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Original Article

Our experience with Endoscopic Transnasal Transsphenoid Resection of Pituitary Adenomas

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INTRODUCTION: The two most common subtypes of Pituitary adenomas are Prolactinomas and non-functioning adenomas. Patients usually present with infertility, diminished libido, galactorrhea, visual manifestations, headache or manifestations of endocrine malfunction. Regarding Prolactinomas, medical treatment is usually administered before surgical resection, as most prolactinomas are highly responsive to it. Since the advent of endoscopic equipment, the transsphenoidal approach has been the surgical method of choice for treatment of pituitary adenomas.

OBJECTIVE: To evaluate the endoscopic transnasal transsphenoidal approach for resection of Pituitary adenomas in our institute in terms of the degree of tumor resection, the clinical, visual and endocrinological outcomes, and the complications.

PATIENTS AND METHODS: This is a retrospective single-institute study of 56 patients who underwent endoscopic transnasal transsphenoidal resection of pituitary macroadenomas and microadenomas in Suez Canal University Hospital from 01 January 2018 to 31 June 2022. We evaluated the endoscopic transnasal transsphenoidal approach for resection of pituitary adenomas in terms of the degree of tumor resection, clinical, visual and endocrinological outcomes, and complications.

RESULTS: In 43 patients (76.8%), gross total resection was accomplished. Endocrinological improvement was seen in 21 out of 24 patients with functioning adenomas (87.5%), including 16 patients with prolactinomas, and visual improvement was seen in 14 out of 16 patients with visual field impairment (87.5%). Seven patients (13%) experienced postoperative diabetes insipidus (DI), including three patients (5%) who had the condition for an extended period. Despite using fibrin glue and a multilayer closure, we had one patient (1.8%) with cerebrospinal fluid (CSF) leak. In this case, surgical exploration was performed, and a high-flow CSF leak was found despite the standard skull base reconstruction performed in the initial operation. A pedicled right middle turbinate flap was used for repair with stoppage of CSF leak. Five of our patients (8.9%) experienced recurrence. We did not experience major morbidities (meningitis, carotid artery or optic nerve injuries), and there were no mortalities.

CONCLUSION: Endoscopic transnasal transsphenoidal resection of pituitary macroadenomas and microadenomas is a safe technique in experienced hands. A sounding knowledge of anatomy along with a detailed study of patients imaging is our map and roadmap.

KEYWORDS: Endoscopic transnasal, Pituitary macroadenoma, Pituitary microadenoma, Transsphenoidal surgery.

INTRODUCTION

Prolactinomas and non-functioning pituitary adenomas are the most common types of pituitary adenomas. Patients may experience headaches, visual manifestations, or manifestations of endocrine dysfunction such as galactorrhea, infertility, or a decrease in libido.[1] In 2017, the World Health Organization (WHO) published the fourth version of its classification of tumors of the endocrine organs.[2] Afterwards, summaries for this classification of pituitary tumors were produced by a number of authors.[3,4] Not all the patients present with symptoms because most adenomas remain asymptomatic, with small size, and do not secrete hormones in excessive amounts.[5]

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Pituitary adenomas are divided into microadenomas (<10mm), macroadenomas (≥10 mm), and giant adenomas (≥40 mm).[6,7] If the brain magnetic resonance imaging (MRI) shows a tumor compressing the optic apparatus, then a formal visual field assessment including perimetry is indicated.[5,6] Evaluation of pituitary function with hormonal profile is crucial. Diabetes insipidus is rarely the presentation of pituitary adenoma.[2] However, two-thirds of these adenomas present with excess hormonal symptoms.[5] In studies that included 1718 patients, 32% to 66% were prolactin-secreting adenomas, 15% to 50% were non-functioning adenomas, 10% were growth hormone (GH)-secreting adenomas, about 4% were adrenocorticotropic hormone (ACTH)-secreting adenomas and less than 1% were thyrotropin-secreting adenomas.[8–14] Hormonal profile analysis is required for patients who have imaging evidence of incidentalomas. Any oversecreting hormones should be handled

appropriately if they are discovered.[5] All patients with pituitary non-functioning macroadenomas should be evaluated for hypopituitarism.[15,16] Hyperprolactinemia may occur due to pituitary stalk dysfunction.[5]

The endoscopic transsphenoidal approach has become the widely accepted treatment modality for the majority of pituitary adenomas.[17] Prolactinomas are very responsive to medical management, therefore, medical treatment is given before surgical resection. An open craniotomy is rarely performed nowadays.[18,19] Transnasal transsphenoidal resection is recommended for patients with enlarging masses or symptomatic tumors with mass effects.[20,21] The transnasal transsphenoidal surgery is indicated for sellar, suprasellar, intraventricular, retro-infundibular, and invasive tumors. The bi-nostril endoscopic approach gives a wide working area. This approach gives a high standard of safety, greater extent of tumor resection, in addition to better quality of life. Better outcomes and fewer complications are achieved along with the learning curve. Using microscopic or endoscopic-assisted microscopic surgery can be done in selected cases.[17]

