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The Combined Use of Acute Regional and Interventional Pain Offers Superior Quality of Life in Palliative Care

Tolga Suvar, MD, Stephen Music, DO, Matthew Tan, MD, and Neal Mehta, MD

Background: Pain is a common symptom associated with cancer and can greatly compromise quality of life, motivation, and further treatments. Intrathecal pump (ITP) offers improved pain scores and clinical outcomes, while reducing the adverse effects of systemic analgesics.

Case Report: A 29-year-old woman with neurofibromatosis type 1 had a malignant peripheral nerve sheath tumor in her right thigh surgically resected. However, one month later, metastatic lesions were found throughout her body. Despite chemotherapy, the disease spread and pain became severe resulting in multiple hospitalizations and halting treatment. Multimodal analgesia was pursued, including regional anesthesia, but she was unable to tolerate the adverse effects of systemic opioids. For long-term analgesia, ITP was pursued, which significantly improved her pain control and quality of life.

Conclusions: In advanced stages of cancer, we highlight the significant benefits ITP offers with improved quality of life and reduced medication side-effect profiles vs systemic analgesics.

Key words: Intrathecal pump, regional anesthesia, palliative care, cancer, chronic pain, opioids

BACKGROUND

Cancer is a leading cause of death worldwide, accounting for approximately 10 million deaths in 2020 (1). Pain is one of the most common symptoms associated with cancer and can greatly compromise quality of life, motivation, and further treatments (2,3). Most cancer patients achieve adequate analgesia with acceptable side effects, but approximately 14% do not, even when treated by experts (4). Although improvements have been made in cancer pain management, undertreatment remains an issue in cancer patients (5). This issue may be exacerbated by the inappropriate use of recommended opioid guidelines for cancer patients, such as inadequate analgesia coverage in the setting of the opioid epidemic and limiting opioid prescriptions (2). Goals of pain management are to optimize therapy in the "5As" of pain outcomes which include: activity, analgesia, adverse effects, aberrant behaviors, and affect (2,6). Goals of "activity" are to optimize patients' functional goals. Analgesia, to provide the most effective pain relief, while limiting the pain regimen's "adverse effects." Aberrant behaviors include avoiding high-risk addiction regimens. The aim of "Affect," in treatment is to reduce pain's influence on the patient's mood (2,6).

Currently, the World Health Organization's 3-tiered "cancer pain ladder" algorithm suggests a stepwise approach to cancer pain to include an initial regimen

From:Rush University Medical Center, Chicago, IL

Corresponding Author: Stephen Music, DO, E-mail: stephen_c_music@rush.edu
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of nonsteroidal anti-inflammatory drugs or acetaminophen and titration on additional medications, such as opioids, from "weak" (e.g., codeine) to "strong" (e.g., morphine) (2,7). However, managing cancer pain is known to be significantly more complex (7). A meta-analysis (2) revealed that 59% of cancer patients undergoing treatment reported pain, and 33% of patients continued to exhibit pain after curative treatment. Evidence illustrates that quality of life and survival are linked to early and effective palliative care, including pain management (2).

The Cancer Pain Trial, a multicenter, multinational randomized controlled study comparing the effectiveness of intrathecal pump (ITP) plus comprehensive medical management (CMM), has illustrated that vs CMM alone, ITP with CMM offered improved clinical success in pain control, reduced adverse effects, and improved survival (4). We present the case of a 29-year-old woman, with a history of neurofibromatosis type 1 (NF1), who developed a high-grade sarcoma and despite treatment, metastatic spread of her disease progressed to various lytic lesions and an oncologic emergency. Her condition resulted in multiple prolonged hospitalizations and halting of chemotherapy. CMM, in addition to a pericapsular nerve group (PENG) block and temporary catheter infusion, was pursued during the third hospitalization, but provided moderate relief at the cost of an intolerable side-effect profile from the CMM regimen. Due to her worsening condition, ITP was pursued, which offered significant improvements to the point where she was able to return home, significantly reduce her oral analgesics, and continue chemotherapy. We aim to highlight the limited use of ITP as an effective treatment for refractory oncologic-related pain when prior management and interventions may be unfeasible.

