J Anesth (2014) 28:937–939
DOI 10.1007/s00540-014-1833-7

SHORT COMMUNICATION

Prolonged post-dural puncture headache in a patient during treatment with selective serotonin reuptake inhibitor: a case report and animal experiment

Takashi Kawano · Tetsuya Takahashi · Noriko Kitaoka · Masataka Yokoyama

Received: 11 February 2014 / Accepted: 4 April 2014 / Published online: 26 April 2014

Abstract We report a case of prolonged post-dural puncture headache (PDPH) in a patient with panic disorder. A 41-year-old woman received spinal anesthesia for interstitial cystitis. She noticed headache after surgery but did not report it to her doctor. As her headache worsened, she was readmitted to the hospital and diagnosed with PDPH 1 month after surgery. She had panic disorder, controlled by treatment with a selective serotonin reuptake inhibitor, sertraline. Conservative treatments were performed for 1 week, but her headache persisted. Successful resolution of PDPH was achieved following two epidural blood patch applications. A recent study showed that the duration of PDPH was prolonged with a history of depression. Therefore, we conducted a reverse translational experiment to investigate the effects of sertraline on the production of cerebrospinal fluid (CSF) in rats. Our results demonstrated that a clinically relevant dose of sertraline decreased the production of CSF. Our findings imply that treatment with sertraline may have contributed to the development of prolonged PDPH in this case.

T. Kawano (✉) · N. Kitaoka · M. Yokoyama
Department of Anesthesiology and Intensive Care Medicine, Kochi Medical School, Kohasu, Oko-cho, Nankoku, Kochi, Japan
e-mail: takashika@kochi-u.ac.jp

T. Kawano · T. Takahashi · M. Yokoyama
Center for Innovative and Translational Medicine, Interdisciplinary Pain Research Team, Kochi Medical School, Nankoku, Kochi, Japan

T. Takahashi
Department of Physiology, Kochi Medical School, Nankoku, Kochi, Japan

Keywords Panic disorder · Selective serotonin reuptake inhibitor · Post-dural puncture headache

We encountered a patient with prolonged severe post-dural puncture headache (PDPH) who had panic disorder controlled by treatment with a selective serotonin reuptake inhibitor (SSRI), sertraline. Here, we describe and discuss our case with the results from an animal experiment.

The patient was a 41-year-old woman for whom bladder distension was scheduled for the treatment of interstitial cystitis. Spinal anesthesia (L4–L5 level) was applied by a fellow of the Japanese Society of Anesthesiologists using a 25-gauge Quincke needle. Mild headache developed after surgery, but the patient did not report it, and she was discharged 2 days later. Urinary bladder symptoms were improved when she visited the outpatient clinic of the urology department 2 weeks after discharge. She did not complain of the headache at this time, but she was aware of it. Later, the headache gradually exacerbated, and it became difficult to work (office work). Thus, she revisited the urology department 1 month after surgery and was referred to our department. On examination, postural headache mainly in the occipital region was noted; it was aggravated in standing and sitting positions and remitted in recumbency. It was occasionally accompanied by nausea. The patient was diagnosed with prolonged severe PDPH and admitted. She had a past medical history of panic disorder, and had been under treatment with an oral selective serotonin reuptake inhibitor (SSRI), sertraline hydrochloride (50 mg/day), for depression-like symptoms for 7 years. The psychotic symptoms had been stable during the past several years, with no problems in daily or social activities.

After admission, conservative treatment with rest, transfusion (2,500 ml/day), oral caffeine (300 mg divided

into three doses), and acetaminophen (400 mg/dose) was initiated. Because no improvement was obtained, a 20-ml epidural blood patch (EBP) was applied at the L3–L4 level on day 7 after admission. The headache markedly improved immediately after EBP, but the effect was lost within several hours. As postural headache persisted, the second EBP was similarly applied on day 14. Her headache remitted thereafter, although a heavy-headed feeling remained, and the patient was discharged on day 17. On head magnetic resonance imaging (MRI), no hemorrhage or tumorous lesion was observed.

