ORIGINAL ARTICLE

Endoscopic Surgery in the Skull Base Unit: Experience in the First 72 Cases

Juan R. Gras-Cabrero,*, Fernando Muñoz-Hernández, b Joan R. Montserrat-Gili, a Pere Tresserras-Ribo, b Manuel de Juan-Delago, c Susan M. Webb, d Anna Aulinas-Masó, e Beatriz Martín-Huerta, f Joan Molet-Teixidó, b Miquel Quer-Agustí, a Humbert Masseguer-Solanch a

a Servicio de Otorrinolaringología, Hospital de la Santa Creu i Sant Pau, Universidad Autónoma de Barcelona, Barcelona, Spain
b Servicio de Neurocirugía, Hospital de la Santa Creu i Sant Pau, Universidad Autónoma de Barcelona, Barcelona, Spain
c Servicio de Radiología, Hospital de la Santa Creu i Sant Pau, Universidad Autónoma de Barcelona, Barcelona, Spain
d IIB-Sant Pau, Centro de Investigación Biomédica en Red en enfermedades raras (Unidad 747), Instituto de Salud Carlos III, Servicio de Endocrinología y Nutrición, Hospital de la Santa Creu i Sant Pau, Departamento de Medicina, Universidad Autónoma de Barcelona, Barcelona, Spain
e IIB-Sant Pau, Servicio de Endocrinología y Nutrición, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
f Servicio de Anestesiología y Reanimación, Hospital de la Santa Creu i Sant Pau, Universidad Autónoma de Barcelona, Barcelona, Spain

Received 22 August 2012; accepted 30 October 2012

KEYWORDS
Multidisciplinary team;
Skull base;
Endoscopic surgery;
Pituitary adenoma;
Cerebrospinal fluid leak

Abstract
Introduction: A multidisciplinary team is essential to develop and expand the indications in endonasal endoscopic skull base surgery.

The aim of this study was to present our experience in a group of patients with skull base lesions treated using endonasal endoscopic approach.

Methods: From January 2008 to January 2012, 72 patients with skull base involvement were diagnosed and treated in our centre.

Results: The mean patient age was 53 years. The different pathologies included 36 pituitary adenomas, 10 cerebrospinal fluid leaks and 5 inverted papillomas as the most frequent pathologies. We performed a transphenoidal transtorial approach in 45 cases, a transmaxillary transpterygoid approach in 4 cases and a transnasal expanded approach in 6 cases. We performed an ethmoidal/sphenoidal approach in 12 patients and a Draf IIb/III procedure in four cases. Total resection was achieved in 61% of patients with pituitary adenomas, subtotal in 22% and partial in 17%. Successful repair was achieved in 86% of CSF leaks. No recurrences were observed in patients with inverted papilloma. Complications were observed in 21 patients (29%), 6 being major complications.

* Corresponding author.
E-mail address: jgras@santpau.cat (J.R. Gras-Cabrero).

© 2012 Elsevier España, S.L. All rights reserved.
Integración de la cirugía endoscópica en una unidad de base de cráneo: experiencia en los primeros 72 casos

Resumen

Introducción: La formación de un equipo multidisciplinar es imprescindible para desarrollar y ampliar las indicaciones en la cirugía endonasal endoscópica de la base de cráneo.

El objetivo de este trabajo es presentar nuestra experiencia en el grupo de pacientes con afectación de la base de cráneo intervenidos con un abordaje endonasal endoscópico.

Métodos: De enero de 2008 a enero de 2012, 72 pacientes con afectación de la base de cráneo fueron diagnosticados y tratados en nuestro centro.

Resultados: La edad media de los pacientes en el momento del diagnóstico fue de 53 años. Las diferentes patologías incluyeron 36 adenomas de hipófisis, 10 fistulas de líquido cefalorraquideo y 5 papilomas invertidos como las más frecuentes. En 45 casos se llevó a cabo un abordaje transesfenoidal, en 4 casos un abordaje transmaxilar transpterigoido y en 6 casos un abordaje transnasal ampliado. En 12 pacientes se realizó un abordaje a través del etmoides y/o del seno esfenoidal y en 4 casos se utilizó un abordaje frontal tipo Draf IIB/III. En el 61% de los adenomas se consiguió una resección total, en el 22% subtotal y en el 17% parcial. El 86% de las fistulas de líquido cefalorraquideo se repararon con éxito. No se evidenció ninguna recidiva en los papilomas invertidos intervenidos. En 21 pacientes (29%) ocurrió algún tipo de complicación, apareciendo 6 complicaciones de orden mayor.