CASE PRESENTATION

Here we present a 29-year-old woman with a medical history notable for NF1 who was found to have a progressive enlarging mass in her right thigh. Biopsy illustrated a malignant peripheral nerve sheath tumor. The mass was surgically resected in December 2022 and was found to be a high-grade sarcoma. At this time, she did not have chemotherapy. She was reportedly doing well postoperatively until one month later - pain began developing in her mid-lower thoracic spine and right hip that radiated to her right lower extremity. Imaging demonstrated metastatic lesions within her lungs, mediastinal lymph nodes, and a right-sided acetabular lytic lesion (stage IV). The patient started chemotherapy and underwent one cycle of doxorubicin and ifosfamide. Upon presentation for her second cycle, she was in severe diffuse pain, rated 10/10 using the visual analog scale (VAS) and unable to continue treatment due to being hospitalized for 6 days due to pain. Despite advancements made in her analgesic regimen, she was admitted twice more due to unrelenting pain in early April 2023 (10 days admission) and a third time (end of April into May 2023 [14 days admission]). Unfortunately, repeat imaging showed additional lytic lesions within her cervical spine C2-C4. At this point, she had no remaining functional quality of life. Her pain was reported in multiple areas, but primarily in her lower thoracic spine, neck, right hip, and below her bilateral knees. It was described as a "shock and stabbing" type of pain that prevented her from moving in any direction, even sleeping. Symptoms were only alleviated by lying down and remaining still. She was unable to tolerate advancements made in her oral analgesic regimen due to adverse effects, such as severe lethargy, constipation, and being bedridden. A right-sided PENG block and catheter infusion (Fig. 1) were pursued for temporary relief, which resulted in improved VAS pain scores rated 6/10 from 10/10. The PENG infusion (0.2 % ropivacaine, at 10 mL/h) was continued for 5 days. Of note, due to cachexia and protein malnutrition, surgery was deferred for her acetabular lytic lesion and she is on weight-bearing restrictions. However, due to severe refractory pain and unwanted side effects, such as severe lethargy to the point of persistent sleeping, from the multimodal analgesic regimen of approximately 300 morphine milligram equivalents (MME)/d, morphine-ITP was pursued for long-term analgesia. The patient's ITP was implanted (April 2023) without complication and the tunneled epidural catheter tip was placed at T11 (Fig. 2). Following the ITP implant, the patient's oral pain regimen was reduced to an as-needed basis (up to 30 MME/d), which consisted of hydrocodone-acetaminophen 5 mg to 325 mg prn. Her pain was reduced by over 70% and she was no longer persistently lethargic, allowing her to return home, offering significant improvements in quality of life, and allowing chemotherapy treatments to resume. Initial ITP settings were set to a continuous infusion over 24 hours of morphine: 1.001 mg/d, (0.042 mg/h). However, due to the unfortunate disease progression and subsequent increased pain demands, her ITP has been carefully titrated to a current dose of 1.875 mg of morphine daily (0.078 mg/h), with patient-controlled

morphine boluses of 1.994 mg; bolus infused over 1 hour, up to 10 times a day. Currently, the patient is continuing and tolerating multiple cycles of chemotherapy with docetaxel and gemcitabine.

In addition to her ITP, her adjunctive analgesia regimen includes fentanyl patch 12 mcg/h q72 h, morphine-immediate release 15 mg po prn (may take up to one a day), lidocaine 5% patch prn and tizanidine 2 mg po prn, maintaining 30 MME/d apart from her morphine ITP. Since the ITP implantation, she reports that overall her pain is well controlled (VAS pain score rated on average 2-3/10), no longer severely lethargic from oral analgesics, and overall very satisfied with her analgesic regimen and the lack of her analgesic regimen's side effects.

