



Original Research Article

Microscopic Trans-sphenoidal surgery in paediatric pituitary adenoma: An institutional experience

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ABSTRACT

Introduction : Pituitary adenoma is common in adult population but rare in pediatric population. Microscopic transnasal trans-sphenoidal surgery (MTTS) is gold standard technique for this. In the last two decades, there is increasing trend for endoscopic trans-sphenoidal surgery for pituitary adenoma. Endoscopic surgery had many well-established benefits over microscopic surgery in case of adult patients. But many surgeons are not fond of using endoscope in pediatric patients because of limited space in children. There is difficulty in maneuvering the endoscope in small nostrils. Present study showed that MTTS is safe and easy procedure in pediatric pituitary adenoma patients.

Materials and Methods : All pediatric patients operated by MTTS technique in single institute by a single neurosurgeon during 2010–2018 were analyzed retrospectively. All patients were below 18 years of age. Data were collected from bed head ticket, operative notes, and discharge summary and histological records.

Results : Total 22 patients were included in the study. The mean age was 14 years ranging from 11 to 17 years. Symptoms were as follows: headache in 46%, menstrual irregularity in 36%, visual disturbance in 32%, feature of acromegaly in 14%, and features of Cushing disease in 23%. Functioning adenoma was found in 20 patients (91%). Among functioning adenoma, prolactinoma comprises 55%, adrenocorticotrophic hormone secretory tumors 22%, growth hormone secretory tumor 14%, and nonfunctioning adenoma 9%. Majority of tumors extending to suprasellar area were prolactinoma (75%). Gross total resection was achieved in 18 cases (82%). Four patients (18%) had postoperative cerebrospinal fluid leak and all these patients were having macroadenoma or giant adenoma. Hormonal profile became normal in 16 patients (80%) out of 20 functioning tumors postoperatively. Seventy-eight percent female patients (seven patients) had improvement in their menstrual irregularity. Transient diabetes insipidus developed in three patients of giant pituitary adenoma.

Conclusion : MTTS is a safe technique in pediatric population. It had minimal morbidity and mortality.

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1. Introduction

Sellar and parasellar masses are 10% of total pediatric brain tumors.¹ In this category, craniopharyngioma ranked top (90%) while pituitary adenoma, Rathke's cleft cyst, germinoma, lipoma, teratomas dermoid, and epidermoids comprise only 10% of lesion.^{2,3} Pituitary adenomas are uncommon tumors in pediatric age and constituting

just 3% of all tumors.^{4,5} Most of these (94–97%) are functional tumors.⁶ This is in contrast to that found in adults populations (44–78% are nonfunctional) found in large series.⁷ Hormonal irregularities are the most common findings in these tumors. Growth hormone (GH) is usually the first pituitary hormone to be suppressed by the pituitary adenoma and adrenocorticotrophic hormone (ACTH) is the last to be affected.⁸ Transnasal trans-sphenoidal approach for pituitary adenoma was used by Hirsch for the first time.⁹ Since then it gradually evolved

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and microscopic trans-sphenoidal approach became the gold standard technique for pituitary adenoma.¹⁰ Now there is trend to remove pituitary adenoma by endoscopic technique because of many benefits as compared with microscopic technique.^{11–13} Although there are tremendous articles favoring the endoscopic endonasal approach, the gloomy part of this approach include, postoperative nasal complaints, cerebrospinal fluid (CSF) leak, and recurrence of tumor as well as intraoperative vascular complications.¹⁴ Pediatric population has some inherited challenges for transnasal approach like small size of nostrils and incomplete pneumatization of sphenoid sinuses. Also one need to remove enough amount of sphenoid bone to reach the Sella if sinus is nonpneumatized or incompletely pneumatized. In this article, we retrospectively study all the pediatric patients below 18 years, operated by microscopic trans-sphenoidal approach in single institute.

