Chapter 7
Cerebrospinal Fluid Fistulae

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Clinical Scenario

A 27-year-old man presented to the Emergency Department (ED) following an assault. He was neurologically intact. He suffered extensive right periorbital swelling and underwent an emergent lateral canthotomy. Upon leaning forward, clear fluid leaked from the patient's right nostril.

7.1 History and Neurologic Exam

A thorough history is very important in determining the etiology of a cerebrospinal fluid (CSF) leak or fistula. A CSF fistula occurs when CSF drains via the paranasal sinuses, external ear, or a cutaneous tract. The terms are often used interchangeably [1]. The leak may also be occult.

7.1.1 Cranial CSF Leaks

Cranial CSF leaks may be divided into those of traumatic/iatrogenic and those of non-traumatic origin.

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7.1.1.1 Traumatic and Iatrogenic

Over 80% of CSF leaks and fistulae result from trauma, including falls and motor vehicle accidents that leave patients with basilar skull fractures [2, 3]. Skull fractures are identified in 6–12% of patients with head injuries [3]. About one fifth of these fractures involve the skull base, and 10–30% of patients with basilar skull fractures will develop a leak or fistula [3]. There is an increased risk of leak in patients with anterior cranial fossa skull fractures [3–5]. Anterior cranial fossa fractures usually result in rhinorrhea, and very rarely oculorrhea [5, 6]. Middle cranial fossa fractures can result in otorrhea or rhinorrhea, as the middle ear communicates with the nasopharynx via the Eustachian tube [5, 7]. Interestingly, there are reports of traumatic leaks following nasal swab testing for the novel coronavirus [8–10]. Sinus and cranial surgery are also risks for iatrogenic leaks.

In patients with a CSF leak following trauma, **perform primary and secondary surveys and rule out life-threatening injuries**. The patient's level of consciousness should be assessed immediately and monitored regularly, and the Glasgow Coma Scale (GCS) score should be recorded. These patients can have additional intracranial pathology, including hematomas, impacted foreign bodies, and depressed skull fractures requiring surgery, and can deteriorate quickly from these injuries [2, 3, 5]. A thorough cranial nerve examination is necessary to evaluate for concomitant olfactory, optic, oculomotor, trochlear, abducens, facial, and/or cochlear nerve injuries [2]. Patients may have obvious anosmia. Occasionally, urgent decompression of these nerves, especially the optic or facial nerve, is necessary [2]. Patients may suffer hearing loss, which can be conductive, central sensorineural, peripheral sensorineural, or a combination of these mechanisms [11]. Evaluate for hemotympanum and look for CSF in the external auditory canal [11].

Provocation maneuvers may also be helpful. Evaluate for headache and other symptoms with position change. In patients with a concern for CSF rhinorrhea, have the patient sit up and lean forward. Evaluate for leakage. Patients with CSF otorrhea may have worsening symptoms when moving the ipsilateral side down [12], and a formal otolaryngology evaluation is warranted.

7.1.1.2 Non-traumatic

Some skull base and ear malformations result in CSF leaks and meningitis in children. Occasionally, these are found after myringotomy/tube placement [13]. Patients with normal labyrinth anatomy can develop leaks from the petromastoid canal, a widened cochlear aqueduct, a persistent Hyrtl's fissure (this usually closes at 24 weeks' gestation), or the facial canal [14]. Spontaneous cranial leaks may be related to increased intracranial pressure (ICP). Evaluate for signs and symptoms of elevated ICP. Rule out idiopathic intracranial hypertension (IIH), which is often seen in young obese females [4]. If there is any concern for IIH, the patient should undergo formal ophthalmologic evaluation.

Fig. 7.1 T2-weighted MRI showing bilateral encephaloceles at the level of Meckel's cave

Symptoms of elevated ICP include headaches that are worse in the morning or while lying flat, nausea, vomiting, pulsatile tinnitus, and blurry vision [4]. Increased ICP can thin and erode the skull base, and the brain can herniate through small defects, forming encephaloceles and meningoencephaloceles [4]. The herniated brain tissue is often not functional and may pose a risk for intracranial infection [15]. Figure 7.1 shows the T2 MRI sequence of a patient with bilateral encephaloceles at the level of Meckel's cave.