Conclusiones: Nuestro centro apuesta por la colaboración multidisciplinar en la cirugía endoscópica de la base de cráneo como línea de excelencia.

© 2012 Elsevier España, S.L. Todos los derechos reservados.

Introduction

The endonasal approach to the skull base has undergone rapid development in recent years, helped by a better understanding of the anatomy of this region, the development of new surgical techniques and reconstruction materials, improvements in imaging studies and navigation systems, and also through interdisciplinary collaboration between different specialties. Thus, the endoscopic endonasal technique used by otolaryngologists in infectious and inflammatory pathologies of the paranasal sinuses began to expand its indications, reaching territories previously treated by other specialties within a few years. However, the main limitation to the progression of this approach was the difficulty in achieving a bimanual dissection, an option so far only offered by the microscope. In 1990, May was the first to describe the endoscopic technique with “4 hands”, allowing 2 surgeons to work in the same surgical field and facilitating treatment of territories which previously seemed inaccessible. Various new pathologies, such as cerebrospinal fluid (CSF) fistulas (or leaks), began to be treated, and it became possible to approach the orbit, the pituitary gland, the anterior skull base, the pterygopalatine fossa and the infratemporal fossa.

Currently, most pathologies located in the skull base are jointly treated by an otolaryngologist and a neurosurgeon using this endoscopic endonasal “4 hands” technique.

The aim of our study is to present our experience analysing the main epidemiological and surgical results of the group of patients with involvement of the skull base, intervened using an endoscopic endonasal approach (EEA).

Methods

The data for the present study were obtained from information contained in the database of our centre, which prospectively collected epidemiological and therapeutic results of skull base pathologies treated exclusively through EEA.

The therapeutic strategy to be followed for each pathology was decided by the Skull Base Committee, which was redefined in 2008, and is comprised by representatives of the Neurosurgery, ENT, Endocrinology, Radiology and Anaesthesiology Services, with occasional advice from an ophthalmologist and/or a pathologist.

A total of 72 lesions with involvement of the skull base were diagnosed between January 2008 and January 2012. Of these, 22% (16/72) were revision surgeries.

All tumours were studied pre- and postoperatively using computed tomography (CT) and magnetic resonance imaging (MRI) scans.

Adenomas were classified into microadenomas and macroadenomas, according to whether tumour diameter was less than or greater than 1 cm, respectively. Invasion of the cavernous sinus was classified according to the lateral extension relative to the internal carotid artery, following the classification proposed by Knoepf et al. Grades 3 and 4 were considered as invasion of the cavernous sinus. The remaining cases (grades 0, 1 and 2) were considered as compression without invasion. A hormonal study was conducted for all pituitary lesions in order to rule out hypersecretion and hypofunction. In addition, an examination of the visual field was carried out if the lesion contacted or
was near the optic chiasm. Tumours secreting growth hormone (GH) were considered cured when GH levels were <1 mcg/l after an oral dose of glucose, with IGF-1 levels within the normal range for the age and gender. In the case of Cushing’s disease, remission was considered upon observation of suprarenal insufficiency (basal cortisol <100 nmol/l [<4 mcg/dl]) and/or when free cortisol urine was undetectable in 24 h or else when morning cortisol suppression was observed after administration of 1 mg dexamethasone at midnight (basal cortisol 50 nmol/l, <1.8 mcg/l). Remission criteria for tumours secreting thyroid-stimulating hormone (TSH) were normalisation of TSH and free T4 after surgery. Remission criteria for tumours secreting follicle-stimulating hormone (FSH) were normalisation of circulating FSH and recovery of menstrual cycles.

Postoperative outcomes were assessed according to tumour resection: total resection (100%), subtotal resection (≥80%) and partial resection (<80%). In addition, we also assessed hormonal evolution for functioning tumours. We performed β2-transferrin detection in nasal and serum secretions, as well as a high resolution CT scan of the skull base for all patients with suspected CSF fistula. We requested isotopic cisternography for cases suffering liquororhea with negative β2-transferrin measurements.

Inverted papillomas were classified according to the Krouse staging system, whilst carcinomas were classified according to the 7th edition of the TNM-UICC system. The minimum follow-up period was 6 months.

