Delayed Emergence After Hepatic Cyst Aspiration and Sclerosis Under Intravenous Sedation

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Prolonged recovery from anesthesia is a cause of concern among anesthesiologists. Time to emerge from anesthesia is multifactorial and associated with patient factors, anesthetic administered and the type and duration of procedure or surgery. In this case, dexmedetomidine drip with local infiltration of lidocaine was used to afford a cooperative sedation for hepatic cyst aspiration and sclerosis with ethanol. On handover to the post anesthesia care unit, the patient was found to be asleep and barely responsive to any stimulus. Analysis of factors that could have caused delayed emergence in this case pointed to ethanol intoxication as the most probable cause. Continuous attention in monitoring and support of the airway, breathing and circulation until the cause is ascertained remains the primary management. The importance of vigilance and continuous monitoring is highlighted.

Keywords: delayed emergence, aspiration and sclerosis of hepatic cyst, dexmedetomidine, ethanol

INTRODUCTION

In otherwise healthy patients who have undergone a relatively short procedure, the incidence of delayed awakening is practically zero.[1] In this case, we have a patient who underwent hepatic cyst aspiration and ethanol sclerosis with ultrasound guidance under conscious sedation. The delay in return to full consciousness was disconcerting.

The aim of this paper is to make healthcare workers aware that even minimally invasive procedures under monitored anesthesia care can still have potentially life threatening complications. The factors that may have contributed to the delay to full awareness are presented. In particular, acute ethanol intoxication was highly suspected.

Case Presentation

A.O. is an 82 y/o female who was admitted due to complaints of one year history of gradual abdominal enlargement, early satiety and weight loss. She was a known cirrhotic with Child Pugh A. There was no history of change in sensorium, disorientation, jaundice or hematemesis. On physical examination, she was awake, alert, conversant, oriented to three spheres, normosthenic with normal cardiovascular, respiratory, neurologic findings, globular abdomen without asterexis or any other signs of cirrhosis. CT scan of the abdomen showed hepatic cysts with hepatomegaly and absence of splenomegaly and ascites. She was scheduled for percutaneous aspiration of hepatic cyst with possible ethanol injection. Pre-operatively, laboratory exams showed normal hemoglobin (118g/L), thrombocytopenia (95 x 10^9/L), normal creatinine (0.62mg/dL), normal bleeding time (3 minutes), normal prothrombin time (15.9 seconds), normal INR (1.17), 75% activity, and elevated alanine aminotransferase (275 U/L). She was given 3 doses of vitamin K 10mg/IV and 2 units of platelet concentrate 1 hour prior to the procedure. Cardiovascular clearance was granted after an unremarkable 2D echo result.

Upon arrival at operating room 20 minutes before the procedure, dexmedetomidine drip at 0.5mcg/kg/hour was started, and nalbuphine 10mg/IV was given. Intraoperatively, blood pressure was maintained at 110-120/70-80 with a heart rate of 60's. She had a Richmond agitation sedation score of -1 to -2 and was able to follow command to shift body sideways. Aspiration of 1800cc straw colored fluid from two cysts was done under ultrasound guidance. After confirming that no communication existed between the cysts and the biliary tree through fluoroscopy, a total volume of 550cc 99.9% ethanol was injected into and remained in the two cysts for 15 minutes then subsequently aspirated. The procedure lasted for 1 hour and 15 minutes. Dexmedetomidine drip was discontinued at the end of the procedure.

She was transferred to the post anesthesia care unit (PACU) responsive but unable to maintain wakefulness. Vital signs at the time of arrival at the PACU was BP 100/60 mmHg, heart rate 57 bpm, RR 19 cpm, temperature 35.9ºC, 100% oxygen saturation with oxygen supplement of 4 LPM via nasal cannula. She was kept normothermic (36.4-36.8ºC). Oxygen supplementation was continued. One hour after PACU admission, she was noted to be flushed, bradycardic (HR 50's) and hypotensive (BP 80/50) for 30 minutes. Blood pressure and heart rate normalized after 2 doses of atropine 0.5mg/IV and ephedrine 10mg/IV were given. On the 2nd hour of the PACU stay, she was noted to be unresponsive. Glasgow coma scale score was 8 (E1V2M5). Pupils were isocoric at 3-4mm and equally reactive to light. Respiratory rate was at 18-19/minute and respiratory depth seemed adequate. Oxygen saturation ranged from 97 -100%. A capnograph was connected and nasal cannula was shifted to an oxygen face mask to monitor end tidal carbon dioxide level ($ETCO_2$). $ETCO_2$ ranged from 35- 40 mm Hg.

