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Undiagnosed catecholamine-secreting paraganglioma and coexisting carcinoid in a patient with MH susceptibility: an unusual anesthetic challenge

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Abstract
The management of a patient with two undiagnosed neuroendocrine tumors and possible malignant hyperthermia (MH) susceptibility poses a unique challenge to the anesthesiologist. We describe a total intravenous anesthetic including an alpha 2-agonist infusion combined with epidurally administered bupivacaine for intra- and postoperative pain management. Alpha 2-agonists may offer improved intraoperative hemodynamic management in patients with catecholamine-secreting tumors and reduce the total dose needed for intravenous anesthetics such as propofol. The latter mechanism may be useful to avert the risk of the propofol infusion syndrome occurring as a consequence of a high cumulative dose following its prolonged administration.

Key words Undiagnosed pheochromocytoma · Carcinoid · Neuroendocrine tumors · Dexmedetomidine · Propofol infusion syndrome

Introduction

The simultaneous occurrence of a catecholamine-secreting tumor such as a pheochromocytoma or paraganglioma and a carcinoid tumor is extremely rare. The annual incidence of catecholamine-secreting neoplasms is estimated to be 2 per 8000000 population, with postmortem studies suggesting a higher incidence (0.1%) [1]. Carcinoid tumors occur with an annual incidence of approximately 2.5 per 100000 population [2]. Preoperative identification of neuroendocrine neoplasms and subsequent optimal medical patient preparation may facilitate intraoperative management and improve perioperative outcomes [3]. However, some patients remain asymptomatic and undiagnosed. Anesthesia and surgery in such patients may lead to a catastrophic consequences [3]. We report our anesthetic management of a patient with a family history of malignant hyperthermia (MH) presenting for multiple tumor resection. While preoperatively undiagnosed, the postoperative histopathology revealed a catecholamine-secreting paraganglioma, as well as a carcinoid.

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Case report

A 35-year-old, 80-kg, 1.63-m-tall woman presented for removal of a mass involving the duodenum and the head of the pancreas, as well as a second lesion located in the left retroperitoneum. The past medical history included polycythemia vera, deep venous thrombosis during pregnancy, and an episode of pericarditis and pancreatitis. A maternal aunt had died of MH during surgery. Our patient had never had surgery and she had not been tested for MH. The family history was negative for neuroendocrine tumors. Except for the topical treatment of rosacea, she was on no medications. Although preoperative biopsy results of the duodenal mass suggested the remote possibility of a neuroendocrine tumor, no further workup was pursued in this asymptomatic patient. The preoperative physical examination was unremarkable. Following placement of a peripheral intravenous catheter and administration of midazolam 2 mg, the patient was brought to the operating room and standard American Society of Anesthesiologists (ASA) intraoperative monitors were attached. A thoracic epidural catheter was introduced at the T8/9 level for postoperative pain management. A dexmedetomidine infusion was started, without a loading dose, at $0.7\,\mu g \cdot kg^{-1} \cdot h^{-1}$, followed by the uneventful induction of general anesthesia with fentanyl 100 µg, propofol 100 mg, and rocuronium $1\,mg \cdot kg^{-1}$ intravenously. After endotracheal intubation, a right radial artery catheter and a

