Spinal cerebrospinal fluid leak as the cause of chronic subdural hematomas in nongeriatric patients

Clinical article

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Object. The etiology of chronic subdural hematoma (CSDH) in nongeriatric patients (≤ 60 years old) often remains unclear. The primary objective of this study was to identify spinal CSF leaks in young patients, after formulating the hypothesis that spinal CSF leaks are causally related to CSDH.

Methods. All consecutive patients 60 years of age or younger who underwent operations for CSDH between September 2009 and April 2011 at Bern University Hospital were included in this prospective cohort study. The patient workup included an extended search for a spinal CSF leak using a systematic algorithm: MRI of the spinal axis with or without intrathecal contrast application, myelography/fluoroscopy, and postmyelography CT. Spinal pathologies were classified according to direct proof of CSF outflow from the intrathecal to the extrathecal space, presence of extrathecal fluid accumulation, presence of spinal meningeal cysts, or no pathological findings. The primary outcome was proof of a CSF leak.

Results. Twenty-seven patients, with a mean age of 49.6 ± 9.2 years, underwent operations for CSDH. Hematomas were unilateral in 20 patients and bilateral in 7 patients. In 7 (25.9%) of 27 patients, spinal CSF leakage was proven, in 9 patients (33.3%) spinal meningeal cysts in the cervicothoracic region were found, and 3 patients (11.1%) had spinal cysts in the sacral region. The remaining 8 patients (29.6%) showed no pathological findings.

Conclusions. The direct proof of spinal CSF leakage in 25.9% of patients suggests that spinal CSF leaks may be a frequent cause of nongeriatric CSDH.

Key Words • chronic subdural hematoma • spinal CSF leak • geriatric • vascular disorders • meningeal cyst

CHRONIC subdural hematomas (CSDHs) are generally regarded to be consequences of head trauma. The most commonly accepted pathophysiological explanation of CSDH is that mild head trauma leads to tearing of bridging veins with subsequent bleeding between the inner layer of the dura mater and the arachnoid, or between the outer and inner layers of the dura, thus creating the hematoma.⁵,¹⁴,²⁸,²⁹ Further and chronic enlargement of the subdural hematoma is believed to be due to microbleedings from fragile walls of sprouting vessels, accumulation of fluid in this newly created space following an osmotic gradient created by blood degradation products, or a combination of these events.⁵,¹⁰ In older patients, mechanical forces related to brain atrophy enable formation and growth of CSDH. A history of mild head trauma in many older patients is suggestive of trauma as a causative agent. In younger patients, brain atrophy is generally not so prominent and a history of head trauma is often not present.

Triggered by our experience with a young man with recurrent CSDH whose recurrence only stopped after...
a spinal CSF leak was sealed, we started to include the search for spinal CSF leakage into a prospective protocol for all consecutive non-geriatric CSDH patients. Our primary objectives were to identify spinal CSF leaks and spinal meningeal cysts in our cohort with the hypothesis that spinal CSF leaks are causally related to CSDH. In this paper we report our findings on the frequency of this condition.

Methods

Study Design

This prospective cohort study was approved by the local ethics committee of Bern University Hospital. All consecutive patients ≤ 60 years old with CSDH verified by CT or MRI who underwent operations between September 1, 2009, and April 12, 2011, were eligible for the study. After formulation of our hypothesis that spinal CSF egress may be a cause of CSDH in younger patients, we distributed the study protocol among all staff of the Departments of Neurosurgery and Neuroradiology at several meetings and conferences that took place beginning 4 months prior to study initiation. Beginning September 1, 2009, all staff from both departments began to screen for patients who underwent operations for CSDH. Furthermore, we used the daily interdisciplinary neurosurgical-neuroradiological conferences, where all elective and emergency cases were presented, as a second screening platform. Patients operated on for a CSDH who were ≥ 60 years of age or younger were eligible for spinal imaging workup. We excluded patients who died early (< 48 hours) due to epilepsy, who presented with recurrent SDH, who were not compliant during spinal imaging, who had recent brain surgery (< 6 months), or who had a shunt system for CSF diversion. As a next step, the computerized and written log books of all operating theaters were screened for patients with CSDH who had not been included in the study. A flow diagram of the number of patients at each stage of the study is provided in Fig. 1. An idealized diagram for how imaging modalities can be used, in order of increasing invasiveness, is shown in Fig. 2.

