

Feasibility of Trans-sphenoidal Surgery for Pituitary Tumors with Parasellar and Suprasellar Extension

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Pituitary adenomas arise from adenohypophyseal cells. The true incidence and prevalence of pituitary adenomas is difficult to establish, but epidemiologic studies suggest a prevalence of about 20 cases per 100,000 populations and an incidence of 0.5 to 7.4 per 100,000 population.^{28,25} An apparent increase in the incidence of pituitary tumors in the last two decades may be related to the introduction of computed tomography (CT), magnetic resonance imaging (MRI), and a variety of radioimmunoassay techniques for pituitary hormones. However clinical problems are relatively rare and the tumors are usually indolent and benign, with very slow growth

Trans-sphenoidal surgery (TSS) is preferred approach for surgical management of pituitary adenoma because of its simplicity, low morbidity and mortality. However, because of narrow surgical corridor of microscopic exposure, direct visualization of cavernous sinus sometime becomes difficult leading to incomplete excision of the tumors extended into the cavernous sinus. Several modifications of this approach have been made to expand the surgical field, but despite ample experience with transsphenoidal surgery, objective data on which tumor expansion and growth pattern allows for radical adenoma resection are still sparse. It is more so in the context of our country where neurosurgical service is very limited.

Therefore we tried to study the feasibility of TSS in removing pituitary tumors with extrasellar extension. We also studied the significance of tumor size and consistency in predicting extent of surgical resection of these tumors.

We found that more is the extrasellar extension of tumor, more difficult it is to completely resect it as expected. Similarly, we also found that tumor size and consistency also significantly influence the extent of surgical resection.

Key words: parasellar extension, pituitary tumors, suprasellar extension, TSS

rates over many years. Although histological invasion into the capsule and surrounding structures is common, only 0.1–0.2% of adenomas develops into frank carcinomas with metastases. However, adenomas may cause major clinical problems from mass effects (causing headache and visual failure from optic chiasm compression), hormone hypersecretion from functioning tumors, and hormone deficiencies from pituitary hypofunction if the residual normal tissue is damaged.¹³

After the first transsphenoidal resection of pituitary tumors by Herman Schloffer in 1907 and repopularization of the approach by Guiot and Hardy the transsphenoidal

approach (TSS) has evolved into the first-line method of treatment for sellar, parasellar and suprasellar lesions.²⁸ With the development of modern microinstruments and the use of operating microscope, transsphenoidal surgery has proven to be a safe and effective method of approaching the sella, however the surgical exposure provided by a microscopic transsphenoidal approach is limited because of narrow surgical corridor and poor direct visualization of cavernous sinus.^{14-17, 22} Several modifications of this approach have been made to extend the surgical field toward the anterior cranial base, the suprasellar region,^{28,11,13,1,3} and the inferolateral portion of the cavernous sinus.^{6,25} Despite ample experience with transsphenoidal surgery, objective data on which tumour expansion and growth pattern allows for radical adenoma resection are still sparse. Therefore we tried to study the feasibility of TSS in removal of pituitary tumors with parasellar and cavernous sinus extension explained by Knosp et al as well as in removal of pituitary tumors with suprasellar extension and their relative morbidity as explained by Hardy. Similarly we also studied how tumor size and consistency affects the extent of surgical resection of pituitary tumors.

Materials and Methods

We retrospectively reviewed the feasibility and therapeutic effectiveness of transsphenoidal approach on 36 cases of pituitary adenoma from Jan 2000 to Jan 2008 undergoing transsphenoidal surgery (TSS) in department of neurosurgery, Kathmandu Model Hospital and Norvic International Hospital in Kathmandu, Nepal. The diagnostic modes, surgical technique and clinical outcome were evaluated in all of these cases.

Radiological grading of tumor extension was done by modified Hardy's method from A to E and by Knosp grading from 0 to 4. Pre operative MRI scans were done with 0.3 tesla MRI scanner and all the pictures were stored in digital form in Departmental data. Coronal as well as Sagittal pictures were studied to classify the parasellar and suprasellar extension of the tumors according to Knosp and Hardy's grading respectively.

For the statistical analysis of this study SPSS 16.0 was used. Outcome of surgery in terms of extent of surgical resection and residual tumor was evaluated considering the predictive factors mainly suprasellar extension, parasellar extension, tumor consistency and tumor size with the help of one way ANOVA (Analysis of Variance) test. Adequate hormonal assay, visual field test were also done in all required cases. After successful transsphenoidal resection of tumor, the cases were followed up for at least

3 years and degree of surgical resection excision was confirmed in post operative MRI. Total excision was considered when post operative MRI scan showed no residual tumor. Near total excision was considered if more than 90% of tumor removed. In the cases where less than 90% and less than 60% of tumor was excised, subtotal and partial excision was considered respectively. Similarly, post operative hormonal as well as visual correction was also evaluated and compared. The cases without post operative images, hormonal and visual assessments, those which had undergone operative procedure other than TSS and those other than pituitary adenomas after histopathological confirmation were excluded from this study. There were 2 post operative deaths (5%) due to Halothene induced liver failure where some degree of residual tumor was seen in CT head done after TSS.

