

Anaesthetic management of laparoscopic assisted bilateral adrenalectomy in a five-year-old child with Cushing's disease

Saffin AP, BSc, MBBCh, DA(SA), Registrar, Walter Sisulu University

Thomas JM, BSc, MBChB, FCA(SA), Paediatric Anaesthetist, Head of Clinical Unit
Red Cross War Memorial Children's Hospital, University of Cape Town

Correspondence to: Andrew Saffin, e-mail: andrew.saffin@gmail.com

Keywords: Cushing's disease, adrenalectomy, laparoscopy, obesity, anaesthesia

Abstract

A five-year-old girl, weighing 42 kg and with a diagnosis of Cushing's disease, presented for bilateral, laparoscopic adrenalectomy.

© Peer reviewed. (Submitted: 2011-04-13. Accepted: 2011-10-07.) © SASA

South Afr J Anaesth Analg 2011;17(6):396-399

Introduction

Cushing's syndrome is characterised by an abnormally high concentration of circulating corticosteroids, and may be caused by injudicious corticosteroid administration, an adrenal tumour, or excessive and uncontrolled stimulation of the adrenal glands by corticotrophin. The latter is known as Cushing's disease, and is due to an overproduction of corticosteroids in response to increased concentration of circulating adrenocorticotrophic hormone (ACTH), produced by a basophilic adenoma of the pituitary gland.¹ Excessive circulating levels of corticosteroids result in characteristic pathophysiological changes that present a range of problems to anaesthetists who are called upon to care for such patients. In this case report, we discuss the preoperative management of such a patient, highlighting the potential and actual problems that we encountered, and how we dealt with them.

Case report

A five-year-old girl was referred to the endocrine clinic with suspected Cushing's syndrome, on the basis of a two-year history of rapid weight gain, poor linear growth, elevated urinary cortisol, and a high, unsuppressed plasma cortisol following a low-dose dexamethasone suppression test. She was noted to have been born at term, via forceps delivery, with a birth weight of 2.5 kg. Her development was normal until her parents noted that, from the age of two onwards, she started to gain weight rapidly.

On presentation to Groote Schuur Hospital, she had the classic signs of Cushing's syndrome: central obesity, moon facies, buffalo hump, abdominal striae and acanthosis nigricans. She weighed 38 kg, with a blood pressure of

145/90 mmHg. She was admitted for further investigations, including a high-dose dexamethasone suppression test, a corticotrophin-releasing hormone (CRH) stimulation test and imaging studies. The results of these tests (Tables I and II) confirmed a diagnosis of Cushing's disease due to microadenomas of the pituitary gland. The pituitary pathology was not deemed operable, as there were multiple small adenomas present. As a result, she was booked for laparoscopic bilateral adrenalectomy. Amlodipine, 2.5 mg twice daily, for blood pressure control, was started.

Anaesthetic management

The patient was seen the day before surgery on a preoperative visit, and was noted to have obvious Cushingoid features, but apart from that, was systemically well (Figure 1). Her blood pressure was 140/90 mmHg and her weight charted at 42.7 kg, representing a gain in weight of 4.2 kg from her presentation six months prior. Airway assessment revealed a normal mandible, but with limited mouth opening, and a Mallampati score of 4. Her neck, while mobile, was not visible because of excessive soft tissue under the chin and upper chest wall. She also had a buffalo hump. In light of these findings, a difficult airway was anticipated with oropharyngeal airways, different laryngoscope blades, laryngeal masks and gum elastic bougies close at hand. On closer questioning of her parents, it was apparent that she was most comfortable lying in a semi-recumbent position at night, and that she did snore when asleep, with occasional spells of apnoea. Examination of her cardiovascular system did not reveal any signs of pulmonary hypertension or cardiac failure. Her respiratory examination was normal. All blood investigations were normal. Specifically, the serum sodium and potassium were normal, and her blood glucose

Table I: High-dose dexamethasone suppression test

Date and time	Plasma cortisol	Plasma ACTH
Day 1: 08h00	492	7.0
Day 2: 08h00	630	Inadequate sample
Day 3: 08h00	228	4.9

These results confirmed a diagnosis of pituitary Cushing's disease, as there was suppression of cortisol and ACTH secretion. This does not occur with adrenal Cushing's, or with ACTH-dependent disease.²

