

Application of Palliative Tunneled Patient-Controlled Epidural Analgesia in Pediatric with Refractory Cancer-Related Visceral Pain and Breakthrough Pain: Case Report

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Abstract:

Background: Managing refractory cancer-related pain in pediatric patients with terminal-stage malignancies presents significant challenges, particularly when complicated by intestinal obstruction and cachexia. Conventional systemic analgesics often prove inadequate or intolerable.

Case presentation: A 10-year-old female with pelvic rhabdomyosarcoma and multiple metastases developed refractory cancer-related visceral pain and breakthrough pain. After three weeks of standardized intravenous opioid therapy, analgesic effect remained unsatisfactory, and the patient developed severe intestinal obstruction and cachexia, rendering oral analgesics intolerable. Following multidisciplinary evaluation, tunneled patient-controlled epidural analgesia (PCEA) was initiated using a subcutaneous tunneling technique with an individualized regimen of sufentanil, ropivacaine, lidocaine, dexmedetomidine, and dexamethasone. The patient received PCEA for over one month, achieving significant pain relief with VAS scores reduced from 4–6 to 0–1 between breakthrough episodes. Breakthrough pain frequency decreased from 15–20 to 6–8 episodes per day, with rapid resolution within 3–6 minutes post-bolus. Muscle strength remained unaffected, activities of daily living and sleep quality improved markedly. Adverse effects were limited to mild hypotension and nausea/vomiting; no serious complications such as infection occurred. The patient maintained emotional

stability and family interaction until peacefully passing away from tumor cachexia after 44 days of PCEA therapy.

Conclusion: This case suggests that palliative tunneled PCEA may be safely and effectively used for pain management in pediatric with terminal-stage refractory cancer-related visceral pain and breakthrough pain, potentially improving quality of life during the end-of-life period when conventional analgesic approaches fail.

Keywords: Refractory cancer-related visceral pain, Breakthrough pain , Patient-controlled epidural analgesia (PCEA), Pediatric, Palliative care

1. Background

Refractory cancer pain[1] is defined as moderate to severe pain caused by the tumor itself or tumor-related therapeutic interventions, which remains inadequately controlled after 1-2 weeks of standardized pharmacologic management and/or is associated with intolerable adverse effects, affecting approximately 10%-20% of cancer pain patients[2]. Pediatric refractory cancer pain is particularly rare and poses significant therapeutic challenges, especially in pediatric with terminal-stage malignancies, where conventional analgesic approaches often prove ineffective. As one of the most debilitating symptoms in pediatric oncology, refractory cancer pain in the terminal stage is frequently characterized by excruciating pain and a profound decline in quality of life, severely compromising both the physical and psychological well-being of patients and their families[3]. Traditional pain management strategies, such as oral or intravenous opioids, are often limited by drug tolerance and severe side effects[4,5] (e.g., constipation, sedation). Patient-controlled epidural analgesia (PCEA), a regional analgesic technique, delivers analgesic agents directly into the epidural space, enabling precise and sustained pain control while significantly reducing systemic drug exposure and related adverse effects[6]. In recent years, PCEA has gained increasing recognition in adult palliative care, demonstrating promising clinical efficacy in managing refractory cancer pain during the terminal stage[6]. Studies indicate that PCEA not only effectively reduces pain scores but also improves emotional well-being and overall quality of life[6]. However, reports on the application of PCEA in pediatric refractory

cancer pain remain limited.

This case report describes a child with pelvic rhabdomyosarcoma who progressed to the terminal stage despite multimodal antitumor therapy. The patient developed refractory cancer-related visceral pain and breakthrough pain, complicated by severe intestinal obstruction and cachexia, which rendered oral analgesics unfeasible and conventional pain control exceptionally challenging. Given the failure of systemic opioid therapy due to inadequate efficacy and intolerable side effects, an alternative interventional approach was required. We present this case alongside a review of relevant literature to explore the efficacy and limitations of PCEA in clinical practice, aiming to provide insights for individualized pain management in children with refractory cancer pain.

2. Case presentation

2.1 General Information

A 10-year-3-month-old female patient (body weight: 17.2 kg) was diagnosed with pelvic rhabdomyosarcoma (embryonal type, stage IV high-risk) with multiple distant lymph node metastases in September 2021. From September 27, 2021 to July 7, 2024, the patient underwent multiple courses of chemotherapy, radiotherapy, and three surgical interventions. Despite these aggressive multimodal treatments, the disease progressed to the terminal stage.