2. Material and Methods

2.1. Patient population

The data for this retrospective surgery were obtained from medical records of patients admitted in the Department of Neurosurgery for pituitary adenoma surgery. Patients younger than 18 years of age, operated between 2010 and 2018 period, were included. All cases operated through microscopic transnasal trans-sphenoidal approach were included. As this is retrospective study so ethical approval was not needed. We had total thirty patients of this age group who were operated by this route. Six of them were craniopharyngioma on histopathology and two patients were recurrent pituitary adenoma, thus excluded from the study. Therefore, this study included total 22 patients of pediatric age group.

Indications for surgery were: pituitary adenoma, nonresponsive or intolerance to medical therapy and in few cases, sudden visual deterioration.

2.2. Endocrine profile

Endocrine profile was done in each case both preoperatively and postoperatively to access the course of disease. Prolactin, insulin-like growth factor 1 (IGF-1), cortisol, and thyroid hormones were measured in all the patients. In case of Cushing disease, normal 24-h urine cortisol level and absence of clinical features were considered as remission. In case of GH secreting tumors, normal IGF-1 level in the absence of radiological lesion was considered as remission of disease.

2.3. Imaging study

Both, contrast enhanced magnetic resonance (CEMR) image and computed tomography (CT) scan was done preoperatively for evaluation of tumor and bony anatomy.

Postoperative CT scan was done on first postoperative day as a routine in all patients to rule out operative site hematoma. CEMR was done at 3 months of follow up to see extent of resection and residual tumors. Radiological recurrence was defined as new lesion after a normal postoperative MR scan.

The clinical finding, endocrine profile, radiological features, operative technique, perioperative course, and morbidity/mortality were taken from discharge summary and histopathological reports.

2.4. Operative technique

Patients were placed in supine position under general anesthesia. Head was elevated to about 20° with slight lateral tilt towards the left side so that surgeon vision could align comfortably with the patient's nasal cavity (Fig 1A). Neck positioned in such a way that jugular vein on left side remain patent and there was no undue traction of brachial plexus on right side. Head was put on horseshoe head rest to facilitate intraoperative maneuverability of head if required by the surgeon. Betadine paint was applied in nasal cavity and on the skin around nose. Right thigh was also prepared for taking fat and fascia lata if needed for sealing the Sellar floor. The cotton strips, soaked with 0.0067% adrenaline saline, were inserted into both nasal cavities between middle turbinate and nasal septum for about 5 min, for nasal vasoconstriction and to augment working space in nasal cavity. For midline lesion, right nasal cavity was used as entry point but if adenoma was in lateral position then approach through contralateral nasal cavity provide better trajectory to visualize the more laterally located tumor. A shorter and smaller diameter nasal speculum inserted in to nasal cavity direct up to sphenoid rostrum. An incision was made in the nasal mucosa at the junction of sphenoid rostrum and bony septum. The septum was shifted to other side by wide opening of speculum. The speculum was locked in position and the surgical approach extended to the anterior wall of sphenoidal sinus. Overlying mucosa was coagulated and stripped off till ipsilateral sphenoid ostium was seen. Care was taken at inferolateral part because of the presence of a branch of sphenopalatine artery. Contralateral mucosa was also stripped off until contralateral ostium was seen. Both sphenoid ostia along with the keel of sphenoid in the midline were in view (Figure 1B). A light-weighted chisel was used to remove the whole block of bone of sphenoid sinus between the two ostia (Figure 1C). This block of bone was used for reconstruction of sellar floor in later stage of procedure in all patients as a routine. Sphenoid sinus opening was increased by using small sizes Kerrison punch in most of the case except in two cases where drill was used due to incompletely pneumatized sphenoid sinus (Figure 1D). Fluoroscopy was used in some case to confirm the midline, superior and inferior limits. Sphenoid sinus septum gives an idea about the midline along with

