CASE REPORT

Cardiac arrest due to baclofen withdrawal syndrome

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SUMMARY

A 41-year-old man presented with postcervical traumatic complete quadriparesis under intrathecal baclofen therapy (ITB) for refractory spasticity. Less than 24 h after having his baclofen pump substituted, he develops hyperthermia, seizures, cognitive depression, acute hypoxaemic respiratory failure and cardiovascular instability leading to mechanical ventilation and vasopressor support. He was transferred to an intensive care unit with diagnosis of community-acquired pneumonia leading to septic shock. He evolved with progressive clinical worsening and multisystem organ failure and cardiac arrest in non-shockable rhythm (pulseless electrical activity)—4 min resuscitation with return of spontaneous circulation. Considering the possible diagnosis of baclofen withdrawal syndrome and, in suspicion of ITB delivery disruption, the catheter system was surgically explored and a leaking tubule attachment was found. Despite aggressive cardiovascular, respiratory and renal support therapy, clinical improvement occurred only after restoration of intrathecal drug delivery. He was discharged from the hospital after 56 days, having returned to baseline status.

BACKGROUND

Baclofen has become the drug of choice for treating patients with severe or intractable spasticity and dystonia of the spinal origin—including post-traumatic plegia—decreasing muscle spasms and pain, and increasing functional motor activity and control.[1] As oral baclofen has unwanted and eventually intolerable central side effects when high doses are needed, the US Food and Drug Administration approved its intrathecal use to optimise administration and reduce secondary effects. It has been shown to be cost-effective, improving the quality of life and optimising daily care, and has become a popular modality.[2]

Approximately 20–30% of patients under intrathecal baclofen (ITB) therapy experience a complication.[3 4] The sudden disruption of its delivery can precipitate an acute withdrawal syndrome that, despite being rare, may lead to cardiac arrest and death.[5 6] Presentation may be as multiple organ failure mimicking several syndromes including sepsis, so a high level of suspicion is needed.[7–10]

Currently, there is no definitive and effective approach to treat this syndrome and numerous agents have varying grades of success in its prevention and treatment.[11–13]

As the implantation of baclofen pumps is increasing, it is likely that emergency physicians will have to treat patients with this kind of condition. To illustrate this and in the hope of raising awareness of this life-threatening complication, we present a case of acute baclofen withdrawal syndrome (BWS) following ITB therapy.

CASE PRESENTATION

A 41-year-old man was admitted to our intensive care unit (ICU) with a possible diagnosis of septic shock, seizure disorder and cardiorespiratory disfunction.

His medical history included a post-traumatic spastic complete quadriparesis with neurogenic bladder after a cervical trauma (C7 level), hypertension, type 2 diabetes mellitus and obesity. He had an ITB pump placed 14 years ago for spasticity refractory to high doses of oral baclofen. At the moment, his baclofen basal continuous infusion was 300 µg/day. He experienced a significant improvement in spasticity and functional capacity without remarkable intercurrences since. In spite of being semidependent, he normally performed his social and familiar roles.

The day before admission he underwent his first ITB pump device substitution (without intrathecal catheter changing). The procedure was uneventful and he was discharged after 24 h. A few hours later, he suddenly developed generalised seizures. The National Emergency System was activated. On presentation to the emergency room of a regional hospital he had generalised tonic–clonic seizures, cognitive depression with Glasgow Coma Scale (GCS) 3, tachycardia (156 bpm), hypotension (83/37 mm Hg) and hyperthermia (41.6°C). This situation evolved with acute hypoxaemic respiratory failure and cardiovascular instability leading to the need of mechanical ventilation and cardiovascular support. The initial investigation included: blood analysis with elevated white cells count (23 000 cells/m^3; 78% neutrophilia), C reactive protein of 24 mg/dL (normal <0.5 mg/dL); thoracic CT scan that revealed a right pulmonary infiltrate, brain CT scan that did not show any acute infarction or bleeding. In this hospital this clinical picture was understood as septic shock due to a community-acquired pneumonia. As there were no available ICU beds, the patient was transferred to our unit, located in a tertiary referral hospital centre.

