Egyptian Journal of Neurosurgery

RESEARCH Open Access

Giant invasive pituitary adenomas: surgical approach selection paradigm and its influence on the outcome—case series

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Abstract

Objective Pointing out our surgical strategy and experience in selection of surgical approaches in giant pituitary adenomas patients and its relation to surgical and clinical outcome.

Methods 31 patients with giant pituitary adenomas (maximum diameter ≥ 4 cm). We analyzed the preoperative clinical presentation, radiological criteria of the tumor, endocrinological profile, approach selected, extent of resection, clinical outcomes and complications.

Results 16 males (51.6%) and 15 females (48.4%). All the patients had a visual complaint (13 had mild impairment (41.9%), 18 had significant visual loss (58.1%). 20 were nonfunctioning (64.6%), 5 prolactin secreting (16%) and 6 growth hormone secreting (19.4%). Surgical approaches included: standard endoscopic endonasal approach in 7, extended approach in 4, transcranial (extended pterional approach) in 3. Staged endoscopic surgery in 5. Extended pterional approach followed endoscopic approach in 12. Gross total resection in 18 (58%) subtotal resection in 8 patients (25.8%) and partial resection in 5 patients (16.2%). The most common complications was tumor recurrence in 8, CSF leakage in 3, Permanent diabetes insipidus in 2, postoperative hydrocephalus in 1, transient 6th CN palsy in 3, and unfortunately only one patient died. 8 had complete Visual recovery, 9 were improved partially, and 11 remain unchanged. Only 3 showed further deterioration of vision.

Conclusions Giant invasive pituitary adenoma is still one of the challenging issues in decision making for selection of the appropriate management strategy. Advancement of the endoscopic surgical techniques made the transsphenoidal approach is the primary choice for management of giant pituitary adenoma. However, the door is still opened for transcranial approach as staged the procedure after endoscopic approach or sole approach for some selected cases.

Keywords Giant, Knosp grade, Endoscopic, Invasive, Pituitary surgery

Introduction

Giant Pituitary adenomas are defined as pituitary tumors with maximum diameter ≥ 4 cm and it constitutes 5–16% of all pituitary adenomas that comprises about 15% of primary intracranial tumors. Different clinical syndromes represent the clinical presentations of giant pituitary adenomas including endocrine dysfunction, visual disturbance, cranial nerve palsy, headache and hydrocephalus related syndromes [1, 2].

The goal of management is to achieve maximum safe resection of the tumor. However such goal is hindered by multiple factors: bizarre extensions of the tumor, tumor size and involvement of critical neurovascular structures [3, 4].

Surgical treatment of giant pituitary adenomas is the treatment of choice and it is considered challenging

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owing to the complexity of neurovascular structures in relation to the tumor. Various surgical approaches are used in the surgical treatment include; the extended pterional approach, the endonasal endoscopic approach, the extended endoscopic endonasal transsphenoidal approach, staged transsphenoidal approach or combined approaches [5, 6].

Selection of the appropriate approach (either transcranial or endoscopic endonasal) depend on sphenoid sellar anatomical relationship, extension of the tumor either to the cavernous sinus or nearby structures, preoperative visual status and tumor criteria including shape and consistency [7, 8].

Many studies addressed the surgical challenges of giant pituitary adenomas and concluded that most of the surgical difficulties are related to the pattern of tumor extension particularly into the cavernous sinus and floor of 3rd ventricle [9, 10].

In this retrospective study we present our experience with surgical management of 31 cases of giant pituitary adenomas that was operated up on in Neurosurgery Department; Mansoura University Hospital aiming at pointing out our strategy and experience in selection of surgical approaches in individual patient and its relation to surgical and clinical outcome in the studied group.

Materials and methods

This retrospective study included the data of a series of patients who were diagnosed radiologically with giant pituitary adenomas at the Department of Neurosurgery, Mansoura University, Egypt. From January 2016 to May 2022, the medical records of 31 patients with giant pituitary adenomas were extracted, reviewed and analyzed.

Patients' data included demographic data (age, sex), preoperative evaluation (visual, endocrinological and neurological) and tumor criteria (i.e., shape, size and extension into nearby neurovascular structures or cavernous sinus invasion). Selected approach, extent of resection, post-surgical complications including cerebrospinal fluid leak and diabetes insipidus, hydrocephalus, endocrinological disturbances at discharge and previous medical treatment.

Patients' selection criteria included: sellar MRI scanning showed pituitary tumor with maximum diameter ≥ 4 cm and histopathological examination of the tumor specimen revealed pituitary adenoma. Patients with previous surgery for such tumors with or without postoperative radiotherapy were excluded from the study.

All patients were subjected to preoperative neuroradiological examination, full endocrinological evaluation (hypothalamic pituitary profile), visual assessment includes visual acuity, perimetry, fundus examination and visual impairment score (VIS) which is developed by German Ophthalmological Society. It was calculated by summation of the scores of the tables for assessment of visual acuity and the visual field defects; the values for both eyes are gathered in each table (Fig. 1). Visual impairment is then classified into four grades based on the scores obtained (ranging from 0 to 100):

