Primary spontaneous cerebrospinal fluid rhinorrhea: a symptom of idiopathic intracranial hypertension?

Clinical article

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Object. The authors aim to identify the characteristics of primary spontaneous CSF rhinorrhea and propose a hypothesis for its pathogenesis.

Methods. Between 2003 and 2009, 21 patients diagnosed with primary spontaneous CSF rhinorrhea underwent surgery in the authors’ hospital. The clinical aspects were retrospectively reviewed, and their characteristics were analyzed.

Results. There were 18 women and 3 men, whose ages ranged from 37 to 74 years (mean 53 years). Body mass index (BMI) ranged from 22 to 58.8 kg/m² (mean 31.2 kg/m²). Eighteen patients (85.7%) were overweight, and 18 (85.7%) suffered from headache or tinnitus before rhinorrhea. Radiological images revealed fully or partially empty sellae in 14 patients (66.7%). The preoperative intracranial pressure (ICP) ranged from 11 to 28 cm H₂O (mean 17.6 cm H₂O), while the postoperative ICP ranged from 21 to 32 cm H₂O (mean 25.5 cm H₂O, p < 0.01). An endoscope-assisted transnasal approach was chosen for the repair. Postoperatively, in 95.2% of patients a cure was achieved. Rhinorrhea recurred in only 1 patient, and a leakage from a new defect occurred in another patient 4 years after the operation. Both patients underwent additional surgery, which was successful. The follow-up period varied from 5 to 75 months with a mean of 34 months.

Conclusions. All patients had direct or indirect evidence of elevated ICP, most patients presented with symptoms of idiopathic intracranial hypertension (IIH), and most patients were women and obese. Primary spontaneous CSF rhinorrhea may be due to IIH, and it is a rare symptom of IIH. When treating or monitoring these patients during follow-up, ICP should be controlled, and other symptoms of IIH should be noted. (DOI: 10.3171/2011.3.JNS101447)

Key Words • cerebrospinal fluid • rhinorrhea • pathogenesis • intracranial hypertension

Cerebrospinal fluid rhinorrhea is a rare and awful disease. It occurs when there is a breakdown in the normal anatomical barrier encompassing the CSF. Regarding the etiology, Ommaya et al.18 classified CSF rhinorrhea into traumatic (accidental or iatrogenic trauma) and spontaneous. Spontaneous CSF rhinorrhea can be caused by tumor, hydrocephalus, congenital anomalies, or other unidentifiable causes. Cerebrospinal fluid rhinorrhea of unidentifiable causes is referred to as primary spontaneous CSF rhinorrhea.17

Primary spontaneous CSF rhinorrhea is a rare entity with some unusual features. It often occurs in middle-aged or older women, and the average BMI is more than 30 kg/m² in most patient series.21,23,26 Ommaya and colleagues18 reported that the condition is caused by focal atrophy and the ICP is normal, but several researchers have recently found that it is related to elevated ICP and have proposed that the high pressure might be the direct cause of the leak.4,20,23,25 Obesity can increase ICP. An empty sella, which occurs in many patients, is now considered radiographic evidence of elevated ICP.

Although the diagnosis and treatment of primary spontaneous CSF rhinorrhea are the same as those for CSF rhinorrhea due to other causes, primary spontaneous CSF rhinorrhea has a reportedly high recurrence rate, ranging from 25% to 87%.1,21,23 In 1994, Clark et al.4 proposed that benign intracranial hypertension, which is also called IIH, was one of the causes of CSF rhinorrhea. When treating patients with CSF rhinorrhea, we began to pay more attention to controlling ICP. Woodworth et al.20 managed ICP in patients with primary spontaneous CSF rhinorrhea postoperatively and reported a success rate of 95%. However, it is still unclear why this condition is common in middle-aged and older obese women. In this article, we attempt to explain the features of primary spontaneous CSF rhinorrhea and propose a hypothesis for this condition’s pathogenesis.
Methods

Patient Population

Between 2003 and 2009, 21 patients with primary spontaneous rhinorrhea were surgically treated by the neurosurgery team at Beijing Tiantan Hospital. The patients' charts were retrospectively reviewed, and the following information was gathered: age, sex, BMI, clinical manifestation, neurological examination, site of bone defect, and pre- and postoperative CSF pressures. The patients underwent strict follow-up. This study was approved by the Capital Medical University Review Board.

