PAIN MEDICINE CASE REPORTS

ISSN 2575-9841

Volume 4, Number 4, pp 131-134

Received: 2019-12-10
Accepted: 2020-03-05
Published: 2020-07-30

From Cancer Treatment to Cancer Survivorship: A Case Report Demonstrating the Dynamic Roles of Intrathecal Drug Delivery System in Various Phases of Cancer Care

Po-Yi Paul Su, MD
Lawrence Poree, MD, PhD
Ann Cai Shah, MD

Background: Until the continued improvements in cancer diagnosis and treatment, many cancers were once considered terminal illnesses. Opioid-based therapy is frequently utilized from the armamentarium for cancer pain treatment since the immediate goals of acute cancer pain management are focused on alleviating pain severity and improving quality of life during this limited time – despite the risks of chronic opioid therapy. However, now, with an expanding cancer survivor population, we lack guidance and tools to assist health care providers and patients in pivoting the focus of cancer pain management from acute relief toward improving function, rehabilitation, and limiting the long-term adverse effects of pain and opioid therapy.

Case Report: Here, we present a case exemplifying the ability of intrathecal drug delivery systems to serve a multitude of roles during the various phases of cancer care: from treating acute cancer-related pain, acting as a tool to wean systemic opioid therapy, to being clinically dormant in situ but ready to serve again in the event of cancer recurrence.

Conclusion: Intrthecal drug delivery systems are effective tools in managing acute cancer pain and can also be adapted to help manage chronic pain in cancer survivors.

Key words: Cancer pain, intrathecal drug delivery system, intrathecal pump, opioid weaning

From: University of California San Francisco, Department of Anesthesia, Division of Pain Medicine, San Francisco, CA

Corresponding Author: Po-Yi Paul Su, MD, University of California San Francisco, 513 Parnassus Ave # S436, San Francisco, CA, 94143,
E-mail: Paul.su@ucsf.edu
Conflict of Interest: None Declared
Disclaimer: There was no external funding in the preparation of this manuscript. Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

BACKGROUND

Guidelines for the management of cancer pain widely support the use of opioids to address cancer pain, with the goal of providing acute relief (1,2). However, as advancements are made in cancer treatment, the prevalence of patients who are cancer-free or live with cancer as a chronic illness has also increased. To better target this expanding population, we must develop evidence-based guidelines that shift the focus toward improving function and limiting the long-term adverse effects of pain and opioid-associated adverse effects. Current guidelines published by the American Society of Clinical Oncology recommend screening for pain at each encounter in an effort to remain vigilant for new-onset pain as an indicator for potential recurrent disease, secondary malignancy, or late-onset oncologic treatment side effects (3). Clinicians are recommended to engage other health professionals such as pain physicians to provide comprehensive pain management care in patients with complex needs.

Pain physicians can offer intrathecal drug delivery systems (IDDS) to successfully treat cancer pain (4). IDDS consist of a catheter positioned in the cerebral spinal fluid to allow for direct delivery of medication to the receptors of the central nervous system (CNS) (5). Long-term therapy requires surgical implantation of a drug reservoir and pump in the subcutaneous tissue connected to the catheter. One advantage of this method compared with parenteral or oral therapy is the ability to limit side effects by decreasing systemic levels of the drug while achieving higher drug concentrations at the site of action in the CNS. Multiple studies have demonstrated that IDDS can improve not only pain severity, but decrease systemic drug toxicities, improve mood, physical function, and survival (4,6). The National Comprehensive Cancer Network guidelines (2) state that the intrathecal route of opioid administration should be considered in patients with intolerable sedation, confusion, and/or inadequate pain management with systemic opioid administration.

Despite evidence supporting IDDS in acute cancer pain treatment, minimal literature exists to guide the use of IDDS in the care of cancer patients as they transition to cancer survivors. We queried the Medline literature database since inception using the terms "intrathecal pump" and "cancer," but found no reports regarding the use of IDDS in the care of cancer survivors. Here we report a case in which IDDS was first used to effectively treat chemotherapy-induced pain, then utilized as a tool to wean opioid therapy; and as the patient entered cancer remission, the IDDS was maintained on reserve, ready to be reactivated against recurrent pain in the event of cancer relapse.

CASE SUMMARY

This is a case of a 55-year-old man with a history of melanoma complicated by metastatic disease to his brain, who underwent surgical resection and radiation therapy. He subsequently underwent adjuvant chemotherapy with ipilimumab, a biological chemotherapeutic, which caused immune-related chronic abdominal pain requiring recurrent hospital admissions for inadequate pain control. He had a negative workup for infectious etiologies. The pain was sharp, stabbing, and burning in the mid- to low abdomen with occasional pain in the right upper quadrant and sternum. His oncologist attempted to treat the underlying colitis with courses of prednisone and infliximab without success. Systemic opioid therapy with various combinations of oral short-acting, long-acting oxycodone and hydromorphone, and transdermal fentanyl (up to ~150 oral morphine equivalents per day) provided some analgesic benefit, but the extent of sedation further worsened his functionality and quality of life.