Multidisciplinary approach cooperation is the keystone for reaching excellent results.[17] Radiotherapy is rarely used as a primary treatment option, and it is usually reserved for individuals who are unable to undergo surgery. Radiation is frequently utilized as an adjuvant therapy when a residual tumor is visible on postoperative MRI. Irradiation is an option in patients who did not achieve adequate reduction in tumor size and/or hormonal levels after medical or surgical treatment or both.[5] The conventional fractionated therapy has been replaced by the newer single higher dose irradiation after careful tumor stereotactic mapping except in very large invasive tumors or tumors in close proximity to the optic chiasm.[22,23] We evaluated the endoscopic transnasal transsphenoidal approach for resection of pituitary adenomas in our institute in terms of degree of tumor resection, clinical, visual and endocrinological outcomes, and complications.

PATIENTS AND METHODS

Study design

This is a retrospective single institute study of patients with pituitary macroadenomas and microadenomas operated upon by the endoscopic transnasal transsphenoidal approach in Suez Canal University Hospital from 01 January 2018 to 31 June 2022. The study has been approved by the Research Ethics Committee of Suez Canal University Faculty of Medicine (Research number 5190), and consent was obtained from all patients.

Participants

Fifty-six patients that underwent endoscopic transsphenoidal resection for pituitary macroadenomas and microadenomas in Suez Canal University Hospital from 01 January 2018 to 31 June 2022 were included. All participants consented to participate in the study.

Clinical and radiological evaluation

The preoperative evaluation was performed by a multidisciplinary team including a neurosurgeon, an otolaryngologist, an endocrinologist, a radiologist, an anesthesiologist and an ophthalmologist. To make a certain diagnosis, a radiologist performed and reported a contrast-enhanced MRI sella. After the patient and his/her family have been consulted and given their approval, a surgical plan was created. Each case was then given a thorough endocrinological and ophthalmological work-up. Prior to surgery, pituitary hormone levels were assessed to compare afterward. An ophthalmologist was consulted in every instance to perform Humphrey's visual field, visual acuity, fundus examinations, and follow-up exams. To establish the nasal anatomy, sphenoidal anatomy, and internal carotid artery proximity to our surgical corridor, computed topography of the paranasal sinuses (coronal, axial, and sagittal) was performed. Otolaryngologists assessed the patient to determine the best course of action. In the anesthesia outpatient clinic, the patient was evaluated for fitness for general anesthesia.

Surgical procedure

In our center, transsphenoidal surgery has been performed exclusively endoscopically from 2010 onward. A neurosurgeon and otolaryngologist couple always perform the entire procedure. We have a medium surgical volume, with over 50 cases a year. We have dedicated Storz equipment (Karl Storz, Tuttlingen, Germany), which includes not only endoscopes (0^o and 30^o), high-definition (HD) cameras, and monitors, but also endoscopic surgical tools like specialized drills, curettes, and dissectors. The authors created a standardized methodology for the procedure, which has enhanced the outcomes and benefited the entire operating room team's ability to operate together. It is also the authors' experience that greater surgical volume benefits the quality of care and efficiency.

The surgeries were performed by neurosurgeons and otolaryngologists. The abdomen and the lateral thigh of the lower limb, which was away from the anesthesiology team working area, was prepared and draped in case of the need for abdominal fat and/or fascia lata graft for closure. The anesthesiologist aspirated 15 cc of venous blood to instill 3 cc each in 5 red-capped serum tubes and lavender-capped serum tubes to be sent to the clinical pathology lab for hospital-made fibrin glue for usage in case of CSF leakage.

In the hospital blood bank, the fibrin glue was made. Three days before surgery, autologous blood donation was encouraged for all patients. In triple blood bags with 70 ml of citrate phosphate dextrose-adenine-1 (CPDA-1) (JMS, Singapore), 450 ml of blood donation

was collected. Within two hours, the red blood cells and plasma were separated by centrifugation for ten minutes. The plasma was frozen and kept at 40°C for 48 hours. In 15 ml of plasma, the cryoprecipitate was suspended. Precipitate containing 7 ml of fibrinogen and factor XIII (a fibrin stabilizing factor) was drawn into a syringe. We utilized autologous thrombin, which was made by taking 15 ml of the patient's blood in tubes, letting it sit for 30 minutes until it clots, and then centrifuging it for 12 minutes before collecting the supernatant (around 10 ml). Afterwards, we combined thrombin and cryoprecipitate in an equal volume. Just before the final 2 minutes of administration into the flaps, we added 2 ml of 50 mg/mL calcium gluconate.[24]

