Status epilepticus in accident and emergency: a difficult case

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Status epilepticus is an acute medical emergency requiring effective immediate treatment to avoid excess morbidity and mortality. It is generally regarded as seizure activity lasting continuously for more than 20 minutes or multiple seizures with incomplete recovery between seizures lasting a total of 20 minutes or more, as this is the period necessary to cause injury to neurons. It is a relatively common presentation in accident and emergency (A&E) practice and it can present considerable difficulties in management. We present a case of status epilepticus that raised several therapeutic issues.

Case report
A 20 year old man was brought to the A&E department by emergency ambulance. He had a past medical history of post-traumatic epilepsy after sustaining a depressed skull fracture eight years earlier. He had been found by his father at home 80 minutes earlier having continuous tonic-clonic seizures. The ambulance crew had administered high flow oxygen via a nasopharyngeal airway and administered 10 mg intravenous (IV) diazepam (Diazemuls) en route to hospital.

On arrival, rapid examination confirmed continuing tonic-clonic status epilepticus. Vital signs were as follows: pulse rate 140 beats per minute, sinus rhythm; respiratory rate 25 per minute; non-invasive blood pressure 130/80 mm Hg; oxygen saturation 98% (on high flow oxygen). He had trismus complicated by copious secretions, but basic airway manoeuvres, a nasopharyngeal airway and suction proved sufficient to maintain a patent airway. There was no evidence of recent, new head injury and his blood glucose was 7.0 mmol/l on bedside testing. He was given IV lorazepam 4 mg with no effect; this was repeated after five minutes, again with no effect.

Background information was available from the patient's father. He had been admitted two weeks earlier in an identical state. The cause of his seizures before was thought to be poor compliance with phenytoin treatment. His father was not sure how well he had been complying with treatment recently. They were due to see the family doctor that evening to discuss his medication, doses and compliance.

Venous blood was sent for basic biochemistry and haematology and a phenytoin level was requested. His previous notes were requested. The laboratory computer was checked and this supported the father's given history: serum phenytoin levels were 21 µmol/l one month before the last admission and 31 µmol/l at the time of the last episode of status epilepticus (normal range 40–80 µmol/l). His previous A&E record was examined and an identical picture to the current situation was seen. Arterial blood gas analysis was as follows: Po2 38.4 kPa; Pco2 5.98 kPa; H+ 52.1 nmol/l and bicarbonate 22.6 mmol/l.

Our impression at this stage was that low serum phenytoin levels were the probable cause of this patient's status epilepticus. We felt that a loading dose of fosphenytoin would probably be therapeutic and given the airway was being maintained without difficulty and arterial blood gases were reasonable, it was not necessary at that stage to proceed to intubation and ventilation.

In view of this, the patient was given 500 mg PE (phenytoin equivalent) of IV fosphenytoin over 20 minutes. With an estimated weight of 60 kg, this was equivalent to approximately 8 mg/kg PE. This had no effect on the continuing seizure activity and he was therefore given a further 500 mg PE of IV fosphenytoin. This again had no effect and a decision was made, in conjunction with the duty intensive care consultant, to proceed to rapid sequence intubation (RSI).

RSI was carried out using alfentanil 1 mg, thiopental 350 mg and suxamethonium 100 mg. Intubation was performed uneventfully but he was noted to continue to seize after the effects of the suxamethonium wore off. He was sedated with intermittent boluses of thiopental as he remained haemodynamically stable. He was then transferred to the intensive therapy unit.

About 15 minutes after intubation, we received the result of the pretreatment phenytoin level, which was 244 µmol/l. This is obviously extremely high and was the probable cause for the prolonged episode of status epilepticus. He was given IV phenobarbitol for the continuing seizures. He was also given multiple dose activated charcoal via a nasogastric tube to hasten the elimination of phenytoin from the circulation.

His seizures were rapidly controlled and he was extubated after 36 hours. A computed tomography scan of the brain showed no new lesion and clinical examination showed no new neurological deficit. He was discharged home five days after admission on phenytoin monotherapy, with arrangements made for neurological follow up.

Discussion
This case raises several issues for the A&E specialist treating status epilepticus. The majority of patients presenting to the A&E department with generalised seizures will have them terminated with IV benzodiazepines. Diazepam has been used extensively in A&E and in the
prehospital situation and is effective. It does, however, have a short duration of anticonvulsant effect (15–30 minutes)7 and can cause profound respiratory depression. Lorazepam is now the preferred benzodiazepine for the treatment of seizures. It has a longer duration of anticonvulsant effect (12–24 hours)2 and is equally effective at terminating seizures.3

Sometimes, as in this case, IV benzodiazepines are ineffective. Traditional teaching would suggest the administration of a loading dose of phenytoin, in the absence of any contraindications. It could be argued that we should have avoided the use of phenytoin, or fosphenytoin (its more modern prodrug), given that he was already on phenytoin therapy. However, our reasoning seems logical, as subtherapeutic levels had been the cause of his previous admissions. Furthermore, it has been recommended that treatment should not be delayed to measure serum drug concentrations.1

Alternatives include phenobarbital (usually only used in infants or after definitive airway control in refractory status epilepticus1) or intramuscular paraldehyde. This is known to have adverse effects (including sterile abscesses, slow onset of action, allergic reactions) and is now not commonly used. IV sodium valproate has been successfully used in status epilepticus1 but is not licensed for that use in the UK.3 Other anticonvulsants could be administered via a nasogastric tube in the intubated patient, but this method suffers from imprecision of dose and slow, unpredictable onset of action in the acute setting.

If these treatments fail, the next stage is induction of general anaesthesia and ventilation to protect the airway and ensure optimum oxygenation. Again, it could be argued that we should have embarked upon RSI earlier in this case, as the patient had already been in status epilepticus for nearly 90 minutes by the time two boluses of IV lorazepam had been given. However, his arterial blood gases did not show a profound metabolic acidosis, which is the hallmark of tonic-clonic status epilepticus, should have alerted us earlier to the possibility that the seizures could have been of an alternative aetiology, for example toxic drug levels. This pointer may have led us to consider earlier intubation and ventilation while waiting to receive the pretreatment phenytoin results. This may at least have avoided the iatrogenic administration of IV fosphenytoin, which compounded the original disorder.

This case should remind A&E specialists that status epilepticus can be a difficult clinical problem in practice. Despite the (usually) obvious aetiology, other factors, including metabolic disturbances, hypoxia, head injury, stroke, intracranial infection, stroke and the possibility of overdose of anticonvulsants (or other seizure inducing drugs), may have to be considered. If toxic seizures are suspected and fail to respond to basic treatment with IV benzodiazepines, early intubation and ventilation should be considered while blood levels are checked urgently. Alternative anticonvulsant treatment, for example phenobarbital, may have to be considered. Treatment must be tailored to the individual situation. Guidelines for the treatment of this condition should take these possibilities into account.

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