On admission to our department, the patient presented multisystem organ failure: haemodynamic instability with tachycardia and severe hypotension (50/20 mm Hg) despite aggressive fluid therapy and increasing doses of vasopressor support with noradrenaline, hyperlactataemia (4 nmol/L) and electrocardiographic abnormalities (ST segment depression) with elevated cardiac enzymes; inefficient oxygenation and ventilation despite ventilator support and increasing sedation (midazolam) and curarisation (rocuronium); acute renal lesion with

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high creatine kinase levels consistent with rhabdomyolysis and oligoanuria; metabolic acidosis and elevation of hepatic enzymes. Empiric broad-spectrum intravenous antibiotics were instituted after microbiological cultures. A few minutes after admission, cardiac arrest in pulseless electrical activity occurred—cardiopulmonary resuscitation instituted during 4 min with return of spontaneous circulation.

INVESTIGATIONS

Blood, sputum, urine and liquor samples were taken for microbiological analysis. Thoracic imaging was repeated. An echocardiogram was performed on bedside.

In suspicion of BWS, the patient's chronic pain and pump delivery system distribution teams were called. We intended to determine the baclofen blood level but it was unavailable in our institution. To assess catheter system integrity, a plain abdominal radiograph was acquired, but it was not conclusive in providing information about catheter integrity. Considering the gravity and emergence of the situation, surgical exploration of the delivery system was considered the most reasonable diagnostic option.

DIFFERENTIAL DIAGNOSIS

Several differential diagnosis were taken into account: baclofen withdrawal, baclofen overdose, autonomic dysreflexia (AD), neuroleptic malignant syndrome (NMS), serotonin syndrome (SS), malignant hyperthermia (MH), cardiac failure, infection/sepsis, intracranial bleeding, hypoglycaemia, Cushing's triad, electrolyte imbalance, status epilepticus, and toxic, metabolic and immune-mediated disorders.[7–10]

Despite the history of spinal cord injury, the patient's lesion was lower than C6 and on presentation he had tachycardia and hypotension, which may rule AD out. No trigger medications for SS or NMS were taken. His family history for MH was negative, no intercurrences during intraoperative or immediate postoperative periods occurred and the calcium level was normal. There were no echocardiographic abnormalities. Metabolic disorders were excluded.

Regarding septic shock, our patient had two important risk factors for sepsis: an indwelling catheter for bladder management and the recent surgical intervention with central nervous system approach and hospitalisation. Pneumonia could have been the focus for an infection, but the severity of hyperthermia, hypotension and rhabdomyolysis was greater than expected. Furthermore, there was no mention of sputum production increment, cough, fever, respiratory distress or other systemic symptoms on previous discharge. Right lower lobe infiltrates are often the result of aspiration pneumonitis in unconscious patients, so it was likely the result, rather than the cause, of the patient's presenting signs. Serial microbiological cultures (including of cerebral spinal fluid) came back negative, except for sputum cultures that came positive, but only later in the patient's course. Additionally, the biochemistry of liquor and CT of the brain were both normal, excluding central nervous system infection. Neither the patient's fever nor his clinical course was markedly modified by antibiotherapy. Therefore, although a respiratory tract infection may have added to the complexity of this patient's clinical picture, it is unlikely that this infection was the only event responsible for the primary shock.

The temporal relationship with the pump replacement (less than 48 h) and the onset of the patient's symptoms makes BWS the most likely cause of this syndrome. Clinical events usually occur within 12–96 h after baclofen administration cessation. The severity and fast evolution of the clinical picture and the combination of symptoms presented at admission corroborated our suspicion. Hyperthermia is typical, usually higher than 40°C and difficult to treat; high heart rates, significant blood pressure lability and even ECG alterations and cardiomyopathy have all been described in association with BWS. The prolonged muscle contraction caused by rebound spasticity led to the need for curarisation in order to improve ventilation and may also have contributed to thermogenesis, hyperthermia and rhabdomyolysis. He also presented seizures, a commonly described feature that may contribute to hyperthermia and rhabdomyolysis.[14 15]

We cannot disregard the possibility of concurrent infection complicating this case. Although it seems highly unlikely that both BWS and sepsis would present on the same afternoon in an otherwise healthy man with tetraplegia, neither diagnosis can be entirely excluded.

