RESEARCH PAPER

Dextrose-Based Prolotherapy for Chronic Post-Surgical Pain: A Novel Peripheral Neuromodulation Approach

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ABSTRACT

Chronic post-surgical pain (CPSP) is a significant and often underrecognized complication of surgery, resulting from complex interactions between nociceptive, neuropathic, and inflammatory mechanisms, with involvement of psychosocial factors. CPSP is associated with substantial functional impairment, psychological distress, and long-term socioeconomic burden. We report two cases of CPSP with distinct clinical profiles. The first case involved a 16-year-old female with persistent localized abdominal pain eight months following an open appendectomy, with features suggestive of peripheral nerve involvement under a keloid scar. The second case described a 21-year-old male with severe, refractory pain in the thoracic area following wide excision of a hemangioma, complicated by marked functional limitation and depressive symptoms. Both patients met the diagnostic criteria for CPSP because no other alternative causes were identified. Multimodal management was implemented, including pharmacological therapy and targeted interventional pain techniques. Both CPSP patient demonstrated significant and sustained pain relief following an prolotherapy intralesional dextrose injection. All procedures were performed under ultrasound guidance using aseptic technique. Written informed consent was obtained from all patients for publication of this case series and accompanying images. Ethical approval was waived as this study represents a retrospective case series with anonymized data. These cases underscore the diverse manifestations and common pathophysiological mechanisms of CPSP across different age demographics and surgical interventions. Individualized, multimodal, and interdisciplinary therapy, particularly the effective application of interventional pain techniques, may provide significant improvements in persistent chronic post-surgical pain. This case series highlights the potential role of combining regional anesthesia with dextrose-based injections as a neuromodulatory strategy in CPSP. While regional blocks provide immediate interruption of nociceptive input, dextrose injections may contribute to longer-term modulation of peripheral sensitization and neurogenic inflammation. This dual-mechanism approach may explain the sustained analgesic effect observed in our patients. Further high-quality randomized controlled trials are needed to strengthen evidence-based treatment strategies.

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INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, resulting from a complex interaction of peripheral, spinal, and supraspinal processes involving multiple neurotransmitters, neuromodulators, and immune mechanisms (Shipton, 2011). Acute postoperative pain is a frequent consequence of surgical interventions resulting from tissue and nerve damage; in certain patients, this pain endures beyond the usual tissue recovery, transforming into chronic post-surgical pain (CPSP) (Bonilla Sierra et al., 2026).

Surgical injury activates peripheral nociceptors and inflammatory pathways, which may lead to peripheral and central sensitization. Prolonged nociceptive input can induce maladaptive neuroplastic changes within the spinal cord and brain, including impaired descending inhibitory control, microglial activation, and increased excitability of nociceptive neurons. For certain individuals, these alterations endure post-tissue repair, promoting the shift from acute to chronic pain (Visser, 2006).

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CPSP represents a substantial clinical and public health burden, with population-based estimates indicating that approximately 2–10% of adult surgical patients develop persistent postoperative pain, and about 1% experience severe and disabling CPSP (IASP, 2021). However, reported incidence varies widely across procedures and study designs, with median rates of 20–30% at 6–12 months postoperatively in certain surgical populations (Macrae, 2008; Rosenberger and Pogatzki-Zahn, 2022). Long-term pain after thoracic surgery is an enormous concern for doctors and patients. More than half of patients are said to have pain that persists for a long time after surgery (Zhang et al., 2022). Procedure-specific differences are well documented, particularly in thoracic surgery, where up to one-third of patients continue to report pain at three months postoperatively (Tawfic et al., 2017).

CPSP is typically characterized as pain that arises or intensifies after surgery, persists for at least three months, is localized to the surgical field or related dermatomes, and cannot be explained by other causes (Clephas et al., 2023). The pain often has neuropathic features, such as hyperalgesia, allodynia, and dysesthesia (Clephas et al., 2023; Rosenberger and Pogatzki-Zahn, 2022). Modern frameworks define CPSP as a complex disorder resulting from the interplay of nociceptive, neurological, inflammatory, and psychosocial factors (Macrae, 2008; Rosenberger & Pogatzki-Zahn, 2022).