7.1.2 Spinal CSF Leaks

Like their cranial counterparts, spinal CSF leaks can be spontaneous or traumatic/iatrogenic. However, **a spinal CSF leak usually presents differently than a cranial leak.** Regardless of the etiology, spinal CSF leaks often cause significant postural headaches that are worse with standing and relieved when lying flat. Occasionally, patients develop subdural hematomas from intracranial hypotension and may present with a rapid decline in mentation [1]. In alert patients with concern for a spinal CSF leak, have the patient move between the flat and upright positions. Assess for headache, nausea, and other symptoms. Altered patients with spinal CSF leaks may improve quickly after being placed flat or in the Trendelenburg position [16, 17].

Calcified disk herniations, usually in the thoracic spine, can cause ventral dural tears that allow CSF egress. Nerve root sleeve tears can also result in CSF leak, and patients can also develop CSF-venous fistulae [18–20]. Fistulae can also form between the spinal subarachnoid space and pleura or mediastinum after spinal surgery, cardiothoracic surgery, chest tube placement, or trauma [1, 21, 22]. Yoshor et al. used non-invasive, positive-pressure ventilation successfully to treat a persistent subarachnoid-pleural fistula. Their patient underwent surgery for an L1 burst fracture, developed the fistula, and failed treatment with a chest tube thoracostomy and lumbar drain prior to this intervention [23].

Ask patients about a personal or family history of connective tissue disorders. Schievink et al. found that there may be an association between spontaneous spinal CSF leak/intracranial hypotension and these disorders [16, 24]. These disorders can also complicate wound healing and the patient's postoperative recovery [25, 26].

7.1.3 Postoperative CSF Leaks

Evaluate the incisions of any postoperative patients with concern for CSF leak. Palpate for a soft collection and look for CSF egress. A contained pseudomeningocele may not pose problems, but persistent CSF leakage impairs wound healing and increases the risk of meningitis [17].

7.1.4 Delayed and Occult CSF Leaks

Most leaks present immediately, but delayed leaks can present weeks to months later with CSF rhinorrhea, otorrhea, or signs of a spinal leak [1]. Occasionally patients have recurrent bouts of meningitis before a diagnosis is made [7, 13, 27, 28]. Some patients are misdiagnosed with allergic rhinitis [29]. A history of trauma, recent or remote surgery, cancer diagnosis, nasopharyngeal swabbing, lumbar puncture, and/or signs and symptoms of a skull base tumor, cancer, or increased intracranial pressure can help elucidate the cause of CSF leak in patients without obvious trauma or risk factors.

The patient in the current clinical scenario presents with obvious signs of facial trauma. The patient should be evaluated for the presence of cranial neuropathies. He should be examined for signs associated with skull base fracture (Battle's sign, raccoon eyes, etc.), as well as for violation of the tympanic membranes. The observation of clear rhinorrhea should immediately raise concern for the presence of a skull base fracture, with clinical evidence of a CSF leak, and prompt further diagnostic evaluation.

7.2 Differential Diagnosis

The differential diagnosis for clear fluid egress or collection depends on anatomic location.

7.2.1 *Cranial*

Broadly, the differential for rhinorrhea includes allergic rhinitis, nonallergic perennial rhinitis, nonallergic rhinitis with eosinophilia, infectious rhinorrhea (bacterial or viral), and vasomotor rhinorrhea (like that seen in cluster headaches) [30]. The differential for otorrhea with temporal bone involvement includes otitis media, cholesteatoma, and tumors, including sarcomas and Langerhans cell histiocytosis [31].

7.2.2 *Spinal*

Pathologies presenting with postural headaches include postural orthostatic tachycardia syndrome (POTS), cervicogenic headaches, and other primary headache disorders [18].

7.2.3 *Postoperative*

Surgical incisions with clear drainage should be evaluated for infection, seroma, and fat necrosis, in addition to CSF leak.

A patient presenting with unilateral clear rhinorrhea in the setting of trauma—as in the current clinical scenario—should prompt further diagnostic evaluation, with a suspicion for an anterior skull base fracture. Other possible etiologies for rhinorrhea are much less likely given the clinical context provided.