2.2 Treatment Course

Upon readmission in July 2024, the patient presented with severe intestinal obstruction, hemorrhagic cystitis, and abdominal pain, which significantly impaired her quality of life. The patient presented with persistent lower abdominal visceral pain for over one month, described as diffuse distending pain (VAS 4-6) with paroxysmal breakthrough colicky pain (VAS 6-8), accompanied by nausea and vomiting. Following diagnosis of malignant bowel obstruction, which precluded enteral analgesics, fentanyl transdermal patches were initiated per expert consensus (grade I, evidence level 1A). An initial dose of 12.5 µg/h was applied as background analgesia, with breakthrough pain managed by intermittent intravenous morphine. Patches were replaced every 72 hours. After one week, due to rescue morphine requirements ≥ 3 times daily, the fentanyl dose was

increased to 25 µg/h, and subsequently titrated up to 100 µg/h as pain progressed. However, this escalation resulted in intractable nausea and vomiting despite antiemetics, prompting a switch to continuous intravenous morphine infusion.

In August 2024, the patient developed recurrent gastrointestinal bleeding and electrolyte imbalances. Following multidisciplinary consultations and discussions with the family, the decision was made to prioritize palliative care, with the family explicitly declining invasive resuscitation measures. From August 5, 2024, the frequency of vomiting increased, and abdominal pain intensified, persisting despite vomiting or defecation. Intravenous morphine (0.01mg/kg/h) administered via a pump provided minimal relief. By August 13, 2024, frequent breakthrough pain episodes necessitated continuous intravenous morphine infusion supplemented with intermittent bolus doses, yielding only slight improvement. As the patient's condition worsened, the morphine dosage was incrementally increased to 60 µg/kg/h. According to the 2006 NCCN Pediatric Cancer Pain Guidelines, this dose falls within the recommended range for continuous intravenous morphine infusion (0.01-0.06 mg/kg/h) in pediatric with refractory cancer pain. At this dosage, the patient developed dose-limiting adverse effects including severe nausea/vomiting (6-8 episodes/day) and persistent somnolence, precluding further dose escalation. Despite intravenous ondansetron (0.15 mg/kg three times daily) and dexamethasone (0.5 mg/kg twice daily), nausea and vomiting persisted. Moreover, VAS scores remained ≥ 6 and breakthrough pain episodes remained at 15–20 per day. Consistent with the 2017 Chinese Expert Consensus on Refractory Cancer Pain[1], which defines refractory pain as inadequate relief despite 1-2 weeks of standard opioid therapy or the presence of intolerable adverse effects, this patient met the criteria for refractory cancer pain.

However, oral adjuvants were contraindicated due to malignant bowel obstruction. Other interventional options were considered but deemed unsuitable: superior hypogastric plexus block posed a high risk of organ injury due to extensive tumor infiltration and adhesions; implantable drug delivery systems were unaffordable and inappropriate given unpredictable survival time. The family preferred a low-risk, reversible technique. Aligned with consensus recommendations, PCEA was ultimately

selected for its technical feasibility, low infection risk, and suitability for patients with limited life expectancy.

2.3 PCEA Implementation

After obtaining written informed consent from the patient's legal guardian and assent from the patient following age-appropriate explanation of the procedure, epidural catheterization was performed on August 26, 2024, under intravenous combined anesthesia with propofol (2 mg/kg), remifentanyl (2 µg/kg), and midazolam (0.15 mg/kg). Spontaneous breathing was maintained, and the puncture site was infiltrated with 1% lidocaine. The patient was placed in the right lateral decubitus position with neck and knees flexed. The T₁₂/L₁ interspace was identified by palpation and confirmed by fluoroscopy. An 18-gauge Tuohy epidural needle was used, and a 20-gauge reinforced radiopaque epidural catheter was advanced 7 cm cephalad into the epidural space. Correct placement was confirmed by loss of resistance to saline, negative aspiration for blood or cerebrospinal fluid, and a negative test dose (3 mL of 1% lidocaine). Given the patient's prolonged bedridden state, severe cachexia, and thin subcutaneous tissue, a subcutaneous tunneling technique was employed as described by Laleh et al.[7]. to reduce the risk of pressure ulcers, infection, and accidental dislodgement (Figure 1). The catheter exit site was meticulously monitored, and dressings were changed regularly to prevent infection.

2.4 Analgesia Protocol and Adjustments

2.4.1 Initial PCEA Protocol and Early Challenges

The initial PCEA regimen was designed in accordance with the NCCN Adult Cancer Pain Guidelines (2024.3 Edition)[8] and published literature[9]. The patient's 24-hour intravenous morphine requirement was converted to an equianalgesic fentanyl dose (100 µg). The initial solution consisted of 15 mg ropivacaine and 100 µg fentanyl, with parameters set at: total volume 100 mL, background infusion 2 mL/h, patient-controlled bolus dose 2 mL/demand, and a 60-minute lockout interval.

