occurring in a 19-year-old South Indian man. To the best of our knowledge, this case is the first of its kind to be reported in the medical literature. The patient had bilateral adrenal pheochromocytomas with an extradrenal pheochromocytoma on the left side, and was successfully operated on after optimal preoperative blood pressure control and factor VIII support.

Keywords: bilateral adrenalectomy, factor VIII concentrate, haemophilia, pheochromocytoma

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INTRODUCTION

Pheochromocytoma accounts for up to 0.6% of the causes of hypertension.[1] Haemophilia occurs at a frequency of one in 10,000 males.[2] We report the occurrence of pheochromocytoma and haemophilia in a single patient.

CASE REPORT

A 19-year-old South Indian man, a known haemophiliac since birth, was referred with a two-month history of paroxysmal hypertension with associated headache, vomiting, palpitation and tremors of the hands. Preliminary workup at the local hospital included an elevated 24-hour urinary vanillyl mandilic acid (VMA) value and computed tomography (CT) imaging of the abdomen that revealed bilateral moderately-enhancing heterodense mass lesions of both adrenal glands. He revealed a history of episodic gum bleeds and excessive bleeding from sites of trauma. He had undergone evacuation of the haematoma in the left shoulder joint done under factor VIII coverage. His father had died seven years ago from uncontrolled hypertension, and had a suprarenal mass which was not evaluated at the time and may have been a pheochromocytoma. One of his two younger brothers, three of his maternal cousins and one maternal uncle were haemophiliacs.

On examination, he had a marfanoid habitus with eunuchoid body proportions. There was a single café au lait spot in the right lower back. Blood pressure during the first visit was 170/100 mmHg. Ocular examination revealed grade 3 hypertensive retinopathy and there was no retinal angioma or corneal nerve thickening. He had normal calcium and calcitonin – 5.56 (normal range 0–50) pg/ml, possibly ruling out MEN 2A. There was no other feature to support a diagnosis of neurofibromatosis or von Hippel-Lindau syndrome, of which pheochromocytoma can be a feature. His haematological workup showed a severe deficiency of factor VIII with levels of < 1% and the absence of an inhibitor to factor VIII. His prothrombin and platelet count were normal. His 24-hour urinary VMA values were 13.1/5,200 ml, 9.7/4,260 ml and 1.8/3,670 ml (normal range 1–8 mg/day). CT of the abdomen showed bilateral adrenal masses, with the right measuring 5 cm × 5 cm and the left a bilobed mass measuring 6 cm × 5 cm. (Fig. 1). Meta-iodo-benzo-guanidine (MIBG) scintiscan revealed bilateral adrenal pheochromocytomas. The left adrenal showed two areas of uptake and was thought to be due to an area of necrosis in the tumour (Fig. 2).

He was prepared for surgery with 14 days of alpha blockade with prazosin extended-release 10 mg twice daily, followed by beta blockade with metoprolol 12.5 mg twice daily. He was loaded with 14 g of oral salt and 3.5 L of water per day. His blood pressure was adequately controlled at the time of surgery. As his factor VIII levels were low preoperatively, he was given 2,500 units of factor VIII three hours prior to the surgery and was planned to have factor VIII maintained at 100% throughout the surgical procedure. A total of 15,750 units were administered in divided doses as subcutaneous injections over the next ten postoperative days to maintain the factor VIII levels at 100%. The surgical approach was debated and the open approach was chosen because of inadequate expertise on bilateral laparoscopic resections, complexity of the left adrenal tumour on imaging and financial constraints. Interestingly, perioperatively, there was a small left-sided extra-adrenal pheochromocytoma along with the bilateral adrenal pheochromocytomas. After the vessel ligation and tumour resection on the left side, there was a marked fall in blood pressure as expected. At this time, noradrenaline infusion was started. On the opposite side after manipulation and ligation of blood vessels with resection of the tumour, there was again an initial rise followed by a marked fall in blood pressure. At this time, adrenaline infusion was started. After bilateral adrenalectomy, the patient was sent to the surgical intensive care unit, where the adrenaline

Department of Endocrinology, Christian Medical College, Vellore 632004, Tamil Nadu, India

Jebasingh KF, MBBS
Senior House Surgeon

Koshy TG, MBBS, MD
Registrar

Paul TV, MBBS, MD, DNB
Consultant

Department of Surgical Endocrinology

Paul MJ, MBBS, MS
Consultant

Abraham D, MBBS, MS
Consultant

Department of Haematology

Viswabandya A MBBS, MD, DM

Correspondence to:
Dr K Felix Jebasingh
Tel: (91) 416 228 3118
Fax: (91) 416 420 3570
Email: felixjebasingh@msn.com