During the 5th hour of the PACU stay, a total of 800mcg naloxone boluses were given but she remained unconscious. Capillary blood glucose was 179 mg/dL. A foley catheter was inserted and urine output was monitored. Repeat CBC (Hgb 148, Hct 0.45, platelets 128 x 10^9/L), serum sodium (142), potassium (3.6), chloride (110) and arterial blood gas showed wide anion gap metabolic acidosis with good oxygenation (pH 7.28, pCO_2 29.4, HCO_3 13.5). Sodium bicarbonate 100 meqs divided into 2 doses were given. After one hour, she regained consciousness.

She was observed for 6 more hours with episodes forof drowsiness and was eventually discharged to the room awake with stable vital signs. While in the room, she had recurring episodes of drowsiness with disorientation for 24 more hours after ethanol injection. She remained anicteric with stable vital signs. Intravenous branched chain amino acid, rifaximin and lactulose were given since concurrent hepatic encephalopathy cannot be entirely ruled out. She was eventually discharged oriented, awake, without episodes of bleeding at the post-op site, 2 days after the procedure.

Discussion

Delayed Emergence

Delayed emergence from anesthesia is often multifactorial. Factors that delay emergence from anesthesia can be grouped into four, namely: patient factor, pharmacologic, surgical, and metabolic factors. [1,2]

Patient Factor

In our case, the patient is a geriatric who has liver cirrhosis with Child Pugh A score without signs of portal hypertension. She has no other comorbidity other than hypertension. Pre-operative history taking, physical examination, laboratory exams, chest xray and 2d-echo showed no evidence of hepatic encephalopathy, pleural effusions, hepatopulmonary syndrome, hepatopulmonary hypertension, hepatorenal syndrome, cirrhotic cardiomyopathy, and coagulation disorders which are associated with chronic liver disease.[3]

Geriatric patients have an exaggerated response to CNS active drugs due to an underlying age related decline in CNS function as well as increased pharmacodynamics sensitivity towards benzodiazepines, general anesthetics and opioids.[4] Old age is also associated with changes in drug pharmacokinetic due to decreased hepatic blood flow and liver mass with reduced hepatic microsomal enzyme function.[5]

Postoperative delirium and cognitive dysfunction (POCD) are topics of special importance in the geriatric surgical population. It is associated with longer hospital stays and increased mortality. Benzodiazepines can precipitate delirium in this population while dexmedetomidine can prevent it.[6,7]

Liver disease affects drug pharmacokinetics as a result of alterations in protein binding, reduced serum albumin, altered volume of distribution and reduced metabolism secondary to abnormal hepatocyte dysfunction.[8,9]

Pharmacologic

Dexmedetomidine was introduced two decades ago as a sedative hypnotic in intubated ICU patients. Its safety and efficacy in sedation of non-intubated patients during surgical and diagnostic procedures has since been studied prospectively.[10] Uses now include sedation for: 1) patients undergoing small or minimally invasive procedures where tracheal intubation is not needed 2) procedures requiring sudden awakening from sedation such as for cooperative clinical examination. [11] When used in therapeutic doses, it is very effective in surgeries that require awake and communicative patients.[12,13] It is metabolized in the liver into inactive metabolites with a mean elimination half-life of 2-2.5 hours with an extraction ratio of 0.71. [14] Use of dexmedetomidine is not contraindicated in hepatic disease but dose adjustments are indicated. In general, the effect of hepatic disease in drugs with high extraction ratio, like dexmedetomidine is predictably altered. Clearance is primarily dependent on hepatic blood flow which is in turn dependent on systemic blood flow. [8,15,16]

