New techniques and technology to repair cerebrospinal fluid rhinorrhea

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Key words
Nasal disorders • Cerebrospinal fluid leak • Surgical treatment • Endoscopic sinus surgery

Summary
Cerebrospinal fluid rhinorrhea occurs as a result of abnormal communication between the subarachnoid space and the pneumatized portion of the skull base, the paranasal sinuses and the middle ear. Conservative measures may be sufficient in the management of cerebrospinal fluid rhinorrhea, but, in some cases, surgical treatment may be required. Transnasal endoscopic techniques are constantly being used in preference to the intra- and extracranial approaches. Recently, image guidance systems have been adopted in neurosurgery, skull base and paranasal sinus surgery. The present report refers to 4 cases of nasal cerebrospinal fluid leak successfully treated with a transnasal endoscopic approach using various techniques and materials to close the bone defect, in 2 of which, the navigation system (Stealth Station® ENT Image Guidance System with Landmark X™ Software, Medtronic, Xomed, Jacksonville, FL, USA) was also used. In all cases, correct localization and repair of the leak was achieved and no major complications occurred. Following a review of the literature, the Authors conclude that, at present, transnasal endoscopic repair of cerebrospinal fluid rhinorrhea is the surgical treatment of choice when the techniques and materials are correctly used. Furthermore, preliminary findings indicate that it is possible to make routine use of the navigation systems and that this technology may be usefully employed, above all, in the management of cerebrospinal fluid leaks.

Introduction
Cerebrospinal fluid rhinorrhea (CSFR) occurs after a breakdown of all the barriers that separate the subarachnoid space from the nose, the paranasal sinuses and the middle ear. In the present report, attention has not been focused on CSFRs due to an interruption of the roof of the tympanic and mastoid cavities. According to Ommaya’s classification, CSFR may be idiopathic, congenital (meningocele or meningoencephalocele, skull base defects, congenital hydrocephalus), or may be caused by a surgical (open and/or endoscopic sinus surgery, skull base surgery), or non-surgical trauma (closed head injuries, open or penetrating injuries, post-traumatic hydrocephalus), or may be secondary to an inflammatory disease

Parole chiave
Patologia nasale • Fistola liquorale • Trattamento chirurgico • Chirurgia endoscopica dei seni paranasali

Riassunto
La rinoliquorrea si realizza in presenza di una fistola liquorale, ovvero una anomala comunicazione tra lo spazio subaracnoideo e la porzione pneumatizzata della base cranica; il naso, i seni paranasali e l’orecchio medio. Terapie mediche e norme comportamentali possono risolvere episodi di rinoliquorrea, ma spesso è necessario ricorrere alla riparazione chirurgica della fistola per evitare le spiacevoli complicanze. Al giorno d’oggi le tecniche endoscopiche transnasali stanno sempre più soppiantando gli approcci intracranici ed extracranici tradizionali grazie anche all’utilizzo dei sistemi di navigazione chirurgica. In questo lavoro gli Autori descrivono 4 casi di fistole liquorali sottoposti ad intervento chirurgico di riparazione con materiali e tecniche diverse, tramite approccio endoscopico transnasale. In 2 casi ci si è avvalsi dell’uso del sistema di navigazione Stealth Station®, Treon™ ENT Image Guidance System with Landmark X™ Software della Medtronic Xomed, Jacksonville, FL, USA. In tutti i pazienti si è riusciti ad individuare la fistola ed a ripararla, non si è avuta nessuna complicanza maggiore, né minore ed al follow-up endoscopico (6-14 mesi) non si è osservata nessuna recidiva. Dopo un accurata revisione della letteratura possiamo affermare che la tecnica endoscopica transnasale costituisce attualmente il trattamento di scelta nella riparazione delle fistole liquorali sempre che tipo di tecnica e materiali vengano correttamente utilizzati. Inoltre i dati preliminari indicano che i sistemi di navigazione possono essere usati routinariamente nella chirurgia endoscopica dei seni paranasali, ma trovano una delle loro maggiori indicazioni proprio nelle riparazione delle fistole liquorali, in quanto consentono una precisa localizzazione del tramite, ed una maggiore tranquillità del chirurgo, anche grazie alla possibilità di eseguire una pianificazione pre-operatoria.
Repair of cerebrospinal fluid rhinorrhea

