

Baclofen Withdrawal Presenting as Irritability in a Developmentally Delayed Child

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Irritability in children has a broad differential diagnosis, ranging from benign processes to life-threatening emergencies. In children with comorbid conditions and developmental delay, the diagnostic process becomes more challenging. This case report describes a developmentally delayed 14-year-old boy who presented with pain and crying caused by a malfunction of a surgically implanted baclofen pump. We describe recommendations concerning the diagnostic evaluation, medical management, and surgical repair. [West J Emerg Med. 2012;13(4):373-375.]

CASE REPORT

A 14-year-old boy with cerebral palsy, developmental delay and seizures was brought to the pediatric emergency department by his parents for “crying constantly,” which began 3 days prior to presentation without apparent reason. The patient had significant cognitive and motor impairment; he was non-verbal and communicated with minimal non-verbal gestures, such as smiles and grimaces. He required assistance for all activities of daily living. Despite administration of ibuprofen at home, his distress increased steadily. Subsequently, he was unable to sleep and had decreased oral intake. The parents denied trauma, fevers, ear discharge, seizure activity, hematuria, dysuria, choking episodes, vomiting, or diarrhea. His last bowel movement on the day prior was soft without any blood. The patient has an intrathecal baclofen pump, which had not alarmed and was examined and refilled two weeks prior by a neurosurgeon at another institution. His parents were unaware of the infusion rate of the baclofen; however, maintenance doses range from 22 micrograms to 1.4 mg daily, depending on patient response. At the time he was taking oxcarbazepine for his seizure disorder; his last seizure was 18 months prior. He had scoliosis and a chronic left hip dislocation. The patient ate a soft pureed diet and some solids by mouth. He had no known drug, food or environmental allergies.

On physical examination, he was crying and appeared uncomfortable, but was intermittently consolable by his parents. He was afebrile, with a heart rate of 145 beats

per minute, blood pressure 130/76 mmHg, respiratory rate 18 breaths per minute, and oxygen saturation 99% on room air. His eyes had no excessive tearing; fluorescein examination revealed no uptake. No foreign body was visualized in the nares or auditory canals; tympanic membranes bilaterally were normal. The chest was clear and the cardiac examination was only significant for tachycardia. The abdomen was soft, non-tender and non-distended; a baclofen pump was palpable in the right lower quadrant; a rectal examination was normal and stool was guaic negative. Examination of the back revealed scoliosis without pain to palpation along the spine. His penile and testicular examination was normal. His extremity examination revealed a deformity of the left hip and no tenderness to palpation, swelling or erythema along the extremities. No skin lesions were noted. At baseline, he was awake, alert, and responded non-verbally with gestures. He moved his eyes in all four quadrants, had no facial asymmetry, localized sounds and tracked objects by turning his head. He had 5/5 strength in all extremities with minor contractures that could be passively ranged bilaterally. He had 2+ to 3+ reflexes bilaterally without clonus. His neurological examination on the day of presentation was significant for increased tone and spasticity in all four extremities and clonus bilaterally at the ankles.

Complete blood count, urinalysis and serum chemistries were within normal limits. Three milligrams of midazolam was administered intravenously resulting in cessation

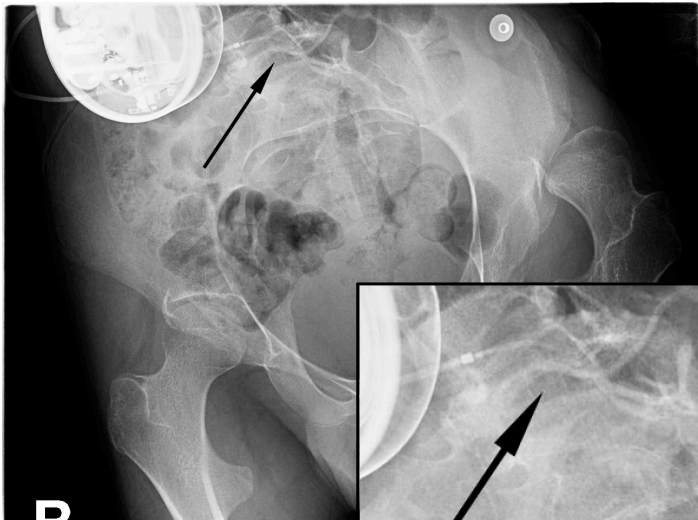


Figure. Radiograph demonstrating chronic left hip dislocation and a discontinuity in baclofen pump catheter (arrow).