right internal jugular venous central line were inserted. Anesthesia was maintained with an infusion of propofol between 50 and 70 $\mu g \cdot kg^{-1} \cdot min^{-1}$ titrated to a bispectral index between 40 and 60 (BIS; Aspect Medical Systems, Newton, MA, USA) and dexmedetomidine at an initial rate of 0.7 $\mu g \cdot kg^{-1} \cdot h^{-1}$. Shortly after laparotomy, the patient's blood pressure (BP) was noted to be 180/110 mmHg, the heart rate increased from mid-70 to 95 beats·min^{-1}; the BIS was as low as 40. In addition to the use of the epidural catheter, hydromorphone 1 mg was administered twice intravenously to blunt the physiologic response to catecholamine release. However, the BP remained elevated and was controlled with 5 mg phentolamine intravenously. At this time a pulmonary artery catheter was introduced to augment hemodynamic monitoring and to tailor the intravenous fluid management. Manipulation of the retroperitoneal mass resulted in hypertension, with a BP reaching 200/125 mmHg and a heart rate of 135 beats·min^{-1}. The hemodynamic parameters improved with intravenous sodium nitroprusside (0.2–1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$), phentolamine, and esmolol. The patient remained hemodynamically labile during retroperitoneal tumor manipulation for approximately 60 min. Following tumor removal, the patient became temporarily hypotensive, requiring volume resuscitation to maintain a diastolic pulmonary artery pressure of 14–15 mmHg and administration of phenylephrine for 30 min. Dexmedetomidine was decreased to 0.2 $\mu g \cdot kg^{-1} \cdot h^{-1}$ and, following hemodynamic stabilization, was returned to 0.4 $\mu g \cdot kg^{-1} \cdot h^{-1}$ until the end of surgery. The propofol infusion was maintained at 50 $\mu g \cdot kg^{-1} \cdot min^{-1}$, and analgesia was achieved with epidural bolus administration of 5 cc bupivacaine 0.5% every 90–120 min. During the 10-h and 49-min surgery, the patient received 10 600 cc of crystalloids, the estimated blood loss was 2300 cc, and the urine output was 910 cc. Following discontinuation of the propofol and dexmedetomidine infusions and reversal of neuromuscular blockade at the end of surgery, the trachea was extubated uneventfully with an awake and comfortable patient. The epidural catheter was removed on postoperative day 4 and the patient was transitioned to oral hydromorphone for pain control. The final histopathology revealed a malignant catecholamine-secreting paraganglioma and a duodenal carcinoid.

Discussion

A history of MH in a family member of a patient presenting for surgery often alters the anesthetic approach to this patient. Commonly, a non-triggering anesthetic will be chosen, which may consist of total intravenous anesthesia (TIVA), or a regional anesthetic technique (with or without sedation), or a combination of the two. Propofol is a frequently used intravenous anesthetic for TIVA and is renowned for its remarkable safety profile in anesthetic practice [4]. However, prolonged administration of propofol in critically ill patients (with acute neurological illnesses or acute inflammatory diseases complicated by sepsis, on catecholamines and/or steroids) may lead to a condition characterized by hyperakalemia, hepatomegaly, metabolic acidosis, heart failure, rhabdomyolysis, and renal failure [5–7]. This condition is known as propofol infusion syndrome (PRIS) and was described in children as well as in adults [5–8]. PRIS occurred after intraoperative propofol infusion during prolonged neurosurgery followed by 20 h of propofol sedation [9]. Concurrent catecholamine administration may act indirectly by increasing propofol requirements or directly by damaging myocytes [5]. While some authors recommend limiting the dose of propofol to 5 $mg \cdot kg^{-1} \cdot h^{-1}$ (70 $\mu g \cdot kg^{-1} \cdot min^{-1}$) if used for more that 48 h [5,7], others suggest an even lower dose limit, of 3 $mg \cdot kg^{-1} \cdot h^{-1}$ (50 $\mu g \cdot kg^{-1} \cdot min^{-1}$) [6]. This lower cumulative dose might have been approached or even surpassed during our prolonged surgery, and endogenous catecholamine surges could have further contributed to a risk for PRIS in our patient. We believe the use of dexmedetomidine facilitated a safe dose range for prolonged propofol use, and improved intraoperative hemodynamics.

Dexmedetomidine is a highly selective alpha 2-agonist with sedative and analgesic properties. Its administration is associated with a reduction of anesthetic requirements and perioperative opioids [10,11]. This agent has been used as an adjunct to regional anesthesia because it has virtually no respiratory depressant effect [10–12]. Its central alpha 2-agonist effects predictably result in decreasing the HR and mean arterial pressure (MAP).

Our patient was scheduled for a long procedure to remove two lesions, in the upper retroperitoneum and abdomen, respectively. The histopathology of these masses was unclear prior to surgery, but a remote possibility existed that either lesion could be a neuroendocrine tumor. The prospect of prolonged surgery, a family history of MH, and the possibility of encountering catecholamine-secreting tumors resulted in our decision to employ a combination of propofol and dexmedetomidine for the induction and maintenance of a TIVA technique, combined with a thoracic epidural catheter for intra- and postoperative pain control. The use of dexmedetomidine allowed for a reduced amount of propofol to maintain general anesthesia. The average propofol infusion rate was 50 $\mu g \cdot kg^{-1} \cdot min^{-1}$, and the depth of anesthesia was assessed clinically, as well as by BIS monitoring. Our patient was medically unprepared for surgery (no alpha blockade, volume expansion, or beta blockade) in the presence of a catecholamine-secreting