Visual acuity

L \ R	1,0	0,6	0,63	0,5	0,4	0,32	0,25	0,2	0,16	0,1	0,08	0,05	0,02	0
	5/5	5/6	5/8	5/10	5/12	5/15	5/20	5/25	5/30	5/50	1/12	1/20	1/50	0
1,00 5/5	0	2	4	6	8	10	12	15	17	20	22	25	27	30
0,8 5/6	2	4	8	10	12	15	17	20	22	25	27	30	32	35
0,63 5/8	4	8	15	17	20	22	25	27	30	32	35	37	40	42
0,5 5/10	6	10	17	20	22	25	27	30	32	35	40	42	45	47
0,4 5/12	8	12	20	22	25	30	32	**35**	37	40	42	47	50	52
0,32 5/15	10	15	22	25	30	35	40	45	47	50	55	57	60	62
0,25 5/20	12	17	25	27	32	40	50	52	55	57	60	65	67	70
0,2 5/25	15	20	27	30	35	45	52	55	57	60	65	70	75	80
0,16 5/30	17	22	30	32	37	47	55	57	60	65	70	75	80	85
0,1 5/50	20	25	32	35	40	50	57	60	65	75	80	85	87	90
0,08 1/12	22	27	35	40	42	55	60	65	70	80	85	90	92	95
0,05 1/20	25	30	37	42	47	57	65	70	75	85	90	98	100	100
0,02 1/50	28	32	40	45	50	60	67	75	80	87	92	100	100	100
0 0	30	35	42	47	52	62	70	80	85	90	95	100	100	100

Visual Field Defect

R \ L											
	0	2	4	5	5	5	5	5	5	5	0
	2	6	8	8	10	14	18	19	20	25	2
	4	8	10	12	14	16	20	21	22	27	4
	5	8	12	14	16	18	22	22	23	28	6
	5	10	14	16	18	20	22	23	24	29	8
	5	14	16	18	20	22	**24**	25	26	31	10
	5	18	20	22	22	24	26	28	35	40	15
	5	19	21	22	23	25	28	30	40	45	20
	5	20	22	23	24	26	35	40	45	48	25
	5	25	27	28	29	31	40	45	48	50	25
	0	2	4	6	8	10	15	20	25	25	0

Fig. 1 Tables containing the results of visual acuity and visual field deficit for calculation of the visual impairment score (VIS). Visual acuity impairment score of 35 of both the right and left eye subsequently 0.2 (2/10) and 0.4 (4/10). Visual field impairment score of 24 for a VIS of 59

- Grade 1 (score 0–25): no or minimal visual impairment
- Grade 2 (score 26–50): moderate visual impairment
- Grade 3 (score 51–75): severe visual impairment
- Grade 4 (score 76–100): subtotal or complete visual impairment

Neuroradiological assessment for every patient included sellar gadolinium enhanced magnetic resonance image (MRI), The degree of parasellar tumor extension can be classified according to the Knosp grading system' while suprasellar extension is qualified in accordance with the Modified Hardys classification system. Furthermore, a computed tomography (CT) scan of the paranasal sinuses to delineate the sphenoid sellar relationship, different types of sphenoid sinus (degree of sphenoid sinus pneumatization), evaluation of the anatomical route to nasal, ethmoidal, and sphenoidal steps and the other bone structures involved in the procedure.

Surgical management

Two surgical approaches were used in this study for achieving resection of giant pituitary adenomas; the trans-sphenoidal approach and extended pterional approach either separately or staged surgery.

Extended pterional approach

A Yasergil standard pterional craniotomy that is modified and expanded by enlargement of the craniotomy to the frontal bone along the lateral sphenoid wing and drilling the roof of the orbit to flatten its surface, giving an unobstructed operative subfrontal corridor and working angles toward the parasellar area. Dural opening through curvilinear fashion over the sylvian fissure and the incision is directed toward the falciform ligament then accessing the tumor.

Endoscopic endonasal approaches

The standard or extended endoscopic approach for giant pituitary adenoma surgery was utilized. binostril four handed techniques; using a 0°, 30° 4-mm endoscope (Karl Storz GmbH & Co. KG, Tuttlingen, Germany). The patient was positioned supine with the head in a neutral position and rotated 10° toward the surgeon. Special consideration toward the steps to achieve safe, effective surgery for giant pituitary adenoma; wide sphenoidotomy through drilling the sellar bone up to the tuberculum sellae or planum sphenoidale above and down to the clival recess below. Wide sellar exposure is crucial to sharply demarcate the important anatomical landmarks of the region including the carotid prominences, opticocarotid recesses (medial and lateral), planum sphenoidale and clivus.

Extended approaches were used in 4 cases to improve our chance for achieving maximum tumor resection.

Reconstruction of the sellar floor using autologous fat was used and was reinforced with a free mucosal flap harvested from the resected middle turbinate if cerebrospinal fluid leakage had occurred. For extended approaches, a vascularized nasoseptal flap based on the sphenopalatine artery was used for skull base reconstruction.

Follow up data included immediate, 1 month, 6 months and I year postoperative and endocrinological, visual and neuroradiological examination.

Results

Demographic data and clinical presentation

The patient group in the current study ($n=31$ patients) included 16 males (51.6%) and 15 females (48.4%) and the mean (range) age was 46.51 (25–67) years. All the screened patients had a visual complaint: visual acuity was declined in 13 patients (41.9%), 7 patients (22.6%) had just perception of light (5 on the right eye, 2 on the left eye), counting fingers for 1 m was detected in 3 patients (9.7%), while no perception of light recorded in 8 patients (25.8%); 5 patients on the left eye and 3 patients in the right eye. Ophthalmoplegia detected in 3 patients (9.7%), oculomotor nerve palsy occurred in 4 patients (12.9%).

The most common other neurological presentations including: headache in 11 patients (35.5%), followed by disturbed conscious level in 8 patients (25.8%), hydrocephalus in 6 patients (20.4%), no apparent neurological deficits in 5 patients (16.1%), then hypothalamic syndrome in 4 patients (12.9%).

Nonfunctioning pituitary giant adenoma in 20 patients (64.6%), while 11 patients had endocrinological imbalance; 5 (16%) adenomas were prolactin hypersecretion, 6 (19.4%) adenomas were growth hormone hypersecretion, while only 3 patients (9.7%) had hypocortisolemia (Table 1).