7.3 Diagnostic Evaluation

Following a thorough history and physical examination, imaging can be very helpful to provide a structural anatomic correlate for clinical observation.

7.3.1 *Cranial*

Obtain a formal otolaryngology consultation when patients have CSF rhinorrhea or otorrhea. Nasal endoscopy, laryngoscopy, and otoscopy may be warranted. Imaging evaluation should start with a high-resolution, noncontrast head CT with soft tissue and bone windows [3]. Evaluate for fracture, congenital, or acquired bony anomalies/defects, air/fluid levels, and pneumocephalus [3, 11]. Also, look for signs of elevated ICP, like an empty sella, and for pneumatized bony sinuses [4]. The lateral recess of the sphenoid sinus, the ethmoid roof, and cribriform plate are common sources of spontaneous leaks [4]. CT cisternography may be helpful when the fistula site is unclear. This study requires a lumbar puncture, with intrathecal injection of an iodinated contrast agent. The patient is tilted with the head down [32]. Thereafter, a high-resolution CT scan is performed, as shown in Fig. 7.2, which demonstrates a CSF leak into the left sphenoid sinus. MR myelography is also feasible but requires off-label intrathecal gadolinium injection. An older method of fistula detection involves intrathecal injection of a radioactive tracer. Pledgets are placed in the nasal sinuses and then examined for radioactivity, with the goal of localizing the leak site [1, 19, 20, 32, 33].

Intrathecal fluorescein injection, first described by Kirchner and Proud in 1960, can be very helpful in the operating room [33]. Fluorescein turns bright green when it encounters CSF, allowing the surgeon to readily visualize the fistula. Figure 7.3 shows intraoperative use of fluorescein during an endoscopic, endonasal resection

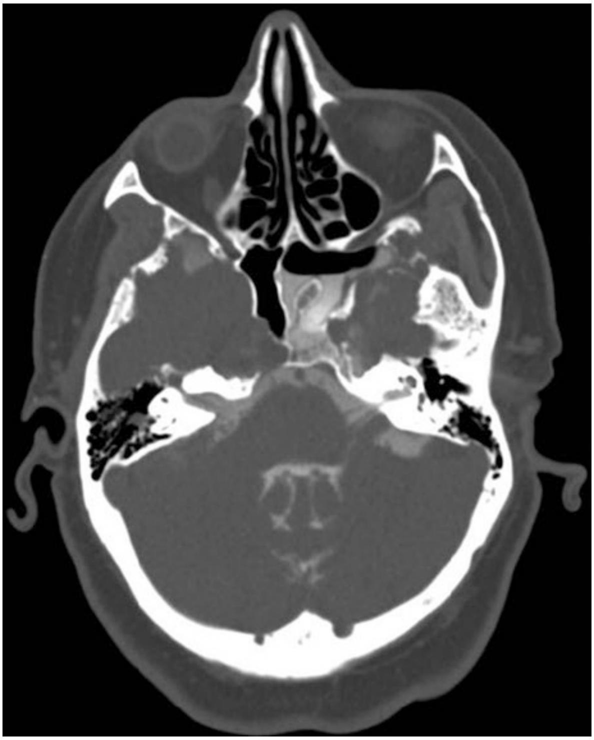

Fig. 7.2 CT cisternogram utilizing Omnipaque contrast demonstrates a CSF leak into the left sphenoid sinus

