ISSN: 2640-4133

Case Report

Advances in Bioengineering & Biomedical Science Research

Anaesthetic Management for Laparascopic Adrenalectomy for Pheochromocytoma as Part of Vonn Hippel-Lindau Syndrome in Child

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Submitted: 15 May 2021; **Accepted:** 19 May 2021; **Published:** 10 Jun 2021

Citation: *G Ivanova, MP Atanasova, G Todorov, K Grozdev, MN Khayat, A Elenkova, R Ivanova, S Zacharieva (2021) Anaesthetic Management for Laparoscopic Adrenalectomy for Pheochromocytoma as Part of Vonn Hippel-Lindau Syndrome in Child. Adv Bioeng Biomed Sci Res 4(2): 59-62.*

Abstract

Pheochromocytoma is a tumor that originates from either chromaffincells in adrenal medulla or in other paraganglia tissues (paragangliomas) of the sympathetic nervous system. It might be familial and associated with hereditary tumors such as Von Hippel-Lindau syndrome and multiple endocrine neoplasia type II. The symptoms are variable related to the level of secreted catecholamine. The most common are hypertension, tachycardia, headache and abdominal pain. The most effective treatment is surgical resection as in recent years, laparoscopic surgery has been more preferred. The perioperative management is quite challenging especially in view of hemodynamic fluctuations. Although there is a considerable amount of information on the management of the adult with phaeochromocytoma, much less has been written concerning children with the disease. We present a case of 9-year-old hypertensive boy with left sided pheochromocytoma, scheduled for excision of tumour. He had presented with complaints of pain in abdomen, excessive sweating, headache and raised blood pressure, as well as family anamnesis for von Hippel-Lindau syndrome (father with confirmed diagnosis). Diagnosis was confirmed by CT scan (abdomen), raised 24-hour urinary catecholamine levels and genetics tests. Preoperative blood pressure was controlled with prazosin (ά-adrenergic blocker). The anaesthetic technique used was general anaesthesia. Child was later discharged on oral antihypertensive.

Keywords: Pediatric hypertension, Pheohromocytoma, Laparoscopic adrenalectomy, Anaesthesia, von Hippel-Lindau Syndrome

Introduction

Phaeochromocytoma (PCC) and paraganglioma (PGL) are rare chromaffin cell tumours which secrete catecholamines and form part of the family of neuroendocrine tumours. They are responsible for 0.5– 2% of cases of secondary hypertension in paediatrics and although rare, are potentially lethal [1]. Phaeochromocytoma and paragangliomas (PPGLs) have a reported annual incidence of two to five cases per million, of which only 10% occur in children [1]. A phaeochromocytoma is a tumour arising from adrenomedullary chromaffin cells that commonly produces one or more catecholamines. A paraganglioma is a tumour derived from extra-adrenal chromaffin cells of either the sympathetic or parasympathetic ganglia. PPGL and PCC may occur as sporadic tumours but may also develop as part of hereditary tumour syndromes reflecting mutations in at least 14 different tumour susceptibility genes. PCC and PGL are inherited in as much as 80% of pediatric cases, and all patients with mutations should be followed closely given the risk of recurrence and malignancy [2]. Major syndromes associated with PPGL include: Multiple endocrine neoplasia (MEN) type 2A and 2B, Neurofibromatosis type 1, Von Hippel-Landau type 2, Carney's triad, The paraganglioma-phaeochromocytoma syndromes involving succinate dehydrogenase gene mutations [1].

The average age at presentation of PCCs and PGLs in paediatrics is 11–13 years, with a male: female ratio of 2:1 [1]. The clinical presentation is variable but sustained hypertension is seen in 60–90% of cases [1]. Patient may present with the classic triad of headaches, palpitations and sweating as well as other symptoms of catecholamine excess such as nausea pallor, tremor, anxiety or other behavioural problems and syncope. Nonspecific symptoms

include blurred vision, abdominal pain, gastrointestinal symptoms, hyperglycemia, polyuria, polydipsia, low-grade fever.