Preoperative tumor radiological criteria

Analysis of the radiological criteria of the tumor showed: the maximum tumor size (the maximum diameter in the axial, coronal, or sagittal plane) was 7.2 cm with the mean diameter 5.41 cm ± SD 0.5. Evaluation of MRI criteria for tumor shape reveled 12 giant pituitary adenomas (38.7%) were multi-lobar shaped, 11 were dumbbell shaped (35.5%) and 8 were rounded shaped (25.8%). Tumor extension were detected in multiple directions in 9 patients (29%), superior extension in 7 patients (22.6%), antero-superior in 7 patients (22.6%), supero-lateral in 4 patients (12.9%) and supero-posterior in 4 (12.9%). Evaluation of suprasellar tumor

Table 1 Demographic data and preoperative neurological, visual and endocraniological presentation

	No. (%)
Demographic data	
Age	46.51 (25–67) years
Sex	
Male	16 (51.6%)
Female	15 (48.4%)
Previous medical treatment:	9 (29.1%)
Follow-up	1–48 months (mean 19.7 months)
Clinical presentations	
Headache	11 (35.5%)
Disturbed conscious level	8 (25.8%)
Hydrocephalus	6 (20.4%)
No neurological deficit	5 (16.1%)
Hypothalamic	4 (12.9%)
Acromegaly	2 (6.5%)
Visual impairment	
Preoperative VIS	Mean ± SD 59.2 ± 13.6
Preoperative degree of visual loss:	
Diminished visual acuity	13 (41.9%)
Perception of light right eye	5 (16.1%)
Perception of light left eye	2 (6.5%)
Counting finger 1 m	3 (9.7%)
No Perception of light right eye	3 (9.7%)
No Perception of light left eye	5 (16.1%)
Preoperative ocular motility	
Ophthalmoplegia	3 (9.7%)
Oculumotor nerve palsy	4 (13.0%)
Preoperative endocrinological profile	
Non functioning	20 (64.6%)
Functioning:	11 (35.4%)
Prolactin secreting	5 (16.0%)
GH secreting	6 (19.4%)
Preoperative hypopituitarism	9 (29.1%)
Hypogonadism	3 (9.7%)
Hypothyroidism	3 (9.7%)
Panhypopituitarism	2 (6.3%)
Diabetes insipidus	1 (3.2%)

extension was classified according to modified Hardy classification in table. Lateral, parasellar and cavernous sinus invasion was evaluated by Knosp classification presented in the Table 2. Sphenoid sinus typing and sphenoid sellar relationship was evaluated by CT scanning paranasal sinus and revealed: pneumatized sphenoid sinus in 25 patients (80.6%), while 6 patients (19.4%) had non-pneumatized sinus; conchal type in 3 patients (9.7%) and presellar type in 3 patients (9.7%) (Table 2).

Table 2 Tumor criteria based on radiological findings Radiological tumor extension and classification Types of sphenoid sinus based on CT paranasal sinuses

Radiological tumor criteria	No. (%)
Tumor diameter	4–7.2 cm (mean ± SD 5.1 cm ± 0.5)
Shape of tumors	
Rounded	8 (25.8%)
Multilobar	12 (38.7%)
Dumbell	11 (35.5%)
Tumor extension	
Modified Hardy classification	
Grade III	8 (25.8%)
Grade IV	19 (61.3%)
Grade V	4 (12.9%)
Cavernous sinus invasion Knosp grading	
Grade 1	2 (6.4%)
Grade 2	7 (22.6%)
Grade 3A	6 (19.4%)
Grade 3B	3 (9.7%)
Grade 4	13 (41.9%)
Types of sphenoid sinus	
Non pneumatized	6 (19.4%)
Conchal type	3 (9.7%)
Presellar type	3 (9.7%)
Pneumatized	25 (80.6%)

Surgical management

Surgery was indicated in cases suffered visual deterioration, unresponsive to medical treatment, electrolyte disturbance and deterioration of conscious level in response to hypothalamic dysfunction or frontal cortical compression and in cases with cranial nerve palsy as a consequence of cavernous sinus invasion.

The standard endoscopic endonasal approach was performed on 7 patients, whereas the extended approach was used to treat 4 patients and the transcranial (extended pterional approach) in 3 patients.

Staged endoscopic surgery was performed on 5 patients. The plan was complete resection in the first surgery. The plan for doing staged transsphenoid approach based on during the first approach we removed most of the sellar component of the tumor without getting the majority of the suprasellar component and fortunately with postoperative MRI done 3 months later it was found descent of the supra sell component into the sella favoring attempting second stage transsphenoidal approach for complete resection.

Transcranial extended pterional approach was planned and used seldomly in 3 patients. Transcranial

Table 3 Surgical approaches used in the studied group

Types of approach	Surgical approaches	No. (%)
Single approach	Endoscopic endonasal approach	11 (35.5%)
	Standard	7 (22.6%)
	Extended	4 (12.9%)
	Transcranial (extended pterional)	3 (9.7%)
Staged approach	Endoscopic endonasal then transcranial	12 (38.7%)
	Transcranial then endoscopic endonasal	3 (9.7%)
	Staged EEA	5 (16.1%)

Table 4 Intraoperative tumor consistency and extent of resection

	No. (%)
Tumor consistency	
Firm	9 (29%)
Soft	15 (48.3%)
Mixed	7 (22.7%)
Extent of resection	
GTR > 90%	18 (58%)
STR > 70%	8 (25.8%)
Partial < 70%	5 (16.2%)

extended pterional approach then endoscopic approach was performed on 3 patients.

Reoperation with extended pterional approach was recommended after endoscopic approach in 12 patients in which the tumor was tough and fibrous in the first endoscopic tanssphenoidal surgery and 3 months follow up MRI showed significant residual tumor (Table 3).

