

CASE REPORTS

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Thyrotoxicosis Factitia in the Anesthetized Patient

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HYPERPYREXIA occurring in the anesthetized patient can be particularly worrisome because malignant hyperpyrexia, a well-described condition, is associated with serious morbidity and mortality. Besides hyperpyrexia, other signs of this usually lethal syndrome include tachycardia and hypercapnia, which can lead to cardiac arrest and death. These signs, however, are not limited to the diagnosis of malignant hyperpyrexia but may occur in other hypermetabolic states as well.

We report a case of hyperpyrexia that occurred during anesthesia and for which the reason was not immediately apparent.

Case Report

A 26-yr-old, 65-kg, 140-cm woman was scheduled to undergo open-reduction, internal fixation of a tripod fracture and mandible fracture. Significant past medical history included Graves' disease diagnosed 5 years previously and initially treated with methimazole followed by definitive radioactive iodide therapy. She had since been receiving thyroid replacement therapy. The patient also had a history of hypertension, well controlled with propranolol. She smoked and had a known history of ethanol, cocaine, and crystal methamphetamine abuse. She denied that she had used any recreational drugs for more than 1 week before surgery. Her surgical history included two cesarean sections performed with regional anesthetic technique. She had had no previous general anesthetics and had no known family history of anesthetic-related deaths or serious complications.

Her medications included levothyroxine 0.1 mg per day and propranolol 40 mg three times per day, both of which she was instructed to continue until the day of surgery by her surgeon. Examination revealed a normal airway and good mouth opening. The patient appeared slightly anxious but did not have symptoms of tremulousness or diaphoresis. She had slight exophthalmus, but her pupils were symmetrical and of normal size. The results of the rest of the ex-

amination and the results of laboratory determinations were normal. According to the patient, results of thyroid function tests, performed at another hospital several months before, were within normal limits.

Before induction, blood pressure was 140/70 mmHg, heart rate 85 beats/min, and oral temperature 36.5°C. Anesthesia was induced with thiopental 500 mg and fentanyl 500 µg, with relaxation by vecuronium to facilitate tracheal intubation. Anesthesia was maintained initially with 1% isoflurane and 70% nitrous oxide in addition to 100-µg boluses of fentanyl.

Within 30 minutes after skin incision, heart rate increased progressively from 90 to 130 beats/min, despite administration of 1,000 µg fentanyl (total) and an end-tidal isoflurane concentration of 2.0% with a 60% nitrous oxide-oxygen mixture. Blood pressure increased slightly, from 110/60 mmHg to 130/80 mmHg. More impressive was that during the next 15 min, maintenance of the patient's end-tidal carbon dioxide tension at 45 mmHg required progressive increases in minute ventilation, from 6,400 to 12,800 ml/min. Furthermore, esophageal temperature began to increase rapidly, and her skin felt hot and moist. A rectal temperature probe confirmed a high temperature, 39.1°C. While an accurate measurement of temperature was being obtained, the heart rate and end-tidal carbon dioxide tension began to decrease slightly, thus relieving some of the urgency in establishing a diagnosis.

The surgeons were immediately notified about the increase in temperature. Isoflurane was discontinued, and anesthesia was maintained with intravenous propofol and fentanyl. Minute ventilation was increased further. A cooling blanket was placed on the patient; ice bags were placed under the axillae and on the groins; and the room temperature was decreased. An arterial blood gas specimen, a blood sample for measurement of thyroid function, and a urine specimen for toxicology screen were obtained.

The results of arterial blood gas analysis, returned within 10 min, were pH 7.43, oxygen tension 141 mmHg, carbon dioxide tension 38 mmHg, and base excess 1.1 mm with a 35% inspired oxygen fraction. Given these findings, malignant hyperpyrexia seemed less likely than initially believed. Therefore, isoflurane administration was restarted, and 2-mg boluses of propranolol to a total of 6 mg over a 20-min period were administered to achieve a heart rate of 100 beats/min. A 2-mg/h propranolol infusion was then begun. As a result of the above maneuvers, the heart rate eventually decreased to 90-100 beats/min; temperature decreased to 36.5°C; and end-tidal carbon dioxide tension decreased and remained at 30-40 mmHg with normal ventilation.