Table II: Corticotrophin-releasing hormone (CRH) stimulation test

Time of blood sample	Plasma cortisol	Plasma ACTH (1.6-13.9 mmol/l)
05h30	863	5.6
09h15 (CRH 1 µg/kg intravenously)	1 013	2.3
09h30	1 147	10.6
09h45	1 518	44.0
10h00	1 488	59.2
10h15	> 1 750	60.3
10h30	> 1 750	49.1
11h00	> 1 750	21.2
11h30	1 497	13.8

These results demonstrate the effect of exogenous CRH on the pituitary, with a corresponding increase in both ACTH and plasma cortisol. This confirms the diagnosis of Cushing's disease.

was 5.8 mmol/l. Premedication of 10 mg midazolam to be taken orally was ordered for the morning of surgery.

On the morning of surgery, the patient was brought to the operating theatre with her mother. Basic monitoring was attached, including electrocardiogram (ECG), pulse oximetry and non-invasive blood pressure (NIBP). As an intravenous cannula was in situ, induction of anaesthesia with propofol (2 mg/kg) was carried out, after initial preoxygenation. Once it was confirmed that bag-mask ventilation was possible, anaesthesia was deepened with sevoflurane 6% in oxygen and her vocal cords visualised and sprayed with 2 ml 2%

lignocaine. A size 5.5 cuffed oral endotracheal tube was placed uneventfully, its position confirmed, and secured at 17 cm at the lip. Anaesthesia was maintained with isoflurane 1.2% in air and oxygen (50%) and muscle relaxation was achieved with a 4 mg intravenous bolus of cisatracurium, followed by an infusion of 0.1 mg/kg/hour. As per the advice of an endocrinologist, the patient received a bolus of 40 mg (1 mg/kg) of hydrocortisone soon after induction. A second large bore (20G) intravenous cannula was placed peripherally in her hand. A 22G, right radial intra-arterial catheter was inserted, in a sterile manner, for intraoperative invasive blood pressure monitoring. Further monitoring included end-tidal CO₂ and core temperature via an oesophageal temperature probe.

Following insertion of the intravenous and arterial cannulae, the patient was turned into the left lateral position, and under strict aseptic conditions, an 18G epidural catheter was placed in the midline at L3/L4 level, and secured with a depth of 3 cm in the epidural space. A bolus of 5 ml of 0.25% bupivacaine with 20 µg clonidine was given, following a negative test dose of 2 ml 1% lignocaine. Three more boluses of 5 ml 0.25% bupivacaine were given, at hourly intervals, before an infusion of 0.2% bupivacaine at 5 ml/hour was started. The patient was positioned in the left lateral position for the right-sided adrenalectomy (Figure 2), before being turned into the right lateral position for the left-sided adrenalectomy. Every effort was made to ensure that pressure points were adequately padded, and her eyes were taped closed.

After an initial intravenous bolus of Ringer's lactate 10 ml/kg over 10 minutes, her blood pressure was well maintained throughout, with mean arterial pressures ranging from 65-90 mmHg. Blood glucose was measured at 6.2 mmol/l soon after induction of anaesthesia, and this climbed to 9.4 mmol/l by the end of surgery. No insulin was administered intraoperatively. Of concern was that her core temperature dropped to 34.8°C over the first two



Figure 1: Typical Cushingoid features apparent at preoperative visit



Figure 2: Patient positioned in left lateral position for right-sided adrenalectomy

hours. This was due to the patient's size not being taken into account when she was positioned on the forced air warmer. It was too small, and should not have been placed underneath the patient, but rather on top of her. Halfway through the procedure, when she was turned into the right lateral position to gain access to the second adrenal gland, an over-body warmer was placed, and by the end of surgery, 90 minutes later, her temperature had risen to 35.8°C.

Surgery was largely uneventful. Access to the adrenal glands was gained laparoscopically via a lateral transabdominal approach, using CO₂ to insufflate the abdomen and keeping intra-abdominal pressures below 15 mmHg. Surprisingly, there was a minimal drop in blood pressure with insufflation, perhaps due to the initial fluid bolus that was administered.