Nalbuphine is an agonist-antagonist opioid that binds to μ-receptors, as well as to κ- and δ-receptors. It is a potent analgesic with low side effect profile. It produces few overt behavioral or autonomic affects even in higher doses. [16] Plasma elimination half-life is 5 hours.[8]

Our patient remained unconscious well over the plasma half-life of both nalbuphine and dexmedetomidine. The age and liver pathology of the patient were taken into consideration but only sedation caused by nalbuphine could be reversed. Naloxone is an opioid antagonist that is used to treat opioid overdose including nalbuphine. [17,18,19,20] It reverses all signs of opioid toxicity. It was given at the 5th hour of the PACU stay.

Classic symptoms of opioid toxicity include apnea, stupor and miosis. Although not all three are always present, respiratory depression is considered the sine qua non of opioid intoxication.[18,19] The patient is stuporous but had normal-sized pupils and adequate respiratory rate. These observations made nalbuphine toxicity unlikely.

Surgical

The procedure entails the insertion of a catheter into the cyst with complete emptying of the contents. A volume of ethanol usually equivalent to 25% of the drained fluid is instilled. Ethanol is often used to destroy the secreting epithelial layer of the cyst wall with marked inflammatory reaction.[22] Patients are rolled from side to side to ensure adequate contact of the ethanol to the entire cyst wall and ethanol is then aspirated out.

Our patient underwent this minimally invasive procedure that lasted for 1.25 hours under sedation with dexmedetomidine infusion and one dose of nalbuphine 1.17mcg/kg. Intra-operative vital signs were stable with no episodes of desaturation with oxygen supplementation via nasal cannula.

Metabolic

Some of the metabolic factors causing delayed emergence from anesthesia include the following: hypoglycemia, hyperglycemia (DKA, hyperosmolar nonketotic coma), electrolyte imbalance (hypo or hypernatremia), hypothermia, hypoxemia, hypothyroidism, hepatic or renal failure, and acidosis.

Capillary blood glucose monitoring did not show hypoglycemia or elevated blood glucose levels enough to cause DKA or hyperosmolar nonketotic coma. Repeat electrolytes showed normal serum sodium and potassium. She was kept normothermic. There was no episode of desaturation. Urine output was adequate. Acute on chronic liver failure (ACLF) leading to hepatic encephalopathy could have been a consideration.

Pre-operatively, she was fully awake and had no changes in sensorium. Physical exam was essentially normal except for enlarged abdomen with palpable slightly tender epigastric mass extending to RUQ._Laboratory exams showed evidence of liver dysfunction. According to the Eastern criteria for ACLF (proposed by either Asia–Pacific Association for the Study of the Liver and Chinese Medical Association), liver failure alone is focused on, and the lower cutoff levels of INR (i.e., >1.5) and serum bilirubin (i.e., 5 mg/dL defined by APASL or 10 mg/dL defined by CMA) are taken to define liver failure.[23] In this patient, these laboratory exams as well as blood ammonia levels were not taken during the comatose state. Hepatic encephalopathy could not have been totally ruled out. The investigation was focused on finding possible precipitating factor and other etiologies instead.

Arterial blood gas showed wide anion gap metabolic acidosis with good oxygenation. Among the causes of wide anion gap metabolic acidosis, ethanol intoxication was the most probable. A blood ethanol concentration would have confirmed the diagnosis; however, the test was unavailable.

Ethanol Intoxication

Hepatic cysts are usually asymptomatic and are detected incidentally by imaging examinations. Symptoms usually arise due to the compression effects of large hepatic cysts on surrounding structures including pain, nausea, vomiting, early satiety and obstructive jaundice.[23] Aspiration-sclerotherapy is an effective means of achieving liver volume reduction and relief of symptoms.[24,25,26,27] It is easy to perform, can be performed on an outpatient basis and leads to few complications. [28]

Ethanol destroys the lining epithelium of the cyst and leads to fibrosis and impedance production of fluid. [29] As a treatment agent, ethanol combines the benefits of being widely available, inexpensive, efficacious, and relatively easy to administer.[30] Complications commonly reported include mild pain, transient increase in temperature, nausea and vomiting. [28] Only one incident of ethanol induced coma after ethanol injection into a hepatic cyst was reported by Wernet in 2008.