Following epidural catheter placement and initiation of PCEA on August 26, 2024(15:30), the intravenous morphine infusion was discontinued once the epidural drug concentration had stabilized. However, contrary to expectations, adequate pain

control was not achieved. Visceral pain and breakthrough pain rebounded significantly, with VAS scores exceeding 6 despite repeated PCEA boluses. At 00:30 on August 27, rescue intervention was required, including resumption of intravenous morphine (16 µg/kg/h) and PCEA adjustments (background rate increased to 5 ml/h, bolus 5 ml). Partial pain relief ($\geq 50\%$ VAS reduction) was achieved within approximately 10 minutes, although the patient still required continuous intravenous morphine at 27 µg/kg/h combined with intermittent boluses. Further adjustments were made on August 27 (10:30). The ropivacaine concentration was increased to 0.2% with background rate 3 ml/h and bolus 5 ml. This reduced breakthrough pain frequency from 15–20 to 12–18 episodes per 24 hours. However, the patient required boluses approximately every hour, with pain relief occurring 8–15 minutes after each bolus (VAS 0–1). After approximately 12 hours, pain gradually intensified again, and repeated PCEA boluses provided inadequate relief, necessitating an increase in intravenous morphine to 45 µg/kg/h.

2.4.2 Protocol Optimization and Rationale for Multi-Drug Approach

At this juncture, the increased background infusion rate and frequent boluses led to rapid consumption of PCEA medication. Simply increasing the local anesthetic concentration or background infusion rate would have heightened concern for local anesthetic toxicity due to increased total ropivacaine intake, particularly given the patient's cachectic state and compromised hepatic function. This approach would have conflicted with the fundamental principle of alleviating pain without adding to the patient's physical burden or risk.

To achieve rapid pain control, a strategic revision of the analgesic approach was undertaken on August 28. Fentanyl was replaced with sufentanil based on morphine-equivalent conversion (100 µg fentanyl/24h to 30 µg epidural sufentanil/24h), with the final dose titrated to 50 µg/24h. Sufentanil was selected due to its higher µ-receptor affinity, better epidural penetration, and longer duration of action[10]. Dose titration was complicated by severe cachexia and hepatic dysfunction. Weight-based dosing using actual body weight risked undertreatment, while ideal body weight calculations increased toxicity risks. To address this challenge and prolong analgesia without

escalating local anesthetic doses, adjunctive medications were considered. Following a comprehensive review of the literature and pharmaceutical instructions regarding drug compatibility, and after confirming the absence of precipitation, turbidity, or color change in each combination, dexmedetomidine (1 µg/ml) and dexamethasone (0.05 mg/ml) were added to the regimen. Dexmedetomidine, an α_2 -adrenergic agonist, was selected to enhance analgesia[11], reduce opioid tolerance, and provide sedation. Dexamethasone[12] was added for its anti-inflammatory effect on visceral pain and its ability to prolong local anesthetic action.

The optimized regimen achieved sustained analgesia, with VAS scores of 0–1 maintained for 8 hours post-bolus and a notable reduction in breakthrough pain episodes to 6–8 per 24 hours. However, each breakthrough episode required 8–15 minutes for complete resolution following bolus administration, during which the patient experienced significant pain. To further optimize the regimen by accelerating the onset of bolus effect and shortening the duration of each breakthrough episode, lidocaine (1 mg/ml) was added after careful consideration[13]. This modification reduced breakthrough pain resolution time to 3–6 minutes, while breakthrough frequency remained stable. Moreover, lidocaine has a faster metabolism compared to ropivacaine, allowing rapid onset with each bolus without accumulating during continuous infusion, thereby minimizing the risk of local anesthetic toxicity.

Throughout the preparation and treatment period, no precipitation, turbidity, or color change was observed. Each batch of solution was used within 24 hours and stored at 4°C when not in use. Close bedside monitoring of vital signs was maintained, with strict protocols in place for managing potential adverse events. The patient and family were fully informed of the off-label nature of this multi-drug combination, and written informed consent was obtained after discussion of potential risks and benefits. This approach was adopted only after conventional therapy failed and following a careful risk-benefit assessment; it should not be interpreted as a general endorsement of polypharmacy.

