Coma mimicking brain death following baclofen overdose

Abstract Baclofen toxicity can be a cause of profound coma with brainstem dysfunction mimicking brain death, and is mainly a clinical diagnosis. Measuring plasma levels is not always possible and may be misleading. Imaging results are usually normal. Electroencephalography may show a pattern of burst suppression. At present no effective specific therapy is available. However, as demonstrated in our case, the prognosis can be good even in severe cases, provided it is recognized early enough, and appropriate supportive measures are instituted.

Key words Baclofen overdose · Coma

Case report

A 59-year-old man was brought to the emergency department after he was found unresponsive at home. On admission he was deeply comatose, with a Glasgow Coma Score of 3/15. His blood pressure was 120/85 mmHg, with a regular heart rate of 72 beats/min and a respiratory rate of 6 breaths/min. He was febrile (38.1°C) and had no tattoos, needle puncture marks, or external signs suggestive of head injury or tongue biting. His pupils were fixed at 3 mm, with neither a direct nor a consensual response to light. Fundoscopy was normal. Oculocephalic and corneal reflexes were absent. He had neither a cough nor gag response to suction. There was no meningealism. His extremities were flaccid, with no spontaneous movement. He did not react to voice or to nail bed or supraorbital pressure. The deep tendon reflexes were reduced in the arms (1/4) and absent in the legs. The plantar responses were absent.

Introduction

The initial diagnostic approach to a patient in coma involves the elucidation of aspects in the history or physical examination which suggest either a structural/focal or generalized/metabolic process. Examination of the pupillary reflexes is usually helpful in this regard, with pupillary reaction usually being preserved in metabolic processes including drug toxicity, and asymmetrically affected in structural processes. However, severe Baclofen toxicity may lead to loss of brainstem function including absence of pupillary reflexes, mimicking a structural brainstem lesion.
Cardiovascular, respiratory, and abdominal examinations were unremarkable. His past medical history was remarkable for chronic musculoskeletal lower back and leg pain for which he had taken various medications, most recently paracetamol with codeine and other tablets which his wife was unable to recall.

In the emergency room he received 50 ml dextrose 50%, 1.2 g naloxone, and 100 mg thiamine, with no improvement. He was intubated and ventilated.

The initial investigations revealed a normal electrocardiogram and chest radiogram. His blood profile showed: hemoglobin 16.0 g/dl, white blood cells 10.9 × 10⁹/l, platelets 265 × 10⁹/l, sodium 143 mmol/l, potassium 3.6 mmol/l, urea 6.7 mmol/l, creatinine 97 µmol/l, and glucose 6.7 mmol/l. Values for serum calcium, liver enzymes, creatine kinase, and coagulation profile were normal. Serum osmolality was 298 mosmol/kg. Arterial blood gases taken immediately after intubation showed a pH 7.30, pCO₂ 49 mmHg, pO₂ 67 mmHg, HCO₃ 23 mmol/l, and base deficit of 3.0 mmol/l. Toxicology screen was negative for salicylates, paracetamol, benzodiazepines, tricyclic antidepressants, cocaine, and phencyclidine. The only positive results were a trace of opiates in his urine and a serum alcohol level of 2.2 mmol/l.

Computed tomography of the head was normal. The cerebrospinal fluid was clear and colorless with red blood cells 12 × 10⁶/l and no nucleated cells, glucose of 4.4 mmol/l, and protein of 465 mg/l. Gram stain was negative. Magnetic resonance imaging of the brain with specific attention to the brainstem was normal. Electroencephalography showed a burst suppression pattern without reactivity to stimulation.

Over the following 12 h he developed hypotension and required vasopressor support. He remained deeply comatose with no spontaneous movement but coughed occasionally with suctioning of the endotracheal tube and also abducted his arms at the shoulder with flexion at the elbow. His pupils remained 3 mm and nonreactive to light, although they dilated somewhat to central pain. Appropriate extracranial movements were observed with the oculocephalic maneuver, and corneal reflexes had returned.

The day following admission his wife presented the bottles containing medications he was taking. According to the dates of prescription, amounts prescribed, and tablets remaining he had consumed a total of 141 Tylenol #3 (paracetamol and codeine) in the preceding 18 days, 187 baclofen (10 mg) tablets in the preceding 11 days, and 7 oxazepam (30 mg) tablets in the preceding 6 days.

Over the following 48 h his neurological recovery continued to the point that he was able to obey commands. His hemodynamics stabilized, vasopressors were discontinued, and he was extubated. He remained persistently febrile with no infective source identified. Repeat computed tomography of his head 48 h after admission showed no abnormalities. After 4 days of intensive care he was transferred to the medical ward, where he remained intermittently confused and disoriented. A neuropsychological assessment revealed moderate impairment in cognitive functions. Repeat electroencephalography 7 days after admission was essentially normal.

On review in the outpatient clinic 6 weeks after discharge he was neurologically normal but continued to complain of musculoskeletal pain. On repeat interview he revealed that because of excessive low back pain he had taken more baclofen than usual the evening prior to admission, which he attributed to being confused due to the effects of the initial few tablets, and not to any suicidal intentions.

**Discussion**

This case demonstrates full neurological recovery in a patient presenting in a deeply comatose state with absent pupillary responses, and indeed apart from preserved but abnormal respiration, absent brainstem reflexes. The most likely diagnosis in this case is that of baclofen toxicity. We were unable to measure baclofen levels at our institution as the techniques are generally available only in research laboratories. There was no other cause of coma. The toxic causation is supported by the complete reversibility. In addition, there was compelling evidence of an ingestion of a large number of baclofen tablets on the day prior to admission.

Baclofen is an analog of the naturally occurring inhibitory neurotransmitter γ-aminobutyric acid (GABA). The inhibitory actions of GABA are thought to occur at the level of spinal interneurons. Its main therapeutic indication is to lessen spasticity secondary to spinal cord disease. In some instances baclofen is prescribed for pain secondary to muscle spasm.

In this patient the electroencephalography performed shortly after admission showed a pattern of burst suppression. This pattern consists of brief paroxysms of activity occurring between periods of little or no electrical activity, indicating the presence of severe diffuse disturbance in brain function. It can be seen as a consequence of an acute anoxic-ischemic insult (i.e., after a cardiac arrest or following a severe head injury). It can also be found in association with overwhelming sepsis, drug overdose, after status epilepticus, and in therapeutically induced coma (i.e., pentobarbital coma). It usually, but not invariably, suggests a poor prognosis. However, some patients (as in this case) make a full neurological recovery. Only a single case report documents the occurrence of this pattern in baclofen toxicity [1].

Baclofen toxicity has been reported after intrathecal and oral administration including iatrogenic, suicidal, and recreational administration [2, 3, 4, 5]. The clinical manifestations are a consequence of an exaggeration of its muscle relaxing effects and of direct central nervous system depression, possibly by stimulation of GABA B receptors in the spinal cord, brainstem and hippocampus. These effects are potentiated by other CNS depressants, for example, alcohol. The onset of clinical toxicity may be rapid, leading to generalized muscular hypotonia, areflexia, coma, respiratory depression, bradycardia, hypotension, and temperature disturbance [4, 5]. Myoclonic jerks and grand mal convulsions have also been reported [3, 5].

Baclofen toxicity is a clinical diagnosis; measuring plasma levels is not always possible, and results can be misleading. The half-life is 3.5 h in therapeutic use but a serum half-life of up to 34 h has been estimated after overdose [3, 6]. Animal experiments with radiolabeled baclofen indicate that concentrations in nerve tissue