

Endoscopic endonasal trans-sphenoid surgery of pituitary adenoma

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ABSTRACT

Endoscopic endonasal trans-sphenoid surgery (EETS) is increasingly used for pituitary lesions. Pre-operative CT and MRI scans and peroperative endoscopic visualization can provide useful anatomical information. EETS is indicated in sellar, suprasellar, intraventricular, retro-infundibular, and invasive tumors. Recurrent and residual lesions, pituitary apoplexy and empty sella syndrome can be managed by EETS. Modern neuronavigation techniques, ultrasonic aspirators, ultrasonic bone curette can add to the safety. The binostril approach provides a wider working area. High definition camera is much superior to three-chip camera. Most of the recent reports favor EETS in terms of safety, quality of life and tumor resection, hospital stay, better endocrinological, and visual outcome as compared to the microscopic technique. Nasal symptoms, blood loss, operating time are less in EETS. Various naso-septal flaps and other techniques of CSF leak repair could help reduce complications. Complications can be further reduced after achieving the learning curve, good understanding of limitations with proper patient selection. Use of neuronavigation, proper post-operative care of endocrine function, establishing pituitary center of excellence and more focused residency and endoscopic fellowship training could improve results. The faster and safe transition from microscopic to EETS can be done by the team concept of neurosurgeon/otolaryngologist, attending hands on cadaveric dissection, practice on models, and observation of live surgeries. Conversion to a microscopic or endoscopic-assisted approach may be required in selected patients. Multi-modality treatment could be required in giant and invasive tumors. EETS appears to be a better surgical option in most pituitary adenoma.

Key words: Neuroendoscopy, nasal cavity surgery, pituitary neoplasm, pituitary adenoma, sphenoid sinus, sphenoid bone surgery

Introduction

Neuroendoscopy has grown rapidly in the last 25 years as a therapeutic modality for treating a variety of brain and spinal disorders.^[1-3] Endoscopic endonasal trans-sphenoid surgery (EETS) is gaining wide acceptance as the first-line treatment of most pituitary adenomas. This article is aimed to review endoscopic Tran's sphenoid management of pituitary tumor. This review is based on 15 years search on this subject on PubMed, Google, and Medline plus.

Investigations

Detailed pre-operative study of CT and MRI scans,^[4] per-operative endoscopic visualization,^[5] and pre-operative three-dimensional modeling of the pituitary adenoma^[6] can provide information about the anatomy of sphenoid sinus, sellar floor, para-nasal sinuses, tuberculum sellae, clivus, position of carotid artery, optic pathways, and infundibulum. A detailed study of lesion and its surrounding structures is important to improve the safety and accuracy of surgery. Although endonasal anatomical variations are frequent, they do not pose a relevant obstacle in the EETS technique.^[7]

Pre-operative thorough examination of endocrinological status, visual field, and visual acuity is also essential. Diffusion tensor imaging assessments with fractional anisotropy and mean diffusivity values may help to estimate the response of visual improvement after surgical therapy in the early post-operative period.^[8]

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10.4103/0976-3147.102615

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Technique

This procedure utilizes a zero or 30 degree endoscope (usually 4 mm wide and 18 cm long). Thirty centimeter long telescope has an advantage over 18 cm scope. It keeps camera away from nasal opening which allows easy manipulations of instruments. General anesthesia is administered and the nasal mucosa of the middle turbinate is injected with a 1:100,000 epinephrine solution to induce vasoconstriction. The epinephrine solution soaked in cotton is also used to induce vasoconstriction of the whole nasal cavity mucosa. Thorough inspection of both the nasal cavities is done to identify normal structure and any anatomical variation. The middle turbinate can be resected or lateralized depending on the type of pathology. It is better to resect turbinate in large lesion to get more space for dissection. This turbinate can be used for sellar reconstruction. In patients with concha bullosa, conchal bone can be removed which can be used for sellar reconstruction after EETS surgery.^[9]