Initial biochemical tests are done to establish and confirm excess secretion of catecholamines and/or their metabolites. This is followed by radiographic studies to identify the location of the tumour. In the paediatric population thorough imaging is particularly important due to the increased incidence of multifocal, extra-adrenal and metastatic tumours. The excessive production of catecholamines is metabolized in the tumor by catecholo-methyl transferase to metanephrins which can be measured in the plasma. They have a sensitivity of 99% (negative tests rule out pheochromocytoma) and should be carried out as the first test in patients with clinical symptoms. The 24 h urinary metanephrins has been found to have high sensitivity (97%) for pheochromocytoma. The product of normalised metanephrin and normetanephrine (100% sensitive and 99% specific) and serum chromogranin A have also been purpose used for diagnostic [3]. The initial radiographic test of choice is cross-sectional imaging of the abdomen and pelvis using either CT or MRI which have similar diagnostic sensitivities. MRI may be preferable in the paediatric population due to the radiation exposure with CT. Functional testing using nuclear scintigraphy with I-labeled metaiodobenzylguanidine (MIBG) is a highly specific test that can confirm the catecholamine-secreting nature of a tumour as well as localise tumours not seen with cross-sectional imaging and may identify other sites of disease. It may be indicated in certain cases [1]. Since the inheritance rate of such tumors is higher than previously described, genetic screening is recommended in all patients, and lifelong follow-up for recurrent tumors is a must [2].

Surgical excision of the tumor, either open laparotomy or laparoscopy, is the definitive management. Laparoscopic adrenalectomy has been increasingly employed to treat adrenal tumors since first reported in 1992 [4]. A laparoscopic approach offers several advantages compared with an open laparotomy such as decreasing fluid shifts that may accompany an open procedure, potentially decreasing the surgical stress imposed on the patient, decreasing the need for postoperative analgesia, shortening postoperative convalescence including an intensive care unit stay, and decreasing the overall hospital stay [5]. The Endocrine Society Clinical Practice Guidelines recommends minimally invasive adrenalectomy (laparoscopic) for most adrenal phaeochromocytomas [6].

Perioperative management of pheochromocytoma is challenging and requires multidisciplinary approach for optimal care and successful outcome. Adequate preoperative evaluation and management of these patients is crucial before surgery and has led to a remarkable reduction in perioperative mortality over the last 60 years. The surgical mortality associated with catecholamine secreting tumours is now of the order of 0–3% [1]. Given the rarity of neuroendocrine tumours in pediatric and even in adult patients, there are no randomized controlled trials looking at the various therapeutic options. The objectives of preoperative preparation include: Arterial pressure control; Reversal of chronic circulating volume depletion; Heart rate and arrhythmia control; Assessment and optimisation of myocardial function; Reversal of glucose and electrolyte disturbances.

Standard practice for preoperative arterial blood pressure control is preoperative α - blockade and is commenced at least 7–14 days prior to surgery. Commonly used α-blockers include phenoxybenzamine, doxazosin and prazosin. In paediatric patients the goal is a blood pressure reduction to <50 percentile for age and height.

Chronic catecholamine excess leads to a contracted intravascular volume. In addition to pharmacological control, a high sodium diet and increased fluid intake are indicated to restore normal circulating blood volume. Fluid intake of at least 1.5 times maintenance rates is suggested in the preoperative period.

A tachycardia may be the result of an epinephrine- or dopamine secreting tumour or may be a reflex tachycardia secondary to α2-receptor blockade. The choice and timing of β-blockade is important1 Children with a catecholamine induced cardiomyopathy present with a wide spectrum of clinical severity. They may not display any signs or symptoms except for perhaps palpitations or arrhythmias [5]. It is therefore crucial that a thorough search for any evidence of cardiac dysfunction is performed pre- operatively. An ECG may reveal ventricular hypertrophy, tachyarrhythmias or myocardial ischaemia. Echocardiography is considered mandatory. Making the diagnosis of a cardiomyopathy is important for several reasons: There is an increased morbidity and mortality in these patients, the myocardial dysfunction may be reversible, the diagnosis has important implications for the child's subsequent management including the anaesthetic technique and intraoperative monitoring. A significant number of children with PPGL and PCC will be found to have abnormalities of glucose tolerance. All children should therefore have at least a random blood glucose test and, if indicated, a fasting blood sugar or glucose tolerance test performed. Electrolyte measurements are necessary to identify catecholamine-induced renal impairment. Cases of severe hypokalemia, due to hyperreninaemia and secondary hyperaldosteronism have been reported in children with PPGL and PCC [1].

