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Successful intralipid-emulsion treatment of local anesthetic systemic toxicity following ultrasound-guided brachial plexus block: case report

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Nguyen Trung Kien[1]
Nguyen Truong Giang[2]
Bui Van Manh[1]
Nguyen Manh Cuong[3]
Ngo Van Dinh[3]
Dinh Cong Pho[4]
Vu The Anh[3]
Dao Thi Khanh[5]
Luu Quang Thuy[6]
Pham Van Dong[7]

[1]Center of Emergency, Critical Care Medicine, and Clinical Toxicology, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam; [2]Department of Cardiothoracic Surgery, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam; [3]Department of Anesthesia and Pain Medicine, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam; [4]Faculty of Medicine, Vietnam Military Medical University, Hanoi, Vietnam; [5]Department of Pharmacy, Military Hospital 103, Vietnam Military Medical University, Hanoi, Vietnam; [6]Center of Anesthesia and Surgical Intensive Care, Vietduc University Hospital, Hanoi, Vietnam; [7]Anesthesia and Pain Medicine, Cho Ray Hospital, Ho Chi Minh City, Vietnam

Background: Local anesthetic systemic toxicity (LAST) is a life-threatening complication that may follow application of LAs through various routes. Despite increasing usage of LA techniques in a large number of health-care settings, contemporary awareness of LAST and understanding of its management are inadequate.

Case presentation: We report two cases who suffered LAST following brachial plexus block for surgery on the upper extremity. The first patient received an ultrasound-guided supraclavicular block with 300 mg lidocaine (6 mg/kg) and 50 mg ropivacaine (1 mg/kg) in 25 mL without epinephrine, and the second patient received an ultrasound guided interscalene block with 200 mg lidocaine (4.5 mg/kg) and 45 mg ropivacaine (1 mg/kg) supplemented with epinephrine 1:200,000. Both patients presented with symptoms of central nervous and respiratory system depression, the first roughly 10 minutes after injection, and the second immediately after withdrawal of the needle. In both cases, thorough recovery was obtained using lipid-emulsion therapy.

Conclusion: The complication of LAST following ultrasound-guided brachial plexus block could be treated successfully applying the American Society of Regional Anesthesia and Pain Medicineprotocol of intravenous administration of lipid emulsion.

Keywords: local anesthetic system toxicity, lipid emulsion

Background

The first documented cases of local anesthetic systemic toxicity (LAST) were about 100 years ago, with the report of 40 deaths related to LAs by the American Medical Association in 1928.[1] Current data have revealed that the primary mechanism of LAST is multifactorial, with varied cellular consequenses in the cardiovascular system and central nervous system (CNS). Several cohort studies from 1993 to 1997 indicated that the incidence of LAST for epidural anaesthesia was about 1.2–11 per 10,000 cases,[2] while incidence after peripheral nerve blockade varied from 2.5 to 9.8 per 10,000.[3,4,5] The year 2006 witnessed the first human patient to be sucessfully resuscitated from LAST by lipid emulsion.[6] Thereafter, there have been some clinical reports confirming reversal of LAST by lipid emulsion in adults and children.[7,8]

Case presentation

Case one

In June 2016, a 73-year-old male patient with a body-mass index (BMI) of aproximately 18.5, was admitted to Millitary Hospital 103 with right-hand injury because of a labor accident requiring an emergency surgery for wound debridement

Correspondence: Pham Van Dong
Anesthesia and Pain Medicine, Cho Ray Hospital, 201 Nguyen Chi Thanh Road, Ward 12, District 5, Ho Chi Minh City 700000, Vietnam
Tel +84 90 391 9391
Email pvdongbvcr@gmail.com

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and reconstruction of index- and middle-finger amputation under supraclavicular block. Biochemical laboratory values and blood formulae were within normal ranges, except for mildly elevated serum AST and ALT levels of 122 U/L and 117 U/L, respectively. Intravenous access was obtained, 2 L/min oxygen by face mask provided, and routine hemodynamic monitoring performed. On physical examination, the patient's vital signs were steady.