Parasellar Extension of Tumor According to Knosp Grading

The proposed classification was based on coronal sections of unenhanced and gadolinium diethylene-triamine-pentaacetic acid enhanced MRI scans, with internal carotid artery serving as the radiological landmark. A midsella coronal MRI scan was chosen as the reference plane. Grade 0 was considered when adenoma did not encroach cavernous sinus space, thus not crossing the tangent of medial aspect of the intra and supra cavernous ICA. In grade 1, tumor crossed the medial tangent without extending beyond the intercarotid line. Further extension beyond the intercarotid line was considered grade 2 and similarly extension beyond the lateral tangent of intra and supra cavernous ICA was considered grade 3. In grade 4, there was total encasement of intracavernous carotid by the tumor. According to this classification, surgically proven invasion of the cavernous sinus space was present in all Grade 4 and Grade 3 cases.

Suprasellar Extension of Tumor According to Modified Hardy's Grading

Modified Hardy's classification is as follows. A; expanding into suprasellar cistern, B: anterior recess of third ventricle obliterated, C: floor of third ventricle displaced, D: Intracranial (intradural) extension of tumor and E: extension into cavernous sinus.

Operative Technique

TSS was performed under general anesthesia with endotracheal intubation with head of the patient elevated

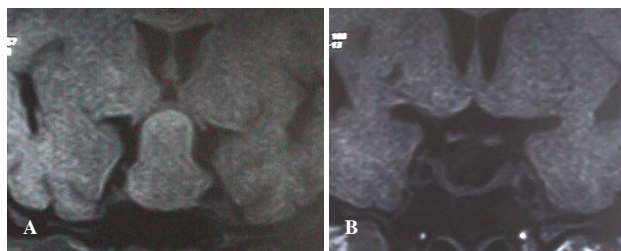


Figure 1. MRI of head coronal section showing huge pituitary tumor with suprasellar (Hardy's B) and parasellar extension (Knosp 2). A. Pre operative MRI. B. Post operative MRI showing complete resection.

20°. All the patients were put on Mayfield 3 pin head fixator. Endonasal approach was chosen in all the cases except in one, which was approached sublabial where the nasal septum was noticed very narrow in the MRI. A sublabial incision was made in the midline beneath the upper lip, at about 1 cm above the gingival-labial sulcus, and extending from one canine to the other as the incision was carried out deep down to periosteum of the maxilla. In endonasal TSS, septum was displaced to the patient's right nostril after the hemitransfixation incision (Fig.2) and the superior aspect of the naris elevated by retractor. Incision was made in the mucosa over the posterior border of cartilaginous septum. The septum was separated from the mucosa and mucoperichondrial plane was developed. An opening was made in the anterior wall of the sphenoid sinus and sellar floor in most of the cases under operating microscope and only in few cases lateral fluoroscopy or portable x-ray was done to confirm the location. The adenomas were carefully dissected and removed. Bleeding from tumor bed usually stopped after a complete extirpation was achieved. Sellar floor was repaired according to the surgeon's choice in required cases however in majority of them only gelfoam was used. In suitable cases the tumor bed and sphenoid sinus were loosely packed with adipose tissue or muscles tissue to prevent cerebrospinal fluid (CSF) leak. Complete excision was considered when post op MRI scan showed no residual tumor.

Results

Out of total 36 cases, 21 (52%) were males and 15 (48%) were females. Eighteen (50%) had purely hormonal, 13 (36%) had visual, 1(2.5%) had raised ICP, and remaining 4 (11.5%) had both hormonal and visual symptoms. Among 20 functioning or hormone secreting adenomas, 10 (45%) were GH secreting, 6 (27%) PRL and 4 (18%) were mixed GH-PRL secreting tumors. In 2 (10%) cases, level of both ACTH

Tumor Type	No of cases	Parasellar extension	No of cases	Suprasellar extension	No of cases
Functional	18	Knosp 0	5	Hardy A	15
Non functionl	14	Knosp 1	9	Hardy B	10
Mixed	4	Knosp 2	10	Hardy C	9
Total	36	Knosp 3	8	Hardy D	1
		Knosp 4	4	Hardy E	1

Table 1. No of cases of pituitary tumors according to their functional, parasellar, and suprasellar classification.

and TSH were low showing features of hypopituitarism. Number of cases according to functional, parasellar and suprasellar extension is as shown in the table 1 (Table 1).

