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Unmasking of thyrotoxicosis during anaesthesia

在麻醉期間甲狀腺毒症的出現

Two cases of subclinical and undiagnosed thyrotoxicosis that presented with unexplained tachycardia during surgery are described. Differential diagnosis and logistics in the management of patients presenting with tachycardia, with or without fever during anaesthesia are discussed. It is emphasised that when encountering unexplained tachycardia during anaesthesia, thyrotoxicosis must be suspected. Investigations for thyrotoxicosis must be carried out in the postoperative period.

本文記述了兩個在亞臨床及未被確定診斷的甲狀腺毒症病例，它們在進行外科手術時呈現心跳加速，但原因不明。本文繼而討論了不論病人在麻醉期間有沒有發燒，如果呈現心跳加速，醫生應對病人作出鑒別診斷和後勤準備。值得強調的是在麻醉期間，如果遇到不能解釋的心跳加速時，應懷疑病人可能患有甲狀腺毒症，在手術後必須進行甲狀腺毒症檢查。

Case reports

Case 1

A 31-year-old healthy labourer with a crush injury to the left index and ring fingers presented for emergency surgery. He had no history of surgery or anaesthesia. Physical examination and preoperative investigations were normal. His preoperative heart rate was 70 beats per minute and he did not have any signs or symptoms of thyrotoxicosis.

Induction of anaesthesia was with fentanyl 100 mg and propofol 200 mg. After insertion of a laryngeal mask airway, anaesthesia was maintained with spontaneous respiration of 66% nitrous oxide in oxygen and 1% isoflurane, using the circle absorber system. Following induction of anaesthesia, the patient became tachycardic (heart rate, 105-125 beats per minute). One hour later, there was increasing tachypnoea (25 breaths per minute) and an increase in arterial carbon dioxide partial pressure ($PaCO_2$) reaching 9 kPa (normal range, 4.7-6.0 kPa) signifying greater carbon dioxide retention. The patient had an anatomically difficult airway (Mallampati grade 3) and thus was given propofol 50 mg and suxamethonium 100 mg for endotracheal intubation, followed by boluses of rocuronium (total dose, 50 mg) and commencement of mechanical ventilation. After intubation, his face was flushed and he appeared pyrexic. A nasopharyngeal temperature probe was inserted, showing a core temperature of 38.2°C. At this stage malignant hyperpyrexia was suspected and a vapour-free anaesthetic machine and circuit were substituted. The surgeon was also alerted to this possibility. After withdrawal of inhalational agents, anaesthesia was supplemented with midazolam. Surgery was completed shortly thereafter. After transferring to the recovery room, the patient was fully awake. Ice water sponging was

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applied and his temperature slowly decreased to 37.5°C. His heart rate, however, remained at 105 to 115 beats per minute.

Postoperative investigations showed the patient had normal renal function. There was an increase in serum creatine kinase (CK) level to 1941 U/L (normal range, 62-297 U/L) and a mixed metabolic and respiratory acidosis (pH=7.22 [normal range, 7.35-7.45], $PaCO_2$=8.4 kPa, oxygen partial pressure= 19.4 kPa [normal range, 10.0-13.3 kPa], bicarbonate ion=21.5 mmol/L [normal range, 23-29 mmol/L], base deficit=3.6). The serum CK level returned to 378 U/L after 24 hours, and the acidosis was self-correcting. The patient's fever also came down after 24 hours. No myoglobinuria was detected. A thyroid function test was performed and the results indicated that he had thyrotoxicosis: serum free thyroxine (T_4) was 54.1 pmol/L (normal range, 13-23 pmol/L) and serum thyroid stimulating hormone (sTSH) was under 0.01 mU/L (normal range, 0.27-4.20 mU/L). The patient was started on carbimazole therapy. Six months later, his thyroid function returned to normal. There was, however, an episode of hypokaelemic periodic paralysis that required hospital admission and observation. His subsequent course was uneventful.

Case 2

A 30-year-old housewife presented for laminectomy and posterior spinal fusion for spondylolisthesis at the L5/S1 level. She had previously had general anaesthesia for appendicectomy, breast mass excision, and uterine curettage. Otherwise, she had no comorbidities. Six months previously, her second child had been delivered by Caesarean section under general anaesthesia. Her postdelivery course was uneventful. Physical examination, blood pressure, temperature, and preoperative investigations were essentially normal, apart from a heart rate of 100 beats per minute, which was attributed to anxiety.

Induction of anaesthesia was with thiopentone 200 mg and fentanyl 200 mg. A 7-mm wire-reinforced endotracheal tube was inserted after administration of cisatracurium 9 mg. Mechanical ventilation was commenced and anaesthesia was maintained with 66% nitrous oxide in oxygen supplemented with isoflurane. The patient was turned to the prone position ready for surgery. At the outset of the procedure, she developed persistent sinus tachycardia (heart rate, 100-120 beats per minute). She, however, had no sweating or other signs of inadequate anaesthesia and her nasopharygeal temperature was normal. Analgesia was supplemented with 6 mg of morphine. Due to the persistent tachycardia, a bolus dose of esmolol 25 mg was administered, followed by an infusion of 50 μg/kg/min. The patient's heart rate was controlled subsequently at 80 to 90 beats per minute.