of patient's crying, relaxation of the upper and lower extremities, and decreased heart rate and blood pressure. An abdominal and pelvic radiograph revealed a chronic left hip dislocation, and discontinuity of the baclofen pump catheter (Figure). The neurosurgical service was consulted, and computerized interrogation of the baclofen pump via wireless device revealed no recent alarms and a sufficient medication volume in the reservoir. Mechanical interrogation via insertion of a needle into the access port was abnormal, with normal forward flow but an inability to aspirate cerebrospinal fluid. Due to the clinical presentation, radiographic findings, and the results of the mechanical interrogation, the patient was diagnosed with a baclofen pump malfunction secondary to disconnection of the tubing. In the absence of severe withdrawal symptoms, 10 mg of oral baclofen 3 times daily was provided with relief of symptoms, and the patient and family were transferred back to the primary neurosurgeon for definitive repair.

DISCUSSION

In children presenting with irritability, a thorough history and physical examination can often narrow an initially broad differential diagnosis and help the clinician determine the need for further laboratory or imaging studies. Children requiring intrathecal baclofen often have spastic neuromuscular disorders as a result of hypoxic ischemic encephalopathy that occurs at birth or from a significant traumatic brain injury. Additionally, they often have significant comorbid conditions, such as global developmental delay and seizure disorders. These children are also susceptible to respiratory illnesses, complications from previous surgeries, and pathologic orthopedic fractures. Since they may not be able to communicate effectively, the history obtained from caregivers is often limited, and the patient may be unable to respond appropriately to the physician's examination. Therefore, a broad differential diagnosis arises from the

common constellation of nonspecific symptoms accompanying irritability. The challenge is compounded by significant comorbidities and the difficulty in obtaining a reliable history and physical examination from a developmentally delayed child.

Infectious processes are often associated with fever; however, localizing signs of infection may be more subtle on physical examination in the significantly impaired child. Evaluation of the tympanic membranes, oropharynx, and skin can identify a child with common infectious causes of pain, such as otitis, pharyngitis, and cellulitis. Special attention should be paid to areas susceptible to decubitus ulcers in children with limited mobility. Critically ill children with meningitis or sepsis may present as toxic and ill appearing with altered mental status and signs of hypoperfusion. It is therefore essential to engage caregivers in the determination of altered mental status, as they will be the best source of the child's baseline status. Intoxications with a wide variety of substances can also cause these concerning symptoms; a history of ingestion or exposure and toxidromic findings on examination can be suggestive of a poisoned child. Intra-abdominal pathologies ranging from constipation to pancreatitis can be associated with symptoms of ileus and localized or peritoneal signs on abdominal examination. A history of decreased and small hard bowel movements, combined with physical findings of stool in the rectal vault, is consistent with constipation. Pancreatitis is diagnosed with a combination of laboratory and radiographic findings in children with a suggestive history and physical examination. Children with surgical conditions, such as appendicitis, intussusception, midgut volvulus, and malrotation, may present with lethargy and ill appearance alone. Along with a history of prior abdominal surgeries and obstructive or infectious symptoms, these conditions are often diagnosed using various radiologic modalities in consultation with pediatric surgeons. In medically complex children with developmental delay, seizures may appear as irritability. Often caretakers will describe alterations in mental status with rhythmic, repetitive movements and post-ictal periods that are consistent with previous seizure patterns in the child. Post-ictal periods will vary among children and include excessive somnolence or a hyperactive agitated state; caregivers may be needed to identify the change from baseline behavior. Renal and reproductive causes of irritability are often acute in onset, severe in quality, and localized to the flank, back, and lower abdomen. It is imperative to perform a genitourinary examination in all impaired boys with irritability, since they will have similar physical findings in testicular torsion but may not localize the pain. The diagnosis of ovarian torsion in non-verbal girls is often directed by a high index of suspicion and consultation with gynecologists. Hematuria and pyuria may accompany pain caused by nephrolithiasis, cystitis, and pyelonephritis. A sterilely obtained urinalysis, culture, and

