Review of first 60 pituitary adenoma cases of a skull base team, one center experience

Osama Hassan  
*Lecturer of Otorhinolaryngology – Head and Neck Surgery, Faculty of Medicine, Cairo University, Cairo, Egypt*,  
oshassan75@gmail.com

Mohamed Fatthallah  
*Lecturer of Neuorosurgery, Faculty of Medicine, Cairo University, Cairo, Egypt.*

Mohamed El Mallawany  
*Lecturer of Neuorosurgery, Faculty of Medicine, Cairo University, Cairo, Egypt.*

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ARTICLE

Review of First 60 Pituitary Adenoma Cases of a Skull Base Team, One Center Experience

Osama Hassan*, Ayman Samir, Mohamed Fatthallah, Mohamed El Mallawany

Faculty of Medicine, Cairo University, Cairo, Egypt

Abstract

Background: Endoscopic endonasal transsphenoid approach of pituitary gland is being effectively replacing microscopic approach. This approach need a lot of training and stepwise learning to reach perfection. This study discuss the experience and pitfalls of an evolving skull base team in one institute.

Aim of the work: Analysis of first sixty pituitary adenomas patients operated by an evolving skull base teams in one institute, and highlighting modifications introduced in their technique.

Methodology: This is a retrospective analytical study of the medical records of first 60 pituitary adenoma patients who had presented to one center and had endoscopic transnasal trans-sphenoidal approach by conjoined skull base team.

Results: There were 60 cases of pituitary adenoma; 23 males, and 37 females. Mean age were 46 years old. 37 cases (61%) had temporal field defect, 22 cases had visual acuity loss, 41 patients (68%) had non-functioning adenomas, and 18% were prolactinomas. Fifty two cases (86.6%) were macroadenoma, and 2 patients (3.3%) were microadenoma. 48 cases (80%) had suprasellar extension, while 19 cases (19%) had parasellar extension. Three cases (5%) were recurrent. Transnasal cavity approach was adopted in 58 cases (96.6%). 4 cases needed middle turbinate resection. Mean operative time was 3 h. Gross total removal of the tumor were achieved in 49 cases (81.6%). Intraoperative CSF leakage occurred in 31 patients (51%). Failure of reconstruction occurred in 4 cases (6.6%). Mean duration of hospital, and ICU stay was 8, 2 days respectively. Postoperative temporary diabetes insipidus occurred in 35 cases (58.3%), 5 of them (8.3%) had permanent DI. Major CNS complications occurred in 2 cases (3%).

Conclusion: The more experience gained the more modifications introduced to improve surgical outcome; more gross total resection rate, less morbidity, and mortality rates, less operative time, better quality of life of patients and less time and effort exhaustion of the team work.

Keywords: Pituitary, Trans-sphenoid, Hypophysectomy, Skull base

1. Introduction

The location of pituitary gland in the bottom of the brain render reaching it trans-cranially a challenging mission. On the other hand, its close proximity to sphenoid sinus give a huge privilege to transnasal approaches. It was traditionally named maestro of endocrine system, as it regulate level and functions of most of body hormones [1]. Pituitary adenomas are the major cause of pituitary dysfunction. They are the third common operated brain tumor (about 10–25% of brain tumors), however much higher incidences in radiology and autopsy studies [2].

They are slowly growing benign tumors that need a very high suspicion level for diagnosis. There are a lot of variation in their pathologic criteria, with multiple classifications based on function, size, extension, and origin of the tumor [3]. Many modalities of treatment were introduced for managing different types of pituitary adenomas; medical, surgical or radiological intervention. Many approaches and techniques were described to deal with pituitary adenoma. Nowadays the endoscopic

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* Corresponding author at: Department of Otorhinolaryngology, Kasr El Ainy School of Medicine, Cairo University, Cairo, 11562, Egypt.
E-mail address: osbashassan75@gmail.com (O. Hassan).

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transnasal approach become the state of art in dealing with pituitary adenoma [4].