Intraoperative finding regarding the tumor consistency: tumor was firm in 9 patients (29%), soft in 15 patients (48.3%) and mixed consistency solid and cystic in 7 patients (22.7%) Table 4

Surgical outcome

Extent of tumor resection was evaluated by immediate follow-up radiology and showed; gross total resection (> 90% of tumor) achieved in 18 patients (58%) subtotal resection (> 70% of tumor) in 8 patients (25.8%) and partial resection (< 70% of tumor) in 5 patients (16.2%) (Table 4). Extent of resection is correlated with the surgical strategy selected are shown in Table 5.

Table 5 Extent of resection in relation to the approach selected

Approach	GTR	STR	Partial
Single endoscopic endonasal	7	3	0
Transcranial (extended pterional)	1	1	1
Endoscopic endonasal then transcranial	8	2	2
Transcranial then endoscopic endonasal	0	1	2
Staged EEA	2	1	0

Table 6 Complications

Complications	No. (%)	EEA	TC
Recurrence–progression	8 (25.8%)	5	3
CSF leakage	3 (9.7%)	3	0
Diabetes Insipidus	2 (6.4%)	2	0
Hydrocephalus	1 (3.2%)	0	1
Hypopituitarism	3 (9.7%)	2	1
Transient CN VI palsy	3 (9.7%)	2	1
Mortality	1 (3.2%)	1	0

Table 7 Visual status outcome

Visual status outcome	No. (%)
Improved	17 (54.8%)
Stationary	11 (35.5%)
Deteriorated	3 (9.7%)
Postoperative VIS	Mean ± SD 41.3 ± 11.2

Complications

Follow-up period ranged from 1 to 48 months (mean follow-up 19.7 months). The most common complications reported was tumor recurrence in 8 patients, CSF leakage in 3 cases (9.7%), Permanent diabetes insipidus in 2 cases (6.4%), postoperative hydrocephalus in 1 patient (3.2%), transient 6th CN palsy in 3 patients, 3 cases developed pan hypopituitarism that required long life hormonal replacement and unfortunately only one patient died (3.2%) as a consequence of hypothalamic injury (Table 6).

Clinical outcomes

Visual

All patients with giant adenoma were subjected to postoperative visual assessment (VF and visual acuity) Preoperative mild diminution of vision was documented in 13 patients, but significant loss of vision was reported by 18 patients. During follow-up, complete recovery was observed in 8 patients, partial improvement in 9 patients,

stationary visual acuity in 11 patients and only 3 patients showed further deterioration of vision. Monitoring the ocular motility during follow-up period revealed no improvement detected in the 7 patients with preoperative ophthalmoplegia and cranial nerve palsy (Table 7).

Endocrine

Post-operative, 2 patients had permanent diabetes insipidus (DI), while 7 patients with transient DI improved on conservative treatment. Among the 6 patients of GH-secreting adenoma, 2 patients (tumors were gross totally resected) with achievement of endocrinological remission, 2 patients received somatostatin analogue and 2 patients were sent for GKRS. All the 5 patients with PRL secreting adenomas were maintained on postoperative medical treatment and 2 of them received conformal radiotherapy beside medical treatment.

Discussion

Giant adenomas are defined in the recent published series as adenomas with a diameter measuring 40 mm and are considered invasive if there is trans-capsular multidirectional intracranial extension. These adenomas have a different aspect of management challenges and concerns in comparison with other types of adenomas. Most of giant pituitary adenoma cases are non-functioning and the clinical presentation is mostly due to visual compression and manifestations related to the tumor extension as hydrocephalus associating the suprasellar tumor extension [6, 11–13]. In our series; all cases has visual presentation, headache in 11 patients (35.5%), disturbed conscious level in 8 patients (25.8%), hydrocephalus in 6 patients (20.4%),and hypothalamic syndrome in 4 patients (12.9%).

Surgery is considered the primary line treatment except for giant prolactinoma that can be initially managed with dopamine agonists. This goal either achieved via one surgical procedure or via staged operations and if complete surgical resection is associated with high incidence of morbidities, part of the tumor must be left to be controlled by adjuvant therapies. Making appropriate choice for the surgical corridor for tumor resection, it is very important to define the advantages of each surgical technique objectively regarding surgical outcome, complication avoidance, experience and preference of the surgeon and tumor characteristics to make the approach as safe and effective as possible. It is essential to provide a balanced assessment of the risks and benefits of each surgical approach [14–16].

Decision making for appropriate surgical approach for giant and invasive adenomas is controversial and sometimes debatable in many surgical series discussing such challenging problem and despite the surgical approach depend up on the experience of the surgical team but from our experience there are many factors that can determine which approach is more favorable regarding the efficacy and safety including; pattern of tumor extension and invasion, anatomical variation of sellar/sphenidal relationship and tumor consistency (Fig. 2).

The transsphenoidal approach is considered in many literature reviews as the first choice for surgical management of giant pituitary adenomas with many advantages including no need for craniotomy and brain retraction and providing a wide panoramic view with high-quality visualization. Advances in the endoscopic transsphenoidal surgery have improved the surgeon's ability to perform surgical procedures to lesions behind the sella with providing access to intracranial lesions, previously thought to be removed only via transcranial route. Large adenomas with significant anterior, posterior, superior and/or lateral extensions have been operated up on through tailored extended endonasal procedures. Despite these advantages, there are several limitations that should be considered. The procedure is technically demanding that require advanced training, some tumor characteristics limit the safe or satisfactory resection of the tumor such as a dumbbell shape, irregular extension, or encasement of cerebral arteries. The reconstruction is certainly one of the more challenging steps of the procedure despite tremendous improvement of such techniques [17–20].