A binostril transnasal transsphenoidal approach was performed. The nose was sterilized with betadine, and adrenaline/saline with dilution 1/100000 was injected submucosally then a nasoseptal Hadad flap was raised bilaterally until exposure of the anterior table of the sphenoid sinus bilaterally. The flap was left aside for reconstruction at the end of the procedure. Usually, the flap was preserved mainly on the side of the greater growth of the tumor, and the other side, if not required later on in reconstruction, was sacrificed. Reversed Hadad flap was used to cover the exposed posterior nasal septum to fasten healing.[25] Posterior septectomy was done. An extensive sphenoidotomy was performed with drilling the rostrum of the sphenoid sinus until full exposure of the sella and carotid bulge bilaterally was obtained. We rarely sacrificed the middle turbinate which was preserved except in cases with inadequate exposure to the sphenoid sinus. To uncover the sella and expose the pituitary, bone removal of the sella turcica was performed until adequate dural exposure was obtained. In cases with Onodi cell presentation, it was opened to complete the sphenoid sinus exposure.

Before opening the dura, the surrounding bony rim should be clear of mucosa so that the bed can be reconstructed at the end of the operation. An ultrasound guide could be used to plan the opening of the dura and avoid injury to the carotid artery. A cruciate incision was made in the dura mater, and the tumor capsule was carefully removed from the inner surface of the dura mater using a dissector. This technique focuses on identifying the tumor capsule at later stages of surgery when tumor debulking makes the capsule more identifiable. The lower pole of the tumor was incised and resected with a ring curette, and the dislocated part was removed by aspiration. We followed standard tumor debulking procedures. This should start downwards, then backward, laterally, and finally upwards. This technique prevents premature diaphragmatic descent and interference with tumor manipulation. Premature exposure and lowering of the diaphragm obstruct the surgeon's vision for definitive tumor removal with the risk of diaphragmatic rupture. The central portion of the tumor should be avoided early as it exerts downward traction on the diaphragm and risks obscuring the sides of the adenoma.

After generous tumor debulking, the medial wall of the cavernous sinus was carefully examined to remove any remaining tumor. The tumor capsule was gently detached from the wall of the cavernous sinus. The angled endoscope provides an enlarged view of the surgical technique for dissecting the tumor capsule away from the medial wall of the cavernous sinus under direct vision, rather than blindly searching for the outer pole of the tumor with a ring curette. This is an important step as blindly aggressive techniques can lead to carotid artery injuries.[26]

Finally, after tumor removal from the sides, the upper part of the tumor was removed. The remaining superior tumor prevents subsequent diaphragmatic depression and definitive tumor removal. The direct line of sight of the microscope cannot adequately visualize the superolateral corners, which are better viewed by the endoscope particularly by the 30° lens. The upper part of the tumor must be manipulated carefully due to the risk of damaging the pituitary stalk.

Using four hands and endoscopic technology, the tumor was debulked and separated from nearby neurovascular systems, with the aim of achieving gross total resection (GTR). The closure was carried out utilizing fat, fibrin glue, and the vascularized nasoseptal flap, which was strengthened by fibrin glue and sponge gel. After surgery, adequate nasal packing was kept in place for 2 to 5 days. Care should be given to removing the sphenoid mucosa during multilayer closure to prevent residual mucoceles.27

Statistical analysis

The authors have created a database using Microsoft Excel® and the statistical packages for social sciences (SPSS) software version 28.0 (IBM Corp, Armonk, NY, USA). We used descriptive statistics to analyze age and follow-up means and standard deviation. Frequencies were used to analyze preoperative characteristics including gender (male/female), recurrence (yes/no), headaches (yes/no), nausea or vomiting (yes/no), blurred vision (yes/no), confusion (yes/no), amenorrhea (yes/ no), galactorrhea (yes/ no), impotence (yes/ no), gynecomastia (yes/ no), hydrocephalus (yes/no) and hemianopsia (yes/no). Frequencies were used as well to analyze postoperative characteristics including extent of resection (subtotal resection (STR) or gross total resection (GTR)), clinical outcome (improved, worsened, unchanged), visual outcome (improved or unchanged according to Humphrey visual fields) and new DI (yes/no). We used an unpaired Student’s T-test to look for significant differences in clinical presentation and outcome between male and female patients. Unpaired Student’s T-test was also used to identify independent predictors of good surgical outcome (gross total resection), clinical outcome (improved symptoms), recurrence, and improved visual function.

