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Case Report

ANESTHESIA AND CRITICAL CARE

ISSN: 2687-7996

Encephalopathy after Erector Spinae Plane Block When Should LAST Be First?

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Abstract

Local anaesthetic systemic toxicity (LAST) is classically described as central nervous system (CNS) excitation followed by cardiovascular collapse. Atypical and isolated CNS presentations are increasingly recognized but may be overlooked, particularly in the absence of clinically apparent seizures or hemodynamic instability. Contemporary case series demonstrate that LAST does not require the classic combination of seizure and cardiovascular collapse, with isolated CNS toxicity accounting for approximately half of reported events. We describe a man in his 70s admitted with a spontaneous pneumothorax due to a ruptured bleb who was also found to have a left upper lobe pulmonary nodule. He subsequently underwent robotic-assisted thoracoscopic wedge resection, pleurodesis, and lymph node sampling, with a preoperative erector spinae plane (ESP) block using 20 mL of liposomal bupivacaine (Exparel) and 10 mL of 0.5% bupivacaine. Approximately four hours postoperatively, he developed visual hallucinations that progressed to profound encephalopathy without clinically apparent seizure or cardiovascular instability. After exclusion of common postoperative causes, empirical 20% intravenous lipid emulsion was administered, followed by prompt improvement in mental status and complete neurological recovery within 24 hours. A focused review of published LAST case reports identified only one prior case with a comparable presentation of isolated encephalopathy without clinically apparent seizure or cardiovascular collapse. This case highlights that LAST should be considered in unexplained postoperative encephalopathy following regional anaesthesia, particularly after fascial plane blocks, even when classic seizure or cardiovascular manifestations are absent.

Keywords: Local Anesthetic Systemic Toxicity; Erector Spinae Plane Block; Bupivacaine; Liposomal Bupivacaine; Encephalopathy; Intravenous Lipid Emulsion

Introduction

Postoperative encephalopathy in the intensive care unit carries a broad differential, with delirium, residual sedation, stroke, and metabolic derangements typically considered first (1). LAST is a rare but potentially fatal complication of regional anesthesia that classically presents with CNS excitation followed by cardiovascular collapse (2,6). Atypical, delayed, and CNS-only presentations are increasingly recognized and can mimic postoperative delirium or emergence phenomena, delaying recognition and treatment (1-3). ESP blocks have gained popularity for thoracic surgery analgesia but require deposition of large local anesthetic volumes into a highly vascular fascial plane, producing peak plasma concentrations comparable to intercostal blocks and a recognized LAST risk (4,5).

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Citation: Alejandro Chapa-Rodriguez, Nirajan Kandel, Hillary Starling, Gabriela Domínguez Arocho, Yasier Medina, Ryan Huttinger, Satyanarayana Vaidy. Encephalopathy after Erector Spinae Plane Block When Should LAST Be First? Anesthesia and Critical care 8 (2026): 112-118.

Received: August 18, 2026
Accepted: August 24, 2026
Published: September 07, 2026

Chapa-Rodriguez A, et al., Anesth Crit Care 2026
DOI:10.26502/acc.0110

This case illustrates a rare presentation of LAST as isolated encephalopathy with hallucinations and frames it within the published epidemiology of LAST presentations to argue for broader clinical suspicion.

Case Presentation

A 70-year-old man weighing 99.7kg with past medical history of essential hypertension, type 2 diabetes mellitus, chronic obstructive pulmonary disease, prior stroke, and prostate cancer in remission. Admitted for spontaneous pneumothorax from a ruptured bleb with a new left upper lobe nodule. He underwent robotic-assisted thoracoscopic wedge resection, pleurodesis, and lymph node sampling under general anesthesia. He received a preoperative bupivacaine ESP block with 20 mL of liposomal bupivacaine (Exparel) and 10 mL of 0.5% bupivacaine for postoperative analgesia. The immediate postoperative period was unremarkable. Approximately four hours postoperatively the patient developed visual hallucinations that progressed over the following four hours to profound encephalopathy with markedly depressed consciousness, eye opening only to noxious stimuli and no verbal response.