### Results

The mean age of patients at diagnosis was 53 years, with a range between 16 and 81 years. In total, 58% of patients (42/72) were females and 42% (30/72) were males. The recorded pathologies included 36 pituitary adenomas, 10 CSF fistulas, 5 inverted papillomas, 4 meningoceles and 4 chordomas, as most frequent pathologies. The distribution of the remaining conditions is shown in Table 1.

A transsellar transphenoidal approach was carried out in 62% of the interventions (45/72), with 6 cases of transsellar approaches expanded to the clivus and 3 cases extended to the sphenoid planum. A transpterygoid transmaxillary approach was employed in 4 cases and an extended transnasal approach was employed in 6 cases (transcribiform in 2 cases, transodontoid in 2 cases and transclival in 2 cases). A total of 12 patients underwent a skull base approach through the ethmoid and/or sphenoid sinus. A Draf-type frontal approach was used in 4 cases (1 Draf III and 3 Draf IIb).

### Pituitary Tumours

In total, 50% of cases were functioning adenomas (18/36), 8 were GH-secreting, 5 were prolactin-secreting, 4 were ACTH-secreting (adrenocorticotropic hormone) and 1 was FSH-secreting. The remaining 50% had no hormonal expression (clinically non-functioning). A total of 38% were diagnosed with symptoms related to hormonal hypersecretion, whilst 22% of cases were incidental findings as the most common form of presentation. The percentage of macroadenomas was 89% (32/36), whilst that of microadenomas was 11% (4/36). Table 2 shows the distribution according to size and functionality.

In total, 34% (11/32) of macroadenomas presented invasion of the cavernous sinus, whilst 72% (23/32) presented invasion-compression of the suprasellar region.

Total resection was achieved in 61% of cases, subtotal in 22% and partial in 17%. Table 3 illustrates the results according to the size of the adenoma and the degree of tumoral resection.

### Table 1: Distribution of the Intervened Pathologies.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Number</th>
<th>Percentage, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pituitary adenoma</td>
<td>36</td>
<td>50</td>
</tr>
<tr>
<td>CSF fistulas</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Inverted papilloma</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Meningocele</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Chordoma</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Basilar impression</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Carcinomas</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Other pathologies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemangioma</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasculitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glomus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningioma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>100</td>
</tr>
</tbody>
</table>

CSF, cerebrospinal fluid.

### Table 2: Distribution of Pituitary Adenomas According to Their Size and Functionality.

<table>
<thead>
<tr>
<th></th>
<th>Non-functioning</th>
<th>ACTH</th>
<th>Prolactin</th>
<th>GH</th>
<th>FSH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microadenoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Macroadenoma</td>
<td>17</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>1</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>4</td>
<td>5</td>
<td>8</td>
<td>1</td>
<td>36</td>
</tr>
</tbody>
</table>

ACTH, adrenocorticotropic hormone; FSH, follicle stimulating hormone; GH, growth hormone.
Hormonal normalisation was achieved in all 8 patients with acromegaly and in the only case of FSH-secreting adenoma. ACTH secretion persisted in 1 patient with Cushing’s syndrome, whilst in 2 patients with prolactinomas, hormonal resolution was not achieved.

A total of 3 patients presented craniopharyngioma with suprasellar extension. Total resection was achieved in all 3 patients, with hormonal deficit being recovered in 1 case. Reconstruction using a nasoseptal flap (Hadad–Bassagasteguy) was performed on all pituitary tumours, previously including fascia lata in those cases in which an intraoperative fistula was observed, as well as in all craniopharyngiomas.

Cerebrospinal Fluid Fistulas – Meningoceles

There were 14 interventions due to CSF fistulas, 4 of them associated with meningocele. In total, 4 patients reported a history of trauma and 3 reported a previous surgical manoeuvre. At least 1 prior episode of meningitis was recorded in 50% of patients (7/14).

There were 7 fistulas located on the roof of the ethmoid, 1 in the cribiform plate, 1 in the clivus and 1 in the sphenoid sinus. Of the meningoceles, 3 were found in the lateral recess of the sphenoid and 1 in the roof of the posterior ethmoid. The fistula was successfully repaired in 86% of cases (12/14).

Malignant Tumours

There were 4 interventions on chordomas located in the clivus, of which 1 female patient had to be reoperated due to tumoral persistence. One case of adenocarcinoma (T3N0) is currently in complete remission at 3 years after surgery and 1 case of adenoid cystic carcinoma (T4bN0) treated with endoscopic surgery after chemotherapy and radiotherapy is currently in complete remission, 6 months after the treatment.