According to Zada et al. experience in managing giant adenoma, He advocates attempting initial tumor delivery via the endoscopic endonasal approach. Technique for a first attempt of tumor delivery with the concept that adenomas with suprasellar extension could be removed via single stage transsphenoidal operation [21]. Tumor descent especially soft tumors could occur spontaneously or even facilitated or provoked by lumbar subarachnoid saline or air injection to facilitate the descent of the suprasellar tumor into the sella. In case of fibrous consistency of the adenoma that can render a complete removal even more difficult and hazardous, one can convert the approach by performing an additional resection of tuberculum and planum, to perform an intradural, extra-capsular resection of the lesion. The technique also provides an adequate approach to tumors extending to the cavernous sinus (Fig. 3a, b).

Insufficient transsphenoidal resection puts patients at risk of postoperative bleeding, edema, and increased mass effect of the residual tumor. In these circumstances a simultaneous transcranial approach is anticipated, and a complementary trans-cranial approach should be initiated. Some surgeons prefer to perform these sequentially, and others advocate simultaneous procedures, especially after the transsphenoidal approach.

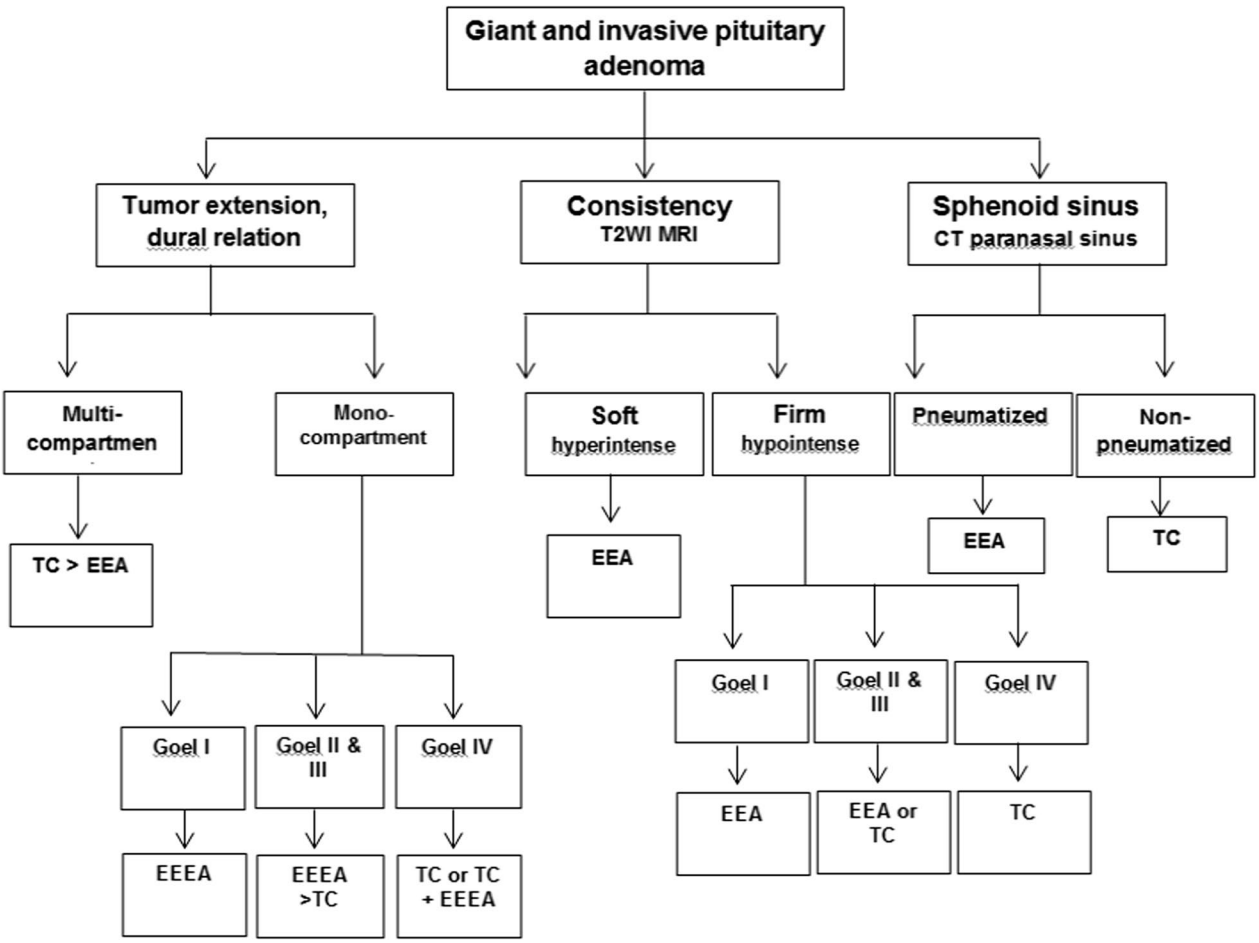

Fig. 2 Proposal for Surgical approach selection algorithm for giant and invasive pituitary adenoma (TC = transcranial, EEA = endoscopic endonasal approach, EEEA = extended endoscopic endonasal approach)

In his series of 29 patients of giant adenomas, Hiroshi Nishioka et al. studied the value of combined approaches in managing giant adenomas regarding potential advantages and limitations. According to his experience, one of the main advantages of "above and below" surgery is adequate and safe optic nerve/chiasm decompression and the avoidance of complications potentially caused by any residual suprasellar tumor. With the simultaneous transcranial approach, the tumor capsule can be dissected from adjacent neurovascular structures facilitating mechanical delivered to the sella. The advantages of a simultaneous technique are that the degree of resection is increased and postoperative bleeding of the residual tumor is minimized. Although the ability to remove such complex tumor is advocated by such technique, several inherent tumor characteristics still exist limiting effective and safe resection. One of them is significant tumor extension in the cavernous sinus. Simultaneous approach also has some disadvantages including longer operation time, higher infection rate, and potential complications associated with both transsphenoidal and transcranial surgery. Therefore, the benefits and risks should be carefully considered before each surgery [22].