Given poor analgesia with intolerable side effects, he underwent an intrathecal pump trial with a staged tunneled intrathecal catheter located at the T9 vertebral level. His pain was most likely multifactorial: neuropathic from chemotherapeutic injury to the autonomic system, and in part nociceptive from bowel injury. We thus provided him with intrathecal boluses of bupivacaine, hydromorphone, and fentanyl, to which he had great analgesic response. A permanent intrathecal pump was implanted the following day. The pump was programmed to deliver a 24-hour dose of 3 mg of hydromorphone, 3.75 mg of bupivacaine, and 22.5 mcg of fentanyl; this was based on his intrathecal medication needs from the trial. The patient was able to discontinue all nonintrathecal opioids immediately postoperatively, his abdominal pain was significantly better managed, and he no longer experienced sedation and cognitive impairment from the oral opioids. The patient subsequently completed his chemotherapy treatments and entered remission. Over the following 6 months, the patient's abdominal pain resolved; as such, the intrathecal opioids were weaned over the course of 8 months by decreasing the rate of delivery and refilling the IDDS with progressively more dilute medications. Following a multidisciplinary discussion with the patient and his oncology and pain management teams, the

decision was made to keep the IDDS in place due to concern that his metastatic malignancy, and his pain, may recur. The intrathecal pump was filled with saline and turned down to its lowest setting of 0.048 mL per day. We established a plan with the patient that in the event of recurrent disease or pain, his IDDS would be again refilled with active medication and the device would be reprogrammed for intrathecal therapy to support his cancer treatments. Three years after permanent implant, he remained in remission, and local irritation around the intrathecal catheter anchor site led to the catheter's explantation with the pump remaining in situ. Ultimately, the pump was also explanted 2 years later as it reached the end of its service life of 5 years. The patient to this date remains off all systemic opioid medications (6 years since IDDS implantation; one year since explant), without limitations in his function, and remains in cancer remission.

DISCUSSION

The use of IDDS has often been reserved for advanced-stage cancer patients as they often have difficult-to-control pain despite following the World Health Organization's analgesic ladder (1). Sometimes the cancer treatment itself can induce intolerable pain that limits the patient's ability to complete the treatment cycles. In this case, IDDS improved the patient's abdominal pain due to chemotherapy-related adverse effects, and eliminated the sedating side effects from systemic opioid therapy. More importantly, IDDS allowed him to complete his chemotherapy treatment, which likely contributed to his cancer survivorship. Echoing previous studies, IDDS can improve pain severity and pain interference on functionality (4,6). Limiting pain interference can improve a patient's performance as reflected in Eastern Cooperative Oncology Group (ECOG) and Karnofsky scores. More studies are needed to investigate the interesting hypotheses of whether early consideration of IDDS can enhance a patient's eligibility for a particular cancer treatment by improving the patient's functional status, and improve treatment adherence by limiting interruptions to treatment cycles due to pain (such as the commonly experienced chemotherapy-related abdominal pain).

In the pursuit of alleviating suffering from acute cancer pain, one often accepts the adverse effects of chronic opioid therapy, including issues of overdose, opioid abuse, increased risk of fractures, cardiovascular events, and endocrinopathies (7). For more and more patients who emerge triumphant from cancer, the balance of risks and benefits of continued opioid therapy may begin to highlight the unwarranted risks of opioids. In non-cancer chronic pain patients, Caraway et al (8) demonstrated that IDDS can provide significant and long-lasting pain relief and can eliminate systemic opioid use. In fact, this method was cited as one of several interventions to effectively reduce or eliminate long-term opioid therapy (9). This case highlights the versatility of IDDS in adapting to the various needs of cancer patients. First, we utilized IDDS to treat chemotherapy-induced neuropathic and nociceptive abdominal pain by using multimodal intrathecal medications. Second, as the patient's pain resolved upon completion of chemotherapy, we successfully eliminated intrathecal hydromorphone (from 3 mg/day) and fentanyl (from 22.5 mcg/day) by weaning via the IDDS. Lastly, IDDS can safely remain implanted without active intrathecal medication and serve as a back-up in the event of relapse. We were prepared to reintroduce intrathecal medications in the IDDS should the patient's clinical scenario change.

