J Anesth (1998) 12:160–163

Journal of
Anesthesia

Clinical reports

Anesthetic management of a patient with acute fatty liver of pregnancy

Naoyuki Fujimura[1], Tetsuo Omote[2], Naoto Inagaki[2], Johji Arakawa[2], Masatoshi Kotaki[2], and Akiyoshi Namiki[1]

[1] Department of Anesthesiology, Sapporo Medical University, School of Medicine, S1 W16 Chuou-ku, Sapporo 060, Japan
[2] Department of Anesthesiology, Asahikawa Red Cross Hospital, 1-1 Akebono, Asahikawa 070, Japan

Key words: Acute fatty liver of pregnancy, Cesarean section, Isoflurane

Introduction

Acute fatty liver of pregnancy (AFLP) is a potentially fatal, uncommon disorder that may complicate the third trimester of pregnancy [1]. In this paper, we present a case of AFLP in which cesarean section was performed under general anesthesia, and discuss the anesthetic management for cesarean section in a patient with this syndrome.

Case report

A 35-year-old woman was admitted to our hospital at 23 weeks of gestation. She had a 5-day of history of general fatigue, appetite loss, nausea, vomiting, and abdominal pain. On physical examination, she appeared jaundiced. Her consciousness was alert. Blood pressure (BP) was 100/50 mmHg, heart rate (HR) was 86 bpm, temperature was 37.1°C, and respiration was 20 breaths per minute. Abdominal examination revealed a 23-week-pregnant uterus. Continuous cardiotocography (CTG) monitoring revealed poor fetal HR variability with a late deceleration pattern. Laboratory data demonstrated acute hepatic impairment and coagulopathy (Table 1). Her previous pregnancy had required cesarean section for cephalopelvic disproportion at 40 weeks but was otherwise uneventful. Since becoming pregnant, she had been checked by an obstetrician regularly and had progressed normally until the 23rd week. She had no past history of liver or gallbladder disease.

Two days after admission, her consciousness became drowsy and she showed flapping tremor. Blood sugar (BS) concentration was 17 mg·dl^{-1}. Fifty percent glucose solution was immediately infused, but the fetal heartbeat disappeared and intrauterine death was confirmed on CTG and ultrasound examination. A CT scan of the liver revealed low-density changes. A clinical diagnosis of acute fatty liver of pregnancy was made, and an urgent cesarean section was considered necessary to avoid the rapid development of fulminant hepatic failure known to occur in acute fatty liver of pregnancy.

No premedication was given. In the operating room, a radial arterial catheter was inserted for continuous BP monitoring. A 3-lead ECG, pulse oximetry, capnography and urinary output monitoring were set up. BP was 100/50 mmHg, and HR was 105 bpm. BS concentration was 245 mg·dl^{-1}. The patient's hepatic encephalopathy was classified as grade II. Anesthesia was induced by a rapid-sequence induction with thiopental 200 mg and succinylcholine 50 mg and maintained with 3 l·min^{-1} nitrous oxide, 2 l·min^{-1} oxygen, and 0.2–0.5% isoflurane. Muscle relaxation was achieved by vecuronium bromide. Arterial blood gas analysis showed pH 7.30, PCO_2 35 mmHg, PO_2 224 mmHg, BE 8.2 mEq·l^{-1}, and BS 277 mg·dl^{-1}. Five units of fresh frozen plasma (FFP), and 700 ml of acetated Ringer's solution were infused during the surgery.

A dead male fetus was delivered and blood loss was estimated as about 200 ml. At the end of surgery, muscle paralysis was reversed with neostigmine 2.5 mg and atropine 1.0 mg. The endotracheal tube was not removed because the patient could not respond to oral commands 60 min after discontinuation of inhalation anesthetics. The patient was transferred to the intensive care unit (ICU) for postoperative management.