Patients with a BMI of 25 kg/m² or lower were considered to be at a normal weight, those with a BMI between 25 and 30 kg/m² were considered overweight, and those with a BMI higher than 30 kg/m² were considered obese. Elevated ICP was defined as ICP higher than 20 cm H₂O. Headache, visual disturbances, and tinnitus were considered symptoms of IIH.

Clinical Management

Conservative treatment includes avoidance of activities that increase ICP (coughing, sneezing, and straining during bowel movements), diuretics such as acetazolamide, and lumbar drainage.

All of the operations were performed under general anesthesia. A transnasal or transcranial approach was selected for patients according to the clinical situation. Postoperatively, all patients were given mannitol for 1 week, and the dosage was decreased gradually.

Follow-Up

Imaging examinations and ophthalmological testing were performed 3 months postoperatively. Patients returned for follow-up visits at 6 months and yearly thereafter. Our main focus was on whether there were symptoms of CSF rhinorrhea and IIH.

Statistical Analysis

Preoperative and postoperative ICP levels were compared using a paired t-test with SPSS 13.0 software. Probability values were obtained from 2-sided tests, with statistical significance defined as p < 0.05.

Results

Patient Characteristics

In this group, 18 (85.7%) of 21 patients were women and 3 (14.3%) were men. Their ages ranged from 37 to 74 years (mean 53 years). The BMIs ranged from 22 to 58.8 kg/m² with an average of 31.2 kg/m². Eight patients were obese, 10 were overweight, and 3 were at a normal weight.

Clinical Presentations and Management

The symptoms are summarized in Table 1. The main clinical symptom was a runny nose. All patients had a continuous or intermittent runny nose. Before the runny nose occurred, 11 patients had intermittent headaches and 9 patients had tinnitus for 1–6 months. Before the runny nose developed, there were 9 cases of tinnitus lasting 1–6 months and 11 cases of intermittent headache seen in a group of 18 patients. When the rhinorrhea occurred, 13 patients had subjective symptoms such as coughing, sneezing attacks, and stuffy nose, and often lowered their heads, thus increasing the ICP. However, the patients' headaches and tinnitus disappeared after the onset of rhinorrhea. Nine patients had a history of meningitis, 3 of whom had recurrent meningitis. None of the patients presented clinically with visual disturbances.

None of the positive signs except runny nose were found during physical examination. Additionally, preoperative ophthalmological examination did not reveal any signs. The physical and chemical characteristics of the CSF were normal both pre- and postoperatively. Through CT scanning, we found that all patients had only 1 bone defect each. These defects were located in the ethmoid sinus (in 13 patients) (Fig. 1), the lateral wall of the sphenoid sinus (in 7) (Fig. 2), and the frontal sinus (in 1), and they were all confirmed at surgery. All patients whose defects were located at the lateral wall of the sphenoid sinus had an excessively pneumatized sinus, and their defects were around the foramen rotundum. Fourteen patients had fully or partially empty sellae (Fig. 3).

Five patients underwent conservative treatment in our hospital or others, and it was effective in 3. However, all of these patients had a recurrence after a period of time, and all eventually underwent surgical repair. A transcranial approach was performed in the patient whose defect was located in the frontal sinus, and an endoscopic approach was used in the others. There were no major postoperative complications.

All patients underwent lumbar puncture pre- and postoperatively. We had direct evidence of ICP variation. Before surgery, the mean ICP was 17.6 cm H₂O (range 21–32 cm H₂O). Only 5 patients had abnormal ICP, but their rhinorrhea was at the latent stage when we measured their ICP. The mean ICP was 25.5 cm H₂O (range 21–32 cm H₂O) 7 days after surgery; all patients had an abnormal ICP and 11 had an ICP higher than 25 cm H₂O. The ICP varied more sharply in patients in whom leakage was more severe. We compared the pre- and postoperative ICP levels by using the paired-samples t-test (p < 0.01). There was a significant difference between them.

