Anaesthetic management of a dopamine-secreting phaeochromocytoma in multiple endocrine neoplasia 2B syndrome

INTRODUCTION

Phaeochromocytoma, a rare neuroendocrine tumour that arises from the cells of chromaffin system, including the adrenal medulla and ganglia of the sympathetic nervous system, can occur sporadically or in conjunction with other endocrine tumours in multiple endocrine neoplasia (MEN) series.[1] Symptoms vary according to the predominant catecholamine secreted by the tumour.[1] Tumours that predominantly secrete norepinephrine (NE) usually present with hypertension, whereas tumours that predominantly secrete epinephrine (E) and dopamine (DA) may present with nonspecific symptoms. Tumours that produce predominantly or exclusively DA are rare.[2] Since hypertension is not a predominant feature of tumours secreting predominantly DA, the anaesthetic management of such patients is different from those secreting NE. We describe here the anaesthetic management of a DA-secreting phaeochromocytoma in a patient with MEN type 2B syndrome.

CASE REPORT

An 18-year-old female patient with growth retardation and primary amenorrhoea was referred to our centre for further evaluation after total thyroidectomy for the medullary carcinoma of thyroid. On pre-operative evaluation, she had no history of hypertension, palpitations, chest pain, sweating or chronic diarrhoea. Her weight and height were 38 kg and 155 cm, respectively. Neuromas were present on the upper lip, tongue, palate and buccal mucosa. Her hospital records showed a maximum blood pressure (BP) of 130/80 mmHg and a minimum of 100/70 mmHg. Her pulse rate was 80 beats/min and regular. All routine blood investigations were within the normal range. An abdominal computed tomography scan revealed an enlarged left adrenal gland with suspected bony metastasis in the lower thoracic and lumbar vertebrae. A well-mixed, 24-h urine sample showed an increased level of DA (1036 mg/day). Urinary E and NE were in the normal range (7.41 mg/day and 67.92 mg/day, respectively). Serum calcitonin was elevated (880 pg/ml). A diagnosis of MEN 2B syndrome was made, and a laparoscopic left adrenalectomy under general anaesthesia was planned. Her thyroid profile was normal.

Prazosin (3 mg b.d.) was started (inadvertently) 4 days prior to surgery and was stopped upon detection on the night before surgery. Thyroid hormone replacement was continued throughout the peri-operative period. Routine premedication in the form of ranitidine (150 mg) and lorazepam (1 mg) PO was given as per institutional practice. Standard non-invasive monitors were used. In addition, invasive arterial as well as central venous pressure monitoring lines were established.

Before the induction of anaesthesia, her BP was 110/80 mmHg. After adequate volume preloading with 15 ml/kg of normal saline, the induction of anaesthesia was performed with midazolam 1 mg, fentanyl 2 mg/kg and thiopentone 3 mg/kg. Endotracheal intubation was facilitated with vecuronium 0.1 mg/kg. Immediately after the induction, the BP dropped down to 60/48 mmHg, and did not respond to a fluid bolus of 200 ml of 0.9% saline. NE infusion was initiated at a rate of 0.15 mg/k/min, and the mean BP was restored to the pre-operative value in 150 s.

Using the anterior transperitoneal laparoscopic method, pneumoperitoneum was created with carbon dioxide gas insufflation at a rate of 4–5 L/min to a pressure of 12 mmHg. The pneumoperitoneum was maintained by a constant gas flow of 200–400 ml/min. Isoflurane (1–1.5%) and intermittent doses of fentanyl and vecuronium were used to maintain the anaesthesia. There was no significant haemodynamic alteration

during laparoscopy. The inotrope was gradually tapered, and later discontinued. The remainder of the intra-operative course was uneventful. Left adrenalectomy was performed. Upon extubation, the patient was shifted to post-anaesthesia care unit. Her BP during the post-operative period was 122/80 mmHg. Intravenous patient-controlled analgesia was used for post-operative pain relief with 40 μg/h fentanyl as a background continuous infusion and 40 μg as a bolus; with a maximum of 4 bolus doses per hour. A lock out period of 10 min was set.

