ORIGINAL ARTICLE

Endoscopic approaches to pituitary lesions: Difficulties and challenges

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Abstract
Introduction and objectives: The evolution of surgical approaches to the pituitary region not only brings benefits to the patient, but also means changes for otolaryngologists, who have to face new difficulties and complications.

The objective of this paper was to present our experience in the endoscopic approach to the pituitary region, assessing the difficulties and complications encountered, and to offer possible elements for improvement.

Material and method: We reviewed the first 40 cases of pituitary approaches we carried out between 2008 and 2011. Interventions were performed by a team of neurosurgeons and otolaryngologists in simultaneous collaboration. We analysed the pathology intervened, complications and difficulties.

Results: There were 37 patients operated on for pituitary tumours and 3 cysts; 34 cases were macroadenomas. The complications were 6 cerebrospinal fluid leaks, 3 with meningitis, 6 diabetes insipidus, 1 pulmonary embolism, 1 hydrocephalus and 4 mild nasal complications.

Conclusions: The frequency and type of complications depend on the extent of the endoscopic approach, patient age, tumour size and suprasellar extension. The use of specific instruments, navigation and preoperative assessment of imaging tests help to minimise complications. Prudent implementation of new approaches, knowledge of techniques and complications, and the analysis of the activity allow further progress in access to skull base pathology.

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Pituitary endoscopic approaches: Difficulties and challenges

PALABRAS CLAVE
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Hipófisis;
Fistula de líquido cefalorraquideo;
Meningitis

Abordajes endoscópicos hipofisarios: dificultades y retos

Resumen

Introducción y objetivos: La evolución de los abordajes quirúrgicos a la región hipofisaria aporta beneficios al paciente, pero también supone cambios para los otorrinolaringólogos que tienen que afrontar nuevas dificultades y complicaciones.

El objetivo de este trabajo es presentar nuestra experiencia en el abordaje endoscópico de la región hipofisaria, valorando las dificultades y complicaciones encontradas, así como los posibles elementos de mejora.

Material y método: Se revisan los primeros 40 casos de abordajes hipofisarios que hemos realizado entre los años 2008 y 2011. Las intervenciones se han realizado por un equipo compuesto por neurocirujanos y otorrinolaringólogos en colaboración simultánea. Se analiza la patología intervenida, las complicaciones y las dificultades encontradas.

Resultados: Fueron intervenidos 37 pacientes con tumores hipofisarios y 3 con quistes. Treinta y cuatro casos eran macroadenomas. Las complicaciones fueron 6 fístulas de líquido cefalorraquideo, 3 de ellas con meningitis, 6 diabetes insípida, un tromboembolismo pulmonar, una hidrocefalia y 4 complicaciones nasales leves.

Conclusiones: La frecuencia y el tipo de complicaciones dependen de la extensión de los abordajes endoscópicos, la edad del paciente, el tamaño del tumor y la extensión supraesfenoidal. La utilización de instrumental específico, navegador y la valoración del preoperatorio de las pruebas de imagen contribuyen a minimizar las complicaciones. La prudencia en la realización de nuevos abordajes, el conocimiento de las técnicas y las complicaciones, así como el análisis de la actividad realizada, permiten seguir avanzando en los accesos a la patología de la base de cráneo.

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Introduction

In the last few decades, a great part of medical development has been based on the complementary overlap and collaboration between different specialists. A specific case in this subject is the use of the nasal endoscopic approach in the treatment of neurosurgical pathology. The first step in this field consists in the approach to the sella turcica and the hypophysis through the nostrils, using the endoscopic techniques employed in Otolaryngology to do so. In fact, this is presently the approach that is becoming the standard for this anatomical zone and also represents a jumping-off point to reach adjacent areas with lower mortality than with other earlier techniques. The advantages of the endoscopic approach with respect to the microscopic one include less blood loss, less need for analgesics, shorter hospital stay and fewer intraoperative complications. Endoscopic approaches for the entire skull base, among which the hypophyseal approach is found, have been described widely and in great detail.

Another important aspect is that, among intracranial tumours in adults, the most frequent are the hypophyseal tumours, which represent from 5% to 20% of all the central nervous system (CNS) tumours. Hypophyseal adenomas can be secreting or non-secreting; the most frequent among the secreting is the prolactinoma. Its treatment of choice is not surgical, it is using dopamine agonists. Next in order of frequency are non-functional adenomas, somatotropinomas, corticotropinomas and thyrotropinomas. When the tumour is smaller than 1 cm, it is considered a microadenoma, while if it is 1 cm or larger, it is a macroadenoma.

