EXTENDED ENDOSCOPIC TRANSTUBERCULUM-TRANSPLANUM APPROACH FOR MANAGEMENT OF SELECTED CASES WITH PITUITARY MACROADENOMAS.

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ABSTRACT

Background: *certain pituitary adenomas are difficult to remove by the standard transsphenoidal approach. Extended Endoscopic Transtuberculum Transplanum Approach (EETA) may offer an alternative to the transcranial route in such cases.*

Aim Of the Work: *We present our experience in Extended Endoscopic Transtuberculum-Transplanum Approach (EETA) for management of selected cases of pituitary macroadenomas in regard to case selection, surgical technique, reconstruction methods, resection rate and clinical outcome.*

Methods: *12 patients with pituitary adenomas that underwent an EETA from March 2018 to June 2022 were reviewed.Clinical outcome and postoperative complications were evaluated.*

Results: *Gross total resection was achieved in 9 (75%) patients, and near total resection (>90%) in 2 (17%) patients. Visual symptoms improved in 8 (67%) patients, and visual deterioration occurred in 1 (8%) patient. Only one patient developed postoperative CSF leak that required reoperation and was successfully managed. One patient developed a serious ischemic stroke.*

Conclusion: *Our experience showed that the EETA offers a viable treatment option in Selected cases of pituitary tumors.*

Key Words*: Pituitary tumors; Endonasal; Endoscopic; Extended approach; Vision.*

INTRODUCTION:

Although most of pituitary adenomas can be successfully removed via the standard transsphenoidal approach either microscopic or endoscopic[1-7], there is some pituitary adenomas that are very difficult to be removed by this approach, these include tumors with very firm consistency, some tumor configurations like: dumbbell shaped adenomas with very tight diaphragma constriction between the sellar and suprasellar component, invasive adenomas invading the diaphragma sella with extension into the subarachnoid space, purely suprasellar adenomas, tumors extending into the anterior cranial fossa with sub-frontal location, invasive adenomas with lateral extension into the parasellar space and cavernous sinus and into the middle cranial fossa, recurrent giant adenomas with large suprasellar extension and multilobular configuration which suggest firm consistency, previous radiation or medical treatment that might cause scar formation and firm consistency[8-12].

Potential surgical approaches for management of such lesions include: microscopic transcranial approaches[7],

staged transsphenoidal approach either microscopic or endoscopic (to allow the undescended suprasellar component to go down into the resection cavity)[13-15], staged or combined microscopic transcranial and transsphenoidal approaches, and extended endoscopic endonasal approaches[8, 10-17], selection of the surgical approach depends on size and shape of the lesion, tumor invasion and extension, and the patient's age, health, and visual function.

The extended endoscopic transtuberculum/transplanum (EETA) approach has been used for surgical management of a variety of midline suprasellar lesions, including Craniopharyngiomas, Tuberculum sella and planum meningiomas[13, 18-24], also has been used for management of selected cases of Pituitary adenomas[8-10, 12, 14-17, 25].

In the past few years, we have used the EETA for management of certain midline skull base lesions. In this report, we are going to present our early experience and surgical technique of this approach in management of selected cases of pituitary adenomas.

AIM OF THE WORK:

We present our experience in Extended Endoscopic Transtuberculum-Transplanum Approach (EETA) for management of selected cases of pituitary macroadenomas in regards to case selection, surgical technique, reconstruction methods, resection rate and clinical outcome.

METHODS

Patient Population and Data Collection:

a retrospective Review for the endoscopic endonasal procedures we performed for management of pituitary macroadenomas by the first and the last authors at Ain Shams university hospital and affiliated hospitals from the time period of March 2018 to June 2022 was done. One hundred and fifty-one procedures were identified. All patients with histologically confirmed pituitary adenoma who performed Extended Endoscopic Transtuberculum-Transplanum Approach (EETA) were included in our study. This study was approved by Ain Shams University Hospital Institutional Review Board (IRB).

The choice of EETA for these patients was based on the 1) Neuroradiological data available before surgery (Dumbbell shaped or multilobular adenomas, tumors extending into the anterior cranial fossa and/or invading the diaphragma and extending into the subarachnoid space, pure suprasellar adenomas, very large recurrent adenomas with large suprasellar and/or intraventricular extension), 2) Operative findings observed in the previous surgery for the recurrent or staged cases (firm consistency of the tumor who failed to descend in the resection cavity), 3) Intraoperative findings in some cases (tumors with firm consistency who failed to descend after resection of the endosellar part of the tumor or diaphragma opening with a narrow constriction or tumors invading the diaphragma).