RESULTS

Epidemiology and clinical presentation

A total of 56 patients were operated upon using the endoscopic transnasal transsphenoidal approach in the period from the beginning of January 2018 to the end of June 2022. Preoperative characteristics were summarized in Table 1. There were 36 males and 20 females. The mean age was 43 years with a range of 20-61 years. There were 49 (87.5%) macroadenomas and 7 (12.5%) microadenomas. There were 10 (17.9%) recurrent cases, and 2 (3.6%) cases were recurrent for the third time (a macroadenoma case and a microadenoma case). The most common clinical symptoms were headaches, amenorrhea, diminution of vision, and visual field affection witnessed in 16 patients (28.6%) (bitemporal hemianopia and bilateral total defect sparing temporal quadrants). We had 16 patients (28.6%) with Prolactinomas who failed medical treatment and/or had compressive symptoms that mandated surgical resection, and 6 patients (10.7%) with growth hormone secreting adenomas who had Acromegalic features. In addition, we have operated on 2 patients (3.6%) with ACTH-secreting adenomas. Thirty-two patients (57.1%) with non-functioning adenomas were operated upon. In our study, we did not have any cases with thyroid stimulating hormone (TSH) secreting adenomas.

Table 1: Preoperative characteristics

Number of patients n=56	
Age in years (mean, range)	(43, 20-61)
Gender	
Males	36 (64.3%)
Females	20 (35.7%)
Size-	
Macroadenoma	49 (87.5%)
Microadenoma	7 (12.5%)
Clinical presentation	
Headaches	26 (46.4%)
Nausea / vomiting	4 (7.1%)
Blurred vision	4 (7.1%)
Confusion	2 (3.6%)
Amenorrhea	8 (14.3%)
Menopause	6 (10.7%)
Galactorrhea	1 (1.8%)
Impotence	4 (7.1%)
Infertility	4 (7.1%)
Gynecomastia	4 (7.1%)
Visual apparatus dysfunction	
- Visual acuity	18 (32.1%)
- Visual field	16 (28.6%)
Acromegalic features	6 (10.7%)
Hormonal disturbances	
Elevated prolactin hormone	16 (28.6%)
Elevated growth hormone	6 (10.7%)
Elevated adrenocorticotropic hormone	2 (3.6%)
Elevated thyroid stimulating hormone	0 (0%)
Elevated follicle stimulating hormone and luteinizing hormone	0 (0%)
Normal hormones (non-functioning adenomas)	32 (57.1%)

Clinical outcome, extent of resection and complications

Surgical results and complications were presented in Table 2. Regarding clinical improvement, visual improvement was noticed in 14 out of 16 patients with visual field affection (87.5%) and endocrinological improvement occurred in 21 out of 24 patients with functioning adenomas (87.5%). Visual field assessment was used as an indicator of visual outcome rather than visual acuity. Based on postoperative MRI in the follow-up period, gross total resection was achieved in 43 patients (76.8%) and 13 patients (23.2%) had subtotal resection. There were 7 patients (12.5%) who had postoperative DI including 3 patients (5.4%) who continued to have DI in the long term. We had only one patient (1.8%) with CSF

leak despite multilayer closure and fibrin glue usage. Our only postoperative CSF leak patient was a case of GH secreting macroadenoma. The patient experienced CSF leak from the right nostril immediately after pack removal. Conservative management was tried but it was not successful. Surgical exploration was done and a high flow CSF leak was found despite our usual skull base reconstruction in the first operation. A pedicled right middle turbinate flap was used for repair and the patient improved with stoppage of CSF leak. There were no statistically significant differences in surgical outcomes between female and male patients. We did not experience any major morbidities (meningitis, carotid artery or optic nerve injuries). Also, there were no mortalities in our series. Five of our patients (8.9%) experienced recurrence. In our study, we followed up our patients, especially those with subtotally resected adenomas and we did not request irradiation for any of them.

Table 2: Surgical outcome and complications

Number of patients n=56	
Extent of resection	
Gross total resection	43 (76.8%)
Subtotal resection	13 (23.2%)
Clinical outcome (symptoms)	
Improved	49 (87.5%)
Unchanged	7 (12.5%)
Visual field	
Improved	14/16 (87.5%)
Unchanged	2/16 (12.5%)
Worsened	0 (0%)
Endocrinological outcome	
Improved after 3 months	21/24 (87.5%)
Complications	
Cerebrospinal fluid leak	1 (1.8%)
Meningitis	0 (0%)
Carotid artery injury	0 (0%)
Postoperative diabetes insipidus	7 (12.5%)
- Temporary	4 (7.1%)
- Permanent	3 (5.4%)
Recurrence	5 (8.9%)

Case presentation

A 55-year-old female patient, married with 5 offsprings the youngest is 15 years old, had a previous endoscopic resection of a Prolactinoma in October 2019. The patient had menopause at the age of 51 years. She presented to us with a history of galactorrhea, headache, and blurring of vision for 5 months. Visual field assessment showed bitemporal hemianopia. Her Prolactin level was 380 ng/mL and MRI sella showed sellar and left parasellar mass 2.3x2.1x1.5 cm **(Fig. 1)**. The operation was done successfully **(Fig. 2)** with improvement of her symptoms and her visual field.