At the end of the 4-hour operation, she was awoken and the effect of the muscle relaxant reversed with neostigmine. In the postoperative period, the patient was awake and comfortable. Her heart rate, however, stayed at 100 to 110 beats per minute after cessation of esmolol. A thyroid function test was performed and the results indicated that she had thyrotoxicosis: serum free T_4 was 43 pmol/L and sTSH was under 0.01 mU/L. The patient was started on carbimazole therapy and made a smooth recovery.

Discussion

The differential diagnosis of intraoperative hyperthermia and hypermetabolism includes malignant hyperpyrexia, thyrotoxicosis, and phaeochromocytoma. The distinguishing features of these conditions are summarised in the Table.[1] Both malignant hyperthermia and thyrotoxicosis are hypermetabolic states with excessive heat production. In malignant hyperpyrexia, anaesthetic agent-triggered calcium release by the sarcoplasmic reticulum leads to escalated excitation-contraction coupling in skeletal muscles, producing muscle rigidity and hyperpyrexia.[2] This process can be aborted by the administration of dantrolene. In thyrotoxicosis, uncoupling of mitochondrial oxidative phosphorylation, including that in muscle cells, leads to hyperpyrexia.

Thyrotoxicosis is one of the most common endocrine disorders in an otherwise healthy young population.[3] Signs and symptoms include a palpable goitre, tachycardia, palpitation, heat intolerance, tremor, anxiety, and weight loss.[4] Depending on the severity of thyrotoxicosis, clinical presentation can be quite subtle. Occasionally, thyrotoxicosis is suspected during the routine preanaesthetic evaluation[5] of patients who appear unduly anxious and usually with other suggestive signs and symptoms. It can then be confirmed or excluded by thyroid function tests. In the two patients reported here, obvious signs and symptoms of thyrotoxicosis were absent during the preoperative visits.

The stress of surgery under light general anaesthesia can trigger off a thyroid storm in susceptible thyrotoxic patients. Thyroid storm is manifested by hyperpyrexia, tachycardia, and hypermetabolism (dramatically increased oxygen consumption with increased carbon

Table. Differential diagnosis of intraoperative hyperthermia and hypermetabolism (modified)[1]

Sign/symptom	Malignant hyperpyrexia	Thyrotoxicosis	Phaeochromocytoma
Hyperthermia	Often present	Often present	May be present
Tachycardia	Usually present	Usually present	Usually present
Acidosis	Usually present	May or may not be present	May be present
Hypertension	May be present	Often present	Usually present
Muscle rigidity	Often present	Absent	Absent
Creatine kinase	Increased	May or may not be increased	May be increased
Myoglobinuria	Often present	Absent	Absent
Other laboratory tests	Hyperkalaemia	Free thyroxine, thyroid stimulating hormone	Urinary vanillylmandelic acid, serum noradrenaline and adrenaline
Response to dantrolene	Positive	Doubtful	May be dangerous

dioxide production),[6] as exemplified in case 1. Hyperpyrexia is also seen in malignant hyperpyrexia under general anaesthesia, where the rate of rise of temperature and the highest temperature reached are important diagnostic features of this condition. Metabolic acidosis, hypoxaemia, and rhabdomyolysis (as evidenced by markedly elevated serum potassium and CK levels), however, are generally of greater magnitude in malignant hyperpyrexia than thyrotoxicosis. Thus, although the serum CK level can be moderately elevated in thyroid storm due to the uncoupling of mitochondrial oxidative phosphorylation in muscle cells,[7] the magnitude of this elevation is much less than that seen in malignant hyperpyrexia, where the rhabdomyolysis can lead rapidly to raised muscle enzymes, myoglobinuria, and acute renal failure. In case 1, the patient's temperature was monitored closely once malignant hyperpyrexia was suspected. After the surgeon had been alerted to this possibility, surgery was completed soon afterwards. Further treatment of malignant hyperpyrexia, a potentially lethal condition, requires prompt administration of dantrolene.

It is interesting to note this patient developed periodic paralysis some 6 months after the operation. Periodic paralysis is a known complication of thyrotoxicosis, and occurs most frequently in young Oriental males.[8] The pathophysiological mechanism of periodic paralysis appears to be related to an increase in the number of cell membrane sodium-potassium pumps, resulting in potassium influx into the cell and hyperpolarisation.[9]

In case 2, where the patient presented with unexplained tachycardia during anaesthesia, differential diagnoses include inadequate anaesthesia, hypovolaemia due to haemorrhage, or obstructed venous return in the prone position. Drugs used for skin infiltration (including adrenaline), atropine, and anaesthetic agents such as droperidol, ketamine, or pancuronium, can also cause tachycardia. After excluding these possible causes, thyrotoxicosis was suspected. Esmolol, which is a short-acting β-blocker, was used successfully to control the heart rate.

Conclusion

When unexplained tachycardia, with or without fever, occurs during surgery, as well as taking measures to control heart rate and temperature, thyrotoxicosis must be suspected and investigated for in the postoperative period. Although the results usually take some time to complete, the diagnosis is important to allow the early institution of antithyroid agents and facilitate further management of complications associated with thyrotoxicosis.

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