Complete hormone assessment of the pituitary gland was performed before surgery and within the 1st week after surgery and repeated after 3 months and subsequently thereafter, when necessary, Preoperative Magnetic Resonance Imaging (MRI) brain with contrast and CT paranasal sinuses were performed for all cases and repeated within 24 hours or a week and after 3 months. Tumor shape was classified based on subjective appearance as either round, dumbbell, or multi-lobular. Tumor location was evaluated for extension into the suprasellar cistern, third ventricle and anterior cranial fossa. Cavernous sinus invasion was graded according to the modified Knosp score[26]. Cavernous sinus invasion was defined radiographically as Knosp grades 3A, 3B, and 4. CT scans were evaluated to assess for bony invasion of the sphenoid sinus, clivus, anterior skull base, and/or orbit.

Neuro-ophthalmology evaluation was performed by visual acuity and Humphrey visual field testing before surgery and approximately 2-4 months postoperatively.

Extent of resection and clinical outcome was evaluated for all patients, Extent of tumor resection was classified as: gross total resection (GTR), near total resection (>90%resection), subtotal resection (> 70% resection), and partial resection (< 70% resection). Clinical outcome was evaluated for visual and hormonal outcome after surgery, and postoperative complications including postoperative CSF leak, hormonal complications including Diabetes Insipidus (DI), postoperative pituitary apoplexy, vascular insults, Neurological deficits and medical complications.

Surgical Technique and Reconstruction:

Patient positioning: The head is slightly extended (5-10 degrees) slightly rotated to the right side to facilitate surgical access and make it more comfortable for the surgeon, the head is slightly elevated above the level of the heart to enhance venous drainage.

Endoscopic Trans-sphenoidal access: A 2-surgeon, 4-handed technique with binostrial access was employed. Latera-lization of both medial turbinate without resection was done in all cases, identification of both sphenoid ostia , harvesting of the nasoseptal flap, posterior nasal septectomy is done to enable us for binostril access and use of 2 or 3 instruments beside the endoscope, wide sphenoidotomy is done in all cases which is very important to help us in identifying the skull base recesses, removal of the sphenoid sinus septa, sometimes we needed to do additional posterior ethmoidectomies to give us more anterior access depending on tumor morphology and the sphenoid sinus pneumatization. Identifying the sellar floor, carotid and optic protuberances, medial and lateral opticocarotid recesses is very important, the Neuro-navigation was used in the recurrent cases where the previous surgical scar might obscure the bony landmarks, the microdrill was used to open the sellar floor, thinning out the tuberculum sella and the planum sphenoidal using a diamond burr with copious irrigation then removing it using a karrison punch, drilling the lateral tubercular strut (medial opticocarotid recess) is crucial to give us a wider corridor for the suprasellar space.

Tumor removal: The tumor was accessed with limited dural opening over the sella using a cruciate incision, the tumor resection is started in the standard endosellar fashion using curettage and suction, in most cases where the tumors were fibrous, such maneuvers were ineffective in obtaining a satisfactory debulking, in such cases, the microdissection and micro-scissors were used for intracapsular tumor debulking, every effort was made to do the maximal excision using the endosellar corridor first and avoid the additional dural opening, when there is a firm, large undescended suprasellar portion or a constriction in the diaphragma sella with large portion of the tumor above it the dura was opened over the tuberculum and the planum after coagulation of the dura over the superior intercavernous sinus (which was obliterated in most cases), bimanual extracapsular dissection of the tumor from the neurovascular structures using the suprasellar corridor will allow pushing down the tumor and further debulking using the endosellar corridor (working using both corridors), after dissection and exposure of the critical structures, completion of the tumor resection using microsurgical technique is carried on, division of part of the diaphragma sella is often necessary to enable us to do this.

Reconstruction: Multilayer skull base reconstruction and covering of the osteo-dural defect using a Fascia lata graft followed by a vascularized nasoseptal flap then a fibrin Glue is the usual reconstruction method we used in most cases. Only in 2 cases different method was used, both cases were a recurrent

cases and the flaps were not available due to cauterization in the previous surgeries, a large fat graft was used to plug the osteo-dural defect with part of the graft inside the resection cavity to close the dead space, then covered by a multilayer reconstruction using fascia lata followed by bone graft worked as a gasket to hold the fascia lata in place and close the bone defect and followed by another fat graft inside the sphenoid sinus.

