

Case Report

Ketamine infusion therapy in an elderly patient with complex regional pain syndrome and major depression

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ABSTRACT

Complex regional pain syndrome (CRPS) is a chronic pain disorder that severely affects mobility and quality of life. This case report describes an 86-year-old man who has a long-standing history of CRPS-related back and leg pain. Traditional treatments, including opioids and duloxetine, did not improve his symptoms, and due to religious beliefs restricting specific interventions, standard hospital care was limited. Given the severity of his symptoms and the refractory nature of his condition, an intravenous ketamine infusion was recommended to improve pain and comorbid depressive symptoms. Following one treatment, the patient exhibited immediate and substantial improvements in pain intensity, mood, and mobility. This case accentuates the importance of culturally sensitive, patient-centered care and suggests the role of ketamine in treating CRPS when traditional therapies are ineffective.

Keywords: Complex regional pain syndrome, Ketamine infusion, Major depression, Chronic pain, Elderly patient, Culturally sensitive care

INTRODUCTION

Complex regional pain syndrome (CRPS) is a debilitating neurological pain disorder affecting one or more limbs, commonly occurring with or without known trauma to the peripheral nervous system. CRPS has previously been defined as Sudeck's atrophy and reflex sympathetic

dystrophy.¹ The condition often develops after a noxious event such as trauma, surgery, or injury; notably, the probability of developing the condition is not related to the severity of the injury. Patients diagnosed with the syndrome typically present with allodynia, hyperalgesia, sudomotor and vasomotor abnormalities, and trophic changes. The diagnosis is made according to the Budapest

criteria, a grouping of signs and symptoms into four distinct categories identified by factor analysis.¹ Although new-onset pain may resolve with aggressive treatments, CRPS patients with symptoms longer than a year rarely improve, and 80% of patients meet the criteria for disability.¹

Conventional pain medications, physical therapy, sympathetic nerve blocks, and transcutaneous electrical stimulation of the nerves have been used to address the intensity of CRPS pain. Although the pathophysiology of CRPS is unclear, prior studies have demonstrated that the activation of N-methyl-D-aspartate (NMDA) receptors increases excitatory transmission of afferent neurons, leading to central sensitization and the development of chronic pain.² In the presence of inflammation, nociceptors spontaneously fire, responsible for the development of chronic pain. Neuropathic pain can also cause nociceptors to alter their characteristics, causing them to be hypersensitive to mechanical, thermal, and ionic stimulation.¹

Intravenous (IV) ketamine in patients with CRPS has been described as a potentially effective treatment for several years; however, randomized placebo trial reports are limited. Ketamine is the most potent clinically available NMDA antagonist, with a well-established role in treating both acute and chronic pain.² Both clinical and experimental evidence have demonstrated the significance of NMDA receptors in long-term potentiation, a key mechanism underlying hyperalgesia, allodynia, and central sensitization, a frequent complaint among CRPS patients, and the NMDA antagonist properties of ketamine are intended to reverse this phenomenon.³ Ketamine's complex effects on the neuroimmune system may in part explain ketamine's analgesic effects in CRPS. Ketamine also interacts with several other receptors, including opioid, gamma-aminobutyric acid, dopamine, muscarinic, nicotinic, and L-type calcium channels, which have been proposed as mechanisms underlying ketamine's efficacy.²

CASE REPORT

The patient was an 86-year-old male and presented to the clinic with a history of debilitating back and left leg pain interfering with his ambulatory ability. He was diagnosed with CRPS in his forties, initially presenting as a popliteal cyst affecting his left knee. A magnetic resonance imaging (MRI) indicated the cyst resulted in compressive neuropathy and weakened distal pulses. Despite the treatment for the popliteal cyst, the symptoms persisted, affected his mood, and led to the subsequent diagnosis of major depressive disorder.

The patient discussed in the study was deeply religious and had prohibitive beliefs against receiving blood products or invasive procedures that could risk transfusion. Due to religious restrictions, the patient was ineligible for specific life-sustaining interventions and was subsequently denied

care by multiple major hospital systems in the United States.

The patient remained adherent to a regimen of pregabalin and transdermal fentanyl; however, these interventions failed to provide adequate symptom relief. His complex history of pain and religious beliefs were considered at the clinic, and it was decided that the serotonin norepinephrine reuptake inhibitor, duloxetine, and occupational therapy would be added to his treatment regimen.