Investigations

Examination showed no rigidity, clones, or fever. Deep tendon reflexes were absent, with flexor plantar responses bilaterally. Non-contrast computed tomography (CT) of the head and CT angiography of the head and neck showed no acute cerebrovascular abnormalities, making a major acute cerebrovascular event less likely. Bedside point-of-care blood glucose, arterial blood gas, chest radiograph, complete blood count, and comprehensive metabolic panel were all unremarkable. There was no response to a trial of flumazenil or naloxone.

Differential Diagnosis

The principal differentials considered included postoperative delirium, residual sedation or emergence phenomenon, acute ischemic stroke or other cerebrovascular events, metabolic encephalopathy, nonconvulsive status epilepticus, and LAST. CT and CT angiography showed no acute cerebrovascular abnormality, while metabolic studies did not identify hypoglycemia, hypercapnia, hyponatremia, or other common metabolic derangements. Absence of response to flumazenil and naloxone reduced the likelihood of residual benzodiazepine or opioid effect. Although nonconvulsive seizure activity and a small acute ischemic lesion could not be definitively excluded without EEG or diffusion-weighted MRI, the patient's rapidly deteriorating mental status and concern for time-sensitive LAST prompted treatment without delaying for further diagnostic testing. The temporal relationship to the bupivacaine ESP block, together with the otherwise unrevealing evaluation, brought LAST to the forefront of the differential diagnosis.

Treatment

Given the recent ESP block with bupivacaine and the systematic exclusion of alternative diagnoses, empirical 20% intravenous lipid emulsion was administered. The patient initially received a 100 mL bolus, after which his mental status improved from profound encephalopathy to intermittent eye opening with persistent confusion. Because neurological recovery remained incomplete, a repeat bolus was administered, followed by continued lipid emulsion infusion. In total, approximately 300 mL was administered by infusion over an estimated 45 minutes. Following repeat dosing, the patient continued to improve without recurrent neurological or cardiovascular deterioration.

Outcome and Follow-up

Mental status improved promptly after initiation of lipid emulsion therapy, with complete neurological recovery within 24 hours. There were no recurrent neurological or cardiovascular events during the remainder of the hospitalization. The patient was discharged with no neurological sequelae.

Discussion

LAST is a recognized but uncommon complication of regional anesthesia, with a contemporary incidence of approximately 1 per 1000 applications (1,7). The rising use of fascial plane blocks, ambulatory catheter infusions, and office-based local anesthetic administration has expanded the population at risk (1,8). ESP blocks in particular produce peak plasma concentrations 30 to 60 minutes after injection and sustained systemic exposure thereafter (4,5); symptom onset four hours post-block, as in our patient, is biologically consistent with this profile.

The clinical spectrum of LAST is broader than the textbook description suggests, and major society guidelines have explicitly broadened the diagnostic criteria (Table 1). The ASRA 2018 Practice Advisory and 2020 Checklist, the Association of Anesthetists 2023 Quick Reference Handbook, and the Japanese Society of Anesthesiologists 2019 Practical Guide each recognize isolated CNS findings, isolated cardiovascular findings, or delayed onset as valid LAST presentations (5-11). Vasques and colleagues analyzed 67 LAST events between 2010 and 2014: isolated CNS toxicity accounted for 50%, combined CNS and cardiovascular toxicity for 36%, and isolated cardiovascular toxicity for 14% (7). Seizure was the most common single feature at 54%, but prodromal symptoms including hallucinations, confusion, slurred speech, tinnitus, and tremor, accounted for 40% of CNS manifestations, more than doubling from 18% in the previous three decades (7,9). The Macfarlane review documented isolated CNS effects in 32% of cases; approximately 53% of manifestations occurred within 10 minutes, 19% between 11 minutes and 1 hour, and 8% after 12 hours (1).

Chapa-Rodriguez A, et al., Anesth Crit Care 2026
DOI:10.26502/acc.0110

Table 1: Comparison of major society guidelines for LAST recognition and management.

