

## LITERATURE REVIEW

# Current insights in CSF leaks: a literature review of mechanisms, pathophysiology and treatment options

Elena Patrascu<sup>1,2</sup>, Claudiu Manea<sup>1,2,3</sup>, Codrut Sarafoleanu<sup>1,2,3</sup>

<sup>1</sup>“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

<sup>2</sup>ENT&HNS Department, “Sfanta Maria” Hospital, Bucharest, Romania

<sup>3</sup>CESITO Center, “Sfanta Maria” Hospital, Bucharest, Romania

## ABSTRACT

A cerebrospinal fluid (CSF) leak occurs when there appears a fistula between the dura and the skull base and it is usually characterized by discharge of cerebrospinal fluid from the nose. Cerebrospinal fluid leaks may have many etiologies, the most common being trauma. The most common site of dural lesion is the cribriform plate of the ethmoid.

Diagnosis can be achieved by a multitude of techniques, high-resolution computed tomography being the modality of choice and it may be completed with magnetic resonance imaging or cisternography.

Treatment may be either conservative, either surgical, related to the cause, the site and the duration of CSF leak. Conservative treatment usually includes strict bed rest, elevated bed head and no straining, nose blowing or stretching, with resolution of the majority of traumatic CSF leaks in seven days. Surgical treatment consists of a variety of approaches (intracranial/extracranial, open/endoscopic). The future trend is represented by minimally invasive endoscopic approaches, with a success rate of almost 90%; however, open transcranial or extracranial interventions still have indications in the surgical management.

CSF leaks must be correctly diagnosed and treated, because the risk of intracranial complications increases 10-fold when the leakage persists.

**KEYWORDS:** cerebrospinal fluid, rhinorrhea, endoscopic, intracranial, grafting.

## INTRODUCTION

The present article is a review of the mechanisms underlying the cerebrospinal fluid leak, as well as the diagnostic and therapeutic methods.

Cerebrospinal fluid (CSF) leak is a severe condition, with lethal risks, because of the high odd of cerebral complications occurrence (meningitis, brain abscess, etc.). Almost 80% of all cases appear in patients with head lesions and craniofacial fractures. Even if in the current medical practice there are advanced technical modalities for the diagnosis, the management and appropriate surgical approaches, difficulties still remain in debate<sup>1</sup>. The main reason for applying rapidly the treatment is the risk of intracranial infectious complications.

## PATHOPHYSIOLOGY

Cerebrospinal fluid is made of water, electrolytes ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Mg}^{2+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Cl}^-$  and  $\text{HCO}_3^-$ ), glucose (60-80% of blood glucose), amino-acids and different proteins (22-38 mg/dL). It has no colour; it is clear, with polymorphonuclear cells and mononuclear cells ( $< 5/\mu\text{L}$ ).

The main site of cerebrospinal fluid production is represented by the choroid plexus, responsible for producing 50-80% of the daily volume. Other production sites are the ependymal superficial layer (almost 30%) and the capillary ultrafiltration (almost 20%).

Cerebrospinal fluid is the final product of the plasma ultrafiltration of the epithelial cells in the choroid plexus, which lines the cerebral ventricles, process catalyzed by  $\text{Na}^+/\text{K}^+$ ATP-ases<sup>1,2</sup>.

The hourly rate of CSF production is 20 ml, with a total daily rate of 500 ml. In the central nervous system, 90-150 ml of circulating CSF can be found at any time. Hydrostatic differences between the production rate and the absorption rate are responsible for maintaining the level of circulating cerebrospinal fluid. A pressure of 10-15 mmHg is considered as a normal value for CSF, while elevated pressures (>20 mmHg) determine high intracranial pressure (ICP)<sup>2</sup>.

CSF leak is a relatively rare, but potentially severe condition, in case of treatment absence. The underlying condition that leads to CSF discharge into the nasal cavities is the disruption of the limits between the rhinosinusal cavities and the anterior and middle cerebral fossae. The communication with the central nervous system may determine multiple infectious complications, with high morbidity and potentially severe patient outcome<sup>3,4</sup>.

Most frequently, we encounter CSF leaks in the anterior cerebral fossa, because it has the most sites of congenital weakness and also the sites that are related to the specific surgery type.

The lateral lamella of the cribriform plate is proved to be involved in almost 40% of the cases, while a frontal sinus walls defect is found in 15% of the cases. The sella turcica, along with the sphenoid sinuses, are also involved in 15% of the times<sup>5</sup>.

In case of endoscopic sinus surgery, we commonly find lesions of the posterior ethmoid wall, near the antero-medial sphenoidal wall, and lesions of the lateral lamella of the cribriform plate. Less frequently, middle or posterior cerebral fossae are involved and, in this particular case, the leak may reach the nasal cavities through the Eustachian tube or the middle ear. In these cases, patients report aural fullness sensation due to an effusion in the middle ear<sup>5</sup>.

## EPIDEMIOLOGY

The underlying etiology of the CSF rhinorrhea determines its frequency. The general classification includes traumatic, iatrogenic and spontaneous/idiopathic causes for CSF leaks (Figure 1).