Ethical approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of Ain Shams University hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

RESULTS:

Patient Demographics and Clinical Presentation:

Twelve patients were included in the study. The mean patient age was 46 years (range 18 – 60) with a male predominance (58%). Visual affection Was the presenting complaint in all the patients (100%), partial or panhypopituitarism was present in Eight patients (67%), two patients had a hormone secreting tumor, one of them presented by a Growth hormone over secretion, and one presented by prolactin over secretion refractory to medical treatment, headache presented in three patients (25%) 6th cranial nerve palsy in one patient (8%). Three (7.3%) patients had prior trans-sphenoidal surgery. No patients had a history of prior radiotherapy (Table 1).

Table 1: *Patient Demographics and clinical presentation.*

Age	46 (18-60) years
Sex • Male • Female	 7 (58%) 5 (42%)
Visual affection	12 (100%)
Endocrinal dysfunction	
• Normal	3(25 %)
• Partial or Panhypopituitarism	8(67%)
• Hyperfunction	2 (16%)
• Headache	3(25%)
Other presentation	
• Hydrocephalus	-
• Cranial nerves deficit	1 (6th nerve palsy)
Recurrence	3 (25%)

Tumor Radiographic Characteristics:

Based on the preoperative MRI, the average tumor volume was 31.8cm^3 (±17.25) (range 9.1-75). The average maximum tumor diameter was 6 cm (3.0-8.0). All tumors had suprasellar extension but anterior cranial fossa with sub frontal extension observed in one patient, tumors extending to the 3rd ventricle were found in 4 (33%) patients, dumbbell shaped configuration of the tumor was present in 5 (42%) patients, while multilobular configuration was present in 6 (50%) patients. Cavernous sinus extension according to modified Knosp score was grade 1, 2, 3a, 3b, 4 in 17%, 67%, 8%, 8%, 0% of patients respectively, Invasion of sellar floor into the sphenoid sinus was found in 3(25%) patients. Invasion of the tumor through the diaphragma Sella into the suprasellar cistern was seen intraoperative in Eight (67%) patients (Table 2).

Table 2. Tumor Radiographic Characteristics

Tumor volume	31.8 (9.1-75)
Maximum tumor diameter	6 (3-8) cm
Shape	
• Single lobe	1 (8%)
• Multilobular	6 (50%)
• Dumble shaped	5 (42%)
Invasion	
• Sphenoid sinus	3 (25%)
• Diaphragma Sella	8 (67%)
• 3rd Ventricle	4 (33%)
Knosp	
• 1 • 2 • 3a • 3b • 4	2 (17%) 8 (67%) 1 (8%) 1(8%) 0

Extent of Resection, Clinical Outcome and Complications:

GTR was achieved in 9 (75%) patients, NTR in 2(17%) patients, and STR resection in one (8%) patient. Visual symptoms improved in 8 (67%) patients, remained unchanged in 3 (25%) patients, while deterioration occurred in one (8%) patient after surgery.

Eleven patients (91%) developed postoperative DI, seven of them were transient and only four (33%) patients were permanent. Only one patient developed a persistent postoperative CSF leak that required reoperation for reconstruction and was successfully managed. Postoperative endocrine function was unchanged in five (42%) patients, five (42%) patients developed a new hormone deficit after surgery, and in the two patients with functioning adenomas (one Growth hormone secreting and the other Prolactin secreting) the hormone remission was achieved after surgery for both. One patient developed a serious ischemic stroke due to perforator vessel injury, this patient died due to medical complications 28 days after surgery (Table 3).

Table 3*. Extent of Resection, Clinical Outcome and Complications*

Degree of resection	
• GTR	9 (75%)
• NTR	2 (17%)
• STR	1 (8%)
Visual outcome	
• Improved	8 (67%)
• Unchanged	3 (25%)
• Worsen	1 (8%)
Hormone remission after surgery for secreting adenomas	2(100%)
Postoperative DI	
• No	1 (8%)
• Transient	7 (58%)
• Permenant	4 (33%)
CSF leak postoperative	1 (8%)
New endocrinal dysfunction	5 (42%)
Ischemic stroke	1 (8%)

Tumor Control and Follow UP:

The mean follows up period was 21 months (SD ±10.2). During this period radiographic tumor recurrence after GTR was detected in only one patient (8%), while radiographic residual tumor progression after STR was non detected. This patient with recurrence was treated with radiosurgery.