CONCLUSIONS

Pain remains a significant and frequent symptom in

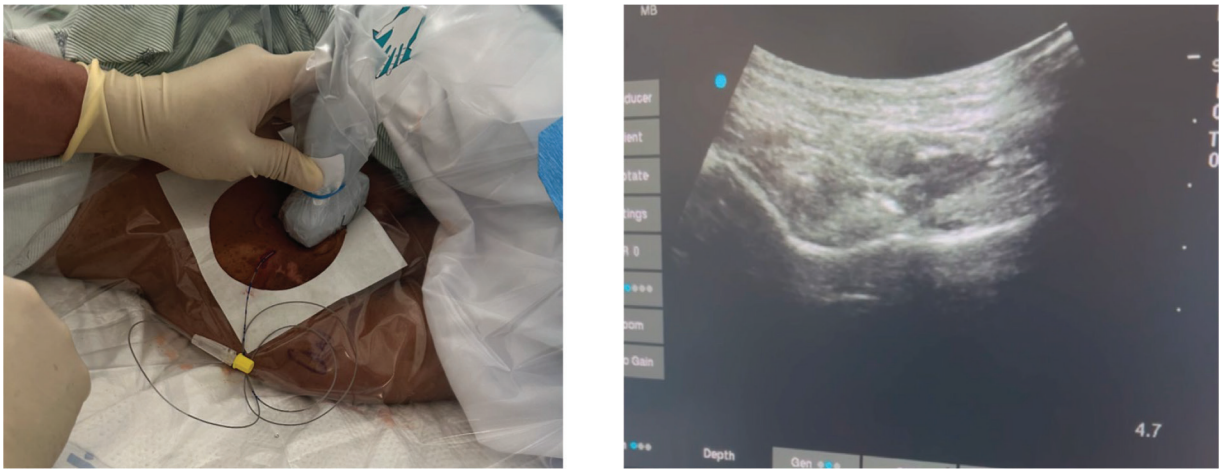

Fig. 1. Right sided pericapsular nerve group (PENG) block and catheter placement under ultrasound guidance.

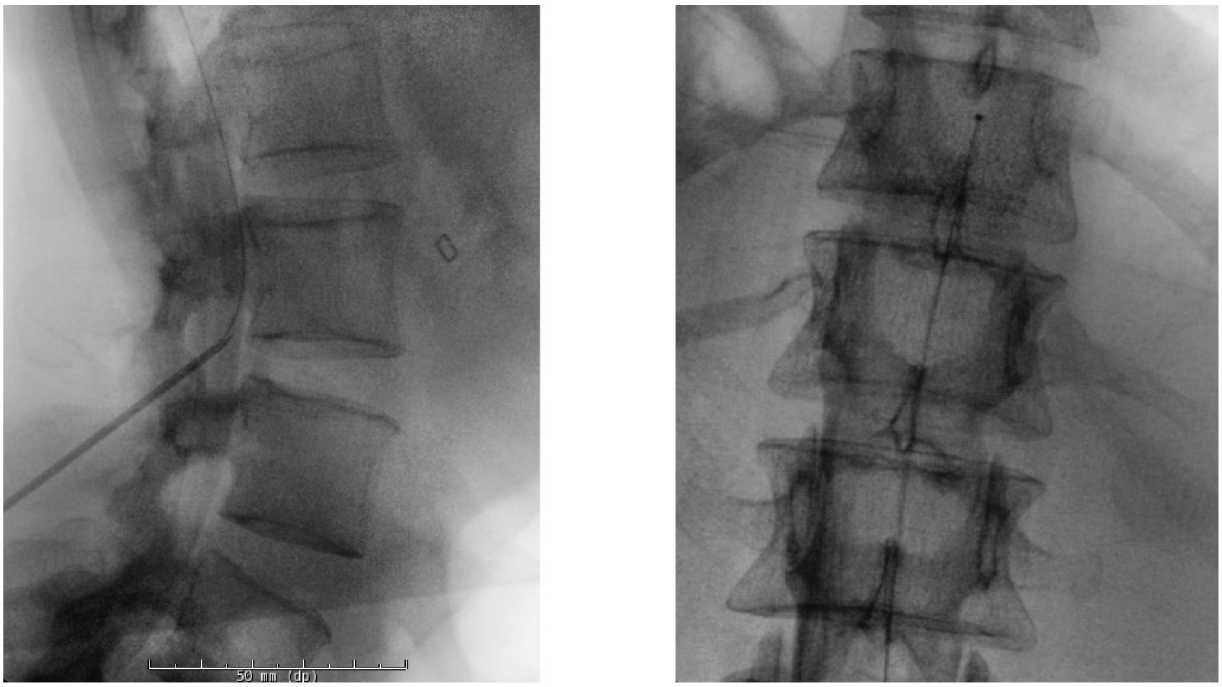

Fig. 2. Intrathecal drug pump catheter placement (Left) and positioning to T11 (Right) under fluoroscopy guidance.