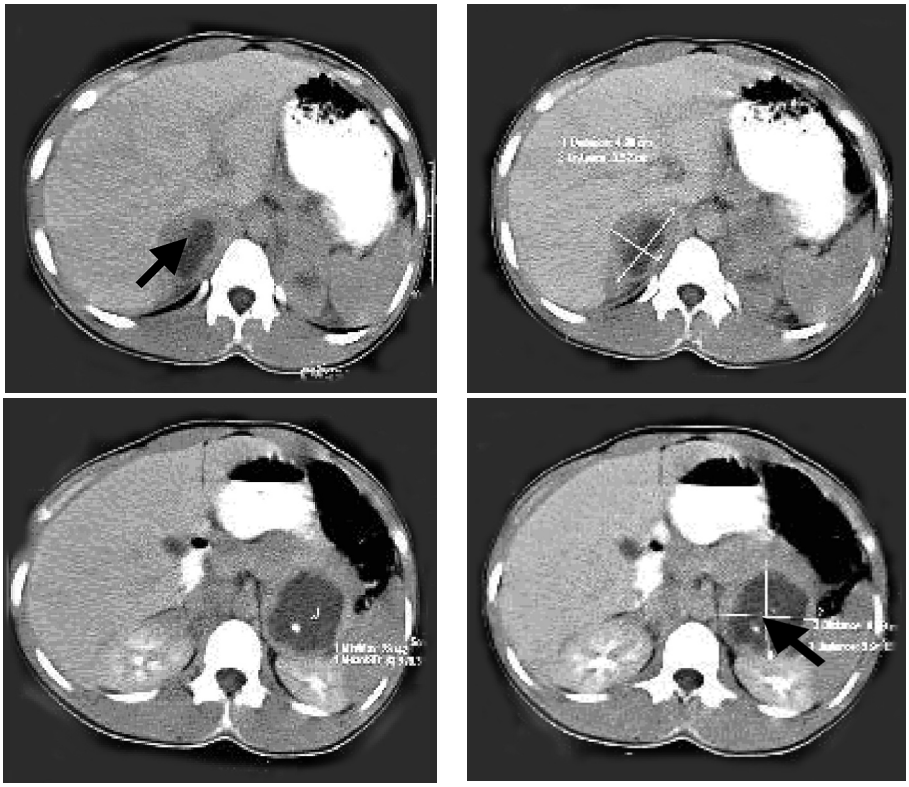

Fig. 1 Axial CT images of the abdomen show the tumour with necrosis and calcification (arrows).

and noradrenaline infusions were slowly tapered and stopped. He was then shifted to the ward after 48 hours. Intraoperatively, the estimated blood loss was about 1.2 L, which was made up of colloids, crystalloids and only 1 pint of whole blood. Postoperatively, his blood pressure normalised and he did not require any antihypertensive medication. Since he had a bilateral adrenalectomy, he was discharged on daily prednisolone and fludrocortisone medications along with hydrocortisone protocol in stressful situations.

DISCUSSION

Pheochromocytoma is very much a vascular tumour; the problem is compounded by the fact that the patient was a haemophiliac. This patient had one potential autosomal hereditary problem – pheochromocytoma (possibly part of MEN 2, although genetic studies were not done) and haemophilia – an X-linked disorder. This situation was handled by the diligent work and meticulous cooperation of endocrinologists, haematologists, endocrine surgeons and anaesthetists. The preoperative preparation of pheochromocytoma involves first establishing alpha adrenergic blockade to stabilise systemic blood pressure, expand intravascular volume and normalise myocardial performance.[3,4] Ideally, a non-competitive alpha blockade is given phenoxybonzamine 10–20 mg orally twice daily for 10–14 days.[5] Selective competitive alpha adrenoceptor blockade with prazosin has also been advocated.[6] Return to normotension facilitates an increase in intravascular volume, which should ideally cause a fall in haematocrit by 5%.[7] Beta blockade is instituted after complete alpha blockade. Induction of anaesthesia is done by intravenous etomidate. Volatile anaesthetic used is desflurane. Intraoperatively, in case of persisting systemic hypertension, there is a role for intravenous sodium nitroprusside infusion. Intravenous magnesium sulphate has been strongly advocated in James' study. Magnesium ions are thought to block the release of catecholamines from the normal adrenal medulla and from adrenergic nerve terminals.[8]

