

Profound Ketamine-Associated Dissociation Preceding Resolution of Refractory Craniofacial CRPS

Hussein Haifa; Atef Haifa, DO; Hamed Sadeghipour, MD

Anesthesiology, SSM Health/Saint Louis University School of Medicine, Saint Louis, Missouri, USA

INTRODUCTION

Complex regional pain syndrome (CRPS) is a chronic pain condition characterized by disproportionate pain relative to the inciting injury, accompanied by sensory, vasomotor, sudomotor, and trophic abnormalities. It most commonly affects a limb, but craniofacial presentations are rare, poorly characterized, and often under-recognized.

Ketamine, an NMDA-receptor antagonist, has an established role in chronic pain management, including as an adjunct for CRPS, largely through its capacity to interrupt central sensitization. However, its therapeutic window overlaps closely with doses that produce dissociative effects, and clinically significant dissociation can occur even when ketamine is given for a purely analgesic purpose. Profound dissociation, amnesia, and hallucinations have each been separately reported with subanesthetic ketamine or esketamine.[1–5]

What has not been well described is a direct temporal link between an episode of profound ketamine-associated dissociation and durable resolution of a refractory pain syndrome. We report such a case: unexpected, complete resolution of longstanding facial CRPS immediately following a profound ketamine-associated dissociative episode, despite the sympathetic block never actually being performed.

CASE HIGHLIGHT: The planned stellate ganglion block was aborted after ketamine-associated dissociation; complete resolution of longstanding facial pain subsequently occurred despite the intended procedure never being delivered.

MATERIALS AND METHODS

- Patient informed consent was obtained for submission of this medically challenging case, and all protected health information was de-identified in accordance with standard case-report practice.
- A focused literature search was performed using PubMed/MEDLINE to identify relevant case reports, clinical trials, and guidelines addressing ketamine and esketamine associated dissociation, amnesia, and hallucinations
- The clinical encounter occurred at an independent outpatient interventional pain clinic. Ketamine was administered intravenously as a periprocedural analgesic adjunct in anticipation of a planned stellate ganglion block, with the goal of reducing procedural discomfort and central sensitization rather than achieving dissociation. Ketamine use for this indication was off-label, consistent with common pain-practice use of the drug outside its FDA-approved indications.

CLINICAL TIMELINE

- Severe traumatic facial injury
- Reconstructive surgery: bilateral sagittal split osteotomies, right condylectomy, Le Fort I advancement → progressive condylar resorption → bilateral total TMJ replacement
- Persistent facial pain disproportionate to findings, refractory to pharmacologic therapy, repeat surgery, and multidisciplinary management → trigeminal-distribution CRPS diagnosed
- Referred for interventional pain management; IV ketamine given as a periprocedural analgesic adjunct in anticipation of a planned stellate ganglion block
- Cumulative 50-mg IV ketamine dose → profound dissociation ("K-hole"); procedure aborted before the nerve block itself was performed
- Follow-up: complete, unprompted resolution of longstanding facial pain — an outcome not previously achieved despite extensive prior treatment

IMAGING

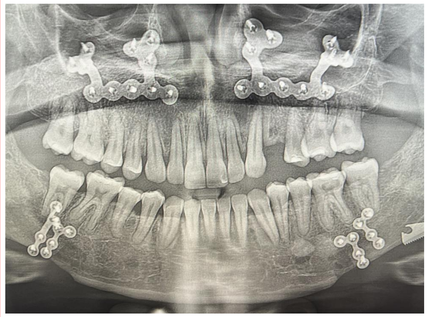


Figure 1: Postoperative panoramic radiograph demonstrating the patient's craniofacial reconstruction and bilateral temporomandibular joint prostheses.

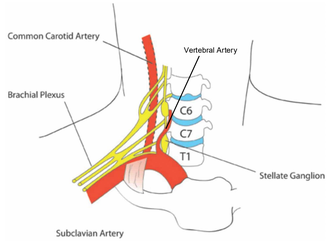


Figure 2: Stellate ganglion (cervicothoracic sympathetic ganglion) block being performed.