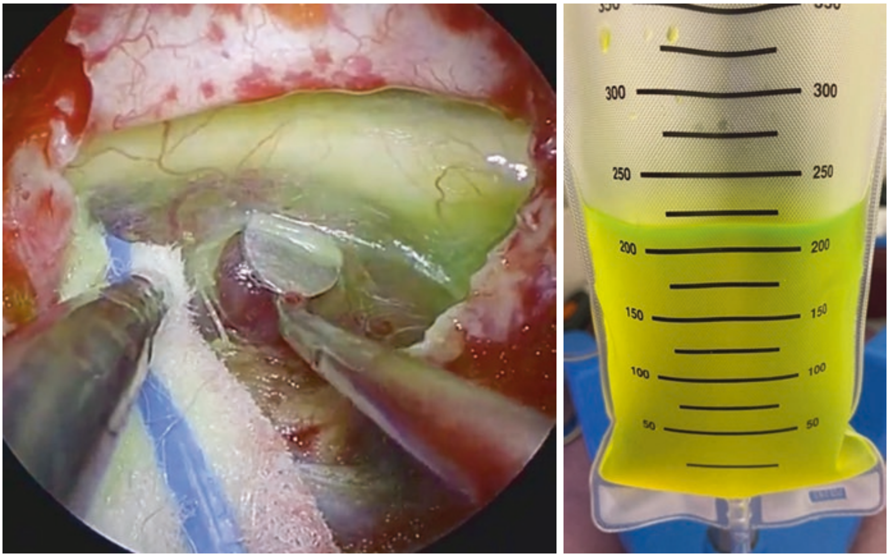

Fig. 7.3 Intraoperative use of fluorescein (left) showing green CSF circulating in the subarachnoid space during an endoscopic, endonasal approach to a craniopharyngioma, and bright green CSF in a lumbar drain system (right) after fluorescein use

of a craniopharyngioma, with green CSF circulating in the subarachnoid space during the procedure (left) and bright green CSF that has reacted with fluorescein in the lumbar drain collection bag (right).

Note that intrathecal use of fluorescein is off-label. Premedicate patients with a steroid (dexamethasone) and an antihistamine (diphenhydramine) [34]. Standard 10% fluorescein dye is diluted to 1% using preservative free saline. One milliliter (mL) of the diluted fluorescein is then mixed with 10 mL of the patient's CSF and slowly injected into the spinal subarachnoid space, usually via a lumbar drain [35]. Rare adverse effects with fluorescein administration include headaches, seizures, vomiting, paresthesias and radiculopathy, hemiparesis, transverse myelitis, and lower extremity weakness [3, 34, 35]. These effects may result from meningeal irritation; the combination of steroids and antihistamine may counter that [34]. Antihistamines also mitigate the increases in plasma histamine seen in patients receiving intravenous fluorescein [36]. Some surgeons apply the dye topically to reduce the risk of a systemic or intrathecal fluorescein injection and necessary lumbar drainage [37].

7.3.2 Spinal

Patients with spinal CSF leaks can be evaluated with noncontrast CT, MRI, myelography (CT or MRI), or newer techniques like digital subtraction myelography [19, 20, 38, 39]. Perform a noncontrast head CT to rule out an extra-axial collection—either subdural hematoma or hygroma. MRI may demonstrate findings associated

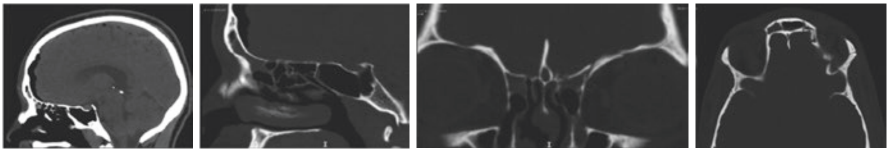

Fig. 7.4 Noncontrast CT head demonstrated pneumocephalus (left image) and skull base fractures (right three images) in a patient with CSF leak following assault

with intracranial hypotension, including diffuse dural enhancement, brain sagging, and venous sinus dilatation [18]. Diffuse dural enhancement is the most common abnormality [18–20]. On spinal imaging, a nerve sheath may dilate or appear irregular at the site of a dural tear and leak. Myelography can occasionally demonstrate contrast extravasation from the subarachnoid space into a vein in patients with CSF-venous fistulas [18, 20, 39].

7.3.3 Unclear Cases

Occasionally, it is unclear if expressed fluid from the nares, ear, or surgical site contains CSF. Two markers indicative of CSF are β2-transferrin and beta-trace protein (βTP). Patients with ocular trauma can have false positive β2-transferrin values, since the aqueous humor contains the substance, and βTP values may be unreliable in patients with bacterial meningitis or renal insufficiency [1, 5, 12]. The β2-transferrin values can take several days to result. βTP testing may be more helpful in some instances when the assay is available and can be performed readily.