DISCUSSION

Our study included 56 patients with pituitary adenomas operated upon by the endoscopic transsphenoidal approach. Regarding visual outcome, improvement was noticed in 14 out of 16 patients with visual field dysfunction (87.5%). Several studies reported visual improvement rates between 79% and 95%.28–30 A meta-analysis of 19 studies published in 2017 showed an 80% improvement in visual field following pituitary adenoma resection.[31]

Regarding the endocrinological outcome, we achieved improvement in 87.5% (21 out of 24 patients) of the patients with functioning adenomas, including 16 prolactinoma patients. Cho and Liau investigated hormonal outcomes in 44 patients with prolactinomas, comparing endoscopic and microscopic approaches. The endoscopic group had a clear significant decrease in prolactin levels, and most patients had normalization of prolactin levels and relief of galactorrhea postoperatively, however, there was no statistically significant difference between the endoscopic endonasal approach and the sublabial transsphenoidal microsurgical approach.[32] Lee's team reported 100% improvement in the endocrinological function postoperatively.[33]

Regarding the degree of resection, gross total resection was achieved in 43 patients (76.8%) and subtotal resection in 13 patients (23.2%). Cappabianca et al. concluded that 90% of their patients operated upon by the endoscopic approach had gross total resection.[34] In

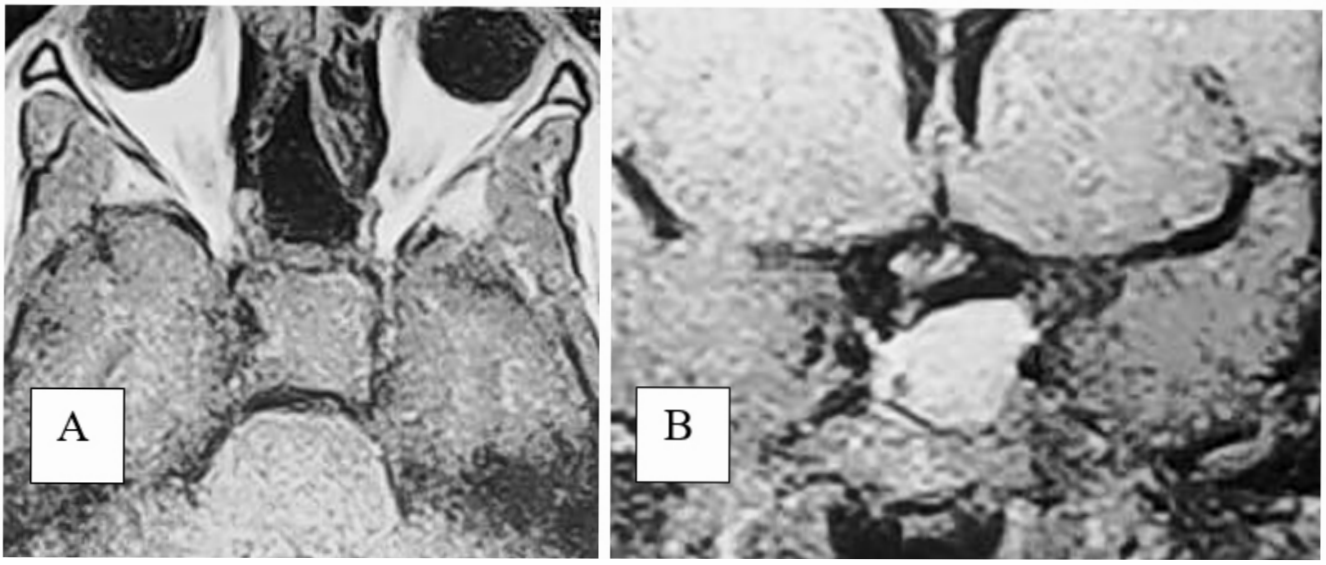

Fig. 1: Preoperative axial (A) and coronal (B) MRI T1WI showing a pituitary macroadenoma.

