Unexplained fitting in three parturients suffering from postdural puncture headache

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We present the cases of three women who, within a 6-month period, suffered post-partum generalized tonic–clonic seizures. All had received an epidural in labour for analgesia and were

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subsequently diagnosed as suffering from postdural puncture headache. All were treated for that headache with Synacthen and one also received sumatriptan before her seizures. All made satisfactory recoveries and were discharged home. None displayed classical patterns suggestive of pre-eclampsia, meningitis, cortical venous thrombosis or any other pathological process that might explain these events adequately, and the specific precipitating factors were left unidentified.

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**Case 1**

A previously fit 37-yr-old primiparous woman with an uneventful pregnancy received epidural analgesia during labour. The hospital notes recorded the epidural procedure as ‘difficult’ but gave no specific details. Uterine contractions were augmented with Syntocinon and the woman had a normal vaginal delivery.

She complained of a headache immediately after delivery and was given acetaminophen with initial good effect. However, the headache returned the following day and was treated with co-proxamol. The headache persisted, becoming progressively more severe and positional, and radiating to the neck. It was then diagnosed as a postdural puncture headache (PDPH). A previous history of migraine effectively treated with sumatriptan was also elicited at this time and she was treated with bed rest, i.v. fluids and sumatriptan 100 mg orally, which resulted in resolution of her symptoms.

She again complained of headache on day 2 after delivery and was given a further dose of sumatriptan, which once again provided good relief. However, the headache recurred and was further treated with compound analgesics and oral fluids.

On day 4, despite analgesics, the headache continued and so she was given i.m. Synacthen 1 mg, and i.v. fluids were recommenced. A blood patch was discussed at this stage. Later that day the headache worsened and she vomited repeatedly. She was given morphine i.m., which relieved the headache, and the vomiting settled with metoclopramide. Her white cell count (WCC) at this time was $10.8 \times 10^9$ litre$^{-1}$.

By day 6, her headache had not resolved and a further dose of Synacthen 1 mg i.m. was given, followed by another dose of sumatriptan 100 mg orally. Until this point in the postpartum period, there had been no abnormal neurological signs and no evidence of hypertension. Then she suffered two short-lived grand mal seizures, which were treated with diazepam 5 mg and then 10 mg i.v. A loading dose of phenytoin was given and she was sedated, intubated, ventilated and transferred to the intensive care unit, where she was noted to have an arterial pressure of 170/100 mm Hg.

The arterial pressure remained elevated for several hours after fitting, and was treated with sublingual nifedipine. She was extubated on day 7. A computed tomography (CT) scan of her head later that day revealed a low-attenuation area in the right occipitoparietal lobe and a smaller area in the left posterior parietal lobe, both suggestive of infarction. A subsequent lumbar puncture was normal. At this time she had no focal neurology, was afebrile and blood urea and electrolytes were normal. The WCC was $15 \times 10^9$ litre$^{-1}$.

She was commenced on carbamazepine with the intention of continuing it for a period of 6 months. She made an uneventful recovery, with no neurological deficit (despite the CT findings) before discharge on day 14.

**Case 2**

A 21-yr-old primiparous woman presented at her local hospital in labour at 39 weeks gestation, having previously been booked at another hospital, where antenatal attendance had been poor. She was generally healthy, suffering only from mild asthma (for which she used a salbutamol inhaler as required), and smoked 20–30 cigarettes per day. During her labour, an epidural was sited uneventfully before she underwent artificial rupture of membranes (ARM) and Syntocinon augmentation. She proceeded to normal vaginal delivery.

On day 1 after delivery she complained of neck pain with headache and a diagnosis of PDPH was made. Oral and i.v. hydration, compound oral analgesics (co-proxamol) and bed rest were prescribed. The possibility of a blood patch was discussed, but she expressed reservations. Because her headache persisted and was ‘making hearing difficult’, she was given Synacthen 1 mg i.m. Her arterial pressure at this time was 120/60 mm Hg and she was afebrile.