Although this approach is not difficult to learn, it provide a challenging learning step ladder to master the technique itself, and methods of avoiding and managing its complications [5].

Main aim pituitary surgery is gross total removal of adenoma with preservation of normal pituitary gland function and/or reaching functional pituitary cure and avoid any insult to cavernous sinus, carotid artery, optic nerves, chiasma, 3rd, 4th, 5th 6th cranial nerves, intercavernous connections, hypothalamus and brain stem [4].

Endoscopy provide better visualization and angled vision in sinonasal surgery which encouraged the neurosurgeons to apply endoscopic techniques for trans-sphenoidal surgery for pituitary adenoma [6].

1.1. Aim of the work

Analysis of first sixty pituitary adenomas patients operated by a beginner skull base team in one institute, and highlighting modifications introduced in the classic adopted technique.

2. Methodology

This is a retrospective analytical study in which the medical records, documents, and videos of the first 60 pituitary adenoma cases subjected to endoscopic nasal trans-sphenoid approach performed by an evolving skull base team in one institute were revised. Cases were operated from 2017 to 2019. This study included cases presented to ENT, and neurosurgical departments with pituitary adenoma.

All cases were assessed by multidisciplinary team composed of rhinologist, neurosurgeon, ophthalmologist, radiologist, and endocrinologist.

All available data were recruited, tabulated in excel sheet and accurately analyzed.

Recruited data included; epidemiological data (age, gender) and history of present illness like presentations of patients; and duration of symptoms). Classification of adenomas according to hormonal profile, and tumor size in MRI.

CT scan of paranasal sinuses was revised to assess status of middle turbinate, septum, sinuses, sphenoid sinus pneumatization, septation, presence of Onodi cells, and dehiscence of carotid artery and optic nerve.

Sellar MRI data was revised regarding site, size, extension and consistency of the tumor, site of normal pituitary gland and presence of apoplexy.

Operative videos, reports, and details were revised to assess operative time, need of blood transfusion, details of technique, and modifications which were done to improve outcome of cases and avoid complications. Also intra-operative complications; CSF leak, reconstruction techniques, and all other complications were recruited.

Reports of immediate post-operative period were analyzed to detect duration of ICU and hospital stay, incidence of post-operative complications and methods of overcoming it. Unfortunately the late post-operative period follow up period is missed in this study.

Although there were a lot of modifications in surgical technique reported throughout this study with gaining more experience, skills, and team work understanding, the basic steps were constant.

After obtaining a written informed consent and explaining all possible complications, pre-op preparation was achieved with intravenous antibiotics and nasal decongestant one day before operation.

On operative day great attention was directed toward instruments, scopes, cameras and other equipments. C-arm X ray and navigation radiology set were available to be used if needed in some cases Fig. 1.

Operation was done under general anesthesia in an anti-trendelenberg position. Sterilization and scrubbing of the face was done leaving eye exposed as well as peri umbilical area and, or lateral side of the thigh.

Nasal phase started with diagnostic endoscopy and decongestion, middle and superior turbinate lateralization was done to localize sphenoid sinus ostium. Downward widening of sphenoid ostium was preceded by downward dissection of rescue flap preserve blood supply of septal mucosa. Then the same procedure was repeated on the other side, nasal septum was separated from sphenoidal rostrum to have what is known as Owle eye appearance Fig. 2, and posterior part was removed to have a wide binostril approach.

Sphenoid phase included widening of the ostium by 2 mm Karisson in all direction. Removal of all anterior wall of sphenoid sinus with trimming of superior turbinate and removal of sphenoid rostrum to expose all posterior and lateral walls of sphenoid sinus. All inter sphenoid phase septa were removed carefully, and sphenoid sinus mucosa was stripped to well visualize bonny landmarks of posterior and lateral walls of sphenoid sinus.

