Original Article

Neuro-ophthalmologic Recovery Following Endoscopic Endonasal Resection of Pituitary Macro-adenomas with Apoplexy

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ABSTRACT

Background: Pituitary apoplexy is a heterogeneous spectrum and infrequent occurrence that may require timely treatment. There is a controversy about which subsets require urgent as opposed to elective surgical or even medical treatment alone.

Objectives: are to study the neuro-ophthalmologic outcome following endoscopic trans-sphenoidal approach for management of pituitary apoplexy.

Patients and Methods: Retrospective analysis of case notes at a single neurosurgical center, Tanta University, Egypt. Twenty Five patients of apoplexy underwent endoscopic trans-sphenoidal approach at Tanta University Hospitals, all patients operated within 48 hours of recent clinical deterioration.

Results. The visual field defects had an improvement of 86%. Ocular paresis and ptosis were improved in all patients ranging from 5 days to two weeks following surgery. Twenty patients out of 25 (80%) had gross total resections. Intra-operative bleeding were venous and easily controlled. Cerebrospinal fluid leakage occurred in only one patient.

Conclusion. Early endoscopic endo-nasal surgical management is an effective and safe treatment modality for treatment of pituitary apoplexy with mass with a low complication rate.

INTRODUCTION

Apoplexy is a medical term that refers to cerebral hemorrhage or other sudden neurological impairment. Pituitary apoplexy occurs when a pituitary tumor (adenoma) either spontaneously hemorrhages or grows in such a way as to compress and cut off its own blood supply, resulting in tumor cell death, bleeding and acute swelling. The hemorrhage- or necrosis-induced swelling can compress the pituitary gland itself, optic nerves, and the nerve that control ocular motility.

Pituitary apoplexy is a rare condition, clinically characterized by headache, visual loss, ocular paresis, and altered mental status caused by sudden hemorrhage or infarction of the pituitary gland. Over the past 20 years, numerous case reports and series have emphasized the association of pituitary apoplexy with a wide variety of medications, procedures, and pathological states such as anticoagulation, endocrinological testing, head trauma, or recent surgery. In most reports, these associated conditions have been qualified as "precipitating factors".

Surgery is performed after stabilization of the patient's medical conditions. One of the preferred surgical treatments for pituitary apoplexy is the endoscopic endo-nasal Approach to resect the tumor and decompress the area. This minimally invasive technique uses the nose and nasal cavities as natural corridors and offers the benefits of no incisions to heal, no disfigurement to the patient, and a faster recovery time.

The pathophysiology of pituitary apoplexy is still a matter of debate. Some authors believe that pituitary apoplexy occurs due to rapid tumor growth that outstrips arterial supply. It is uncertain whether the pathological process is a primary hemorrhage or whether the event is really a hemorrhagic infarction.

The tumor size appears to be a major factor, but it is known that even smaller adenomas can bleed. Another rationale for pituitary apoplexy could be the tumor tissue growing inside the narrow space situated between the pituitary stalk and diaphragma sellae leading to constriction of the thin vascular net adjacent to the stalk, and finally ischemia, necrosis and hemorrhage on the anterior lobe and tumor tissue.

PATIENTS AND METHODS

This retrospective study includes twenty five patients of pituitary macro adenomas presented with apoplexy, operated in Tanta University Hospitals from May 2012 to July 2015. Inclusion criteria considered all patients with neuro-ophthalmologic deterioration, in whom histopathology revealed pituitary adenoma. Seventeen patients had hormonally inactive adenoma, one patient with GH-adenomas and seven patients with prolactin secreting macro adenomas. All patients were subjected to full history taking, neurological examination focusing on recent neurological and/or...
ophthalmologic deterioration. Preoperative hormonal assay, CT paranasal sinuses and dynamic contrast enhanced MRI sella were done. The magnetic resonance imaging was more sensitive than computed tomography for identifying hemorrhage. Endoscopic endo-nasal tumor removal was performed 1-2 days following hospital admission. Surgeries were performed with the endo-nasal endoscopic approach through both nostrils (3 hands technique). Using Karl Storz ® THUMFART Irrigation and Suction Endoscope, it was possible to always have a clear endoscopic view. Following lateralization of the middle turbinate, we performed drilling of the sphenoid face starting through the sphenoid ostium. The same steps were done on the left nasal cavity with the addition of right side endoscopic view control of the left side admitted Karl Storz ® OSTRUM 360° Rotating Antrum Punch to back-bite the posterior nasal septum. This was followed by drilling of the sellar floor and incision of the dura. Tumor removal was achieved using combined use of curette and suction tube through both nostrils, followed by a blunt curved suction tube to remove remnants on the wall of the cavernous sinus bilaterally. Finally, the sellar floor is sealed by fibrin glue, followed by packing of the nasal cavity, to decrease mucosal bleeding, (Figure 1).