At the end of surgery, volatile anaesthetics were discontinued, the neuromuscular relaxation was reversed with neostigmine 0.05 mg/kg, co-administered with glycopyrrolate 0.01 mg/kg, and only when she was awake, and able to maintain her own airway, the patient's trachea was extubated. She was propped up on bolsters to keep her in her most comfortable preoperative positioning (Figure 3). In this way, she maintained her own airway adequately, and saturations were 98% on nasal prong oxygen at 2 l/minute. She was transferred to the intensive care unit (ICU) for further management and did very well, remaining there for two days. Epidural analgesia was continued via infusion while in the ICU, at a rate of 5 ml/hour 0.2% bupivacaine. She reported discomfort only from one of the port sites not covered by the block at approximately T8 level. This was managed well with simple analgesics. She was discharged from hospital five days postoperatively for further follow-up under the endocrinologist's care.

Discussion

Patients with Cushing's syndrome and Cushing's disease present a multitude of challenges for the anaesthetist. The



Figure 3: Patient propped up on bolsters after surgery, in most comfortable preoperative position

classical problems of glucose intolerance, hypertension, electrolyte abnormalities, susceptibility to infection, and obesity with attendant airway problems are well described, and indeed were evident in our patient.¹ In light of this, we planned our anaesthetic management to ensure optimal care for our patient, including anticipation of a difficult airway, strict aseptic technique for invasive procedures, regular monitoring of blood glucose, and close attention to positioning.

Cortisol promotes protein breakdown and gluconeogenesis in the liver, and antagonises the effects of insulin. This action maintains normal blood glucose during fasting. Cortisol also displays a weak mineralocorticoid effect.³ The effects of excessive circulating levels of corticosteroids therefore results in glucose intolerance, and may lead to the development of type 2 diabetes. Electrolyte changes include sodium retention and potassium loss, with a resultant expanded extracellular volume and hypertension.²

Fortunately, on her preoperative workup, our patient did not display evidence of overt glucose intolerance, nor any obvious electrolyte abnormalities. However, plasma glucose and electrolytes were checked hourly throughout the surgical procedure, and we were prepared to correct any abnormalities.

Cortisol maintains a low-level anti-inflammatory state in the body, and when present in excess, has a powerful anti-inflammatory and immunosuppressive effect, inhibiting pain, swelling, cellular immunity, wound healing and repair.⁴ This results in an overall predisposition to infection and poor surgical wound healing. In light of this, all invasive procedures relating to the anaesthetic, such as epidural placement and intra-arterial cannulation, were carried out under strict aseptic conditions.

Especially in long cases (four hours and 45 minutes here), body temperature maintenance is an issue for all patients undergoing anaesthesia. A fall in body temperature results in undesirable physiological changes, including myocardial irritability, platelet dysfunction, prolonged neuromuscular blockade, and a predisposition to infection. In this incidence, the body temperature fell below 35°C, putting the patient at risk of myocardial contractility dysfunction, arrhythmias and clotting abnormalities.⁵

The combination of thin skin, hypothermia and obesity puts the patient at risk of developing pressure sores. The positioning of these patients needs to be meticulous when they undergo anaesthesia. All potential pressure points in our patient were padded with Gamgee® pads and silicone supports. In older patients with Cushing's syndrome or disease, in the light of potential osteoporosis and the risk of long bone fractures during positioning, care must also be taken.

Obesity is one of the pathognomonic signs of Cushing's syndrome, and has far-reaching consequences for the anaesthetist. Of great concern is the effect on the cardiovascular system, as these patients are at risk of obstructive sleep apnoea, with resultant pulmonary and cardiovascular disease. Therefore, a detailed cardiovascular history and examination is essential, and depending on these findings, further investigation may be required. Obesity can also make intravascular access a problem. In our case, peripheral cannulation was easy, but taking into account the anatomy of the neck and the groin, we elected not to insert a central venous cannula. This was due in part to technical difficulty with insertion, and in part to minimise the risk of line sepsis.

Compounding all of the above problems was the fact that the surgery was to be carried out laparoscopically. This added another dimension to some of the problems that we potentially faced. These included difficulty with ventilation, problems with maintaining blood pressure due to decreased venous return, and the possibility of a pneumothorax or air embolus, considering the length of surgery. We were also aware of the potential for catastrophic bleeding because of the proximity of the surgery to the inferior vena cava on the right side. To this end, we had large-bore intravenous access, warm fluids at hand, and two units of blood crossmatched.