Spinal Imaging

For MRI, a Magnetom Avanto 1.5-T or Magnetom Verio 3-T (Siemens) machine was used. The following sequences were employed: T1-weighted, T2-weighted, magnetization-prepared rapid acquisition gradient echo (MPRAGE), and sampling perfection with application of optimized contrasts using different flip angle evolutions (SPACE) with multiplanar reconstructions. In cases of intrathecal contrast application, gadopentetate dimeglumine (Magnevist, Bayer) at a standard dose of 0.5 ml dissolved in 9.5 ml CSF was administered via a lumbar puncture at the L3–5 level.

Myelography was performed using a Siemens Artis Zee Monoplan System (Siemens). A maximum dosage of 30 ml of iodine contrast material was administered after lumbar puncture using an atraumatic puncture kit. Postmyelography CT was performed on a LightSpeed Ultra scanner (GE) immediately after myelography and again 4 hours later in selected cases.

Stepwise Protocol of the Search

After a review of existing imaging results or suggestions of CSF leaks, 3-T SPACE imaging of the complete spinal axis was conducted. Next, 0.5 ml of contrast medium (Magnevist) was injected intrathecal, and T1-weighted MRI of the spinal axis was completed. Myelography was then performed, and finally, postmyelography CT was completed. If a CSF leak was identified, the imaging algorithm was stopped with the least invasive study. Example images from a patient are provided in Fig. 3; following the diagnosis of a CSDH (Fig. 3A), spinal imaging without contrast demonstrated extrathecal fluid accumulation (Fig. 3B). The CSF fistula was then proven by fluoroscopy (Fig. 3C) and postmyelography CT (Fig. 3D).

Classification of Spinal Imaging Findings

We classified the findings of the spinal imaging according to the likelihood of pathological CSF outflow from the intrathecal to the extrathecal space on a scale from 0 to 5 in an ascending manner (Table 1): no pathological findings (category 0), detection of spinal meningeal cysts in the sacral region (category 1), detection of spinal meningeal cysts in the cervicothoracic region (category 2), detection of extrathecal fluid accumulation on spinal MRI without intrathecal contrast application (category 3), detection of extrathecal fluid accumulation on spinal MRI with intrathecal contrast application (category 4), and direct visualization of outflow of intrathecally administered contrast (iodine) from the intrathecal to the extrathecal space under fluoroscopy (category 5). The proof of an existing CSF leak (categories 4 and 5) was defined as the primary outcome.

Surgery for CSDH

Whenever possible, the patients were operated on under local anesthesia via the 2-bur-hole technique; drain insertion was performed if it was considered safe, after careful rinsing with large amounts of normal saline solution. For nonliquified space-occupying blood clots, open craniotomy under general anesthesia was the first procedure or a backup procedure.

Postsurgical Care

All patients were admitted to the intermediate care unit or the intensive care unit after surgery. The drains were left in place, restricted to 10 ml/hr and 120 ml/day, for a maximum of 48 hours. Mobilization of patients was started on the day of surgery.

Treatment of Spinal CSF Leak

In cases in which a spinal CSF leak was detected, the following treatment algorithm was used: 1) bed rest for as long as 3 days; 2) undirected blood patch at the L3–4 level (with an option to repeat the treatment if necessary); 3) directed blood patch under fluoroscopy or CT guidance (with an option to repeat the treatment if necessary); and 4) microsurgical exposure and closure of the CSF leak. For treatment options 3 and 4, the exact site of the
CSF leak had to be known. Depending on the severity of symptoms, the escalation from an undirected treatment (1 or 2) to a directed treatment (3 or 4) was accelerated, including emergency neuroradiological workup to find the spinal CSF leak and to enable directed treatment.

