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Case Report

Local Anesthetic Systemic Toxicity Joint Management in the Prehospital Environment: A Case Report

Alberto Gabrieli, MD[1], Caterina Barberi, MD[2], Caterina Compostella, MD[1], Michela Azzolini, RN[1], Andrea Butturini, RN[1], Gabriele Larger, RN[1], Lara Boldo, RN[1], Matteo Paganini, MD[1,*], Roberta Levato, RN[1], Andrea Ventura, MD[1]

[1] *Trentino Emergenza Emergency Medical Service, Trento Healthcare Trust, Trento Healthcare Trust (APSS), Trento, Italy*
[2] *Emergency Department, S. Maria del Carmine Hospital, Rovereto, Trento Healthcare Trust, Trento Healthcare Trust (APSS), Trento, Italy*

A B S T R A C T

Local anesthetic systemic toxicity (LAST) is a potentially life-threatening complication that may occur after local anesthetic injection. After reaching the systemic circulation, cardiovascular and central nervous system derangements may appear, with potentially fatal complications if left untreated. The pillars for LAST treatment are advanced life support measures, airway and seizure management, and a 20% lipid emulsion intravenous administration. When occurring in the prehospital setting, LAST is difficult to recognize, mostly because of its features overlapping with other acute conditions. Prompt treatment is also challenging because lipid emulsion may not be routinely carried on emergency vehicles. This article reports a case of LAST occurring in a dental ambulatory located in a remote location within the Italian Alps in which effective communication among different components of the same regional health care system (dispatch center, prehospital teams, and hospital network) led to fast lipid emulsion retrieval en route and on-site toxicity resolution. This case can inspire future operational changes, such as antidote networks available to prehospital emergency medicine crews, avoiding unnecessary deployment of antidotes on ambulances or helicopters, which is difficult to preserve without increasing management costs. However, to be established, such a network would need protocols to facilitate antidote retrieval, training focused on toxidromes recognition, and improved communication skills among different professionals involved in prehospital emergency medicine.

Local anesthetic systemic toxicity (LAST) is a potentially life-threatening complication that may occur with local anesthetics (LAs) regardless of the administration route. After tissue infiltration or a nerve block, LA may accidentally reach the systemic circulation, leading to different degrees of toxicity. Cardiovascular and central nervous system (CNS) derangements are the 2 most dangerous complications of this rare adverse reaction. The recommended treatment for LAST consists of advanced life support measures, airway and seizure management, and a 20% lipid emulsion intravenous administration. This case report describes how effective communication between the hospital and prehospital systems in a high-performance organizational network led to localization and retrieval en route in a short time of a lifesaving drug with a positive impact on patient outcomes.

Case Report

In a dental practice of a peripheral town within the Italian Alps, an 89-year-old woman experienced syncope after receiving local anesthesia with articaine + epinephrine for a supraperiosteal infiltration. After the call made by the dentist, an advanced life support ambulance (staffed with a certified nurse and emergency medical technicians) was emergently dispatched. At that point, the patient lost consciousness, manifesting generalized seizures with sphincteric incontinence.

Upon the ambulance arrival, medical control was notified of the following clinical picture: reduced level of consciousness with left-sided limb weakness, peripheral oxygen saturation of 75%, hypotension (75/45 mm Hg), peripheral cyanosis, and normal heart rate (HR) (84 bpm, possibly due to beta-blocker use).

*Address for correspondence: Matteo Paganini, MD, Trentino Emergenza Emergency Medical Service, Trento Healthcare Trust, Trento Healthcare Trust (APSS), via Pedrotti 16, 38121, Trento, Italy.
E-mail address: matteo.paganini@apss.tn.it (M. Paganini).

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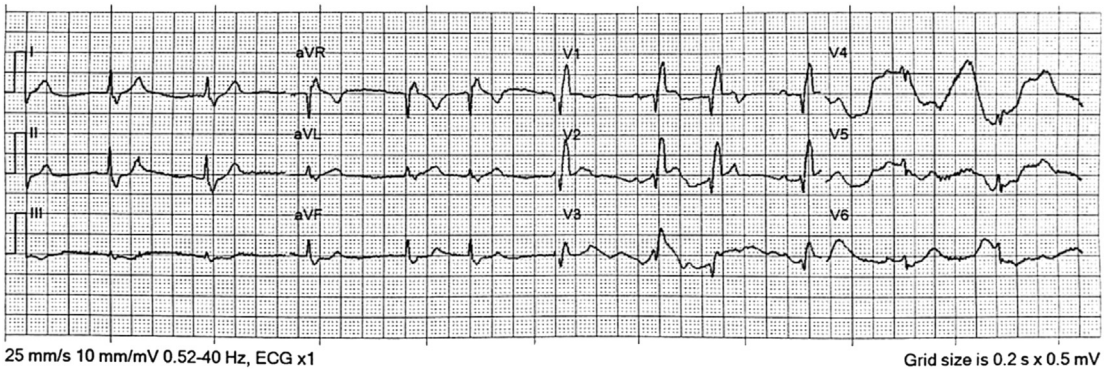

Figure 1. The patient's electrocardiogram showing sinus rhythm with a prominent terminal R wave in aVR (but R/S ratio < 0.7) and corrected QT interval within normal ranges.

