Pseudo-cerebrospinal fluid rhinorrhea

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Because of its potentially serious sequelae, cerebrospinal fluid (CSF) leakage following surgery for lesions of the cranial base is given immediate attention by neurosurgeons. Despite a multitude of approaches used to prevent its occurrence, CSF leakage complicates up to 30% of difficult skull-base tumor operations.

The authors describe the cases of 11 patients who developed a syndrome, not previously described in the literature, termed "pseudo-CSF rhinorrhea." This syndrome occurs after surgery of the cranial base, usually involving dissection or removal of the petrous or cavernous carotid artery, the greater superficial petrosal nerve, and the pericarotid sympathetic plexus. It is characterized by nasal stuffiness and nasal hypersecretion and is sometimes accompanied by facial flushing. The symptoms are characteristically exacerbated by exertion or by elevated ambient room temperatures. Lacrimation is typically absent ipsilateral to the pseudo-CSF rhinorrhea. It is believed that pseudo-CSF rhinorrhea developed in these patients because of a relative imbalance of the regulatory autonomic supply of the nasal mucosa.

KEY WORDS - cerebrospinal fluid leak - rhinorrhea - cavernous sinus

During the last decade, a multidisciplinary approach to patients with lesions of the skull base has allowed surgeons to treat a multitude of pathologies successfully. The complications of such surgery can be categorized into those affecting the neural, vascular, bone, soft-tissue, and systemic structures of the brain. Postoperative cerebrospinal fluid (CSF) leakage was recognized early in the era of modern skull-base surgery as a complication due to the transgression of meningeal, bone, and soft-tissue spaces (particularly the paranasal sinuses) and has led to the development of a variety of approaches to prevent its occurrence. Despite such approaches, CSF leakage is reported to occur in up to 30% of operations for skull-base lesions.

We describe a complication, seen in 11 patients, that mimics CSF rhinorrhea due to transgression of the paranasal sinuses. If not properly identified, this complication may lead to multiple invasive investigations and even unsuccessful attempts to repair the basal, bone, and soft-tissue structures.

Clinical Material and Methods

During the period from 1983 to 1991, 200 patients with lesions of the cavernous sinus underwent surgery and a further 100 patients had exposure of the petrous carotid artery during surgery at our center. Within these groups, 11 patients were identified who complained of rhinorrhea associated with exertion. The hospital and outpatient records of these patients were reviewed in detail and form the basis of this report.

Results

All patients had undergone exposure, mobilization, or resection of their ipsilateral petrous internal carotid artery (ICA) and/or cavernous sinus ICA during skull-base surgery. This included manipulation and/or division of the pericarotid artery sympathetic nerve plexus and division of the greater superficial petrosal nerve in most cases. During the postoperative course, all patients described persistent symptoms of nasal hypersecretion of clear fluid which occurred characteristically following exertion. Six patients noted that rhinorrhea was associated with an increase in body or ambient room temperature and two other patients noted that rhinorrhea was also exacerbated by intense emotional feelings. One patient experienced facial flushing associated with the rhinorrhea. Patients typically had diminished or absent lacrimation ipsilateral to the rhinorrhea. None exhibited computerized tomography (CT) features such as fluid in the sinuses suggestive of a CSF leak. The clinical details of the 11 patients who experienced the syndrome are outlined in Table 1. Three illustrative cases are presented in detail below.
### TABLE 1