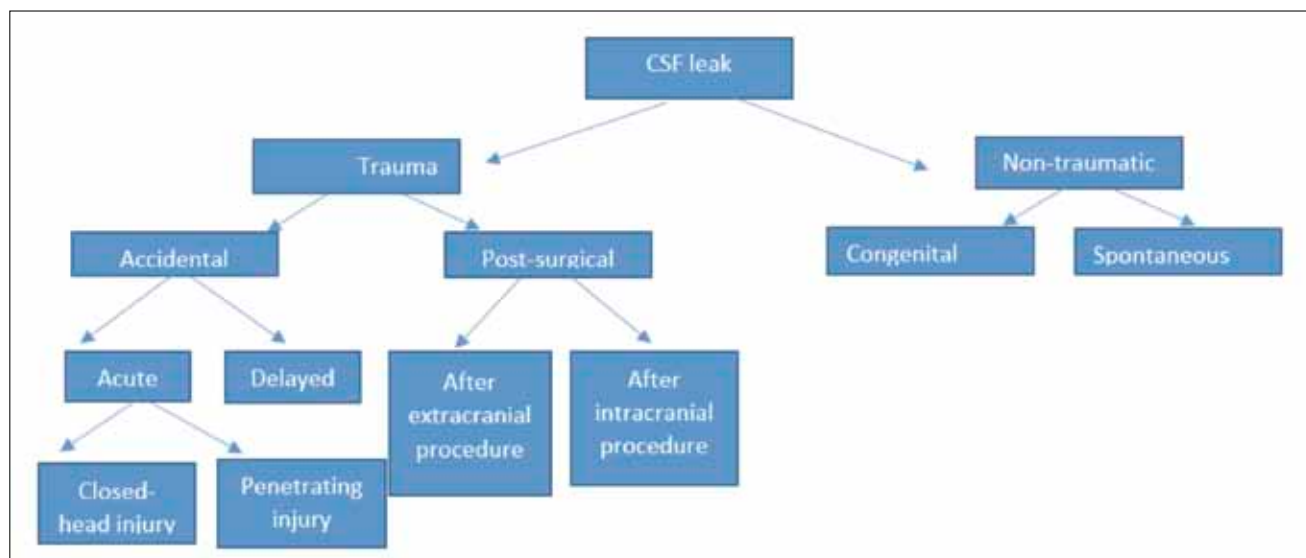
### *Traumatic CSF leaks*

This category is usually divided into iatrogenic and non-surgical causes.

Traumatic causes (penetrating and blunt cranio-facial lesions) represent approximately 80% of all CSF leaks, being most common in young males. Basilar skull fractures are involved in 12-30% of cases, more common in the anterior cranial fossa. At this level, the dura has a high adherence to the skull base and it can easily be affected by injuries. When examining the cases with major head trauma, only 2-3% of them determine a CSF leak<sup>6</sup>.

Regarding the latency of occurrence, they are classified as immediate or delayed: 60% are present in the first 3-4 days after the incident, 70% are present in the first 7 days and 95% are present in the first 3 months after trauma. For a CSF leak to appear immediately after an injury, a bony fracture or defect must be found, along with a dural lesion. Most patients with a CSF leak consequent to an accidental trauma (motor vehicle accident) present immediately. In case of delayed posttraumatic leakages, a previously intact dura may herniate during time through a bony defect of the skull base. As other theories postulate, it is possible for the bony defect and dural tear to coexist, but the leakage only occurs after the cerebral hematoma necrosis or after the wound contraction<sup>2</sup>.

Iatrogenic trauma represents 16% of traumatic cases for CSF leak. Basically, any surgical intervention



**Figure 1** Classification of cerebrospinal fluid leak

adjacent to the skull base may provoke an iatrogenic CSF rhinorrhea. Skull base lesions may vary in dimensions, from a simple bony crack to great (>1 cm) defect, along with dural disruption of the dura mater and, eventually, cerebral tissue.

In the previous decades, neurosurgical interventions (craniotomy, excision of pituitary tumors or suprasellar masses) were the most common causes of iatrogenic CSF leak. Otolaryngology procedures (septoplasty, endoscopic sinus surgery), may determine skull base defects and CSF rhinorrhea. Nowadays, FESS (functional endoscopic sinus surgery) became the number one cause of iatrogenic CSF leaks, with an odd of appearance less than 1% of total surgical endoscopic procedures.

The most frequent site of lesion during ESS (endoscopic sinus surgery) procedures is the lateral lamella of the cribriform plate (80%), usually right-sided, because of the thickness of the bone in the anterior skull base. Other sites of common injuries include the frontal sinus (8%), the sphenoid sinus (4%) and the posterior fovea ethmoidalis. What surgeons have to keep in mind is that, once the CSF leak is produced, the goal remains the intra-operative repair of the injury, through a variety of techniques (free-mucosal, fat tissue or muscle fascia).

Compared to traumatic leaks, iatrogenic CSF leaks occur in only 50% of patients during the first week after the surgery. In most of the cases, the patients are already discharged when the leakage appears. It is important to inform the patient about the most frequent symptoms present in case of a CSF leak.

#### *Tumoral CSF leaks*

In case of benign tumors, their rhythm of growth does not usually determine CSF rhinorrhea. There are also cases of locally aggressive tumors, like inverted papilloma and neoplasms (nasopharyngeal carcinoma, osteomas), that may erode the bone in the anterior cranial fossa. The bony destruction by mass effect may lead to local inflammation and potential dural disruption. Even though the tumors by themselves do not determine CSF rhinorrhea, the resection surgery typically provokes immediate leakage. The surgeon should be aware of this complication and should be able to repair the defect, through transcranial or endoscopic procedures.

#### *Congenital CSF leaks*

Persistence of the anterior neuropore after birth may determine the herniation of the meninges through the anterior cranial fossa (meningo-encephaloceles). These are uncommonly associated with CSF leaks. Meningo-encephaloceles usually appear in childhood like an intranasal or extranasal tumoral mass, transilluminating, which expands when the

child cries (Furstenberg sign). Suspicion should be kept in mind in case of all pediatric intranasal tumoral masses, especially those arising from the midline. The biopsy should be performed only after we have obtained complete imaging investigations<sup>7</sup>.

Persistent craniopharyngeal canal is another congenital lesion that may determine CSF rhinorrhea. Primary Empty Sella Syndrome is a congenital condition that may lead to CSF leak and it may be associated with intracranial tumors, hydrocephalus or Pseudotumor cerebri.

#### *Spontaneous CSF leaks*

Spontaneous CSF leak appears in patients without any antecedent causes, but as a consequence of an intracranial process, elevated intracranial pressure (ICP). High-pressure leaks appear to be involved in 45% of the non-traumatic cases of CSF leaks.

In literature, there are named different causes of high intracranial pressure, but the most frequent remains the idiopathic mechanism. Some studies show that obstructive sleep apnea syndrome is also correlated to elevated ICP. Elevated intracranial pressure is increasingly common, most frequent in obese females and it is thought to appear due to constant pulsations of arachnoid granulations. The anterior cranial base dura is affected by the CSF pressure variations, due to multiple factors (respiration and arterial pressure fluctuations, Valsalva-like maneuvers when blowing the nose), that may lead also to dural lesions in the bony floor defects.