In addition to surgical and nociceptive factors, psychological factors such as anxiety, depression, negative affect, pain catastrophizing, and poor sleep quality are consistently associated with an increased risk and prevalence of CPSP, with evidence suggesting a more pronounced impact among women (Tawfic et al., 2017; Rosenberger and Pogatzki-Zahn, 2022). Furthermore, the intensity of acute postoperative pain has emerged as one of the strongest and most reproducible predictors of pain chronification across surgical populations (Tawfic et al., 2017).

CPSP is associated with significant long-term consequences, including reduced quality of life, functional impairment, increased healthcare utilization, and socioeconomic burden (Clephas et al., 2023; Rosenberger and Pogatzki-Zahn, 2022). Pediatric patients are similarly affected, with persistent postoperative pain reported after appendectomy, particularly among females and those with greater surgical scar length (Palabiyik and Demir, 2021).

As the number of surgeries around the world continues to rise, CPSP is likely to remain a major clinical problem. Early identification of high-risk patients and implementation of optimized, multidisciplinary perioperative pain management strategies are therefore essential to prevent the transition from acute to chronic pain. In this particular setting, we present two examples of CPSP: one in a teenager who had an appendectomy and the other in a young adult who had a thoracic surgery. These examples show the clinical features, treatment difficulties, and responses to interventional pain management.

CASE PRESENTATION

Case 1

A 16-year-old female presented with persistent abdominal pain localized to the previous appendectomy site eight months following an open appendectomy performed in December 2024. The pain had been present for eight months, occurring intermittently with episodes of severe exacerbation reaching a Numeric Rating Scale (NRS) score of 10. The pain was localized just inferior to the surgical scar, without radiation. It was sometimes aggravated by physical activity but could also occur at rest. She denied nausea and vomiting. Intermittent constipation occurred every 2–3 weeks but was considered normal by the patient, and she continued to pass flatus.

The patient had self-administered ibuprofen 400 mg with minimal relief (NRS reduction from 10 to 8). Celecoxib provided marked improvement (NRS 10 to 1). She had previously attended a pain clinic and received gabapentin 300 mg daily, while the pediatric surgery clinic prescribed paracetamol and diclofenac sodium. During one week of combination therapy, she reported complete pain resolution.

On examination, vital signs were stable. The abdomen was non-distended. A keloid scar was identified at the prior surgical site, with focal tenderness localized inferior to the scar. No palpable mass was detected. Plain abdominal radiography and postoperative abdominal ultrasonography revealed no significant abnormalities. Given the localized neuropathic characteristics of the pain and exclusion of intra-abdominal pathology, the patient was diagnosed with chronic post-surgical pain (CPSP), likely secondary to peripheral nerve entrapment, and was referred to the pain clinic for targeted interventional management.

At the pain clinic, an ultrasound-guided diagnostic and therapeutic procedure was performed. Initial scanning focused on the region corresponding to the post-appendectomy scar. The right lateral cutaneous nerve was successfully identified within the fascial plane between the *musculus obliquus internus* and *musculus transversus abdominis*, consistent with its expected anatomical course. Notably, the nerve appeared to be located in close proximity to fibrotic tissue, with a clinical impression suggestive of perineural entrapment associated with post-surgical scar formation. This finding was considered the primary generator of the patient's neuropathic pain.

A targeted perineural hydrodissection was subsequently performed using a mixture of 12.5% dextrose and 0.5%

lidocaine (total volume 3 mL). The procedure aimed to mechanically separate the nerve from surrounding adhesions, restore neural gliding, and alleviate compressive forces, while simultaneously providing immediate analgesia through local anesthetic effect. Following perineural intervention, a focused intralesional injection was administered directly into the keloid scar at the site of maximal tenderness, utilizing the same solution of 12.5% dextrose and 0.5% lidocaine. This approach was intended to address both nociceptive input from the scar tissue and underlying neurogenic inflammation, as well as to promote local tissue remodeling. This combined strategy integrates mechanical decompression (hydrodissection), neural desensitization, and proliferative modulation, targeting both peripheral nerve pathology and scar-related pain generators. At three-week follow-up, the patient demonstrated marked clinical improvement, with pain intensity reduced to NRS 1–2, accompanied by significant restoration of functional capacity and daily activity tolerance.