For the patient in this case scenario—suspected to have a cranial CSF leak of traumatic origin—noncontrast CT head (Fig. 7.4) showed significant scattered pneumocephalus (left), and bone window revealed fractures of the bilateral orbits, cribriform plate, ethmoid bones, and frontal sinus (right).

7.4 Clinical Decision-Making and Next Steps

Cranial and spinal CSF fistulae can require different treatments.

7.4.1 Cranial

Initial treatment of a cranial CSF leak includes bedrest with the head elevated. It is important to minimize straining, coughing, sneezing, and nose blowing. Laxatives and cough suppressants may be helpful. Acetazolamide can reduce CSF pressure by reducing CSF production; monitor for metabolic acidosis. Over 70% of traumatic CSF rhinorrhea cases and almost all CSF otorrhea cases resolve with these measures [1, 12]. Spontaneous leaks often require intervention [1, 3, 12]. While these patients are at risk for developing meningitis and brain abscess, prophylactic antibiotics are not recommended. A Cochrane review including five studies and 208 patients with CSF leaks from basilar skull fractures found no benefit of antibiotic administration [40].

Patients with cranial CSF leaks who fail to respond to conservative measures after 5–7 days can undergo lumbar puncture or lumbar drain placement [41]. Patients with lumbar drains must be monitored in the ICU, as overdrainage can lead to tentorial herniation and death [12, 41]. The goal of drainage is to lower the CSF pressure and let the fistula heal [1, 3, 15]. If the leak persists, additional workup and direct surgical repair may be needed. Also, consider surgery in patients with spontaneous leaks [1].

A range of surgical approaches are available for management of cranial origin CSF leaks; the choice of surgical procedure depends in part upon the anatomic localization of the leak and in part upon the comfort of the operative team with various techniques. The fistula site should be located with imaging preoperatively and/or fluorescein intraoperatively. Aid from otolaryngology can be helpful during endoscopic cases, when a CSF fistula involves the inner or middle ear, and in patients with bony anomalies [13, 27].

Extracranial approaches to the fistula, including endoscopic, endonasal surgeries, are often successful in patients with CSF rhinorrhea and anterior skull base pathology. Frontal sinus fractures can also be repaired through extracranial approaches, using a bicoronal, forehead (within a crease or existing laceration), or naso-orbital incision to allow exposure and repair of the frontal sinus [5]. Intradural approaches may be needed for large defects that cannot be closed through the endoscopic, endonasal route. Sometimes direct primary dural repair is feasible; pericranial flaps can reinforce the closure and seal off other defects. Fibrin glue is helpful in adhering the pericranium to the dura [3, 15].

Fat, fascia, dural substitutes, and fibrin glue can be used to plug and seal bony defects; a multilayer closure may be necessary and is most effective [1, 3, 13, 15, 27]. Nyquist et al. used a DuraGuard (Biovascular Corp, Minneapolis, MN, USA) inlay, fat, fascia lata, and fibrin glue in small leaks, and incorporated MedPor (Stryker Corporation, Kalamazoo, MI, USA), vomer bone, or titanium plates as needed in their series of endoscopically repaired leaks [15]. Vascularized grafts from the mucosa or turbinates and nasoseptal flaps can also be helpful [42, 43]. For large leaks, some surgeons use a "gasket seal" technique [15, 44]. A large soft tissue graft, like fascia lata, is placed in the defect, and then buttressed with a rigid graft like bone or MEDPOR® (Stryker, Kalamazoo, MI). The soft tissue graft should circumferentially surround the rigid graft. A vascularized flap and fibrin glue are used on top of the repair [15, 45].

