Intracranial Hypertension After Treatment of Spontaneous Cerebrospinal Fluid Leaks

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Four patients, aged 10 to 44 years, with spontaneous cerebrospinal fluid (CSF) leaks and intracranial hypotension developed intracranial hypertension after treatment of their CSF leaks. The leak was at the spinal level in all patients (thoracic level, 2; lumbar level, 1; and undetermined, 1). One patient responded to an epidural blood patch. Three patients responded to surgery, of whom 2 had not responded to prior epidural blood patches. Treatment resulted in complete resolution of symptoms, including orthostatic headaches and disappearance of magnetic resonance imaging abnormalities. However, all patients later developed steady headaches different from their previous headaches. None had recurrence of magnetic resonance imaging abnormalities or any evidence of occlusion of cerebral venous sinuses. All had increased CSF opening pressures. One had bilateral papilledema, and another had no venous pulsations on examination of fundi. Follow-up was possible in 2 patients. One responded well to treatment with acetazolamide, and the other improved gradually and was asymptomatic within several months.

Most, if not all, cases of spontaneous intracranial hypotension result from spontaneous cerebrospinal fluid (CSF) leaks. Only a few of these leaks are at the skull base (mainly the cribiform plate), whereas most occur at the level of the spine, particularly the thoracic spine.1 Modern neuroimaging techniques have enabled physicians to identify the level or even the site of the leaks in many patients and implement epidural injections or surgical treatments in those in whom conservative treatments have failed. Single or multiple epidural blood patches are effective in relieving the symptoms in a substantial proportion of these patients.2 Success with epidural injection of colloids,3,5 crystalloids,6,8 or fibrin glue9 has also been reported occasionally. Most patients who have CSF leakage sites that have been accurately identified on imaging studies and in whom multiple epidural blood patches have failed respond well to surgical corrections.10 The response to surgical treatments is often durable, but occasionally symptoms may recur because of reopening of a previous leak or development of new leaks at different sites. During the past decade, several patients have presented to the Mayo Clinic in Rochester, Minn, with intracranial hypotension, orthostatic headaches, and documented CSF leaks who were treated successfully but subsequently developed a different type of headache and were found to have developed intracranial hypertension. In previous publications dealing with CSF leaks, this phenomenon has been mentioned briefly.1,11

REPORT OF CASES
Case 1
A 10-year-old girl previously in good health began to experience severe orthostatic headaches and photophobia. In recumbency, she was essentially asymptomatic. She had no history of antecedent trauma. A maternal grandfather and his sister, a maternal grandmother and her brother, and 2 paternal uncles had abdominal aortic aneurysms. Results of the patient’s neurologic examination were normal. However, she had hyperflexible joints, hyperextensible skin, high-arched palate, and dilation of the aortic root on echocardiography. Head magnetic resonance imaging (MRI) revealed low-lying cerebellar tonsils and diffuse pachymeningeal enhancement. A computed tomographic (CT) myelogram revealed a single diverticulum approximately 1 cm in diameter at T12 through L1. The CSF pressure was low and not measurable. A trial of caffeine was ineffective. An epidural blood patch offered complete relief but only for 2 days. A second epidural blood patch had no effect. The patient subsequently underwent surgery, and through a T12 hemilaminectomy, the meningeal diverticulum was identified and ligated.

After surgery, the headaches resolved, and the patient quickly resumed her usual activities. Two weeks after surgery, she fell from a flight of stairs, and 2 days later she began to experience orthostatic headaches with increasing severity. A trial of bed rest and caffeine failed to relieve her symptoms. Three weeks postoperatively, she underwent

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indium In 111 cisternography and CT myelography. These studies showed CSF leaks at C7 and T1 bilaterally. Dilated root sleeves were again noted at the T6, T9, T10, and T11 levels. No leak was appreciated at the site of her prior repair. The patient was treated with bed rest, caffeine, and subsequently 2 more epidural blood patches. Gradually, the orthostatic features of the headaches blurred, and finally the orthostatic headaches resolved within a few months to be replaced by severe constant headaches and nausea and vomiting to the point of dehydration that required hospitalization. Although the neurologic examination showed no neurologic deficits, the optic disc margins were blurred, and venous pulsations were absent. Head MRI showed no abnormal pachymeningeal enhancement, and spine MRI revealed only postoperative changes of the previous T12 laminectomy. The CT myelogram showed a contained extra-arachnoid pocket of fluid to the left of the mid line from C3 to T3 without spread in the epidural space and soft tissues on delayed images. The CSF opening pressure was 220 mm H₂O.

