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Continuous Epidural Saline Infusion for the Treatment of Low CSF Pressure Headache

BETH E. GIBSON, M.D.,* DENISE J. WEDEL, M.D.,†
RONALD J. FAUST, M.D.,† RONALD C. PETERSEN, M.D., PH.D.‡

Postural headache is a complication of dural puncture, resulting from continued leakage of cerebrospinal fluid (CSF) through the dural rent with subsequent loss of buoyancy of the brain and traction upon pain-sensitive structures (meninges, blood vessels) when assuming an upright position. The syndrome is one of fronto-occipital headache in the upright position, which may be accompanied by nausea/vomiting, diplopia, tinnitus, or diaphoresis. A similar syndrome can occur spontaneously (*i.e.*, without recent dural puncture or trauma). It has been termed Schaltenbrand's syndrome, spontaneous aliquorrhea, and spontaneous or primary intracranial hypotension.

We describe a patient with a 6-week history of spontaneous postural headache and diplopia who was successfully managed with a continuous infusion of epidural saline.

CASE REPORT

A 44-yr-old woman presented with a severe postural headache. Approximately 6 weeks prior to admission, after working in her pumpkin patch, she had gone into the house and sat down to eat when she noted the rapid onset of severe headache that felt as though the "top of her head was going to blow off." After lying down, the headache was gone within 15 s. The headache returned each time she assumed an upright position. After 2 days of bedrest, she reported to her local hospital where a head computer-assisted tomagraphy was normal. She was observed for 1 day and discharged. The headache resolved, and she had no complaints for the next 2–3 days. Then, at home while showering, the headache recurred with the same intensity, and was definitely postural in nature.

By 2 weeks prior to admission, the intensity of the headache had increased. She was confined to bed, was nauseated, and had begun to notice diplopia with lateral gaze which was worse on the right side.

She again reported to her local hospital, where a repeat computer-assisted tomagraphy of the head and a three-vessel cerebral angiogram was negative. Two lumbar punctures were performed. The first was a "dry tap," and the second was reported as "low CSF pressure." A radioisotope cisternogram reportedly showed "increased activity along the nerve root sleeves in the thoracic area at locations of cyst formation or spontaneous leak" and early appearance of the dye in the bladder.

Her past medical history was significant for a L_{4-5} spondylolisthesis, and "sciatica" in 1986 that was treated conservatively. She did have a history of migraine headaches, which were typically unilateral with no associated symptoms. She emphatically insisted that those headaches were different from her present headache. She had undergone a thyroidectomy in 1986.

The physical examination was essentially normal, except for the neurological examination that was remarkable for bilateral sixth cranial nerve palsies, symmetrical hyperreflexia, and unsustained clonus.

A lumbar puncture was performed under fluoroscopic guidance, and the opening pressure in the horizontal position was zero. With a 30° head-up tilt, the CSF pressure was 55 mm H_2O, and rose appropriately with Valsalva. CSF examination revealed three white blood cells, 18 red blood cells, a glucose of 60 mg/dl, and a protein of 102 mg/dl (14–45), and was negative for xanthochromia. Magnetic resonance imaging of the head and spine showed thin subdural collections over both hemispheres consistent with small bilateral subdural hygromas, and the spinal cord was negative for pathology. Head computer-assisted tomagraphy confirmed these findings. A repeat radioisotope cisternogram was performed, and an area of increased activity was identified near the spinal nerve outlet at T_5 on the right side. There was early appearance of activity in the kidneys and bladder that was suspicious for CSF leakage into the epidural space at T_5.