Sellar phase started with opening of the sellar bonny floor either by gentle pressure with dissector or gauge and hummer, and widening of sellar opening with 1 or 2 mm Kararrison up to the 4 blues. Incising of the dura with no 11 scalpel or sickle knife, and microscissors was used sometimes for extension of dural cut Fig. 3.
Tumor removal stage started with biopsy before total tumor removal with different types of curettes and suction tips.

Reconstructive phase started after achieving total gross tumor removal with delicate meticulous observation of any arachnoid defect and planning of its closure with different types of reconstructive materials mainly abdominal fat Figs. 4,5. A grading system and reconstruction scheme was followed in last cases. In G0 CSF leak (no detected leak), we used did not repair anymore, while in grade 1 CSF leak (leak without detectable defect), one layer repair is used using fat or fascia or nasal local flap or graft, while in grade 2 (defect less than 2 mm) multilayers repair was adopted. CSF diversion methods were adopted in grade 3 (defect more than 2 mm). At the end anterior nasal pack and stent were left in patients’ nose.

During post-operative period: the patients is on antibiotics, electrolytes daily checked, 24 h urine is calculated, nasal blowing is avoided, straining in all kinds was restricted.

Nasal packing was removed around day 3 post-operative and patients were discharged if remained uneventful, stents were removed after 7–10 days.

3. Results

This study included 60 patients presented to an evolving skull base team with various types of pituitary adenomas. All cases were candidate of endoscopic endonasal trans-sphenoid surgical excision.

There were 23 male (38%), 37 female (62%). Mean age was 46 years with the youngest 23 years, and the oldest 78 years old.

Thirty seven patients (61%) presented with temporal field defect, 8 patients (13.3%) had intact visual field, while 15 patients (25%) did not have full visual field assessment due to emergency situation or severe visual affection. Thirty two patients (53%) had decreased visual acuity; 18 of them (30%) had unilateral visual loss, and 14 patients (23%) had bilateral visual acuity affection. The mean duration of visual loss was 2 months; this short period because patients sought medical advice soon after visual affection.

Four patients (6%) presented with cranial nerve affection other than optic nerve mainly 3rd and 6th cranial nerves, while 14 patients (23%) presented with pituitary apoplexy (sudden headache, deterioration of vision and or conscious level, and symptoms of increased intracranial pressure) Fig. 6. Fifty one patients (85%) presented with vague persistent headache of different characters.
Forty one patients (68%) presented with non-functioning adenomas, while 11 cases (18%) were prolactin secreting adenoma, 4 cases (7%) were Cushing disease and 4 cases (7%) were growth hormone secreting adenoma.

While revising preoperative CT scans of the patients, it was found that; 9 patients (15%) had conchal middle turbinate, one patient (1.6%) had paradoxical middle turbinate. Also 6 patients (10%) had ethmoidal opacity; 4 of them were proved to be inflammatory polyps, and the other 2 cases were invasive adenoma as proved intraoperatively. Onodi cell (posterior extension of ethmoid sinus) was found in 18 cases (30%).
Sphenoid sinus pneumatization was post sellar in 31 cases (51.6%), sellar in 26 cases (43.3%), and 3 cases (5%) had presellar pneumatization. Vertical intersphenoid septation were multiple in 19 cases (31.6%), 41 cases (68.3%) had single vertical intersphenoidal septum. Intersphenoid septations were intimately directed to carotid artery in 28 cases (46.6%). Sphenoid sinus was opacified in CT scan in 11 cases (18.3%); 8 cases (13%) were tumor extension through sellar floor defect and the other 3 cases were secondary sphoeiditis.

Regarding MRI finding; fifty two cases (86.6%) were macroadenoma (more than 1 cm), 6 cases (10%) were mesoadenoma (average 1 cm), and 2 cases were microadenoma (3.3%). The site of displaced normal pituitary gland could be identification and anticipated by MRI in 38 cases (63.3%).

Fig. 5. A) grade 2 arachnoid defect with CSF leak B) reconstruction of arachnoid defect with abdominal fat as 1st layer.