**Patient Outcome**

Outcome was assessed after 6 months during regularly scheduled follow-up visits in the outpatient clinics. Patient outcome was based on the modified Rankin scale (mRS) score, working status, major neurological deficits, dependency, and living situation.

**Statistical Analysis**

For descriptive statistics, data are expressed for continuous variables as means, standard deviations, and medians. Associations between categorical variables such as multiple recurrence, bilateral hematoma, head trauma, and CSF leak were calculated using a 2-sided Fisher exact test. Multiple logistic regression analysis was applied to consider the event of a CSF leak or of a recurrent CSDH in relation to explanatory variables by forward selection. Because the sample size and the number of events were small, only a few explanatory variables and no interactions could be investigated together. The statistical analysis was conducted using SAS Enterprise Guide (version 4.3). A p value < 0.05 was considered indicative of a significant result.

**Results**

**Patient Characteristics and Clinical Findings**

Nineteen men and 8 women, with a mean age of 49.6 ± 9.2 years (median 52.0 years), were included in the study (Table 2). Patient 1, who presented in November 2008 and whose clinical course led to the formation of our hypothesis, was included in the final analysis. The leading symptoms included headaches, neurological deficits, cranial nerve deficits, decreased level of consciousness, and seizures (Table 2). Fifteen patients (55.6%) had
a history of head trauma, 1 patient was taking oral anticoagulants, and 4 patients were taking aspirin. Orthostatic headaches prevailed in 1 patient and were retrospectively documented in 2 additional cases. Thus, although the chief complaint of 15 patients was headache, for 12 of these patients the headache was not orthostatic; overall, 24 patients had no orthostatic symptoms.

Characteristics and Treatment of CSDH

Chronic SDHs were unilateral in 20 patients (74.1%) and bilateral in 7 patients (25.9%; Table 2). Initial treatment was via 2-bur-hole trephination (25 cases), via 2-bur-hole trephination with conversion to craniotomy (1 case), and craniotomy (1 case). One patient showed a yellowish subdural fluid collection (hygroma, 3.7%), and 26 (96.3%) showed typical hematomas. Ten patients (37.0%) had recurrent CSDH treated with a total of 14 procedures. All patients who underwent operations for multiple recurrences had a proven CSF leak (3 of 7 with a leak vs 0 of 20 without a leak; p = 0.012).

Results of Spinal Imaging

According to our classification system (Table 1), 5 patients had a spinal CSF leak proven by direct visualization of contrast material outflow (category 5) and 2 patients had a spinal CSF leak proven by extrathecal contrast material accumulation after intrathecal application (category 4), resulting in 25.9% of patients with a proven CSF leak as the primary outcome. Spinal cervicothoracic meningeal cysts (category 2) were found in 9 patients (33.3%), including patients with multiple cysts. Cysts in the sacral region only (category 1) were detected in 3 cases (11.1%). No pathology (class 0) was found in 8 patients (29.6%). The specific imaging findings and imaging modalities used per patient are listed in Tables 2 and 3. Three (43%) of the 7 patients with proven CSF leaks had a history of head trauma as compared with 15 (75%) of 20 patients without a proven leak (p = 0.175). Imaging comprised 46 spinal MRI procedures, 15 myelographies, 13 postmyelography CT scans, 1 cisternography, and 1 nuclear medicine examination.

Treatment of Spinal CSF Leaks

Eight patients, including 7 with proven CSF leaks and 1 without spinal pathology but with recurrent CSDH, were treated with 13 epidural blood-patching procedures. Three patients underwent 4 spinal microsurgical operations for closure of the leak. Two of these patients needed microsurgery after repeated blood patching.