Beginning in 2008, endoscopic techniques have been used in approaching hypophyseal tumours in our hospital, otolaryngologists and neurosurgeons collaborating in teams. At present, all the approaches are performed with this procedure.

The objective of this article was to present our experience in the transsphenoidal endoscopic approach of the first 40 cases performed in our hospital, analysing the pathology causing the surgery, the difficulties and complications found and the development of the procedures as we increased the number of cases. In addition, we assessed possible elements for improving the technique and the results.

Material and method

We present a retrospective study on the first 40 cases of approach to the hypophyseal area via endonasal endoscopy performed in our hospital. These operations were carried out between 2008 and 2011 during the process of establishing a skull base unit between the Otolaryngology and Neurosurgery Services, consisting of physicians from both services in simultaneous collaboration. For the surgeries, we analysed the distribution by age and sex, as well as the type of adenoma, classifying them into microadenomas (smaller than 1 cm) and macroadenomas (1 cm and larger), and secreting or non-secreting.

The preoperative assessment included ophthalmologic, otolaryngological, endocrinological and radiological studies, using magnetic resonance (MR) and CAT scans for the radiological data. Evaluating the sphenoid sinus with imaging tests made it possible to analyse the degree of sinus...
pneumatization. This, in turn, let us foresee the existence or lack of anatomical references for the approach to the area. If necessary, it also enabled us to program the navigator to carry out the surgery, either for this reason or due to the extension of the lesions over the suprasellar diaphragm.

Otolaryngological participation consisted of preparing the surgical route, maintaining the best visibility possible so the neurosurgeon could excise the tumour and then close the sphenoid defect. We used 0° viewing and 4 mm diameter. If it was necessary to explore areas not visible with this view, we used 30°. The neurosurgical navigator was the optical Brain Lab (BrainLAB, Heimstetten, Germany), with 2 emitting/receiving infrared cameras that were reflected in spheres fixed to the signalling point. The surgeon’s criteria and the pathology involved decided the use of the navigator, as long as it could be clinically useful.

The otolaryngological part began with the introduction of patches with vasoconstrictor into the nostrils. After removing them, a middle turbinectomy was performed through the right nasal fossa; the Hadad nasoseptal flap used to close the sellar defect was then prepared, placing it in the cavum during the intervention. The nasal septum of the sphenoid rostrum was luxated and approximately 1 cm was resected from the posterosuperior section of the nasal septum to allow 4-hand work in both nostrils. The sphenoid sinuses were opened using a motor and drill and the existing interseptal walls were eliminated. Next, all the sphenoid mucosa was eliminated, locating the sella turcica, eliminating its bony part up to the dura mater in the hypophysis area. From that moment on, it was the work of the neurosurgeon to complete the surgical field and remove the lesion. The otolaryngologist maintained the visual field as clean, centred and unobstructed as possible. When the neurosurgeon considered the excision completed, any possible meningeal defects were closed. The otolaryngologist then finished the closure by placing the nasal septal flap and various resorbable materials. The borders of the flap were fixed with oxidized cellulose (Surgicel®) and covered with a biological sealant (DuraSeal®); over this a layer of absorbable gelatin sponge (Spongostan®) was placed so that the Foley catheter used to maintain these materials in position did not stick. A Silastic® splint was introduced in each nostril to prevent sequelae, along with a Merocel® pack. The nasal pack was removed at 48 h and the Silastic® splints were left in place for 3 weeks.

If rhinoliquorrhoea was suspected, the diagnosis was first confirmed by determination of the beta-trace protein. The patient was then reintervened in cases of high output; in cases of low output fistulas, a lumbar drainage was placed for 48–72 h and the development was assessed, intervening again if there was inadequate evolution.

Results

In the first 40 cases handled with this technique, there were 24 males and 16 females, with a mean age of 60 years (ranging from 32 to 84 years). The interventions were for macroadenoma in 34 patients, microadenomas in 3 patients and for sellar cysts in the 3 remaining patients. The most frequent tumour type was non-functioning adenoma, which presented in 27 cases. There were 4 GH-producing tumours and 3 prolactinomas.

In 15 patients the cavernous sinus was affected, with 5 bilateral cases, 5 right sinus and 5 left. Imaging studies made it possible to verify that in all cases there was appropriate pneumatization of the sphenoid sinus. There was only 1 case in which the pneumatization was insufficient for locating the references needed for the approach to the sella turcica and the hypophysis, although this did not prevent performing the procedure. In 20 patients the lesion extended over the level of the sellar diaphragm. In 8 cases the tumour occupied the lumen of the sphenoid sinus and, in 1 case, the tumour reached the mucosa of the nasopharynx and the sphenoidethmoidal recess.