After conscious sedation with intravenous 100 µg fentanyl and 20 mg propofol, an ultrasound-guided supraclavicular brachial plexus block was performed with 300 mg lidocaine (6 mg/kg) and 50 mg ropivacaine (1 mg/kg) in 25 mL. Aspiration every 2–5 mL was negative. Verbal communication was sustained during the procedure to monitor mental status and reduce the risk of intraneural injection.

About 3 minutes after the block, the patient felt numbness in his arm. Motor block assessed by Bromage score indicated level 2. Roughly 10 minutes after withdrawal ofg the needle, the patient became confused, unconscious, and then apneic. SpO_2 decreased from 100% to 50%. Supported ventilation via face mask with 100% oxygen was applied for 5 minutes, and SpO_2 recovered to a normal range of 98%–100%. Hemodynamics were stable throughout this period. Spontaneous breathing returned to a rate of 18 per minute, but the patient was still unconscious and did not respond to verbal commands or deep pain stimulation anymore. Pupils were a normal size and replied adequately to light.

At 20 minutes after loss of consciousness, intravenous 10% lipid-emulsion therapy was initiated with a bolus dose of 3 mL/kg (150 mL) for 1 minute. Immediately after completion of the bolus dose, the patient opened his eyes, responded well to verbal commands, and achieved full recovery. We did not use continuous infusion of lipid emulsion, and the surgical procedure continued for 64 minutes under brachial plexus anesthesia. The patient was transferred to the postoperative care unit with normal hemodynamic and respiratory parameters. He was discharged after 7 days of treatment.

Case two

In March 2018, a 32-year-old female patient was admitted to Military Hospital 103 for treatment of an osteoma in the upper head of the left humerus. She had undergone seven operations before, and was scheduled to undergo left glenohumeral joint-replacement procedure. The old surgical site was still swollen and secreting purulent exudate. The patient had an asthenic body habitus with a BMI of 18.5 (1.55 m and 45 kg). ThLaboratory values related to cardiac and pulmonary function were within normal physiological limits. Vital parameters were observed continuously on a Nihon Kohden monitor, oxygen was given via face mask at a rate of 5 L/min, and an 18 G intravenous needle was placed. Her mental status was normal. Vital signs immediately before anesthesia indicated heart rate (HR) 84 beats/minute, blood pressure (BP) 125/55 mmHg, and SpO_2 100%.

An interscalene block was performed under ultrasound guidance. Lidocaine (200 mg) and 45 mg ropivacaine with epinephrine 1:200,000 were administered after ensuring that the tip of the needle was indeed within the plexus cover on the ultrasound screen and there was no blood aspiration in the syringe. While the last 5 mL of anesthetic was being injected, the patient suddenly felt dizzy and reported a metallic taste with perioral and tongue numbness. The anesthesiologist aspirated a small amount of blood in the syringe, stopped the injection, and withdrew the needle. The patient showed clouding of consciousness and slowing response to verbal commands. Vital signs at this time were HR 88 beats/minute, BP 127/60 mmHg, and SpO_2 100%. Around 30–40 seconds after stopping injection, HR increased to 140 beats/minute, BP increased to 201/130 mmHg, SpO_2 maintained 100%. Two minutes after stopping the injection, the patient lost consciousness completely, breathed very slowly, and was provided ventilation support via face mask and manual resuscitator. The monitor showed that hemodynamic values had returned to the patient's baseline: HR 89 beats/minute, BP 119/74 mmHg, and SpO_2 100%. The cardiac rhythm was sinus, and she remained stable.

Ten minutes after LA administration, the patient was given an intravenous injection of 20% lipid emulsion 70 mL for 1 min (3 mg/kg), followed by an infusion of 150 mL for 15 minutes. After the bolus dose of lipid emulsion, the patient regained consciousness, responded well to verbal commands, and was oriented to name and age. After a further 20 minutes, the patient was completely conscious, communicated well, and was fully oriented. Her left upper extremity continued to manifest signs of effective sensory and motor brachial plexus blockade: 2/5 motor strength (movement possible, but not against gravity). She continued to report perioral and tongue numbness. After 2 hours, 20 minutes, patient was transferred to the inpatient ward, where we continued to observe her progression. After 48 hours, the patient had achieved complete recovery and there were no sequelae.