Histological examination revealed a well encapsulated phaeochromocytoma of 1.0 cm × 0.8 cm × 0.8 cm size with adrenal hyperplasia. Two weeks after the surgery, the 24-h urinary DA levels returned to normal (570 μg). The patient was later discharged from the hospital with a yearly follow-up advice. Until date, the patient remains free from disease with no signs of recurrence or malignancy.

DISCUSSION

Multiple endocrine neoplasia type 2 can be classified into three subtypes: MEN 2A, MEN 2B and familial medullary thyroid carcinoma without any other endocrine manifestations (MEN 2C). While all three subtypes exhibit high risk for development of medullary carcinoma of the thyroid, MEN 2A and MEN 2B are increasingly associated with phaeochromocytoma (approximately 50%).[3] Phaeochromocytomas in patients with MEN 2 are usually discovered after the presentation of medullary thyroid cancer.

Most functional phaeochromocytomas usually secrete a combination of NE and E. Owing to deficiency of DA-β-hydroxylase, the enzyme that converts DA to NE, patients with DA-secreting tumours are frequently normotensive and have nonspecific symptoms. The absence of hypertension is assigned to the vasodilatory action of DA on the renal and mesenteric vasculature. Compared to NE and E, DA has poor alpha-receptor affinity. Pre-operative α-blockade, routinely used in NE-secreting tumours to prevent a hypertensive crisis during tumour manipulation, is not recommended for DA-secreting tumours. As there is little alpha-receptor stimulation, any alpha-receptor blockade in this context can result in severe hypotension and cardiovascular collapse due to the unopposed hypotensive action of DA. As evident from this case, the intra-operative hypotension in the patient is explained by excessive pre-operative alpha-blockade.

Although prazosin, a selective α_1-adrenoceptor blocker, has high clearance (4–5 ml/min/kg) and short elimination half-life (2–3 h), the residual alpha-receptor blockade effect can be potentiated by the accompanying vasodilatory effect of induction agents. The hypotension encountered could be managed with NE infusion. Nevertheless, the hypotensive effect of irreversible pre-operative α-blockade may persist for a longer duration (>24 h), and may be resistant to NE or E. As such, vasopressin may be helpful in such situations.[4] Metyrosine, a tyrosine analogue with no α-blocking effects, has been advocated in the treatment of DA secreting tumours as it inhibits tyrosine hydroxylase which converts tyrosine to dihydroxyphenylalanine (rate limiting step in the catecholamine synthesis).[5]

Two distinct classes of DA-receptors, D_1 (vasodilatation) and D_2 (inhibition of NA release from neurons), are functionally supposed to exist in the peripheral tissues.[6] D_1-receptor deficient mice have been shown to have elevated BP than the control mice, suggesting a hypotensive action of DA.[7] Diminished D_1-receptor activity has been described in patients with essential hypertension.[8] Persistent elevation of BP after the resection of DA-secreting tumours has been observed in certain instances, probably due to unopposed release of NA from postganglionic sympathetic neurons following the removal of the source of excess DA.[9]

Amid the various anaesthetic techniques that have been effectively employed for the resection of phaeochromocytoma, Prys-Roberts has suggested a technique comprising a mid to low thoracic epidural combined with adequate general anaesthesia, and selective adrenergic antagonists to control haemodynamic surges in response to tumour manipulation.[1] No regional technique was combined in this case; however, due to the potential risk of precipitate hypotension owing to pre-operative α-adrenergic blockade.

CONCLUSION

Dopamine secreting phaeochromocytoma can be asymptomatic and can be a part of MEN syndrome. Pre-operative alpha-blockade is unnecessary, and often hazardous in such tumours. NE infusion, if required, can be started at the time of induction to prevent a life-threatening hypotension.

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