The surgical procedure proceeded uneventfully. The patient emerged from anesthesia, and the trachea was extubated. When she was alert, the events that took place in the operating room were discussed with her. It was discovered at that time that the patient had taken her morning medications before surgery as instructed. The problem, however, was her decision at that time to take 14 levothyroxine tablets to make up for the pills that she had forgotten to take during the previous 2 weeks.

The thyroid function studies from the intraoperative blood sample revealed the following: total thyroxine 27.1 µg/dl (normal 4.5-12.0

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$\mu\text{g}/\text{dl}$), free thyroxine greater than 7.2 ng/dl (normal 0.9–2.1 ng/dl), total triiodothyronine (T_3) 479 ng/dl (normal 65–200 ng/dl), and thyroid-stimulating hormone 0.07 $\mu\text{IU}/\text{ml}$ (hyperthyroid <0.3 IU/ml). The toxicology screen was positive only for ultra–short-acting barbiturate.

The patient remained hemodynamically stable postoperatively and was told to discontinue taking levothyroxine until follow-up with her internist.

Discussion

The patient's medical history offered numerous possibilities for a hypermetabolic state during anesthesia. However, malignant hyperpyrexia was immediately suggested based on the development of symptoms (hyperpyrexia, hypercapnia, and tachycardia) during a patient's first exposure to a known triggering agent, isoflurane. For 20 min, it was tempting to initiate treatment for malignant hyperthermia, but the patient lacked a positive family history for that condition, and the muscle rigidity or masseter muscle spasm that often accompany malignant hyperpyrexia did not occur. Moreover, although she had sinus tachycardia, no malignant dysrhythmia developed. Furthermore, lack of the concomitant metabolic acidosis largely excluded this diagnosis. Had a severe acidosis or base deficit been noted, the procedure would have been canceled immediately and dantrolene administered, with treatment focused on the malignant hyperthermia.

Another possibility in the differential diagnosis included thyroid storm. There have been several reports of cases of life-threatening thyrotoxicosis during anesthesia that have mimicked malignant hyperthermia, even to the extent that dantrolene has been administered.^{1–3} Our patient had a known history of hyperthyroidism secondary to Graves' disease yet had received definitive treatment with radioactive iodide. As is common, this treatment had rendered the patient hypothyroid, which resulted in her being given thyroid replacement therapy. Moreover, during the preoperative period, apart from slight anxiety, she did not display any of the stigmata of thyrotoxicosis.

Her history of drug intoxication offered yet another possibility to explain her hypermetabolic state. Rosenberg *et al.* cite several cases of hyperthermia secondary to drug intoxication with cocaine and amphetamine,⁴ drugs our patient was known to abuse. She denied, however, that she had used any recreational drugs for more than 1 week before surgery. More convincingly, the results of toxicology analysis were negative for these drugs.

Our patient's symptoms resulted from her ingestion of supraphysiologic quantities of thyroid hormone before surgery. This syndrome is well described as thyrotoxicosis factitia,⁵ a disorder not uncommon in patients with underlying psychiatric disorders who take the hormone either inadvertently or for malingering. Unfortunately, our patient did not display thyrotoxic symptoms until after anesthesia had been administered, the delay after ingestion presumably resulting from the time required for drug absorption, conversion to T_3 , and onset of its metabolic effects at the cellular level. This delay has been studied by LeBoff *et al.*⁶ and Valente *et al.*,⁷ who demonstrated a significant increase in serum T_3 4 h after ingestion of large quantities of levothyroxine. They have suggested that a significant component to this increase in serum T_3 may result from the contamination of levothyroxine preparations with T_3 . These hypothesized phenomena may explain the onset of our patient's signs in the middle of the procedure. In addition, fasting is known to increase absorption of the drug and may have influenced the timing of the symptoms.