Fig. 6. MRI sella showing heterogenicity of pituitary apoplexy.
Forty eight cases (80%) had suprasellar extension of the pituitary adenoma, while 19 cases (31.6%) had parasellar extension with different grades of extensions according to knosp classification Fig. 7.

In this study 3 patients (5%) were recurrent adenomas; 2 of them after endoscopic approach and another one recurred after transcranial approach.

Mean operative time was 170 min. Twelve cases required blood transfusion. Trans-septal endoscopic approach was tried in 2 cases only with subsequent shift to classic transnasal approach later because of difficult technique due to limited place for instruments, and manipulations. Trans-nasal cavity approach was adopted in 58 cases (96.6%).

Partial middle turbinate resection was inevitable in 4 cases (6.6%) due to concha bullosa and bulbous first part. Superior turbinate trimming was needed in all cases (100%) to exposing all face of sphenoid sinus and its lateral wall. Five cases (8.3%) needed limited septoplasty for septal deviation and or spurs. Ethmoidectomy was done in only one case (1.6%) due to presence of polyp. Injury of the septal branch of sphenopalatine arteries occurred in 4 cases (6.5%) and controlled by cauterization.

Normal pituitary gland could be identified clearly intraoperatively in 48 cases (80%), while in 12 cases, it was difficult to differentiate between normal gland and adenoma.

Dural incision was wide (extend to 4 blues) in 45 cases (75%). Inter cavernous connections were injured in 6 cases (10%), all were micro adenoma, and could be managed by compression.

Three cases (5%) had fibrous pituitary adenoma. Residual adenomatous tissue in supra and parasellar areas could be detected intraoperatively by the use of 30° endoscope in 23 cases (38.3%). Gross

![Fig. 7. MRI scan showing supra and para sellar extension of invasive pituitary adenoma.](image-url)
total removal of the tumor were achieved in 49 cases (81.6%).

Early arachnoid descent occurred in 11 cases (18.3%), while arachnoid did not descend to obliterate sellar cavity in 15 cases (25%).

Intraoperative CSF leakage occurred in 31 patients (51%); 30 patients were reconstructed with double layer abdominal fat, and one case had multilayer repair. Failure of reconstruction occurred in 4 cases (6.6%); two of them needed revision reconstruction, while the other 2 patients improved with conservative measures. Moreover two cases had intra-operative CSF diversion (shunt and lumbar drain).

Mean duration of nasal pack removal was 3 days (range between 2 and 5 days). Mean duration of hospital stay was 8 days (range between 5 and 20 days), while mean duration of ICU stay was 2 days (range from 0 to 5 days).

Postoperative temporary diabetes insipidus occurred in 35 cases (58.3%), Only 5 cases (8.3%) continued to had permanent DI (long life vasopressin dependant).

Major CNS complications occurred in 2 cases (3%) in the form of CNS infection and Hematoma. Three cases (5%) had minor wound complications (hematoma and gaping).

CNS complications occurred in 2 cases (3%) in the form of CNS infection and Hematoma. Three cases (5%) had minor wound complications (hematoma and gaping).

In this study forty one patients (68%) had non-functioning adenomas, while 11 cases (18%) had prolactinoma. Also Singh et al. 2018 [7] described 79% of adenomas were non-secretary whereas 21% were growth hormone (GH) secreting tumors. On the other hand, Hofstetter; s team in 2011 [15] in their study reported 35% of pituitary adenomas were non-secreting and most common secreting tumor were prolactinoma (40%) followed by growth hormone secreting tumor (20%) and ACTH secreting tumor (10%). Also Aiyer and Uperti 2020 [10] in their study had (43%) clinically non-functioning (21.4%) prolactinoma.

CT scanning was very important to assess bony structure, anatomical variation of septum and
sphenoid sinus, and planning for surgical steps for operation [10].

Regarding sphenoid sinus pneumatization in this study; most common type was post sellar (51.6%), sellar (43.3%), and presellar (5%). Being opacified in CT scan in 11 cases (18.3%); 8 of them (13%) were tumor extension. While Aiyer and Upreti 2020 [10] reported the sellar type being the most common and favourable type (93%)

Preoperative MRI brain was the cornerstone investigation modality. It identifies the site, size, extension of lesion, and its neurological and vascular relationships [10].