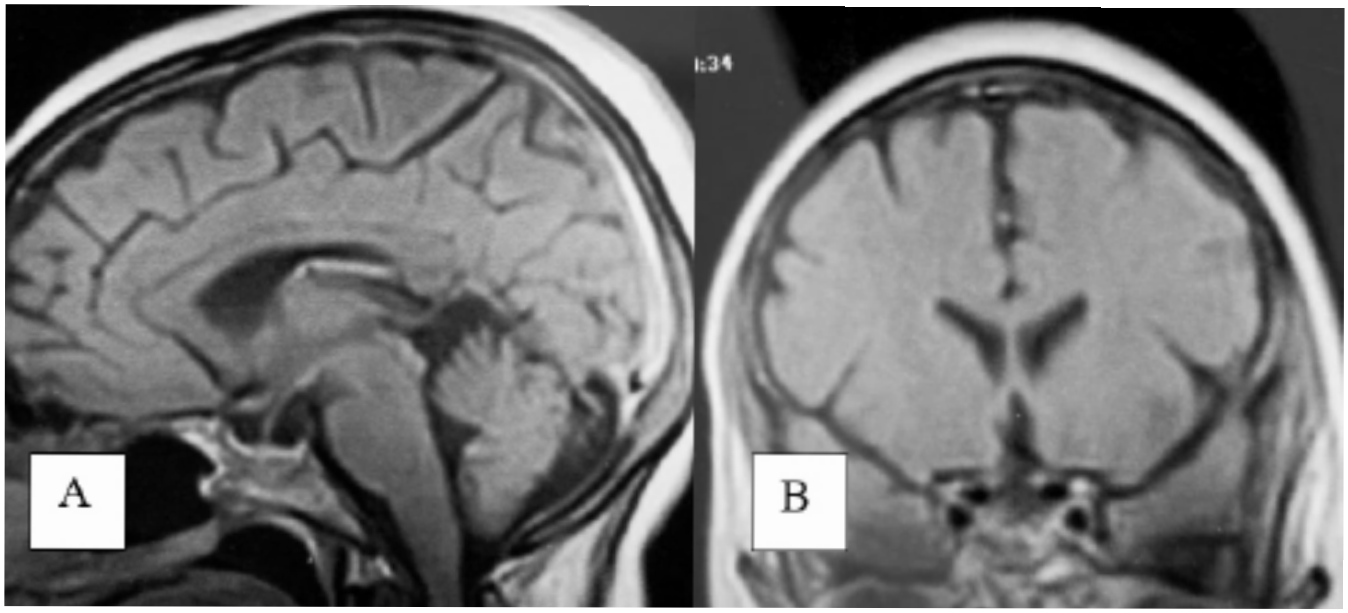

Fig 2: Sagittal (A) and coronal (B) MRI T1WI of the same patient three-month postoperatively.

a systematic review and meta-analysis by Li et al in 2017, which included 2272 patients in 23 studies, the endoscopic approach showed beneficial effects on the gross total resection rates compared to the microscopic approach.[35] Also, in another meta-analysis with 8257 pituitary adenomas patients in 2018, there was 74% gross total resection rate using the endoscope compared to 66% using the microscope.[36]

Regarding the complications, there were 7 patients (12.5%) who developed postoperative DI including 3 patients (5.4%) who continued to have DI in the long term. Neal et al. found a rate of DI in the endonasal endoscopic group around 7%.[37] In an American national database with 5891 patients published in 2022, there was a 10.2% incidence of postoperative DI.38 Similarly, Ajlan et al. and Gondim et al. reported a 10% rate of long-term DI.[39,40] A meta-analysis described a 15% incidence of DI.[41]

Regarding CSF leak, we had only one patient (1.8%) with CSF leak despite multilayer closure and fibrin glue

usage. The rate of CSF leakage in an American national database including 5891 patients was 8.35%.[38] Duz et al. reported that CSF leakage occurred in 11% of his endoscopic group.[42] A paper published in 2020 with 270 patients, including pituitary adenomas among other pathologies, found a 9% incidence of CSF leak.[43] In a meta-analysis done by Gao et al. in 2014, they concluded that the endoscopic transsphenoidal approach is safer and more effective than microscopic surgery in the treatment of pituitary adenomas. They also mentioned that with increasing experience of the neurosurgeon, the complications rate decreases.[44]

Study limitations

Our study limitations include the small sample size, as we are a medium-sized university hospital, and the relatively short follow-up period. Long-term follow-up is highly recommended in the future papers.

CONCLUSION

Endoscopic transnasal transsphenoidal resection of pituitary macroadenomas and microadenomas is a safe technique in experienced hands. Our guide and direction come from a thorough understanding of the anatomy and a careful examination of the patient's imaging. Multidisciplinary cooperation between neurosurgeons and otolaryngologists is highly recommended especially if the same staff worked together for years, making the surgery flow homogenously. A very good improvement in the visual field is expected, and the postoperative DI even if it is permanent is managed with life-long desmopressin. Fortunately, major morbidities and mortalities are quite uncommon in qualified hands. The steep learning curve mandates dedicated learning, attending cadaveric courses, and being involved in operations for years to build up a safe endoscopic neurosurgeon.