Fig. 1 a-h: a: Preoperative sagittal T1 weighted post contrast MR image showing pituitary macro adenoma with large supra-sellar extension. b: Preoperative coronal T2 weighted image showing hyper intense signal involving the left portion of the of the tumor (arrow head) denoting infarction. c: Postoperative sagittal T1 weighted post contrast MR image showing gross total tumor removal. d: Postoperative coronal T1 image with contrast showing normal pituitary gland on the right side (arrow head). e: Endoscopic intraoperative image showing tumor resection with the combined use of curette (arrow head) through right nostril and suction tube through left nostril (double arrow head). f: Removal of the remaining tumor on sellar wall using blunt curved suction tube. g: Endoscopic intraoperative view inside the sella showing redundant diaphragma sellae after gross total resection of the tumor with the normal pituitary gland to the right side (arrow head). h: Final intraoperative image with fibrin glue sealing the sellar floor.
Surgical outcomes for non-functioning adenomas were quantified as gross total or subtotal on the basis of postoperative magnetic resonance imaging. Dynamic contrast enhanced MRI sella was routinely performed one month, six months following surgery and yearly thereafter. For functionally active adenomas, the resections were quantified as gross total or subtotal, and postoperative endocrinial assay were performed to assess the hormonal disturbance recovery.

**RESULTS**

Over the time period of 3 years, endoscopic endonasal trans-sphenoidal surgeries were performed for twenty five patients with pituitary apoplexy (sudden onset of neuro-ophthalmologic symptoms, an intraoperative finding of hemorrhage and or radiological signal intensity changes within the adenoma). The study sex distribution had eight female patients, (32%) and seventeen male patients, (68%). The average age was 37 years (range, 19-55 years).

**Table 1: Clinical presentation of 25 patients of pituitary apoplexy and post-operative improvement rate.**

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Frequency</th>
<th>Totally resolved</th>
<th>Improved</th>
<th>Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual deterioration</td>
<td>22</td>
<td>15/22</td>
<td>4/22</td>
<td>3/22</td>
</tr>
<tr>
<td>Ocular paresis</td>
<td>6</td>
<td>5/6</td>
<td>1/6</td>
<td>0/6</td>
</tr>
<tr>
<td>Ptosis</td>
<td>4</td>
<td>3/4</td>
<td>1/4</td>
<td>0/4</td>
</tr>
<tr>
<td>Hyper-prolactinemia</td>
<td>7</td>
<td>0/7</td>
<td>5/7</td>
<td>2/7</td>
</tr>
<tr>
<td>Growth hormone hyper-secretion</td>
<td>1</td>
<td>1/1</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Headache</td>
<td>20</td>
<td>15/20</td>
<td>5/20</td>
<td>0/20</td>
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The most common clinical presentations were visual deterioration (88%) and headaches (80%). Visual deterioration was confirmed by perimetry where sixteen patients had typical bi-temporal visual field loss and six patients had mixed bilateral field defects. Six Patients had ocular paresis due to affection of oculomotor nerve and four patients had Ptosis (unilateral). An elevated prolactin level was the most common hormonal abnormality, occurring in 28%. (Table 1)

**Post-operative**

Our postoperative outcomes indicate that the visual deterioration had an improvement of 86%. The visual field defects totally resolved in fifteen patients, improved in four patients and remained unchanged in three patients. Regression of the field defects was documented with automated perimetry. Ocular paresis and ptosis were improved in all patients ranging from 5-15 days following surgery. The level of hormone in functioning adenomas also had an apparent remission. Among the seven patients who had prolactinomas, five patients had remarkable decrease in serum prolactin level while two of them remained unchanged to be controlled by medical postoperative dopamine analog. One patient with growth hormone secreting adenoma had hormonal resolution as well.

A total of twenty patients out of twenty five (80%) had gross total resections. In the patients with hormonally active adenomas (eight patients), five patients had gross total removal (62%) and three had subtotal removal, and in patients with hormonally inactive adenomas, fifteen had gross total removal (88%), (Table 2).

**Table 2: Extent of surgical resection**

<table>
<thead>
<tr>
<th>Type of Adenoma</th>
<th>Gross Total Resection</th>
<th>Partial Resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonally Active adenoma</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Hormonally Inactive adenoma</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>5</td>
</tr>
</tbody>
</table>

Postoperative complications were reported in a total of eight patients. Seven patients developed postoperative diabetes insipidus, being transient in six cases with remission within one month following surgery, and persistent in one patients requiring hormonal replacement. Transient CSF leakage was noticed in one patient managed for four days using spinal drainage till remission.

**DISCUSSION**

In early 1898, Bailey et al described the first case of pituitary tumor associated with hemorrhage, and there have been numerous case reports and series dealing with this lesion published in the literature since then. The endoscopic Endo-nasal transsphenoidal approach for management of pituitary lesions is considered superior to microscopic approach in terms of wider viewing angles allowing direct visualization at the
suprasellar region or various anatomic corners as well as being minimally invasive.