Regardless the causes of high intracranial pressure, the secondary mechanisms are the same: the pressure exerted on the thin sites of the anterior skull base (lateral cribriform lamella, lateral recess of the sphenoidal sinus) determine ischemia by vessels compression, bone thickening and bony remodeling, with a defect formation. Through this defect, the dura may herniate and form meningoceles or, if the defect is big, the cerebral parenchyma can also herniate through (encephalocele)<sup>8</sup>.

A study conducted by Lieberman et al on patients with spontaneous CSF rhinorrhea proved that they had multiple simultaneous bony defects in the skull base<sup>4</sup>. The researchers found that intracranial hypertension represents a determining factor for the appearance of these defects.

There are also described CSF leaks cases associated with normal intracranial pressure, representing 55% of non-traumatic cases of CSF rhinorrhea.

## **DIAGNOSIS**

In order to institute rapidly the optimal treatment and have a favourable prognosis, it is essential to make

the diagnosis correctly. The diagnostic steps are well established and we must have a detailed anamnesis, physical examination and paraclinical investigations.

#### *Anamnesis*

The first step of the diagnosis of CSF leak should be based on the patient's detailed anamnesis, followed, after clinical suspicion, by laboratory tests for CSF markers<sup>9</sup>. Diagnosis is easier to be made in the case of the patients with recent surgeries or trauma than in other patients. In case of delayed fistulas, there are some difficulties of diagnosis and the CSF leak may appear also years after the trauma. In these cases, it is possible to misdiagnose the leak as a vasomotor or allergic rhinitis<sup>10</sup>.

The most frequent symptom in CSF leak is clear, watery nasal discharge from a single nostril, but if the trauma occurred recently, it can be mixed with blood. In the supine position, the volume of nasal discharge may increase. Leakage can also be intermittent due to the accumulation of cerebrospinal fluid in one paranasal sinus and its externalization through the nostril when the head position changes (the "reservoir sign")<sup>11</sup>.

The patients may also experience a salty taste. Most of the patients do not have headache, but the presence of this symptom should increase the suspicion of high intracranial pressure and intracranial lesions<sup>12,13</sup>. It is important if the headache disappears with the leakage. Anamnesis should reveal the presence of meningitis associated with the leak.

In some cases, associated symptoms may help us localize the site of the leak. Presence of anosmia (60% of post-traumatic rhinorrhea) is a sign of an injury of the anterior fossa and olfactory area<sup>14</sup>.

Optic nerve deficit and visual impairment suggest a lesion of the sellar tuberculum, the posterior ethmoidal cells or the sphenoid sinus. In case of recurrent meningitis, patients should undergo evaluation for the defects that expose the meninges to the upper airways, regardless of the presence or absence of CSF leak<sup>15</sup>.

In the acute phase, right after the trauma, patients may have epistaxis, chemosis, periorbital ecchymosis, visual impairment, anosmia or cranial nerve deficits (most frequently, I-III and V-VII) and meningitis<sup>6,16-18</sup>.

In the chronic phase following the trauma, patients may experience intermittent nasal watery discharge, recurrent meningitis or brain abscess, headaches, salty/sweet taste in the rhinopharynx, hyposmia. The risk of developing posttraumatic recurrent meningitis varies from 12.5% to 50%, with a rate of 29.4% of neurological complications<sup>16</sup>.

Being able to differentiate CSF rhinorrhea from other nasal secretions remains the cornerstone of diagnosing CSF fistulas.

In the case of patients with severe posttraumatic CSF rhinorrhea, the diagnosis is clear and needs only a confirmation. In some cases, the presence of blood clots or epistaxis secondary to facial fractures may complicate the diagnosis, as well as the latency of appearance of CSF rhinorrhea<sup>18</sup>.

#### *Physical examination*

Physical examination consists of complete rhinologic, otologic, ophthalmologic and neurologic evaluations.

Clinical examination and nasal endoscopy may reveal the presence of encephaloceles or meningoceles. When the patient performs the Valsalva maneuver or when both jugular veins are compressed (Queckenstedt-Stookey test), we may identify the presence of the CSF leak. In many cases, the physical evaluation may not be conclusive, especially in those patients with intermittent CSF leakage<sup>19</sup>.

In some cases, we may observe the "target sign", which expresses the ability of cerebrospinal fluid to migrate and to create a bull's eye stain, surrounding the central bloody spot, on a filter paper. This traditional sign has however low specificity and it can also be produced by tears or saliva<sup>20</sup>.

Clinical examination of the patients with bilateral rhinorrhea does not offer much information for finding the site of the defect. When the midline structures (the vomer, crista galli) are disrupted, cerebrospinal fluid may leak paradoxically to the opposite nostril.

#### *Laboratory tests*

Laboratory tests are very important for diagnosing CSF leak. From all the tests that have been proposed over the years, only one managed to remain the gold standard in determining the presence of cerebrospinal fluid and that is the test for beta-2-transferrin.

Beta-2-transferrin is a protein of the central nervous system, produced under neuraminidase activity. Because it is not normally found in the nasal secretion, its presence is an indirect marker of CSF rhinorrhea. For the test, it is necessary to collect a volume of 0.5 ml of fluid. The test is highly sensitive (99%) and specific (97%)<sup>21</sup>.

Other tests include beta-trace protein, found in the cerebrospinal fluid (35-fold higher levels than serum), heart tissue and plasma, but it has lower specificity than beta-2-transferrin. It may be elevated in cases of renal insufficiency, multiple sclerosis, central nervous system tumors. Nevertheless, the test has the advantage of being quickly to perform, in about 15 minutes, being able to detect very low levels of CSF in the nasal secretion. Other advantages of the beta-trace protein are similar to the beta-2-transferrin test: non-invasive, repeatable, easy sample collection methods, elevated sensitivity<sup>21-24</sup>.

In the past, glucose testing was performed, because it was easy and it was the most available marker, but it was proved that it has poor sensitivity and specificity<sup>25,26</sup>

#### *Imaging methods*

The following step in diagnosing CSF leak, after clinical suspicion, is based on the imaging methods. After the confirmation of the CSF rhinorrhea, the next step consists in identifying its exact site and establishing the optimal treatment. Localizing the site is, basically, the most important aspect that allows us to expect a successful repair. Imaging investigations are the gold standard in this case.

