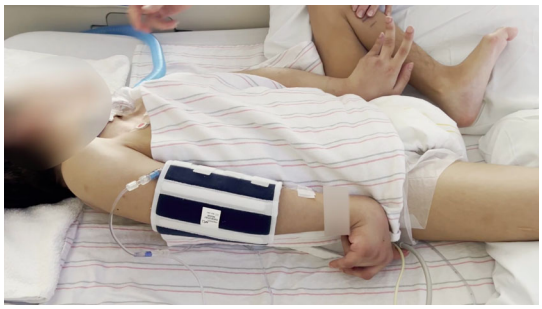
Movement Disorders
CLINICAL PRACTICE
LETTER: NEW OBSERVATION

Combination Intrathecal Pharmacotherapy for Refractory Status Dystonicus in Dyskinetic Cerebral Palsy

Francesca Papoff, MD,[1,2] Katerina Bernardi, MD,[3] Kristin Buxton, MSN, RN, CPNP,[4] Stacey Cook, MD, PhD,[5] Weston Northam, MD,[6] Scellig Stone, MD, PhD, FRCSC,[6] Charles Berde, MD, PhD,[7] Darius Ebrahimi-Fakhari, MD, PhD,[3] and Kathryn Yang, MBChB, FRCPC[3,*]

Status dystonicus (SD) is a life-threatening hyperkinetic movement disorder emergency increasingly recognized in children with dyskinetic cerebral palsy (DCP).[1] Current clinical practice guidelines conditionally recommend intrathecal baclofen (ITB) and globus pallidus internus deep brain stimulation (GPi-DBS) for severe refractory dystonia in DCP; however, the underlying evidence remains limited, and individual therapeutic responses are heterogenous.[2] We describe a patient with severe DCP and recurrent refractory SD in whom combined intrathecal pharmacotherapy was associated with a substantial and sustained reduction in health care utilization.

The patient is a 21-year-old young man with DCP secondary to extreme prematurity. His baseline examination was notable for severe generalized dystonia, spastic tetraplegia, fixed upper and lower limb contractures, with Gross Motor Function Classification System level V and multiple medical comorbidities (Video 1). Over several years, recurrent episodes of SD led to repeated prolonged hospitalizations in intensive care, often exceeding 6 months per year. Sequential trials of more than 10 dystonia-directed therapies were ineffective. An ITB pump

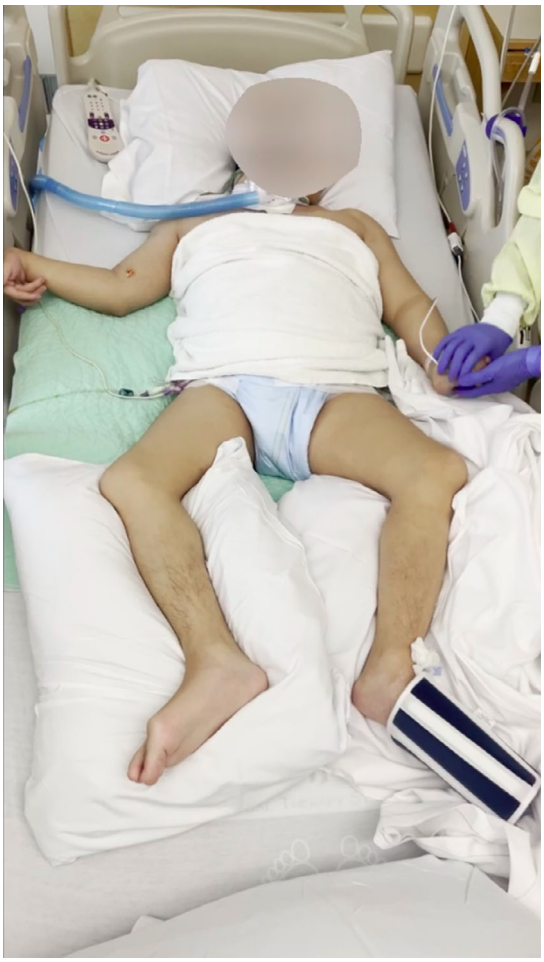


Video 1. Clinical examination of this 21-year-old male patient with dyskinetic cerebral palsy during hospital admission for status dystonicus, requiring mechanical ventilatory support. The video demonstrates severe generalized dystonia with fixed bilateral wrist contractures. Marked cachexia is noted, reflecting the chronic severity of the movement disorder. Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.70753