Address correspondence to: N. Fujimura
Received for publication on October 11, 1996; accepted on March 23, 1998

Table 1. Perioperative laboratory data

Data	Adm	Preop	Postop	PostPE	POD1	POD3	POD5	POD7	POD14
PT (10–12s)	13.8	12.6	12.4	12.1	13.3	12.2	12.3	12.1	11.0
APTT (26–28s)	39.1	39.9	45.0	42.7	46.6	36.7	30.9	32.0	29.3
HPT (70–130%)	70	100	100	110	85	88	95	135	130
Fibrinogen (200–400%)	213	177	180	181	169	228	297	450	450
AT-III (79–120%)	19	15	59	58	40	65	75	69	70
FDP-E ($-75\,ng\cdot ml^{-1}$)	374	413	680	433	334	493	367	450	295
AKBR (≧1.0)			0.43		1.29	0.89	2.03	1.19	
BUN ($6–20\,mg\cdot dl^{-1}$)	11	25	27	23	14	13	11	10	12
Cre ($0.6–1.3\,mg\cdot dl^{-1}$)	1.5	2.6	2.6	2.1	1.7	0.6	0.7	0.6	0.6
GOT ($10–40\,IU\cdot L^{-1}$)	430	240	193	70	87	80	98	43	88
GPT ($4–50\,IU\cdot L^{-1}$)	450	380	300	71	70	55	58	28	43
LDH ($200–500\,IU\cdot L^{-1}$)	275	286	344	297	292	324	348	286	339
Tbil ($0.2–1.0\,mg\cdot dl^{-1}$)	3.6	3.4	3.8	2.0	3.4	4.6	4.4	4.5	4.7
TP ($6.5–8.2\,mg\cdot dl^{-1}$)	7.5	6.1	5.7	5.3	4.9	6.1	7.1	6.9	7.6
ChE ($7.0–19.0\,IU\cdot L^{-1}$)			3.7		8.3	11.7	13.7	11.8	11.6
RBC ($12–15 \times 10^4\cdot ml^{-1}$)	11.7	11.8	11.9	8.5	7.3	8.9	9.2	9.0	10.3
WBC ($4000–8500\cdot ml^{-1}$)	8300	29600	27400	20100	18560	15280	15490	14860	6640
Plt ($10–40 \times 10^4\cdot ml^{-1}$)	20	18	16.6	8.0	8.0	9.2	9.1	14	37

PT, Prothrombin time; APTT, activated partial thromboplastin time; HPT, hepaplastin time; AT-III, antithrombin-III; FDP-E, fibrin degradation products-E fractionation; AKBR, arterial ketone body ratio; BUN, blood urea nitrogen; Cre, creatinine; GOT, glutamic-oxaloacetic transaminase; GPT, glutamic-pyruvic trans-aminase; LDH, lactate dehydrogenase; Tbil, total bilirubin; TP, total protein; ChE, cholinesterase; RBC, red blood cells; WBC, white blood cells; Plt, platelets; Adm, admission; Preop, preoperation; Postop, postoperation; PostPE, post plasma exchange; POD, postoperative day.

Electroencephalographic examination in the ICU showed grade II hepatic encephalopathy. Plasma exchange (PE) and hemodiafiltration (HDF) were performed to prevent prolongation and deterioration of hepatic encephalopathy. The patient was treated with PE (FFP, 4000ml) for 3h using Plasmacure filters (Kawasumi Laboratory, Tokyo, Japan) 3h after the surgery. Then the patient was treated with HDF for 3h using FB-90UGA filters (Nissho, Osaka, Japan). Two hours after the initiation of PE, her consciousness became clear and she was able to respond to verbal commands. The patient was extubated uneventfully. Hepatic encephalopathy was not recognized during the postpartum period.

A liver biopsy confirmed the diagnosis of AFLP on the 22nd postoperative day. Laboratory studies for acute and chronic viral hepatitis were negative. The patient was discharged from our hospital in excellent condition on the 25th day.

Discussion

AFLP initially has nonspecific symptoms such as headache, fatigue, malaise, nausea, vomiting, and abdominal pain [1]. As with our patient, laboratory data usually show a modest elevation of transaminase, usually up to around 300 units but rarely above 500 units. The bilirubin level may be normal early in the course of the disorder but will rise if the pregnancy is not terminated. Alkaline phosphatase, blood urea nitrogen, and creatinine levels are elevated. Maternal liver function usually improves upon termination of the pregnancy, with rapid normalization of the elevated aminotransferase level [2].

If unrecognized or untreated, AFLP may progress to fulminant hepatic failure with jaundice, encephalopathy, disseminated intravascular coagulation, uncontrollable gastrointestinal bleeding, and death [1]. The immediate termination of pregnancy is recommended for recovery from AFLP. It is supported by the finding that no patient has yet recovered from AFLP before delivery [3]. The diagnosis of AFLP should be done rapidly, because the maternal and fetal lives depend on the immediate termination of pregnancy.

