



Trans-Septal Trans-Sphenoidal Surgery For Pituitary Adenomas: A Retrospective Study

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Abstract

In this retrospective study 100 patients of pituitary adenoma who underwent Trans-septal Trans-sphenoidal surgery over 10 years period were evaluated. The mean presenting complaints of these patients were headache and decreased vision. Majority of tumors in our study were non functioning adenomas (39%) followed by prolactinomas (38%), growth hormone producing tumors constituted 20%, where as cortisol secreting adenomas were 3%. There was no operative mortality in our series. Post-op CSF rhinorrhoea was noted in 3 patients - out of these one patient required surgical repair of fistula in immediate post-operated period while other two patients were managed with lumbar drain. Total excision of tumor was attained in 38% of patients as these were evaluated by post-operated CT scan and MRI with contrast. 30% of patients were given radiotherapy immediately after the surgery. These were patients in whom residual tumor was more than 1 cm in size and the hormone levels did not return to normal. The patients were followed up from 9 months to 10 years with a mean follow up of 4 years. There were total of 18 recurrences on follow up study.

Key Words

Pituitary adenoma, Transsphenoidal Excision

Introduction

Pituitary adenomas are benign monoclonal tumors that arise from the cells comprising of the anterior pituitary gland. They account for approximately 15% of all intracranial tumors. The treatment options available are medical therapy and surgery. Their appropriate use depends on the histological type of adenoma and its size. Early decompression of optic nerve or chiasma should be done. Radiation therapy also is an important adjunct in the management of pituitary adenoma (1,2).

The pituitary adenomas can be approached by trans - cranial and trans - sphenoidal routes. The trans sphenoidal approach to the pituitary gland is more direct and less time consuming than a trans cranial operation. Suprasellar extension of a pituitary adenoma, even when massive does not contraindicate the trans-sphenoidal approach, since the suprasellar portion of the tumor usually descends into the sella turcica as the intrasellar portion is being removed. Most dumbbell-shaped tumors may also be dealt with trans - sphenoidally (1,2).

However it is unsuitable if the pituitary adenoma has significant extension into the middle or anterior cranial fossa. In such cases, the transcranial approach allows better access to the tumor.

Material & Methods

This is a retrospective study. It includes 100 patients of pituitary adenoma who underwent Trans-septal Trans-sphenoidal surgery at Grant Medical College Hospital Mumbai over 10 years period from Jan 1997 to Jan 2006. It is a tertiary level hospital with referral of patients from state of Maharashtra and adjoining states. The patients were evaluated in terms of their size of adenoma, modes of presentation, endocrinal abnormalities, histopathological types and outcome, the number of recurrences on follow up and the treatment given for the recurrences.

Investigations:-Hormonal study - Growth hormone, prolactin, cortisol, FSH, LH, TSH, T3 & T4 levels. Visual Perimetry; X-ray skull sellar view; CT Scan with contrast with coronal cuts; MRI with contrast.

All patients were operated by Trans-septal Trans-sphenoidal approach using operating Microscope. In twenty patients endoscope assistance was also used (00 and 300 endoscopes) to have better view inside the sella after excision of the tumor to see the extent of tumor removed. Post operatively patients were kept in intensive care unit. Post operative serum electrolytes, urine specific gravity, strict Intake - output balance was monitored

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lumbar drain was used in those cases where CSF leak was suspected. The patients were assessed for any post-op complications. Post operatively, the improvement in patient's symptomatology was assessed by clinical examination. The extent of tumor removed was assessed by post-operative CT scan. Hormonal profile was performed on tenth post-operative day and at 3 months on follow up. Long term follow up was assessed in terms of residual visual deficit and hormonal assessment. Patients were followed up regularly with neuroophthalmological examination and repeat CT/MRI scan and hormonal assessment. Follow up ranged from 9 months to 10 years. Minimum period of follow up was taken as a 9 months. All data was tabulated and analyzed scientifically.

Criteria For Cure was defined as

1. Prolactinomas:- Patients who were asymptomatic and had a normal serum prolactin level of <25 ng/ml and no recurrence on MRI study on follow up for 5 years are considered cured.

2. Growth Hormone:-The growth hormone level of 10 ng/ml after surgery is considered as criteria for cure. A sustained rise of hormone over a 12 month period was classified as recurrent endocrinopathy.

3. Non-secretory adenomas:-The success of surgery for non secretory adenomas was measured with following parameters.

- a. Improvement in vision.
- b. Radiographic removal of tumor.
- c. Paucity of complications.

Tumor Recurrences was defined as: Recurrences were classified into three categories.

1. Those with clinical symptoms
2. Those seen on CT /MRI scan without clinical symptoms.
3. Those with endocrinologic evidence.