Two large-bore peripheral intravenous (IV) cannulas were placed, and a 500-mL normal saline bolus was administered. In the meantime, an electrocardiogram (EKG) was obtained (Fig. 1), demonstrating a sinus rhythm with an HR of 70 beats/min, enlarged QRS complexes, and ischemia-like alterations in the anterior leads. Because of the minimal hemodynamic response to IV fluids, the clinical picture, and the acute EKG alterations, the helicopter emergency medical team (a medical crew composed of an anesthesiologist and a nurse) was activated.

Given the peculiar clinical presentation after LA administration, a high suspicion for LAST arose during dispatch. With the helicopter already en route, the dispatch center's doctor promptly contacted the local community hospital to obtain 20% lipid emulsion (Intralipid, Fresenius Kabi Italia S.r.l., Isola della Scala, Italy) from the anesthesia department. The helicopter retrieved the medication and arrived at the dental practice, finding the patient in respiratory distress with HR increased to 117 beats/min and still hypotensive (85/50 mm Hg). Her Glasgow Coma Scale score was 9 (E2 + V2 + M5) with anisocoria (left > right), and her blood glucose was 109 mg/dL. Strength and sensory deficits progressed to all 4 limbs. After IV administration of Intralipid (100-mL bolus), the clinical picture improved significantly; her blood pressure increased to 145/70 mm Hg, HR normalized to 85 beats/min, peripheral oxygen saturation reached 99% with O_2 administration, and her Glasgow Coma Scale score improved to 14 (E3 + V5 + M6) with resolution of neurologic deficits (except amnesia for the event). Immediately after reaching hemodynamic stabilization, the patient was transferred to the district's referral hospital, maintaining a continuous Intralipid infusion according to currently established protocols. She was hospitalized in a subintensive ward for 3 days, monitoring EKG, troponin, and neurologic status, and was eventually discharged home without sequelae.

Discussion

LAST is an uncommon, life-threatening complication of LA administration.[1] The main risk factors are represented by the dose and volume of the LA administered; extremes of age (infants and elderly); low body mass; and cardiovascular, hepatic, renal, or metabolic dysfunction.[2] The reported incidence of LAST is low, with events reported in 2 to 2.8 per 10,000 peripheral nerve blocks in recent literature, although the number could be underestimated because of misdiagnosis.[3] A small percentage of patients develop severe symptoms (3.5%), for whom treatment with Intralipid becomes crucial; despite appropriate therapy, less than 0.5% die as a result of LAST.

To minimize the chance of an adverse reaction, LA selection is fundamental. The patient's allergies, age, and comorbidities[4] should be weighed against each anesthetic's features. For example, bupivacaine (a lipophilic LA) is more cardiotoxic than shorter-acting LAs (such as lidocaine),[2] even at small doses, potentially causing cardiovascular symptoms without prior CNS effects. Also, doses should be carefully calculated during the initial assessment and injected after aspiration to avoid inadvertent intravascular administration.[5,6] Before administering LA, it is advisable to calculate the maximum dose according to the ideal weight and the type of local anesthesia, although the serum concentrations of LAs depend not only on the dose itself but also on the injection technique, place of injection, and the addition of additives to the LA.

From a pathophysiological point of view, cardiovascular and CNS manifestations are caused by membrane-based voltage-gated sodium channel blockade, thus hampering sodium influx, depolarization, and generation of action potentials.[2,3] Within the CNS, the net effect is a disruption of inhibitory neuron depolarization, leading to neural excitation and seizures or involuntary muscle activation. At higher LA plasma levels, CNS depression can occur, resulting in altered mental status, coma, and respiratory arrest.[5] In the cardiovascular system, LAs can affect myocardial contractility or worsen an already compromised cardiac function. Also, the conduction system can be affected, leading to PR, QRS, and QT interval prolongation. In particular, the QT interval can be prolonged due to potassium channel (efflux) blockade.[3] Overall, cardiac toxicity is considered the most important factor influencing LAST severity and patient's survival.[7]

Notably, the addition of vasoconstrictors, such as epinephrine, can dramatically slow the absorption of LAs from the injection site, improving safety and prolonging the anesthesia.[4] In dentistry, articaine seems to be the most appropriate anesthetic[8] because of its shorter duration effect in soft tissues and lower pain reported by patients during the immediate postoperative period.[9] Moreover, in commercially available articaine solutions, epinephrine is in low concentration (from 1:100,000 to 1: 200,000), thus reducing the risk of adverse reactions. Any recommendation on the maximal safe LA dose can be valid only in reference to a specific nerve block procedure.[1]