Society / Region	Current Document (ref)	Diagnostic Recognition	First-Line Treatment	ILE Dosing (20%)	Notable Points
ASRA (US)	3rd Practice Advisory 2018 (5); Checklist 2020 update (6)	Recognizes isolated CNS, isolated CV, delayed onset, and atypical presentations as valid LAST events.	Lipid emulsion at first signs of toxicity; airway, seizure control with benzodiazepines.	<70 kg: 1.5 mL/kg bolus then 0.25 mL/kg/min. ≥70 kg: 100 mL bolus then 250 mL over 15–20 min. Repeat bolus or double infusion if inadequate.	Most widely cited international standard. 2020 update emphasizes early lipid use and simplified weight-based dosing.
Association of Anaesthetists (UK)	Quick Reference Handbook 3-10, June 2023 (10)	Sudden altered mental status, severe agitation, loss of consciousness with or without convulsions, OR cardiovascular collapse.	Stop LA, call for help, ABC, lipid emulsion. Reduced-dose vasopressors.	1.5 mL/kg bolus over 1 min, then 15 mL/kg/h infusion. Repeat bolus up to 2× at 5 min intervals. Max 12 mL/kg cumulative.	Highlights pancreatitis as ILE complication. Registry reporting encouraged.
JSA (Japan)	Practical Guide, J Anesth 2019 (11)	Recognizes CNS prodrome, seizure, CV depression, and atypical/delayed presentations; explicit attention to differential diagnosis postoperatively.	Stop LA, airway/breathing support, seizure control, lipid emulsion, modified ACLS for LA-induced arrest.	Aligned with ASRA dosing: 1.5 mL/kg bolus then 0.25 mL/kg/min infusion.	Strong emphasis on prevention and availability of ILE wherever LAs are used.
AHA / ACLS (US)	2020 AHA CPR & ECC Guidelines, Part 3 (30)	LAST as a special-circumstance cardiac arrest; reversible cause to consider after recent LA use.	Standard ACLS with addition of lipid emulsion per ASRA; consider extracorporeal support for refractory arrest.	Defers to ASRA 2020 dosing.	Frames LAST within special-circumstance resuscitation.

Reference numbers in column two correspond to the reference list. ASRA = American Society of Regional Anesthesia and Pain Medicine; AAGBI = Association of Anesthetists; JSA = Japanese Society of Anesthesiologists; AHA = American Heart Association; ACLS = Advanced Cardiac Life Support; ILE = intravenous lipid emulsion; ABC = airway, breathing, circulation; LA = local anesthetic.

Despite this guideline convergence, most clinicians anchor on the classic teaching: seizures progressing to hemodynamic collapse. In practice the threshold for invoking LAST often becomes the simultaneous presence of CNS and cardiovascular instability, a combination that occurs in a minority of published cases. To contextualize our case, we performed a focused PubMed search across "lidocaine", "bupivacaine", "liposomal bupivacaine", "ropivacaine", and "local anesthetic" associated with systemic toxicity terms. The search identified 81 records, after removal of 35 duplicates, 46 unique publications were assessed for eligibility. Twenty-eight were excluded, leaving 18 publications reporting 21 LAST cases for inclusion in Table 2 (12-29). Of the 21 cases, 11 presented with isolated CNS prodromal or seizure-dominant features, five with combined CNS and cardiovascular involvement, two with isolated cardiovascular toxicity, two with atypical multisystem manifestations, and one with isolated encephalopathy without clinically seizure or hemodynamic instability. Only one prior case (29) presented with isolated encephalopathy in the absence of clinically seizure or hemodynamic instability, a pattern our case shares.

Search strategy: PubMed searches were performed using "lidocaine associated systemic toxicity," "bupivacaine associated systemic toxicity," "liposomal bupivacaine associated systemic toxicity," "ropivacaine associated systemic toxicity," and "local anesthetic associated systemic toxicity." The searches identified 81 records. After removal of 35 duplicate records, 46 unique publications were assessed for eligibility. Twenty-eight publications were excluded: 12 were not relevant to the clinical question, 10 did not describe confirmed local anesthetic systemic toxicity, five could not be adequately assessed because full text was unavailable or toxicity could not be confirmed, and one described a non-comparable transdermal lidocaine presentation. Eighteen publications reporting 21 LAST cases were included. The present case is displayed separately and is not included among the 21 cases identified by the literature search. Reference numbers in the author column correspond to the reference list. Highlighted row indicates the present case. ILE = intravenous lipid emulsion; TAP = transversus abdominis plane; TKA = total knee arthroplasty; RA = rheumatoid arthritis; ESP = erector spinae plane.

