Endoscopic Endonasal Transsphenoidal Approach for Pituitary Adenomas
(Our Experience in Avoiding Complications)

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ABSTRACT
Background: The endoscope was used in trans-sphenoidal surgery for sellar lesions by Gerard Guiot more than 40 years ago. Interest in endonasal endoscopic transsphenoidal surgery has increased. Objectives: This article presents our experience in the endoscopic trans-sphenoidal approach of the first sixty cases performed in our hospital, analyzing the pathology causing the surgery, the difficulties and complications found and the development of the procedures.

Patients and Methods: A retrospective study of the first sixty cases of pituitary adenomas operated via endonasal trans-sphenoidal endoscopy that was carried out between 2008 and 2014. Results: In sixty cases of pituitary adenomas operated via endonasal trans-sphenoidal endoscopy, there were forty five females and fifteen males, with a mean age of 54 y (18 to 65 years). Macroadenoma was present in fifty patients and microadenomas in ten patients. Non-functioning adenoma was present in 32 cases while 18 cases had prolactinomas and 10 cases had GH-producing tumors. MRI was done 3 and 6 months after the surgery. It was shown that total resection was achieved in 70% of the cases, subtotal in 18.3% and partial resection in 11.6%. In ten patients (16.6%) a cerebrospinal fluid (CSF) leak occurred postoperatively. Five cases achieved resolution using conservative measures, while another five required surgery to control the fistula. Three cases were died (5%), two cases died from meningitis and the third case didn’t recover after surgery for pituitary apoplexy.

Conclusion: For most pituitary tumors, endoscopic endonasal transsphenoidal approach is the most appropriate route. It provides excellent exposure of the sella and adequate working space. There is less postoperative pain with short hospital stay and minimal complications. As time has passed and our surgical experience has increased, complications have become fewer.

INTRODUCTION

The pituitary gland lies within a bony depression called sella turcica within the sphenoid bone at the base of the brain. Access to the sella is limited from above by the optic nerves and chiasm and the circle of Willis, from laterally by the cavernous sinuses and internal carotid arteries and from behind by the brain stem and basilar artery. These vital structures protecting its superior, lateral, and posterior borders have led to the preferred surgical routes to tumors of the gland being from below through trans-sphenoidal approach.3

The pituitary tumors are the third most common primary intracranial tumors. It was believed to account for 5% to 20% of all the central nervous system (CNS) tumors.8,18 The pituitary adenomas arise from adenohypophysis may be microadenomas or macroadenomas, secreting or non-secreting. The most frequent among the secreting is the prolactinoma. The clinical manifestations of the pituitary adenomas are due to either compression or hormonal disturbances.2,23

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Significant advances in the recognition and management of pituitary adenomas have taken place over the last decade. Highly sensitive hormonal assays and magnetic resonance imaging with gadolinium enhancement have led to earlier and more frequent diagnosis of pituitary adenomas.24

The possibility of removing the brain through the nose without disfiguring the face was already known to the ancient Egyptians, five-thousand year ago. The endoscope was used in trans-sphenoidal surgery for sellar lesions by Gerard Guiot more than 40 years ago, but his experience remained mostly isolated for a long time. Subsequently, ENT surgeons acquired confidence with the endoscope while performing functional endoscopic sinus surgery. This was followed by Jho and Carrau, who pioneered the pure endoscopic approach to pituitary lesions ten years ago, and by Cappbianca group in Naples. After these reports, which highlighted the advantages of this technique in the treatment of sellar lesions, interest in endonasal endoscopic transsphenoidal surgery has increased, to the point that several centers around the world are now currently using the technique with some personal variations.4,6,15,26
PATIENTS AND METHODS

We present a retrospective study of the first sixty cases of pituitary adenomas treated surgically via endonasal trans-sphenoidal endoscopy. These operations were carried out between 2008 and 2014. We analyzed the distribution by age and sex, as well as the type of adenoma, classifying them into microadenomas (smaller than one cm) and macroadenomas (one cm and larger), and secreting or non-secreting.

Preoperative assessment included ophthalmologic, otolaryngological, endocrinological and radiological studies, using magnetic resonance image with gadolinium (MRI) and CT scans nasal and paranasal sinus for the radiological data. Evaluating the sphenoid sinus with imaging tests made it possible to assess the degree of sinus pneumatization. This, in turn, let us to see the existence or lack of anatomical references for the approach to the area. We used the endoscopic endonasal approach to the sella, which was performed via an anterior sphenoidotomy, through the existing sphenoid ostium, without the use of a trans-sphenoidal retractor and with a rigid endoscope as the sole visualizing tool. Records of all the patients were kept by our department, with the duration of follow up ranging from 6 months to 18 months after the procedure.