Patient Outcome

Outcome according to the mRS score at 6 months was a score of 0 for 15 patients, a score of 1 for 9 patients, and a score of 2 for 3 patients (Table 2). One of the
patients with an mRS score of 2 had suffered an ischemic stroke 8 years earlier with persistent hemiparesis. All 27 patients lived independently at home and 25 (92.6%) returned to their previous work status. All patients were available for follow-up.

Multiple Logistic Regression

The dependence of a CSF leak event was considered with respect to the following variables: sex, trauma, orthostatic headache, oral anticoagulation/aspirin, and bilateral CSDH. Only the lack of orthostatic headache (OR = 0.030, p = 0.030) and the presence of bilateral CSDH (OR = 21.33, p = 0.017) had significant impacts on the occurrence of a CSF leak. The model assumptions and fit were checked (area under the curve = 0.836). The same model assumptions were used for the recurrence event with the same variables and also CSF leak. In this case, the presence of bilateral CSDH (OR = 17.8, p = 0.03) and lack of trauma (OR = 0.059, p = 0.023) were significant factors. The model assumptions and fit were also checked (area under the curve = 0.889). Because of the small sample size with not many events in the explanatory variables, these results should be considered with caution. Multiple recurrences were also considered, but because there were only 3 such events among the 27 patients, a multiple logistic regression did not produce an acceptable result. However, this event was dependent on CSF leak (p = 0.012, Fisher exact test) and trauma (p = 0.029, Fisher exact test).

Discussion

With this prospective search for spinal pathologies in a consecutive neurosurgical series of non-geriatric patients with CSDH, we found an unexpectedly high rate of spinal CSF leaks (25.9%). Although spinal CSF leaks have been described as a potential cause of CSDH in rare cases, spinal CSF leakage has not been regarded as a frequent diagnosis and is therefore not included in a standard workup. Our findings suggest that investigation of spinal CSF leakage should be a mandatory part of a dedicated workup. In addition to the 25.9% of patients with directly proven CSF leaks, 33.3% of patients were found to have spinal cervicothoracic meningeal cysts. These cysts have been proposed as the cause or likely cause for spinal CSF outflow.

Cerebrospinal Fluid Leakage as a Cause of CSDHs

Spinal outflow of CSF may lead to sagging of the brain, which may tear congested bridging veins and thus enable formation of a CSDH. A causal relationship between CSF outflow and CSDH is supported by the formation of CSDH as a complication of lumbar puncture, spontaneous intracranial hypotension (SIH), and neurosurgical shunting procedures. Spinal anesthesia, spinal microdiscectomy with a dural tear, or any neurosurgical procedure associated with excessive CSF outflow.

Until now, the clinical relevance and incidence of spinal CSF outflow for non-geriatric patients with CSDH has not been documented and is very likely underestimated. The prevailing diagnostics focus on iatrogenic mechanisms (such as spinal tap or CSF shunts) leading to CSF loss, whereas an occult, idiopathic, or acquired form of spinal CSF leakage that leads to CSDH is currently not regarded as a relevant differential diagnosis and is thus not routinely investigated. To our knowledge, a systematic study of spinal CSF leakage in patients with CSDH has never been performed or reported.

Because SIH is a possible diagnosis leading to CSDH, we specifically inquired about orthostatic symptoms at admission, and again during outpatient follow-up visits, including questioning of relatives. This led to identification of 3 patients (11%) with some orthostatic component. The majority of subdural fluid collections in SIH reported in the literature are hygromas (which do not usually require evacuation); in contrast, in our series there were only 4% hygromas and the remaining 96% were hematomas. Both disorders, CSDH and SIH, occur with the same incidence of about 5 per 100,000 people. Thus, it is extremely unlikely that a simultaneous occurrence of these disorders would happen by chance in 25.9% of a group of patients.

The presence of a spinal CSF leak might lead to different clinical phenotypes (SIH or CSDH), which raises pathophysiological considerations. Whether there are different kinds of spinal CSF leaks with specific anatomical or functional (flow) characteristics, with some leading to SIH and others to CSDH, or whether the clinical manifestations change over time or represent a spectrum of a disease, is unknown.