These findings have several important implications for the bedside recognition of LAST. Hemodynamic instability is absent in roughly half of confirmed LAST cases (12-20); anchoring on the combination of CNS and cardiovascular findings therefore delays treatment in approximately half of patients. The CNS prodrome is heterogeneous and easily mistaken for other postoperative phenomena. Hallucinations and visual disturbances (16-18), dysarthria with focal motor signs (21), perioral numbness with confusion (12), and progressive encephalopathy (29, present case) all fall within

Chapa-Rodriguez A, et al., Anesth Crit Care 2026
DOI:10.26502/acc.0110

Table 2: LAST presentations in published case reports identified through targeted PubMed search.

Author / Year (ref)	Drug	Route / Block Type	Initial Presentation	Pattern
Isolated CNS — prodromal / seizure dominant (11 cases from 9 publications)				
Martin 2024 (12)	Lidocaine	Infiltration (therapeutic dose)	Perioral numbness, seizure-like activity, confusion	Prodromal + seizure
Chan 2025 (13)	Lidocaine	In-office infiltration	Tremors, perioral/facial paresthesias, spasticity, generalized tonic-clonic seizure	Prodromal + seizure
Jayanthi 2016 (14)	Lidocaine	Various (3 cases)	Seizure (3 cases)	Seizure
McMahon 2022 (15)	Lidocaine	Pediatric infiltration	Status epilepticus	Seizure
Chiang 1996 (16)	Lidocaine	Regional infiltration	Headache, tinnitus, visual/auditory disturbance, muscle twitching, trismus; later agitation, hallucinations, verbosity	Prodromal (hallucinatory)
Adeleye 2020 (17)	Tetracaine	Topical/local	Seizure	Seizure
Burch 2023 (18)	Lidocaine	Hematoma block (wrist)	Slurred speech, difficulty opening eyes, red/black flashing lights	Prodromal (visual)
Satsumae 2008 (19)	Ropivacaine	Brachial plexus block	Convulsions	Seizure
Yasgur 2025 (20)	Bupivacaine	Regional anesthesia	Seizure; severe hypertriglyceridemia following high cumulative-dose ILE	Seizure + ILE complication
CNS + cardiovascular involvement (n=5)				
King 2024 (21)	Lidocaine	Procedural (pacemaker placement)	Dysarthria, bilateral arm shaking, sinus tachycardia	CNS + CV
Zhu 2025 case 1 (22)	Ropivacaine + lidocaine	Brachial plexus block (uremic pt)	Unresponsive to verbal/painful stimulus; BP 182/113, HR 78, SpO2 87%	CNS + CV
Zhu 2025 case 2 (22)	Ropivacaine + lidocaine	Brachial plexus block (uremic pt)	BP 166/85 to 185/92 mm Hg, unable to wake up	CNS + CV
Sun 2025 (23)	Ropivacaine	Rectus sheath catheter (post-hepatectomy)	Altered mental status, perioral numbness, hypotension, new conduction abnormalities	CNS + CV / ILE complication
Basta 2023 (24)	Liposomal bupivacaine	Intercostal nerve block	Seizures and hypotension	CNS + CV
Isolated cardiovascular (n=2)				
Boleyn 2023 (25)	Liposomal bupivacaine	TAP block	Cardiac arrest	CV only
Maulidi 2012 (26)	Tetracaine	Topical (premature neonate)	Bradycardia	CV only
Atypical / multisystem (n=2)				
Robles 2024 (27)	Lidocaine	Infiltration	Bradycardia, hypotension, acute pancreatitis	Atypical (pancreatitis)
Kapenda 2022 (28)	Ropivacaine	Local infiltration analgesia (TKA)	Respiratory distress with impaired consciousness	CNS + respiratory
Isolated encephalopathy without clinically apparent seizure or cardiovascular collapse — rare (n=1 prior + present case)				
Baic 2026 (29)	Local anesthetic (regional)	Regional anesthesia (RA patient)	Arm numbness, then fixed non-dynamic gaze, slowed incoherent speech, involuntary upper-limb movements	Encephalopathy
Present case	Bupivacaine	ESP block (thoracic surgery)	Visual hallucinations progressing to encephalopathy (eye opening to noxious only, no verbal response)	Encephalopathy