The pathogenesis of PDPH is currently thought to be caused by cerebrospinal fluid (CSF) leakage [1]. The mean duration of PDPH is ~5 days, and it spontaneously remits within 1 week in most patients without any treatment [2]. In our patient, however, 1 month had passed after dural puncture when PDPH was diagnosed. Similar to this case, several cases of spinal anesthesia-induced PDPH persisting for several months or years without initial treatment have been reported [3–6]. All these published previous reports, as well as our case, showed that PDPH was resolved by EBP, although the mechanism of prolonged PDPH remains unclear.

Recently, van Oosterhout et al. [7] prospectively investigated the PDPH developmental pattern in patients who underwent dural puncture and observed an association between PDPH and a past medical history of depression. Interestingly, a past medical history of depression was involved in the prolongation, but not the incidence, of PDPH [7]. However, the underlying mechanisms of this relationship remain to be elucidated. On the other hand, previous studies have showed that serotonergic signaling could decrease the production of CSF [8, 9], which is also associated with the pathogenesis of PDPH. In our case, therefore, we suspect that the sertraline may be one potential causal factor for prolonged PDPH. To confirm this hypothesis, we decided to investigate the effects of sertraline on the production of CSF in rats after approval from the Kochi University Animal Experiment Committee.

Male Wistar rats (6 weeks old, body weight 145–180 g) were used in this study. The production of CSF was assessed as previously described, with slight modifications [10]. Under pentobarbital (30 mg/kg, intraperitoneal) anesthesia, the head was fixed at a 30° head-up position using a stereotaxic apparatus. Body temperature was monitored by a rectal probe and maintained at around 37 °C by a heating lamp throughout the experiment under anesthesia. Pulse rate, arterial oxygen saturation, and mean arterial blood pressure were also measured noninvasively. After suboccipital craniotomy, the cisterna magna was exposed. After confirming complete hemostasis, a 3 × 15 mm filter paper, weighed beforehand, was inserted into the cisterna magna to absorb CSF (Fig. 1a). The filter paper