CASE REPORT

A 33-year-old male developed chronic facial pain and temporomandibular joint (TMJ) dysfunction after severe traumatic facial injury. His surgical course was extensive: reconstruction included bilateral sagittal split osteotomies, right condylectomy, and Le Fort I maxillary advancement, followed by progressive condylar resorption that subsequently required bilateral total TMJ replacement, seen on postoperative imaging (Figure 1).

Despite this structural reconstruction, he continued to experience persistent, severe facial pain that was disproportionate to examination findings and refractory to pharmacologic therapy, repeated surgical intervention, and multidisciplinary pain management. CRPS involving the trigeminal distribution was ultimately diagnosed — an uncommon presentation given the syndrome's typical predilection for the extremities.

Given the failure of conventional management, he was referred for interventional pain management and scheduled for a stellate ganglion block (Figure 2), a sympathetic block commonly used for craniofacial and upper-extremity CRPS. Intravenous ketamine was administered as a periprocedural analgesic adjunct prior to the block.

After a cumulative dose of 50 mg, he developed profound dissociation characterized by complete detachment from his surroundings and an inability to meaningfully interact with staff — a presentation clinically resembling a "K-hole," more typically associated with recreational ketamine misuse than with carefully titrated periprocedural dosing. Staff managed the episode supportively, including playing soft, calming music to help ground and reassure the patient through the dissociative state. Given the severity of the response, the procedure was aborted before the stellate ganglion block was ever performed.

At follow-up, and without any additional intervention, the patient reported complete resolution of his longstanding facial pain — an outcome he had not achieved despite years of surgery, pharmacologic therapy, and multidisciplinary pain management.

CLINICAL OBSERVATION AND PROPOSED MECHANISM

Ketamine is a non-competitive antagonist at the NMDA receptor, acting at the phencyclidine binding site within the receptor's ion channel. NMDA receptors are central to spinal "wind-up," the progressive amplification of pain signaling that underlies central sensitization in CRPS; blocking them can interrupt this amplification even after the peripheral injury has been surgically addressed.

NMDA receptors are also densely expressed on inhibitory cortical interneurons. Antagonism there disinhibits downstream glutamatergic neurons, producing a surge of cortical glutamatergic activity — the leading mechanistic explanation for ketamine-associated dissociation.

The analgesic and dissociative effects therefore arise from the same receptor mechanism occurring simultaneously in different neural circuits — a plausible physiological rationale for the temporal association observed in this case, and a reason the magnitude of dissociation may loosely track the degree of central NMDA blockade achieved.

DISCUSSION

Marked dissociative and perceptual effects have been well documented during therapeutic ketamine exposure, including void-like dissociation,[1] esketamine-associated dissociation,[2,3] low-dose ketamine-associated amnesia,[4] and vivid hallucinations.[5] These reports establish dissociation as a dose-related, predictable phenomenon rather than a unique reaction.

What distinguishes this case is the outcome that followed: pain resolution occurred despite abortion of the planned sympathetic block, the maneuver that was intended to treat his CRPS was never delivered, yet his pain resolved anyway. This cannot establish causality, but it suggests a relationship between ketamine-associated altered consciousness, central pain processing, and analgesic response that warrants further study. It also underscores a broader point: dissociative side effects, often viewed purely as adverse events, may in some cases correlate with therapeutic benefit.

Management of an acute dissociative episode is primarily supportive, as the state is typically self-limited. Staff used grounding techniques soft music and tactile/temperature sensory input to reorient the patient, consistent with grounding strategies used more broadly in dissociative states. The evidence base here mainly addresses prevention: benzodiazepine co-administration reduces the incidence and severity of ketamine emergence reactions,[11,12] and current sedation guidelines recommend a calm, low-stimulation recovery environment.[13] Sensory-grounding approaches like those used here follow this same principle, though they remain unstudied as a formal treatment for ketamine-associated dissociation. While these measures likely did not shorten the episode itself, they plausibly reduced the patient's distress and may be a reasonable low-risk addition to periprocedural protocols.

SUMMARY

A profound ketamine-associated dissociative episode preceded complete, unexpected resolution of this patient's refractory craniofacial CRPS pain. The planned stellate ganglion block — the procedure ketamine was meant to support — was aborted and never performed.

This temporal association raises the possibility that ketamine-associated modulation of central pain processing, via the same NMDA mechanism responsible for the dissociation, contributed to the analgesic response; however, causality cannot be established from a single case.

REFERENCES