2.4.3 Final Regimen and Clinical Outcomes

The final optimized regimen consisted of sufentanil (0.5 µg/ml), ropivacaine (2 mg/ml),

lidocaine (1 mg/ml), dexmedetomidine (1 µg/ml), and dexamethasone (0.05 mg/ml), with a background infusion of 5 ml/h, a patient-controlled bolus of 5 ml per demand, and a 60-minute lockout interval. Following stabilization of this regimen, satisfactory analgesia was achieved: visceral pain was well controlled (VAS 0–1), breakthrough episodes were reduced to 6–8 per 24 hours and resolved within 3–6 minutes after bolus administration, without increasing the patient's physical burden or the risk of nausea and vomiting. Progressive dose and concentration adjustments, with background infusion rates up to 8 mL/h and ropivacaine concentrations up to 0.25%, maintained inter-episode VAS scores ≤ 2 and breakthrough pain frequency < 10 episodes per 24 hours (Table 1). Over 44 days of therapy, this individualized PCEA regimen provided satisfactory pain control until the patient's death from tumor cachexia on October 8, 2024.

2.5 Monitoring and Management During PCEA

Throughout PCEA therapy, intermittent monitoring of vital signs (heart rate, blood pressure, respiratory rate, oxygen saturation) was performed alongside dynamic pain assessments. Functional evaluations included lower limb muscle strength (Medical Research Council scale), bowel/bladder function (daily recording of voiding/defecation frequency), activities of daily living (Barthel Index), and sleep quality (Pittsburgh Sleep Quality Index, PSQI). Adjustments to the analgesic regimen were guided by real-time clinical responses. Primary adverse effects included hypotension and nausea/vomiting, with preserved lower limb muscle strength allowing early bedside toileting. Nighttime sleep quality improved significantly, with restful sleep during pain-free intervals. No serious complications (e.g., epidural infection, catheter dislodgement, or drug hypersensitivity) occurred. Despite complex epidural drug combinations, no significant drug interactions or incompatibilities were observed under individualized dosing and close monitoring.

With disease progression and upward titration of local anesthetic concentrations/background infusion rates, lower limb mobility remained intact. Transient bilateral foot numbness occurred in the supine position but did not disrupt rest during pain-free periods. Mild hypotension responded to fluid resuscitation and

baseline rate adjustments. Nausea/vomiting increased to 6-8 episodes per day, primarily opioid-related though potential intestinal obstruction progression was considered. To mitigate the nausea-pain exacerbation cycle, background rates were dynamically optimized post-regimen stabilization to identify the minimal effective dose balancing analgesia and side effects, supplemented by glucocorticoids and tropisetron for antiemetic support.

2.6 Multidisciplinary Support and Clinical Outcomes

Following the transition to palliative care, a multidisciplinary team—including specialists from anesthesiology, pediatric oncology, palliative care, clinical nutrition, and social work—convened regular family conferences to facilitate shared decision-making, and coordinate holistic care while addressing psychosocial needs. At the time of palliative care referral, the patient was in a state of tumor cachexia and receiving continuous intravenous morphine infusion with inadequate analgesic effect. She remained in significant distress, lying in a passive flexion position of the hips and knees, and was completely bedbound for toileting. After PCEA initiation on August 26, 2024, visceral pain improved markedly. The patient was able to rest quietly in a semi-recumbent position and achieved limited ambulation and bedside toileting. As disease progressed, the ropivacaine concentration in the PCEA regimen was gradually increased. Visceral pain remained well controlled, and intermittent breakthrough pain episodes were rapidly relieved within 3–6 minutes following bolus administration, attributable to the inclusion of lidocaine. The addition of dexmedetomidine provided both analgesic and anxiolytic effects. Between breakthrough episodes, the patient remained calm, communicated effectively with family and healthcare providers, and engaged in simple activities with support from hospital social workers. Transient bilateral foot numbness occurred occasionally; bedside activities were reduced accordingly to prevent falls.

In the final phase of life, the palliative care team provided psychological and spiritual support to both the patient and her family. The patient came to accept her impending death peacefully, fulfilled several personal wishes, and participated in discussions regarding her own funeral arrangements. During the last 48 hours of life, hematemesis

and melena gradually worsened, and the patient became progressively somnolent due to tumor cachexia and metabolic disturbances. Visceral pain remained adequately controlled with the existing PCEA regimen, though intermittent breakthrough pain continued. Initially, the patient was able to describe her pain and self-administer bolus doses. As she weakened and could no longer clearly express pain, her family administered bolus doses every 2.5 hours based on their observation of breakthrough pain patterns. No additional sedative medication was required. The patient died peacefully on October 8, 2024, surrounded by her family, after 44 days of PCEA therapy. No intravenous opioids or palliative sedation were needed during the final days. Family members expressed satisfaction with pain management throughout the treatment course and actively participated in pain assessments and care decisions.