Outcome

All of the patients were stable and were discharged from the hospital 7 days after surgery. All patients underwent follow-up, and the mean follow-up time was 34
months (range 5–75 months). One patient had a recurrence, and one patient had a second leakage at another site 4 years after the first operation. Both patients underwent additional surgery to treat the new occurrence of rhinorrhea. The success rate of the first attempt was 95.2%, and the success rate of the second attempt was 100%. Two patients had tinnitus 42 and 59 months postoperatively. Their symptoms were controlled by oral diuretics. None of the patients reported headache or visual disturbances. No patient presented with papilledema at 3 months postoperatively.

**Discussion**

Cerebrospinal fluid rhinorrhea that does not have any identifiable cause is generally referred to as primary spontaneous. However, we believe that all diseases have a real cause. Similar to those reported in the literature, the following characteristics were noted in our series: the majority of patients were middle-aged or older women, most patients’ BMIs were abnormal, the defect location was mainly in the ethmoid (cribriform plate and ethmoid roof) or the lateral wall of the sphenoid sinus, an empty sella existed in many patients, ICP was elevated in all patients postoperatively, and some patients presented clinically with symptoms of IIH. It is quite interesting that IIH has similar features, and these 2 diseases may be related to each other. Primary spontaneous CSF rhinorrhea may be due to IIH, and it may be a rare symptom of IIH.

Table 2 shows that the 2 diseases are very similar in demographics (except age), clinical presentation, and imaging findings. Idiopathic intracranial hypertension was diagnosed according to the modified Dandy criteria as follows: signs and symptoms of increased ICP, no localized signs except abducens nerve palsy, CSF opening pressure higher than 25 cm H$_2$O with normal CSF composition, and normal neuroimaging findings (no other causes of intracranial hypertension have been identified).$^6$

Some authors have also reported that patients with CSF rhinorrhea had features of IIH. Although some data were not very precise, the authors provided evidence that both of these diseases are similar. The published data are summarized in Table 3 and are a nice addition to our data.$^4,11,20,24–26$

**Intracranial Pressure**

As with primary spontaneous CSF rhinorrhea, IIH is also a diagnosis of exclusion. Intracranial pressure is the most important index to diagnose IIH. Most ICP levels measured preoperatively were in the normal range. The preoperative ICP may be higher before the onset of rhinorrhea, and rhinorrhea may reduce the ICP due to CSF leakage. In 1 study, the removal of 15–25 ml of CSF re-
TABLE 2: Comparison of characteristics associated with primary spontaneous CSF rhinorrhea and IIH

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Rhinorrhea</th>
<th>IIH</th>
</tr>
</thead>
<tbody>
<tr>
<td>age group</td>
<td>middle-aged, older</td>
<td>young</td>
</tr>
<tr>
<td>sex</td>
<td>female</td>
<td>female</td>
</tr>
<tr>
<td>BMI</td>
<td>obese, overweight</td>
<td>obese</td>
</tr>
<tr>
<td>empty sella</td>
<td>common</td>
<td>common</td>
</tr>
<tr>
<td>symptoms</td>
<td>runny nose, headache, tinnitus</td>
<td>headache, tinnitus, visual disturbances</td>
</tr>
<tr>
<td>ICP</td>
<td>all abnormal, &gt;50% w/ ICP &gt;25 cm H₂O</td>
<td>&gt;25 cm H₂O</td>
</tr>
</tbody>
</table>

duced the pressure to lower than 10 cm H₂O. The patients who had abnormal ICP preoperatively were at the latent stage of rhinorrhea. Therefore, the pressures obtained postoperatively might represent the real states of the patients. The postoperative ICP levels were significantly higher than those obtained preoperatively. Although almost 50% of patients had an ICP lower than 25 cm H₂O, there was a trend toward increasing ICP. The elevation may be progressive and chronic. Liang et al. reported that remote tumors causing rhinorrhea preoperatively were all benign tumors and provided evidence that the formation of rhinorrhea due to intracranial hypertension was a chronic process. Considering the influence of long-standing rhinorrhea, the pressure may be higher when rhinorrhea occurs. At that moment, all patients in our series could be included in the criteria for IIH.

