

Case Report

Local Anesthetic Systemic Toxicity Following General and Epidural Anesthesia in A patient with a History of Muscle Relaxant-induced Anaphylaxis

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We here report that a 71-year-old Japanese woman with a history of anaphylaxis induced by muscle relaxants had local anesthetic systemic toxicity (LAST) following an abdominal surgery under general anesthesia with combined spinal-epidural anesthesia without muscle relaxants. The total dosages of local anesthetics reached 0.67 mg/kg of ropivacaine and 11.5 mg/kg of lidocaine over 12.5 h to obtain sufficient muscle relaxation for surgery. Regional anesthesia is useful in cases in which muscle relaxants are to be avoided during a surgery. However, especially for a patient with risk factors and prolonged surgery, precautions should be taken to prevent LAST.

Key words: muscle relaxant-induced anaphylaxis, local anesthetic systemic toxicity, epidural anesthesia, abdominal surgery

In patients with a history of anaphylaxis induced by muscle relaxants, an alternative method for achieving muscle relaxation during surgery is needed, but few guidelines and review articles are available regarding such alternatives [1]. Anesthesiologists thus encounter the predicament of how to provide adequate muscle relaxation without muscle relaxants. Theoretically, the addition of spinal and epidural anesthesia to general anesthesia could achieve stable muscle relaxation, but an increased use of local anesthetics can cause local anesthetic systemic toxicity (LAST).

Here, we report a case in which LAST occurred after abdominal surgery performed under general anesthesia with combined spinal-epidural anesthesia, in a patient with a history of anaphylaxis induced by rocuronium bromide.

Case Report

A 71-year-old Japanese woman (60 kg, 152 cm, body mass index 26.0 kg/m²) was admitted to the hospital with lower abdominal pain and was diagnosed with a left iliopsoas muscle abscess and pyonephrosis. She had diabetes mellitus preoperatively. Her surgical history included a total abdominal hysterectomy with bilateral salpingo-oophorectomy, a uterine sarcoma resection, endovascular stent grafting into the left common iliac artery, and coil embolization of the left internal iliac artery. She had no allergies and no significant family history on admission. Laboratory test results were within normal ranges, with the exception of a white blood cell count at 14,790 μl^{-1} and a C-reactive protein level at 25.47 mg/dl.

A computed tomography scan indicated that the

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abscess cavity extended from a stent in the left common iliac artery to the plug in the left internal iliac artery, and it showed that stent occlusion had induced collateral inflow vessel development in the left leg. We initially chose to create a femoro-femoral bypass before abscess drainage. During the induction of general anesthesia for the bypass surgery, an anaphylactic reaction occurred, including hypotension, tachycardia and systemic erythema; the surgery was thus cancelled.

The result of an intradermal test conducted 20 days later suggested a causative role for rocuronium bromide and remifentanyl, and it revealed a cross-sensitivity to vecuronium bromide. We then completed a femoro-femoral bypass with the patient under general anesthesia without muscle relaxants or remifentanyl. We planned to remove the patient's artificial materials and perform intraperitoneal drainage and a left nephrectomy with her under general anesthesia with combined spinal-epidural anesthesia and without muscle relaxants or remifentanyl.

The patient was monitored by electrocardiography, noninvasive blood pressure (BP) recording, and pulse oximetry in the operating room. Her vital signs were normal: BP 121/75 mmHg, heart rate (HR) 89 beats/min, and SpO₂ 94% on room air. We inserted an epidural catheter (Th12/L1) and confirmed that there was no backflow of cerebrospinal fluid or blood; we subse-

quently administered 20 mg isobaric bupivacaine into the subarachnoid space. We used 40 mg of propofol and 200 µg fentanyl for the induction of general anesthesia and then intubated the patient with the inhalation of 3% isoflurane with a spray of 4% lidocaine onto the vocal cords.