Other Pathologies

There were 4 patients diagnosed with sinonasal inverted papilloma and frontal sinus involvement (Krouse T3) who were operated exclusively with an EEA (1 Draf III and 3 Draf IIb) with no reports of recurrence after a minimum follow-up period of 6 months. One patient presented an inverted papilloma originating in the sphenoid sinus, and remains free of recurrence, 3 years after surgery.

Two patients underwent surgery for decompression of the cervical spine with removal of the odontoid process due to a malformation of the cranio cervical junction (basilar impression). Resections and biopsies were performed in 1 case of vasculitis, 1 case of plasmacytoma, 1 glomus and 1 cavernous sinus haemangioma.

Complications

Complications appeared in 29% (21/72) of cases, with 6 major complications: 3 CSF leaks, 1 injury to the internal carotid in its parasellar portion, 1 intraventricular haemorrhage and 1 case of meningitis. The 3 postoperative fistulas occurred in the immediate postoperative period in 3 patients who underwent surgery for macroadenoma, accounting for 8% (3/39) of pituitary procedures. Two of these cases required lumbar drainage in the immediate postoperative period. Minor complications occurred in 15 cases: 4 cases of postoperative anosmia, 1 case of epistaxis requiring surgical revision, 6 instances of transient diabetes insipidus and 4 cases of hypopituitarism in patients without prior hormonal alterations.

Discussion

Establishing a multidisciplinary team provides professionals with the knowledge and experience of others and enables them to address problems in the most effective way possible. An example is endoscopic endonasal surgery of the skull base, where otolaryngologists and neurosurgeons work together in a team with “4 hands”. At present, different centres are becoming increasingly experienced in the management of pathologies in this region.

Most centres conduct their first “4 hands” procedures in pituitary gland surgery and thus gain sufficient experience to tackle other pathologies, enabling advances in more comprehensive approaches. In the early 20th century, the Viennese otolaryngologist Oskar Hirsch,9 was the first to carry out a transspHENoidal approach without external incisions. After a long period of neglect, surgeons like Norman Dott, Gerard Guiot and Jules Hardy fostered the current development of transspHENoidal surgery, mainly through the introduction of intraoperative fluoroscopy and microscopy.10

In the 1990s, Jankowski11 was the first to perform pituitary surgery exclusively using the endoscope. Subsequently, Sethi,12 the Pittsburgh school13 and the Italian school14–16 eventually popularised and developed this surgical approach route. At our hospital, endoscopic surgery was introduced in the late 1980s and the first case series was published in 1991 by Ademà and Masserué.17 The service continued to gain experience in this type of approach, culminating with the first endoscopic, transspHENoidal, “4 hands” surgical procedure, conducted in collaboration with Hospital Universitari Mutua de Terrassa, in 2005. Fig. 1 shows the historical evolution of this technique and the main events taking place at our hospital in recent decades.9–20

This technique has made it possible to maintain the results obtained with the microscopic approach in the treatment of pituitary adenomas, minimising endonasal iatrogenic damage21 and even improving results in some locations, such as the suprasellar and parasellar regions.22

In a recent metaanalysis, Tabaei et al.23 published total or subtotal resection percentages over 75%, reaching figures of 85%–100% in some series which included only non-functioning adenomas. In our short experience, we have obtained similar resection figures, despite a high percentage of macroadenomas, although the number of patients treated is still limited.

The rates of complete resection in craniopharyngiomas operated by EEA are high, above 85%, with some publications placing them above the transcranial approach.24,25 In our series, we present 3 cases with complete resection of the lesion. The main dilemma in these lesions lies in the
extent of resection. The endoscopic route allows an infrachiasmatic approach without a need to manipulate adjacent neurovascular structures. This contributes to the preservation of pituitary functions and an improvement of visual involvement due to optic nerve decompression. Nevertheless, occasional involvement of the pituitary stalk by tumours represents an alteration thereof, either directly, by the lesion, or indirectly, by involvement of its irrigation, with subsequent panhypopituitarism, despite performing a correct dissection under direct vision.

The EEA is currently the technique of choice in most CSF leaks of the anterior skull base. Wingard\textsuperscript{18} was the first to describe the endoscopic closure of a fistula during an ethmoidectomy.