RESULTS

In the first sixty cases surgically treated with this technique, there were forty five females and fifteen males, ranging from 18 to 65 years with a mean age of 54 years. The interventions were for macroadenoma in fifty patients, microadenomas in ten patients. The most frequent tumor type was non-functioning adenoma, which presented in thirty two cases. There were eighteen prolactinomas and ten GH-producing tumors. In non-functioning macroadenoma visual deterioration was the most common presenting symptoms and signs in functioning macroadenoma followed by acromegalic features. In eight patients the cavernous sinus was affected. In forty patients the lesion extended over the level of the sellar diaphragm. Imaging studies made it possible to verify that in all cases there was appropriate pneumatization of the sphenoid sinus with sellar location of the sphenoid sinus in fifty six cases and presellar location in four cases. Sphenoid sinus with single septum was found in twenty four patients and with multiple septa in thirty six patients.

Most cases (fourty eight) were operated through bilateral nasal opening, middle turbinectomy was done in twelve cases. Intraoperative, four cases were fibrous & non suckable and failed to be totally removed, in most cases (fourty four) we were able to identify the normal gland. Pituitary apoplexy was found in six patients (Table 2).

<table>
<thead>
<tr>
<th>Intraoperative finding</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of normal Pituitary</td>
<td>44</td>
</tr>
<tr>
<td>Apoplexy</td>
<td>6</td>
</tr>
<tr>
<td>Fibrous non suckable tumor</td>
<td>4</td>
</tr>
</tbody>
</table>

In ten patients (16.6%) a cerebrospinal fluid (CSF) leak occurred postoperatively all of them was macroadenoma. Five cases of fistula achieved resolution using conservative measures, while another five required surgery to control the fistula. In six patients, CSF leak was accompanied by meningitis, which presented 48-72 h after the fistula.

Meningitis resolved with antibiotic therapy in three cases, one case was operated again to repair the CSF fistula, and two cases died. There were no cases of meningitis without CSF fistula. All cases of CSF leak occurred in patients with macroadenomas that extended beyond the sellar diaphragm. In the immediate postoperative period, fourteen patients presented diabetes insipidus (three persistent & eleven transient). Six patients developed persistent panhypopituitarism after surgery. Compression symptoms improved shortly after operation while hormonal symptoms showed improvement later on. We had three cases of visual deterioration.

With respect to the endoscopic approach, the patients have had otolaryngological follow-ups at least six months following surgery. The complications observed have been; four cases of epistaxis that needed plugging on two occasions, four cases with nasal synechiae lacking clinical impact, three cases of sphenoid sinusitis and three cases of moderate dry rhinitis (Table 3).
Table 3: Postoperative complications

<table>
<thead>
<tr>
<th>Neurosurgical complication</th>
<th>Otolaryngological</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF</td>
<td>Epistaxis</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Synechia</td>
</tr>
<tr>
<td>DI</td>
<td>Sphenoid sinusitis</td>
</tr>
<tr>
<td>Visual deterioration</td>
<td>Dry rhinitis</td>
</tr>
<tr>
<td>Hormonal</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td></td>
</tr>
</tbody>
</table>

To assess the neurosurgical results, MRI was taken 6 months after the surgery. It was shown that total resection was achieved in 70% of the cases as shown in figure 1 & 2 while resection was subtotal in 18.3% and only partial resection in 11.6% (Table 4).

Table (4): Extent of tumor resection

<table>
<thead>
<tr>
<th>Degree of tumor removal</th>
<th>No</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>42</td>
<td>70%</td>
</tr>
<tr>
<td>Subtotal</td>
<td>11</td>
<td>18.3%</td>
</tr>
<tr>
<td>Partial</td>
<td>7</td>
<td>11.6%</td>
</tr>
</tbody>
</table>

As regard improvement after operation, 80% of patients with visual affection were improved. Headache improved in 60% of patients while all the patients with ptosis were improved (Table 5).

Table (5): Improvement after operation

<table>
<thead>
<tr>
<th>Symptoms / Signs</th>
<th>No</th>
<th>Improved</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual</td>
<td>30</td>
<td>24</td>
<td>80%</td>
</tr>
<tr>
<td>Headache</td>
<td>20</td>
<td>12</td>
<td>60%</td>
</tr>
<tr>
<td>Amenorrhea, galactorrhea and infertility</td>
<td>12</td>
<td>8</td>
<td>66.6%</td>
</tr>
<tr>
<td>Acromegalic features</td>
<td>10</td>
<td>6</td>
<td>60%</td>
</tr>
<tr>
<td>Impotence &amp; galactorrhea</td>
<td>4</td>
<td>4</td>
<td>100%</td>
</tr>
<tr>
<td>Disturbed conscious level</td>
<td>2</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>Ptosis</td>
<td>2</td>
<td>2</td>
<td>100%</td>
</tr>
</tbody>
</table>

Regarding mortality, three cases died (5%), two cases died from meningitis and the third case had presented by pituitary apoplexy and disturbed conscious level (GCS 7) and after the operation he did not recover from anesthesia, was admitted in ICU on mechanical ventilation and died three days after the operation.