Anesthesia was maintained with 0.7-1.2% isoflurane and the administration of fentanyl as required. After the effect of spinal anesthesia had diminished, we administered 0.2% ropivacaine and 1.5-2% lidocaine through the epidural catheter. The time course of the dosages of intraoperative local anesthetics during surgery is shown in Fig. 1. A rectal perforation was identified intraoperatively; a colostomy was thus added to the scheduled surgical procedures. Lidocaine was administered as a bolus in addition to a ropivacaine infusion when we determined that muscle relaxation was inadequate. The patient's vital signs were stable: SpO₂ 99%, HR 70-100 beats/min, and systolic BP 90-130 mmHg. There were no adverse events such as arrhythmia.

The durations of surgery and anesthesia were 10 h 29 min and 12 h 31 min, respectively. The total volumes of fluid and blood transfusions, intraoperative blood loss, and urine output were 6,230 ml (red blood cells, 1,680 ml; fresh frozen plasma, 1,200 ml; platelets, 200 ml), 2,855 ml, and 1,300 ml, respectively. The total dosages of ropivacaine and lidocaine were

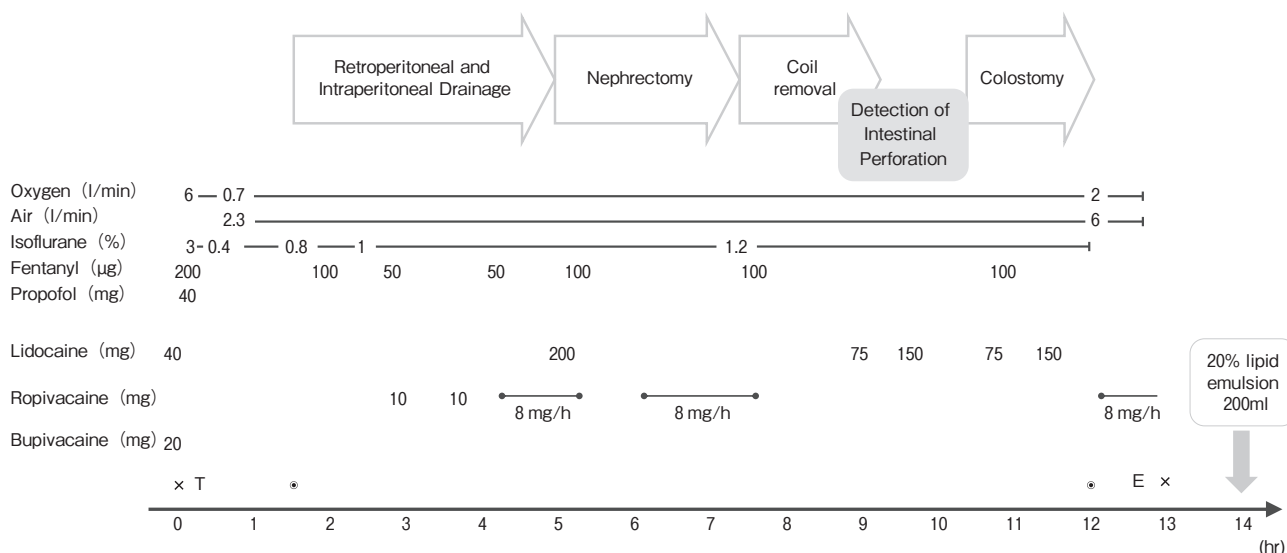


Fig. 1 The dosing timeline of local anesthetics and lipid emulsion; lidocaine and ropivacaine were injected into the epidural space and bupivacaine was injected into the subarachnoid space. A cross symbol: entry and exit to the operation room. A double circle: start and end of the surgery. T; intubation, E; extubation.

40 mg (0.67 mg/kg) and 690 mg (11.5 mg/kg), respectively.