Nevertheless, controversies regarding appropriate surgical corridor to start with for resection of giant adenomas still exist and trans-cranial approach continues to play a primary role in the management of giant and invasive pituitary adenomas despite its associated higher surgical morbidities in comparison to the trans-sphenoidal route.

Transcranial approach is often considered the first choice for adenomas with excessive suprasellar or parasellar extension and transgression of dura with significant invasion into subarachnoid spaces, subfrontal and temporal lobes especially those with nearly normal-sized sella turcica or with anatomical variations of sphenoid sellar relationship particularly conical type sphenoid sinus hindering the transsphenoidal approach (Fig. 4a and b). Also, the trans-cranial approach is also considered

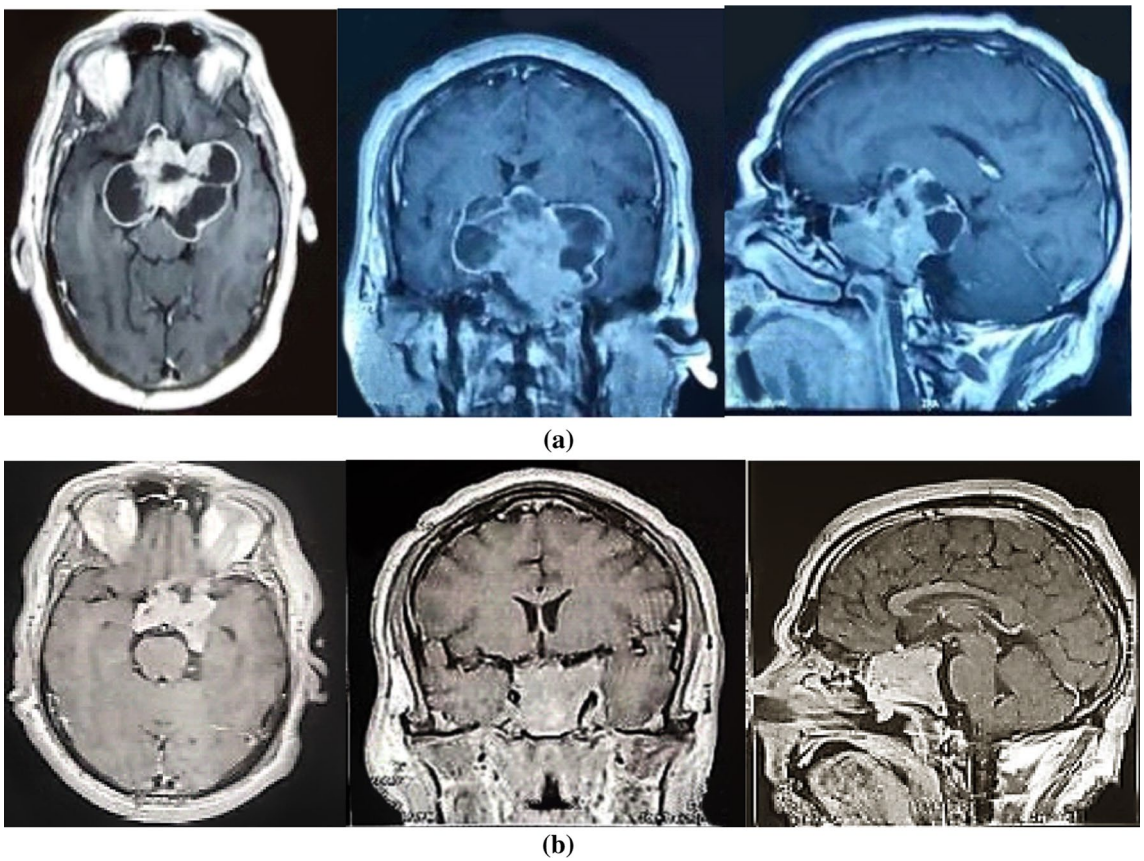

Fig. 3 **a** A male patient 50 years with progressive deterioration in vision for 2 years (left eye: counting finger 25 cm, Right eye: hand movement). Preoperative post-contrast MRI brain: giant large partially cystic partially solid pituitary adenoma (3.8*7.7*5.2 cm). **b** Three months postoperative (transsphenoidal excision and biopsy) post contrast MRI brain: optic chiasm was decompressed, tumor burden was reduced and vision was improved (Left eye: counting finger 1 m, Right eye: counting finger 50 cm)

the primary surgical corridor for giant fibrous adenomas presented with significant visual loss with difficult optic pathway decompression via the trans-sphenoid approach. The most important limitation of transcranial surgery is that intrasellar portion of the tumor is more difficult to visualize and remove, particularly in the setting of prefixed optic chiasm. Residual adenomas can be removed by second stage trans-phenoidal approach 3 months later or managed with radiation therapy depending on the location of the residual tumor [6, 23].

The goal of surgery should be achieving gross total tumor removal if possible, however achieving such goal should consider the patient safety without exposing the patient to surgical morbidities especially those considered life threatening like hypothalamic and/or thalamic injury. The decision to attempt radical tumor resection rather than less aggressive surgical resection should be determined with considering the patient's age and wishes, overall conditions, and tumor characteristics and pattern of extension. In high-risk circumstances, decompression of the optic pathway with effective reduction of tumor mass is an accepted policy to achieve clinical improvement with minimal co-morbidities. Small residual tumor can be followed with serial magnetic resonance imaging scans for any signs of regrowth, which may not occur for years while large residual adenomas can be managed via a multimodality management strategy after achieving surgical resection surgery (Fig. 5a and b).