Table 4. *demographics and tumor morphology of the series reported per patient.*

Case number	Age/Sex	Hormone secretion	Previous treatment	Tumor Configuration	Tumor Invasion	Cavernous sinus Knosp grade
1	51/M	No	No	Dumbbell shaped	-	3
2	27/M	Prolactin secreting	Medical (Cabergoline)	Sellar, Suprasellar with anterior cranial fossa extension	Clivus, Sphenoid, Diaphragma	2
3	60/F	No	Endoscopic endonasal	Giant with suprasellar and 3rd ventricle extension	Diaphragma, 3rd ventricle	2
4	34/F	No	No	Sellar, Suprasellar with arachnoid invasion and encasement of ACA	Diaphragma	1
5	47/M	No	Endoscopic	Dumbbell shaped	-	2
6	51/M	No	Microscopic	Dumbbell shaped	-	2
7	45/F	No	No	Giant with Suprasellar extension	Sphenoid	2
8	56/M	No	No	Giant with suprasellar and 3rd ventricle extension	Diaphragma, 3rd ventricle	2
9	60/F	No	Endoscopic	Giant with suprasellar and 3rd ventricle extension	Diaphragma, 3rd ventricle	2
10	35/F	No	No	Dumbbell shaped	Diaphragma, Sphenoid sinus	2
11	55/M	No	No	Dumbbell shaped	Diaphragma	2
12	18/M	No	No	Giant with suprasellar and 3rd ventricle extension	Diaphragma, 3rd ventricle	2

Table 5*. Intraoperative findings, repair technique, clinical outcome, resection rates and complications reported per patient.*

Case No.	Tumor consistency	Repair technique	(CSF leak)	Other Complications	Visual outcome	Postop. endocrine function	Extent of resection	Follow up (months)
1	Firm	fascia lata, nasoseptal flap	No	DI transient	improved	unchanged	GTR	36
2	soft	Multilayer (fat and fascia lata)	No	No	unchanged	Hormone remission	GTR	24
3	Firm	Multilayer (fat and fascia lata)	No	Ischemic stroke, medical complication, death	unchanged	worsened	GTR	-
4	Soft	fascia lata, nasoseptal flap	No	DI transient	improved	unchanged	STR	9
5	Firm	fascia lata, nasoseptal flap	No	DI permanent	One eye worsened	worsened	NTR	48
6	Firm	Multilayer (fat and fascia lata)	Y, Lumbar drain	No	improved	unchanged	NTR	24
7	Firm	fascia lata, nasoseptal flap	No	DI, transient	improved	worsened	GTR	12

8	Soft	fascia lata, nasoseptal flap	No	DI, transient	unchanged	worsened	GTR	6
9	Firm	fascia lata, nasoseptal flap	No	DI permanent	improved	worsened	GTR	6
10	soft	fascia lata, nasoseptal flap	No	DI, transient	improved	unchanged	GTR	12
11	Firm	fascia lata, nasoseptal flap	No	DI permanent	Worsen	unchanged	GTR	24
12	Soft	fascia lata, nasoseptal flap	No	DI, transient	improved	worsened	GTR	12

Figure 1. Example of tumor extending into anterior cranial fossa. A case of prolactin secreting adenoma, 27 years old male with history of prolactin secreting adenoma refractory to medical treatment the tumor is extending into the anterior cranial fossa (a) and invading the sellar floor and the clivus (arrows) (b). postoperative MRI after extended transtuberculum approach showing GTR of the tumor with complete hormone remission (c)