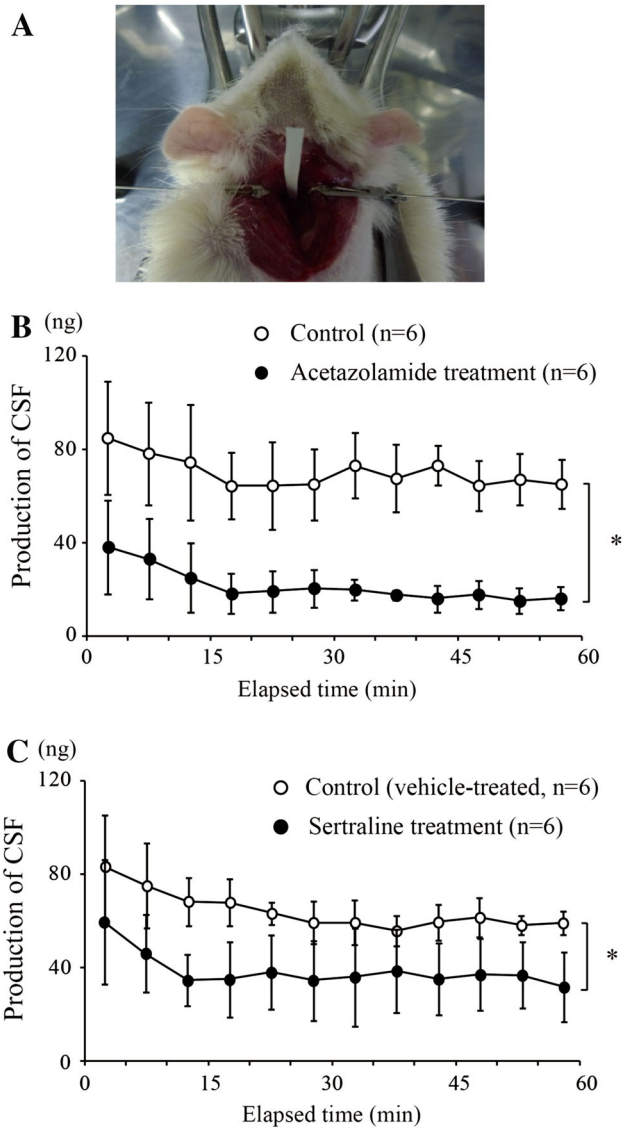

Fig. 1 Measurement of cerebrospinal fluid production in rats. **a** Photograph of experimental model. A filter paper is placed in the exposed cisterna magna. The influence of acetazolamide (**b**) and sertraline (**c**) on time-course changes in cerebrospinal fluid (*CSF*) production is shown. Mean increase (±standard deviation) in filter paper weight over 5 min is presented as cerebrospinal fluid production ($n = 6$ in each group). Statistical analyses were performed using a two-way analysis of variance with repeated measures ($^*p < 0.05$)

was replaced every minute, and the increase in the weight was measured as an index of CSF production. Stable CSF production could be recorded (Fig. 1b). The CSF volume was significantly reduced by pretreatment with a carbonate dehydratase inhibitor, acetazolamide (5 mg/kg, intraperitoneal), which inhibits CSF production (Fig. 1b). Next, the influence of sertraline on the production of CSF was then investigated. In rats treated with sertraline at the estimated clinical dose for humans (10 mg/kg/day, intraperitoneal) daily for 2 weeks, the production of CSF was significantly

decreased compared to that in control rats treated with the solvent (dimethyl sulfoxide, DMSO; Fig. 1c). There were no significant differences between the groups for arterial oxygen saturation level, pulse rate, and mean arterial blood pressure during the experimental procedure. Although our animal experiment cannot be directly translated to humans, the current findings suggest that oral SSRI-induced reduction of CSF could contribute the development of prolonged PDPH. Most of the currently used antidepressants, not limited to SSRI, are known to increase serotonin concentration in the brain [11]. Therefore, our finding implies that a similar mechanism might be involved in the relationship between a past medical history of depression and persistence of PDPH. Further clinical or epidemiological investigations should be necessary to confirm our current speculation.

In conclusion, we encountered a patient under treatment with an oral SSRI for panic disorder who developed persistent PDPH. Accumulated information and the results of the animal experiment suggested that oral SSRI-induced reduction of CSF production may be involved in the pathogenesis of prolonged PDPH.

References

1. Turnbull DK, Shepherd DB. Post-dural puncture headache: pathogenesis, prevention and treatment. Br J Anaesth. 2003;91:718–29.
2. Lybecker H, Djernes M, Schmidt JF. Postdural puncture headache (PDPH): onset, duration, severity, and associated symptoms. An analysis of 75 consecutive patients with PDPH. Acta Anaesthesiol Scand. 1995;39:605–12.
3. Klepstad P. Relief of postural post dural puncture headache by an epidural blood patch 12 months after dural puncture. Acta Anaesthesiol Scand. 1999;43:964–6.
4. Abouleish EI, Rashid S. Successful epidural blood patch 2 years after post-lumbar puncture headache. Am J Emerg Med. 1995;13:683–4.
5. Abouleish E. Epidural blood patch for the treatment of chronic post-lumbar-puncture cephalgia. Anesthesiology. 1978;49:291–2.
6. Wilton NC, Globerson JH, de Rosayro AM. Epidural blood patch for postdural puncture headache: it's never too late. Anesth Analg. 1986;65:895–6.
7. van Oosterhout WP, van der Plas AA, van Zwet EW, Zielman R, Ferrari MD, Terwindt GM. Postdural puncture headache in migraineurs and nonheadache subjects: a prospective study. Neurology. 2013;80:941–8.
8. Faraci FM, Mayhan WG, Heistad DD. Effect of serotonin on blood flow to the choroid plexus. Brain Res. 1989;478:121–6.
9. Conn PJ, Sanders-Bush E. Regulation of serotonin-stimulated phosphoinositide hydrolysis: relation to the serotonin 5-HT-2 binding site. J Neurosci. 1986;6:3669–75.
10. Li X, Kong H, Wu W, Xiao M, Sun X, Hu G. Aquaporin-4 maintains ependymal integrity in adult mice. Neuroscience. 2009;162:67–77.
11. Richelson E. Pharmacology of antidepressants. Mayo Clin Proc. 2001;76:511–27.