The outcome of managing giant pituitary adenomas depends on many factors including patient's clinical presentations, size and pattern of tumor expansion, the chosen surgical corridor, and the post-operative adjuvant treatment. According to many literature reviews, the endoscopic trans-sphenoid corridor has promising results in comparison to the transcranial corridor regarding extent of tumor resection, endocrinological and visual outcome and surgery related complication rates. In our study, a gross total resection of more than 90% of the tumor that was achieved in 18 patients (58%) subtotal resection which is comparable to previous reports [5, 11, 24, 25].Visual outcome and recovery depends on: Degree of visual loss, Onset of visual affection, Duration

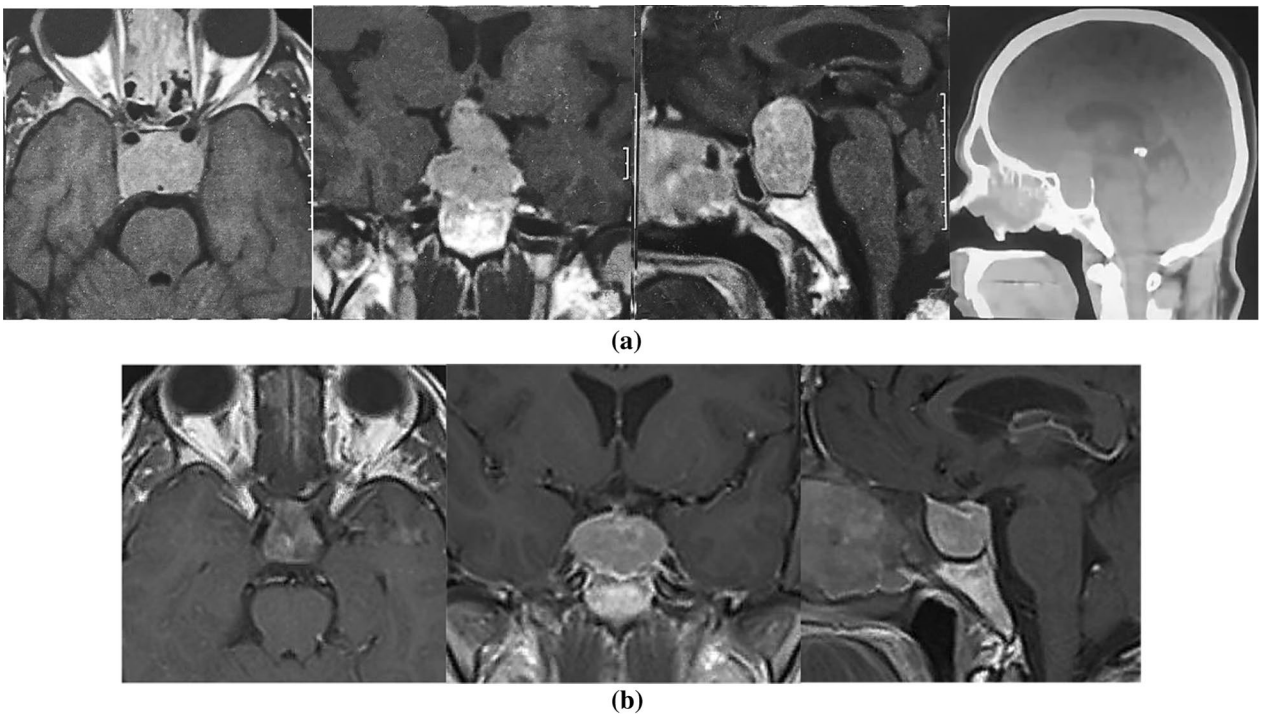

Fig. 4 **a** 49 year old male patient with giant pituitary adenoma and conical type sphenoid sinus was operated upon through extended pterional approach. **b** One month Postoperative MRI post-contrast showing decompression of the optic apparatus and reduction of the tumor mass

of manifestation, surgical approach Chosen. In our series; 17 patient have been improved (54.8%); 8 experienced complete visual recovery while 9 have been partially improved and 11 patients had stationary visual status (35.5%).

Postoperative mortality with endoscopic surgery is reported to be less than 1% and mostly happened from ICA injury, hypothalamic injury, and meningitis due to CSF leakage. The most common complication following endoscopic approach is CSF leakage. The rate of such complication is dramatically decreasing in sequential reviews owing to the advancements of skull base reconstruction techniques. A systemic review published in 2019 by Marigil Sanchez et al. reported a rate of CSF leakage of 8.8% in 431 patients of giant pituitary adenomas while in our series 9.7% in 31 patients. Unfortunately one patient died (3.2%) in our series as a consequence of hypothalamic injury while other review reported mortality of 1.9% and 20.8% of new endocrinological deficit either due to adenohypophyseal deficit or diabetes insipidus. In our series; permanent diabetes insipidus reported in 2 cases (6.4%), pan hypopituitarism has been developed in 3 patients (9.7%) that required long life hormonal replacement.

Unlike craniopharyngiomas, surgical treatment of giant pituitary adenomas has lower incidence of hypothalamic damage because craniopharyngiomas often invade the hypothalamus and radical resection can cause irreversible hypothalamic damage, while giant pituitary adenomas usually displace rather than invade the hypothalamus allowing avoiding serious hypothalamic injury [12].

In light of our reported complications; prevention and lowering the incidence of CSF leakage may be feasible if we prepare a meticulous reconstruction plan for the skull base in cases of endoscopic approach and in our series the otolaryngologist member of our endoscopic skull base team is fixed the "same surgeon".