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. It is a safe and efficient minimally invasive approach. This has been concluded from the results of the case series enriching the neurosurgical literatures. To carry out endoscopic approaches, specific equipment and instruments are essential.

The frequency and type of complications depend on the extension of the endoscopic approach, tumor size, suprasellar extension, complexity of the pathology, presence of anatomical alterations and patient age. 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 study, this complication occurred in ten patients, 16.6%, which is at the limit of high rate. However, it should be remembered that we are analyzing a period that include the learning curve for a new surgical technique, in which the number of complications is usually higher.

As it is a new surgical approach to the sella, we started with cadaveric dissection four times before starting to operate. During the first procedures, we tried to select the cases carefully and we started with simple and straightforward cases as patients with non-functioning macroadenoma with well pneumatized sinus. With respect to the learning curve, we started to...
get confident and familial with the approach after about ten procedures. The data in the literature are few and variable, ranging from the consideration that there is no learning curve to see 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 stabilize. In our case, the percentage of patients with CSF fistula was 23.3% for the first thirty cases; this dropped by half, to 10% in the following thirty cases. Shahinian reported 3 cases of CSF leak among the first ten operations, while in the last sixty five operations, he reported only two cases.

All cases of CSF leak were associated with macroadenoma with suprasellar extension. CSF leak was treated by complete bed rest, application of lumbar drain for five days, and antibiotic coverage which were sufficient in five cases. In the other five cases endoscopic re-interventions were done with placement of thick fascia lata graft, fat and fibrin glue that resolved the problem. The usage of a single layer reconstruction technique as applying fat only usually not enough, in contrary to multi-layer technique.

Although our sample is relatively small, we can conclude that multi-layered reconstruction techniques are relatively superior to a single layered one. This conclusion is supported by the results of other studies. For a successful surgery and in order to prevent the CSF leak and related complications, skull base reconstruction is an important step of endoscopic transphenoidal surgery (EETS), particularly in extended surgery. Using Autologous Fibrin Sealant (AFS) combined with multilayer reconstruction technique is a safe and effective method to prevent CSF leak in large defects following EETS.

Infectious complications are related to the presence of CSF fistula. There was a fistula in every case of postsurgical meningitis. 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 extension of the pathology treated with these techniques.

Vascular complications (no cases in our series), 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 extended skull base approaches are performed, reaching up to 10% or 15% in the very extended approaches. Injury to the cavernous segment of the ICA upon transphenoidal surgery is a rare, but potentially fatal complication. Thorough preparation for surgery – the study of neurovisualization data, improvement of the transsphenoidal approach technique and correct identification of the middle line is of great importance to reduce risk for the development of this complication.

Worsening of pituitary function after surgery was in six patients 10%, as a new anterior pituitary insufficiency detected during the postoperative endocrine evaluation. Cappabianca et al. experienced 9.3% anterior pituitary insufficiency in their study which included hundred and forty six patients.

In our series, we had no neurological lesions of cranial nerves but we had three (5%) cases of visual deterioration. In the literature, the endoscopic approach to hypophyseal tumors is associated with a rate of loss of visual acuity in 0.3% - 2.6% of the cases. Patients presenting with severely compromised vision should be managed in the ICU postoperatively for a minimum of 72 hours, preserving their mean arterial pressure around 85 mm Hg. In addition, Kassam et al advocated intracisternal papaverine injection when facing a situation with a potential risk for vasospasm, avoiding balloon packing, avoiding over packing, under packing, follow up of conscious level to minimize the risk of intrasellar hematoma.

Focusing on otolaryngological complications, it is notable that they are few in number and of little clinical importance, in spite of the extensive surgical manipulation in the nose with the removal of the middle turbinate. The standard middle turbinate extirpation makes it possible to have a wider, more comfortable operating field and does not cause important nasal complications from the clinical point of view. In our series we did middle turbinectomy in twelve cases, ten cases were acromegalic with hypertrophied nasal mucosa and two cases were had narrow nasal cavity.

On the other hand, posterior septostomy (forty eight cases in our study) allows two 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.

Most commonly, death is caused by vascular events or infectious complications, particularly meningitis. Kassam et al., mentioned that they had mortality rate of 0.9% in their study which included 800 cases. We had mortality rate of 5% (three cases).

**CONCLUSION**

For most pituitary tumors, endoscopic endonasal transsphenoidal approach is the most appropriate route. It provided excellent exposure of the sella and adequate working space. We confirmed that improved visualization allowed the surgeon to identify and avoid injury to the vital structures leading to fewer complications with better outcome. The best strategy for dealing with surgical complications is to avoid it.
Cadaveric dissection is a very important step to start with followed by Good training that is very essential in endoscopic surgery. This technique produces less postoperative pain and shortens hospital stay with minimal complications. The endoscopic approach has become our preferred approach to sellar lesions.

REFERENCES