**Characteristics of patients with pseudo-CSF rhinorrhea**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs.)</th>
<th>Sex</th>
<th>Location of Tumor</th>
<th>Surgical Approach</th>
<th>Procedure</th>
<th>Symptoms</th>
<th>Invasive Investigations</th>
<th>Repair Procedure</th>
<th>Side vs. Surgery</th>
<th>Type of Discharge</th>
<th>Lacrimation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>42</td>
<td>F</td>
<td>It sphenocerebrospinal fluid meningioma (CS meningioma)</td>
<td>FTC, OZO</td>
<td>divided</td>
<td>divided</td>
<td>PE rhinorrhea</td>
<td>Iohexol cisternogram</td>
<td>VP shunt, frontal fossa repair</td>
<td>Ipsilat</td>
<td>Clear, colorless</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>F</td>
<td>rt CS PC meningioma</td>
<td>1: ST/IT OZO 2: preretro-sigmoid</td>
<td>exposed</td>
<td>divided</td>
<td>PE &amp; T rhinorrhea</td>
<td>Iohexol &amp; radionuclide cisternograms</td>
<td>None</td>
<td>Ipsilat</td>
<td>Clear</td>
</tr>
<tr>
<td>3</td>
<td>44</td>
<td>F</td>
<td>It CS PC meningioma</td>
<td>FTC, OZO</td>
<td>divided</td>
<td>divided</td>
<td>PE rhinorrhea</td>
<td>Iohexol cisternogram</td>
<td>None</td>
<td>Ipsilat</td>
<td>Clear</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>F</td>
<td>It CS ICA aneurysm, pituitary adenoma</td>
<td>FTC, OZO</td>
<td>divided</td>
<td>divided</td>
<td>PE, E, &amp; T rhinorrhea; facial flushing</td>
<td>None</td>
<td>None</td>
<td>Bilat†</td>
<td>Mucus</td>
</tr>
<tr>
<td>5</td>
<td>56</td>
<td>F</td>
<td>It CS PC meningioma</td>
<td>FTC, OZO</td>
<td>repair</td>
<td>divided</td>
<td>PE rhinorrhea</td>
<td>None</td>
<td>None</td>
<td>Ipsilat</td>
<td>Clear</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>F</td>
<td>CS meningioma</td>
<td>FTC, OZO</td>
<td>exposed</td>
<td>divided</td>
<td>PE &amp; T rhinorrhea</td>
<td>None</td>
<td>None</td>
<td>Ipsilat</td>
<td>Clear, slightly thick</td>
</tr>
<tr>
<td>7</td>
<td>64</td>
<td>F</td>
<td>It CS PC meningioma</td>
<td>FTC, OZO, exposed</td>
<td>divided</td>
<td>PE &amp; T rhinorrhea</td>
<td>None</td>
<td>None</td>
<td>Ipsilat</td>
<td>Clear‡</td>
<td>It eye constantly dry, rt eye normal</td>
</tr>
<tr>
<td>8</td>
<td>43</td>
<td>F</td>
<td>It sphenoorbital CS PC meningioma</td>
<td>FTC, OZO</td>
<td>exposed</td>
<td>divided</td>
<td>PE &amp; T rhinorrhea</td>
<td>None</td>
<td>None</td>
<td>Ipsilat</td>
<td>Clear liquid</td>
</tr>
<tr>
<td>9</td>
<td>56</td>
<td>M</td>
<td>It CS PC neurilemoma</td>
<td>FTC, OZO</td>
<td>exposed</td>
<td>divided</td>
<td>PE &amp; T rhinorrhea</td>
<td>None</td>
<td>None</td>
<td>Ipsilat</td>
<td>Clear, moderately thick</td>
</tr>
<tr>
<td>10</td>
<td>62</td>
<td>F</td>
<td>rt CS hemangioma</td>
<td>FTC, OZO</td>
<td>exposed</td>
<td>divided</td>
<td>PE &amp; T rhinorrhea</td>
<td>Iohexol cisternogram</td>
<td>Sphenoid sinus repair</td>
<td>Ipsilat</td>
<td>Clear, colorless, thick</td>
</tr>
<tr>
<td>11</td>
<td>42</td>
<td>M</td>
<td>Invasive pituitary adenoma</td>
<td>FTC, OZO</td>
<td>exposed</td>
<td>divided</td>
<td>PE rhinorrhea</td>
<td>Iohexol cisternogram</td>
<td>VP shunt, frontal fossa repair</td>
<td>Ipsilat</td>
<td>Clear, watery mucus</td>
</tr>
</tbody>
</table>

* CSF = cerebrospinal fluid; ICA = internal carotid artery; GSPN = greater superficial petrosal nerve; CS = cavernous sinus; PC = petroclival; FTC = frontotemporal craniotomy; OZO = orbitozygomatic osteotomy; ST/IT = subtemporal/infratemporal; PE = parieto-external; T = with increased room temperature; E = with emotion; VP = ventriculoperitoneal.

† Patient had previous transphenoidal and transethmoidal surgery.

‡ Patient's left nostril dry when sneezing, but has rhinorrhea in hot humid weather or during exercise.

### Illustrative Cases

**Case 1**

This 42-year-old woman developed left-sided earache and nausea in February, 1982. She subsequently underwent two attempts at resection of a left sphenocavernous sinus meningioma which were incomplete and complicated by mild left-sided halopiasia of the first division of the fifth cranial nerve (V1). Later in 1982, she spontaneously lost vision in the left eye and, in 1983, she underwent another incomplete resection of the residual meningioma. The ICA was injured during this operation and was progressively occluded with a Silverstone clamp. She was given radiation treatment in 1984 and was subsequently treated for panhypopituitarism.

In 1987, the patient was referred to our center. Between that time and February, 1989, she developed a progressive partial third nerve palsy and burning facial pain in the V1 distribution. In February, 1989, she underwent complete resection of the residual tumor via a left frontotemporal craniotomy combined with an orbital osteotomy. During this procedure, the occluded ICA was divided; because of the firm nature of the tumor, a piecemeal intracavernous resection was car-

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ried out, working between the oculomotor (third cranial) nerve and V\textsubscript{1}, between the V\textsubscript{1} and V\textsubscript{2} divisions of the trigeminal nerve and through Parkinson's triangle. The oculomotor nerve and V\textsubscript{1} component of the trigeminal nerve were excised because they were infiltrated by tumor. The dura was closed in a watertight fashion and the orbital apex closed with a fascia lata graft. The frontal sinus was xenectrated of mucosa and packed with fat.

