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Educational case report

Intrathecal management of complex regional pain syndrome: A case report and literature

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HIGHLIGHTS

- Complex regional pain syndrome is a painful condition resulting from trauma.
- Intrathecal drug delivery systems can provide significant pain relief.
- Severe side effects from the medications and hardware failure are possible.
- Only morphine, baclofen, and ziconotide are approved for intrathecal use.
- Intrathecal pumps should only be used on highly selected patients.

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ABSTRACT

Background and purpose: Complex regional pain syndrome (CRPS) is a painful condition typically resulting from a traumatic event. Pain control in these patients is often difficult and requires a multimodal approach. Our objectives are to present a single intrathecal pain management regimen for CRPS and provide a literature review of intrathecal pain management options in CRPS.

Methods: Case report from an academic pain management clinic.

Case report: We present the case of a 29-year-old female with a past medical history of multiple lumbar spine surgeries and lumbar post-laminectomy syndrome who presented to clinic with CRPS type II of the bilateral lower extremities. After failing conservative measures, she underwent placement of a successful intrathecal drug delivery system.

Conclusion: The use of intrathecal medications is useful for pain control in CRPS patients.

Implications: We provide a framework for treatment of CRPS, which could be useful for practitioners dealing with this difficult and painful condition.

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1. Introduction

Complex regional pain syndrome (CRPS) is a painful condition typically resulting from a traumatic event. CRPS type I often follows a minor injury, while CRPS II follows a known nerve injury. Pain persists beyond the typical time period that one would expect from the initial injury, and may be accompanied by allodynia and hyperalgesia. In addition to pain, patients will often experience oedema and sympathetic dysfunction, seen clinically by changes in skin colour, temperature, sweating, and hair and nail growth [1].

Pain control in these patients is often difficult and will require a multidisciplinary approach. Pharmacotherapy, interventional

procedures, and nonpharmacological coping skills have all proven to be beneficial in obtaining satisfactory pain scores in these patients [1].

2. Case description

We present the case of a 29-year-old female with a past medical history of multiple lumbar spine surgeries and lumbar post-laminectomy syndrome who presented to clinic with CRPS type II of the bilateral lower extremities causing severe neuropathic pain, skin discoloration, profound temperature changes, and oedema. Initially, she was treated with multiple oral agents, including opioids, tramadol, pregabalin, gabapentin, amitriptyline, duloxetine, and topiramate, but did poorly due to medication side effects and drug ineffectiveness. She then underwent a failed spinal cord stimulator trial. Following this, the decision was made to attempt intrathecal options and she received an intrathecal

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injection of 75 mcg fentanyl which was successful. At that point, a Medtronic SynchroMed II programmable intrathecal drug delivery system was placed without complications and she was started on a 0.2 mg/day morphine infusion. At her two week follow-up visit her pain was improved though still suboptimal so an infusion of bupivacaine was initiated. Over the course of several clinic visits and dosing adjustments, the patient found pain control with 0.5897 mg/day morphine and 3.334 mg/day bupivacaine. At the last follow-up visit, five months after placement of the intrathecal drug delivery system, her pain continued to be substantially improved, and she was happy with the outcome, improved quality of life, and greater functionality.

3. Comment

Intrathecal drug delivery systems have been used for various indications since the 1980s. It was not until 1991 that the Food and Drug Administration approved a programmable implantable infusion pump. Since that time, the indications and medications used for intrathecal drug delivery have expanded. Currently, intrathecal pumps are used for both malignant and nonmalignant chronic pain conditions [2]. Indications for intrathecal pain management include patients with failed back surgery syndrome, spinal cord injury-induced spasticity, CRPS, chronic pancreatitis, neuropathies, and rheumatoid arthritis. However, before any intrathecal device can be implanted, the patient must undergo psychiatric evaluation since the presence of depression, anxiety, suicidal ideation, or personality disorder has been associated with poorer outcomes following intrathecal medication administration [3]. In addition to the above contraindications, intrathecal pumps are not indicated in patients who are unable to have the pump refilled, require anticoagulation with inability to discontinue, have significant coagulopathies, are hemodynamically unstable, have cerebrospinal fluid outflow obstruction, are septic, have intracranial hypertension, or have an infection at the site of catheter or pump insertion [3].