In our case, the fetal heartbeat disappeared just after an occurrence of sudden and profound hypoglycemia before surgery. Maternal starvation- induced ketosis provoked fetal ketonemia, hypoxia, and fetal lactic acidosis [4]. The death of the fetus might be associated with maternal hypoglycemia due to inadequate glycolysis accompanied by liver failure [5]. Hypoglycemia was still recognized 10 days after the surgery. A study of AFLP showed that hypoglycemia was detected in almost all the patients, requiring continuous intravenous infusion of hypertonic glucose solution for up to 1 week after delivery [6]. Hypoglycemia causes a deterioration in the level of consciousness or irreversible damage to cerebral function. Careful monitoring of

BS concentration is needed during the perioperative period.

Advanced AFLP often shows coagulation abnormalities [1,4,7]. Upper gastrointestinal bleeding due to the Mallory-Weiss syndrome or to a duodenal ulcer, or other hemorrhages, are attributed to coagulation abnormalities. In our patient the coagulation abnormality was indicated by prolonged PT and APTT. The elevated level of FDP-E and the reduced fibrinogen reflected intravascular coagulation. Although the intraoperative infusion of 6 units of FFP improved the PT, the APTT remained prolonged after surgery. This suggested the progression of hepatic impairment. Reduced antithrombin-III (AT-III) was still recognized 7 days after surgery. Hepatic synthesis remained defective for several days. Severe AT-III depression is associated with intravascular coagulation in AFLP [8]. Infusion of AT-III and FFP should be facilitated in patients with AFLP.

It is difficult to predict a clinical course in patients with AFLP who have given birth. Elevated serum glutamic- oxaloacetic trans-aminase (GOT) and glutamic- pyruvic trans-aminase (GPT) fall rapidly within 24 to 48 h and return to normal levels within 2 weeks after delivery. Most patients will begin to improve 2 to 3 days postpartum, but in some cases a transient worsening is noted [4,7]. Burroughs et al. [7] described two patients who died within 24 h of delivery. These patients did not recover from deep hepatic coma, despite the induction of labor, and had a rapidly progressive downhill course. In our case, electroencephalography showed grade II hepatic encephalopathy in the postpartum period. Hypoglycemia, the lower value of the arterial blood/ketone body ratio (AKBR), and elevated plasma creatinine (Cre) showed severe hepatic and renal impairment. We performed PE and HDF to prevent prolongation and deterioration of hepatic encephalopathy. After the first treatment of PE and HDF, the patient's consciousness became clear. Hepatic encephalopathy was not recognized after that. AKBR returned to normal levels immediately after PE and HDF. AKBR serves as an indicator of the degree of metabolic derangement [9]. PE and HDF might improve intracellular metabolic derangements with AFLP.

There are some studies that describe the anesthetic management of patients with AFLP [10–12]. Antognini et al. [10] avoided general anesthesia, which may cause the deterioration of liver function and liver blood flow, and they performed epidural anesthesia after correcting coagulopathy by infusion of vitamin K and FFP. Corke et al. [11] chose general anesthesia and emphasized that regional anesthesia was contraindicated in AFLP because of the coagulation abnormality with a risk of an epidural hematoma.

Hemolysis, elevated liver enzyme activity, and low platelet count (HELLP syndrome) represents a severe preeclampsia spectrum. The clinical signs and symptoms and the laboratory data of HELLP syndrome are similar to those of AFLP. Anesthetic management of HELLP syndrome is depend on the underlying preeclampsia condition, such as intravascular volume, adequacy of blood pressure control, and bleeding tendency [13,14]. General anesthesia is recommended in cases with apparent bleeding tendency [15].

General anesthesia was performed in our patient because there was no time to correct the coagulopathy before the surgery. Hepatic synthesis remained defective for several days after the surgery. It seems to be prudent to choose general anesthesia with isoflurane in AFLP.

Isoflurane (1 MAC) anesthesia preserves hepatic blood flow [16]. The 30% reduction in mean arterial pressure induced by isoflurane is not associated with a deterioration in the hepatic oxygen supply [17]. Hepatic venous oxygen saturation is greater and hepatotoxicity is less during isoflurane anesthesia than during halothane anesthesia [16,18]. Sevoflurane at concentrations less than 2.0 MAC produces only moderate changes in hepatic perfusion, and these changes are similar to those produced during isoflurane anesthesia [19]. However, sevoflurane anesthesia with 70% of preoperative systolic blood pressure depresses liver function and hepatic blood flow [20]. Therefore, isoflurane may be one of the most appropriate choices in AFLP.