The laboratory studies also supported the diagnosis, with marked increase in serum thyroxine, free thyroxine and serum T_3 , as well as markedly suppressed TSH concentrations.

The treatment for this condition should be similar to that of thyrotoxicosis of any origin. The first line of therapy should include use of a β -adrenergic blocking drug. Our patient's symptoms abated soon after we administered propranolol, and she remained hemodynamically stable throughout the rest of surgery and the recovery period. One would expect similar results with the ultra–short-acting β antagonist esmolol. Though not used in this case, glucocorticoid treatment also may have been beneficial because it inhibits conversion of tetraiodothyronine to the more active T_3 . Other interventions, had the diagnosis been confirmed during the case, could have included placement of a nasogastric tube for purposes of gastric lavage and treatment with cholestyramine, which interferes with thyroxine absorption. Unlike thyrotoxicosis secondary to Graves' disease, treatment with antithyroid drugs such as iodine, propylthiouracil, or methimazole would have little benefit in thyrotoxicosis factitia, because these drugs primarily inhibit synthesis and release of thyroid hormone from the gland.

In addition to providing an example of thyrotoxicosis factitia during anesthesia, this report emphasizes that hyperpyrexia during anesthesia may have any of a variety of causes.

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Successful Use of Inhaled Nitric Oxide for Treatment of Severe Hypoxemia in an Infant with Total Anomalous Pulmonary Venous Return

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INFANTS with total anomalous pulmonary venous return (TAPVR) often present with heart failure or cyanosis or both.¹ These infants become severely cyanotic and acidotic, and their condition may deteriorate rapidly.² Mechanical ventilation, along with sedatives and muscle relaxants, is often used to stabilize the children's condition preoperatively. However, urgent operation usually is necessary.² Nitric oxide (NO) has been identified as an endothelium-derived relaxing factor,³ and the addition of low-dose NO to inspired gas has been shown to provide selective pulmonary vasodilation both in animals and in humans.^{4,5}

We describe an infant with TAPVR in whom inhalation of low-dose NO was used successfully to treat life-threatening hypoxemia.

Case Report

A 4-month-old, 6,210-g boy was admitted to the hospital with a 6-day history of cyanosis after an upper respiratory tract infection. He had been born at full term and had no history of previous illness. At the time of admission he was tachypneic but not hypotensive. Arterial blood gas values were pH 7.36, carbon dioxide tension 43 mmHg, oxygen tension 37 mmHg, and base excess 0 mEq/l while he breathed room air. A chest radiograph showed a dilated heart with hypervascular lungs. Oxygen therapy and mechanical ventilation were commenced, but the patient's condition did not improve. He was transferred to our intensive care unit 2 days later.

On admission to intensive care unit, echocardiography demonstrated an atrial septal defect, marked enlargement of the right atrium and ventricle, and tricuspid regurgitation. Doppler ultrasound by the tricuspid gradient method⁶ estimated the systolic pressure gradient between the right ventricle and right atrium at 40 mmHg, indicating the presence of pulmonary arterial hypertension. Although the sites of the entry of the individual pulmonary veins into the systemic venous circulation were not clearly identified, TAPVR was suggested.

Mechanical ventilation with a SERVO 900C ventilator (Siemens-Elma, Stockholm, Sweden) was started with an inspired oxygen fraction (FiO₂) of 1.0, a tidal volume of 60-70 ml, and 3-5 cmH₂O positive end-expiratory pressure while fentanyl, midazolam, and vecuronium were administered. However, the child exhibited cyanosis and increasing metabolic acidosis.

Seventeen hours after admission (on day 2), peripheral cyanosis became severe. Arterial blood gas values were pH 7.11, carbon diox-

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