In the current study (86.6%) of cases were macroadenoma (10%) of cases were mesoadenoma, and (3.3%) of cases were microadenoma (80%) of cases had suprasellar extension, while (31.6%) of cases had parasellar extension.

Some authors reported incidence of suprasellar extension in 71%, sellar with parasellar extension in 7% and combined extensions in 7% of cases [7]. Ammirati et al. 2012 [6] in their meta-analysis of 5643 patients with pituitary adenoma have reported 79.75% incidence of macroadenoma with 28% showing intracavernous extension.

Throughout the revision of medical data, many modifications and improvements in the management of patients were documented.

Great attention were delivered to obtain informed written consent. Counseling providers were shifted from neurosurgeon alone to all team members; rhinologist and endocrinologist. Team members counseling and discussion became a mandatory step in preparation. Much care was provided to operative room preparations, included equipment, instruments, consumables, portable imaging systems, and distribution of equipment and personnel in operative room. Operative room preparations had taken much time and effort at the start until all medical and para medical staff had established his role well, and hence it had gone smoothly in a harmony.

Transnasal approach was adopted in 96.6% of cases. It has the advantage of being binostril four-hand technique, giving space for two surgeons to operate, and easy instrument manipulations. Preoperative local decongestants concentration had been increased to 1/1000. While reviewing operative videos, it was noticed that the manipulation of turbinates had become gentler and nasal mucosa were treated with cutting forceps rather than stripping. In the last cases, cautery of middle, and superior turbinates was minimized as much as possible to avoid atrophic rhinitis and olfactory dysfunction. Removal of sphenoid rostrum, and all parts of all inter sphenoid septations was meticulously performed in last cases for widening the exposure of the sphenoid sinus. Also with more experience, sphenoidal sinus mucosa was pushed away rather than stripped.

The principle of dural opening has been shifted from small safe cruciate incision to large X incising reaching the 4 blues. After proper coagulation of inter-cavernous connection whenever encountered. Dural incision was wide (extend to 4 blues) in 45 cases (75%). Intraoperative bleeding was better and more efficiently dealt with by the 2 surgeon collaboration where one of the team member holding the endoscope for proper visualization of the bleeding point and the other having 2 free hands for suction and hemostasis.

Before tumor removal, biopsy had been an essential step for pathological examination, also more time and effort were directed to identification of normal pituitary gland, and inspection of tumor bed before & after tumor removal with angled endoscopes. Normal pituitary gland could be identified intra-operative in 48 cases (80%) which is an important step for post-operative preservation of hormonal functions.

Residual adenomatous tissue in supra and para sellar areas could be detected intra-operative by the use of 30° endoscope in 23 cases (38.3%) which is one of the upper hand privileges for endoscopy over the microscopic technique formerly done by the neurosurgeon solely. Gross total removal of the tumor was achieved in 49 cases (81.6%). it was evident by viewing both medial walls of cavernous sinus, arachnoid membrane superiorly, sellar floor inferiorly, and dura over brain stem posteriorly. Post-operative routine MRI was no adopted in our cases. In a study of 16 cases, total resection of lesion was evident in 64% cases whereas in 36% it couldn’t be achieved. They assess residual tissue by post-operative MRI [7]. Ammirati et al.2012 [6] in their meta-analysis of 38 studies described residual lesion incidence 33%. Also Aiyer and Upreti 2020 [10] noted incidence of residual tumor was 43%. Gross total resection grades were reported in 26 studies and ranged between 14 and 91% (median: 63.5%). This wide variation of percentage was related to difference in operating surgeons’ experiences [11]. Factors affecting ability to reach gross total resection were size, and extention of tumor especially parasellar intra cavernous sinuses extension, in addition to experience of surgeons [9,10,15,16].