location of adenoma if correlated with preoperative MR scan. Sphenoid septum removed and sphenoid mucosa was coagulated to prevent postoperative mucocoele formation. Considering the pediatric age only bare minimal removal of sellar floor bone was done with thin curette and drill. The boundaries of this operative space were as follows: superiorly tuberculum sellae, laterally carotid tubercles, and inferiorly the sellar floor. After initial opening in Sella, it was widened with the help of fine punch rongeurs. A cruciate incision was given in dura and all four flaps were coagulated to stop bleeding (Figure 1E). For removal of adenoma, surgeon had to remain in extra-arachnoidal plain. Anterior lobe of pituitary usually compressed to a thin-layer tissue around the tumor. This normal pituitary gland is seen in preoperative T-1-weighted MR scan as thin layer of increased intensity around the tumor. Preservation of this thin layer is the key to prevent long-term postoperative complications. Most of the adenoma were large and came up to surface, so tumor-arachnoid plain was easily found and tumor removed with the help of ring curettes. In cases where adenoma was small and not come to surface, incision was given at junction of normal looking gland and discolored gland if found. Tumor removal was started from inferior part then going to lateral part over the cavernous sinus. Superior portion of the tumor was removed in the last as the case in prevent early fall of arachnoid membrane. In case when suprasellar part did not come down, a positive end expiratory pressure was employed to facilitate the fall of this portion of tumor. At last, pseudocapsule, which is mainly made of adenoma tissue, was separated from normal pituitary gland. When tumor was completely removed the arachnoid of the diaphragma sellae gradually fell down in the sellar cavity. Small piece of gelatinous sponge and surgicell were used to fill the resection cavity. The small piece of sphenoid bone that was kept carefully was put across the dura with lateral edge inserted under the dura for adequate stability. Small fat graft put in the cavity and sealed with fibrin sealant in the last for extra safety to prevent CSF leak (Figure 1F). Nasal cavity irrigated copiously with saline and all blood clots removed. Vaseline gauze was not used in any case for nasal packing.

3. Result

Twenty-two patients were included in the study. Eleven were boys and rest were girls (50%). The mean age was 14 years ranging from 11 to 17 year. The most common symptoms were headache in 46% (10 patients) followed by menstrual irregularity in 36% (eight patients). Visual disturbance found in 32% (seven patients), feature of acromegaly in 14% (three patients), and features of Cushing disease in 23% (five patients). No patient was presented with apoplexy in this study.

Frequency of various type of adenoma was given in Figure 2. The mean of maximum dimension of tumor

was 23.05 mm, ranging from 6 to 60 mm. There were 5 patients with microadenoma (23%), 14 patients of macroadenoma (64%), and three patients had giant pituitary adenoma (14%). Suprasellar extension was found in eight patients (36%). Prolactinoma formed 75% (six cases) and nonfunctioning adenoma were 25% (two cases) of these tumors extending to suprasellar area. Cavernous sinus invasion was present in four cases (18%) of which all were prolactinoma (100%). Incomplete pneumatization of sphenoid sinus was present in two cases (9%) only. Gross total resection (GTR) was achieved in 18 cases (82%) and subtotal resection (STR) in four cases (18%) only. Radiological absence of tumor in postoperative MR scan was considered as GTR of tumor. All the cases of subtotal resection were those having cavernous sinus invasion (Figure 3). All these were prolactinoma on histopathology and received medical therapy to control their residual tumor at follow-up visit. One of these four patients also received radiotherapy for hormonal control. Four patients (18%) had postoperative CSF leak and all these patients were having macroadenoma or giant adenoma. All patients having visual symptoms (seven cases) became normal as recorded in postoperative follow up records. Hormonal profile became normal in 16 patients (80%) out of 20 functioning tumors postoperatively. Remaining four patients (all were prolactinoma) received medical therapy for control of their residual tumors and hormones. Menstrual irregularity was improved in seven female patients (78%) out of nine patients. Two female patients, in whom only subtotal resection could be achieved due to invasion of cavernous sinus, received postoperative medical therapy. One female patient also received radiotherapy for hormonal control. Three patients of giant pituitary adenoma developed diabetes insipidus postoperatively and improved gradually. Permanent diabetes insipidus was not developed in any case. There was no postoperative mortality in this study.

