

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 fluroxene.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 adrenalectomy for pheochromocytoma, 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 oxaloacetic transaminase and bilirubin levels had been normal. Since that time, hormone replacement consisting of dexamethasone, levthyroxine and fludrocortisone had been maintained.

Physical examination upon admission was unremarkable with the exception of the surgical lesion. Roentgenogram of the chest, electrocardiogram, and values for complete blood count, urinalysis, serum electrolytes, serum calcium and liver function studies were normal. Premedication consisted of morphine, 10 mg, and scopolamine, 0.5 mg. Anesthesia was induced with thiopental, 500 mg, and maintained with enflurane, 1.5 to 2.5 per cent in nitrous oxide-oxygen 50 per cent. Five hours were required for excision of the mass in the neck and radical neck dissection. Arterial blood pressures ranged from 100/60 to 125/70 torr, compared with a preoperative value of 120/70 torr. Blood loss was replaced with Plasmanate, 500 ml, and one unit of whole blood. Hydrocortisone, 200 mg, was given intravenously during the procedure.

Four hours postoperatively, the patient's temperature increased, with spikes as high as 39 C (oral) over the next ten days. This was accompanied by anorexia and malaise, which gradually resolved

over the following month. No rash or arthralgia was present at any time, and there was no evidence of wound, pulmonary, or urinary infection. Postoperative hemoglobin was 13.8 g/100 ml, and leukocyte counts ranged from 7,700 to 9,300/cu mm.

Liver function tests were markedly abnormal. On the tenth postoperative day, 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 hemagglutination. 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, sepsis, hypotension, or pre-existing hepatic disease can probably be excluded. The rapid

† Lymphocytes from the patient and two normal volunteers were prepared and assayed for lymphocyte transformation by the method of Cullen *et al.*⁵ Transformation was not observed in any of the preparations either during or following exposure to enflurane, 0.2 per cent, or halothane, 0.14 per cent, for five days.

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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 Cohen² 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.⁶ 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."⁷

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.

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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 anes-

thesia has been reported by Gerbershagen and Kennedy.¹ However, it is not usually recognized among the potential complications of this anesthetic.

REPORT OF A CASE

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.

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