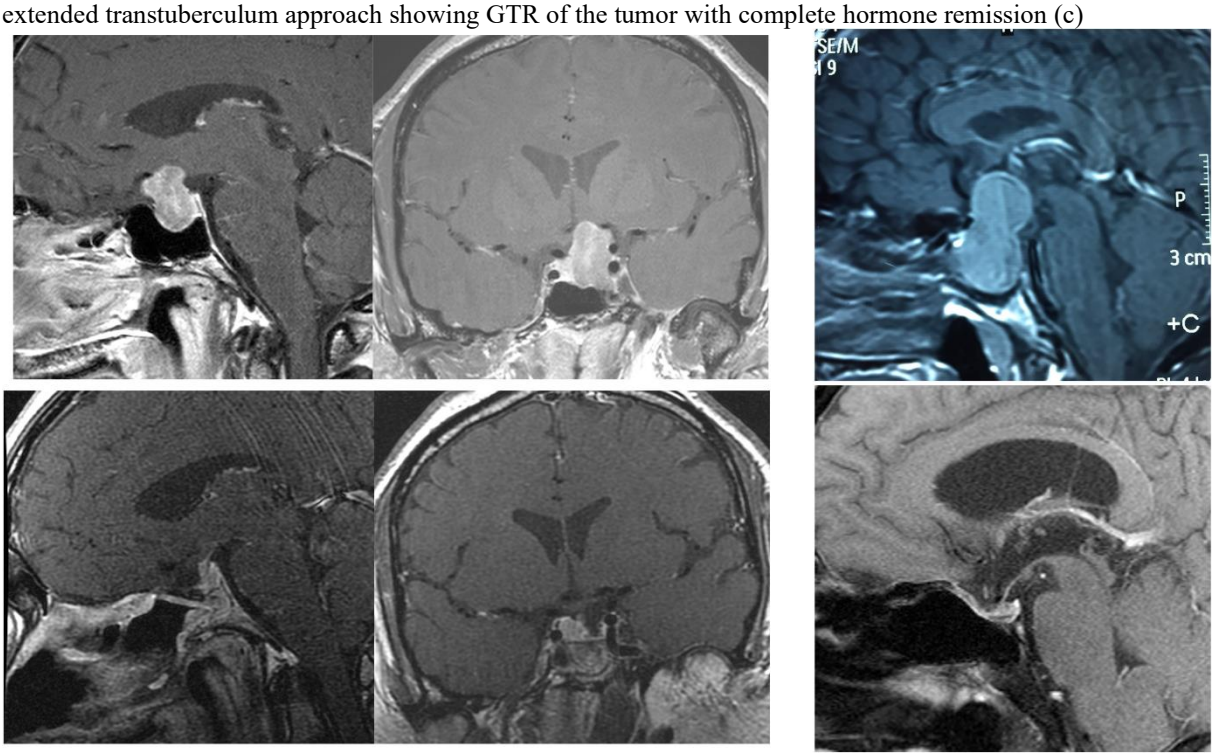

Figure 2. Examples of management of fibrous adenomas in our series. Case 1(a): Preoperative sagittal (left) and Coronal MRI (right) showing pituitary adenoma extending into suprasellar space and abutting both anterior cerebral arteries, the tumor was very fibrous. (b) Postoperative sagittal (left) and Coronal MRI (right) after EETA showing gross total resection of the tumor. Case 2 (c): Preoperative sagittal MRI showing dumbbell shaped pituitary adenoma extending into suprasellar space, the tumor was very firm. (d) Postoperative sagittal MRI after EETA showing gross total resection of the tumor.