[1]Department of Developmental Neurosciences, IRCCS Stella Maris Foundation, Pisa, Italy; [2]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [3]Movement Disorders Program, Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA; [4]Baclofen Pump Program, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA; [5]Complex Care Services, Division of General Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA; [6]Department of Neurosurgery, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA; [7]Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

***Correspondence to:** Dr. Kathryn Yang, Movement Disorders Program, Department of Neurology, Boston Children's Hospital, Harvard Medical School, 300 Longwood Avenue, Boston, MA 02115, USA; E-mail: kathryn.yang@childrens.harvard.edu
Keywords: dyskinetic cerebral palsy, intrathecal pharmacotherapy, status dystonicus.
Francesca Papoff and Katerina Bernardi have contributed equally to this study.
Financial disclosures: The authors declare no other financial relationships related to the submitted work.
Funding agency: Research in the Ebrahimi-Fakhari Laboratory is supported by the National Institute of Neurological Disorders and Stroke (K08NS123552, 1U54NS148312), the Spastic Paraplegia Foundation, the Dystonia Medical Research Foundation, the Boston Children's Hospital Translational Research Program, the Boston Children's Hospital TIDO Accelerator Award.

Received 21 April 2026; revised 15 June 2026; accepted 17 July 2026.
Published online 00 Month 2026 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mdc3.70753



Video 2. Clinical examination of the same patient at age 22 following the initiation of combination intrathecal pharmacotherapy. The patient was admitted for a tracheitis. On examination he remains mechanically ventilated. Compared to Video 1, overall muscle tone is reduced; however, there is persistent lower limb spasticity with prominent bilateral clonus. Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.70753

was implanted at the age of 7 and, at the age of 20, bilateral GPi-DBS was performed[1]; neither provided meaningful benefit, and his DBS was ultimately deactivated.

With conventional interventions exhausted, at the age of 22, the existing intrathecal pump (Medtronic SynchroMed, continuous-infusion mode) was reprogrammed to deliver a continuous admixture of baclofen, clonidine, and bupivacaine, aiming to attenuate involuntary hyperkinetic movements while modulating spinal nociceptive input (Fig. S1). The final optimized doses were as follows: baclofen 633.9 μg/d (26.41 μg/h), clonidine 31.66 μg/d (1.31 μg/h), and bupivacaine 12.03 μg/d (0.50 μg/h).

Clinical improvement was marked (Video 2). Retrospective analysis of hospital utilization showed a stepwise reduction after pump reprogramming: total inpatient days fell from 251 days in 2022 to 159 days in 2024 and 91 days in 2025; mean length of admission decreased from 42 days to fewer than 7 days, with lengthening interadmission intervals (Fig. 1). Moreover, after the implantation he gradually gained weight (+11.7 kg from August 2024 to March 2026), and mean creatine kinase (CK) levels improved over time, reflecting a reduction in sustained dystonic muscle activity. Importantly, there were no serious adverse events (Supporting Information Text: Adverse Effects and Tolerability).

The mechanisms underlying this response remain incompletely understood. Visceral pain and discomfort from gastrointestinal dysmotility are recognized precipitants of SD.[3] In patients with profound intellectual disability, nociception is often underrecognized, potentially sustaining a self-reinforcing pain–dystonia cycle.[4] Intrathecal bupivacaine may attenuate this cycle through segmental nociceptive blockade, though this hypothesis requires formal evaluation. Notably, emerging preclinical evidence implicates spinal circuits as independent contributors to dystonia pathogenesis: spinal cord–restricted *Tor1a* deletion in a DYT1-*TOR1A* mouse model produces a fully penetrant dystonic phenotype in the absence of supraspinal pathology, supporting spinal mechanisms as a therapeutic target.[3] These findings provide a mechanistic rationale for spinally delivered pharmacotherapy, although generalization from genetic models to acquired etiologies warrants caution.

Combination intrathecal pharmacotherapy is established for refractory cancer pain and has been reported for spasticity in cerebral palsy,[5] but its application to SD has not been described previously. Limitations of this single-case observation include the inability to distinguish combination-specific effects from nonspecific motor suppression and uncertainty about generalizability to less severely affected patients. Whether this combination alters the natural course of SD also cannot be determined. Nevertheless, our observation suggests that simultaneous modulation of motor and nociceptive spinal pathways may represent a viable therapeutic strategy for refractory SD in severe DCP when standard interventions have been exhausted and warrant prospective evaluation in larger cohorts.

Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Manuscript preparation: A. Writing of the first draft, B. Review and critique.

F.P., K.B.: 1A, 1B, 1C, 2A, 2B
K.B., S.C., W.N., C.B.: 1B, 2B
D.E.F., K.Y.: 1A, 1B, 1C, 2B

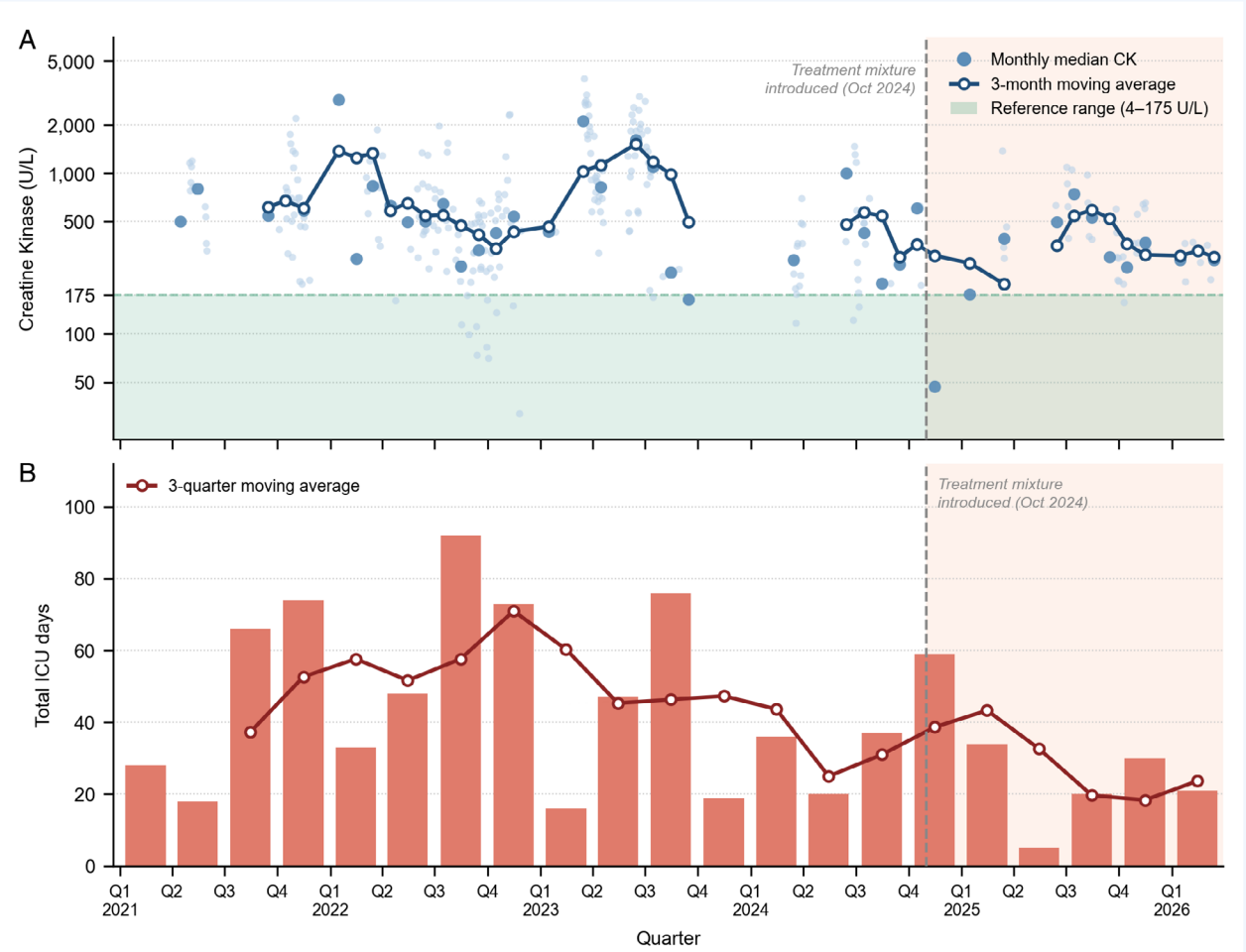


FIG. 1. Longitudinal serum creatine kinase levels and intensive care unit burden before and after initiation of combination intrathecal pharmacotherapy. (**A**) Serial serum CK concentrations (U/L) measured during hospitalizations from April 2021 to March 2026. Small circles represent individual daily CK values (daily mean where multiple assays were obtained on the same date); large filled circles represent monthly median CK values. The line with open circles denotes the 3-month moving average of monthly medians. The shaded band and dashed horizontal line indicate the laboratory reference range (4–175 U/L; ULN: 175 U/L). A total of 289 measurements were available; 93% exceeded the ULN (median 544 U/L; mean ± SD, 758 ± 656 U/L). (**B**) Total ICU days per calendar quarter from Q1 2021 to Q1 2026 (50 admissions; 852 total ICU days over the study period). Bars represent quarterly ICU day totals. The line with open circles denotes the three-quarter trailing moving average of quarterly ICU days, illustrating the longitudinal trend in hospitalization burden. In both panels, the vertical dashed line marks the date of intrathecal pump reprogramming to a continuous admixture of baclofen, clonidine, and bupivacaine (October 31, 2024); the shaded region to the right of this line denotes the post-reprogramming period. Data are presented descriptively; no formal statistical comparisons were performed. CK, creatine kinase; ICU, intensive care unit; SD, standard deviation; ULN, upper limit of normal.

Acknowledgments

The authors thank the patient and patient's family for supporting research on movement disorders.

Disclosures

Ethical Compliance Statement: This study was conducted in accordance with institutional and ethical standards. The case report was reviewed and determined that formal IRB approval was not required for this single-patient report. Written informed consent was obtained from the patient's parents and documented in the medical record. We confirm that all authors have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Financial Disclosures and Conflicts of Interest