In June, 1989, a ventriculoperitoneal shunt was inserted to relieve the patient's progressively severe headaches associated with rhinorrhea, presumably secondary to hydrocephalus. Although the headaches were relieved, the left nostril rhinorrhea continued. She then underwent transsphenoidal packing of the sphenoid sinus with negative results of an iohexol cisternogram. She continued to note leakage of clear fluid from her left nostril, particularly during exercise; flexing her head forward and Valsalva maneuvers did not exacerbate the fluid leakage.

In September, 1989, via a bifrontal craniotomy, the frontal sinus was xenectrated of mucosa and packed with fat and a pericranial flap was placed to repair the presumed frontal fossa defect. A repeat iohexol cisternogram for persistent rhinorrhea was negative in April, 1990; however, the patient continues to complain of leakage of clear fluid from her left nostril following exercise. The fluid has tested negatively for β\textsubscript{2} transferrin.

Case 2

This 32-year-old woman presented for evaluation of a 2-year history of progressive supraorbital headaches, accompanied by intermittent numbness of the right side of the face and body, a 3-month history of progressive right ptosis, and pituitary dysfunction. She had a negative CT scan during investigation of infertility 8 years prior to her current admission.

A large right cavernous sinus petroclival meningioma was resected in two stages. The middle fossa tumor as far back as the tentorial incisura was resected via an orbitozygomatic approach, during which the greater superficial petrosal nerve was divided, the horizontal and vertical segments of the petrosal ICA were exposed, and the cavernous sinus was entered superiorly and laterally between the fourth cranial nerve and the V\textsubscript{1}, V\textsubscript{2}, and V\textsubscript{3} divisions of the fifth cranial nerve. Two weeks later, gross total resection of the tumor was completed through a right posterior subtemporal, pre- and postganglionic approach achieved by partial petrous bone resection and retromastoid craniectomy.

Follow-up magnetic resonance imaging has not revealed tumor recurrence; however, the patient has noted leakage of clear fluid from her right nostril upon exercising and whenever the ambient room temperature rises above 80°F. She uses artificial tears to provide moisture to the right eye. Radioisotope and iohexol cisternograms have shown no recurrence; however, the artificial tears have not been effective in providing adequate moisture.

Case 4

This 39-year-old woman with Cushing's disease had undergone three attempts at resection of a pituitary adenoma: two transphenoidal and one transethmoidal. The last resection (transethmoidal) was complicated by an injury to the ICA. Postoperatively, she suffered several episodes of severe epistaxis and an aneurysm of the intracavernous carotid artery was identified. Embolization of the external carotid artery was attempted to stop the epistaxis prior to the discovery of the aneurysm. Balloon test occlusion of the ICA was not tolerated clinically.

On July 27, 1988, a saphenous vein bypass graft of the ICA was placed in an end-to-end fashion from the horizontal petrous ICA to the supraclinoid ICA, sacrificing the ophthalmic artery, the greater superficial petrosal nerve, and the periarterial sympathetic plexus. Despite intraoperative hypertension, the patient had a mild hemiparesis and expressive dysphasia as well as a third cranial nerve palsy and trigeminal hyperpathia postoperatively. Her immediate postoperative deficits have largely resolved; however, in April, 1991, she began to notice severe left facial flushing in all three trigeminal divisions associated with rhinorrhea following exercise, sudden startling, or with emotion. Lacrimation in the left eye is absent. The symptoms of rhinorrhea have resolved with administration of topical sympathomimetic agents.

Discussion

Anatomy

The preganglionic parasympathetic fibers of the nasal mucosa arise from cell bodies in the superior salivatory nucleus and emerge from the brain stem in the nervus intermedius. The fibers leave the geniculate ganglion at the facial hiatus to form the greater superficial petrosal nerve, which runs parallel to the ICA to join the postganglionic sympathetic fibers from the periarterial ICA plexus and form the nerve of the pterygoid canal (vidian nerve). The parasympathetic fibers synapse at the sphenopalatine ganglion and are then distributed to the nasal mucosa and the lacrimal gland, where they represent the secretory-motor supply. The sympathetic fibers of the vidian nerve arise from the stellate, middle cervical, and superior cervical sympathetic paracervical ganglia. These unmyelinated postganglionic fibers form a periarterial plexus around the ICA to reach the cavernous sinus, where they run with divisions of the oculomotor nerve and the first and second divisions of the trigeminal nerve to eventually reach the glands of the nasal mucosa (Fig. 1). Malcolmson\textsuperscript{4} demonstrated that stimulation of the cervical sympathetic chain produces vasoconstriction of the nasal mucosa, which is abolished after section of the vidian nerve. This suggests that the most important sympathetic innervation to the nasal mucosa is via this nerve. Conversely, stimulation of the parasympathetic fibers causes congestion of the cavernous tissue of the nose and secretion of fluid.
Pseudo-cerebrospinal fluid rhinorrhea