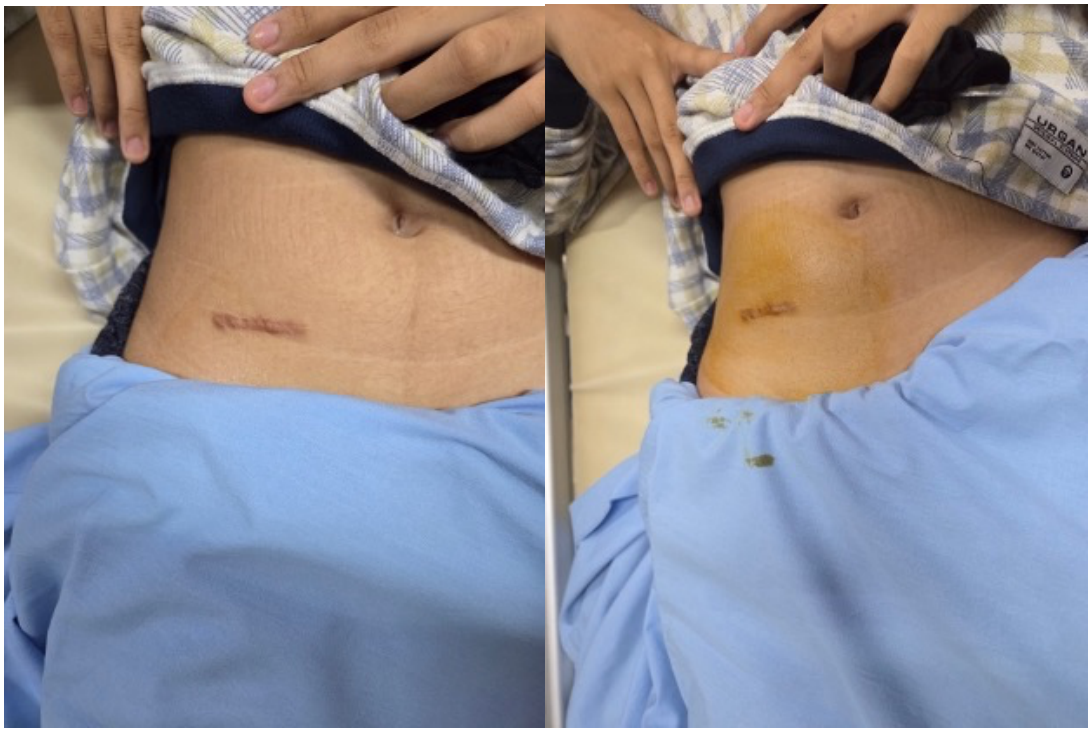

Figure 1. Clinical photograph showing the surgical site.