Chapa-Rodriguez A, et al., Anesth Crit Care 2026
DOI:10.26502/acc.0110

the prodromal spectrum but resemble postoperative delirium, emergence phenomena, or focal cerebrovascular events more than they resemble the textbook description of LAST. In a postoperative patient receiving sedation, analgesia, and antiemetics, these features are routinely attributed to medication effect or expected postoperative cognitive dysfunction. Seizures associated with LAST may be difficult to control and require prompt treatment with antiepileptic drugs alongside lipid emulsion therapy. Refractory seizures will remain until lipid emulsion is administered, supporting the role of lipid as both first-line treatment and diagnostic confirmation rather than a measure of last resort (1-6). The same principle may extend to non-seizure presentations: when clinical suspicion for LAST is high and alternative diagnoses have been reasonably excluded, empirical lipid emulsion should not be delayed while awaiting definitive confirmation. In our patient, the progression from hallucinations to deep encephalopathy four hours after a bupivacaine ESP block, with exclusion of imaging-detectable cerebrovascular causes, common metabolic derangements, and benzodiazepine or opioid effect, satisfied this threshold. Empirical 20% lipid emulsion administered per ASRA 2020 dosing produced prompt clinical improvement with complete recovery within 24 hours, providing additional clinical support for the diagnosis (6). Although lipid emulsion is central to the treatment of LAST, cumulative dosing should be monitored carefully. ASRA guidance recommends an upper limit of approximately 10 mL/kg of lipid emulsion during the first 30 minutes of resuscitation, while the updated 2020 checklist recommends a maximum cumulative dose of 12 mL/kg. In our 99.7-kg patient, the total administered dose was approximately 5.0 mL/kg, well below these limits (5-31). Excessive administration has been associated with severe iatrogenic hypertriglyceridemia and other complications (20). LAST should be considered when any unexplained neurological or cardiovascular change occurs within hours of local anesthetic administration, not only when both systems are involved. The diagnostic threshold should be temporal proximity to a regional block plus exclusion of alternatives, rather than the textbook combination of seizure and collapse. This posture aligns with current international guidance (5,6,10,11). More specifically, the use of liposomal bupivacaine in our patient warrants consideration, as its prolonged-release formulation may be relevant to the delayed onset of toxicity observed in this case. Exparel is a prolonged-release formulation of bupivacaine that uses DepoFoam technology, in which bupivacaine is encapsulated within micro-sized multivesicular liposomes (MVLs), allowing sustained local release for 48-72 hours. MVLs are characterized by a honeycomb-like structure, with the inner aqueous phase divided into multiple non-centric chambers that support prolonged drug release. (32) The sustained release mechanism of Exparel has been studied but is not fully understood at this time. Manna et al , proposed a triphasic release profile. The first stage consists of an initial burst release, thought to reflect unencapsulated or surface-bound bupivacaine. This is followed by a lag phase characterized by slow diffusion through lipid membranes, potentially accompanied by lipid rearrangement. A secondary release phase then occurs, largely attributed to particle erosion (33). Compared with immediate-release bupivacaine, liposomal bupivacaine produces prolonged systemic exposure and a delayed pharmacokinetic profile, which may extend the temporal window during which systemic toxicity can occur. The 20 mL Exparel formulation contains 266 mg of bupivacaine, providing a substantial amount of drug available for absorption. In this case, the patient also received 50 mg of immediate-release bupivacaine HCl with 266 mg of liposomal bupivacaine, corresponding to a bupivacaine HCl-to-Exparel ratio of approximately 1:5.3. This was within the manufacturer-recommended maximum ratio of 1:2 for concomitant administration; however, the systemic toxic effects of local anesthetics are additive. Therefore, a high index of suspicion should be maintained when new neurologic or cardiovascular abnormalities arise following regional anesthesia, particularly when no alternative explanation is apparent. Notably, current prescribing information recommends a maximum perineural Exparel dose of 133 mg for approved nerve blocks, whereas our patient received 266 mg in an off-label ESP block (35). Whether this higher perineural dose contributed to the development of systemic toxicity cannot be determined from a single case and should be explored in future studies evaluating dose-dependent systemic exposure and LAST risk with liposomal bupivacaine used in fascial plane blocks.

