

Local anesthetic systemic toxicity: An adverse drug reaction that could be mistaken for drug anaphylaxis

Toxicidade sistémica dos anestésicos locais: Uma reação adversa medicamentosa que pode ser confundida com anafilaxia

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To the editor,

Suspected hypersensitivity reactions to local anesthetics (LAs) are a common cause of referral to Allergy and Clinical Immunology Departments. Adverse drug reactions to LAs have been estimated to occur in 2.5-10% of patients, the vast majority comprising non-immune mediated reactions like overdose, toxic levels from compromised metabolism, intravascular administration of LAs not intended for intravenous use, anxiety from the needle puncture, or the systemic effects

of added epinephrine (1,2). True hypersensitivity immune-mediated reactions to the currently used aminoamide LAs are very rare, they are estimated to contribute to less than 1% of all cases (1,2).

An 18-year-old male patient with no relevant past medical history was referred to our Allergy and Clinical Immunology Department for evaluation of a suspected hypersensitivity reaction to LAs. On two different occasions, six months apart, the patient developed generalized tonic-clonic seizures during sleep approximately six hours after receiving LAs for teeth extraction (articaine in the

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first episode and lidocaine in the second). The patient described that repeated injections were necessary for adequate anesthesia, and reported no other symptoms. Neurological evaluation, including brain computed tomography, magnetic resonance imaging and electroencephalogram, was unremarkable except for a small parietal cavernoma. He had no previous history of seizures and is currently free of events after more than two years. No LAs have been administered since. After consideration, the events did not suggest a hypersensitivity reaction, and a diagnosis of local anesthetic systemic toxicity (LAST) was considered likely.

LAST is a potentially life-threatening complication of the use of LAs. The reported incidence is as high as 1-2 cases per 1.000 nerve blocks, but an increasing proportion of cases are being reported in the setting of local tissue infiltration of LAs or intravenous administration of lidocaine (3). Toxicity is related to the plasma concentration of LAs and is thought to result from the impairment of ionotropic and metabotropic cell signaling and, importantly, mitochondrial function (3). Signs and symptoms include perioral paresthesia, dysgeusia, tinnitus, lightheadedness, tremor, dysarthria, and confusion, which may progress rapidly to seizures, coma, hypotension, cardiac arrhythmias, and cardiac arrest. Although typically presenting immediately (when resulting from an intravascular injection) or in the first hour after administration (when resulting from systemic uptake), delayed onset has been reported (3,4). In our case, we hypothesize that the presence of the parietal cavernoma may have contributed to a lower seizure threshold. We recommended that the subsequent use of LAs occurs in-hospital, with meticulous avoidance of intravascular injection, careful attention to dosing, and prolonged monitoring. Management of LAST consists of respiratory and circulatory support, suppression of seizures, and administration of intravenous lipid emulsion 20% (3,5). Lipid emulsion antagonizes the systemic toxicity of LAs, and early administration has been recommended. Appropriate up-to-date publications can

be consulted for dosing details, for example, the American Society of Regional Anesthesia and Pain Medicine 2020 checklist (5).

In summary, neurological or cardiovascular symptoms after the administration of LAs, particularly when unaccompanied by typical allergic manifestations, should prompt consideration and treatment of LAST. Importantly, all physicians dealing with LAs should be aware of this potentially fatal complication and of its management. Allergy specialists, in particular, must consider this possibility in the workup of suspected allergy to LAs and when administering LAs in drug provocation tests. A multidisciplinary evaluation by allergists and anesthesiologists is warranted to manage these cases.

Conflict of interest

The authors have no conflict of interest to declare.

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