CSF fistulas in the middle fossa can also be repaired using extracranial approaches, including transmastoid and transnasal approaches through the maxillary sinus [46]. Intracranial, intradural approaches risk injury to the vein of Labbe,

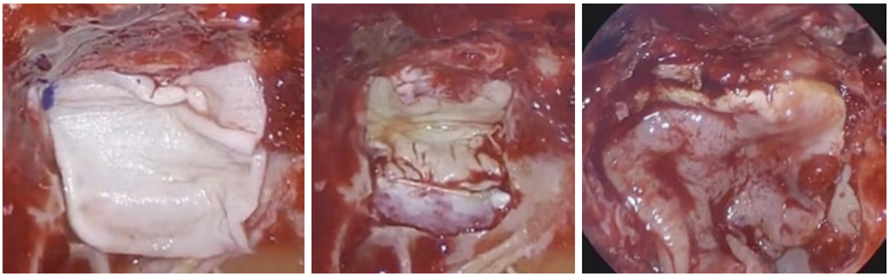

Fig. 7.5 CSF leak repair with a dural substitute (left) that is eventually tucked under the native dura (middle), covered with Surgicel® (not shown; Johnson & Johnson, New Brunswick, NJ, USA) and then sealed with a nasoseptal flap (right)

but extradural approaches may require traction on the facial nerve [3, 47]. Pericranial grafts are again helpful [3]. Prevent mucocele formation either by stripping away mucosa as needed (and "cranializing" the frontal sinus) or by ensuring that the mucosa has a safe pathway to drain its secretions [48]. The multilayer closure described above can be used during these operations [15, 45]. Figure 7.5 shows a dural substitute and nasoseptal flap used in skull base reconstruction after an endoscopic, endonasal tumor resection.

A lumbar or external ventricular drain can be used to minimize CSF pressure on the repair in the perioperative period. The patient should be monitored for the development of significant pneumocephalus after leak repair with CSF diversion [1, 12, 13, 15, 41]. If multiple surgeries fail to resolve a cranial or spinal leak, consider CSF diversion with a shunt. CSF diversion may also be needed in patients with increased intracranial pressure [15, 49]. These patients may not develop signs and symptoms of hydrocephalus until after fistula repair [1, 15, 38]. A classic example of this phenomenon is the postoperative Chiari decompression patient who returns with a CSF leak at the surgical site—ultimately determined to have occurred due to unrecognized, co-morbid hydrocephalus.

7.4.2 *Spinal Leaks*

CSF leaks and fistula from penetrating trauma generally require direct surgical repair. Often there will be other serious injuries to address, especially in penetrating trauma [2, 22, 48]. Iatrogenic CSF leaks are more common than their traumatic counterparts. Unfortunately, iatrogenic postoperative leaks can significantly impair patients' recovery, increase the risk of serious infection, and add to health care costs [50]. Durotomies that occur during minimally invasive, tubular procedures like microdiscectomies can be challenging to repair primarily. Faltings et al. present two cases in which patients undergoing microdiscectomies experienced CSF leaks [51]. Both had complete resolution of their symptoms following administration of an epidural blood patch (EBP). Some patients also can be managed conservatively, and the incision can be oversewn as needed [1].

Woodruffe et al. advocate for primary repair, use of a fibrin glue, and consideration of lumbar drain placement at the index surgery [50]. In their series, delayed re-exploration was associated with longer hospital stay and increased infection risk. In general, patients with lumbar leaks should be flat for 24–48 h postoperatively to minimize pressure on the repair although there is some debate on this topic [17]. Patients with cervical and thoracic leaks should be positioned upright for a similar period to divert CSF away from the repair by gravity. Surgical drains should be used with caution; some argue that the suction generated by them can pull CSF, weaken the surgical repair, and impair fistula closure [17, 50]. Patients who undergo multiple unsuccessful attempts at repair should be considered for shunt placement [50].

7.4.3 Spontaneous Leaks

Conservative measures can be tried in patients with spontaneous intracranial hypotension and spinal CSF leak, but these may fail in upwards of 80% of patients [18]. Medical management includes hydration, caffeine, and bed rest [19]. The next line of treatment is an EBP. Multiple authors report success using EBP in patients with disc herniations or spontaneous nerve sheath tears [1, 18, 19]. Long-segment blood patch can be performed in patients when workup has failed to identify a specific leak source [19].

