Hepatocellular Dysfunction without Jaundice after Enflurane Anesthesia

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Hepatic injury, ranging in severity from slight alterations in hepatic enzyme functions to massive necrosis, has been associated with the administration of halothane,1,2 methoxyflurane,3 and fluoroence.4 The following case report suggests that enflurane may also be capable of producing hepatic damage in rare individuals.

REPORT OF A CASE

A 40-year-old Caucasian man with multiple endocrine adenomatosis (Sipple's syndrome) was admitted to the Clinical Center of the National Institutes of Health for evaluation of a mass in the neck. Eight years previously he had undergone bilateral adenectomy for phaeochromocytoma, followed in three weeks by total thyroidectomy for medullary carcinoma of the thyroid. Halothane had been administered for both procedures, without clinical evidence of hepatic injury. Postoperative serum glutamic pyruvic transaminase had increased from a preoperative value of 10 U to 900 U (normal: 5 to 35 U). Serum glutamic oxaloacetic transaminase was 370 U (normal: 8 to 40 U). Total bilirubin increased slowly to the upper limit of normal (1.2 mg/100 ml). The eosinophil count increased from a preoperative value of 1 per cent to 6 per cent on the third postoperative day and remained above normal for two weeks. Hepatitis B antigen was negative by radioimmunoassay, and hepatitis B antibody was not detected by passive haemagglutination. Antimitochondrial antibodies were not present 15 days after operation, and studies of lymphocyte transformation done at this time were negative. Liver biopsy was not performed.

During the febrile period, the patient received maintenance hormone replacement with the addition of hydrocortisone. When discharged from the Clinical Center on the twenty-first postoperative day, he had recovered fully with the exception of mild malaise and minimal elevation of serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase. The patient was told that he might have had an "allergic response" to enflurane and that if anesthesia should become necessary in the future, enflurane and other halogenated anesthetics should be avoided.

DISCUSSION

The hepatic abnormalities in this patient may or may not have been related to the administration of enflurane. Indeed, residual halothane in the anesthetic apparatus may have been the precipitating agent. Other causes of postoperative hepatic dysfunction, including hypoxia, nonanesthetic drugs, septis, hypotension, or pre-existing hepatic disease can probably be excluded. The rapid

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onset of fever, limited time course and failure to detect viral antibodies or antigens argue against viral hepatitis' being the cause of this disorder.

Laboratory and clinical abnormalities in this patient were similar to those found by Lecky and Cohen in a patient who received halothane. However, examination of our patient failed to demonstrate antimitochondrial antibodies, and his lymphocytes were not stimulated when exposed to enflurane or halothane in vitro. Several possibilities might account for failure to observe lymphocyte stimulation. First, the lymphocyte cultures were tonometered with enflurane, while other investigators have exposed the cultures directly to liquid anesthetic. Second, the dose of anesthetic and duration of exposure may have been incorrect. Third, enflurane alone may not be an adequate antigen; perhaps a protein-bound metabolite is required. Finally, the patient may not have had enflurane hypersensitivity. If he did, alteration in lymphocyte function may not have been a feature of the disease, just as it is not always a feature of "halothane hepatitis."12

We do not feel that a single case report should indict enflurane as an hepatotoxin. However, unexplained fever and malaise following enflurane anesthesia should be thoroughly investigated and taken into account when considering further exposure of such a patient to halogenated agents.

REFERENCES


Sinus Bradycardia and Asystole during Spinal Anesthesia

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Sinus bradycardia rapidly followed by cardiac asystole was observed in a young, healthy patient 34 minutes after induction of spinal anesthesia. This complication in two healthy male volunteers receiving spinal anesthe-

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A healthy 29-year-old male graduate student, height 5 feet, 11 inches, weight 160 pounds, was to undergo elective bilateral vasovasotomy for infertility. The only previous anesthetic had been an uneventful spinal anesthesia with tetracaine, 12 mg, for bilateral hydrocele repair. The patient was premedicated with morphine sulfate, 8 mg, diazepam, 10 mg, and scopolamine, 0.2 mg, intramuscularly an hour prior to induction of anesthesia. Just before induction of subarachnoid block, blood pressure was 120/60 mm Hg and pulse rate was 68/min.