List of abbreviations

ACTH: Adrenocorticotropic hormone.
CPDA: Citrate phosphate dextrose-adenine-1.
CSF: Cerebrospinal fluid.
DI: Diabetes insipidus.
GH: Growth hormone.
GTR: Gross total resection.
HD: High definition.
MRI: Magnetic resonance imaging.
SPSS: Statistical packages for the social sciences.
STR: Subtotal resection.
TSH: Thyroid stimulating hormone.
WHO: World Health Organization.

Disclosure

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REFERENCES:

1. Lake MG, Krook LS, Cruz SV. Pituitary adenomas: An overview. *Am Fam Physician.* 2013;88(5):319-327.
2. Lloyd RV, Osamura RY, Klöppel G, et al, eds. WHO Classification of Tumours of Endocrine Organs. 4th edition. *Lyon: IARC.* 2017.
3. Lopes MBS. The 2017 World Health Organization classification of tumors of the pituitary gland: A summary. *Acta Neuropathol.* 2017;134(4):521-535.
4. Mete O, Lopes MB. Overview of the 2017 WHO classification of pituitary tumors. *Endocr Pathol.* 2017;28(3):228-243.
5. Molitch ME. Diagnosis and treatment of pituitary adenomas: A review. *JAMA.* 2017;317(5):516-524.
6. Buchfelder M, Schlaffer S. Imaging of pituitary pathology. Handb Clin Neurol. 2014;124:151-166.
7. Raverot G, Jouanneau E, Trouillas J. Management of endocrine disease: Clinicopathological classification and molecular markers of pituitary tumours for personalized therapeutic strategies. *Eur J Endocrinol.* 2014;170(4):R121-R132.
8. Daly AF, Rixhon M, Adam C, et al. High prevalence of pituitary adenomas: A cross-sectional study in the province of Liege, Belgium. *J Clin Endocrinol Metab.* 2006;91(12):4769-4775.
9. Fontana E, Gaillard R. Epidemiology of pituitary adenoma: Results of the first Swiss study [Article in French]. Rev Med Suisse. 2009;5(223):2172-2174.
10. Fernandez A, Karavitaki N, Wass JAH. Prevalence of pituitary adenomas: A community-based, cross-sectional study in Banbury (Oxfordshire, UK). *Clin Endocrinol (Oxf).* 2010;72(3):377-382.
11. Raappana A, Koivukangas J, Ebeling T, et al. Incidence of pituitary adenomas in Northern Finland in 1992-2007. *J Clin Endocrinol Metab.* 2010;95(9):4268-4275.
12. Gruppetta M, Mercieca C, Vassallo J. Prevalence and incidence of pituitary adenomas: A population based study in Malta. *Pituitary.* 2013;16(4):545-553.
13. Tjörnstrand A, Gunnarsson K, Evert M, et al. The incidence rate of pituitary adenomas in western Sweden for the period 2001-2011. *Eur J Endocrinol.* 2014;171(4):519-526.
14. Agustsson TT, Baldvinsdottir T, Jonasson JG, et al. The epidemiology of pituitary adenomas in Iceland, 1955-2012: A nationwide population-based study. *Eur J Endocrinol.* 2015;173(5):655-664.

15. Freda PU, Beckers AM, Katznelson L, et al. Pituitary incidentaloma: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96(4):894-904.

16. Cheer K, Trainer PJ. Evaluation of pituitary function. *Handb Clin Neurol.* 2014;124:141-149.

17. Yadav Y, Sachdev S, Parihar V, et al. Endoscopic endonasal trans-sphenoid surgery of pituitary adenoma. *J Neurosci Rural Pract.* 2012;3(3):328-337.

18. Swearingen B. Update on pituitary surgery. *J Clin Endocrinol Metab.* 2012;97(4):1073-1081.

19. Ammirati M, Wei L, Ciric I. Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery: A systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry.* 2013;84(8):843-849.

20. Molitch ME. Nonfunctioning pituitary tumors. *Handb Clin Neurol.* 2014;124:167-184.

21. Chanson P, Raverot G, Castinetti F, et al. Management of clinically non-functioning pituitary adenoma. *Ann Endocrinol (Paris).* 2015;76(3):239-247.

22. Loeffler JS, Shih HA. Radiation therapy in the management of pituitary adenomas. *J Clin Endocrinol Metab.* 2011;96(7):1992-2003.

23. Ding D, Starke RM, Sheehan JP. Treatment paradigms for pituitary adenomas: Defining the roles of radiosurgery and radiation therapy. *J Neurooncol.* 2014;117(3):445-457.