High-resolution computed tomography (CT) examination, with axial, coronal and sagittal reconstructions is the imaging method of choice used for identifying skull base defects, associated with cerebrospinal fluid rhinorrhea (Figure 2). The images should be 1 mm thick<sup>27</sup>.

CT scans are able to demonstrate the presence of skull base defects after iatrogenic or accidental trauma, as well as various anatomic conditions, hydrocephalus or pneumocephalus and tumoral masses<sup>28</sup>. It is recommended to make CT scans in all cases of suspected bony defects of the skull base.

Supplementary, the CT scan may be used in conjunction with intrathecal contrast substance (iopendylate), the imaging modality being termed CT cisternography. The study is much more invasive, but it has greater accuracy in identifying the exact location of a bony defect and a CSF leak. CT cisternography is proved to have almost 100% rate of detection when the patient has an active CSF leak. In cases of intermittent leaks, this rate of detection is hardly 60%<sup>29</sup>. In order to perform this investigation, we must place, under endoscopic control, pledgets in the anterior plate of the cribriform, in the middle meatus or in the sphenoidal recess. When radioactivity is regis-



**Figure 2** Cranio-facial CT scan, coronal section – 2 areas of posttraumatic disruption of the right ethmoidal roof.

tered through the pledgets, the diagnosis of fistula is sure, although the technique does not provide data about the exact site.

Another imaging method used is magnetic resonance imaging (MRI), with high specificity for soft tissue lesions and CSF. It is able to differentiate the CSF leak of other intrasinusoidal fluids, due to the hyperintense signal on T2-weighted imaging characteristic for a CSF leak<sup>30</sup>. MRI may also be used with intrathecal dye administration to improve its accuracy. This imaging modality has a lower specificity than CT in detecting defects of the skull base and the price is much higher.

Magnetic resonance imaging cisternography, performed with intrathecal administration of Gadolinium contrast medium, is a method whose accuracy needs to be proved by further studies.

There are also cases of occult fistulas, in patients with recurrent meningitis, without CSF rhinorrhea, when the diagnosis becomes much more difficult and all imaging methods should be put in balance, for an optimal therapeutic decision.

#### *Intrathecal tracers*

In the past years, there have been many nuclear medicine tests used for localizing the site of CSF leaks, but the disadvantages are greater than the information provided.

Radionuclide cisternography is a method that requires intrathecal administration of a radioactive tracer (Technetium99, I131, Indium111). Pledgets must be placed in the sites of CSF leak suspicion. The method is not in the current use, because it is hard to perform, it does not identify intermittent leak and the radioactive isotope is absorbed into the blood<sup>31,32</sup>.

Many surgeons identify the area of CSF leaks by injecting Fluorescein intrathecally, both preoperatively and intraoperatively. The patient is roughly examined 30-60 minutes later with an endoscope. In most of the cases, Fluorescein coloration can be observed without any filters. In case of small defects, the fluid is detectable only by using filters, black light. The method is not FDA approved, as it may become neurotoxic in high doses. The accuracy of the test depends on the surface of the dural disruption, fluid volume, time of examining after injection, as well as the rate of fluorescein turnover<sup>33</sup>.

## **TREATMENT OPTIONS OF CSF LEAKS**

The treatment of CSF leak can be divided into conservative and surgical management. Usually, posttraumatic CSF leak resolves only with conservative treatment, but in the case of spontaneous CSF leaks, surgical therapy is recommended.

In case of refractory CSF leaks, we must apply complex therapeutic methods, which consist of observation, CSF reduction and surgery (intracranial or extracranial procedures). Negative prognostic factors in the management are loss of consciousness on admission and the coexistence of intracranial lesions within posttraumatic CSF leaks<sup>34</sup>. Practitioners must decide carefully the optimal time and the way of treating this condition.

Conservative treatment is efficient in posttraumatic leaks, taking into consideration that they have a great odd of spontaneous resolution. Basically, conservative management consists of bed rest<sup>35</sup>.

The patient must stay in bed, for 7-10 days, keeping the head of the bed elevated at 15-30 degrees, in order to reduce CSF pressure at the level of the basal cisterns. Stool softeners must be used, for reducing the strain and the level of intracranial pressure. The patient must not strain, cough, blow his nose, neither to perform heavy lifting. It has been shown that, using this management, 75-80% of all traumatic CSF rhinorrhea may spontaneously resolve in seven days.

Antibiotherapy in case of CSF leak still remains controversial. It is used for preventing the appearance of intracranial infections, like meningitis<sup>36</sup>. Many studies have noticed no difference in the prevention of the cerebral complications with or without antibiotics. The administration of antibiotics during FESS is acceptable, because, due to the intracranial invasion, meningitis may occur.

When there is an increased ICP, diuretic use should be considered. For example, acetazolamide, a diuretic that inhibits the conversion of water and CO<sub>2</sub> to bicarbonate and H<sup>+</sup>, can lower ICP by reducing the activity of Na<sup>+</sup>/K<sup>+</sup> ATP-ases responsible for CSF production. Thus, acetazolamide can be a useful adjunct in the treatment of patients with spontaneous CSF rhinorrhea associated with elevated intracranial pressure<sup>37,38</sup>, but care should be taken to the side effects (e.g. diarrhea, nausea, metabolic acidosis, polyuria, paresthesia).

An adjunctive method is also the lumbar drain and it should be taken into consideration after the failure

of 5-7 days of the previous management. Continuous drainage is preferred over intermittent drainage, because it prevents CSF pressure spikes. The recommended rate for CSF drainage must be about 10-15 cc/hr, in order to prevent adverse effects, like nausea, headaches and emesis<sup>39</sup>. It should be noted that lumbar drain is not recommended for initial management following skull base surgery or large bony defects. A study conducted by Albu et al.<sup>40</sup> noticed that, in patients with closed head trauma and CSF rhinorrhea, leakage time may be diminished by the early placement of a lumbar drainage.