The patient was treated with acetazolamide, 250 mg twice daily. Her headaches resolved within several days. At telephone follow-up 3 months later, she was back at school and pain free. Acetazolamide use was discontinued a few months later. She has remained headache free except for occasional tension-type headaches.

Case 2

A previously healthy 18-year-old female student was hospitalized for severe occipital headache, nausea, and gogginess. Neurologic examination results showed no focal or lateralizing abnormalities. The results of a head CT scan were normal. The severe sudden headache resolved, but she continued to have a pronounced orthostatic headache in the upright position associated with nausea and sometimes emesis. Head MRI showed diffuse pachymeningeal gadolinium enhancement, low-lying cerebellar tonsils, and thin bilateral subdural fluid collections over cerebral convexities. Spine MRI and CT myelography revealed extra-arachnoid fluid from C5 through L3, but no specific site of the leak was identified. After an epidural blood patch, the nausea and emesis resolved. The orthostatic headaches also began to dissipate after a few weeks to be replaced by a more steady headache. Results of head MRI approximately 2 months after the blood patch was placed were normal, but the headaches lingered. A subsequent CSF examination approximately 9 months later showed an opening pressure of 200 mm H₂O.

Approximately 6 months after this study, the patient was reexamin ed; she still had constant occipital headaches with fluctuating intensity that sometimes extended to the vertex and retro-orbital regions. At the height of severity of the headaches, she would also feel nauseated. Neurologic examination showed no neurologic deficits. The CT myelogram revealed contained left ventral extra-arachnoid fluid from T1 through T3. There was no epidural egress of the fluid, and no site of any CSF leak was noted. The CSF opening pressure was 210 mm H₂O.

Case 3

A 35-year-old woman with a complex history of insulin-dependent diabetes mellitus, hypertension, diabetic nephropathy, neuropathy, retinopathy, and a renal transplantation 2 years earlier was undergoing immunosuppressive treatment. In the preceding 20 months, she had experienced lingering holoccephalic but primarily bifronto-occipital headaches associated with neck pain and definite orthostatic aggravations. Several MRIs had shown diffuse pachymeningeal enhancement. Multiple CSF examinations had revealed nonobtainable, low, or sometimes low-normal opening pressures along with elevations in CSF protein concentrations ranging from 70 to 453 mg/dL. The results of CSF cytologic and bacteriologic analysis had been consistently negative, and CSF sugar levels were never low in proportion to plasma glucose concentrations.

A right frontal meningeal biopsy was performed elsewhere, and the specimen was sent to the Mayo Clinic in Rochester, Minn. The biopsy specimen was noted to show findings similar to those seen previously in patients with CSF volume depletion, in that there was a thin zone of fibroblasts and thin-walled small vessels in an amorphous matrix in the subdural aspect of pachymeninges, reminiscent of organized subdural hygroma. No inflammation or infiltration was noted. Subsequently, the patient received 2 epidural blood patches, each resulting in resolution of the headaches for 1 week. Later the patient was referred to the Mayo Clinic.

The patient’s lingering headaches had persisted, but the orthostatic features were substantially less. Head MRI showed diffuse pachymeningeal gadolinium enhancement but less marked than on MRIs obtained elsewhere (before epidural blood patches). Indium In 111 radioisotope cisternography revealed little activity over the convexities even at 48 hours. Spine MRI showed extradural fluid extending from the upper thoracic to upper lumbar levels. Iopamidol myelography followed by CT revealed extradural egress of contrast from T3 to T8. The CSF opening pressure was 146 mm H₂O. The CSF protein level was 211 mg/dL, but cell counts, cytologic test results, and bacteriologic test results were normal. In mid-July 1995, a T4 through T8 laminectomy was performed, and, on exposure of dura and introduction of indigo carmine through a lumbar drain, multiple confluent thoracic diverticula were outlined, emanating from almost the entire thoracic dura in
Postoperatively, the patient was kept recumbent for 72 hours and was subsequently allowed to move. She reported substantial decrease in her headaches, and within a few weeks, she became entirely headache free for approximately 4 to 5 months, when she began to experience onset of continuous holocephalic headaches without diurnal variation or relationship to posture, activity, or Valsalva-type maneuvers. These headaches were decidedly different from her previous headaches. Neurologic examination showed no new developments. Head MRI revealed resolution of the previously noted abnormal meningeal enhancement. The CSF examination results showed that the total protein concentration had now decreased to 88 mg/dL. Cell count and cytologic test results were normal. However, the opening pressure was high at 215 mm H₂O. The patient did not keep her return appointment.

