Acute Liver Failure following Minor Outpatient Surgery: A Case Report

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ABSTRACT

Hepatotoxicity associated with inhalation anesthetics is a known rare occurrence. Sevoflurane, one of the newest generation agents, has a more ideal safety profile due to its lack of airway irritation, rapid onset of action, and quick elimination. However, based on several case reports, sevoflurane has been associated with acute liver toxicity following surgery. Literature review reveals other reports demonstrating an association between inhaled anesthetics and acute liver damage.

A 90-year-old Caucasian man with chronic renal insufficiency, but otherwise relatively healthy and active, suffered a displaced nasal fracture from a fall. There was no syncope or loss of consciousness. After primary care in the emergency room, he was referred to plastic surgery for treatment of his nasal fracture. Visible deformity and airway compromise was noted for which early closed reduction was recommended. Following medical clearance through his internist, he underwent a 30 minute procedure under general anesthesia in an outpatient surgery center.

Sevoflurane was used along with propofol and nitrous oxide. Surgery and recovery were uneventful. Follow-up on post-operative days 1 and 5 did not reveal any problems. On post-operative day 10, he presented to the emergency room with constipation and jaundice. Work-up for painless jaundice ensued; no biliary obstruction was found, though he was noted to have a bilirubin of 12 mg/dL and markedly elevated transaminases. He rapidly developed respiratory failure and worsening of his chronic renal failure. Unfortunately, the patient continued to deteriorate and passed away 26 days after surgery.

Although a rare event, acute liver failure from exposure to inhalation anesthetics has been reported. With our patient, his advanced age including chronic renal failure likely contributed to the development of liver failure that then precipitated multiple system failure and a rapid demise. This case report reminds us that even the most minor of procedures can have major consequences.

CASE PRESENTATION

A 90-year-old Caucasian male with a history of chronic renal insufficiency sustained a nasal fracture after a fall. He denied any loss of consciousness and noted bleeding from his nose. He was treated at a local emergency room, where a
displaced nasal fracture was diagnosed and a laceration of the dorsum of the nose was repaired. Medications included tamsulosin, aspirin, sodium bicarbonate, calcitriol, amlodipine, and sevelamer. He was noted to be allergic to diazepam. He was referred to the office for consultation one day after initial presentation. After displacement of the nasal fracture and some airway compromise was noted on physical exam, early closed reduction was discussed. Medical clearance was arranged through his internist and the surgery was scheduled for 10 days after initial presentation. The patient was given cephalaxin as prophylaxis for infection. Closed reduction of the nasal fracture was performed in an outpatient surgery center under general anesthesia with a laryngeal mask airway using sevoflurane, propofol, and nitrous oxide. Dexamethasone and cefazolin were also given. He tolerated the anesthesia and procedure well. At one day follow-up the patient was doing well aside from minor typical post-surgical discomfort. He returned again 5 days after surgery to remove the splint and was improving. The next visit was scheduled for one month later. However, 10 days after surgery, he came to the emergency room complaining of inability to have a bowel movement.

Initial evaluation revealed jaundice with an elevated bilirubin and abnormal liver function panel. Abdominal ultrasound and computed tomography scan were performed. Results from both were negative for gallstones, biliary dilation, and masses. Magnetic resonance cholangiopancreatography (MRCP) was unremarkable. During the course of hospitalization, he was seen by several consultants including a gastroenterologist, pulmonologist, cardiologist, nephrologist, vascular surgeon, and infectious disease specialist. His renal function declined and dialysis was begun. Medications included buspirone, calcitriol, darbepoetin alfa, fluconazole, levosulbutamol, levofloxacin, methylprednisolone, multivitamin, piperacillin/tazobactam, and sevelamer. The patient had a worsening course related to progression of his renal insufficiency and possible aspiration pneumonia. Further testing found no evidence of cholelithiasis but he was noted to have multiple hepatic cysts. A hepatitis panel came back non-reactive. Sputum cultures were positive for yeast although blood and urine cultures were negative. In the end, the patient succumbed to multi-organ failure, unable to recover from his liver, respiratory, and renal failure. The family refused hospice evaluation and 37 days after initial presentation, he was noted to be unresponsive with no spontaneous respirations, pulse or blood pressure. The patient was pronounced dead.