Sphenoid ostium is identified which lies usually 1-1.5 cm superior to the choana. A naso-septal flap is raised if needed.^[10] The pedicled naso-septal flap may not be sufficient in large dural defect especially in children less than 14 years of age.^[11] Bilateral naso-septal flaps could be required in these cases.^[12] The naso-septal flap must be raised at the beginning of the operation to protect the posterior pedicle during the expanded approach. In most pituitary tumor cases, an intraoperative cerebrospinal fluid leak is not expected but may be encountered. In these cases, a "rescue" flap approach can be used.^[13] In 1999, Dr. Gustavo Hadad and Dr. Luis Bassagaisteguy, from Argentina, developed a flap based on sphenopalatine artery, the vessel with the largest possible vascular territory in the nose. The sphenopalatine artery is the terminal branch of the internal maxillary artery, and it enters the nose through the sphenopalatine foramen. At the foramen, it then divides into two branches. The posterior branch (septal artery) runs over the rim of the posterior choana on the sphenoid in the sub-mucosal plane. This fact allows the flap to be harvested from the nasal septum in a sub-perichondrial and sub-periosteal fashion. The anterior limit is at the entrance of the nostril. It should be designed as long as possible. Posteriorly, incision follows the posterior border of the nasal septum and then arches over the choana. Part of the superior nasal septal mucosa is left to preserve olfaction.

Endoscope is positioned superiorly at 12 o'clock in right nostril to optimize the available space. Suction is usually entered into the 6-o'clock position in the right nose and dissecting instruments can be introduced through the left nostril. Sphenoid ostium is enlarged with Kerrison

rongeurs. Sphenoid rostrum and posterior vomer is removed to open the whole anterior wall of the sphenoid sinus. This creates the desired single rectangular cavity and allows identification of key anatomical landmarks. The medial optico-carotid recess (OCR), carotid protuberance, the sellar face, clival recess and the strut of bone over the superior inter-cavernous sinus (SIS) should be recognized. The medial OCR represents the ventral surface of the medial clinoid and is the key anatomical landmark in this region. An entry at the level of the medial OCR allows simultaneous access to the carotid canal, optic canal, sella turcica, and medial cavernous sinus. It is analogous to a "key hole" during a conventional pterional craniotomy. The medial OCR does not need to be opened for the removal of pituitary tumors unless there is significant suprasellar and lateral extension toward the optico-carotid cistern. The sphenoidotomy is widened to include the lateral recess of the sphenoid extending lateral to the carotid canal especially for the expanded approach. The exposure is then extended rostrally to expose the posterior cells of the ethmoid sinus and the planum-tuberculum junction. Finally, the floor of the sphenoid is resected back to the level of the clivus. This is particularly important in the case of macroadenomas with significant suprasellar extension. By reducing the floor of the sphenoid, a greater caudal-to-rostral trajectory into the suprasellar space is created. Any intrasphenoidal septations must be removed with care, because the paramedian septations often lead to the internal carotid artery. The sphenoid sinus mucosa is removed and the venous bleeding is controlled by irrigation with warm saline. Wide opening of sella is better for removal of large tumor. Removal of the bone overlying the SIS is imperative for lesions extending into the anterior cranial fossa. Bone removal over the sellar face should extend laterally over the medial portions of each cavernous sinus and rostro-caudally to expose both the superior and inferior inter-cavernous sinus. Surgeons who are beginner in endoscopy may fail to undertake an adequate exposure sometimes. This eliminates the primary advantage of endoscopic surgery of delivering divergent focal light and magnification which facilitates superior visualization and dissection. Combination of micro-curettes and micro dissectors are used to remove tumor within and above the sella. Endoscopic tumor resection uses techniques identical to those of microsurgery (internal debulking, capsular mobilization, and extracapsular dissection of neurovascular structures, along with coagulation and capsule removal).