In 37 patients a nasal septal flap was used to repair the defect. In 1 case, this was not done because the tumour extended to the nasal mucosa; in another 2 cases of microadenomas, resorbable materials were used for closing. In 6 patients a cerebrospinal fluid (CSF) fistula was produced; in 3 patients this was accompanied by meningitis, which presented 48–72 h after the fistula and was resolved with antibiotic therapy. There were no cases of meningitis without CSF fistula. Three cases of fistula achieved resolution using conservative measures, while another 3 required surgery to control the fistula. All fistula cases occurred in patients with macroadenomas that extended beyond the sellar diaphragm and made it necessary to open it. One of the patients who had a CSF fistula with surgical resolution developed hydrocephalus and needed the placement of a ventriculoperitoneal shunt.

In the immediate postoperative period, 6 patients presented diabetes insipidus and 1 patient developed a pulmonary thromboembolism that resolved with medical treatment. Four patients developed persistent panhypopituitarism after the surgery.

With respect to the endoscopic approach, the patients have had otolaryngological follow-ups at least 6 months following surgery. The complications observed have been: 1 case of epistaxis that needed plugging on 2 occasions, 2 cases with nasal synechiae lacking clinical impact and 1 case of moderate dry rhinitis.

To assess the neurosurgical results, an MR was taken 6 months after the surgery. It was shown that total resection was achieved in 53% of the cases, subtotal in 29% and only partial resection in 18%.

Discussion

At present, anterior skull base and hypophyseal area approaches are performed using endoscopic techniques. Earlier, the microscopic approach was used, but there are comparative studies that have shown that in endoscopic approaches blood loss is less, less analgesia is needed, the hospital stay is shorter and there are fewer intraoperative complications. To carry out endoscopic approaches, specific equipment and instruments are essential, as is the collaboration between otolaryngologists and neurosurgeons. The increase in the number of operations in which this collaboration is required and the need for the individuals trained in these techniques to be the ones that perform this type of intervention make it helpful and even necessary to
create skull base units to allow for incorporating these techniques in the services offered in some of the hospitals in our health network. In our hospital collaboration between the Neurosurgery and Otolaryngology services is common, which facilitated the possibility of implementing these procedures.

As time has passed and our surgical experience has increased, complications have become fewer (Table 1). The frequency and type of complications depend on the extent of the endoscopic approach, tumour size, suprasellar extension, complexity of the pathology, presence of anatomical alterations and patient age (Table 2).

A CSF fistula is a complication that can present in both the endoscopic approach and the microscopic approach, with a frequency ranging from 2% to 15% according to the series published. In our case, this complication occurred in 6 patients, 15%, which is at the limit of a high rate. However, it should be remembered that we are analysing a period that includes the learning curve for a new surgical technique, in which the number of complications is usually higher. With respect to the learning curve, the data in the literature are few and variable, ranging from the consideration that there is no learning curve to seeing the need for a great number of cases. However, it seems that between 20 and 30 interventions of this type can cover this period until results stabilise. In our case, the percentage of patients with CSF fistula was 20% for the first 20 cases; this dropped by half, to 10%, in the following 20.

Infectious complications are related to the presence of CSF fistula. There was a fistula in every case of postsurgical meningitis. However, the presence of meningitis did not determine the choice of the procedure to repair the fistula.

The closure procedure was independent of the presence of previous infection. The resolution of the fistula was not related either favourably or unfavourably with the existence of previous infection. Although in the literature the procedures and materials used in CSF fistula closure vary widely, in our case there were 3 endoscopic reinterventions with placement of thick fascia and fat that resolved the problem.

The literature contains reports of other intracranial infections as complications of endoscopic skull base surgery, such as cerebral abscesses, which are more related to cases of extensive intradural approaches, with an incidence rate that can reach up to 30% in some series. The fact that we have not had any cases of intracranial abscesses is probably related to the number of cases in the series and to the extension of the pathology treated with these techniques up to now.

Vascular complications, which are serious and usually involve a life-threatening situation, are described as having a frequency between 0.3% and 0.6% in hypophyseal approaches. This figure rises sharply when wider skull base approaches are performed, reaching up to 10% or 15% in the very extended approaches.

In our series, we had no neurological lesions of cranial nerves or definitive visual deterioration; quite the contrary, 3 patients who had presented loss of visual acuity improved with the surgery. However, in the literature, the endoscopic approach to hypophyseal tumours is associated with a rate of loss of visual acuity in 0.3%–2.6% of the cases. Hydrocephalus and the need for ventriculoperitoneal shunting is also described as a late complication for this type of surgery, although it is uncommon.