Discussion

The typical manifestation of LAST often originates with prodromal symptoms, such as dizziness, tinnitus, perioral numbness, agitation, and confusion. These may be followed by CNS derangements, such as excitation (eg, confusion, muscle twitching, or seizure), depression (eg, drowsiness, obtundation, coma, or apnea), cardiovascular derangements, such as hypertension, tachycardia, bradycardia, asystole, or ventricular arrhythmias, or a combination thereof. In our first case, the symptoms of CNS dysfunction appeared without any prodromal signs, whereas the second one followed the classical progression in which CNS toxicity was preceded by altered sensoria (dizziness, metallic taste, perioral and tongue numbness). The differential diagnosis for these symptoms may comprise drug allergy, pulmonary embolism, cardiovascular crisis, and LAST. The typical symptoms of type 1 anaphylaxis include urticaria, bronchoconstriction, hypotension, nausea, and vomiting. Neither patient presented with any of these signs. In addition, the incidence of allergic reaction to amide LAs is extremely low, and thus a diagnosis of drug allergy may be ruled out. Pulmonary embolism is typically characterized by pain, altered mental status, tachypnea, normoxia, tachycardia, and hypertension. Although our two patients exhibited some changes in perceptual condition and some cardiovascular signs, their physical and laboratory examinations showed no risk factors or evidence of pulmonary embolism. Unconsciousness and apnea in the first patient is unlikely to have been a result of the fentanyl or propofol that was administered for sedation, because verbal contact was maintained during the procedure and his symptoms did not begin until >10 minutes after the procedure had been completed. Given the nature and progression of their symptoms associated with brachial plexus blockade, we established a diagnosis of LAST in both cases.

Recent data have demonstrated that atypical types account for about 40% of LAST,[9] and in 68%–77% of cases CNS toxicity, presenting as seizures or coma, is the most prevalent attribute.[10,11] It is clearly evident that the two patients presented with CNS symptoms (altered mental status followed by unconsciousness). It is noteworthy that the short-lived increase in HR (140 beats/minute from a baseline of 88 beats/minute) and BP (201/130 mmHg from a baseline of 127/60 mmHg) in the second patient was likely related to the effect of epinephrine used as an indicator of inadvertent intravascular injection, rather than the presentation of cardiovascular toxicity. The majority of LAST events take place immediately following injection of LAs.[2] However, recent data have also revealed that delayed onset may happen at a variety of time points up to several hours following commencement of an administration. Whether LAST presents with an early or delayed onset depends on the mechanism that leads to the event. LAs thatreach the circulation via systemic absorption from surrounding tissue often result in postponed presentation, whereas accidental intravascular injection leads to rapid exhibition.[12] This mechanism may explain why the onset duration for LAST in the first case was 10 minutes, while the event happened immediately in the second case.

The risk factors of toxicity include the type and dose of LA, injection around a vessel-rich region, preexisting pulmonary, cardiac, and nervous system vulnerability, extremes of age, needle or catheter placement without imaging devices, and small or limited muscle mass.[12] Precautions employed in our two cases to minimize the occurence of LAST included use of ultrasound guidance, aspiration before injecting to detect intravascular needle placement, use of epinephrine as an indicator for accidental intravascular injection, and optimizing the dose according to patient weight. In the first patient, however, 6 mg/kg lidocaine and 1 mg/kg ropivacaine without epinephrine was a significantly high dose, especially for a 73-year-old and 18.5 BMI patient with modest muscle mass. Skeletal muscle plays an important role as a depot for systemically absorbed LAs.[13] Similarly, although the dose:weight ratio of anesthetics in the second patient was not really high (approximately 4.5 mg/kg lidocaine and 1 mg/kg ropivacaine with epinephrine), the risk was still substantial for such a diminutive patient. According to Felice and Schumann,[14] the maximum dose of lidocaine is 6–8 mg/kg. However, the emergence of LAST may be related more to plasma concentration than the total amount of drug injected.[15] Symptoms of toxicity may occur at concentrations of 6 μg/mL, convulsions may be seen at 10 μg/mL, and cardiovascular collapse at levels of 30 μg/mL.[16] We lacked the laboratory support to examine these patients' serum LA concentration.