The decision to explant or retain the IDDS ultimately rests with the informed consent of the patient. One major advantage for maintaining the IDDS in situ is the rapid ability to initiate intrathecal therapy – not only for recurrence of cancer pain but also for unforeseen non-cancer pain conditions such as chronic lower back pain. From an economics perspective, since the substantial cost of IDDS occurs at the time of surgical implantation, cost savings accrue with increased longevity of the system. A recent economic evaluation demonstrated the cost-saving potential of IDDS compared to conventional medical management in as early as 2 months (10). Any future use of the implanted IDDS will be potentially less costly and more efficacious than conventional medical management. Additionally, elective explantation exposes the patient to risks associated with surgery such as surgical site infection, bleeding, seroma, and catheter-related injuries (11,12). On the other hand, retention of foreign bodies also poses a risk for infection. The risk of surgical site infection varies from 2% to 8% (13). While the majority of infections occur within the first 2 months, infections can occur after many years as the pump is accessed for refills (14). Specific make and models of IDDS carry individual magnetic resonance imaging (MRI) compatibility limitations. While many IDDS currently in use are MRI-conditional for common MRI scanners, explantation may be warranted in order to safely obtain specific MRI sequences required for the care of the patient. Lastly, as is the circumstance in this

case, pocket site or anchor site irritation may also lead a patient to request explantation of a dormant IDDS.

An intrathecal pump filled with saline set to the lowest rate can not only optimize the battery life of the device (15) but can eliminate the need for frequent pump refills and the associated procedural and infection risks. While there are no guidelines specifying the frequency of clinical follow-up and reassessment for a saline-only IDDS, we reasoned echoing cancer-specific surveillance recommendations as a potential framework, since possible recurrence or secondary malignancy must be considered when conducting assessment of pain (3). For example, every 3 to 6 months for the first 2 years and progressing to annually as clinically indicated for melanoma surveillance (16).

IDDS is proving to be more than a salvage therapy in cancer patients, although more formal studies are needed to examine broader applications of IDDS in cancer patients. We provided a proof of concept that IDDS can be used in a temporary fashion to facilitate the management of pain severity and interference from cancer pain and its related treatments, as well as a tool to help cancer survivors to transition toward restoring functionality and long-term pain rehabilitation by eliminating long-term opioid therapy.

REFERENCES

1. World Health Organization. ***WHO Guidelines for the Pharmacological and Radiotherapeutic Management of Cancer Pain in Adults and Adolescents.*** Geneva: World Health Organization; 2018.
2. National Comprehensive Cancer Network. Adult Cancer Pain (Version 2.2019). www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Date Accessed 05/10/2019.
3. Paice JA, Portenoy R, Lacchetti C, et al. Management of chronic pain in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. ***J Clin Oncol*** 2016; 34:3325-3345.
4. Smith TJ, Staats PS, Deer T, et al; Implantable Drug Delivery Systems Study Group. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: Impact on pain, drug-related toxicity, and survival. ***J Clin Oncol*** 2002; 20:4040-4049.
5. Deer TR, Pope JE, Hayek SM, et al. The Polyanalgesic Consensus Conference (PACC): Recommendations on intrathecal drug infusion systems best practices and guidelines. ***Neuromodulation*** 2017; 20:96-132.
6. Thimineur MA, Kravitz E, Vodapally MS. Intrathecal opioid treatment for chronic non-malignant pain: A 3-year prospective study. ***Pain*** 2004; 109:242-249.
7. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain - United States, 2016. ***MMWR Recomm Rep*** 2016; 65:1-49.
8. Caraway D, Walker V, Becker L, Hinnenthal J. Successful discontinuation of systemic opioids after implantation of an intrathecal drug delivery system. ***Neuromodulation*** 2015; 18:508-516.
9. Frank JW, Lovejoy TI, Becker WC, et al. Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: A systematic review. ***Ann Int Med*** 2017; 167:181-191.
10. Stearns LJ, Narang S, Albright J, et al. Assessment of health care utilization and cost of targeted drug delivery and conventional medical management vs conventional medical management alone for patients with cancer-related pain. ***JAMA Netw Open*** 2019; 2:e191549.
11. Deer TR, Pope JE, Hayek SM, et al. The Polyanalgesic Consensus Conference (PACC): Recommendations for intrathecal drug delivery: Guidance for improving safety and mitigating risks. ***Neuromodulation*** 2017; 20:155-176.
12. Frizon LA, Sabharwal NC, Maiti T, et al. Removal of intrathecal catheters used in drug delivery systems. ***Neuromodulation*** 2018; 21:665-668.
13. Engle MP, Vinh BP, Harun N, Koyyalagunta D. Infectious complications related to intrathecal drug delivery system and spinal cord stimulator system implantations at a comprehensive cancer pain center. ***Pain Physician*** 2013; 16:251-257.
14. Tunkel AR, Hasbun R, Bhimraj A, et al. 2017 Infectious Diseases Society of America's clinical practice guidelines for healthcare-associated ventriculitis and meningitis. ***Clin Infect Dis*** 2017; 64:e34-e65.
15. SynchroMed® IsoMed® 8626, 8627, 8637, 8472 Implantable infusion systems. Information for prescribers (includes MRI eligibility information). [package insert]. Minneapolis, MN: Medtronic, Inc.; 2017-06-01.
16. Trotter SC, Sroa N, Winkelmann RR, Olencki T, Bechtel M. A global review of melanoma follow-up guidelines. ***J Clin Aesthet Dermatol*** 2013; 6:18-26.