(erosive lesions such as mucoceles, polypoid disease and fungal sinusitis, osteomyelitis of the skull base), or a neoplasm invading the skull base. The amount of CSF lost is often clinically insignificant and becomes evident bending the head forwards or with any manoeuvre that increases intra-cranial pressure. Often conservative measures, such as bed rest, raising of the head, avoiding strenuous activities, decrease in CSF pressure with spinal drains or drugs, may lead to an improvement in CSFR. Surgical treatment is indicated when patients do not respond to these procedures, when a CSF leak has been identified during endo-nasal surgery and when infectious meningitis is found to be secondary to a fistula between the nose or the paranasal sinuses and the anterior cranial fossa.

Over the last twenty years, transnasal endoscopic techniques have gradually been preferred to intra- and extra-cranial approaches in the surgical management of CSFR. Recently, image guidance systems have become easier to use and have been extensively applied, in neurosurgery, skull base and paranasal sinuses surgery.

In the present report, personal experience is described in the management of nasal CSFR leak, repaired with a transnasal endoscopic approach, with/without navigation systems.

Patients and methods

Case n. 1, a 20-year-old male with Apert syndrome for which he had undergone, in childhood, frontal decompressive cranioplasty. The patient came to our attention 40 days after an open head injury due to the onset of CSFR. Magnetic resonance (MR) showed a post-traumatic hydrocephalus, with a bilateral subdural hematoma and a right ethmoidal leak (Fig. 1). A lumbar drain was initially positioned but the patient developed bacterial meningitis. Transnasal endoscopic repair of the posterior ethmoidal fistula was then performed.

Case n. 2, a 70-year-old male showed an idiopathic CSFR and was initially treated unsuccessfully with acetazolamide. MR revealed the presence of a meningoencephalocele within the right ethmoid (Fig. 2) and was, therefore, submitted to surgical treatment by means of a transnasal endoscopic approach.

Case n. 3, a 59-year-old male, presenting an inverted papilloma with histological evidence of malignant degeneration, underwent external removal of the lesion by a paralateronasal approach. After surgery, the patient developed CSFR due to a leak in the posterior wall of the frontal sinus which was repaired endoscopically using a (Stealth Station® Treon™ ENT Image Guidance System with Landmark X™ Software, Medtronic, XOMED, Jacksonville, FL, USA) (Fig. 3).
Fig. 2. Case n. 2. Magnetic resonance (MR), in sagittal and coronal planes, reveals meningoencephalocele within right ethmoid (arrows).

Fig. 3. Case n. 3. Intra-operative view showing leak in posterior wall of frontal sinus. With the Treon™ ENT Image Guidance System with Landmark X™ (Medtronic), localization of fistula, at CT scan, allows precise and safe repair of fistula. Crossair on screen provides real-time localization of instrument in 3D reconstructions of previously acquired CT images of patient.
Case n. 4, a 49-year-old female presented with CSFR after a closed head injury. Imaging showed a lesion involving the lateral wall of the left sphenoid sinus. The patient was first treated, unsuccessfully, with a lumbar drain and drug therapy (mannitol). The fistula was repaired by means of a transnasal endoscopic approach and using a navigation system (Stealth Station® Treon™ ENT Image Guidance System with Landmark X™, Software, Medtronic, OMED, Jacksonville, FL, USA) (Fig. 4).