This may be secondary to ethanol systemic absorption or unintentional intravascular injection.[30] Wernet et al [31] proposed that ethanol can be directly

absorbed through the cyst wall formed by an epithelium which resembles biliary epithelium and a stroma made of thin layer of connective tissue. The high volume (550cc) of ethanol used could have contributed to the volume absorbed even if contact time with the cysts wall only lasted for 15 minutes each.

Van Sonnenberg et al (1994)[32], reported a maximal ethanol blood level of 1.02g/L 1 hour after injection. Blood alcohol concentration needed to produce intoxication varies due to different levels of tolerance to it. CNS depression is produced by binding the GABA receptor and by acting as an antagonist of the NMDA receptor.

The patient is a geriatric with liver dysfunction and no history of alcoholic beverage drinking. Ninety-five percent of ethanol is metabolized in the liver. Impaired metabolism and minimal tolerance to alcohol may have produced the comatose state.

Ideally, a blood ethanol concentration level and blood ammonia levels can be taken to differentiate between acute ethanol intoxication and hepatic coma; however, blood ethanol level determination was not available in the hospital. We believed our geriatric patient initially had ethanol intoxication over hepatic encephalopathy since she remained anicteric with Child Pugh A score with no signs of coagulopathy. Serum electrolytes and blood glucose were taken to rule out any other underlying cause. When she then had episodes of disorientation back in her room, concurrent hepatic encephalopathy could not be ruled out. Measures (rifaximin, lactulose) to lower blood ammonia level were instituted.

Treatment of ethanol intoxication is primarily supportive. Most feared complication of ethanol intoxication includes hypoglycemia and respiratory depression.[33] Patients' respiration and ability to maintain the airway should be closely monitored. Intubation and mechanical ventilation should be done as indicated. Hypoglycemia occurs secondary to ethanol's inhibition of gluconeogenesis. Blood glucose monitoring should be done. The patient in this case was breathing adequately with no signs of respiratory depression. Capillary blood glucose levels ranged from 160-179.

In addition to the two complications, serum electrolyte determination was also done because other metabolic derangements such as hypokalemia, hypomagnesemia, hypocalcemia and hypophosphatemia may be present in alcohol intoxication.[26] Acetaldehyde acetate, a metabolite of ethanol, may also produce hypotension by inducing peripheral vasodilatation. Intermittent hemodialysis is the most efficient way of rapidly lowering serum alcohol levels.[34]

Wide anion gap metabolic acidosis in ethanol intoxication can occur from lactic acidosis or alcoholic ketoacidosis. The management of metabolic acidosis is by treating the underlying cause. Alcoholic ketoacidosis on the other hand, occurs in the background of chronic alcoholic abuse with binge drinking and starvation. Treatment is giving dextrose and saline for hydration. Our patient was not starved and she was hooked to a dextrose containing fluid from the preoperative period making alcoholic ketoacidosis unlikely.

Conclusion

Aspiration of hepatic cyst and sclerosis is minimally invasive requiring a short procedural time, virtually no blood loss and no incision. Monitored anesthesia care with sedation using dexmedetomidine was used to keep the patient comfortable and cooperative without the propensity for respiratory depression; however, she became unarousable in the PACU. Vigilance and continuous monitoring of patients are essential roles of anesthesia providers even in seemingly simple cases. In this case, the interplay of the patient's age, hepatic dysfunction, drugs, drug interaction and ethanol use were contributory to the adverse event. Continuous, meticulous, and vigilant monitoring together with supportive care is again emphasized for a good outcome.

Ethical Considerations

The authors declare no conflict of interest. A written informed consent was obtained from the patient prior to writing the draft of this case report. (consent forms attached)

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