In summary, we reported general anesthesia for a patient with acute fatty liver of pregnancy undergoing cesarean section. General anesthesia with isoflurane was chosen because of the coagulation abnormality and to preserve hepatic blood flow and function. This case report emphasizes the need for recognition and therapy for rapidly progressive hepatic failure which produces symptoms such as hypoglycemia, coagulopathy, and encephalopathy during the perioperative period.

References

1. Kaplan MM (1985) Acute fatty liver of pregnancy. N Engl J Med 313:367–370
2. Riely CA, Latham PS, Romero R, Duffy TP (1987) Acute fatty liver of pregnancy: a reassessment based on observations in nine patients. Ann Intem Med 106:703–706
3. Ebert EC, Sun EA, Wright SH, Decker JP, Librizzi RJ, Bolognese RJ, Lipshutz WH (1984) Does early diagnosis and delivery in acute fatty liver of pregnancy lead to improvement in maternal and infant survival? Dig Dis Sci 29:453–455
4. Wasserstrum N (1992) Issues in fluid management during labor: general considerations. Clin Obstet Gynecol 35:505–513
5. Sherlock S (1983) Acute fatty liver of pregnancy and the microvesicular fat disease. Gut 24:265–269

6. Reyes H, Sandoval L, Wainstein A, Ribalta J, Donoso S, Smok G, Rosenberg H, Meneses M (1994) Acute fatty liver of pregnancy: a clinical study of 12 episodes in 11 patients. Gut 35:101–106
7. Burroughs AK, Seong NH, Dojcinov DM, Scheuer PJ, Sherlock SVP (1982) Idiopathic acute fatty liver of pregnancy in 12 patients. QJ Med 204:481–497
8. Liebman HA, McGehee WG, Patch MJ, Feinstein D (1983) Severe depression of antithrombin III associated with disseminated intravascular coagulation in women with acute fatty liver of pregnancy. Ann Int Med 98:330–333
9. Ozawa K, Aoyama H, Yasuda K, Shimahara Y, Nakatani T, Tanaka J, Yamamoto M, Kamiyama Y, Tobe T (1983) Metabolic abnormalities associated with postoperative organ failure. Arch Surg 118:1245–1251
10. Antognini JF, Andrews S (1991) Anaesthesia for cesarean section in a patient with acute fatty liver of pregnancy. Can J Anaesth 38:904–907
11. Corke PJ (1995) Anaesthesia for cesarean section in a patient with acute fatty liver of pregnancy. Anaesth Intens Care 23:215–218
12. Thomas SD, Boyad AH (1994) Prolonged neuromuscular block associated with acute fatty liver of pregnancy and reduced plasma cholinesterase. Eur J Anaesthesiol 11:245–249
13. Patterson KW, O'Toole DP (1991) HELLP syndrome: a case report with guidelines for diagnosis and management. Br J Anaesth 66:513–515
14. Crosby ET (1991) Obstetrical anaesthesia for patients with the syndrome of haemolysis, elevated liver enzymes and low platelets. Can J Anaesth 38:227–233
15. Kinouchi K, Fukumitsu K, Yanagi K, Fukami S, Matsuyama M, Hiramatsu K, Takeuchi M, Miyamoto Y, Kitamura S (1996) HELLP syndrome and anesthetic management. Masui 45:617–623
16. Goldfarb G, Debaene B, Ang ET, Roulot D, Jolis P, Lebrec D (1990) Hepatic blood flow in humans during isoflurane-N_20 and halothane-N_2O anesthesia. Anesth Analg 71:349–353
17. Gelman S, Dillard E, Bradley EL (1987) Hepatic circulation during surgical stress and anesthesia with halothane, isoflurane, or fentanyl. Anesth Analg 66:936–943
18. Brown BR, Gandolfi AJ (1987) Adverse effects of volatile anesthetics. Br J Anaesth 59:14–23
19. Frink EJ, Morgan SE, Coetzee A, Conzen PF, Brown BR (1992) The effects of sevoflurane, halothane, enflurane, and isoflurane on hepatic blood flow and oxygenation in chronically instrumented greyhound dogs. Anesthesiology 76:85–90
20. Kobayashi M (1996) The effects of sevoflurane and isoflurane on hepatic blood flow in man. Masui 45:281–286