**SURGICAL PROCEDURES**

Following pre-operative antibacterial prophylaxis, surgery was carried out under general anaesthesia in order to avoid major complications due to infection. The endoscopic equipment consisted of rigid optic fibres of 0° and 30°. The patient was placed in a supine position with the head turned toward the surgeon. When no CSFR was evident, positive pressure ventilation was employed to increase intracranial pressure (Valsalva’s manoeuvre). Once the leak was identified, the mucous tissue was cleaned from the bony borders and any fibrous tissue was removed in order to allow close contact between the graft and the bone. Dissection was extended to allow correct placement of the graft. Two slides of synthetic dura (Tutoplast®) were then placed over the defect with the edges pushed under the bony borders (underlay technique). Fibrin glue (Tissucol®) human fibrin glice by BAXTER, Pisa, Italy was used to improve adhesion of the graft. Finally, the mucoperichondrium, obtained from the quadrangular cartilage, was positioned in order to recreate the nasal anatomy resembling, as closely as possible, the original form. In this patient, a new surgical adhesive material (BIOGlue®), Cryolife®, Inc. Kennesaw, Georgia, USA) was used, polymerization of which begins immediately after application, reaching a bonding strength within 2 minutes. This material avoids the use of abdominal fat. Nasal packing with Merocel® Pope Epistaxis Packing by MEDTRONIC, XOMED, Jacksonville, FL, USA supported the graft after the surgical procedure. Image-guided endoscopic surgery was performed in Cases 3 and 4, employing The Stealth Station Treon™ with LandmarkX™ (Medtronic Sofamor Danek, Memphis, Tenn., USA), a computerised surgical navigation system based on optic technology and using both passive and active reflecting systems. It can acquire computed tomography (CT) and magnetic resonance (MR) images from various sources (CD-ROM, ZIP drive, LAN) and reconstruct them in any of the three planes, or produce three-dimensional im-

**Fig. 4.** Case n. 4. Intraoperative view. Crossair on image shows tip of suction positioned in lateral wall of left sphenoid sinus. After opening anterior wall of left sphenoid sinus, the leak was well localized and then repaired with BIOGlue surgical adhesive, mucoperichondrium and, finally, fibrin glue (Tissucol®).
The advances made in technology, the increased experience in the field of endoscopic sinus surgery, but also the increase in iatrogenic leaks occurring during this kind of surgery and the need to close them carefully without delay have allowed rapid development of this technique. 3,4 Patient history, nasal endoscopy, and, when possible, β2 transferrin dosage, in the sample, represent three important steps in the diagnosis of CSFR. 3 In spontaneous CSFR, axial and coronal CT scans and MR are always necessary in order to identify, when possible, defects in the skull base bones, to carefully evaluate the patient’s local anatomy, to exclude the presence of a meningocele or meningoencephalocele or intra-cranial hypertension and, finally, to plan and perform image-guided surgery. When all these diagnostic procedures fail to clarify the clinical suspicion of CSFR, fluorescein-nasal endoscopic evaluation, by means of an intra-thecal injection of 5% sodium fluorescein through a lumbar drain, could be performed. 4 A possible alternative could be intra-operative positive pressure ventilation which increases intra-cranial pressure (Valsalva’s manoeuvre) thus making the leak visible.

When the defect has been clearly identified, the margins must be prepared, and the mucosa removed to allow graft uptake. Local anatomy must be preserved, as far as possible, and only when absolutely necessary, should a complete ethmoidectomy, with or without resection of the middle turbinate, be performed.

Various grafts have been used with almost identical results: mucoperiosteum, mucoperichondrium, bone, cartilage, fat, fascia. These can be classified as: simple free (mucoperichondrium and mucoperiosteum), combined free (bone and simple grafts), composite (simple layers not separated from the underlying bone, such as the middle turbinate, or the septal cartilage with its mucosa) and pedicled graft that, obviously, must be large enough to cover the defect. Free abdominal fat is the preferred material to obliterate the sphenoidal sinus, if leaks are detected in the roof or the lateral wall. 5,7 Recently, new synthetic materials have become available to close the defects of the barrier.