**DISCUSSION**

The use of anesthesia, since its inception over 150 years ago, has revolutionized the practice of surgery. More than 60,000 patients in the US undergo surgical procedures daily under general anesthesia.\(^1\) Sevoflurane, fluoromethyl 2,2,2-trifluoro-1-(trifluoromethyl) ethyl ether, is one of the most commonly used volatile anesthetic agents used for induction and maintenance of general anesthesia. Aside from desflurane, sevoflurane has the most rapid onset of action and dispersal.\(^2\) Sevoflurane became available in Britain and North America in 1995.\(^3\) Due to its pleasant smell and minimal airway irritation, sevoflurane can be inspired at high concentrations without side effects or discomfort, making it an ideal volatile agent.\(^4\)

In addition to therapeutic benefit, inhaled anesthetics often have side effects. Liver damage from drugs is among the leading causes of acute liver failure. This liver failure occasionally necessitates liver transplantation in Western nations.\(^5\) More specifically, based on a study of drug-induced hepatic failure causing death or
transplant in Sweden, anesthetics were some of the most common drugs associated with fatal outcomes. In this case report, we present a patient who developed rapid liver failure shortly after minor surgery under general anesthesia, and discuss the possible contributing factors and the possible primary causative factor as sevoflurane.

Without an autopsy the exact cause of death cannot be confirmed. However, we believe that the patient likely succumbed from multi-system failure beginning with acute liver failure secondary to the inhalation anesthetic. Previous case reports demonstrate similar situations with an association between inhalation anesthesia and acute liver damage. Severe hepatic injury from sevoflurane specifically is rare but it has been described in published case reports. The injury is marked by acute increase in serum transaminase levels and appearance of jaundice within 2 to 21 days after exposure. The acute injury may be self-limited and resolve in 4 to 8 weeks or can be severe and associated with irreversible liver failure. A strong risk factor is previous exposure to any of the halogenated anesthetics. Although this patient was not obese, a study comparing obese to non-obese patients undergoing abdominal surgery using sevoflurane demonstrated a significant increase in liver enzymes in obese patients as compared to non-obese patients.

We suspect that the patient’s chronic renal failure and advanced age made him more vulnerable to the potential hepatic damage induced by sevoflurane. A similar situation was detailed in a case report of 47-year-old woman who underwent kidney transplantation using sevoflurane and died of fulminant hepatitis. The common variable here is limited kidney function. The combination of exposure to acetaminophen, known for potential liver toxicity, and sevoflurane can potentiate the damage.

The mechanism of sevoflurane-induced hepatotoxicity is suspected to be similar to that of halothane. Halothane is oxidized by hepatic cytochrome P-450 yielding products which bind covalently to liver proteins rendering them immunogenic. Sevoflurane also produces an immunogenic response when it is metabolized by CYP2E1 to trifluoroacetylated reactive intermediate. The attachment of these reactive intermediates to proteins induces the formation of antibodies that attack the liver cells, resulting in acute damage.

Despite the research indicating an association between sevoflurane use and acute liver damage, this case report still leaves several questions unanswered. Most of the literature indicates that liver damage occurs more commonly following repeated exposure to inhalation anesthetics. Our patient only received sevoflurane once and we are unable to confirm if he had received sevoflurane during previous surgeries. Therefore a question remains, what is the incidence of acute liver damage from a single exposure to sevoflurane? In addition, without an autopsy, we are unable to confirm the exact cause of death. We have focused on exposure to sevoflurane, as a possible cause of liver failure in this patient, however there are a myriad of other potential causes including ischemia, sepsis, viral infection and other drug-induced injury. This case report reminds us that even the most minor of procedures can have major consequences. We must always remain cognizant of this potential as we manage our patients and balance the risks and benefits of treatments every day in practice.

**LEARNING POINTS**

1. Despite the multitude of benefits, the use of inhaled anesthetics can cause serious complications.
2. There is an association between inhaled anesthetic use and acute liver failure, especially when used repeatedly.

3. Sevoflurane is one of the most commonly used volatile anesthetics.

REFERENCES