tumor, potentially increasing the risk for major morbidity and mortality due to intraoperative cardiovascular and/or cerebrovascular catastrophes [3,13]. Although difficult to prove, we believe that we might have experienced even more pronounced intraoperative hemodynamic alterations in the absence of an alpha 2-agonist infusion. Even in a properly prepared patient it is not uncommon to encounter hypertensive episodes (even crises) during tumor manipulation [13]. Pretreatment of patients for pheochromocytoma surgery with clonidine, a less selective alpha 2-agonist, was associated with a reduced release of catecholamines, a decrease in MAP and HR, and an increase in SVR [13]. Dexmedetomidine use during anesthesia for pheochromocytoma resection has been reported previously [14,15]. Central nervous system (CNS) alpha 2 receptors can be found presynaptically as well as postsynaptically. Activation of presynaptic alpha 2 receptors reduces norepinephrine release (negative feedback loop). Activation of postsynaptic alpha 2 receptors leads to hyperpolarization of the membrane [11] or membrane inhibition. Both mechanisms could explain the beneficial hemodynamic effect of dexmedetomidine during operation in our patient.

Pain was well controlled by thoracic epidural analgesia using bupivacaine. However, perioperative neuraxial blockade for pheochromocytoma surgery is controversial because the sympathetic block does not protect against catecholamine surges [16], and hypotension from neuraxial blockade may result in profound reflex catecholamine release.

Conclusion

We have described the successful anesthetic management of an MH-susceptible patient presenting with an undiagnosed catecholamine-secreting paraganglioma and a coexisting carcinoid. The combination of a trigger-free total intravenous anesthetic technique consisting of propofol and dexmedetomidine with the use of epidural analgesia may have contributed to this excellent outcome. The safety and efficacy of alpha 2-agonists during anesthesia for neuroendocrine tumor surgery remains to be determined in future studies.

References

1. Barakat MT, Meeran K, Bloom SR (2004) Neuroendocrine tumors. Endocr Relat Cancer 11:1–18
2. Oberg K (2003) Diagnosis and treatment of carcinoid tumors. Expert Rev Anticancer Ther 3:863–877
3. Voros DC, Smirniotis B, Argyra E, Vadalouka A, Siafaka L, Papadimitriou J (1995) Undiagnosed pheochromocytomas in the perioperative period. Eur J Surg 162:985–987
4. Short TG, Young Y (2003) Toxicity of intravenous anaesthetics. Best Pract Res Clin Anaesthesiol 17:77–89
5. Vasile B, Rasulo F, Candiani A, Latronico N (2003) The pathophysiology of propofol infusion syndrome: a simple name for a complex syndrome. Intensive Care Med 29: 1417–1425
6. Ernest D, French C (2003) Propofol infusion syndrome—report of an adult fatality. Anaesth Intensive Care 31:316–319
7. Kang TM (2002) Propofol infusion syndrome in critically ill patients. Ann Pharmacother 36:1453–1456
8. Koch M, DeBacker D, Vincent JL (2004) Lactic acidosis: an early marker of propofol infusion syndrome? Intensive Care Med 30:522
9. Liolios A, Guerit JM, Scholtes JL, Raftopoulos C, Hantson P (2005) Propofol infusion syndrome associated with short-term large-dose infusion during surgical anesthesia in an adult. Anesth Analg 100:1804–1805
10. Ramsay MAE, Luterman DL (2004) Dexmedetomidine as a total intravenous anesthetic agent. Anesthesiology 101:787–790
11. Jorden VSB, Tung A (2002) Dexmedetomidine: clinical update. Semin Anesth Periop Med Pain 21:265–274
12. Arain SR, Ebert TJ (2002) The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. Anesth Analg 95:461–466
13. Sprung J, Kinney MO, Warner MA (2002) Anesthetic aspects of laparoscopic adrenalectomy for pheochromocytoma. Semin Anesth Periop Med Pain 21:35–45
14. Wong AYC, Cheung CW (2004) Dexmedetomidine for resection of a large pheochromocytoma with invasion into the inferior vena cava. Br J Anaesth 93:873
15. Schumann R, Joseph N, Zabala L, Schwaitzberg SD, Lechan RM (2003) Hypertensive crisis inducing rhabdomyolysis during laparoscopic resection of a large pheochromocytoma: a case report. J Clin Anesth 15:540–544
16. Graham GW, Unger BP, Coursin DB (2000) Perioperative management of selected endocrine disorders. Int Anesthesiol Clin 4:31–67