TREATMENT

Despite all the critical care measures and adjuvant therapy, and considering BWS the most probable diagnosis, it was assumed that definitive treatment would include urgent restoration of drug delivery, preferably by the same route and dosage as before interruption. In this context, 100 µg bolus of intrathecal baclofen was given.

To exclude any dysfunction of the infusion system, surgical exploration of the catheter system was then performed: pump status and function, catheter and connections' integrity were checked and the pump was refilled with drug at a proper concentration. A probably leaking tubule attachment between the catheter and the pump was found. Catheter and its connections were substituted.

A bolus dose of 400 µg was administered intrathecally and the continuous infusion was resumed at 400 µg/day. Despite this, the patient remained without supply for additional 24 h because of a programming error.

As a consequence of the initial shock and low perfusion status, an impairment of liver and renal function occurred. Sustained low-efficiency dialysis (SLED) was begun on the third day.

Empiric antibiotic treatment was maintained for 11 days.

To overcome the difficulty in weaning the patient from mechanical ventilation, proper care was taken through a tracheostomy tube since the 12th day.

OUTCOME AND FOLLOW-UP

Over the following days after baclofen delivery reinstitution, a clinical improvement was seen: sedation and curarisation needs dramatically decreased and the patient remained non-feverish and haemodynamically stable. Frequent pulmonary atelectasis implied a difficult weaning off the ventilator. Spontaneous ventilation succeeds after 25 days. Neurological function was regained, except for the remarkable muscular hypotonia, which led to the need of an intensive rehabilitation programme and progressive adjustment and reduction of the ITB infusion rate to his baseline (300 µg/day). SLED was maintained until the 14th day, normal renal function was achieved before ICU discharge.

No further intercurrences occurred during the 29 days course of aggressive management in the ICU, after which the patient was transferred to the physical medicine department to resume his rehabilitation programme with improvement of his physical status, namely in his daily life activities and mobility. He was discharged from hospital after 56 days without oxygen supplementation. Rehabilitation programme was maintained in a specialised physiatrist hospital.

At a 3-month follow-up he was evaluated in the chronic pain department, having returned to his baseline status.

DISCUSSION

This clinical case raises the discussion over the difficulties about diagnosing and treating patients with ITB pumps in proper time. Adequate and prompt diagnosis may be extremely challenging but can make the difference between mild symptoms and high morbidity and even mortality. There are few BWS cases described and its presentation and gravity may be diverse.

The literature is unanimous about the cornerstones of treating BWS: reinstitution of baclofen and supportive care, the latter focused on diminishing acute exacerbations in muscle spasticity, treating blood pressure lability and preventing central nervous system complications such as seizures and delirium.[12 13] Although commonly given to patients experiencing withdrawal, oral baclofen is not adequate to replace large intrathecal doses, in which case treatment should focus on repairing or replacing the malfunctioning intrathecal pump with the goal of resuming baclofen delivery to intrathecal space as promptly as possible. The use of adjuvant therapy such as benzodiazepines, low-dose propofol infusion, cyproheptadine, dantrolene or tizanidine represents a reasonable option based on currently available clinical experiences and reports.

Our attention should also focus on preventing abrupt discontinuation of the therapy: careful pump implantation, filling and programming techniques are essential.[16]

Learning points

- Baclofen withdrawal syndrome is rare but with increasing use of intrathecal delivery systems, patients are more likely to be seen by acute physicians.
- Prevention of abrupt discontinuation of intrathecal baclofen therapy requires careful pump implantation, filling and programming techniques.
- A high level of suspicion is needed as this diagnosis may be clinically occult or mimic several syndromes.
- Early recognition, reinstitution of baclofen and proper intensive care management are mainstays to prevent potentially fatal sequelae.
- Patients should be well educated about this potentially lethal complication. If available, the contact number of a well-trained physician (regarding intrathecal pump management) should be given if there are any fear of complications.

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