4. Discussion

Trans-sphenoidal microscopic pituitary surgery is a testified method for pituitary adenoma over past many decades. In a survey done by Ciric et al. in 1997 showed the lowest incidence of complications by trans-sphenoidal route in pituitary adenoma surgery in any practical setting.¹⁰ Large tumors had a tendency to compress this gland to a peripheral thin sheet but they remain in extra-arachnoidal plain and push the diaphragm upward. Surgeon's operative work must have to be extra-arachnoid to avoid any damage to pituitary gland and its postoperative long-term complication.¹⁵ To remain in extra-arachnoid plain is also necessary to prevent unwanted CSF leak. Microscopic pituitary surgery has the advantage of three-dimensional view as compared to the two-dimensional view in endoscopic surgery. Because of this, it is difficult to access the depth of operative field in endoscopic technique. This is one of the causes

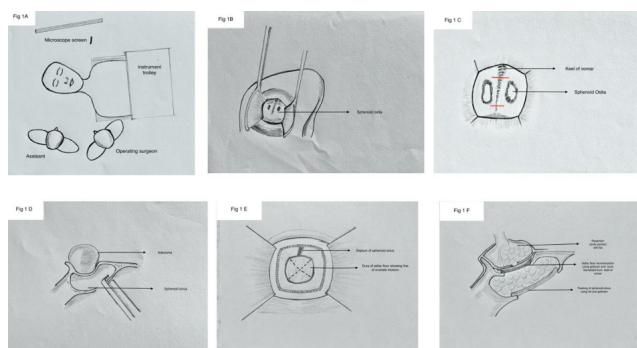


Fig. 1: **1A:** Showing patient positioning and position of surgeon and assistant during surgery, **B:** Exposure of rostrum of sphenoid and sphenoid ostia, **C & D:** Showing frontal and lateral view of enlargement of sphenoid ostia. For this we use small chisel and bone is cut along red lines and preserved for reconstruction of sellar floor. Space is further enlarged with a Kerrison punch. **E:** After dural exposure at sellar floor, the dura is opened in a cruciate manner. **F:** Lateral view of Sella after decompression of the tumor. Resection cavity is packed with gelfoam and fat (in some cases), sellar floor is reconstructed with bone which was harvested during sphenoidotomy. Sphenoid sinus is packed with gelfoam and fat (in cases where sinus is large)

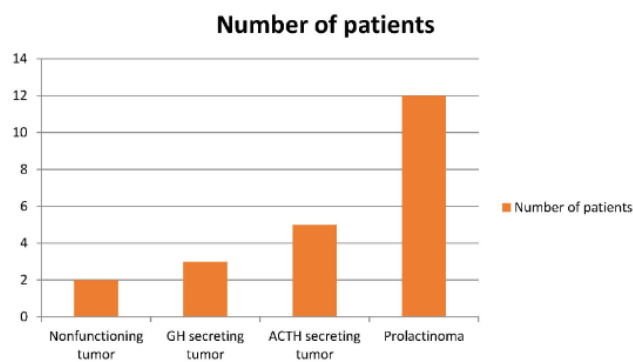


Fig. 2: Showing distribution of the various pathological types among the patients in this study

responsible for majority of vascular complication associated with endoscopic technique like intracerebral hemorrhages, midbrain stroke, and posterior cerebral artery and internal carotid artery injury.^{16–19} Small sizes of nostrils in pediatric populations also give the advantage to microscopic trans-sphenoidal surgery over endoscopic surgery because of limited operative corridor to work with instruments. Small nostrils is challenging for endoscopic procedure unless concurrent turbinectomy or ethmoidectomy is performed. However, this increases the postoperative nasal complications like empty nose syndrome Senior.^{20,21} In a study done by Haddad SF in 1991 showed that trans-sphenoidal microscopic surgery gives good result with few complications, little morbidity, and near zero mortality in adults and children.²² Pneumatization of sphenoid sinus