Subdural effusions may resolve after EBP alone. Therefore, patients who have brain MRI hallmarks of intracranial hypotension that include extra-axial collections should be considered for EBP [19]. Direct drainage may result in worsening of the extra-axial collections, risking neurological decline and a need for further surgery [16, 52]. Collections can also recur if the underlying leak is not addressed [52]. Figure 7.6 shows the noncontrast head CT of a patient who underwent a craniotomy for tumor resection, with an intraoperative lumbar drain. She was readmitted several days later with worsening positional headaches and an epidural fluid collection. Her symptoms resolved and scan improved after an EBP was placed. She was discharged approximately 24-h after the EBP and did not require additional treatment.

An EBP can also help patients with persistent headaches following lumbar puncture or drainage. If a blood patch fails, consider targeted fibrin glue injection [18, 19, 53]. If that also fails, consider surgery and direct repair of the fistula after successfully localizing the lesion [18, 20]. Surgery may require nerve root ligation since most leaks occur in the thoracic spine, this is generally tolerated [20].

Occasionally, patients treated for spontaneous intracranial hypotension (SIH) develop rebound intracranial hypertension. In a series of 113 patients, Schievink et al. found rebound high-pressure headaches in 27% [54]. These patients were more often female, younger, and had spinal extradural CSF collections. Some of the patients who developed intracranial hypertension also suffered from transverse sinus stenosis. These patients may require shunt placement [4, 15, 54].

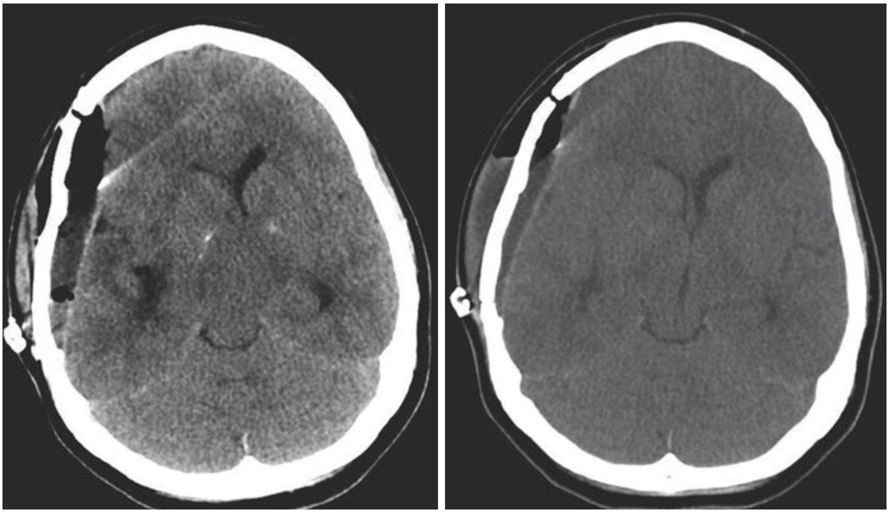

Fig. 7.6 Noncontrast CT head showing an epidural fluid collection and air following craniotomy with lumbar drain (left). Following epidural blood patch, the patient's postural headaches resolved completely, and a post-procedure CT head performed 18 h later showed decrease in the collection (right)

The patient in the current clinical scenario was admitted to the intensive care unit, placed on bedrest, and started on acetazolamide. The cerebrospinal fluid rhinorrhea persisted despite these measures. A lumbar drain was placed, with five milliliters of CSF drained hourly for 5 days. Serial X-rays were performed to monitor for pneumocephalus. The drain was clamped without return of rhinorrhea, and the patient was discharged home without further intervention.

7.5 Clinical Pearls

- All patients with head injuries, especially those with basal skull fractures, should be evaluated for CSF leak.
- Spinal injuries, fractures, and surgery can also cause CSF fistula formation.
- A fistula can go unrecognized for days, months, or even longer. Intermittent and slow leaks can be difficult to diagnose, and patients with spinal CSF leaks may be treated for headaches and other problems before a leak is considered.
- Various imaging modalities and dyes are useful for locating the fistula site and guiding repair.
- Treatments for CSF leaks depend on the location and etiology, and can include conservative management, blood patches, and surgery.
- Prophylactic antibiotics are not recommended.
- An untreated CSF leak or fistula can lead to meningitis, pneumocephalus, brain or spine abscess, hydrocephalus, and death.

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