Relevance of Spinal Meningeal Cysts

The incidence and natural history of spinal meningeal...
Spinal CSF leakage and chronic subdural hematoma

al cysts are not exactly known. Small perineural cysts in the region of the sacrum appear to have a benign course.9 Spinal meningeal cysts have been regarded as the source of CSF outflow,3,22 and Schievink and his group suggested that these are, together with imaging and clinical features, a diagnostic criterion for spinal CSF leaks.20 Spinal CSF leaks in combination with anticoagulation treatment were recently suggested as a cause of CSDH, particularly in elderly patients.22 Interestingly, all 3 reported patients in that study had spinal cervicothoracic cysts (33.3%, comparable to the current cohort) but none had a proven CSF leak. To take this into consideration, our classification differentiates proven CSF outflow (categories 4 and 5) from the mere presence of spinal cysts (categories 1 and 2).

<table>
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<tr>
<th>Variable</th>
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<tr>
<td>age (yrs)</td>
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<td>males (n = 19)</td>
<td>mean age ± SD (yrs) 48.1 ± 9.7, median age 51.0</td>
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<td>females (n = 8)</td>
<td>mean age ± SD (yrs) 53.1 ± 7.1, median age 55.5</td>
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<td>leading symptoms (multiple)</td>
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<td>location of CSDH</td>
<td>rt 11, lt 9, bilat 7</td>
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<td>mRS score at 6 mos</td>
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Patient Profile and Risk Factors

The reported incidence of recurrent CSDH varies from 3% to 39%,17,24,27,30 with reports of second or multiple recurrence ranging from 2% to 9%.17,24,26,27 Our series showed a high rate of first (33.3%), second (11.1%), and third recurrences (3.7%), but no reference group of nongeriatric patients with CSDH is available for comparison. Multiple recurrences occurred significantly more often in patients with proven CSF leaks (categories 4 and 5) as compared with patients without such leaks. What makes the multiple recurrences noteworthy is the fact that in 4 of the 7 current cases, the recurrence of the CSDH only stopped after the CSF leak was sealed. This finding supports the hypothesis of a causal relationship between CSF outflow and CSDH.

Other researchers have reported that patients with recurrent CSDH have a lower incidence of head trauma than patients without recurrent CSDH,13 as was also the case in the current series. In addition, bilateral CSDH and young age appear to involve a higher risk of recurrence.8,12,26,27 The current report describes an association of bilateral hematomas, orthostatic headaches, and multiple CSDH recurrences with a proven CSF leak. Based on our current observations, we suggest that criteria such as young age, early or multiple CSDH recurrence, continuing or unexplained clinical deterioration, orthostatic headaches, or the presence of bilateral CSDH should initiate the search for spinal CSF leaks.

Conclusions

Spinal imaging results are challenging the pathogenetic concept of CSDH in nongeriatric patients. Our results support the hypothesis that spinal CSF leakage is a frequent cause of CSDH in young patients, which could influence the diagnostic and therapeutic management of these patients. Potential spinal CSF leaks should be methodically investigated in young patients and in patients with certain risk factors.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Beck, Raabe. Acquisition of data: Beck, Gralla, Fung, Ulrich, Schucht, Fichtner, Andereggen, Gutbrod, Z’Graggen, Reimert, Ozdoba, Raabe. Analysis and interpretation of data: Beck, Gralla, Fung, Ulrich, Gosau, Hattingen, Z’Graggen, Hüsler, Ozdoba, Raabe. Drafting the article: Beck, Fung, Gosau, Hattingen, Z’Graggen, Hülsler, Ozdoba, Raabe. Critical revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Beck. Statistical analysis: Hülsler, Beck. Study supervision: Beck.

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References


TABLE 3: Neuroradiological workup of all patients studied*

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* CM (it) = intrathecal application of contrast media; CM (iv) = intravenous application of contrast media.
† Case 1 was the only patient to also undergo 1 cisternography and 1 nuclear medicine examination.
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