In selected cases (Table 1), surgical intervention remains the only valuable method in the management of CSF leak. This treatment is only contraindicated in the patients medically unstable for a general anesthesia. The surgical management of CSF rhinorrhea depends on the cause, location and severity of the leak.

General principles applicable in the management of CSF leaks are the following: (1) to treat meningitis and hydrocephalus, before performing any surgical procedure; (2) to identify the dural defect site and extension; (3) to dissect the bone and dural defect; (4) to directly repair the dura, when possible; (5) to close by grafts, when the direct dura repair is impossible.

Preoperative CT scans should be performed. If available, the stereotactic image-guided technique is valuable in identifying the dural defect (Figure 3). A multidisciplinary team formed of otolaryngologist, anaesthesiologist and neurosurgeon is essential for a favourable outcome.

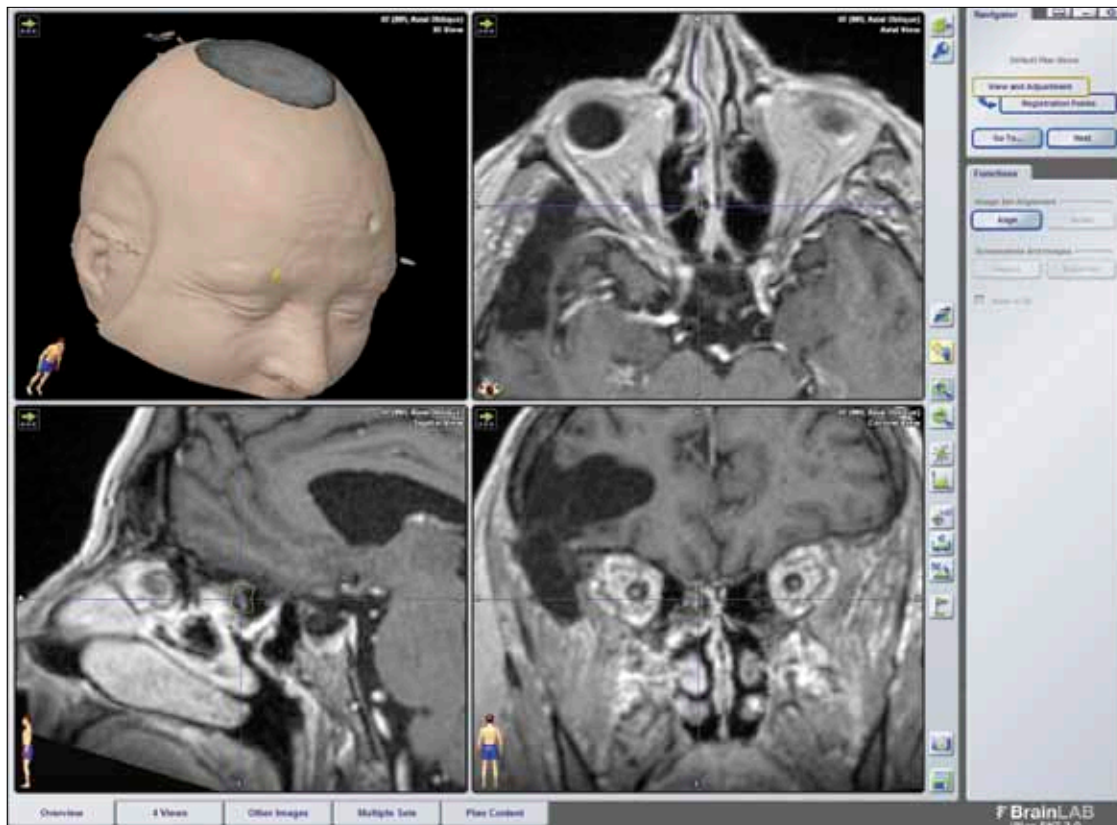
In cases of iatrogenic CSF leaks, the moment of repair should be at the same time as the principal surgery.

The surgical treatment of CSF leak is divided into intracranial and extracranial intervention.

Intracranial approaches are used in case of comminuted or extended skull fractures and hemorrhages in cranial fractures or contusion, which require craniotomy<sup>25</sup>. The main advantage of this technique is the direct visualization of the dural defect and cortical in-

**Table 1**  
**General Indications of Surgical Intervention**

Recurrent episodes of meningitis and permanent leak, despite conservative treatment	High pressure leaks and hydrocephalus
Large pneumocephalus (> 2ml), despite conservative management	Imaging appearances for decreased probability of natural dural repair (bone erosion, skull base comminution, soft tissue interposed in the bony edges)
Acute traumatic/post-operative leaks that persist or recur in 10-13 days after conservative treatment	CSF leaks and congenital brain dysplasia; especially after an episode of meningitis
Intermittent/delayed leak	



**Figure 3** Intraoperative navigation-guided system image – disruption of the posterior region of the left ethmoidal roof and a 5-6 mm meningocele, at 2 cm anteriorly of the anterior sphenoidal wall.

juries, which allows a better patching of the disruption. The disadvantages (high morbidity, increased hospitalisation, anosmia, cerebral injuries with seizures and behaviour disorders) are important and must be minimized as much as possible<sup>18,41</sup>.

Once the endoscopic surgery entered in the common use, the surgical treatment of CSF leaks changed significantly. Being able to expose the nasal roof allowed to identify the site of the CSF leak and improved the postoperative outcome<sup>42</sup>.

Nowadays, endoscopic intranasal surgery is the method of choice in the management of CSF leaks, due to its reduced morbidity (no brain retraction, no additional risk of anosmia) and its great field of vision. Nevertheless, this method must identify very precisely the site of the fistula, in order to correctly place the graft<sup>43-47</sup>. Several different endoscopic approaches have been developed, according to the dural defect localization.