3. Discussion

3.1 Refractory Cancer Pain

Refractory cancer pain is defined as pain that does not respond to standard opioid and/or co-analgesic therapy[14]. It is classified as mixed pain, exhibiting both nociceptive and neuropathic characteristics[15], with primary etiologies including direct tumor invasion of neural tissues, release of inflammatory mediators, vascular ischemia, and organ dysfunction [16]. Chronic pain caused by tumor progression often induces peripheral and central sensitization, leading to inadequate efficacy of conventional analgesic regimens. The 2006 NCCN Guidelines for Pediatric Cancer Pain Management[4,5] emphasize comprehensive pain control through individualized pharmacotherapy (e.g., opioids and NSAIDs) and multidisciplinary collaboration (including pain assessment, psychological interventions, and family support), aiming to alleviate pain and improve quality of life while addressing the unique needs of special populations (e.g., neonates and terminally ill pediatric). However, these guidelines do not specifically address the assessment and management of refractory cancer pain in pediatric patients. Current clinical practices for pediatric refractory cancer pain are primarily based on expert consensus for adult refractory cancer pain and pediatric-specific studies.

3.2 Challenges in the Assessment of Pediatric Refractory Cancer Pain

While pediatric pain assessment can and should utilize validated pediatric-specific tools,

the evaluation of refractory cancer pain in children may still need to integrate concepts from adult refractory pain definitions due to the relative lack of pediatric-specific diagnostic criteria for this particular condition. Specialized assessment tools help characterize pain subtypes: the ID Pain Scale for neuropathic pain screening, the DN4 questionnaire, and the Alberta Breakthrough Pain Assessment Tool for breakthrough pain evaluation. These tools are primarily validated in adults. In pediatric refractory cancer pain assessment, they serve as references to guide evaluation and are used alongside pediatric-specific instruments[17], given the lack of pediatric-specific diagnostic criteria for this condition. Pediatric assessments must further integrate age-specific developmental considerations, focusing on pain attributes (nature, intensity, location, triggers, aggravating/alleviating factors), psychosocial dimensions (social-emotional functioning, family dynamics), medication history, non-pharmacological interventions, and input from both patients and caregivers[17]. The complexity of pediatric refractory cancer pain—driven by diverse pathophysiological mechanisms, marked interindividual variability, overlapping pain types, and psychosocial influences—significantly complicates therapeutic optimization, exacerbates management challenges, and diminishes quality of life. In this case, a comprehensive evaluation guided by the NCCN Pediatric Cancer Pain Guidelines[4,5] and refractory cancer pain expert consensus[1] confirmed diagnoses of visceral and breakthrough cancer pain. The patient presented with persistent lower abdominal distension pain lasting over one month (VAS scores of 4-6) and frequent breakthrough episodes (15-20 per 24h), accompanied by nausea and vomiting. Pain exacerbation occurred with physical activity and vomiting, with partial post-emetic relief. The ward physicians, following pediatric cancer pain management guidelines and considering the patient's cachexia and hepatic impairment, developed an individualized analgesic strategy—including oral ibuprofen suspension, fentanyl transdermal patch, and continuous intravenous morphine—which was sequentially introduced, adjusted, and replaced based on the patient's pain status and treatment response. Although these regimens played a crucial role in the early phase of pain management, progressive pain escalation and the emergence of opioid-related adverse effects increasingly limited their use, necessitating

a shift in analgesic strategy.