Use of liposomal bupivacaine for ESP block is not among the currently established regional nerve-block indications in the United States; current prescribing information limits established regional analgesia indications to interscalene brachial plexus, popliteal sciatic, and adductor canal blocks. Accordingly, the four-hour onset of neurological symptoms in our patient is biologically compatible with ongoing systemic exposure, although the temporal relationship cannot establish that the liposomal formulation itself caused the delayed or CNS-predominant phenotype. The slower release also means that it may require an extended observation. In the case we are presenting the team elected to watch the patient for a minimum of 24 hours after lipid emulsion was given to monitor for any residual signs of LAST, but none appeared. Exparel use has increased since its earlier years on market. Expanded FDA indications for its use accompanied by a strong push to focus on opioid sparing approaches to analgesia will likely increase its utilization (34). Given this information, it would be prudent to consider LAST on the differential diagnosis for many hours after a nerve block with Exparel. The prolonged-release mechanism of Exparel may have contributed to the delayed onset of symptoms in this case by extending the period of systemic bupivacaine

Chapa-Rodriguez A, et al., Anesth Crit Care 2026
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exposure. However, whether this pharmacokinetic profile also influenced the predominantly neurologic presentation, rather than producing seizures or cardiovascular toxicity, cannot be determined from a single case.

Conclusion

LAST may present as isolated encephalopathy with hallucinations in the absence of clinically apparent seizures or cardiovascular instability, an uncommon but recognized phenotype within the published spectrum of toxicity. Because a substantial proportion of reported LAST events lack hemodynamic instability, waiting for the classic combination of CNS excitation and cardiovascular collapse may delay recognition and treatment. Following fascial plane blocks such as the ESP block, systemic absorption of local anesthetic can produce delayed neurological manifestations that may be mistaken for postoperative delirium, residual sedation, or emergence phenomena. Current guidance from major professional societies recognizes isolated, atypical, and delayed presentations of LAST. Accordingly, when LAST is strongly suspected and alternative causes have been reasonably excluded, intravenous lipid emulsion should not be delayed solely because clinically apparent seizures or cardiovascular instability are absent.

Acknowledgements: none

Funding: none

Competing Interests: The authors declare that they have no competing interests.

Patient consent: Written informed consent for publication of this case report was obtained from the patient.

Data Availability: Not applicable. No datasets were generated or analyzed for this case report. All relevant clinical information is contained within the manuscript, with identifying information omitted to protect patient confidentiality.

AI Use Disclosure

ChatGPT (OpenAI) was used to assist with language editing (grammar, flow and prose), manuscript organization, and refinement of selected sections. All clinical information, literature interpretation, references, and final manuscript content were independently reviewed and verified by the authors, who take full responsibility for the accuracy and integrity of the work.

Author contribution statement

N.K.: Conceptualization, investigation, data curation, and writing, original draft. A. C-R.: Conceptualization, methodology, literature review, data interpretation, writing, original draft, writing/review and editing, and project administration. S.V.: Supervision, clinical interpretation, and review. Gabriela Domínguez Arocho: Pharmacotherapy review, treatment-data verification, clinical interpretation, and writing, review and editing. Hillary Starling: Pharmacotherapy review, literature review related to liposomal bupivacaine and intravenous lipid emulsion, clinical interpretation, and writing, review and editing. R. H.: Conceptualization, review Y. M.: Conceptualization review, manuscript edits, supervision.

All authors reviewed and approved the final manuscript and agreed to be accountable for the accuracy and integrity of the work.

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