In our patient, thiopentone and 2% isoflurane was used for induction. Intravenous magnesium sulphate was given at 1 g/hour for a total of nearly 2.5 hours. Vecuronium was used as a muscle relaxant. The other special condition in this boy was haemophilia. Haemophilia is treated with factor VIII concentrate. The amount of factor VIII required depends on the plasma level of factor VIII needed to treat the specific bleeding episode – it must also be sufficient for the distribution of factor throughout the body and clearance from plasma.[9] In the case of major surgery, normal factor VIII must be maintained at around 100% during the perioperative and postoperative periods. During the induction of anaesthesia in haemophiliac patients, intramuscular

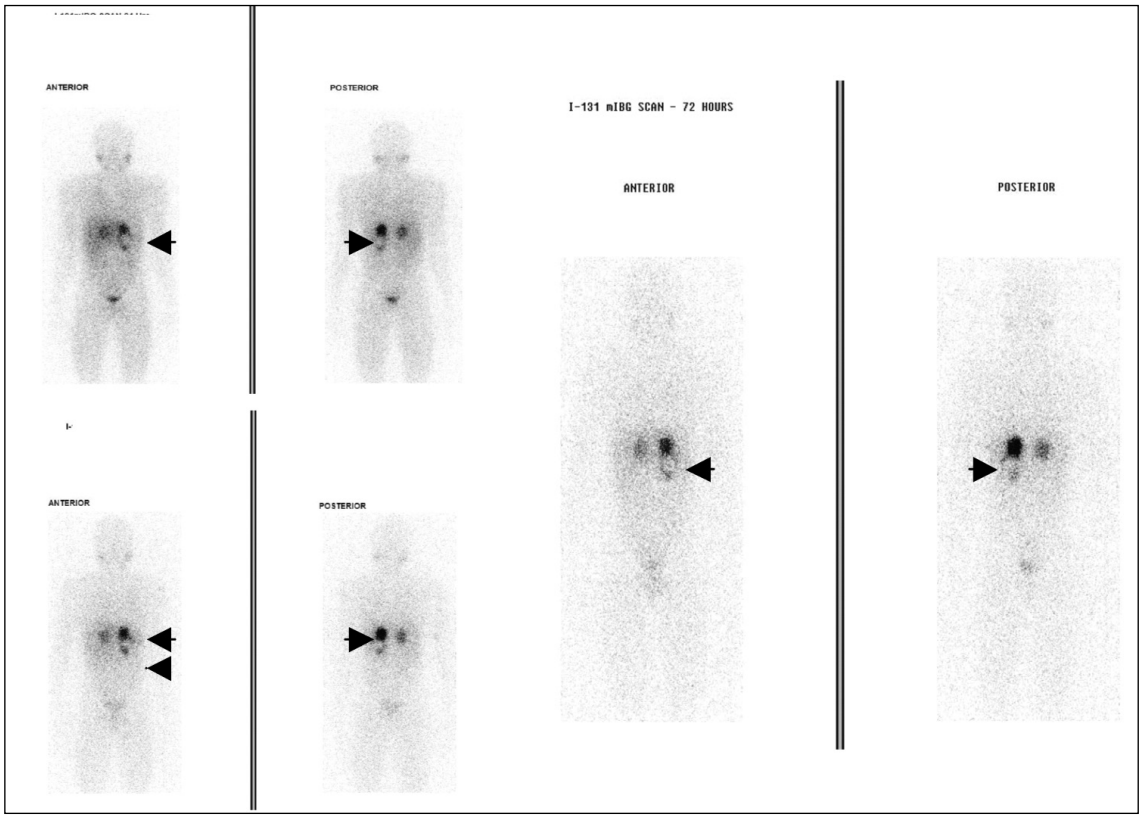

Fig. 2 MIBG scintiscans show bilateral increased uptake suggestive of bilateral pheochromocytomas. The arrows show the left side with two areas of uptake – the adrenal and extra-adrenal components.

injections are generally avoided.[10] Sometimes, tracheal incubation may result in haematoma in the surrounding structures.

Since the widespread availability of factor VIII concentrate, surgery in patients with haemophilia has become much safer, with operative mortality falling to below 1% and enabling complex elective procedures to be carried out.[11] Major abdominal operations such as gastrectomy, colectomy, splenectomy and cholecystectomy have been reported by single institutions with a low risk of morbidity related to bleeding and comparable to normal patients.[12,13] Hitherto, excision of a highly vascular tumour such as pheochromocytoma in a haemophiliac has not been reported. We place on record the performance of this complex operation by the open approach with no haemorrhagic complications. It remains to be seen if a laparoscopic approach would also be a safe option. Given the advantage of a less extensive incision and dissection coupled with the aid of magnification offered by laparoscopy, we would expect it to be well-suited to surgery in haemophiliacs. Although our patient had a family history of pheochromocytoma and haemophilia, genetic evaluation was not done as the appropriate technology was not available. However, blood was collected and stored for future genetic studies.

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