3.3 Comprehensive Treatment Strategies and Advances in Minimally Invasive Techniques

Therapeutic options for pediatric refractory cancer pain remain limited, with current strategies predominantly extrapolated from adult cancer pain management. Although multimodal analgesia combining opioids, NSAIDs, and adjuvant analgesics is widely employed, prolonged opioid use often leads to tolerance and adverse effects, complicating pain control. Guideline-recommended approaches[18] prioritize etiological treatment for breakthrough pain with identifiable triggers, while WHO guidelines endorse opioids as the cornerstone for moderate-to-severe cancer pain via oral, transdermal, subcutaneous, or intravenous routes, supplemented by NSAIDs, adjuvants, and antidepressants[3, 19]. Bone metastatic pain may be managed with bisphosphonates, denosumab, or radioisotopes[20]. Despite systematic pharmacotherapy, 10%-20% of patients progress to refractory pain due to inadequate efficacy or intolerable side effects[2]. The 2017 Refractory Cancer Pain Consensus advocates therapeutic adjustments, including opioid rotation or minimally invasive interventions. Recent advances in interventional techniques-such as patient-controlled analgesia (PCA)[21], neurolytic procedures[22], percutaneous vertebroplasty[23], radioactive seed implantation[24], regional nerve blocks[25], and epidural[6] or intrathecal drug delivery systems[26] offer effective alternatives. PCEA, characterized by procedural simplicity, low cost, and minimal infection risk, is particularly suitable for patients with a life expectancy ≤ 6 months[27]. PCEA delivers medications directly to the spinal dorsal horn, blocking nociceptive transmission while reducing systemic drug exposure and central sensitization[19, 28], demonstrating superior efficacy over intravenous routes in reducing breakthrough pain and enhancing end-of-life quality[6]. Segmental epidural catheter placement (C5-T6 for cervicobrachial pain, T6-T12 for abdominal pain, L1-L5 for pelvic/leg pain, and sacral for perineal pain) optimizes analgesia duration and dose requirements, with higher placements yielding prolonged effects at lower doses.

In this case, morphine was titrated from 30 $\mu\text{g/kg/h}$ to 60 $\mu\text{g/kg/h}$ based on analgesic

response. Despite dose escalation, pain control remained suboptimal (VAS ≥ 4) with frequent breakthrough episodes (15-20/day). Further increase was precluded by the emergence of unacceptable opioid-related adverse effects, including severe nausea/vomiting (6-8 episodes/day) and persistent somnolence, despite optimized antiemetic therapy. Concurrent intestinal obstruction precluded guideline-recommended oral adjuvants (gabapentin, amitriptyline), while severe cachexia and hepatic dysfunction further complicated management. The coexistence of refractory visceral pain and frequent breakthrough episodes, compounded by therapeutic limitations, necessitated a paradigm shift. Several interventional options were considered. Superior hypogastric plexus block, an absolute indication for pelvic visceral pain, was initially discussed with the family. However, it was ultimately not performed due to extensive tumor infiltration in the retroperitoneum and pelvis, coupled with a history of multiple surgeries, radiotherapy, and chemotherapy, which resulted in severe abdominal adhesions and a significantly increased risk of injury to adjacent organs. Implantable drug delivery systems (IDDS) were also considered but deemed unsuitable because of the family's limited financial resources and the unpredictable survival time, which made a costly, permanent device less favorable. Given the patient's poor prognosis, the family expressed a strong preference for a low-risk, reversible, and titratable analgesic technique over a permanent neurolytic procedure. Aligned with the 2017 Consensus[1] recommendations for opioid-tolerant cases with uncontrolled pain, PCEA was implemented given its technical feasibility, low infection risk, and suitability for short life expectancy. This intervention addressed anatomical specificity (mid-thoracic epidural catheter for abdominal pain), minimized systemic toxicity, and mitigated central sensitization, ultimately achieving rapid analgesia (3–6 minutes post-bolus) and improved quality of life.

3.4 Pharmacological Optimization and Clinical Outcomes of Epidural Analgesia in Refractory Cancer Pain

The efficacy and safety of PCEA depend critically on drug selection and synergistic combinations. PCEA regimens typically incorporate local anesthetics[6], opioids[29], $\alpha 2$ -adrenergic agonists[30], glucocorticoids[31], NMDA receptor antagonists[32], and

adjuvant agents [33, 34], each targeting distinct neural pathways to achieve multimodal analgesia. Local anesthetics (e.g., ropivacaine, bupivacaine, levobupivacaine) serve as the cornerstone of PCEA by blocking sodium channels to inhibit nociceptive transmission, offering prolonged analgesia with low systemic toxicity[6]. Lidocaine[13], with its rapid onset, is particularly effective for breakthrough pain control, though excessive doses risk cardiovascular depression and neurotoxicity. Opioids (e.g., morphine[35], fentanyl, hydromorphone[36], sufentanil[29]) are often combined to enhance analgesia while reducing local anesthetic requirements. Studies demonstrate that epidural opioids achieve comparable pain relief to systemic administration with fewer side effects[37]. A recent network meta-analysis confirmed that combinations of local anesthetics with opioids, including sufentanil-bupivacaine, provide superior analgesia for patient-controlled epidural analgesia[38]. α 2-Adrenergic agonists like dexmedetomidine[11] and clonidine[34] prolong local anesthetic duration and provide sedation and antisympathetic effects, particularly beneficial in neuropathic pain, albeit with risks of hypotension and bradycardia. Glucocorticoids (e.g., dexamethasone[31]) mitigate inflammatory pain by suppressing cytokine release and extending analgesic duration, though they may induce hyperglycemia and immunosuppression. NMDA antagonists (e.g., ketamine[11]) counteract central sensitization in refractory pain but may transiently elevate blood pressure or impair cognition. Adjuvant agents (e.g., vitamin B[12], calcitonin[33], neostigmine[39], methadone[40]) further broaden therapeutic utility. In this case, a PCEA regimen combining sufentanil, ropivacaine, lidocaine, dexmedetomidine, and dexamethasone achieved tailored analgesia: sufentanil addressed persistent visceral pain, ropivacaine provided sustained relief with reduced bolus demands, lidocaine rapidly alleviated breakthrough episodes, dexmedetomidine enhanced analgesia with sedation, and dexamethasone suppressed inflammation. Individualized dosing and close monitoring prevented significant drug interactions or incompatibilities. This strategy not only reduced opioid consumption and hepatorenal metabolic burden but also improved sleep quality and overall functional status. Compared to intravenous patient-controlled analgesia (PCIA), PCEA demonstrated superior efficacy in terminal cancer pain