An epidural catheter was placed at L_{2-3} by the anesthesia pain service, and 10 ml of preservative free normal saline was injected. The patient sat up and noted a marked improvement in her headache symptoms. Based on this response, a continuous epidural infusion of normal saline at 20 ml/h was begun. She was kept at bedrest except to sit for meals. After 48 h of this therapy, during which she showed continued relief of her headache and nausea, the infusion was discontinued. The catheter was left in place for another 24 h, and she was allowed to ambulate. Her headache did not return, and she began to note some improvement in her visual disturbances. A repeat computer-assisted tomagraphy scan prior to discharge showed resolution of the subdural collections. The patient remained headache-free at 4 months follow-up, and her sixth cranial nerve palsies had resolved.

DISCUSSION

The syndrome of primary intracranial hypotension was first described in 1938 by Schaltenbrand.[1] He used the term "spontaneous aliquorrhea," and proposed three possible mechanisms: 1) decreased CSF production secondary to a vasomotor disturbance within the choroid plexus; 2) increased reabsorption of CSF; and 3) CSF leakage through tears in the dura mater. Of these, the most likely cause seems to be CSF leakage. A number of the reported cases of this syndrome have been preceeded by relatively minor trauma, and one

* Instructor in Anesthesiology.
† Assistant Professor of Anesthesiology.
‡ Assistant Professor of Neurology.

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Address reprint requests to Dr. Gibson: Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota 55905.

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had a documented dural sleeve tear at L_{3-4} diagnosed by myelography.[2,3]

Two separate reports have used lumbar radioisotope cisternography to aid in the diagnosis of spontaneous low CSF pressure headaches.[4,5] Neither demonstrated a definite CSF leak, but they did show rapid disappearance of the isotope from the spinal axis and early appearance within the kidneys and urinary bladder, which was felt to be consistent with leakage into the epidural space and rapid vascular uptake.

As mentioned earlier, the symptoms of spontaneous low CSF pressure syndrome are identical to those seen in the typical post-dural puncture headache patient. CSF pressure is very low (<70 mm H_2O), and examination typically reveals moderate elevation of protein and an increased cell count.

Most cases of spontaneous low CSF pressure headache resolve spontaneously between 2–16 weeks.[3,6–8] As with post-dural puncture headache, conservative measures, such as bed rest, analgesics, and hydration, may be of some benefit. Failing that, or should the patient continue to deteriorate symptomatically as did the one we report here, some intervention may be warranted.

The treatment of low CSF pressure headache secondary to dural puncture has been extensively reviewed in the literature.[10–12,13–16] An established technique, the epidural blood patch, results in a 90–97% success rate. Although not as successful as a blood patch, epidural saline, either by intermittent injections or by continuous infusion, has also been used both prophylactically and for treatment of post-dural puncture headaches.[13–17]

For the treatment of spontaneous low CSF pressure headache, saline and blood have been injected both intrathecally and epidurally with some degree of success.[2,5,6] Gaukroger and Brownridge[9] recently reported a case that responded initially to 60 ml of intrathecal Ringer's solution, but subsequently recurred. An epidural blood patch was done the next day with immediate and long-term relief.

In our case, we were hesitant to proceed directly to epidural blood patch for several reasons. Although the leak had been localized at the T_5 level, we had no information as to the etiology of the leak or its size. Presumably, if the hole were large enough and/or the pressure in the epidural space became great enough, the injected blood could enter the subarachnoid space. The concern here is primarily a theoretical one, as Ravindran *et al.*[18] demonstrated in dogs that the injection of autologous blood into the subarachnoid space is not associated with any neurologic consequences. Nevertheless, caution would advise against indiscriminate placement of blood into the subarachnoid space.

Technically, the performance of an epidural at the T_5 level is more difficult than in the lumbar area due to the sharp angle of the spinous processes and a narrower epidural space. In patients with very low CSF pressures, the likelihood of an unrecognized subarachnoid injection also increases. The possibility of cord compression from an epidural hematoma or blood patch becomes greater in the thoracic than in the lumbar area, again due to the narrower epidural space.