After surgery, the patient breathed spontaneously and opened her eyes, although she could not follow simple verbal instructions. Her pupils were equally 2.5 mm in size. We extubated the patient after a confirmation of adequate laryngo-pharyngeal and esophageal-bronchial reflexes in the operating room. Her cardiorespiratory status was stable. After transfer to the intensive care unit, the recovery of consciousness remained insufficient and the patient showed involuntary movements of her extremities. Because LAST was suspected based on the intraoperative dosages of local anesthetics, we intravenously administered 100 ml of a 20% lipid emulsion. The patient's consciousness and involuntary movements immediately improved; she was able to speak and complain of pain. She was uneventfully discharged to the ward on the third postoperative day.

Discussion

Abdominal surgery for this patient with a history of muscle relaxant-induced anaphylaxis was completed under general anesthesia with epidural and spinal anesthesia and without any muscle relaxants. Postoperatively, the patient showed delayed emergence and involuntary movements of the extremities caused by LAST, which improved after an intravenous injection of lipid emulsion.

Regional anesthesia, including epidural anesthesia, is an effective approach to achieve muscle relaxation without the use of muscle relaxants. The use of a high concentration of local anesthetics can block thick and long motor fibers during epidural anesthesia [2-4]. However, there is no objective method to evaluate the degree of muscle relaxation at this time. We administered primarily a ropivacaine infusion; we added a bolus of lidocaine when motor fiber blocking was needed to secure a surgical field or when the surgeon required muscle relaxation. We might thus have used an excess of local anesthetics.

The appropriate dosage of lidocaine to block motor fibers has not been reported. Becker *et al.* proposed that the maximum individual dose of lidocaine without epinephrine should not exceed 4.5 mg/kg of the patient's body weight and that the maximum total dose should not exceed 300 mg for normal healthy adults [5]. They

also contended that the maximum recommended individual dose of lidocaine with epinephrine should not exceed 7 mg/kg; the maximum total dose should not exceed 500 mg [5].

LAST is associated with the absorption of anesthetic agents, metabolic efficiency and muscle mass, as well as the total amount of local anesthetics [6]. The reported risk factors of LAST are age (<16 or >60 years old), smaller muscle volume (particularly with regard to neonates, infants, and weakened elderly patients), female gender, and comorbidities (primarily cardiac diseases, liver disease, diabetes mellitus, *etc.*) [6]. Our patient had three risk factors: age, female gender, and diabetes mellitus.

The plasma lidocaine concentration during epidural anesthesia reaches a peak level within 15-20 min and then decreases gradually; repeating the injection gradually increases the concentration [7]. In our patient's case, the dosage of lidocaine used as local anesthesia was 450 mg in the last 4 h of the surgery. Thus, the LAST observed in our patient could have occurred because of the intraoperative dosage of local anesthetics, her clinical symptoms, and the immediate effect of the intravenous lipid emulsion, which has been described as an effective treatment for LAST in some guidelines [6,8]. The use of a 20% lipid emulsion for LAST was officially permitted by our institutional committee because it had not yet been approved in Japan.

Importantly, some precautions can be taken to prevent LAST during surgery involving muscle relaxation with local or regional anesthesia, including the reduction of the total amount of local anesthetics as much as possible. First, combined spinal-epidural anesthesia is a good choice, and continuous spinal anesthesia may provide an option to maintain muscle relaxation using a lower dose of local anesthetics. Second, local anesthetics containing epinephrine are useful because epinephrine can limit the maximal blood concentration and prolong the period of peak concentration [9]. A recent study reported that a combined epidural injection of local anesthetics with fentanyl or dexmedetomidine augments the duration and quality of epidural anesthesia and analgesia [10,11]; therefore, this combined injection may reduce the overall requirement for local anesthetics.

In conclusion, we treated LAST that occurred after an abdominal surgery under general anesthesia with combined spinal-epidural anesthesia in a patient with a

history of anaphylaxis induced by muscle relaxants. When patients with contraindications for the use of a muscle relaxant undergo surgery with epidural anesthesia, the cumulative amount of local anesthetics may be high, especially during a long surgery; some precautions are thus needed to prevent LAST.

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