The patient adhered to the duloxetine and occupational therapy for three months, but unfortunately, this approach failed to yield meaningful improvement in either his pain or depressive symptoms. Given the refractory nature of his condition, and after exhausting conventional treatment options, a trial of ketamine infusions was considered. The decision was made with careful consideration of the patient's religious beliefs and pending medical clearance for the procedure.

Table 1: Clinical course and treatment timeline.

Clinical stage	Intervention(s)	Outcome
Initial presentation (age 40s)	Popliteal cyst treatment	Persistent CRPS symptoms, later depression diagnosis
Long-term management	Pregabalin, transdermal fentanyl	Inadequate pain relief
Adjunctive therapies	Duloxetine + occupational therapy (3 months)	No meaningful improvement
Pre-ketamine status	Wheelchair-bound, severe pain, poor sleep, low appetite	Poor quality of life
Ketamine infusion (0.5 mg/kg IV over 40 min)	Subanesthetic dose, continuous monitoring	Rapid and substantial pain relief; improved mood and mobility; ambulated independently at discharge

Outcome

The patient presented to the clinic in a wheelchair for initiation of ketamine treatment, describing significant pain along with a one-week history of difficulty sleeping and lack of appetite. A subanesthetic dose of ketamine at 0.5 milligrams per kilogram was administered intravenously over a forty-minute period, with continuous monitoring by medical personnel. The infusion was well tolerated and elicited a rapid and pronounced reduction in pain intensity. Following the treatment, the patient who

had previously required a wheelchair due to severe pain and functional limitation, demonstrated improved mobility and was able to ambulate independently at discharge without the need for assistive devices.

DISCUSSION

Chronic pain conditions such as CRPS are closely intertwined with psychiatric comorbidities, particularly major depressive disorder. The high burden of sustained, severe pain can profoundly impact emotional regulation and cognitive function, leading to the emergence or exacerbation of depressive symptoms. Depression is not merely a reaction to pain but often coexists in a reciprocal relationship, each intensifying the other's severity and complicating treatment outcomes.⁴ Neurobiological findings further support this link, suggesting shared pathophysiological mechanisms involving central sensitization, impaired monoaminergic transmission, and dysregulated stress response systems.⁵ Additional studies emphasized that depression is not only more prevalent among chronic pain patients but is also predictive of worse functional outcomes and increased healthcare utilization.⁶ Moreover, chronic pain and depression share overlapping symptomatology, including sleep disturbances, fatigue, and concentration difficulties, often making differential diagnosis and treatment particularly challenging.⁷ This bidirectional relationship underscores the importance of integrated, multidisciplinary approaches in managing CRPS complicated by depressive illness.

The antidepressant effects of ketamine are well-documented in psychiatric literature and may also impact the affective aspects of CRPS.⁸ Chronic pain and depression are commonly comorbid, and there is a reported bidirectional relationship between depression and pain severity. Based on the available data collected, functional neuroimaging studies have found that ketamine exerts its effects in cortical areas that are shared between patients with CRPS and major depressive disorder.⁹ Reportedly, intermediate doses of intravenous ketamine have yielded varying degrees of pain relief and decreased major depressive disorder symptoms.⁸

This case illustrates the profound impact of ketamine therapy in a patient with complex medical, neurological, psychiatric, and ethical challenges. The analgesic effect likely stemmed from NMDA receptor antagonism in central sensitization pathways, while its antidepressant benefit is consistent with ketamine's effects on glutamatergic modulation and neuroplasticity.

His recovery is particularly notable given the barriers to care imposed by religious beliefs, advanced age, and prior treatment failures. The case also underscores the importance of integrated, culturally sensitive care and the need for clinicians to consider ketamine in treatment-

resistant CRPS, particularly when conventional approaches are contraindicated or refused.

CONCLUSION

Ketamine infusion therapy was used as a non-conventional approach in the case of an elderly patient with CRPS and major depression. The patient's religious beliefs enhanced the complexity of his care, and as a result, he had difficulty establishing care. The intervention restored his mobility, improved depressive symptoms, and enhanced quality of life. This case highlights ketamine as a therapeutic option in patients with refractory pain and psychiatric distress, particularly when treatment options are ethically or medically limited.

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