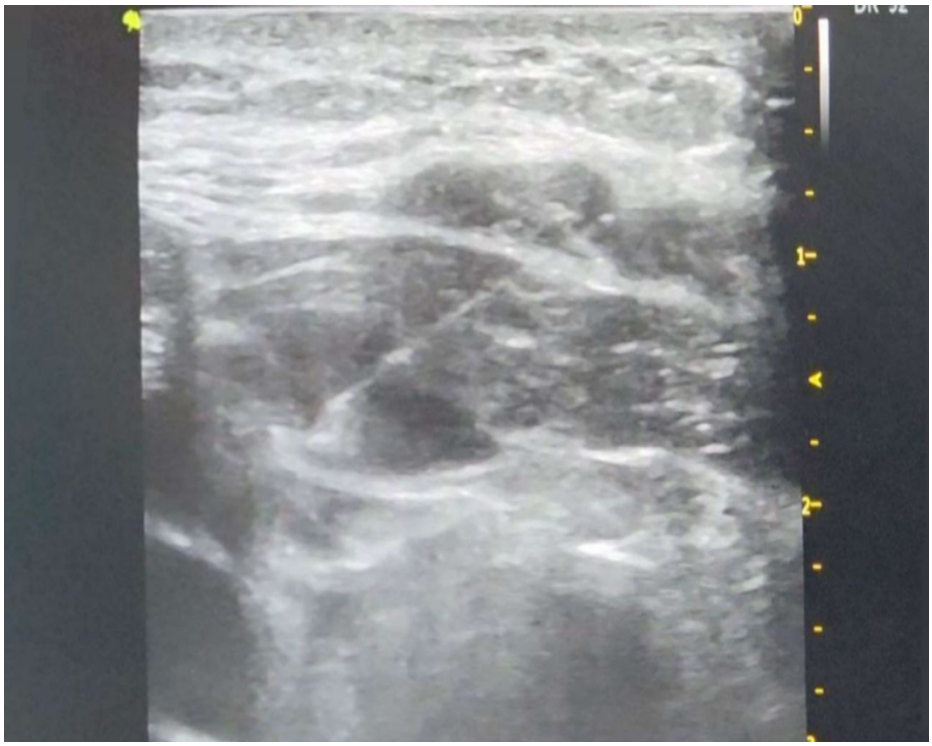

Figure 2. Ultrasound-guided hydrodissection of the lateral cutaneous nerve within the fascial plane between the internal oblique and transversus abdominis muscles

Figure 3. Intralesional Injectional with 12.5% Dextrose and Lidocaine 0.5%

Case 2

The second case involved a 21-year-old male presenting with severe, persistent pain localized to the site of prior wide hemangioma excision involving the posterior to lateral thoracic region (T3–T10), performed two years earlier. The pain had been continuous since surgery, with intensity ranging from NRS 9–10, and was refractory to multimodal pharmacological therapy, including sustained-release morphine sulfate (20 mg twice daily), paracetamol (500 mg four times daily), gabapentin (weight-adjusted dosing), and alprazolam. The patient exhibited significant functional impairment and psychological distress. Based on clinical evaluation and exclusion of alternative etiologies, the patient was diagnosed with chronic post-surgical pain (CPSP) and referred for interventional pain management.

An ultrasound-guided erector spinae plane block (ESPB) was performed as the initial intervention, targeting the ipsilateral thoracic region corresponding to the pain distribution. The block was administered using ropivacaine 0.5% (30 mL), with the primary objective of achieving rapid analgesia through regional neural blockade. Following the procedure, the patient experienced a marked reduction in pain intensity to NRS 2–3. However, two days post-intervention, pain recurred, albeit with reduced duration and severity compared to baseline.

Two weeks after the initial ESPB, a targeted intralesional prolotherapy injection was performed using a combination of 12.5% dextrose and 0.5% lidocaine, administered along the area of maximal tenderness within the surgical scar region. This intervention resulted in a reduction of pain intensity from NRS 8–9 to 5–6. A second session of intralesional prolotherapy using the same solution was conducted two weeks later, leading to further significant improvement, with pain reduced to NRS 1–2.

Notably, following these sequential interventions, the patient was able to discontinue all prior oral analgesic medications, including opioids and adjuvant agents, with sustained functional improvement. This staged interventional approach highlights the role of initial regional blockade (ESPB) for acute pain modulation, followed by prolotherapy targeting chronic peripheral sensitization and scar-related nociceptive generators, resulting in durable analgesic outcomes.

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Figure 4. Clinical photograph showing the post-surgical site.

DISCUSSION

Chronic post-surgical pain (CPSP) is an unintended adverse outcome after surgery that affects approximately 10–50% of surgical patients worldwide and causes a significant clinical problem with substantial functional, psychological, and socioeconomic consequences (Fuller et al., 2023; Thapa and Euasobhon, 2018). CPSP not only impairs quality of life but also raises therapeutic challenges for clinicians due to its complex pathophysiology and varied presentation. The present case series shows this complexity through two distinct cases of CPSP following different surgical procedures to emphasize various risk profiles and management considerations.

According to the International Classification of Diseases, Eleventh Revision (ICD-11), CPSP is defined as pain that develops or increases after surgery, persists beyond normal tissue healing (≥3 months), is localized to the surgical site or related dermatomes, and cannot be explained by alternative causes such as infection, malignancy, or pre-existing pain conditions, often with neuropathic features (Macrae, 2008; Rosenberger and Pogatzki-Zahn, 2022). Based on the location, duration, and exclusion of alternative causes of pain, both patients in this series met these diagnostic requirements.