Demographics

Primary spontaneous CSF rhinorrhea and IIH are common in obese women. In our series, women accounted for 85.7% of patients. This percentage is close to that for IIH reported by Bruce et al. Complying with rigid criteria, they found the percentages of female and male patients to be 91% and 9%, respectively. Obesity is related to elevated ICP; Badia et al. proposed that central obesity could cause increased intraabdominal pressure and subsequent elevation of ICP. However, in our study the percentage of obese patients is less than that for IIH. Only 8 of 21 patients were obese and 10 were overweight; elsewhere, the frequency of obesity in patients with IIH has been reported to range from 71% to 94%. Woodworth et al. reported that 82.1% of obese patients were diagnosed as having primary spontaneous CSF rhinorrhea. The percentage of obese patients was in accordance with IIH.

The patients with rhinorrhea were older than those with IIH. The mean age of our patients was 53 years, and the mean age at onset of IIH has been reported as 28–35 years. Woodworth et al. reported that 82.1% of obese patients were diagnosed as having primary spontaneous CSF rhinorrhea. The percentage of obese patients was in accordance with IIH.

Formation of Rhinorrhea

Before rhinorrhea occurred, 18 patients presented with symptoms (headache and tinnitus) of IIH, which disappeared as soon as rhinorrhea occurred. Headache and tinnitus are the most common symptoms of IIH; they may be caused by elevated ICP, and their disappearance would be related to the reduction in ICP caused by rhinorrhea. The duration of the symptoms was short. We speculate that the elevation of ICP is gradual; patients can suffer a slight alteration at first, but when the pressure exceeds the range that one can tolerate, the symptoms occur. Although visual disturbance is also one of the common symptoms of IIH, none of our patients experienced visual symptoms. Ophthalmological examination did not reveal any findings in our patients preoperatively or 3 months postoperatively. Based on the results of our literature review (Table 3), we note that visual disturbance and papilledema have been reported previously. Seth et al. reported rates of visual disturbance and papilledema as 10.5% and 9.4%, respectively, which are not as high as the rate of IIH. The Dandy criteria have been recently amended so that the presence of papilledema is no longer a requirement for IIH diagnosis. Digre et al. reported that visual fields were more likely to be normal in patients with IIH without papilledema than in those with papilledema. Therefore, we believe that our patients’ symptoms were in accord with the diagnosis of IIH. Rhinorrhea, which could reduce ICP and relieve the symptoms, should be a result of elevated ICP. It may provide other evidence that IIH precedes rhinorrhea.

An empty sella is common in either primary sponta-

TABLE 3: Review of the literature of patients with primary spontaneous CSF rhinorrhea

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Mean Age (yrs)</th>
<th>% Female</th>
<th>BMI (kg/m²)</th>
<th>Symptoms &amp; Signs</th>
<th>CSF Pressure (cm H₂O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clark et al., 1994</td>
<td>4</td>
<td>38</td>
<td>100</td>
<td>NR</td>
<td>headache, papilledema</td>
<td>32</td>
</tr>
<tr>
<td>Law et al., 1999</td>
<td>1</td>
<td>56</td>
<td>100</td>
<td>NR</td>
<td>headache</td>
<td>NR</td>
</tr>
<tr>
<td>Ransom et al., 2006</td>
<td>1</td>
<td>53</td>
<td>100</td>
<td>NR</td>
<td>headache, visual change</td>
<td>30</td>
</tr>
<tr>
<td>Seth et al., 2010</td>
<td>39</td>
<td>57.7</td>
<td>85</td>
<td>38.5</td>
<td>headache, tinnitus, diplopia, papilledema</td>
<td>24</td>
</tr>
<tr>
<td>Suryadevara et al., 2007</td>
<td>2</td>
<td>49.5</td>
<td>100</td>
<td>obese</td>
<td>headache, visual loss, papilledema</td>
<td>24–26</td>
</tr>
<tr>
<td>Woodworth et al., 2008</td>
<td>56</td>
<td>61</td>
<td>77</td>
<td>36.2</td>
<td>NR</td>
<td>27</td>
</tr>
</tbody>
</table>