management, offering procedural simplicity, low infection risk, and broader clinical applicability.

3.5 Limitations and Future Directions of PCEA in Refractory Cancer Pain

While PCEA can provide effective analgesia in refractory cancer pain, its clinical application has several limitations. First, as a single case report, our findings are inherently limited in generalizability. Second, the multi-drug epidural combination used in this patient (ropivacaine, sufentanil, lidocaine, dexmedetomidine, dexamethasone) represents an off-label approach; although we confirmed physical compatibility and maintained close monitoring, this practice is not standard and should not be generalized without further evidence. Third, in applying the strict definition of refractory cancer pain, we acknowledge that although a multi-mechanistic antiemetic regimen (ondansetron and dexamethasone) was employed, not all possible antiemetic combinations (e.g., including haloperidol or NK1 receptor antagonists) were attempted before the patient was deemed refractory—an important consideration when evaluating opioid tolerability. Additional limitations include contraindications (e.g., bleeding diathesis, local infection), dependence on specialized nursing resources and institutional expertise, and the need for rigorous catheter monitoring to prevent complications such as infection or malposition. The efficacy of PCEA may also be limited in patients with multifocal pain. Finally, evidence on pediatric PCEA remains sparse, with no large-scale randomized trials validating long-term safety and outcomes. Future prospective studies should focus on optimizing drug combinations, dosing protocols, and patient selection criteria to maximize clinical benefits while addressing implementation challenges across diverse care settings.

4. Conclusion

Management of pediatric refractory cancer pain requires a dynamic, individualized approach distinct from conventional postoperative analgesia. End-stage cancer pain involves persistent high-intensity stimulation with progressive worsening, often complicated by factors that create vicious cycles. Key lessons include: (1) multimodal analgesia combining long-acting agents for sustained background control with rapid-onset drugs for breakthrough episodes; (2) adequate background infusion volumes to

minimize rescue bolus frequency; (3) adjuvants such as dexmedetomidine and dexamethasone for enhanced analgesia and reduced opioid-related side effects; (4) continuous dynamic follow-up with documentation of pain scores, bolus frequency, rescue latency, and adverse effects; (5) family involvement in pain assessment and recording; (6) rigorous catheter care to prevent infection; and (7) multidisciplinary teamwork ensuring effective communication and collective decision-making.

For this pediatric patient with refractory cancer pain unresponsive to conventional therapy, PCEA proved a viable alternative. The individualized regimen, integrating epidural opioids, local anesthetics, and adjuvants with close monitoring and hospice principles, provided effective analgesia while preserving dignity and quality of life. These experiences suggest that PCEA, when tailored to the patient's evolving needs and supported by a multidisciplinary team, is a valuable option for managing refractory cancer pain in terminally ill children.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions

- Youbing Tu: Data curation, Investigation, Writing – original draft
- Sijia Zhou: Methodology, Palliative care supervision
- Ningning Cui: Project administration, Pain management
- Caiqi Yang: Resources, Validation
- Liang Xu: Conceptualization, Supervision, Writing – review & editing

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Ethics statement

Written informed consent was obtained from the minor's legal guardian, for the publication of any potentially identifiable images or data included in this article.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