The pathogenesis of CPSP is complex and multifactorial, involving interactions between patient-related and surgery-related factors. Patient-related factors include genetic susceptibility, prior pain experiences, psychological vulnerability, and psychosocial context, whereas surgery-related factors encompass the type and approach of surgery, the extent of neural injury, anesthetic techniques, perioperative analgesia, and postoperative complications (Macrae, 2008; Rosenberger and Pogatzki-Zahn, 2022). Although the length of operation and the degree of tissue damage affect the probability of CPSP, the type of injured tissue and the involvement of brain structures seem to be particularly significant factors.

The first case involved a 16-year-old female who developed persistent abdominal pain eight months following an open appendectomy. Localized to the inferior aspect of the surgical scar, the pain is occasionally present at rest and exacerbated by activity. Severe exacerbations of pain even reached NRS 10. On physical examination, there was no sign of visceral pathology, but there was focal tenderness beneath a keloid scar. The prevalence of CPSP after appendectomy in children and adolescents is rising. Palabiyik and Demir (2021) reported a prevalence of 18.4% six months after open appendectomy in children, with female sex and longer scar length identified as independent risk factors. These findings are consistent with the clinical profile of our patient. Additional studies have emphasized the role of postoperative pain intensity, sleep disturbance, and sex-related vulnerability in long-term pain outcomes among children and adolescents (Stamer et al., 2021).

In abdominal surgery, chronic postoperative pain is frequently attributed to peripheral mechanisms such as nerve injury or entrapment involving the thoracolumbar nerves supplying the anterior abdominal wall. Evidence showing that transverse abdominis plane (TAP) blocks guided by ultrasound and targeted neural blockade can effectively relieve pain in a subset of patients supports this idea, pointing to a peripheral source of pain rather than

persistent visceral pathology (Eisenberg, 2004; Wylde et al., 2017).

In the first patient, CPSP was managed at the pain clinic using a targeted interventional approach consisting of ultrasound-guided identification of the right lateral cutaneous nerve, followed by perineural hydrodissection with 12.5% dextrose (D12.5%) combined with 0.5% lidocaine, and subsequent intralesional injection of D12.5% with 0.5% lidocaine at the keloid scar site.This combined intervention aimed to address both peripheral nerve entrapment within the abdominal wall fascial plane and nociceptive input originating from the post-surgical scar tissue. Following the procedure, the patient reported marked improvement, with significant reduction in pain intensity and restoration of functional activity. Comparable outcomes have been reported by Skinner and Lauder (2007), who described significant pain relief and improved quality of life in pediatric patients with chronic abdominal wall pain following targeted regional interventions such as rectus sheath block with local anesthetic, with some patients achieving complete and sustained resolution after a single treatment.

The second case involved a 21-year-old male presenting with severe, persistent thoracic pain following wide excision of a hemangioma involving the posterior to lateral thoracic region (T3–T10). The pain was continuous, functionally disabling, and associated with depressive symptoms, and was refractory to multimodal pharmacological therapy, including opioids and adjuvant analgesics. Thoracic surgery is recognized as a high-risk procedure for the development of CPSP, primarily due to intercostal nerve injury, extensive tissue dissection, and prolonged nociceptive input. Neuropathic pain features are particularly prevalent in thoracic CPSP and are often associated with greater pain severity and functional impairment compared to CPSP following other surgical procedures (Tawfic et al., 2017).

A staged interventional strategy was employed. Initially, an ultrasound-guided erector spinae plane block (ESPB) was performed using ropivacaine 0.5% (30 mL) on the ipsilateral side of pain, with the aim of achieving rapid analgesia through regional neural blockade. This resulted in a significant reduction in pain intensity to NRS 2–3. However, partial recurrence of pain was noted within two days, although with reduced duration and severity compared to baseline. Two weeks following ESPB, the patient underwent a targeted intralesional prolotherapy injection using a combination of 12.5% dextrose and 0.5% lidocaine, administered along the area of maximal tenderness within the surgical scar. This resulted in a reduction of pain from NRS 8–9 to 5–6. A second session of intralesional prolotherapy, performed two weeks later, led to further substantial improvement, with pain reduced to NRS 1–2, accompanied by marked functional recovery and discontinuation of all prior oral analgesic medications.