* NR = not reported.
Primary spontaneous cerebrospinal fluid rhinorrhea

neous CSF rhinorrhea or IIH. It may be the radiographic evidence of elevated ICP, because reversible empty sella syndrome has been reported in cases of documented intracranial hypertension after successful reduction of ICP with diuretics or shunt treatment.12,13 Maira et al.14 performed continuous ICP monitoring in 11 patients with idiopathic empty sella syndrome. Twenty-seven percent had elevated ICP when they were awake, and an additional 45% had elevated ICP when they were in REM sleep. Only 27% had normal ICP at all times.

As with other etiologies, the defects seen in our series were mainly located in the ethmoid sinus and the lateral wall of the sphenoid sinus. The cribiform plate is the thinnest bone in the body. The body of the sphenoid is formed by the fusion of pre- and postphosphene centers of ossification. Tiny defects in the sphenoid bone might arise as the sinuses develop. If the sphenoid sinus is excessively pneumatized, the bone will be thinner and the defect may be larger. Among the aging population, there is focal atrophy of the mucous membrane or nerve,6 so the bone may be more fragile. With the continuous effect of high-pressure CSF pulses, the bone defect forms gradually and the skull base becomes eroded, allowing rhinorrhea to occur.

Management

To sum up, in our series, elevated ICP has an impact on the weakened skull base; primary spontaneous CSF rhinorrhea may be both the result and a rare symptom of IIH. However, it is not enough to cure primary spontaneous CSF rhinorrhea by controlling ICP. Conservative management has little effect on primary spontaneous CSF rhinorrhea and may increase the risk of meningitis, so surgery should be performed as soon as the condition is diagnosed. The outcome of conservative treatment in our series was disappointing. The purpose of conservative treatment is to decrease ICP and encourage the defect to heal spontaneously. Even though conservative treatment is sometimes effective, ICP would again become elevated, and the already weakened skull base may be destroyed again, thereby causing a recurrence. Primary spontaneous CSF rhinorrhea is an indication for surgery. Surgical treatment, with the help of decreasing ICP, is an effective method to cure rhinorrhea, and we have attained a satisfactory success rate. However, 3 of 21 patients presented with clinical symptoms a long time after surgery. One patient had a new defect and 2 had slight tinnitus; these symptoms could be the result of IIH. To reduce these symptoms, it is also very important to control ICP postoperatively. Idiopathic intracranial hypertension is a self-limited condition in some cases.16 There are no sufficient studies of any treatment modality for IIH, so the evidence base for management decisions is poor. There are generally only 2 reasons to treat patients with IIH: severe intractable headache and optic neuropathy.16 Asymptomatic patients should be observed regularly.2 We advised our patients to control their weight and pay attention to the related symptoms of IIH postoperatively. In the follow-up period, no patient had severe symptoms of IIH, so we did not undertake any invasive intervention in them.

Conclusions

The patients in our series had the following characteristics: most were middle-aged or older obese women, the defect location was mainly in the ethmoid (cribiform plate and ethmoid roof) and the lateral wall of the sphenoid sinus, and empty sella syndrome was noted in many patients. There was significant variation in ICP pre- and postoperatively. Idiopathic intracranial hypertension has features similar to those of CSF rhinorrhea, including obesity, female sex, and empty sella syndrome, and our patients presented clinically with the symptoms of IIH pre- and postoperatively. Primary spontaneous CSF rhinorrhea may be due to elevated ICP and is a rare symptom of IIH. When treating these patients, we should control intracranial hypertension. When conducting the follow-up, we should observe whether patients have symptoms of IIH.

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: Liu, C Wang. Acquisition of data: Yang, B Wang. Analysis and interpretation of data: Liu, Yang. Drafting the article: Yang. Critically revising the article: Liu, C Wang. Reviewed final version of the manuscript and approved it for submission: Liu, C Wang. Statistical analysis: B Wang.

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