Baysinger *et al.*[19] recently reported successful use of epidural saline infusions in two cases of post-dural puncture headache that had failed treatment with epidural blood patch. Although not as effective as the blood patch, epidural saline may be indicated in certain patient populations.[17,19]

Our patient experienced relief of her headache after a 10-ml bolus, and had no complaints of ocular or back pain, either with the bolus, or during the 48-h infusion at 20 ml/h. The catheter was removed 24 h after the infusion was discontinued.

Spontaneous low CSF pressure headache is a rare syndrome. This case is unique in that a definite leak of CSF was documented by radioisotope cisternography, and it occurred in the thoracic rather than the lumbar region. This is the first reported case of spontaneous low CSF pressure headache successfully treated with a continuous lumbar epidural infusion of saline. The treatment did not produce any untoward side effects, and avoided any potential risks of an epidural blood patch.

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Halothane Hepatitis Patients Generate an Antibody Response Toward a Covalently Bound Metabolite of Halothane

A. K. HUBBARD, PH.D.,* T. P. ROTH, B.S.,† A. J. GANDOLFI, PH.D.,‡ B. R. BROWN, JR., M.D., PH.D.,§ N. R. WEBSTER, PH.D., M.B., CH.B., F.F.A.R.C.S.,¶ J. F. NUNN, PH.D., M.D., F.R.C.S., F.F.A.R.C.S.**

Halothane hepatitis (HH), a rare complication of halothane anesthesia, may in part result from an immune mediated injury. Investigators speculate that this immune response is due to the alteration of hepatocyte proteins by halothane or, more probably, one of its reactive intermediates formed during metabolism.[1,2] Epidemiologic data in humans support an association between this disease and an immune response.[3–7] Multiple administrations of halothane increase the incidence and intensity of hepatitis, the interval between anesthetic and jaundice is shorter after two or more exposures than after a single exposure,[3] and patients are reported to evidence rash, arthralgia, and peripheral and/or hepatic eosinophilia.[4] Moreover, early studies noted that, in patients with HH, an increased frequency of anti-mitochondrial and anti-smooth muscle antibodies,[5] anti-thyroid antibodies,[6] and anti-nucleic acid antibodies[7] were present.

Previous investigations have suggested that the potential antigen in a halothane-induced immune response is not the parent drug, but, instead, a biotransformation intermediate of halothane which alters the antigenicity of liver cell constituents by serving as a hapten.[8] Thus, the antigenicity of the hepatocyte membrane protein may be altered by biotransformation intermediates of halothane generated through either an oxidative [trifluoroacetyl halide (TFA)] or a reductive (free radicals or carbene intermediates) pathway.[9]

Work in other laboratories describe a humoral immune response in patients with liver complications following halothane anesthesia that is directed toward a hepatocyte protein altered by a reactive intermediate of halothane. These patients with fulminant halothane hepatitis evidenced a circulating antibody that appeared to react with the surface of rabbit hepatocytes altered by halothane exposure.[10,11] In both an antibody-dependent cellular cytotoxicity assay and an immunofluorescent test using hepatocytes from rabbits exposed to halothane, this antibody could be detected only in sera from halothane hepatitis patients, and not from individuals with other liver complications. In addition, sera from two surgeons with hepatic damage following occupational exposure were also positive for this antibody.[12] More recent studies using the sensitive and highly quantitative enzyme-linked immunosorbent assay (ELISA) have noted that sera from HH patients will

* Research Assistant Professor, Department of Microbiology, University of Arizona.
† Research Assistant, Department of Anesthesiology, University of Arizona.
‡ Associate Professor, Department of Anesthesiology, University of Arizona.
§ Professor and Head, Department of Anesthesiology, University of Arizona.
¶ Member of Scientific Staff and Consultant, Division of Anaesthesia, Clinical Research Centre.
** Head, Division of Anaesthesia, Clinical Research Centre.

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Address reprint requests to Dr. Gandolfi: Department of Anesthesiology, University of Arizona, Tucson, Arizona 85724.

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