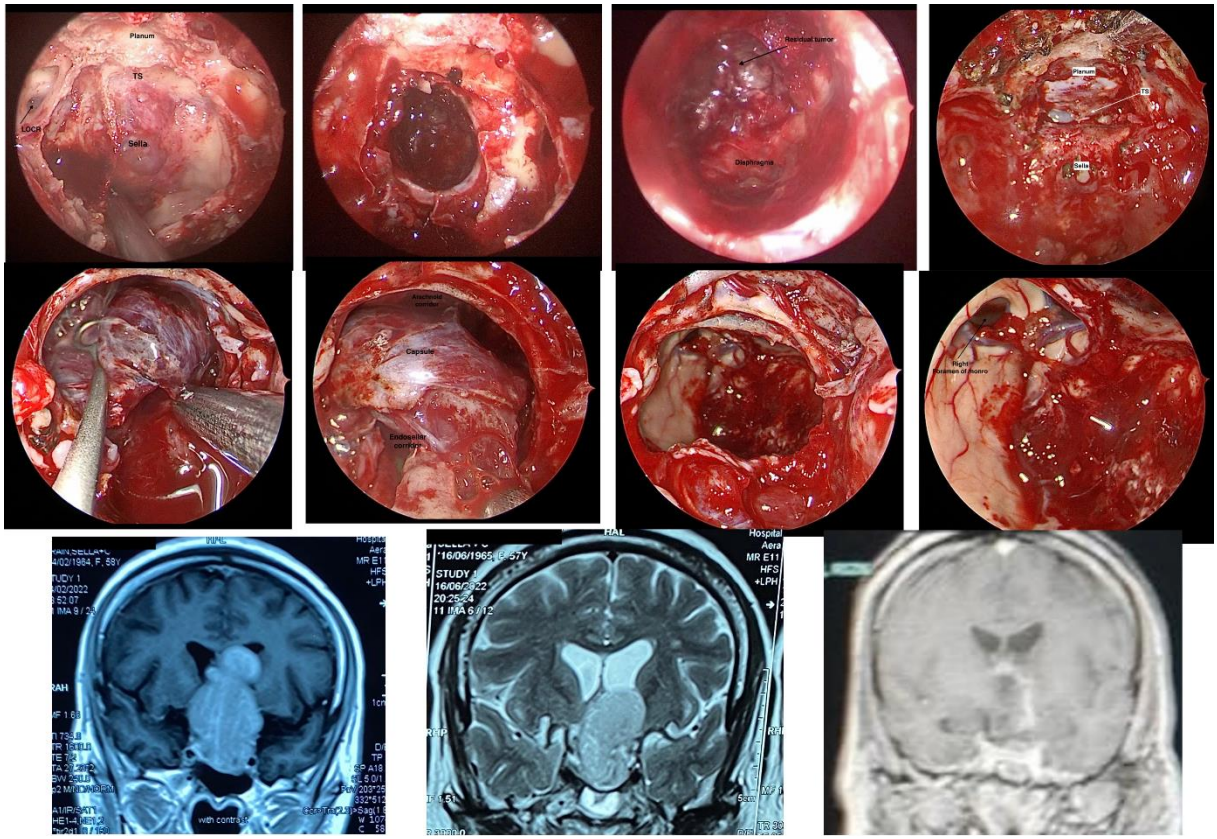

Figure 3. A case we did a 2 staged endonasal approaches for, the 1st using the standard endosellar approach and the second using the extended transtuberculum transplanum approach. in the 1st surgery we exposed the sella, tuberculum, planum and the parasellar recesses but we only worked through the sella and we did good debulking of the lesion which was firm invading the diaphragma sella and extending to the suprasellar cisterns (a, b, c) we left this part of the tumor for a second stage surgery, repeated MRI after 3 months showed significant descent into the resection cavity. we went again using the endonasal approach after drilling of the tuberculum and planum (d) we opened the dura over the tuberculum, and we did extracapsular dissection of the tumor from the neurovascular structures using the arachnoid corridor and using both corridors the endosellar and the arachnoid corridor we completed excision of the tumor (e, f). at the end of tumor excision, we can see the invaded floor of 3rd ventricle, both foramina of Monroe and the lateral ventricles (g, h), MRI showing the tumor before the 1st surgery (i), 3 months after the 1st surgery (j) and 5 days after 2nd surgery showing GTR of the tumor (k)

DISSCUTION:

EETA offers a unique surgical exposure for the tumors difficult to be removed using the standard approach due to large or firm undescended suprasellar tumor portion, blind curettage or dissection may cause transgression of instruments into the subarachnoid space which might cause injury of the optic apparatus or the critical vessels. extension of the dural opening over the Tuberculum sella and planum offers two corridors to approach the tumor simultaneously, the endosellar (sub-diaphragmatic) corridor for maximal intracapsular tumor debulking, and a suprasellar (intra-arachnoidal) corridor to allow for a bimanual extracapsular dissection of the suprasellar part of the tumor from the critical neurovascular structures under direct vision to allow for a safe maximal tumor resection.

Transcranial microscopic approaches has been used for management of pituitary adenomas difficult to be removed by standard transsphenoidal approach, however anato-mical relationship of certain tumors may favor the extended transtuberculum approach over the anterior cranial approaches especially tumors extending to retro-chiasmatic and sub-chiasmatic space as

manipulation of the stretched nerves and chiasma from above might cause visual deterioration[9,11&17], also some tumors with large sellar components especially those invading the sellar floor and the clivus are very difficult to remove by transcranial approach, the EETA offers a wide surgical exposure to facilitate dissection of the tumor from the optic apparatus and critical vessels without manipulation. In one case with a functioning hormone secreting prolactinoma not responding to medical treatment the tumor had a large sellar component invading the sellar floor and the clivus, also there was a large portion extending into the anterior cranial fossa above the tuberculum and the planum sphenoidal, the EETA was used for management of this tumor and GTR of the lesion was achieved with complete hormone remission (Figure 1).