24. Faisal M, Salem S, kamel N, et al. Effect of autologous fibrin glue on seroma reduction after modified radical mastectomy for breast cancer: A randomized controlled trial. *Ann Med Surg (Lond).* 2021;63:102135.

25. Hadad G, Bassagasteguy L, Carrau RL, et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: Vascular pedicle nasoseptal flap. *Laryngoscope.* 2006;116(10):1882-1886.

26. Hendricks BK, Cohen-Gadol A. Pituitary adenoma: Diagnosis and operative considerations. *Neurosurgical Atlas, Inc;* 2016.

27. Dolci RLL, Encinas WE, Monteiro AA, et al. Closure of skull base defects after endonasal endoscopic resection of planum sphenoidale and tuberculum sellae meningiomas. *Asian J Neurosurg.* 2020;15(3):653.

28. Jahangiri A, Lamborn KR, Blevins L, Kunwar S, Aghi MK. Factors associated with delay to pituitary adenoma diagnosis in patients with visual loss. *J Neurosurg.* 2012;116(2):283-289.

29. Monteiro ML, Zambon BK, Cunha LP. Predictive factors for the development of visual loss in patients with pituitary macroadenomas and for visual recovery after optic pathway decompression. *Can J Ophthalmol.* 2010;45(4):404-408.

30. Danesh-Meyer HV, Wong A, Papchenko T, et al. Optical coherence tomography predicts visual outcome for pituitary tumors. *J Clin Neurosci.* 2015;22(7):1098-1104.

31. Sun M, Zhang ZQ, Ma CY, et al. Predictive factors of visual function recovery after pituitary adenoma resection: A literature review and meta-analysis. *Int J Ophthalmol.* 2017;10(11):1742-1750.

32. Cho DY, Liau WR. Comparison of endonasal endoscopic surgery and sublabial microsurgery for prolactinomas. *Surg Neurol.* 2002;58(6):371-375.

33. Lee SY, Alias A, Izaini Ghani AR, Long Bidin MB. Endocrinological outcome of endoscopic transsphenoidal surgery for functioning and non-functioning pituitary adenoma. *Malays J Med Sci.* 2019;26(3):64-71.

34. Cappabianca P, Alfieri A, Colao A, Ferone D, Lombardi G, De Divitiis E. Endoscopic endonasal transsphenoidal approach: An additional reason in support of surgery in the management of pituitary lesions. *Skull Base Surg.* 1999;9(2):109-117.

35. Li A, Liu W, Cao P, et al. Endoscopic versus microscopic transsphenoidal surgery in the treatment of pituitary adenoma: A systematic review and meta-analysis. *World Neurosurg.* 2017;101:236-246.

36. Almutairi RD, Muskens IS, Cote DJ, et al. Gross total resection of pituitary adenomas after endoscopic vs. microscopic transsphenoidal surgery: A meta-analysis. *Acta Neurochir (Wien).* 2018;160(5):1005-1021.

37. Neal JG, Patel SJ, Kulbersh JS, et al. Comparison of techniques for transsphenoidal pituitary surgery. *Am J Rhinol.* 2007;21(2):203-206.

38. Al-Qurayshi Z, Bennion DM, Greenlee JDW, et al. Endoscopic pituitary surgery: National database review. *Head Neck.* 2022;44(12):2678-2685.

39. Ajlan AM, Abdulqader SB, Achrol AS, et al. Diabetes insipidus following endoscopic transsphenoidal surgery for pituitary adenoma. *J Neurol Surg B Skull Base.* 2018;79(2):117-122.

40. Gondim JA, Almeida JPC, Albuquerque LAF, et al. Giant pituitary adenomas: Surgical outcomes of 50 cases operated on by the endonasal endoscopic approach. *World Neurosurg.* 2014;82(1-2):e281-e290.

41. Goudakos JK, Markou KD, Georgalas C. Endoscopic versus microscopic trans-sphenoidal pituitary surgery: A systematic review and meta-analysis.

Clin Otolaryngol. 2011;36(3):212-220.

42. Duz B, Harman F, Secer HI, et al. Transsphenoidal approaches to the pituitary: A progression in experience in a single centre. *Acta Neurochir (Wien).* 2008;150(11):1133-1139.

43. Hannan CJ, Almhanedi H, Al-Mahfoudh R, et al. Predicting post-operative cerebrospinal fluid (CSF) leak following endoscopic transnasal pituitary and anterior skull base surgery: A multivariate analysis. *Acta Neurochir (Wien).* 2020;162(6):1309-1315.

44. Gao Y, Zhong C, Wang Y, et al. Endoscopic versus microscopic transsphenoidal pituitary adenoma surgery: A meta-analysis. *World J Surg Oncol.* 2014;12:94.