imaging can differentiate between these causes. Of special note, developmentally delayed children are often diapered or require regular catheterization due to a neurogenic bladder. These populations are especially susceptible to urinary tract infections. In children with limited mobility, pathologic fractures from osteopenia may occur with minimal force, and no history of significant trauma may be elicited. Fractures can be identified in children with swelling, bruising, and pain on palpation at the site of fracture. Ocular trauma, foreign bodies, splinters, and hair tourniquets are common causes of irritability and can be identified by careful examination of the skin and extremities and fluorescein examination of the eyes.

Baclofen is an analog of gaba-aminobutyric acid, which inhibits excitatory neurotransmitter release in the brain and spinal cord.^{1,2} Intrathecal delivery of baclofen via a surgically implanted device placed subcutaneously in the abdominal wall with an indwelling spinal catheter, began in the 1990s as a method of reducing spasticity secondary to cerebral palsy. The most common complications include infection and malfunction of hardware, which occur in 9-10% and 21-33% of patients, respectively. Among hardware malfunctions, catheter-related causes predominate.²⁻⁶ Baclofen withdrawal syndrome can occur from 1 to 3 days following cessation of therapy with increased spasticity, fever, seizures, dysphoria, labile blood pressure, pruritus, and paresthesias. Left untreated, patients may progress to rhabdomyolysis, multi-organ system failure, and death. The differential diagnosis includes sepsis, seizure, neuroleptic malignant syndrome, malignant hyperthermia, autonomic dysreflexia, and other toxic, metabolic, and immune-mediated disorders.^{1,7} Diagnosis involves radiographic evaluation of the hardware, computerized interrogation of the device to determine medication volume and presence of any malfunction, and mechanical interrogation via insertion of a syringe transcutaneously into the device port to assay its ability to deliver the medication to the patient. Neurology, neurosurgery, or anesthesia service consultations are often required for the computerized and mechanical interrogation of a suspected malfunctioning device. Treatment includes administration of baclofen and benzodiazepines, orally or intravenously, to reduce symptoms. Because there is no direct conversion from intrathecal to oral or intravenous dosing of baclofen, the dose must be titrated to achieve relief of withdrawal symptoms. Cyproheptadine, a sedating antihistamine with antimuscarinic, serotonin-antagonist, and calcium-channel blocking actions, has also shown some effectiveness among adults in the treatment of acute baclofen withdrawal.^{1,8} The usual dose is 4-8 mg every 6-8 hours. In our patient, the initial dose of midazolam resulted in relief of symptoms. Midazolam, a benzodiazepine, is a GABA agonist like baclofen but acts on GABA-A instead of GABA-B receptors; however, it produces a similar effect on spinal reflexes and reduces muscle tone.

Our patient did not have the classic signs of complete baclofen withdrawal, presenting only with increased spasticity

and dysphoria manifested as irritability; more severe signs and symptoms such as hyperthermia, seizures, and labile blood pressures were not present. This may have been due to the partial absorption of baclofen from the discontinuous catheter. Although hardware malfunction must be in the differential diagnosis, a complete examination and careful consideration of other etiologies causing irritability in a nonverbal, medically and cognitively impaired child is warranted. In these children, irritability can be a manifestation of minor to life-threatening conditions, and a concise history and careful physical examination can often determine the underlying cause, and reduce the need for an extensive diagnostic workup.

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