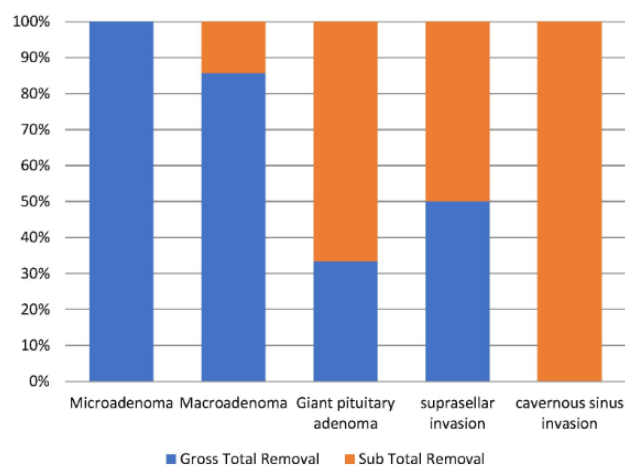


Fig. 3: Showing possible surgical excision of the tumor based on size and parasellar extension.

is also a matter of concern in pediatric populations. Two patients in this study had incomplete sphenoid sinus pneumatization. In both cases, high-speed drill was used to make a corridor in the sphenoid sinus to reach the floor of Sella. It would be very difficult for endoscope to negotiate and navigate through this narrow bony corridor. The key points for good results are the mastering the anatomical details of location along with vast experience in trans-sphenoidal surgery especially in children. In a large series of 136 pediatric patients reported by Minderman and Wilson, the percentage of various adenoma was as follows: prolactinoma (52.9%), ACTH secreting adenoma (30.9%), GH secreting tumor (8.8%), Nelson syndrome (4.4%), and only 2.9% nonfunctional tumors.⁶ This was comparable to the data found in our study. The percentage in our study is as follows: prolactinoma (55%), ACTH secretary adenoma (22%), GH secretary adenoma (15%), and nonfunctioning adenoma was 9% (Fig. 2). GTR was done in 18 patients (82%) in this study as compared to 75% in the study done by Tarapore et al.¹⁴ STR was achieved in four patients. All these patients had cavernous sinus invasion (100%). These were also the same patients whose hormonal profile didn't become normal after surgery and needed postoperative medical therapy and even radiotherapy in few. Invasion to cavernous sinus and volume greater than 10 cm³ are the two factors that preclude GTR in adenoma as shown in the study by Hofstette et al.²³ We got similar results in this study as all patients in whom only subtotal resection could be achieved, were macroadenoma and had cavernous sinus invasion. Hormonal profile came down to normal in 16 patients (80%) out of 20 patients of functioning adenoma. Four patients who had residual tumor in cavernous sinus, continued to have elevated hormones level. They received postoperative medical therapy for elevated hormone.

Postoperative CSF leak occurred in four patients (18%). Two patients were managed by simple conservative management while two patients needed lumbar drain for recovery. In various studies done by different authors, the percentage of CSF leak mentioned is from 0% to 2–3%.^{21,24,25} In this study, the incidence of CSF leaks were more than other studies. Mastering in skull base reconstruction is the key to reduce these incidences of CSF leak. Repeated surgery was not required in any case.

5. Conclusion

Microscopic trans-sphenoidal surgery is a gold standard treatment for adult pituitary adenoma. Now there are numerous articles that prove the efficacy of this technique in pediatric populations also. However, some authors only do endoscopic pituitary surgery in pediatric patients but there are very few articles that compare both the techniques. Small nostrils and incomplete pneumatization of sphenoidal sinus are the two major challenges for endoscopic surgery in children. This study concludes that microscopic trans-sphenoidal surgery had good outcome in pediatric pituitary adenoma with minimal perioperative complication.

6. Source of funding

None.

7. Conflict of interest

None.

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