It is easily recognized that the main reason for the toxicity in the second patient was the unintended intravascular administration of anesthetics. Although performing regional anesthesia under ultrasound guidance offers several potential advantages, including the use of smaller volumes of LAs and direct visualization of the drug's spread, thus reducing the risk of inadvertent intravascular injection of LAs,[17–19] incomplete visualization of the

needle or movement during injection may still result in intravascular injection. Evidence for intravascular injection in this case were aspiration of blood during injection of the last 5 mL of anesthetics, the immediate symptoms experienced by the patient, and the elevation of HR and systolic BP 30–40 seconds after injection. A rise in HR of at least 10 beats/minute or an increase in systolic BP of at least 15 mmHg may imply an intravascular injection. The increase in HR and BP cannot have been a cardiovascular effect of LAST, because it existed for a very short time, there was no other dysrhythmia, and electrocardiogramphy showed a continuous sinus rhythm.

Presently, seizure control, advanced cardiac life support, and prompt lipid-emulsion therapy are the three pillars in the algorithm of treatment for LAST. Seizure activity can be treated effectively by intravenous benzodiazepines or barbiturates (eg, phenobarbital). Supplemental oxygen is necessary for any patient undergoing LAST, but for severe cases with hemodynamically unstable arrhythmia, apnea, or cardiac arrest, immediate invasive airway management or circulatory support should be considered. The goals are to guarantee adequate ventilation and sufficient organ perfusion, especially of the heart, brain, and kidneys, with well oxygenated bloodand to prevent progression of acidosis until commencement of lipid-emulsion therapy.[16] Our two patients did not have seizures or cardiovascular dysfunction, so seizure management and advanced cardiac life support were unnecessary. They were provided supplemental oxygen at a rate of 5 L/min and given ventilation support via facial mask and manual resuscitator as needed.

Weinberg recommended that lipid infusion should be initiated as early as possible and vasopressor drugs not be used as it may worsen acidosis and precipitate arrhythmia.[16] According to the American Society of Regional Anesthesia and Pain Medicine,[20] 20% lipid-emulsion therapy should include a bolus over 2–3 minutes of 100 mL for patients >70 kg or 1.5 mL/kg if the patient is <70 kg (ideal body weight). Following the bolus, it recommends an infusion of 200–250 mL over 15–20 minutes if patient is >70 kg or 0.25 mL/kg/min if the patient is <70 kg, to be continued for at least 10 minutes after circulatory stability has been attained. If circulatory stability is not attained, consider rebolus or increasing infusion to 0.5 mL/kg/min. Because the 20% commercial product was not available, we utilized an equivalent dose of 10% emulsion with 3 mL/kg (150 mL) bolus, with prompt resolution of signs and symptoms of toxicity. In the second patient, the initial dose of lipid emulsion was given after 10 minutes with a bolus injection of 70 mL 20% lipid emulsion for 1 minute and then continuous intravenous injection of 150 mL for 15 minutes, with a similarly prompt recovery. The rapid effect of lipid emulsion can be explained by its multifactorial mechanism, where lipid employs a scavenging effect (also known as the "lipid sink") in which a large lipid phase in the serum is able to extract LAs from the plasma. There is also a direct metabolic effect in which mitochondrial lipid metabolism is impeded,[21] thus lowering tissue acidosis and reducing carbon dioxide production. It has a role in activating calcium and potassium channels as well.

Conclusion

Ultrasound-guided peripheral nerve block carries a risk of LAST. We recommend following the American Society of Regional Anesthesia and Pain Medicine protocol of lipid-emulsion therapy as soon as possible if there are any changes in CNS or cardiovascular function related to usage of LAs.

Ethics approval and consent to participate

The case reports received approval for publication from the Ethics Committee of 103 Military Hospital.

Consent for publication

Written informed consent for publication of the clinical details and clinical images was obtained from the patients.

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Disclosure

The authors report no conflicts of interest in this work.

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