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Figure 1

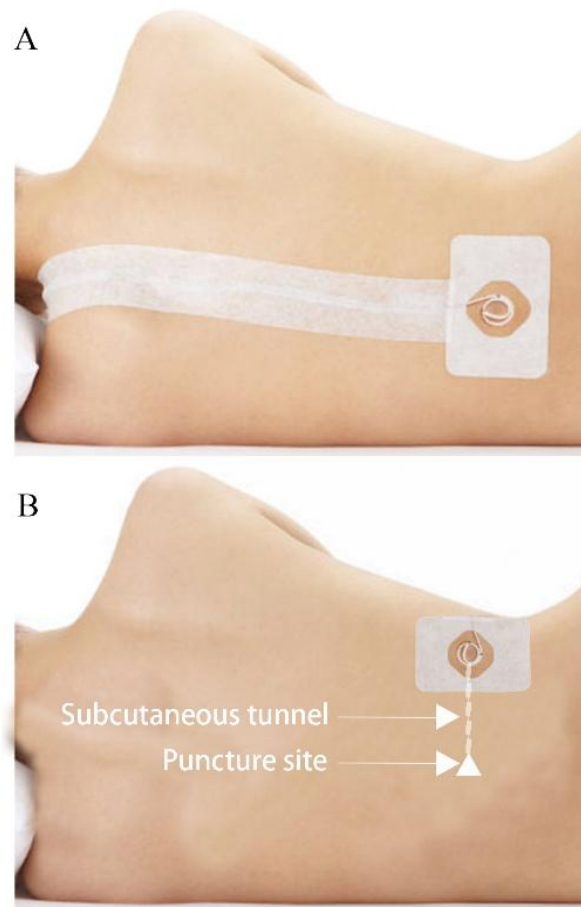


Figure 1 A. Conventional epidural catheter fixation method: After catheter insertion, the external portion of the catheter is secured along the spine with adhesive tape. B. Subcutaneous tunneling technique: Following catheter insertion, a 2-mm horizontal incision is made at the catheter exit site. A Tuohy needle is reinserted 9 cm laterally from the initial puncture site, with its tip advanced through the pre-made incision. The epidural catheter is threaded retrograde through the Tuohy needle. After needle removal, the catheter is redirected away from the spinal insertion point, emerging through a distal skin exit site for secure fixation.

Table 1: Patient-Controlled Epidural Analgesia (PCEA) Protocol and Dynamic Adjustments

Table 1: Patient-Controlled Epidural Analgesia (PCEA) Protocol and Dynamic Adjustments			
Date	Analgesic Regimen	Infusion Parameters	Clinical Course and Adjustments
2024-08-26 2024-08-27	0.15% ropivacaine + fentanyl (1 µg/mL)	Background: 2–5 mL/h Bolus: 2–5 mL Lockout: 60 min	Initial PCEA failed to achieve adequate pain control despite rate escalation. Pain rebounded (VAS >6) after discontinuing IV morphine, requiring resumption of IV morphine (16–27 µg/kg/h) and frequent PCEA boluses (hourly, 8–15 min to relief).
2024/8/27	0.2% ropivacaine + fentanyl (1 µg/mL) + IV morphine	Background: 3–5 mL/h Bolus: 5 mL Lockout: 60 min	Ropivacaine increased to 0.2%. Breakthrough frequency reduced from 15–20 to 12–18/24h, but patient still required hourly boluses (8–15min to VAS 0–1). Pain recurred after 12 h, requiring IV morphine increase to 45 µg/kg/h.
2024-08-28 2024-09-06	0.2% ropivacaine + sufentanil (0.5 µg/mL) + dexmedetomidine (1 µg/mL) + dexamethasone (0.05 mg/mL)	Background: 3.5–5 mL/h Bolus: 5 mL Lockout: 60 min	Fentanyl replaced with sufentanil for better epidural penetration. IV morphine discontinued 1 h after PCEA optimization. Pain well controlled (VAS 0–1 for 8 h post-bolus), breakthrough reduced to 6–8/24h (8–15 min to relief). Background rate titrated (3.5–5 mL/h) to balance analgesia and increased vomiting.
2024-09-06 2024-10-08	0.2–0.25% ropivacaine + sufentanil (0.5 µg/mL) + dexmedetomidine (1–2 µg/mL) + dexamethasone (0.05 mg/mL) + lidocaine (1 mg/mL)	Background: 5–8 mL/h Bolus: 5 mL Lockout: 60 min	Lidocaine added to accelerate onset; breakthrough resolution shortened to 3–6 min. Dexmedetomidine increased to 2 µg/mL for better control. Background rate progressively increased (5→8 mL/h) and ropivacaine to 0.25% as disease progressed. Breakthrough frequency maintained at <10/24h with inter-episode VAS ≤2 until patient's death on October 8, 2024.