Intrathecal medications along with the recommended maximum concentrations, initiation doses, maximum doses, and side effects can be found in Table 1 [2,4]. Medications are selected based on the patient's past medical history and response to the screening trial. Only morphine, baclofen, and ziconotide are approved for intrathecal use, though a variety of medications are used today [5]. Morphine is the standard medication for intrathecal opioid initiation [2].

While there are distinct side effects from the medications, there are some adverse events due to the catheter/pump system. Postop-

erative subarachnoid haemorrhage is an uncommon complication and risk increases with the use of anticoagulant agents. To reduce this risk, it is important to get a thorough and accurate medication history from the patient before proceeding with the procedure. Catheter displacement and persistent cerebrospinal fluid leakage has been seen in as many as 20% of patients [3]. Catheter breakage can be identified clinically by increasing pain or withdrawal symptoms. Infection is most commonly seen at the abdominal surgical site. This risk can be decreased by the use of strict sterile technique and prophylactic antibiotics. *Staphylococcus epidermidis* is the most common organism identified [2]. Infection rates range from 2% to 5% [3].

The literature surrounding use of intrathecal therapies for CRPS largely consists of case reports. Kapural et al. in 2009 reported on seven cases of intrathecal ziconotide for the treatment of CRPS [6]. The patients had an age range from 14 to 52 years with a mean of 32 years. Six out of seven patients suffered from CRPS type I. All but one patient had never received intrathecal therapy before undergoing a successful intrathecal trial. Three of the seven patients had ziconotide monotherapy, while the four other patients received ziconotide plus an opioid. Five patients had a >30% improvement of their pain scores and increased activity levels. Four patients were able to wean off of the intrathecal pump and manage their pain with oral agents alone. Three patients had skin or oedema changes after ziconotide initiation, which resolved spontaneously with continued infusion. Four patients experienced urinary retention.

That same year, Munts et al. described the use of intrathecal glycine for pain and dystonia in CRPS [7]. Nineteen patients with CRPS type I had an intrathecal pump placed with infusion of glycine over a four week time period and normal saline over a different four week time period. They found no difference in pain scores or dystonia between the use of intrathecal glycine and normal saline, and reported that the use of intrathecal glycine was ineffective for pain control and dystonia in CRPS.

In 2013 van der Plas et al. discussed the efficacy of intrathecal baclofen on different pain qualities in CRPS [8]. Every three months the 10 pain qualities of the neuropathic pain scale were evaluated in 42 patients receiving intrathecal baclofen. Results showed a significant improvement in global intense, dull, and sharp pains during the first six months. After this time period, scores plateaued despite increases in baclofen dosing.

Rauk et al. in 2015 reported on the use of intrathecal clonidine and adenosine in CRPS [9]. Twenty-two patients received either intrathecal clonidine (100 mcg) or adenosine (2 mg). They found no difference in pain scores between the two groups 2 h after

Table 1
Intrathecal medications and the recommended maximum concentrations, initiation doses, maximum doses, and side effects.

Medication	Maximum concentration	Initiation dose per day	Maximum dose per day	Side effects
Morphine	20 mg/ml	0.1–0.5 mg	15 mg	Granuloma formation, peripheral oedema, hormonal changes, respiratory depression, immunosuppression
Hydromorphone	15 mg/ml	0.02–0.5 mg	10 mg	Granuloma formation, peripheral oedema, hormonal changes
Ziconotide	100 mcg/ml	0.5–2.4 mcg	19.2 mcg	Increased risk of suicidality, psychiatric changes, dizziness, headache, sleep changes, motor weakness, urine retention
Fentanyl	10 mg/ml	25–75 mcg	No known upper limit	Granuloma formation
Bupivacaine	30 mg/ml	1–4 mg	10–30 mg	Weakness, urine retention, hypotension, respiratory depression
Clonidine	1000 mcg/ml	40–100 mcg	600–1000 mcg	Hypotension, sedation, peripheral oedema, arrhythmia, rebound hypertension
Sufentanil	5 mg/ml	10–20 mcg	No known upper limit	Granuloma formation
Baclofen	2 mg/ml	50 mcg	2 mg	Weakness, hypotonia, sedation, constipation, erectile dysfunction, loss of sphincter control, respiratory depression

Source: Reproduced with permission from Deer et al. [4].

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