Gross total removal is impossible in tumor with knosp classification grade 4, and difficult in grade 3 A &3 B.
In the early cases, we did sellar and sphenoid sinus fat packing in all cases regardless presence, absence or grade of CSF leak. Modification introduced in managing intra-operative CSF leak is the strict following of a grading system of arachnoid defect size and adopting a scheme for reconstruction, and avoiding sphenoid fat packing. Intra-operative CSF leakage occurred in 31 patients (51%); 30 patients were reconstructed with double layer abdominal fat, and one case had multilayer repair. Failure of reconstruction and post-operative CSF leak occurred in 4 cases (6.6%). This goes with the results of Singh et al. 2018 where post-operative CSF leak was seen in one Patient out of 16 (6.3%). They repair all surgical defects using fat, bone and septal mucosa [7]. This is similar to the results of Aiyer, Upreti2020 [10] who states that only one patient developed post-operative CSF leak. They elevated posteriorly based nasoseptal (Hadad-Bassagasteguy) flap in all cases without incidence of flap necrosis [3]. In another study performed by Cappabianca and colleagues 2004 [17] intra-operative C.S.F leak occurred in 90 of their 242 patients (37.1%) who underwent endoscopic pituitary surgery [17].

Early arachnoid Descent occurred 11 cases (18.3%). One of the effective modifications introduced is trial of gentle arachnoid pushing superiorly with small cottonoid in cases of early descent to inspect posterior part of the sella. This was difficult at the start as it need synchronous and well oriented team work.

With gaining experience duration of nasal pack, hospital stay, and ICU admission were reduced to the minimum needed period to improve quality of life. Also treating post-operative complications had been introduced effectively and without delay which mean decrease conservative measures chances. Mean duration of nasal pack removal was 3 days (range between 2 and 5 days). Mean duration of hospital stay was 8 days (3–17 days). In agreement with this study, Other studies reported mean hospital stay was 13.54 days (Range 08–21 days) [7,13].

In this study major CNS complications occurred in 2 cases (3%), while in another study post-operative complication rate was 71% of cases. One patient with growth hormone secreting adenoma developed meningitis followed by septicemia and expired on seventeenth post-operative day [7]. The incidence of complications after trans-sphenoid surgery ranges from 0.4 to 17% [6].

The most common complication in our study was transient diabetes insipidus (35 cases) (58.3%). It is not really considered a result of excessive manipulation of the infundibulum during surgery and occurs within 24–48 h postoperatively.

In a study conducted by Ammirati et al. 2012, diabetes insipidus occurred in 4 (28.6%) patients, three of them improved with iv fluids and vasoressin sprays, while only one case (7%) developed permanent diabetes insipidus [6]. While Singh et al. 2018 [7] had 21% had transient Diabetes Insipidus (hyponatremia).

One recent survey among neurosurgeons found a significant correlation between the number of pituitary adenomas resections performed and post-operative complication rates (p < 0.05) [9].

Shou et al. 2016 [16] claimed that after completing 30 to 40 endoscopic surgeries, teamwork harmony and shared experiences between neurosurgeons and rhinologist were well established and then a harder surgery with more extensive adenomas can be tried [16].

5. Conclusion

Fully illustrative counseling between team members and patients is crucial throughout the preoperative and post-operative period.

The difficulty and complexity of OR theater preparations, four handed, double surgeon technique, learning curve of the endoscopic transnasal approach had been changed from being a limitation for the team at the beginning, to be a valuable advantage of the technique after gaining well experience.

The more experience gained the more modifications introduced to improve surgical outcome; more gross total resection rate, less morbidity, and mortality rates, less operative time, better quality of life of patients and less time and effort exhaustion of the team work.

Ethical approval for research involving human participants

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee

Informed consent

Informed consent was obtained from all individual participants included in the study.

Conflict of interest

Osama Hassan declares that he has no conflict of interest. Mohamed El Mallawany declares that he
has no conflict of interest. Mohamed Fatallah declares that he has no conflict of interest.

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