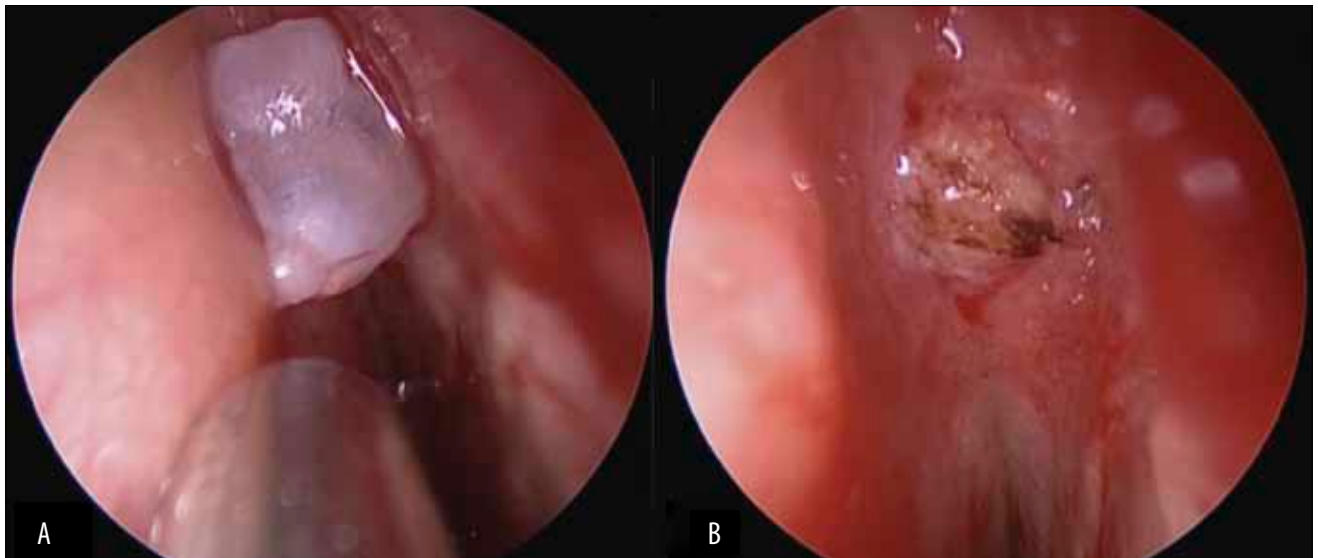
The main step of an endoscopic treatment is the good exposure of the dural defect, using also, in low flow cases, intrathecal fluorescein. Initially, if an encephalocele is found, it should be removed carefully. For a good exposure, the surgeon must expose 0.2-0.5 cm of the bone surrounding the defects and the remaining mucosa inside the defect must be excised be-

fore repairing, in order to prevent mucocele formation; it also stimulates osteogenesis and it improves graft acceptance<sup>43,48</sup>.

In the current practice, various types of grafts are used, but their size should be no bigger than 30% of the defect dimension. The types of grafting material are cartilage (septum), bone (septal, mastoid tip, iliac crest), septal or turbinate mucosa, fascia (fascia lata, temporalis), abdominal fat, pedicled septal flaps or turbinate flaps<sup>49</sup>. It is important to remind that the pedicled flaps may tint or fold and contract.

There are many facts that may influence the option for a certain graft type: defect size and location, level of intracranial pressure, personal experience and material availability<sup>50</sup>.

The techniques of grafting can be divided into: overlay (directly over the defect), underlay (between the dura mater and the bony defect) and combined methods. For the reinforcement after the graft placement, fibrin glue and autologous abdominal fat are also used. A mucosal fragment from the septum of the middle turbinate may be also placed as an overlay graft. To better seal the defect, fascia (temporalis muscle or fascia lata) offer additional support (Figure 4). After all the grafts are set in place, the defect repair is fixed with Gelfoam® and non-absorbable nasal pack-



**Figure 4** Left ethmoidal roof dura defect and meningocele – intraoperative endoscopic aspect, before (A) and after (B) ablation and grafting with temporalis fascia and human fibrin glue.

ing, to increase pressure on the site. Surgeons must pay attention not to obliterate the adjacent sinus ostia.

The size of the dura defect is an important parameter when planning the surgical intervention, regarding the number of layers and the type of graft material. During dura obliteration, we must apply the main principle - “watertight closure”.

The studies have shown that, when the defect has less than 2 mm, the type of grafting is not important for the success of the intervention. For defects of 2-5 mm, it is recommended to use overlay grafts (mucosal graft or flap), in absence of important dural lesions. If the fracture is comminuted, we should use composite graft. For defects greater than 5 mm, composite grafts or grafts made of mucosa and bone are the method of choice.

Postoperative care should consist of bed rest, with the head of the bed elevated at 15-30° for 3-5 days. The blood pressure should be kept at a normal value and antibiotherapy should be administered.

## CONCLUSIONS

Cerebrospinal fluid leaks represent a serious, potentially severe condition, which requires immediate diagnosis and appropriate treatment, because, in its absence, the risk of meningitis increases by 10 fold. The most frequent etiology remains the traumatic lesions, either from iatrogenic or surgical causes.

The therapeutic results depend on the cause, size of the dural defect, timing of applying the treatment and patient comorbidities. Usually, in approximately 7-10 days, under conservative treatment of the most post-traumatic CSF leaks, complete resolution in ex-

pected<sup>51</sup>, while spontaneous CSF leaks usually require surgical intervention.