oncology. Intractable pain due to an oncologic emergency can result from a fracture or impending fracture of the weight-bearing bone that is typically seen in advanced stages of cancer (2). Despite the availability of opioids, non-opioid analgesics, and advancements in comprehensive medical management, undertreatment in oncologic-related pain remains common (5). Greco et al (5) illustrated that 43.4% of cancer-related pain is undertreated. However, patients suffering from "intractable pain" may not tolerate the side-effect profile of increased opioid demands (i.e., profound lethargy, severe constipation), which are important contributors to failed pain therapies (4,5). In these circumstances, interventional techniques have been effective to eliminate or significantly control pain without the adverse effects of systemic analgesics (5). The Cancer Pain Trial showed that ITPs have provided superior analgesia with less systemic toxicity, and may improve survival in patients with intractable pain after appropriate therapy (4). The European Society of Medical Oncology, in 2019, also recommended intrathecal analgesia for refractory pain or in patients experiencing pain in various anatomic locations (3). Furthermore, ITPs being implanted devices pose a reduced risk of infection vs percutaneous means of intrathecal opioid administration (3).

In our case, the patient experienced intractable pain due to her pathologic fracture and other various locations resulting in hospitalization and halting of chemotherapy. Furthermore, due to her refractory pain and increased analgesic demands despite a multimodal analgesic regimen, including regional anesthesia, she was unable to tolerate any functional status or attain any quality of life, let alone proceed with any life-prolonging oncologic therapies. The National Comprehensive Cancer Network recommends providers consider all pain management interventions in the context of patient-specific goals for comfort, function, and safety (2). According to Dupoiron (3), intrathecal opioid administration should be considered in patients with intolerable sedation, confusion, and/or inadequate pain management with systemic opioid administration. Furthermore, the Polyanalgesic Consensus Conference, in 2017, strongly recommended ITP use in treating cancer pain with a high level of evidence (level I, rank A), and recommended that it is no longer mandatory to proceed with a trial prior to permanent implantation (3,8). In our case, permanent ITP was quickly pursued due to the severity of the patient's condition, inability to continue chemotherapy, and disability from her increased analgesic demands, such as severe lethargy resulting in persistent sleeping.

Following ITP implantation, the patient immediately noted a significant pain reduction by at least 70% with an MME reduction by 10 times. Her MME was reduced from 300 mg/d to 30 mg/d with the remaining oral analgesics available on an as-needed basis. She was also able to return home vs requiring further hospitalizations due to her drastic improvements in functional status after ITP. Since implantation in April 2023, the patient's pain scores have been maintained around 2-3/10 VAS score, with an MME of 30 mg/d while continuing to receive chemotherapy, and all while not experiencing debilitating adverse systemic effects from high narcotic requirements. The patient has also maintained higher than anticipated pain reduction scores (> 70%) following ITP implantation. One study (4) showed that 12 weeks post-ITP implantation pain scores were decreased by approximately 47%.

Furthermore, Smith et al 2005 (4) noted that patients who received ITP therapy had improved cancer survival, (median survival > 100 days) with 52% to 59% alive at 6 months compared with 32% of the non-ITP group. Studies have also suggested that patients with ITP therapy provided a cost-neutral benefit in stages of advanced metastatic disease vs alternative methods, such as external epidural catheter, home intravenous patient-controlled analgesia, or other expensive therapies (3,4).

Lastly, despite ITP's effectiveness and availability for decades, it remains underutilized despite a high level of efficiency and being widely recommended (8,9). The American Society of Pain Neuroscience conducted a survey yielding a response from 159 providers utilizing ITP in their practice, with representation from > 5 specialties, including anesthesiology, physiatry, neurosurgery, and neurology (9). In 2020, there were 602,350 cancer deaths in the United States (10). Cancer being the second-leading cause of death in the United States, ITP consideration should be expanded in order to effectively manage the high incidence of cancer pain, especially at advanced stages of the disease (3,10). However, the complex implementation, management, and invasiveness in a palliative context are acknowledged limitations (3).

As we illustrates when comprehensive medical management proves ineffective, and the patient is suffering severe disability and/or increased analgesic demands, ITP should be considered in select patients. ITP has been shown to provide superior analgesia and the ability to preserve quality of life with improved clinical outcomes, while minimizing unwanted adverse effects of systemic opioids.

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