On day 2, she was still complaining of difficulty hearing and was feeling very sleepy. Despite this, she refused to comply with advice to remain in bed. Oral analgesia was changed to codeine and she received a second dose of
Synacthen 1 mg i.m. Her arterial pressure and temperature remained normal.

On day 3, although she was still sleepy, her headache was improving, resulting in her refusal of a third dose of Synacthen. On day 4, she refused all analgesics and was generally uncooperative despite the persistent headache. On day 5, she suffered a generalized tonic–clonic seizure, during which she became cyanosed. The fit resolved spontaneously and, although post-ictal, she was responding to command, moving all four limbs, her pupils were equal and reactive and she did not have papilloedema. Observations immediately after the seizure revealed an arterial pressure of 120/60 mm Hg and a heart rate of 100 beats min⁻¹. Blood tests revealed that blood sugar was 4.1 mmol litre⁻¹, WCC 16.8×10⁹ litre⁻¹ and uric acid 0.31 mmol litre⁻¹. Urea and electrolytes, liver function tests and full blood count were all normal. Midstream urine, sputum and blood culture samples taken at this time were all later reported as negative for bacterial growth.

A second fit, 1 h later, was treated with diazepam 10 mg i.v. She was then intubated and ventilated and a CT head scan was performed. The scan showed small ventricles and meningeal hyperaemia. In the intensive care unit she was treated with phenytoin, cefotaxime and benzylpenicillin and was extubated later that day.

On day 6 she returned to the labour ward after having had a magnetic resonance imaging scan (MRI) of her brain, which was reported as normal. She self-discharged on day 12, still complaining of headache, and was lost to follow-up.

**Case 3**

This previously fit and well 33-yr-old primiparous lady also had an uneventful pregnancy. She was induced with Prostin vaginal pessaries and then ARM at term plus 13 days and sustained a dural tap on insertion of an epidural in labour. She underwent lower segment Caesarean section (LSCS) under general anaesthesia for failure to progress.

On day 1, she complained of frontal head and neck ache on sitting up and was diagnosed as having a PDPH. She had no neurological symptoms or signs at this time and was afebrile. She was treated with oral compound analgesics and i.v. fluid, and blood patch treatment was discussed.

On day 2, she still complained of headache, which was relieved by lying flat and taking regular oral analgesics. She was given Synacthen 1 mg i.m. but continued to complain of headache the following day and so was given a second dose of Synacthen 1 mg i.m. She was then encouraged to mobilize and i.v. fluids were discontinued.

She was given a third dose of Synacthen 1 mg i.m. on day 4, but by day 6 she was complaining of spots in front of her eyes, blurred vision and headache. She suffered a grand mal fit and became peripherally cyanosed (arterial pressure 170/100 mm Hg), but recovered spontaneously with facemask oxygen. After resolution of the fit, her arterial pressure was 126/71 mm Hg, pulse 80 beats min⁻¹, arterial oxygen saturation 95% and temperature normal. She was catheterized, i.v. access was established and i.v. hydration was resumed, but she was also allowed oral fluids.

At this time the midwife noted that the patient had a swollen face and feet, but neurological examination proved unremarkable. Clotting screen, urea and electrolytes, liver function tests and full blood count were all normal, uric acid was 0.45 mmol litre⁻¹ and there was only a trace of protein in her urine. Later the same day, she again complained of headache and as her arterial pressure was recorded as 163/102 mm Hg, she was given nifedipine 10 mg orally. She had a non-contrast CT brain scan which was reported as normal. A loading dose of phenytoin was given, followed by maintenance therapy of 300 mg per day.

On day 7 her arterial pressure was still elevated, at 153/100 mm Hg, and an MRI of her brain was reported as showing a small infarct near the left trigone (near the posterior horn of the left lateral ventricle) and small focal ischaemic areas in the white matter. She was prescribed oral aspirin 75 mg daily and enoxaparin 40 mg s.c. Phenytoin was subsequently discontinued gradually and she made an uneventful recovery.