![Diagram of nasal anatomy](image)

**Fig. 1.** Artist's drawing demonstrating the autonomic supply of the nasal mucosa. GSPN = greater superficial petrosal nerve; n. intermed. = nerve intermedium; VII = seventh cranial nerve; N. = nerve; ICA = internal carotid artery; sup. = superior.

**Pathophysiology**

In 1943, Fowler described unilateral vasomotor rhinitis in a patient after extirpation of the left stellate ganglion. Further evidence that sympathetic denervation produces a parasympathomimetic state in the nasal mucosa was demonstrated by Millonig, et al., who described the nasal stuffiness that followed cervical sympathectomy for various conditions. Hamberger described nasal stuffiness and nasal hypersecretion in patients who underwent removal of their stellate ganglia and section of the second, third, or fourth thoracic ganglia for the treatment of angina pectoris. These clinical findings describing the effects of sympathectomy on the nasal mucosa were confirmed in animal studies by Krajina, et al., and Whicker, et al., in the early 1970's. Furthermore, Golding-Wood succeeded in that the symptoms of nasal hypersecretion associated with vasomotor rhinitis by section of the greater superficial petrosal nerve were seen in a small craniotomy.

Thus, the pathophysiological explanation for the nasal hypersecretion seen in our patients likely relates to the parasympathomimetic state caused by surgical interruption of the sympathetic innervation of the nasal cavity after skull-base surgery. The exacerbation of symptoms following exertion or during hot weather likely represents a relative hyperemia of the affected nasal mucosa, due to the parasympathomimetic state with its concomitant nasal hypersecretion.

That the syndrome occurs despite sectioning of the greater superficial petrosal nerve can be reconciled as follows. One explanation may be that, in a minority of patients, there is parasympathetic reinnervation of the nasal mucosa without concomitant sympathetic rein-

**Diagnosis**

Cerebrospinal fluid leakage following skull-base surgery is a well-recognized complication that may lead to bacterial meningitis. Rhinorrhea may be due to a breach of the paranasal sinuses abutting the meninges, which have been violated surgically or traumatically. Another possibility is that rhinorrhea may be secondary to a CSF fistula from the posterior fossa to the nose via opened mastoid air cells and the eustachian tube. Cerebrospinal fluid rhinorrhea is usually identified by the patient or by the nursing staff who notes the leakage of clear fluid from the patient's nose. In questionable cases where the medical history is unclear or the findings are uncertain, assay of the fluid for β transferrin has been advocated as the most sensitive and specific test for identification of the fluid as CSF. Our cases presented such clear histories of rhinorrhea in the setting of surgical procedures well known to be at risk for postoperative CSF leakage that the fluid was assumed to be CSF without biochemical confirmation. In several cases, if we had had the opportunity to obtain biochemical evidence (β transferrin) that the nasal fluid was, in fact, not CSF, we could have avoided investigations and repeat surgery.

The diagnosis of pseudo-CSF rhinorrhea is made if the following features are present: 1) A skull-base procedure involving exposure, manipulation, and/or resection of the petrous or cavernous ICA and the associated autonomic nerves in the region has been performed. 2) Rhinorrhea occurs ipsilateral to the surgical procedure, which is typically exacerbated following exertion. An increase in room temperature, or feelings of intense emotion may also worsen the rhinorrhea. The rhinorrhea may begin within months or up to 2 years postoperatively, particularly if the capability to exercise has been limited due to a prolonged period of rehabilitation. 3) Lacrimation is absent ipsilateral to rhinorrhea. 4) Physical examination confirms the presence of rhi-
norhea and rules out signs of meningitis. 5) Testing of the fluid for β₂ transferrin is negative. The response to sympathomimetic agents or parasympathetic antagonists lends further support to the diagnosis.

If symptoms are bothersome to patients, the syndrome can be treated with a sympathomimetic amine such as pseudoephedrine or parasympathetic blockers such as atropine and intranasal atrovent in an attempt to restore autonomic homeostasis to the nasal mucosa.

Conclusions

We recommend that patients with apparent CSF rhinorrhea, in the appropriate clinical settings, have the fluid assayed for β₂ transferrin before other investigations or surgery aimed at repair of the leakage are undertaken. A high index of suspicion for the syndrome we have described will allow the astute clinician to manage these patients appropriately.

References


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