**Conflict of interest:** The authors have no conflict of interest.

**Contribution of authors:** All authors have equally contributed to this work.

## REFERENCES

1. Mantur M., Łukaszewicz-Zajęc M., Mroczko B., Kulakowska A., Ganslandt O., Kemoni H., Szmitkowski M., Drozdowski W., Zimmermann R., Kornhuber J., Lewczuk P. - Cerebrospinal fluid leakage—reliable diagnostic methods. *Clin Chim Acta.*, 2011;412(11-12):837-840. doi: 10.1016/j.cca.2011.02.017. Epub 2011 Feb 17.
2. Nuss D.W., Constantino P.D. - Diagnosis and management of cerebrospinal fluid leaks: highlights of the instructional courses of the American Academy of Otolaryngology - Head Neck Surgery. *Otolaryngol Head Neck Surg.*, 1995;8:79-95.
3. Schlosser R.J., Bolger W.E. - Nasal cerebrospinal fluid leaks: critical review and surgical considerations. *Laryngoscope*, 2004;114(2):255-265.
4. Lieberman S.M., Chen S., Jethanamest D., Casiano R.R. - Spontaneous CSF rhinorrhea: prevalence of multiple simultaneous skull base defects. *Am J Rhinol Allergy.*, 2015;29(1):77-81. doi: 10.2500/ajra.2015.29.4121.
5. Lemonnier L.A., Tessema B., Kuperan A.B., Jourdy D.N., Telischi F.F., Morcos J.J., Casiano R.R. - Managing cerebrospinal fluid rhinorrhea after lateral skull base surgery via endoscopic endonasal eustachian tube closure. *Am J Rhinol Allergy.*, 2015;29(3):207-210. doi: 10.2500/ajra.2015.29.4146.
6. Eljamel M.S., Foy P.M. - Post-traumatic CSF fistulae, the case for surgical repair. *Br J Neurosurg.*, 1990;4(6):479-483.
7. Woodworth B.A., Schlosser R.J., Faust R.A., Bolger W.E. - Evolutions in the management of congenital intranasal skull base defects. *Arch Otolaryngol Head Neck Surg.*, 2004;130(11):1283-1288.
8. Woodworth B.A., Prince A., Chiu A.G., Cohen N.A., Schlosser R.J., Bolger W.E., Kennedy D.W., Palmer J.N. - Spontaneous CSF leaks: a paradigm for definitive repair and management of intracranial hypertension. *Otolaryngol Head Neck Surg.*, 2008;138(6):715-720. doi: 10.1016/j.otohns.2008.02.010.
9. Park J.I., Strelzow V., Friedman W.H. - Current management of cerebro-

