HYPERPYREXIA OF UNCERTAIN ORIGIN

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Hyperpyrexia occurring in a 27-year-old woman undergoing eye surgery is described. The cause, although open to doubt, appeared to be a thyroid storm.

CASE REPORT

A 27-year-old woman presented for surgical re-correction of divergent strabismus. A previous operation had been performed under nitrous oxide in oxygen and ether anaesthesia when she was 11 yr old. She had been healthy otherwise, apart from long standing “nervousness” accompanied by tremor. She had a 3-year-old child and had been taking oral contraceptives for 3 yr. She had no specific complaints and her weight was constant.

On examination she was a plump, anxious woman. The heart rate was regular at 86 beat min⁻¹, arterial pressure was 160/90 mm Hg, and no abnormalities were noted apart from the presenting condition.

On the morning of operation the patient became acutely anxious while still in the ward and was given papaveretum 10 mg and hyoscine 0.2 mg i.v. Despite this, she was still tearful and distressed when she arrived in theatre about 45 min later.

Anaesthesia was induced with methohexitone 100 mg, followed by suxamethonium 80 mg, which produced slight muscle fasciculation, and a cuffed tracheal tube was introduced without difficulty. Nitrous oxide, oxygen and halothane were then administered, the concentration of the latter being increased to 4% and trichloroethylene added for a few minutes because the patient failed to “settle”. The operation commenced.

Fifteen minutes after induction of anaesthesia the respiratory frequency remained rapid and the patient felt hot to the touch. An electric rectal thermometer indicated 38 °C and the heart rate was 120 beat min⁻¹. Two diagnoses were considered, malignant hyperpyrexia and thyroid storm. With the latter possibility in mind, propranolol 2 mg was injected i.v. via an indwelling needle. Some suxamethonium present in the tubing of this needle caused transient cessation of breathing. After 5 min there had been no improvement and an infusion containing procaine 400 mg was commenced.

Twenty-five minutes after induction of anaesthesia the rectal thermometer indicated 42 °C but the peripheral skin colour remained satisfactory and there was no muscle rigidity. Nonetheless malignant hyperpyrexia was diagnosed, the procaine was infused quickly and tubocurarine 30 mg was given i.v. to enable artificial ventilation to be undertaken. The surgeon then completed the operation rapidly and ice packs were applied to the body, with the result that at 40 min, the rectal temperature had decreased to 36.8 °C.

On the assumption that this was malignant hyperpyrexia, dexamethasone 100 mg and frusemide 40 mg were injected i.v. and an infusion of 100 ml of mannitol 20% was administered. Artificial ventilation was continued in the intensive therapy unit and the bladder was catheterized. By this time the patient’s excellent clinical condition was matched by a series of normal laboratory investigations and she was allowed to breathe spontaneously after removal of the endotracheal tube 3 h after anaesthesia had commenced. The body temperature increased again during the following 4 h to 38.8 °C, but settled after the administration of chlorpromazine 75 mg i.m. and an aspirin suppository. The patient was discharged from hospital 2 days later.

All the initial laboratory investigations were within normal limits except for a slight increase of the blood glucose concentration (13 mmol litre⁻¹) which could be attributed to dexamethasone. Investigations included serum electrolytes, creatine phosphokinase, lactate and blood-gas analysis. Blood coagulation profile and 24-h urinary catecholamine excretion were also normal.

Three weeks later thyroid function tests showed (normal range in parentheses):

- T₃ uptake 64% (92-117%) low value in hyperthyroidism
- Serum T₄ 13.8 µg dl⁻¹ (4.5-13) high value in hyperthyroidism
- Free thyroxine index (FTI) 21.6 high value in hyperthyroidism

These results are all indicative of hyperthyroidism. The free thyroxine index (FTI) is intended to eliminate the effect of variations in thyroid binding proteins, such as their increase by the contraceptive pill. Of the above tests, it is the most indicative of hyperthyroidism.

The patient was referred to a physician (Dr M. J. T. Peaston) who noted a heart rate of 100 and wide arterial pressure (160/90 mm Hg) but no evidence of toxicity other than a fine tremor. He considered the patient to be thyrotoxic, but repeated the previous tests, FTI being 17.0, and requested a thyroid microsomal antibody test which was positive. These results were confirmatory, therefore.

Treatment was commenced with propranolol and neomercazole and appeared to be beneficial, especially as regards the patient's nervousness. She soon refused to attend the hospital again, however. A muscle biopsy had by then been performed by Dr Ellis at the Department of Neuropathology in Leeds and was normal, thus excluding malignant hyperpyrexia.

**DISCUSSION**

The reason for the increase in temperature in this patient remains obscure. A thyroid "storm" arising from pre-existing thyrotoxicosis would be the most likely explanation in view of the subsequent findings. Such crises have been described in patients who were apparently normal before operation and who were undergoing surgery not involving the thyroid gland (Nemec et al., 1970; Shehata, 1974). It has been demonstrated also that stress or the exhibition of anaesthetic agents such as ether and halothane may cause an increase of the blood thyroxine concentration (Oyama et al., 1969), and such a mechanism might be postulated in this case. Against this conclusion are the short clinical course, since thyroid storms rarely abate in less than 24 h, the rapid response to treatment and the absence of overt clinical thyrotoxicosis after operation. Conversely, an increase of catecholamine concentrations could have triggered a thyroid crisis, since these are now considered to be the mediators of the majority of manifestations of thyrotoxicosis. This view accords with the failure to demonstrate an increase of thyroxine concentration during thyroid crises and the known efficacy of propranolol and reserpine in controlling symptoms.

The patient was acutely anxious before operation and would be expected to have an increased blood catecholamine concentration, although this was not sufficient to increase the 24-h urinary excretion above the upper limit of normal. Since it is now considered that sensitivity to catecholamines induced by thyroid hormones, rather than an increase in their concentration, is the cause of the manifestations of thyrotoxicosis, a transient increase in catecholamines might explain the phenomena described.

Lastly it is possible to speculate on the role of halothane, alone or in combination with the above factors, in uncoupling oxidative phosphorylation within cells and thereby producing excessive energy as heat. Snodgrass and Piras (1966) have demonstrated this uncoupling action of halothane in rat liver mitochondria, although it was not associated in their experiment with increased energy production.

**ACKNOWLEDGEMENTS**

I would like to thank Dr M. J. T. Peaston, PH.D., M.R.C.P., for his advice and Drs Ellis and Harriman of the Hyperpyrexia Investigation Unit at Leeds for their assistance and performance of the muscle biopsy. I am grateful for the help afforded me by Dr R. Taylor, consultant physician at Kidderminster General Hospital.

**REFERENCES**