Outcome of TSS in Tumors with Parasellar Extension

Among 24 cases graded 0-2, all had total excision except one (4%) where the consistency of tumor was firm and thus had only near total excision, whereas of other 12 cases graded 3-4, four (33%) had total (**Figure 1, A&B**), seven (59%) had near total and one(8%) had only partial excision, requiring second transcranial surgery. There were two post operative deaths which belonged to grade 3-4. Broadly, 36 cases were classified into two groups, Knosp 0-2 and Knosp 3-4 and ANOVA test was performed comparing the tumor resection of two groups. ANOVA showed statistically significant difference in the extent of tumor resection between the two groups ($P<0.01$) suggesting less the parasellar extension, more is the surgical resection.

Outcome of TSS in Tumors with Suprasellar Extension

Among 25 cases graded A-B, total excision was possible in all except in two (8%), where only near total excision was achieved (**Figure 2, A&B**). In nine cases graded C, total excision was seen only in five cases (55%) in post operative MRI. One case of grade D had only partial excision requiring transcranial approach in second attempt and in another one of grade E, near total excision was possible. Broadly, 36 cases were classified into two groups, Hardy's A-B and Hardy's C-E and ANOVA test was performed comparing the tumor resection of two groups. ANOVA showed statistically significant difference in the extent of tumor resection between the two groups ($P=0.02$) suggesting less the suprasellar extension, more is the surgical resection.

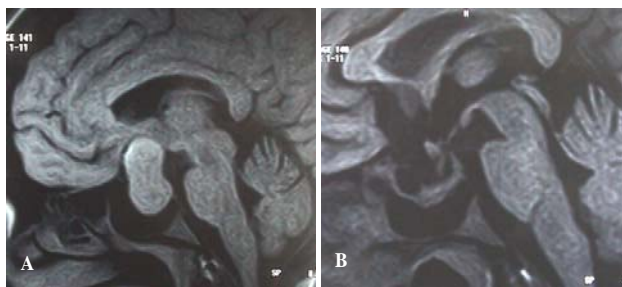


Figure 2. MRI of head, sagittal section, showing huge pituitary tumor with suprasellar (Hardy's B). A. Pre operative MRI. B. Post operative MRI showing complete resection.

Outcome of TSS According to Consistency of Tumor

Most of the tumors were soft and semisolid, hence easily suckable. Only in four cases (11%), tumors were firm in consistency and three of them were PRL secreting adenomas that underwent bromocriptine therapy. Total excision was possible in only one case even though the tumor was big, however in another case where the tumor was small without marked extension, only near total excision was possible due to its consistency. The other 2 tumors were very big with massive supra or parasellar extension. Total excision could be achieved in all cases with soft tumor consistency except in five (15.5%) where the tumors were very big with massive parasellar and/or suprasellar extension. ANOVA test was performed comparing the tumor resection of two groups, soft and firm. ANOVA showed statistically significant difference in the extent of tumor resection between the two groups ($P=0.01$) suggesting softer the tumor, more is the surgical resection.

Outcome of TSS according to Size of tumor

In this series, 26 (72%) cases were macroadenoma, tumor size being more than 1 cm. In ten (28%) cases size of the tumor was less than 1 cm, which was considered microadenoma. In all the cases of microadenoma, total excision of tumor was achieved, however in nine cases (34%) of macroadenomas, some degree of residual mass was seen in post operative MRI scan. ANOVA test was performed comparing the tumor resection of two groups, micro and macroadenoma. ANOVA showed statistically significant difference in the extent of tumor resection between the two groups ($P=0.02$) suggesting smaller the tumor, more is the surgical resection.

Post Operative Hormonal and Visual Correction

In all cases partial or complete visual and hormonal recovery was seen post operatively. Complete visual correction was noticed in 21 (59%) cases presenting with visual complaints (**Figure 3, A&B**) and in 15 cases (41%) there was only some degree of visual improvement. Likewise, in 15 cases (68%) of functional adenomas, complete hormonal recovery was obtained following TSS within 3 months.

Post Operative Recurrence and Use of Radiotherapy

In three years follow up, recurrence was seen in only 1 case of TSS, where only partial excision could be achieved. The residual was approached transcranially obtaining subtotal excision. All the cases were routinely evaluated in follow up and none of them required radiotherapy (RT) so far. However, in one case of near total excision RT was advised by another surgeon outside Nepal and in this particular case post RT hypopituitarism was seen requiring long term steroid therapy.

