

Perioperative Management in a Child with Familial Bilateral Pheochromocytoma

Saurabh Joshi*, Chetan Saraya, Shri Prakash Singh, Jasbir Singh Khanuja and Umesh Kumar Valecha

B L Kapur Super Specialty Hospital, New Delhi, India

Abstract: *Purpose:* Diagnosis and perioperative management of bilateral adrenal pheochromocytoma with a successful outcome is an apt combination of clinical knowledge and anaesthetic skills. Detailed history, meticulous physical examination, relevant laboratory investigations along with good preoperative pharmacological optimization and fluid resuscitation plays an important role in the perioperative period. Genetic testing and counseling should be offered to all the family members of patients suspected of familial predisposition. We report the anesthetic management of 10 year old male child with bilateral adrenal pheochromocytoma with family history of disease.

Clinical Features: A10-year old male, presented to our pediatric outpatient clinic with gradually increasing holocranial headache, blurring of vision, sweating, photophobia, progressive quietness in nature and poor performance in school, increased thirst and urine output for one week along with pain over bilateral lower limbs and difficulty walking without support for 20days. Parents also reported two episodes of generalized convulsions with one episode of opisthotonic posturing and up rolling of eyes, which was sustained for 50 min. Family history of three sudden deaths, and father, a known case of pheochromocytoma along with clinical presentation, raised the suspicion of familial pheochromocytoma.

Conclusion: Though pheochromocytomas are rare tumours, a high level of suspicion in paediatric age group, where patients don't present with classical symptoms, leads to early diagnosis and management and prevents catastrophic events. Young patients with bilateral disease and positive family history should be offered genetic testing. Preoperative catecholamine blockade and meticulous anaesthetic and surgical management are the keys to successful perioperative management of bilateral pheochromocytoma.

Keywords: Pheochromocytoma, Familial, Bilateral, Anesthetic management.

INTRODUCTION

Pheochromocytomas are the neuroendocrine tumors of chromaffin cell origin with a rare incidence of 2-8 cases per million [1, 2]. Patients usually present with signs and symptoms of sympathetic overstimulation. Detailed personal and family history along with radiological imaging helps in early diagnosis and treatment of this tumor. In this article, we report anesthetic management of a 9-year-old male presenting with seizures and headache diagnosed to have bilateral pheochromocytoma in subsequent investigations.

CASE REPORT

A 10-year-old male, presented to our pediatric outpatient clinic with gradually increasing holocranial headache, blurring of vision, sweating, photophobia, progressive quietness in nature and poor performance in school, increased thirst and urine output for one week along with pain over bilateral lower limbs and difficulty walking without support for 20 days; two episodes of generalized convulsions with one episode of opisthotonic posturing and uprolling of eyes, which was sustained for 50min. Family history of three

sudden deaths and father, a known case of pheochromocytoma along with clinical presentation, raised the suspicion of familial pheochromocytoma. Physical examination revealed heart rate of 122 beats per minute, with low volume, regular pulse and a blood pressure (BP) of 170/116 mm of Hg. Otherwise physical examination was unremarkable. Biochemistry reports including thyroid function tests, parathormone levels, and serum aldosterone and serum electrolytes were normal.

Ultrasound (USG) abdomen revealed a hypochoic nodular lesion measuring 3.5 * 2.9cm at left renal hilum. CT angiography revealed multiple nodular intensely enhancing lesions in right suprarenal region and intensely enhancing rounded lesion in left suprarenal region anterior to left renal vein with no evidence of renal artery stenosis, and a possibility of bilateral adrenal pheochromocytoma. USG neck was done to negate thyroid involvement. Nerve conduction velocity studies of bilateral lower limbs were normal. MIBG Scan showed increased uptake in bilateral adrenal glands. Urinary catecholamines confirmed the diagnosis (Epinephrine= 113.94 µg/g creatin, norepinephrine= 6598.51µg/g creatin, dopamine= 304.08µg/g creatin, VMA= 105.56 mg/g creatin). Free plasma normetanephrine was 2484pg/ml. Patient was started on oral Phenoxybenzamine 10mg thrice a day

*Address correspondence to this author at the B L Kapur Super Specialty Hospital, New Delhi, India; Tel: 011-30403040; E-mail: soshijo@gmail.com

and Amlodipine 10 mg once daily. Tablet Atenolol 12.5 mg two times daily was added one week later. With increasing control of BP and heart rate amlodipine was gradually withdrawn. After 14 days of treatment and achieving orthostatic hypotension (125-108/88-70mmHg) and volume expansion with fluid resuscitation, he was posted for laparoscopic pheochromocytoma excision. Stress response to adrenal stimulation was controlled by titrating nitroprusside infusions, boluses of intravenous diltiazem and labetalol. Maximum BP response was 220/110mmHg. With left adrenalectomy, a fall in blood pressure to 75/45 mm Hg was managed by titrating noradrenaline. Again, during manipulation of right adrenal gland, a surge in BP was noted. Noradrenaline was switched off and nitroprusside was switched on. After bilateral adrenalectomy, patient was switched back to noradrenaline infusion which was gradually tapered by the end of the surgery to put the patient off vasopressor. Blood sugar was monitored hourly. Injection hydrocortisone 50mg was given as a bolus dose. Patient was shifted to pediatric ICU, was later shifted to ward and then discharged home uneventfully with advice for regular follow up visits. His antiepileptics and Tablet Hydrocortisone 7.5 mg was prescribed as replacement therapy. In the initial 2 weeks after the surgery patient maintained a BP of 130-140/80-90mmHg which gradually reduced by third week to 110/70mmHg. Fludrocortisone was added in the third week. Histopathology report confirmed the diagnosis. Counseling for genetic analysis is done. Patient was followed for a month after surgery.