According to Castelnuovo et al. 5 mucoperichondrial and/or mucoperiosteal free flap can be used to close small defects (<3 mm) of the ethmoid cribiform plate and the posterior wall of the sphenoid sinus,
while combined grafts are required for defects >3 mm. In the present cases, we preferred an overlay technique, but the overlay technique seems to yield comparable results 8. We used fibrin glue in order to enhance the adhesion of the graft and stop bleeding 9 and in case n. 4, we successfully used a new strong surgical adhesive (BIOGlue®) with a very short polymerization time which completely obliterated the sphenoid sinus, avoiding the use of abdominal fat.

The success rate of the endoscopic approach in closing nasal CSF leaks is extremely high reaching 90% after the first attempt and rising to 96% after a second surgical procedure 8 10 independently of the cause and size of the defect, choice of material and technique employed 11 12. Meningitis, chronic headache, pneumoencephalus, intra-cranial hematomas, frontal lobe abscess, anosmia, failure to repair the fistula or recurrence with signs of meningeal irritation have been reported as a sequela of trans-cranial endoscopic repair 8.

Peri-operative antibiotic administration appears to contribute to reducing the risk of meningitis following skull base surgery 13, albeit not all Authors agree on this issue 14; Choi and Spann 15 found a significantly higher incidence of meningitis in patients who received prophylacticy antibiotics as compared to those who did not.

Computer-aided surgery is an interesting technology which found one of its major indications in the treatment of CSF leaks. In fact, it reduces peri-operative complications and increases the success rate giving a precise localization of the radiologically marked point of probable leak and allowing a safer surgical procedure due to the high confidence level of the surgeon. Furthermore, it represents a powerful educational tool and can also be used in telemedicine and consulting.

Today, image-guidance systems fall basically within two main types of tracking technologies: electromagnetic and optical, both of which present advantages and disadvantages 16-19.

The electromagnetic systems are based on the reaction between the ferromagnetic components (receiver) and the magnetic field (generated by a transmitter located on the head of the patient), allowing the position of the surgical instrument to be identified. The main limitation of these techniques is that only specific, disposable instruments can be used; nevertheless, with careful handling, it is possible to use each headset and suction tubes for between five and seven successive operations 19 20.

Optical systems can use images acquired with a CT scan, a MR image or a positron emission tomography (PET) scanner, after placing of markers. These markers, or fiducials, are designed to be imaged and then localized in both the image space and the physical space. Once the surgeon has prepared and positioned the patient for surgery, it is necessary to register patient or physical space to image space before images can be used interactively. Once the accuracy of the registration has been assessed, the tracked instrument is moved, in physical space, and the corresponding position, in image space, is displayed and used as a guide during the surgical procedure 21. Optical systems have some drawbacks, such as increased registration time, the need to maintain a clear line of sight between the camera and the instruments and more complex hardware and software which can increase the risk of intra-operative malfunction. On the other hand, these systems allow the use of standard endoscopic sinus instruments, without the concern for interference due to metals.

The main disadvantages limiting widespread, successful, implementation of computer-aided surgery are: the cost 22-25, the time needed for the procedure 17 26-29, the, as yet, not satisfactory capacity to discriminate, which is still around 1.5 mm (due also to the intrinsic limitations of the acquiring systems). It must also be pointed out that this is not real-time technology and does not reflect changes in anatomy occurring during the surgical procedures. Computer-aided surgery, performed with the patient positioned in a live magnetic resonance suite, is only a technology and is still far from having truly widespread clinical application 30.

Conclusion

The high success rate and low morbidity of transnasal endoscopic surgery used in the repair of CSFR make it the surgical treatment of choice, quite apart from the techniques and materials employed. Proper use of imaging techniques is essential for success of the procedure. Preliminary findings indicate that it is possible to make routine use of the navigation systems and that one of the major indications, for this technology, is to be found in the approach to CSF leaks. Larger and more detailed studies are needed in order to determine whether safety during surgery can be improved and the duration of surgery reduced.

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Received: February 11, 2004
Accepted: March 25, 2004

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