From a systemic point of view, complications not directly related to this type of intervention are also presented, such as pulmonary embolism (in 4% of the cases) or severe pneumonia (in 2%). In general, between 3% and 7% of the patients undergo a systemic complication and this rate rises with age, reaching up to 32% in those older than 70.

Endoscopic skull base approaches cause defects that require reconstruction. For this purpose, several types of pedicled nasal flaps in the anterior, posterior or infraturbinate areas have been proposed. In all the cases in which the lesion did not reach the nostril, we prepared a pedicled nasoseptal flap in the posterior nasal artery to cover the mucous defect of the sphenoid sinus, similar to that described by Hadad et al.

Focusing on otolaryngological complications, it is notable that they are few in number and of scant clinical repercussion, in spite of the extensive surgical manipulation in the nose with the removal of the middle turbinate and fashioning of the nasoseptal flap. The standard middle turbinate extirpation makes it possible to have a wider, more manageable operating field and does not cause important nasal complications from the clinical point of view. However, another alternative would be the lateral luxation of the middle and superior turbinates, without needing to eliminate them. On the other hand, excising an area posterior to the nasal septum allows 2 surgeons to work more easily, improving operating field view and clarity, as well as making it easier to introduce instruments and handle them in the surgical field. Our nasal complications have been similar to those described in the literature.
When a technique is introduced, there are usually some limitations or weaknesses. However, these did not prevent us from performing the procedures or reduce the possibilities of providing the patients with these approaches. At the very start, there were coordination problems derived from the novelty in carrying out this type of procedures; these were solved in a short period of time as these techniques were established as the standard for treating these lesions. In the first few cases, an additional difficulty had to do with the use of the normal instruments in traditional hypophyseal surgery instead of the specific instrumentation for the endoscopic approach. This was rapidly solved by the acquisition of material more appropriate for these techniques.

It was not possible to carry out olfactometry on the patients included in our study; however, recent publications point to possible effects on olfaction from performing the pedicled septal-mucosal flap.33 None of our patients reported clinical discomfort worthy of mentioning, even though we have not tested this factor objectively.

Imaging techniques in the preoperative study are essential for orientation in the access route. We generally used MR scans as, in the majority of the patients, it was the technique that had been used to study the sella turcica and hypophysis. The CAT scans were used in a few cases in which the MR was insufficient to evaluate the nasal and paranasal structures that influence the approach. With these imaging tests, it is possible to assess the size of the lesion, its extension to the cavernous sinus or the level of the suprasellar diaphragm (Fig. 1) and the possible involvement of adjacent structures, such as compression of the optic chiasm, carotid arteries or cranial nerves. These factors can be determinant in the choice of the approach to the lesion, even mandating the need to perform an open route instead of the endoscopic approach or the need for a combined procedure for correct lesion treatment. It should be remembered that suprasellar extension, especially over the plane of the hypothalamus and the floor of the third ventricle, has been linked to worse postoperative results.34,35

Although involvement of the cavernous sinus is not a contraindication for the transsphenoidal endoscopic approach, its presence limits the possibilities of tumour resection.36 Involvement of the entire carotid circumference also limits these, even though widened approaches are used. Some authors feel that the lateral limit of the endoscopic approach would be in the lateral extension to the cranial nerves.37 Other factors that can make an open approach advisable are retrosellar extension, tumour consistency, brain oedema or invasion, previous surgical or radiotherapy treatment, circumferential involvement of the arteries of the Circle of Willis or cases in which the tumour completely surrounds the chiasm or some of the optic nerves.38

The navigator can make surgery easier and reduce surgical time. However, the imaging studies used to diagnose this pathology do not always comply with the requirements for navigation, which means that if navigation is needed the study has to be repeated. That is the reason why it was not used in all our cases, only in those whose imaging study was compatible with the navigator or whose complexity or previous imaging studies led us to foresee some special difficulty in accessing the lesion, whether due to its size or to the anatomical placement of the structures.

**Conclusion**

Our initial experience with these 40 cases of approaches to hypophyseal lesions is in line with the data published in the literature; some of them are at the higher limit, such as the CSF fistulas (explained by the learning curve), while other data occur with much less frequency than what has been published, such as cerebral infections (probably due to the number of cases). Prudence in performing new approaches, knowledge of the surgical techniques and precaution against complications, as well as analysis of the activity carried out, will make it possible to continue progressing in this form of access to skull base pathology. We should increase the number of patients and continue analysing our work to be able to advance in extending the approaches and the complexity of the pathology treated.
Conflict of Interests

The authors have no conflicts of interests to declare.

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