Intraoperative monitoring includes ECG, pulse oximeter, capnography, temperature probe, arterial line, CVP.

Case report

A 9-year-old boy was admitted in endocrinology clinic with complaints of high BP – up to 160/100 mmHg, and periodically fevers without any other signs of infections. A week before admission, when complaints occurred, an abdominal ultrasonography revealed a rounded formation above right kidney. His father is diagnosed with Von Hippel – Lindau syndrome (VHLS) de novo mutation in VHL gene, repeated occurrence of Pheochromocytoma/Paragangleoma (PCC/PGL) and multiple surgeries. Urinary catecholamine concentration was measured – Normetanephrine

3985 ng for 24 hours (ref – up to 600 ng). MRT was performed – rounded formation above right kidney, connected with adrenal gland, size – 2.8x2.5 sm. Molecular - genetic analysis – mutation c.499C>T,p.Arg167Trp in VHL gene. Patient was diagnosed with right sided PCC within VHLS. The decision of surgery was reached and preoperative therapy with α-blocker - doxazosin 1 mg twice daily, was started. The laparoscopic adrenalectomy was scheduled in 3 weeks.

Pre-operative medical exam revealed – weight 37 kg, height 145 sm, BP 120/80 mmHg, HR – 75 min- 1. Other investigations - complete blood count, plasma glucose, urea, electrolytes were, within normal limits. ECG and echocardiography were normal. He was kept nil orally for 6 hours on maintenance fluid therapy to avoid dehydration and morning doses of oral antihypertensive were continued. Early premedication – 20 mg of Omeprazole the night before surgery and in the morning of surgery. Standard monitors were attached – SpO2, NIBP, ECG. His pre-operative HR 85 min-1, BP 124/68 mmHg, SpO2 100%. Two peripheral intravenous cannula 20 and 24 gauge was established and Midazolam 0.08 mg kg-1, Atropine – 0.02 mg kg-1, Lidocaine 0.5% - 1.5 mg kg-1, Fentanyl 0.8 μg kg-1, Methylprednisolon mg kg-1 were administrated i.v. as immediate premedication. Vasodilators and inotropes were kept ready. After preoxigenation anesthesia was induced with Propofol 4.5 mg kg-1 and Atracurium 0.5 mg kg-1. The trachea was intubated with 6.0 mm cuffed tube. Postinduction vitals-BP 130/70 mmHg, HR 90 min-1. Urinary catheter was placed and right internal jugular vein was cannulated. The anaesthesia was maintained with Sevoflurane 2.6 vol% in Oxygen, intermittent doses Fentanyl (in total 0.03 μg kg-1 h-1 with premedication) and Atracurium 0.15 mg kg-1. Postoperative nausea and vomiting were prevented with Dexamethason 4 mg i.v and Ondansetron 2 mg i.v administrated immediately after induction. There were no significant blood pressure fluctuations after placing the patient at left lumbar position, dissection and tumor manipulation. Clipping of vena centralis led to fall of BP, restored with crystalloids, colloids and norepiniphrin infusion - 8-24 μg min-1. Total fluids infusions were 800 ml of crystaloids and colloids. Urine output was estimated as 2.7 ml kg-1 h-1 at the end of procedure. Analgesia was achieved with Acetaminophen 13 mg kg-1 i.v. three times daily, Tramadol 1 mg kg-1 i.v. and Lidocain 0.5% infiltrated into the port site. At the end of surgery, the vitals were stable on norepinephrine infusion at 0.02 μg kg-1 min-1. Patient was extubated and transferred to ICU for strict monitoring of BP and blood glucose concentration. Norepinephrin infusion was interrupted after the transfer to ICU on stable BP, HR and blood glucose level. On first postoperative day patient was discharged from ICU. Five days after surgery child was hemodynamically stable without any medications, discharged and called for follow up a month after surgery when presented with normal BP, normal metanephrines concentrations, without any symptoms of hypocortisolism.