**Discussion**

The differential diagnosis of post-partum seizures includes: epilepsy; drug/alcohol withdrawal; pre-eclamptic toxaemia (PET); meningitis; space-occupying lesion; cerebral venous thrombosis (CVT); metabolic disturbance, (e.g. calcium and glucose); thrombotic thrombocytopenic purpura (TTP); PDPH and certain treatments for PDPH, such as caffeine, sodium benzoate and sumatriptan. Investigation of the condition should include: arterial pressure and temperature measurement; urine and blood cultures; full blood count; urea and electrolytes; bone minerals; glucose; clotting; bleeding time; fibrinogen; liver function tests and erythrocyte sedimentation rate; EEG; CT head; lumbar puncture (if not contraindicated) and MRI to exclude CVT if appropriate.

None of the three ladies had a history of alcohol or drug abuse or of epilepsy. TTP and metabolic disturbance were excluded in all three by laboratory blood analysis. CT scanning failed to show potentially causal space-occupying lesions. None of the three women had any of the fluctuating motor or sensory focal neurological signs that are normally associated with CVT and two of the three had normal MRI scans. No convincing evidence of meningitis or PET was found, with only transitory post-ictal arterial pressure rises seen in two of the women.

After dural puncture, the continued loss of cerebrospinal fluid (CSF) leads to decreased volume and pressure of the CSF compartment.¹ This can cause a downward pulling or stretching of the intracranial contents as a result of the negative spinal–cranial pressure gradient. Cranial nerves, vessels, dura and brain parenchyma may be injured by
stretching, leading to complications such as sixth nerve palsy, seizures, subdural haematoma and, very rarely, subarachnoid haemorrhage. Decreased CSF pressure creates an abnormal pressure gradient between the cerebral vasculature and the CSF. As veins are thin-walled and, within certain limits, will adjust passively to pressures in and around them, it is likely that negative pressure on the outside of the vein wall will result in vasodilatation. In addition, a sudden decrease in CSF volume is proposed to further propagate vasodilatation via activation of vascular adenosine receptors.

Although PDPH is often self-limiting or resolves within 24 h of conservative treatment, such as analgesics and fluid therapy, the potential significant complications of the condition lead us to treat it more aggressively after this period. Reversal of the postdural puncture cerebral vasodilatation with vasoconstrictors has been tried with both caffeine and sumatriptan. Sumatriptan is a vasoconstrictor of pathologically dilated arterial vessels and its actions may be dose-dependent and show regional variations. Its use is cautioned in pregnancy and breast-feeding. Seizures have been reported with the use of both sumatriptan and i.v. caffeine.

In pre-eclampsia, women have a relatively dehydrated intravascular circulation and a vasoconstricted cerebral vasculature. PET can present post-partum and is seen as a spectrum of clinical disease. Post-partum eclamptic fits lead to cerebral vasospasm, ischaemia and infarction. In women with both PET and PDPH, the use of vasoconstrictors to treat the PDPH would seem unwise. Indeed, there may be a group of women with subclinical PET who would be at increased risk of cerebral infarcts if their PDPH were treated with vasoconstrictors.

The mode of action of Synacthen in the treatment of PDPH is unknown. It was given in this hospital for many years before recent requirements for audit and evidence-based medicine and thus no evaluation of its use as a treatment in this centre exists. Indeed, it was discontinued as a therapy for PDPH shortly after these three cases occurred. There are no published large-number trials in which the efficacy and side-effect profile of this treatment for PDPH have been fully evaluated. To date there are no reports in the literature of patients suffering seizures secondary to Synacthen therapy.

Currently, the most widely used treatment for unresolving PDPH is an aseptically performed epidural blood patch. However, recurrent headache is a common event unless the blood patch is delayed by at least 48 h, and the influence of the volume of blood injected is unclear.

In these cases, it seems likely that the Synacthen was ineffective and the seizures were caused by the complications of untreated dural puncture. Further evaluation of the efficacy of Synacthen is needed before its use in the treatment of PDPH. Also, further evaluation of the effects of cerebral vasoconstrictors in the treatment of PDPH, particularly in women with PET, is needed before they are used routinely. Indeed, one of these three women may have suffered seizures as a result of sumatriptan therapy.

References

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