Success rates usually range between 88% and 94%,\textsuperscript{26} similar to those obtained in our series. In general, in our centre this condition is treated by the otolaryngologist. \textit{A priori}, for small fistulas we employ \textit{fascia lata} covered by a mucosal graft, either free or pedicled. In larger fistulas we attempt to place a double layer of \textit{fascia lata}, inside and outside the bone plane, covered by a pedicled mucosal flap. It is essential to remove the protruding sac in cases of meningocele associated to a fistula. In the case of a fistula located in the posterior wall of the frontal sinus or the presence of multiple posttraumatic defects, we perform a combined external and endonasal approach, with the help of the neurosurgeon.

The EEA is the technique of choice in most benign lesions of the paranasal sinuses and fossa, such as inverted papillomas, fibrous seous lesions or vascular lesions. Currently, involvement of the anterior skull base does not represent a limitation for this approach, since purely endoscopic approaches can be employed for lesions involving the middle cranial fossa. Inverted papillomas and nasopharyngeal angiofibromas are the 2 benign pathologies which have focused most interest, with excellent results being obtained. Our centre has accumulated extensive experience in the treatment of inverted papillomas, and this has allowed us to observe the evolution from the classical external approach to the EEA, which we currently employ to deal with most of these lesions. None of the lesions in our series had its origin in the frontal sinus. Invasion thereof appeared in 10% of cases,\textsuperscript{27} in fact representing a progression of the disease from neighbouring regions towards the frontal sinus. In total, 4 patients underwent an exclusively endoscopic approach through a Draf III/IIb-type endonasal approach.

The number of publications referring to the resection of malignant tumours using an EEA has increased in recent years.\textsuperscript{28-31}

The technique involves less surgical morbidity and better postoperative quality of life. However, the greatest drawback lies in obtaining negative oncololgical margins. The European Society of Rhinology\textsuperscript{32} considers tumour extension requiring orbital exenteration, a maxillectomy which does not include the medial wall of the sinus, involvement of the anterior and/or lateral frontal sinus, involvement of the dura mater lateral to the optic nerve and invasion of the brain parenchyma, as absolute contraindications for EEA. Nicolai et al.\textsuperscript{33} presented a wide range of tumours operated exclusively with EEA, with a 5-year adjusted survival of 94% for adenocarcinomas, 60% for squamous cell carcinomas and 100% for adenoid cystic carcinomas. When analysing these excellent results we should consider that 64% of tumours were T1-T2 Initial lesions, with adenocarcinoma being the most common histology.

At our centre, we employed this approach in carcinomas of the nasoethmoidal complex without involvement of the cribriform plate and without extensive involvement of the lamina papyracea (or orbital lamina) and the roof of the ethmoid (T1-T2) or as palliative treatment for unresectable tumours. The objective of the multidisciplinary committee is to expand these indications to more extensive tumours as experience increases.

The progressive increase in indications has been partly aided by an improvement in the reconstruction of skull base...
defects through the design of different nasal flaps enabling large defects to be sealed. At present, the percentage of CSF leaks in skull base surgery at experienced centres is below 5%, a similar figure to that obtained at our centre. We currently perform a nasoseptal flap in all pituitary tumours, although almost 90% are macroadenomas. We consider using other materials and free flaps for future microadenoma surgeries, in order to be more conservative with the nasal mucosa and reserve this excellent nasoseptal flap only for macroadenomas and other lesions which cause extensive defects in the skull base.

The endonasal approaches, especially the expanded, cause postoperative crusts in the nasal fossa as main morbidity and, less frequently, hyposthesia or olfactory alterations. Major complications include neurovascular lesions, such as CSF fistulas and lesions of large vessels. Kas-sam et al. reported vascular haemorrhage in 0.9% of cases among 800 intervened patients. In our series we observed 2 cases of haemorrhage, 1 lesion of the internal carotid and 1 case of ventricular haemorrhage.

The endoscopic endonasal technique continues its remarkable evolution. The main drawbacks regarding the microscope, such as the lack of bimanual dissection and the absence of visualisation in 3 dimensions, have been solved through the “4 hands” technique and the appearance of 3D endoscopes. In recent years, robotic systems have started to be used in head and neck injuries, as well as in some locations in the skull base. These systems provide excellent 3D vision and accuracy, and will be a significant part of the constant evolution of this surgical technique.

Conclusions

The creation of reference centres which accumulate a sufficient number of pathologies is essential in order to further develop the technique and expand the applications of skull base surgery. Our centre is committed to multidisciplinary collaboration in endoscopic skull base surgery as a route to achieve excellence.

Conflict of Interests

The authors have no conflict of interests to declare.

References