All practitioners administering LA, especially in an out-of-hospital setting, must be aware of LAST to recognize and treat it promptly. However, LAST management is poorly known, as previously noted by Oksuz et al.[10] Little effort is sufficient to improve LAST awareness (eg, by establishing periodical simulations and implementing visual aids and flowcharts in the clinical environment).[11]

According to the medical literature, the pillars for LAST treatment are advanced life support measures, airway and seizure management, and 20% lipid emulsion intravenous administration.[2,4] Per the American Society of Regional Anesthesia recommendations, an IV bolus should be provided over 2 to 3 minutes with subsequent infusion over 15 to 20 minutes based on ideal body weight.[3,12] In case of refractory cardiovascular instability, another bolus can be repeated every 5 minutes. This infusion should not be used in patients allergic to egg yolk phospholipids and soybean oil.

Although the full mechanism of action of lipid emulsion still remains unclear, a multimodel theory has developed over the years. Historically, 20% lipid emulsion was thought to act as a "lipid sink"[1]

through its ability to take up lipophilic moieties (LAs) and transfer them to sites of storage and detoxification.[3] However, the scavenging effect is not sufficient to explain the rapid recovery after antidote administration. A second and more powerful effect seems to act directly at the level of the myocardium: 20% lipid emulsion may improve sodium channel function, increasing cardiac output through a combination of volume and direct cardiotonic effects once the cardiac concentration of drug drops below ion channel–blocking thresholds. Inotropy is also potentiated through increased myocyte intracellular calcium inflow. Finally, lipid emulsion acts as a fatty acid energy substrate to the myocardium itself, counteracting the deleterious effect of LAs on fatty acid delivery to the mitochondria.[4]

In this case, the treating dentist did not immediately recognize the intoxication, and the advanced life support ambulance personnel initially interpreted the clinical picture as an acute neurologic event. Delays in disease identification are known to worsen patients' outcomes, especially in intoxications. Prehospital emergency medicine personnel should be trained in toxicology to improve toxidrome recognition because this task could be extremely challenging for the dispatch center personnel who cannot visit the patient.

When the dispatch center personnel integrated the information collected on site by the ambulance crew, namely, the clinical picture plus the recent articaine administration, sharing them with medical control, the suspicion of LAST arose immediately. Unfortunately, not all antidotes can be carried in emergency vehicles for 2 main reasons. First, some drugs require particular storage; second, given the low incidence of such toxidromes, antidotes may expire without being used and increase overall costs. To overcome this obstacle, the dispatch center personnel contacted the local hospital on the helicopter route to retrieve the lipid emulsion and bring it to the patient within minutes. Effective communication among different components within the same regional health care system (dispatch center, prehospital emergency medicine teams, and the hospital network) allowed fast resource collection and time optimization, leading to the best possible solution for drug retrieval and toxicity on-site resolution.

In a recent work published by Setrinen Hansen et al[13] regarding the interface between rural and urban Swedish emergency departments, the authors discovered that strong interpersonal relationships among colleagues were crucial factors in job satisfaction and execution, with decisive implications in patient management. Logistical challenges encountered by physicians were frequently solved, sometimes by adopting "improvised" solutions. Similarly, in our prehospital emergency system, frequent online meetings and multisite joint training favor interactions between professionals and different districts' crews. The flexibility and adaptability of the transport system are great resources, helping to create alternative solutions.[13]

Likewise, the possibility of mutual exchange of resources in case of emergency medical treatment on the territory can be achieved only when good communication is present and protocols are established. However, should an unpredicted problem arise during rescue deployment, the operations center needs to be aware of the localization of resources, especially antidotes.

In the present case, the crucial exchange of information between intra- and prehospital emergency professionals allowed the retrieval of an antidote that was not available in advanced rescue vehicles but was readily accessible by contacting the hospital en route and organizing the physical pickup along the way, allowing the patient to be stabilized and her life to be saved. As previously demonstrated, effective communication affects organizational performance,[14] and simulation-based interprofessional training was shown to improve effective team communication.[15]

In conclusion, we advise that prehospital emergency systems develop LAST treatment protocols and training in toxicology to improve toxidrome recognition and treatment. It would be desirable that a network of antidote repositories be identified in each hospital network in case of toxicology emergencies to organize timely retrieval by the local emergency medical system. Also, health care personnel communication skills should be strengthened through continuous training to improve patient safety.

Declaration of Competing Interest

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CRediT authorship contribution statement

Alberto Gabrieli: Conceptualization, Methodology, Writing – original draft. **Caterina Barberi:** Writing – original draft. **Caterina Compostella:** Methodology. **Michela Azzolini:** Writing – review & editing. **Andrea Butturini:** Writing – review & editing. **Gabriele Larger:** Writing – review & editing. **Lara Boldo:** Writing – review & editing. **Matteo Paganini:** Conceptualization, Methodology, Writing – original draft. **Roberta Levato:** Supervision. **Andrea Ventura:** Supervision.

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