Medical therapy of Cushing's disease includes the drugs, metyrapone, which inhibits the 11 β -hydroxylase enzyme involved in steroid synthesis, and ketoconazole, which has steroidogenesis inhibitor actions. Adult patients presenting with severe Cushing's disease have been treated with infusions of etomidate to inhibit steroid production while being prepared for surgery. Greening et al published a case report of the use of etomidate in a child presenting with uncontrolled hypercortisolaemia in preparation for surgery.⁶ This did not appear to be necessary in our patient, as she was not in extremis on presentation.

In this case, access to the adrenal glands was obtained via a lateral transabdominal approach. Schreinemakers et al have recently shown that retroperitoneal adrenalectomy is a safe and effective alternative, avoiding the increased chance of injury to intra-abdominal organs, combined with a shorter operating time.⁷ This procedure is carried out in the prone position. If a bilateral adrenalectomy is to be performed, avoiding the need to reposition the patient is an additional advantage.⁷ However, the prone position is not without its own set of complications. The benefits and risks of anaesthesia and surgery need to be weighed up.

Microscopic endonasal transsphenoidal pituitary surgery is another option for the treatment of pituitary adenomas in

children. A recent publication has shown that it is a safe and well-tolerated option for pituitary tumours in children, and that this surgery results in minimal morbidity.⁸ However, all patients required postoperative supplemental hormone therapy. In our case, the pituitary tumour was not deemed operable, and hence bilateral adrenalectomy was the preferred surgical treatment. As a result of this, the patient will require lifelong corticosteroid and mineralocorticoid supplementation. In the light of this, long-term follow-up of the patient is mandatory. Up to 20% of patients may present for emergency care because of steroid deficiency or an Addisonian crisis.⁹

Bilateral adrenalectomy is also a risk factor for the development of Nelson's syndrome. This is associated with the development of progressive cutaneous hyperpigmentation due to excessive ACTH released from a pre-existing adenoma. The loss of negative feedback on the adenoma may also allow it to increase in size, producing mass effects in the brain. The development of Nelson's syndrome may occur more commonly in the paediatric population.¹⁰ Prior pituitary irradiation is protective against the development of Nelson's syndrome.⁹

In summary, paediatric and adult patients with Cushing's syndrome present the anaesthetist with a cluster of challenges that require careful consideration and management. For such cases, meticulous planning is essential, and multidisciplinary team discussion pre-operatively is extremely beneficial.

References

1. James MFM. Anaesthesia for patients with endocrine disease. Oxford: Oxford University Press, 2010; p. 144.
2. Hutton P, Cooper G. Fundamental principles and practice of anaesthesia. London: Martin Dunitz, 2002; p. 488.
3. Rang HP, Dale MM, Ritter JM, Flower RJ. Pharmacology. 6th ed. Philadelphia: Churchill Livingstone, 2003; p. 431-432.
4. Davies M, Hardman J. Anaesthesia and adrenocortical disease, continuing education in anaesthesia, critical care and pain. 2005;5(4):pages.
5. Kirkbride A, Buggy D. Thermoregulation and mild peri-operative hypothermia. Br J Anaesth. CEPD Reviews. 2003;3(1):pages.
6. Greening JE, Brain CE, Perry LA, et al. Efficient short term control of hypercortisolaemia by low-dose etomidate in severe paediatric Cushing's disease. Horm Res. 2005;64(3):140-143.
7. Schreinemakers JM, Kiela GJ, Valk GD, et al. Retroperitoneal endoscopic adrenalectomy is safe and effective. Br J Surg. 2010;97:1667-1672.
8. Tarapore PE, Sughrue ME, Blevins L, et al. Microscopic endonasal transsphenoidal pituitary adenectomy in the pediatric population. J Neurosurg Pediatrics. 2011;7(5):501-509.
9. Hawn MT, Cook D, Deveny C, Sheppard B. Quality of life after bilateral adrenalectomy for Cushing's disease. Surgery. 2002;132(6):1064-1069.
10. Thomas CG, Smith AT, Griffiths J. Nelson's Syndrome after Cushing's disease in childhood: a continuing problem. Surgery. 1984;96(6):1067-1077.