DISCUSSION

Pheochromocytomas and paragangliomas are neural crest cell tumors which originate from the chromaffin cells in adrenal medulla and parasympathetic/sympathetic ganglia, respectively [3]. With a reported incidence of pheochromocytomas of about 2-8 cases per million [1,2] and about 10-20% of these cases occurring in pediatric age group, treating a pediatric familial bilateral pheochromocytoma is an unusual and difficult task. These tumors are mostly associated with catecholamine production and therefore present with clinical symptoms of sympathetic over activity like the classic triad of episodic headache, sweating, and tachycardia [4, 5]. Pediatric patients, however, usually present clinically with sustained hypertension, slow mental activity, and poor performance in school or work instead of classical triad [2]. In our case, the patient presented with headache, blurring of vision, sweating, photophobia and history of

seizures, gradually decreasing performance at school. In 6-7% of cases, pheochromocytoma was found to be associated with familial syndromes [6]. Most of the pheochromocytoma in pediatric patients are benign, localized to their site of origin and are cured by surgical resection alone [7]. Though, childhood pheochromocytomas are bilateral and mostly form a part of a familial syndrome [3, 8] such as von Hippel-Lindau disease (VHL), multiple endocrine neoplasia (MEN2), neurofibromatosis, tuberous sclerosis and Sturge-Weber syndrome, and as a component of multiple endocrine neoplasia (MEN 2); in our case it was not found to be a part of any syndrome after thorough clinical examination and lab investigations. Genetic studies were refused by the patient's family due to financial reasons. Clinical presentation, family history of 3 sudden deaths, father having undergone a pheochromocytoma surgery, significantly high levels of catecholamines and their metabolites in blood and urine constituted the preoperative diagnosis of familial pheochromocytoma. Hypertension, sweating and headache suggest pheochromocytoma, with 91% sensitivity and 94% specificity [3]. Computed tomography (CT) scans and magnetic resonance imaging (MRI) has a sensitivity of 75%-100%, though with low specificity. The ¹³¹I-MIBG, (¹³¹I-Metaiodobenzylguanidine gammagraphy), in combination with platelet normetanephrin, has (100%) sensitivity. Positron emission tomography (PET) scan has a better image resolution using tracer (18-fluorodihydroxyphenylalanine), compared to MIBG, with a sensitivity reaching 100% [9, 10]. Plasma free metanephrines have a high sensitivity and specificity [11].

Timely diagnosis and management of pheochromocytoma prevents high catecholamine level related complications viz. myocardial infarction, cerebrovascular accident, renal injury, and arterial aneurysms [9]. Most critical factor in preoperative management is to achieve a good catecholamine blockade to reduce the hemodynamic instability during exaggerated catecholamine release at the time of tumor resection [12].

Catecholamines cause hemodynamic effects through α - and β -adrenergic receptors. α -effects cause arteriolar constriction leading to hypertension; and, diminished insulin secretion and enhanced gluconeogenesis and glycogenolysis leading to hyperglycemia. β effect increases cardiac contractility and heart rate. Subjects present mostly with weight loss due to high basal metabolism, and signs and

symptoms of sympathetic over activity. Differential diagnosis of pheochromocytoma includes other causes of hypertension like renal artery stenosis, coarctation of the aorta, and tumors like neuroblastoma. Sequential preoperative α -blockade followed by β -blockade and replenishment of intravascular volume through increased fluid intake helps in achieving fluid optimisation prior to surgery. β -blockade is contraindicated until effective α -blockade has been established to prevent unopposed α -adrenergic stimulation by catecholamine excess. Phenoxybenzamine, a nonselective alpha adrenergic blocker in doses up to 1mg/kg/day is used for alpha blockade. Adverse effects include reflex tachycardia and sedation, and the long half-life of the drug can lead to sustained hypotension after tumor resection. Prazosin and doxazosin are selective alpha-1 antagonists associated with less reflex tachycardia. Beta blockers, like metoprolol, atenolol and propranolol effectively prevents tachyarrhythmias due to high catecholamine levels [13,14].

In our patient 10 mg of phenoxybenzamine was given to the patient thrice followed by addition of atenolol 25mg and 12.5 mg in morning and evening respectively, aiming to generate orthostatic hypotension [15]. So the patient was on phenoxybenzamine, atenolol and amlodipine for 14 days, aiming for optimal blood pressure control prior to the surgery. Dosing was titrated according to his blood pressure readings, which were ranging between (125-108/88-70mmHg).

In the postoperative period, steroid and mineralocorticoid supplementation plays important role depending on whether adrenal cortex has been spared or not. In our patient, hydrocortisone was added in the immediate postoperative period followed by addition of fludrocortisone as total adrenalectomy was done. He will be monitored closely with biweekly visits initially and monthly and three monthly visits later on along with metanephrine studies and yearly PET studies [16]. Patient and his family have been instructed to report signs of catecholamine excess (diaphoresis, tachycardia, flushing, headache, and hypertension) to us as rapidly as possible should they develop between clinic visits. Genetic testing counseling to the patient's family is done on a regular basis [17, 18].

CONCLUSION

Though pheochromocytomas are rare tumors, a high level of suspicion in pediatric age group, where

patients don't present with classical symptoms, leads to early diagnosis and management and prevents catastrophic events. Young patients with bilateral disease and positive family history should be offered genetic testing. Preoperative catecholamine blockade and meticulous anesthetic and surgical management are the keys to successful perioperative management of bilateral pheochromocytoma.

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