A dumbbell-shaped adenoma configuration is not usually an indication for the extended transsphenoidal approach. A lot of cases can be treated with the standard transsphenoidal approach, but sometimes the tumor consistency is not soft enough and the diaphragma opening is very narrow and the manipulations to deliver the suprasellar component from it is not possible, in these cases EETA facilitate extracapsular dissection, debulking and pushing down the suprasellar component with partial division of the diaphragma, this was done in three cases in our series.

Firm or Fibrous adenomas, either denovo or with history of previous medical treatment, radiation therapy or previous surgery especially those with significant suprasellar extension are difficult to treat using the standard transsphenoidal approach, blind dissection of the suprasellar component is hazardous and extracapsular dissection of the tumor from the neurovascular structures facilitate safe debulking and excision, Five cases in our series was firm or rubbery in consistency and we were able to achieve GTR or NTR in all the cases (Figure 2).

Postoperative necrosis, hemorrhage or swelling in the residual part of the tumor after partial tumor resection (postoperative apoplexy) is a documented complication, although it is uncommon it is mostly associated with serious morbidity and mortality due to rapid compression on the adjacent critical neurovascular structures[27-29], so leaving significant portion of the tumor behind is always associated with some risk of serious postoperative complication, a staged endoscopic endonasal approach was planned in one case in this series, this case was a giant pituitary adenoma with maximal tumor diameter of 8 cm, there was no parasellar extension but the tumor was invading the floor of the 3rd ventricle and extending into the lateral ventricle, good tumor debulking of the lesion was done but there was significant undescended suprasellar component firm in consistency, we opted for a second stage after 3 months to give a chance for the residual part to descend into the resection cavity and fortunately no apoplexy occurred, then we went again using the extended transtuberculum approach as the tumor was firm, a gross total resection of the tumor was achieved (Figure 3).

The main concern for the use of the EETA for these selected pituitary adenomas includes the substantial increase in potential morbidity compared with a simpler standard transsphenoidal technique, mostly the increased risk of CSF leak. However, in this report only one case with postoperative CSF leak occured, thanks to the multilayer reconstructive techniques and vascularized nasoseptal flap coverage the risk of postoperative CSF leak has decreased substantially to the level that it is not considered an obstacle for this approach nowadays, but it is still relatively higher compared to the standard approach.

This approach also is technically demanding, and use of specific endoscopic microsurgical instruments designed for expanded approach like microscissors,

hooks, and micrograsping forceps is very critical to enable us to properly dissect and resect the tumor efficiently and safely.

Conclusion:

Our early experience showed that the EETA offers a potentially viable treatment option in certain pituitary tumors which are difficult to remove by the standard trans-sphenoidal approach with high rates of tumor resection and visual improvement and low rates of complications. However, successful removal of these tumors requires significant experience in endoscopic endonasal cranial base surgery and longer follow-up and larger series are needed to establish the efficacy of this approach.

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The study was retrospective review of the records so informed consent of the patients was not needed.

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استخدام المدخل الجراحي الأنفي الموسع لإستئصال أنواع محددة من أورام الغدة النخامية.

مينا منير و محمد حلمي و احمد نجاتي و سامح محمد حفني و خالد الشاذلي

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الخلفية: بعض اورام الغدة النخامية لايمكن استئصالها بالمدخل الجراحي الأنفي التقليدي، المدخل الأنفي الموسع يمثل بديل جيد لجراحات فتح الجمجمة في بعض الحالات. نستعرض في هذه الدراسة خبرتنا في استخدام المدخل الجراحي الأنفي الموسع في علاج بعض حالات أورام الغدة النخامية ونستعرض اختيار نوعية الأورام، تفاصيل إجراء الجراحة، نسبة استئصال الورم و نتائج الجراحات.

الطرق: تم استعراض نتائج اجراء ١٢ جراحة باستخدام المدخل الأنفي الموسع من حيث نسبة الإستئصال وتعافي النظر ومضاعفات الجراحة.

النتائج: تم استئصال الورم بشكل كامل في ٧٥٪ من الحالات، تعافي النظر في ٦٧٪ من الحالات، تسرب السائل النخاعي حدث في حالة واحدة وتم علاجها بشكل ناجح، مريض واحد حدثت له جلطة خطيرة بعد الجراحة، متوسط فترة المتابعة ٢١ شهر.

الاستنتاج: المدخل الأنفي الموسع هو بديل جيد لاستئصال بعض أورام الغدة النخامية