Fascial plane blocks such as ESPB have gained increasing attention due to their ability to provide multilevel analgesia with a favorable safety profile (Macaire et al., 2020). By facilitating cranio-caudal spread along the fascial plane adjacent to the dorsal rami and paravertebral space, ESPB can modulate both somatic and neuropathic pain components, making it particularly useful as an initial intervention in thoracic CPSP (Forero et al., 2016; Tawfic et al., 2017).

In contrast, intralesional dextrose prolotherapy may contribute to longer-term pain control through mechanisms involving peripheral neuromodulation, reduction of neurogenic inflammation, and modulation of nociceptive signaling, thereby addressing the underlying chronic pain generators that are not fully resolved by regional blockade alone.

The pathophysiological mechanisms underlying CPSP are similar in both patients, despite variations in age, sex, surgery site, and pain distribution. Peripheral sensitization at the site of injury and central sensitization within the spinal and supraspinal pain networks both lead to pain chronification. Tissue and axonal injury trigger inflammatory and immune responses, leading to neurotransmitter release, microglial activation, ectopic neural firing, and persistent hyperexcitability of dorsal horn neurons (Shipton, 2011; Rosenberger and Pogatzki-Zahn, 2022). Supraspinal alterations, including impaired descending inhibitory modulation and altered brain network connectivity, further perpetuate chronic pain.

Clinically, CPSP is frequently associated with hyperalgesia, allodynia, and dysesthesia, reflecting sustained central sensitization. Approximately 35–57% of patients with CPSP exhibit neuropathic pain features, which are associated with higher pain intensity, functional limitation, and poorer quality of life (Macrae, 2008). While inflammatory and neuroplastic mechanisms may predominate in visceral and abdominal surgeries, neuropathic mechanisms are more prominent following thoracic and nerve-injuring procedures (Kehlet et al., 2006). The progression to chronic pain is not merely a biological process but a dynamic phenomenon influenced by psychological, social, and temporal elements. Psychological distress, encompassing anxiety, depression, negative affect, and pain catastrophizing, has been continuously demonstrated to elevate the probability of CPSP and prolonged opioid utilization, with a notably pronounced effect in female patients. (Franqueiro et al., 2024; Rosenberger and Pogatzki-Zahn, 2022; Tawfic et al., 2017). The second example demonstrated the reciprocal

association between psychological factors and pain, as successful pain management was associated with a reduction in depressive symptoms.

Current findings for the pharmacological prevention and treatment of CPSP is constrained, with the majority of recommendations being from research on alternative chronic and neuropathic pain disorders (Thapa and Euasobhon, 2018). While anticonvulsants, antidepressants, topical agents, and cautious opioid use may benefit selected patients, systematic reviews have not demonstrated consistent long-term preventive effects of pharmacological strategies alone (Shipton, 2011; Rosenberger and Pogatzki-Zahn, 2022). In contrast, regional anesthesia and interventional pain techniques play an important therapeutic role in established CPSP, particularly in patients with localized, refractory pain. By interrupting persistent nociceptive input and modulating central sensitization, targeted nerve blocks may provide sustained analgesia and functional recovery in carefully selected patients (Wylde et al., 2017).

The current cases underscore the importance of individualized, multimodal, and interdisciplinary approaches in the management of chronic post-surgical pain (CPSP). Prompt identification of high-risk patients, optimization of perioperative analgesia, reasonable opioid use, and timely referral to pain specialists for interventional management may facilitate more effective and timely pain control, while mitigating psychological distress and adverse long-term consequences. Despite the clear advantages of interdisciplinary approaches in CPSP management, there remains a lack of high-quality randomized controlled trials, highlighting the need for further research to establish robust, evidence-based treatment protocols.

CONCLUSION

CPSP represents a significant clinical and socioeconomic challenge across age groups and surgical procedures. These two cases illustrate the diverse presentations and shared pathophysiological mechanisms of CPSP, emphasizing the need for a biopsychosocial, patient-centered approach to prevention and management. Interventional pain techniques may offer meaningful benefit in refractory cases and should be considered as part of a comprehensive treatment strategy.

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