Results (Table.1; Fig 1&2)

The patients in our series ranged from 21 to 58 years of age with an average age of 36.41 years. Age group with maximum occurrence of pituitary adenoma was in fourth decade. There was male preponderance with male to female ratio of 1.17 to 1. The main presenting complaints were headache (64%) and decreased vision (56%). Endocrine abnormalities as presenting complaints were less common. Acromegalic features were noted in 20% and amenorrhoea was present in 16% of all the patients who were included in our study. Galactorrhoea was present in 8% and decreased Libido was present in 6% of patients. The most common visual field defect noted on examination was incomplete bitemporal hemianopia. These patients were evaluated for their tumor

characteristics using CT scan with contrast and MRI with contrast, Suprasellar extension of tumor was noted in 58% of patients. The tumor was located in sella in 32% of patients. All patients underwent trans-septal transphenoidal excision of pituitary adenoma. Endoscope assistance was used in 20% of cases using 0 and 30 degree endoscopes in order to have better view of sella during and after excision of tumor.

There was no operative mortality noted in our series. The incidence of transient diabetes insipidus was 14%. CSF rhinorrhoea was noted in 3% and meningitis was noted in 1% of cases No patient had diabetes insipidus lasting for more than 3 months. One patient with CSF rhinorrhoea required surgical repair of fistula in immediate post-op period. Other two patients were managed with lumbar drain. One patient with meningitis was treated with broad spectrum antibiotics. A full recovery of vision was achieved post - operatively in 35 (60%) patients and incomplete visual improvement was noted in 14 (25%) patients. Amenorrhoea persisted in 7 patients where as Menses were regained in 9 patients. Galactorrhoea improved in 5 patients and libido improved in 4 patients. Results of Endocrine studies: Hormonal evaluation was done on 10th postoperative day and at 3 months on follow up. All patients had decrease in hormone levels as compared to pre operative levels. The patients were followed up from 9 months to 10 years with a mean follow up of 4 years.

There were total of 18 recurrences on follow up study. A patient was considered to have a clinical recurrence when either old visual symptom returned or a new visual deficit occurred and neuroradiological studies confirmed the presence of recurrent tumor growth. 12 patients with clinical recurrence were reoperated and were given Radiotherapy post-operatively. Ten patients out of these were operated by trans nasal approach, whereas two patients were operated by transcranial approach - these patients had significant extension of tumor into anterior cranial fossa and parasellar location. Four patients who were harbouring prolactinomas were given drug therapy - Bromcriptine/Cabergoline. Two patients who were harbouring nonfunctioning adenomas were directly given radiotherapy. In these cases the recurrent tumor was parasellar in location. These patients showed good response to radiotherapy.

Radiotherapy: 30% of patients were given radiotherapy immediately after the surgery in whom residual tumor was more than 1 cm. in size and the hormone level did not return to normal. 32 patients with subtotal excision were followed up in whom the residual tumor was less than 1 cm. and was adjacent to vital areas

Table 1. Elevated Hormone Levels (n=61) (At 10th day and at 3rd Month)

Type of Hormone	Hormone Level Compared To Pre-Op Level		
		On 10 th day (No. of pts.)	At 3 rd month (No. of pts.)
Polactin (n=38)	Improved	38	38
	Normal	11	14
Growth Hormone	Improved	20	20
	Normal	5	7
Cortisol (n=3)	Improved	3	3
	Normal	1	1

like optic chiasma. These patients were subjected to re-surgery and radiotherapy if the tumor was increasing in size or the patient had recurrence of symptoms.

The conventional external beam radiation was used. A total of 45-50 Gy. is delivered over 4-5 weeks at a daily dose of 1.8 to 2.0 Gy., for 5 days in a week.

Discussion

The trans - sphenoidal approach that has been used in our cases is the recommended approach for most enclosed tumors even with large suprasellar extension, provided the tumor extends symmetrically in the midline above the sella turcica. Locally or diffusely invasive tumors with downwards extension into the sphenoid sinus and lateral extension towards the cavernous sinus are also suitable for trans - sphenoidal surgery, since the procedure allows a massive debulking of the tumor prior to radiation therapy. Irregular multinodular, fungating tumors or eccentric extensions into the frontal, temporal or posterior fossa dictate an intra cranial transfrontal approach (1).

Trans-septal Trans-sphenoidal approach for pituitary adenomas is a better suited technique as it is a less intrusive operation; secondly the surgeon comes straight down on to the tumor and can preserve the normal pituitary tissue, there is negligible risk of epilepsy and also the recovery of vision and the visual fields is quicker because the optic nerves and chiasma are not manipulated. The Trans-septal approach used in our cases gives adequate exposure of the floor of sella and the tumors extending above the sella can be effectively removed. The size of nares is rarely a problem encountered. Care should be taken not to fracture the septum too far superiorly because the anterior cranial fossa may be entered. Similarly the approach should follow the floor of the nasopharynx to avoid a misdirected entry into the cranium. The sublabial approach, although it was once the most common corridor of access, is now used only in procedures for which

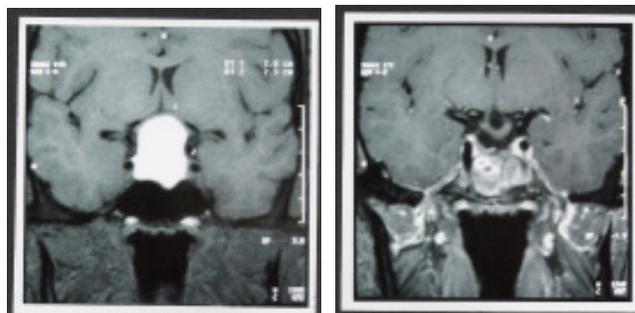


Fig 1 & 2. Pre-op MRI of a Patient of Pituitary Adenoma with Suprasellar Extension and Post-op MRI of the Same Patient Showing Total Excision of the Adenoma with Postoperative Changes in Sphenoid Sinus

endonasal exposure is inadequate. These include extended anterior cranial base procedures, patients with small nasal apertures, and in pediatric patients in whom the nose is too small to accept a standard sized speculum (2).