Author disclosures are available in the Supporting Information.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. ■

References

1. Vogt LM, Yang K, Tse G, et al. Recommendations for the Management of Initial and Refractory Pediatric Status Dystonicus. *Mov Disord* 2024; 39(9):1435–1445. https://doi.org/10.1002/mds.29794.
2. Fehlings D, Agnew B, Gimeno H, et al. Pharmacological and neurosurgical management of cerebral palsy and dystonia: clinical practice guideline update. *Dev Med Child Neurol* 2024;66(9):1133–1147. https://doi.org/10.1111/dmcn.15921.
3. Pocratsky AM, Nascimento F, Özyurt MG, White IJ, Sullivan R, O'Callaghan BJ, et al. Pathophysiology of Dyt1- *Tor1a* dystonia in mice is mediated by spinal neural circuit dysfunction. *Sci Transl Med* 2023; 15(694):eadg3904. https://doi.org/10.1126/scitranslmed.adg3904.
4. Peacock DJSJ, Vithlani K, Clarke GA, Patel M, Joseph AA, Horvath G. Pediatric Status Dystonicus: a single-center 10-year retrospective review. *Mov Disord Clin Pract* 2025;12(12):2247–2252. https://doi.org/10.1002/mdc3.70282.
5. Ratnasingam D, Woehrlen T, Koerber S, Drenth E, Marupudi N, Concepcion M, et al. Utilizing combination intrathecal baclofen and analgesic medication to manage spasticity and pain in patients with pediatric-onset disability: case series. Byrne R, Kim H, Najarian R, Ramsey J, Thomas S, curatori. *J Pediatr Rehabil Med* 2024;17(1):57–66. https://doi.org/10.3233/PRM-220100.

Supporting Information

Supporting information may be found in the online version of this article.

Figure S1. Anteroposterior (left) and lateral (right) chest and abdominal radiography showing high implantation of the catheter device terminating at the T5 level (white arrows).

Data S1. Adverse effects and tolerability. No adverse effects attributable to long-term intrathecal bupivacaine in combination with baclofen and clonidine—such as new or worsening constipation, urinary retention, motor weakness beyond baseline—were observed over the follow-up period. Doses have been periodically retitrated in response to intercurrent clinical changes (e.g., transient temperature fluctuations, which were pre-existing and which we did not attribute to the intrathecal regimen), but no formal attempt at dose reduction or withdrawal of the combination infusions has been undertaken to date, given the magnitude and durability of the clinical benefit.

Data S2. COI_Disclosure.