Case 4

This patient, whose case has been reported previously,11,13 presented in 1984 at the age of 34 years with a 2-year history of daily orthostatic headaches relieved by recumbency. There was associated nausea and emesis for which he had undergone several gastrointestinal studies, with negative results, including CT of the abdomen. Neurologic examination results were normal. Unenhanced head MRI showed descent of the cerebellar tonsils to the level of C1. The CSF examination results showed an opening pressure of 142 mm H₂O, normal protein and sugar concentrations, but a primarily lymphocytic pleocytosis (21 cells/mm³). Several subsequent CSF examinations were performed in an attempt to determine the then unexplained pleocytosis. The results of protein, sugar, cytologic, and microbiologic studies all remained normal. The opening pressures, however, were low in some of these taps. Decompressive suboccipital craniectomy and C1 and C2 laminectomy for a presumed type I Chiari malformation were performed in August 1987. Subsequently, the headaches improved but did not resolve.

In 1994, at the age of 44 years, the patient presented with not only increasing orthostatic headaches in the preceding 3 years and recurrence of the associated nausea and sometimes emesis but also fluctuating bowel and bladder incontinence, hiccups, and dizziness. On examination, there were no neurologic deficits. Gadolinium-enhanced head MRI showed postoperative changes of the previous suboccipital craniectomy but also diffuse pachymeningeal gadolinium enhancement and magnetic resonance evidence of descent of the brain (low-lying cerebellar tonsils to the level of C2, obliterated perichiasmatic cisterns, and flattening of the optic chiasm) and enlarged pituitary (Figure 1, A). The CSF opening pressure was 60 mm H₂O with a protein concentration of 60 mg/dL and a white blood cell count of only 4 cells/mm³. Indium In 111 radioisotope cisternography showed a collection of left upper lumbar parathecal activity. On subsequent CT myelography, this proved to correspond to a meningeal diverticulum at the left L2 neural foramen (Figure 1, B and C). In retrospect, the same diverticulum could be seen on abdominal CT that had been performed 8 years earlier to try to determine the patient’s then unexplained nausea and emesis.

Subsequently, the patient underwent surgery to stop the CSF leak. A left L2 laminectomy revealed extradural
CSF and the meningeal diverticulum. The CSF leakage was terminated after ligation of the diverticulum. When the patient was reexamined 2 months after surgery, all his preoperative symptoms had resolved, but he reported that 1 week after surgery he had noted intermittent visual symptoms initially in the form of vague double vision and later visual blurring. The neurologic examination results were normal except for the presence of a bilateral papilledema along with a hemorrhage inferior to the left optic disc (Figure 2), whereas the patient’s preoperative formal neuro-ophthalmologic evaluation results had been entirely normal. The visual complaints resolved in 4 months along with pronounced improvement of papilledema and disappearance of hemorrhage. Follow-up head MRI showed resolution of the previously noted abnormalities (Figure 1, D). The patient was completely free of symptoms and had normal neurologic examination results.

DISCUSSION
Cerebrospinal fluid is a circulating body fluid sometimes referred to as the third circulation. A minute portion of the CSF is secreted by the brain capillaries and enters the ventricles, passing through the ependyma. A large portion of the CSF, however, is formed by the choroid plexus, which has structural and functional similarities to the collecting tubules of the kidneys and is essential for maintaining the compositional integrity of this fluid.14

Cerebrospinal fluid is formed at a rate of approximately 0.35 mL/min or 500 mL/d. The CSF volume is often quoted as 150 mL, but this is based on old and autopsy data. The average CSF volume in adults, based on magnetic resonance volumetric studies, is 210 mL when the mean ± SD cranial CSF volume has been calculated as 157±59 mL (less in young persons and more in older persons who have larger ventricles and more generous subarachnoid spaces and cisterns).15,16 Spinal CSF volume from the T11-12 interspace to the sacral terminus of the dural sac has been calculated as 49.9±12.1 (less for obese than nonobese persons).13 Therefore, the entire CSF is turned over a few times each day. Normally, only a tiny portion of the CSF is absorbed into the cerebral vessels through simple diffusion, whereas a large portion of the CSF is absorbed into the cerebral veins and venous sinuses by arachnoid villi via a valvelike direct flow mechanism called bulk flow.17,18 In humans, despite limited data, in general the rate of formation of CSF is thought to be relatively constant.19 No convincing evidence has been presented to indicate that increased CSF formation can occur in any condition other than choroid plexus papilloma20,21 or possibly in vitamin A neurotoxicity.19 With a person in the horizontal position, lumbar, cisternal, and presumably intracranial CSF pressures are equal and approximate 5 to 15 mm Hg, which equals 65 to 195 mm of CSF.19