Discussion

Transsphenoidal approach has become the preferred approach for surgical management of pituitary adenoma because of its low morbidity and mortality.^{23, 7, 12, 19, 10} Factors determining extent of excision are cavernous sinus invasion, suprasellar extension, size and consistency of the tumor. Several authors suggested cavernous sinus invasion or parasellar extension as a reason for an incomplete excision.^{7, 9, 4} Hashimoto et al¹² and Saito et al²⁶ discussed the fibrous or woody nature of some pituitary tumors that had large quantities of connective tissue and intraoperative difficulty in bringing them down into the sella. On the other hand, soft tumors and those containing fluid rendered themselves to a radical excision irrespective of their size. Therefore we also tried to study the factors and their significance in determining the surgical outcome of pituitary adenoma following TSS.

The anatomic location of the pituitary gland determines its tendency to expand laterally toward the cavernous spaces. Because there are no lateral bony boundaries to the pituitary fossa, tumor expands mainly in the lateral directions. It is mentioned that 6% to 10% of pituitary adenomas involve the cavernous sinus^{2, 8} and are considered to be invasive.^{21, 20} However, in our study 36% of the cases had cavernous sinus involvement, this may be because of late presentation of the patients. Despite their size, clinical signs of cavernous sinus invasion occur

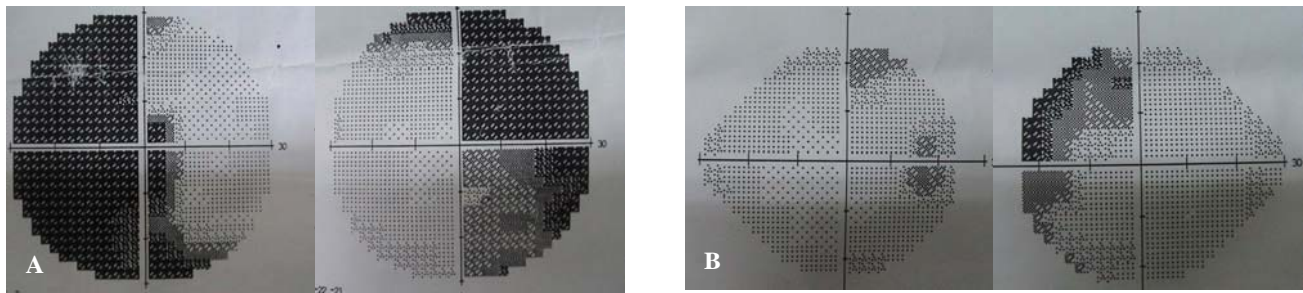


Figure 3. Visual field perimetry, A. preoperative perimetry showing bitemporal hemianopia, B. postoperative perimetry showing visual field improvement.

late because the intracavernous cranial nerves are lateral to the intracavernous internal carotid artery (ICA).⁵ Cavernous sinus invasion corresponds to biologically aggressive neoplasms and increases the morbidity and mortality associated with **surgical** procedures,²⁹ even if the tumor remains histologically benign in most of the cases.²⁴ Total encasement of the intracavernous ICA by the tumor is the most reliable MR imaging sign of cavernous sinus invasion, but this sign occurs very late,²⁷ thus tumor crossing the lateral intercarotid line is a very helpful sign for the diagnosis of cavernous sinus invasion.¹⁸

We focused on the feasibility of TSS in excision of pituitary adenoma with suprasellar as well as parasellar extension and nature of consistency determining the degree of excision. We found that the possibility of total excision is significantly high in pituitary tumors with Knosp 0-2 ($p < 0.01$) or Hardy A-B grades ($p = 0.02$) as compared to more extensively extended tumors as has been found in other previous studies. As the size and extension of tumor increases, the radical excision becomes more difficult. In our series radical excision was possible in only 40% of cases graded Knosp 3-4 and in about 50% in cases graded modified Hardy C-D. Similarly our study also shows that consistency ($p = 0.01$) and size of tumor ($p = 0.02$) also significantly determines the extent of surgical excision of the tumors. However, irrespective of degree of surgical excision, partial to complete visual and/or hormonal correction was observed in all the cases in this series. Routine follow up of all the cases with residual tumor has been uneventful and no post operative radio or chemo therapy has been recommended in this study.

Conclusions

TSS is preferred approach for surgical management of pituitary adenoma because of its low morbidity and mortality. Among various predictive factors of extent of surgical excision, our study showed greater the extrasellar

extension of tumor, greater is the possibility of residual mass. Similarly, tumor size and consistency are also statistically significant factors in predicting extent of surgical excision of these tumors. However, post operative visual and/or hormonal improvement can be expected in all cases irrespective of degree of surgical excision provided they are not completely impaired preoperatively. Being benign and slow growing tumor, even the residuals can be observed in routine follow up without requiring radio or chemotherapy after surgery.

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