Conclusion

Giant invasive pituitary adenoma is still one of the challenging issues in decision making for selection of the appropriate management strategy. Advancement of the endoscopic surgical techniques made the transsphenoidal approach is the primary choice for management of giant pituitary adenoma. However, the door is still opened for transcranial approach as staged the procedure after endoscopic approach or sole approach for some selected cases. Selection of the surgical approach either utilized as a single or staged depend on variable tumor criteria including preoperative tumor shape, volume, size, extension and dural relationship with the tumor, invasiveness (Knosp, Hardy classification). Tumor consistency (tumor intensity

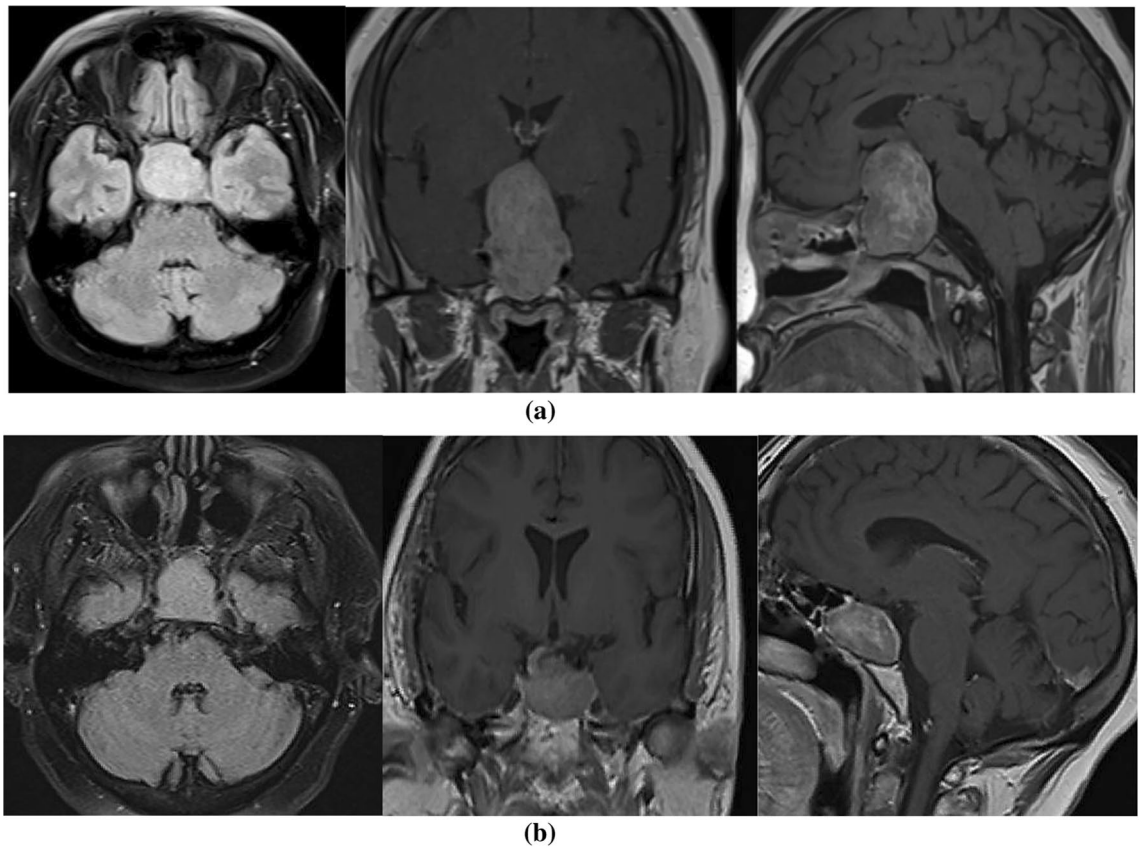

Fig. 5 **a** A case of 50 years old female patient with giant pituitary adenoma underwent staged surgery (initial transsphenoidal surgery 3 years ago then presented with visual deterioration and planned for transcranial approach). **b** One month postoperative (extended pterional) MRI scan of the brain showing decompression of the optic chiasma

on T2-weighted MRI) and sellar sphenoid sinus relationship as well as preoperative visual status and endocrinological profile. Proper selection of the suitable surgical approach is crucial in achieving and maximizing extent of tumor resection and lowers the rate of complications.

Abbreviations

CN	Cranial nerve
CSF	Cerebro-spinal fluid
CT	Computed tomography
DI	Diabetes insipidus
GH-secreting adenoma	Growth hormone-secreting adenoma
GKRS	Gamma knife radiosurgery
MRI	Magnetic resonance imaging
VF	Visual field
VIS	Visual assessment score
ICA	Internal carotid artery

Acknowledgements
This study was conducted by the authors and no funds, grants, or other support was received.

Author contributions
All authors contributed to the study conception and design, read and approved the final manuscript for submission and publication. Contribution to the study was organized according to: MS contributed to conceptualization, methodology, formal analysis and investigation, writing original draft preparation and supervision, ANT contributed to conceptualization, methodology, formal analysis and investigation writing original draft preparation and supervision. SS contributed to: original draft preparation, resources. HS contributed to: methodology, writing review and editing WKZ contributed to: conceptualization, writing review and editing. All authors read and approved the final manuscript.

Funding
No funds or grants were provided for the study.

Availability of data and materials
All data related for this study are available for sharing upon request.

Declarations

Ethics approval and consent to participate
This study was approved by the IRB of Mansoura University Faculty of Medicine. This article does not contain any studies with human participants performed by any of the authors.

Consent for publications
All data and records of patients were approved for publications by authors and involved patients.

Competing interests
All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria;

educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Received: 6 March 2023 Accepted: 10 April 2023
Published online: 29 June 2023

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