- spinal fluid rhinorrhea. *Laryngoscope*, 2009;93(10):1294-1300.
10. Kerr J.T., Chu F.W.K., Bayles S.W. - Cerebrospinal fluid rhinorrhea: diagnosis and management. *Otolaryngol Clin North Am.*, 2005;38(4):597-611.
  11. Meco C., Oberascher G. - Comprehensive algorithm for skull base dural lesion and cerebrospinal fluid fistula diagnosis. *Laryngoscope*, 2004;114(6):991-999.
  12. Mokri B., Atkinson J.L., Piepgras D.G. - Absent headache despite CSF volume depletion (intracranial hypotension). *Neurology*, 2000;55(11):1722-1724.
  13. Mokri B., Hunter S.F., Atkinson J.L.D., Piepgras D.G. - Orthostatic headaches caused by CSF leak but with normal CSF pressures. *Neurology*, 1998;51:786-790.
  14. Mathias T., Levy J., Fatakia A., McCoul E.D. - Contemporary approach to the diagnosis and management of cerebrospinal fluid rhinorrhea. *Ochsner J.*, 2016;16(2):136-142.
  15. Bernal-Sprekelsen M., Alobid I., Mullol J., Trobat F., Tomas-Barberan M. - Closure of cerebrospinal fluid leaks prevents ascending bacterial meningitis. *Rhinology*, 2005;43(4):277-281.
  16. Cassano M., Felippu A. - Endoscopic treatment of cerebrospinal fluid leaks with the use of lower turbinate grafts: a retrospective review of 125 cases. *Rhinology*, 2009;47(4):362-368. doi: 10.4193/Rhin08.175.
  17. Scholsem M., Scholtes F., Collignon F., Robe P., Dubuisson A., Kaschten B., Lenelle J., Martin D. -Surgical management of anterior cranial base fractures with cerebrospinal fluid fistulae: a single-institution experience. *Neurosurgery*, 2008;62(2):463-469;discussion 469-471. doi: 10.1227/01.neu.0000316014.97926.82.
  18. Yilmazlar S., Arslan E., Kocaali H., Dogan S., Aksoy K., Korfali E., Doygun M. - Cerebrospinal fluid leakage complicating skull base fractures: analysis of 81 cases. *Neurosurg Rev.*, 2006;29(1):64-71. Epub 2005 Jun 4.
  19. Bolger W.E., Kennedy D.W. - Nasal endoscopy in the outpatient clinic. *Otolaryngol Clin North Am.*, 1992;25(4):791-802.
  20. Dula D.J., Fales W. - The 'ring sign': is it a reliable indicator for cerebral spinal fluid? *Ann Emerg Med.*, 1993;22(4):718-720.
  21. Warnecke A., Averbek T., Wurster U., Harmening M., Lenarz T., Stöver T. - Diagnostic relevance of beta2-transferrin for the detection of cerebrospinal fluid fistulas. *Arch Otolaryngol Head Neck Surg.*, 2004;130(10):1178-1184.
  22. Meco C., Arrer E., Oberascher G. - Efficacy of cerebrospinal fluid fistula repair: sensitive quality control using the beta-trace protein test. *Am J Rhinol.*, 2007;21(6):729-736.
  23. Meco C., Oberascher G., Arrer E., Moser G., Albegger K. - Betatrace protein test: new guidelines for the reliable diagnosis of cerebrospinal fluid fistula. *Otolaryngol Head Neck Surg.*, 2003;129(5):508-517.
  24. Schnabel C., Di Martino E., Gilsbach J.M., Riediger D., Gressner A.M., Kunz D. - Comparison of beta2-transferrin and beta-trace protein for detection of cerebrospinal fluid in nasal and ear fluids. *Clin Chem.*, 2004;50(3):661-663.
  25. Chan D.T., Poon W.S., IP C.P., Chiu P.W., Goh K.Y. - How useful is glucose detection in diagnosing cerebrospinal fluid leak? The rational use of CT and Beta-2 transferrin assay in detection of cerebrospinal fluid fistula. *Asian J Surg.*, 2004;27(1):39-42.
  26. Kosoy J., Trieff N.M., Winkelmann P., Bailey B.J. - Glucose in nasal secretions. Diagnostic significance. *Arch Otolaryngol.*, 1972;95(3):225-229.
  27. Lund V.J., Savy L., Lloyd G., Howard D. - Optimum imaging and diagnosis of cerebrospinal fluid rhinorrhoea. *J Laryngol Otol.*, 2000;114(2):988-992.
  28. Naidich T.P., Moran C.J. - Precise anatomic localization of a traumatic sphenethmoidal cerebrospinal fluid rhinorrhea by metrizamide CT cisternography. *J Neurosurg.*, 1980;53(2):222-228.
  29. El Gammal T., Brooks B.S. - MR cisternography: initial experience in 41 cases. *AJNR Am J Neuroradiol.*, 1994;15(9):1647-1656.
  30. Eljamel M.S., Pidgeon C.N., Toland J., Phillips J.B., O'Dwyer A.A. - MRI cisternography, and the localization of CSF fistulae. *Br J Neurosurg.*, 1994;8(4):433-437.
  31. Jeon T.J., Lee J.D., Lee B.I., Kim D.I., Yoo H.S. - Radionuclide cisternography in spontaneous intracranial hypotension with simultaneous leaks at the cervicothoracic and lumbar levels. *Clin Nucl Med.*, 2001;26(2):114-116.
  32. Horikoshi T., Ikegawa H., Uchida M., Takahashi T., Watanabe A., Umeda T. - Tracer clearance in radionuclide cisternography in patients with spontaneous intracranial hypotension. *Cephalalgia*, 2006;26(8):1010-1015.
  33. Liu H.S., Chen Y.T., Wang D., Liang H., Wang Y., Wang S.J., Wang Y., Chen G.Q., Zuo H.C. - The use of topical intranasal fluorescein in endoscopic endonasal repair of cerebrospinal fluid rhinorrhea. *Surg Neurol.*, 2009;72(4):341-345; discussion 346. doi: 10.1016/j.surneu.2009.03.034. Epub 2009 Jul 15.
  34. Jones N.S., Becker D.G. - Advances in the management of CSF leaks. New techniques will improve the management of unilateral clear nasal discharge. *BMJ*, 2001;322:122-123.
  35. Albert B., Leibrock L.G. - Neurological approaches to cerebrospinal fluid rhinorrhea. *Ear Nose Throat J.*, 2005;71:300-305.
  36. Ratilal B.O., Costa J., Pappamikail L., Sampaio C. - Antibiotic prophylaxis for preventing meningitis in patients with basilar skull fractures. *Cochrane Database Syst Rev.*, 2015;28(4):CD004884. doi: 10.1002/14651858.pub4.
  37. Gosal J.S., Gurmey T., Kursu G.K., Salunke P., Gupta S.K. - Is acetazolamide really useful in the management of traumatic cerebrospinal fluid rhinorrhea? *Neurol India.*, 2015;63(2):197-201. doi: 10.4103/0028-3886.156280.
  38. Carrion E., Hertzog J.H., Medlock M.D., Hauser G.J., Dalton H.J. - Use of acetazolamide to decrease cerebrospinal fluid production in chronically ventilated patients with ventriculopleural shunts. *Arch Dis Child.*, 2001;84(1):68-71.
  39. Caballero N., Bhalla V., Stankiewicz J.A., Welch K.C. - Effect of lumbar drain placement on recurrence of cerebrospinal rhinorrhea after endoscopic repair. *Int Forum Allergy Rhinol.*, 2012;2(3):222-226. doi: 10.1002/alr.21023. Epub 2012 Feb 16.
  40. Albu S., Florian I.S., Bolboaca S.D. - The benefit of early lumbar drain insertion in reducing the length of CSF leak in traumatic rhinorrhea. *Clin Neurol Neurosurg.*, 2016;142:43-47. doi: 10.1016/j.clineuro.2016.01.016. Epub 2016 Jan 13.
  41. Friedman J.A., Ebersold M.J., Quast L.M. - Post-traumatic cerebrospinal fluid leakage. *World J Surg.*, 2001;25(8):1062-1066.
  42. Tosun F., Gonul E., Yetiser S., Gerek M. - Analysis of different surgical approaches for the treatment of cerebrospinal fluid rhinorrhea. *Minim Invasive Neurosurg.*, 2005;48(6):355-360.
  43. Dodson E.E., Gross C.W., Swerdloff J.L., Gustafson L.M. - Transnasal endoscopic repair of cerebrospinal fluid rhinorrhea and skull base defects: a review of twenty-nine cases. *Otolaryngol Head Neck Surg.*, 1994;111(5):600-605.
  44. Hegazy H.M., Carrau R.L., Snyderman C.H., Kassam A., Zweig J. - Transnasal endoscopic repair of cerebrospinal fluid rhinorrhea: a meta-analysis. *Laryngoscope*, 2000;110(7):1166-1172.
  45. Lee T.J., Huang C.C., Chuang C.C., Huang S.F. - Transnasal endoscopic repair of cerebrospinal fluid rhinorrhea and skull base defect: ten-year experience. *Laryngoscope*, 2004;114(8):1475-1481.
  46. Lopatin A.S., Kapitanov D.N., Potapov A.A. - Endonasal endoscopic repair of spontaneous cerebrospinal fluid leaks. *Arch Otolaryngol Head Neck Surg.*, 2003;129(8):859-863.
  47. Marshall A.H., Jones N.S., Robertson I.J.A. - CSF rhinorrhoea: the place of endoscopic sinus surgery. *Br J Neurosurg.*, 2001;15(1):8-12.
  48. Spetzler R.F., Zabramski J.M. - Cerebrospinal fluid fistulae: their management and repair. In: Youmans J.R., editor. - *Youmans Neurological Surgery*. 3rd ed. Philadelphia (PA): WB Saunders Company, 1990;p.2269-2289.
  49. Elmors S.M., Khafagy Y.W. - Endoscopic management of spontaneous CSF rhinorrhea with septal graft and middle turbinate rotational flap technique: a review of 31 cases. *Ear Nose Throat J.*, 2014;93(6):E14-E19.
  50. Landeiro J.A., Flores M.S., Lazaro B.C.R., Melo M.H. - Surgical management of cerebrospinal fluid rhinorrhea under endoscopic control. *Arq Neuro-Psiquiatr.*, 2004;62(3b):827-831.
  51. Adams A.S., Francis D.O., Russell P.T. - Outcomes of outpatient endoscopic repair of cerebrospinal fluid rhinorrhea. *Int Forum Allergy Rhinol.*, 2016;6(11):1126-1130. doi: 10.1002/alr.21810. Epub 2016 Sep 14.