In this study, pituitary apoplexy was defined on basis of clinical signs essentially correlated with imaging and histopathological evidence. Based on recent neuro ophthalmologic deterioration, the most common clinical presentation were visual deterioration 88%, ocular paresis 24%, and ptosis 16%. Together with headache, neuro ophthalmologic deterioration are the most frequently reported clinical findings in most studies 8,9,10,11. This could be explained by sudden volume expansion within the tumor leading to upward compression affecting the chiasm, or on side walls bounded by cavernous sinus with subsequent compression on oculomotor nerve and or trochlear nerve leading to ocular paresis. Ptosis may result from either oculomotor nerve affection or compression of the sympathetics within the cavernous sinus inducing Horner syndrome.9,11

There is a debate about the optimum timing for surgery where some authors support early, but not necessarily emergency, decompression at the time of presentation with apoplexy in the hope of obtaining more improvement in vision. Early surgical decompression has been claimed to improve not only neuro ophthalmologic but also endocrine outcomes9,10,11. Definitive treatment for apoplexy patients requires both surgical (such as surgical decompression of the sellar, suprasellar space, and cavernous sinus) and medical aspects (such as hormonal replacement therapy) to be addressed 10,13.

Our results found that early surgical intervention (first 48 hours) were associated in improvement in visual field defects, and ocular paresis in 86%, and 100%, respectively. Visual acuity improvement is significant during the first two weeks following surgery, with no further significant improvement after this period. Visual field defects significantly improved during the first two weeks postoperatively and further improvement was noticed during the first three months. This is similar to the data reported by Kristof and co-workers who published the results of visual outcome in a recent retrospective study, where surgery resulted in improvements in visual acuity, visual field defects, and ocular paresis in 88%, 95%, and 100%, respectively 14.

Ocular paresis is more likely to resolve after apoplexy than any visual loss 8. Kaplan et al15 and Symon and Mohanty 16 both noted the resolution of ocular paresis with surgery in all 10 patients. In their study, Zhang et al 9 noted improvement in 82% of patients with ocular paresis all operated upon within the first 24 hours. Our results were similar to previous surgical series, with some recovery from ocular paresis in all affected patients and a full recovery of normal eye movements in 83% of patients.

The extent of tumor resection was verified by dynamic post contrast MRI sella, 1 month postoperative to reveal any residual tumor. We reported gross total tumor resection in 80% of cases, in all of them downward descent of diaphragm was observed intraoperatively. Only two cases out of five with partial resection showed descent in diaphragm sellae. Our results are nearly similar to those of Zhu et al17, who reported gross total resection of 82%. Zhang et al in 201119 reported 88.5% gross total tumor resection based on post-operative MRI without declaration if done with contrast or dynamic staged contrast imaging. Several authors have reported gross tumor removal rates of 62-93%.18,19.

To our updated knowledge, the definition of gross total resection showed some variation in literature. Koumouroussi et al in 201320 in their study of giant macroadenomas reported gross total resection rate of only 66%. They considered the degree of resection near total when more than 90% of the tumor was resected. Yang et al21 designed their own definition of total resection using software-calculated volumetric measurement. They rendered 3D adenoma reconstruction pre and postoperative to quantify total resection based on tumor volume reduction. Nevertheless they overlooked the means of differentiating normal pituitary gland from tumor tissue that requires dynamic imaging and careful neuro-radiological evaluation.

In this study, post-operative remission of hormonal hypersecretion, was reported in 71.4% for prolactin secreting tumors and 100% for GH secreting tumors. Hormonal remission following trans-sphenoidal pituitary surgery is a common improvement ranging from 65-100% in variable studies 22,23,24.

Some Complications were reported in our study none of them resulted in mortality or neurological morbidity. Persistent postoperative diabetes nisipidus, was noticed in only one patient requiring hormonal replacement. Taransient CSF leakage was also reported in one patient managed by spinal drainage for 4 days till remission. These narrow spectrum complications are similar to the result concluded by Santos AR et al and White et al. 25,26.

CONCLUSIONS

Early endoscopic endonasal transsphenoidal approach is an effective modality to treat patients with pituitary apoplexy. Patients with field defects should be referred as soon as possible (before 48 hours) for surgery. Ocular paresis is more likely to complete resolution after early intervention for apoplexy than visual deterioration. The true limitation of this approach is the extension of the tumor beyond the lateral wall of the cavernous sinus precluding gross total resection. The
complication rate is relatively low with long period of training and clear management strategy prospects.

Declaration

The author(s) declare no conflict of interest or any financial support and confirm the approval of the submitted article by the concerned ethical committee.

REFERENCES