All our patients had experienced CSF volume depletion that resulted from CSF leaks, and each had developed a symptomatic increase in intracranial pressure. None of our patients had a history of any symptoms or signs that could have pointed to preexisting intracranial hypertension before the onset of the manifestation of the CSF leak. None had empty sella syndrome or a history of migraine. In 2 of our 4 patients, adequate close follow-up was possible, and in each, symptoms did not last more than a few months. The mechanism of this “rebound”-increased intracranial pressure is intriguing and not entirely understood. One possibility is induction of increase in CSF production in response to prolonged CSF volume depletion. A subsequent cessation of the leak will therefore lead to increased intracranial pressure for variable periods until a normal balance between production and resorption of CSF is established.

Figure 2. Case 4. Photographs of right (R) and left (L) optic fundi show bilateral papilledema. On the left, there is hemorrhage inferior to the optic disc.
Another possible mechanism might be a disturbed mechanism of CSF resorption and a slowing of the bulk flow as a consequence of a prolonged CSF leak. This may render the resorptive mechanism dysfunctional for some time until enough function of the resorptive mechanism is established to allow a relatively normal balance between CSF production and resorption.

Each of these hypotheses is subject to serious criticism. An absorptive defect at the level of the arachnoid villi is considered a major etiologic factor in some cases of communicating hydrocephalus. Therefore, hydrocephalus should be expected if a disturbed resorptive hypothesis is entertained. However, observations in experimental normal-pressure hydrocephalus suggest that ventricular dilation may not be the consequence of decreased CSF absorption but rather related to abnormal transmantle pressure that results from blockage of free flow of CSF on the cerebral convexities. Although none of our patients had hydrocephalus, absence of hydrocephalus does not rule out decreased CSF absorption.

Similarly, in choroid plexus papilloma, the only clinical entity definitely known to be associated with increased CSF production, hydrocephalus is frequently noted. This is commonly presumed to be due to increased CSF production. However, alternative explanations have been presented by noticing that (1) approximately two thirds of choroid plexus papillomas directly obstruct the flow of the CSF, (2) not all choroid plexus papillomas are associated with hydrocephalus, and (3) arachnoiditis andependymitis have been noted in brains of patients with choroid plexus papillomas in several careful neuropathologic studies. All these observations raise the possibility of decreased absorption rather than increased production as the cause of hydrocephalus in patients with choroid plexus papillomas, and absence of hydrocephalus does not rule out the possibility of presence of increased CSF production. The resorptive capacity of arachnoid villi is unknown, but it should be higher than the rate of CSF production. Therefore, absence of hydrocephalus in our patients does not rule out either theory of increased CSF production or decreased CSF resorption.

In idiopathic intracranial hypertension (pseudotumor cerebri), despite an increase in intracranial pressure, hydrocephalus is absent, and indeed cerebral ventricles are typically normal in size or perhaps even somewhat small. The mechanism of increased intracranial pressure in pseudotumor cerebri is undetermined and has been subject to much discussion and controversy. Several theories, including increased resistance to CSF absorption, increased CSF production, and increased venous sinus pressure, have been proposed. We have no data on our patients regarding any increase in CSF production or any decrease in CSF absorption. Furthermore, venous manometric studies were not performed in any of these patients, but on follow-up MRIs and magnetic resonance venography, none had cerebral venous occlusive disease. One could argue that our patients may have originally had increased intracranial pressure and subsequently had self-decompression due to CSF leaking through a weak dural defect and again developed increased intracranial hypertension when the leak was sealed. I have noted this phenomenon previously in 1 patient. There was no clinical or imaging evidence, however, that any of the 4 patients described herein had prior increased intracranial pressure. None had any abnormality of optic discs during the time they were symptomatic with CSF leak. No patient was obese or had empty sella syndrome.

In conclusion, a likely self-limiting increase in intracranial pressure may occur in some patients after treatment of CSF leaks. This can present as headaches different from patients’ original headaches. Whether the cause is a self-limiting increase in CSF production, an increase in resistance to CSF absorption, or a different mechanism remains speculative. Also unanswered is the issue of whether this rebound-increased intracranial pressure is noted in only some patients or only becomes symptomatic in some patients. Future research may provide insight into some of these observations and may further our knowledge of CSF dynamics.

Since submission of this manuscript, I have seen another patient with increased intracranial pressure after treatment of spontaneous CSF leak. Her headaches improved with acetazolamide.

REFERENCES
[published correction appears in Anesthesiology. 1988;69:638].