As regards the complications, there was no mortality following transsphenoidal operation in our series. No patient had diabetes insipidus lasting for more than three months. CSF rhinorrhoea was noted in 3% of patients. It is comparable to the results published by Black *et al* in 1987 (3). Amongst the patients having CSF rhinorrhoea one patient required surgical repair of fistula in immediate post-op period. Other two patients were managed with lumbar drain. CSF rhinorrhoea is a constant potential problem in post-op period. In carrying out the Transsphenoidal procedure the surgeon can be faced with a choice between complete resection and high likelihood of CSF leak or grossly incomplete resection. We have been increasingly willing to risk CSF leakage to obtain as radical a tumor resection as possible. Curettage, however, especially against the diaphragm, must be gentle and the pituitary curettes should not be used to pull tissue off the diaphragm. The surgeon's ability to perform a gross total tumor removal with no demonstrable evidence of a residual tumor tissue in the postoperative CT scan appears to be influenced by the diameter of the suprasellar tumor extension and the consistency of the tumor. Total excision of the tumor is easy in case of soft and cystic tumors as compared to hard and septate tumors. The results of our study were comparable to the study by Ivan Ciric *et al* (4) and also the results published by Black *et al* (5) as shown in table No. 2, 3 & 4. It is noticeable that the absence of residual tumor tissue on the postoperative CT scan is only significant within the limitation of the resolution capabilities of a CT scan. The salutary effect of Bromcriptine and cabergoline on hyperprolactinemia, galactorrhoea and infertility has been well documented. Since bromcriptine and cabergoline are not tumoricidal,

Table 2. Comparison with Past Study

	IVAN CIRIC et al (1983) (n=108)	Our study (n=100)
A) Incidence of visual symptoms on presentation	58%	56%
B) Improvement of visual symptoms after surgery	63%	85%
C) Cases with Normal Post-Op hormone levels.		
1) Prolactinomas		
2) Growth hormone secreting Adenomas	27%	37%
	26%	34%
D) Completeness of Tumor removal on Post-op CT scan	41%	38%

Table 3. Comparison with Past Study

Complications	Black et al (1997) (n=255)	Our study (n=100)
1) Diabetes insipidus < 3 months	17%	14%
2) CSF rhinorrhoea	2.7%	3%
3) Meningitis	0.4%	1%

discontinuation of medical therapy, however results in a recurrence of hyperprolactinemia in a majority of patients. Drug therapy was given in those cases of prolactinomas in whom the prolactin levels did not return to normal and in those who did not regain menses after the surgery.

Bromocriptine should not be viewed as an exclusive therapy but rather as an adjuvant therapeutic modality to be used prior to or following incomplete removal of a large prolactin secreting pituitary tumor (6). Transsphenoidal resection is indicated for patients with deterioration of vision, patients not responding to medical therapy (7). Transsphenoidal resection is the primary treatment modality for acromegaly and a successful resection results in a rapid reduction of growth hormone levels and can be achieved with very low morbidity and mortality even in older patients. Also good preservation of pituitary function is there, avoiding the need for life long hormone replacement (8,9). Transsphenoidal surgery also remains the main modality for treatment of non functioning pituitary adenomas. 39% of the patients in our series were non functioning adenomas. The patients had good improvement in vision following operative resection of the tumor (10,11).

Conclusion

Trans-septal Trans-sphenoidal microsurgery for both large and small pituitary adenoma done by experienced surgeons have acceptable morbidity & mortality. An endocrine cure was seen in 37% of patients with prolactinomas & in 34% of patients with growth hormone secreting tumors. Therefore, Trans-septal Trans-sphenoidal removal of pituitary adenomas has a high

Table 4. Incidence of Recurrences as Observed by Clinical, CT and Endocrine Evidence

Follow up period (yrs)	IVAN CIRIC et al (1983) (n=108)		Our study (n=100)	
	Total cases	Recurrences	Total cases	Recurrences
<2	22	0	21	0
2-4	40	4	44	8
5-6	20	3	25	6
7-8	17	4	6	2
>8	9	2	4	2
Total	108	13	100	18

probability of accomplishing endocrine cure with preservation of normal pituitary function. Post operative radiation therapy appears to play a greater role in the prevention of recurrences. This approach gives a good exposure of the floor of sella & therefore to accomplish gross tumor excision. We hereby recommend this approach for removal of pituitary adenoma.

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