Discussion

Pheochromocytoma is a rare condition, especially in children. Some big centers for children health and pediatric surgery in Europe, Asia and North America report less than a single case per year 4,7,8,9. The large number of cases in children is as part of hereditary tumor syndromes as MEN type 2A and 2B, Neurofibromatosis type 1, Von Hippel Lindau syndrome as in the reported case. Pheochromocytoma is a potentially curable cause of secondary hypertension in pediatric patients. Hypertension due to pheochromocytoma in children tends to be more sustained rather than paroxysmal in adults. Clinical manifestations are seen due to release of epinephrine and norepinephrine resulting in constriction of arteriolar and venous segments as the predominant catecholamine in children is norepinephrine Other common symptoms are headache, palpitations, sweating, abdominal pain, hyperglycemia, weight loss. Diagnosis is usually confirmed by raised urinary catecholamine levels and their metabolites and measurement of 24-hour free urinary catecholamine is the best confirmatory test. Localisation of tumour is accurately done by CTscan, MRI, MIBG. The definitive treatment of PCC is surgical excision with preferences of laparoscopic adrenalectomy [6]. Despite many advances, there is no specific anaesthetic protocol and consistent recommendations from the literature for pheochromocytoma management. Most authors, working on the problem, recommend strict preoperative preparation, including arterial pressure control with α blocker, reversal of chronic circulating volume depletion, heart rate and arrhythmia control, assessment and optimisation of myocardial function, reversal of glucose and electrolyte disturbances. In our case patients was prepared with Doxazosin for arterial blood pressure control, ECG revealed no arrhythmia, Echocardiography was normal as well as laboratory tests.

Intraoperative management is based on close monitoring including ECG, NIBP and/or IPB, pulse oximetry, capnography, temperature, urinary output, and vascular access - CVC, large bore peripheral venous access. Goals of anaesthetic management should aim at avoiding drugs or maneuvers which produce a catecholamine surge - stress, anxiety, pain, hypoxia, hypercarbia, providing optimal surgical conditions and suppression of the responses to endotracheal intubation with deep plane, surgical stimulation, tumour handling and devascularisation, maintain cardiovascular stability with short acting drugs, maintain normovolemia and hemodynamics after tumour resection. We used as premedication Midazolam i.v., Lidocaine 0.5% i.v., Fentanyl i.v., Atropine i.v.. Monitoring in our case was per recommendations except arterial line and invasive blood pressure. CVC and 2 large bore peripheral cannula were established. The preferred agents for induction were propofol and atracurium. Sevoflurane was used because it doesn`t sensitize the heart to catecholamines. Fentanyl was used for intraoperative analgesia while tramal and acetaminophen were administrated for postoperative analgesia. Vasodilators and inotropes were kept ready. We met no need for using vasodilatators or β-blockers during surgery. After removing the tumor, a short infusion of norepinephrine was administrated. Laparascopic retroabdominal right adrenalectomy was performed. The anaesthesia, we performed, and postoperative period went uneventful. Our ap-

proach was similar to quoted authors and in maximum conformity with pathopfisiological mechanisms of PCC and with this particular patient. Long-term follow-up on patients with hereditary PCCs cannot be stressed enough given the lifelong risk of recurrence and metastatic disease. Laboratory testing with serum/urine metanephrines should be performed yearly and patients should undergo imaging studies intermittently and as clinically indicated based upon symptoms and/or positive laboratory testing at follow-up visits. Smaller pediatric and adult case series recommend follow- up at 6 weeks and between 6 months and 1 year following initial surgery, then annually [2]. The follow- up of our patient was performed 5 weeks after surgery, revealed normal catecholamine levels.

In conclusion the anesthesia and postoperative period in our patient were uneventful, based on strict pre-operative preparation, deep multimodal anaesthesia, achieved with drug`s doses estimated in advance and close monitoring of NIBP, HR, cardiovascular volume and blood glucose concentration. We consider our approach successful [7, 8].

Acknowledgements related to this Article

Assistance with the letter: none

Financial support and sponsorship: This article is published with the financial support of Medical University Sofia.

Conflicts of interest: none

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