Cerebrospinal fluid (CSF) leak if encountered can be repaired with fibrin glue, fat, and fascia lata and vascularized nasoseptal flap. CSF diversion techniques have been reported to manage CSF leak. A simple

purely synthetic repair of low-grade CSF leaks with a hydrogel sealant is described.^[14] Another simple and quick technique involving layered fibrin glue and gelatin sponge is also effective.^[15] More complex defects after pituitary surgery should be repaired with button graft technique.^[16] Multilayer technique, using autologous materials such as fat, fascia lata, bone, and mucoperiosteum, is frequently used for large defect.^[17,18] In recent cases, dural opening has been sutured.^[19] The trans-septal approach preserves the total septum which can be used for future reconstructions.^[20]

The bilateral endonasal approach provides a wide working area as compared to single nostril approach.^[21,22] After anterior sphenoidotomy, the endoscope can be fixed or can be held by the assistant in one nostril and the instruments can be inserted through any of the nostril. The bilateral endonasal approach provides a wide working area without the need for special instruments. Mucosal dissection can be modified (unilateral or bilateral dissection) depending upon tumor extension. This approach is better suitable for more extensive tumors. Binostril approach is strongly advocated especially for all expanded endoscopic approaches. Special transnasal trans-sphenoidal speculums with interchangeable blades and unique blade angulations were found to be safe. It allows optimal exposure and can be used interchangeably with microscopic or endoscopic techniques.^[23]

Traditional boundaries of the trans-sphenoidal approach can be extended in antero-posterior and lateral planes.^[24-26] The evolution of the endoscopic endonasal trans-sphenoidal technique, which was initially reserved only for sellar lesions, has lead to a progressive possibility to access the skull base from the nose. This route allows midline access and visibility to the suprasellar, retrosellar and parasellar space without brain retraction. This technique allows us to treat a variety of suprasellar and parasellar lesions which were traditionally approached by trans-cranially. Detailed knowledge of anatomy is must to properly perform this technique and to avoid complications. CSF leak remains a challenge and proper cranial base reconstruction and sealing of the leak is important. Such extended endoscopic approaches require an advanced and specialized training. Endoscopic endonasal transposition of the pituitary gland and its stalk can provide a valuable corridor to the retroinfundibular region with preservation of pituitary function.^[27] The interpeduncular cistern, including the retroinfundibular area, is one of the most challenging regions to approach trans-nasally. The pituitary gland and the infundibulum guard the region when an endonasal route is undertaken. Superior transposition of

the pituitary gland and infundibulum can be performed to access this complex region. Preservation of normal pituitary function can be achieved in over 85% cases but remains a concern in this technique. This approach should only be pursued once significant experience with endoscopic endonasal approaches has been acquired.

The capsule of the tumor is the compressed normal pituitary gland. The normal adenohypophysis was more often found at histopathology in the extracapsular excisions, rather than in the intracapsular excisions. The trans-sphenoidal pseudocapsule-based extracapsular resection approach provides a more effective and safe alternative compared to the traditional intracapsular technique.^[28] Better tumor removal, good remission and lower recurrence rate could be achieved compared to intracapsular approach. Gross total extracapsular dissection may be accomplished either by using a standard approach to the pituitary fossa or by extending the exposure. This technique could need removal of a portion of the planum sphenoidale and division of the superior inter cavernous sinus especially in tumors with suprasellar extension. Separation of the tumor from the normal gland, stalk, and cavernous sinus contents could be possible. It should be noted that the improved visualization provided by the endoscope does allow extracapsular dissection in many cases but it is not always possible especially in giant tumor. Intracapsular resection has also been found to be a safe and effective treatment.^[29]

One has to pay proper attention to anatomical considerations for endoscopic endonasal skull base surgery in pediatric patients.^[30] Various Neuronavigation techniques can make reoperation easier, faster, and safer.^[31-37] Open low-fields intraoperative MRI, using contrast-soaked cottonoid packing in the tumor resection cavity, can be used to monitor the precise extent of tumor removal.^[38] Integrating MR angiography into surgical neuronavigation provides superior visualization of the carotid arteries.^[39]

Soft-tissue removal is often a rate-limiting aspect in endoscopic procedures, especially when the tissue is dense or fibrous. Ultrasonic aspiration^[40] and other instruments can be used to remove tissue, without generating heat, through the working channel of the endoscope.^[41] The side-cutting tissue resector is also safe, easy to use, and effective tool for non vascularized firm tumors.^[42] The ultrasonic bone curette is a useful tool for bone removal.^[43] The pulsed laser-induced liquid jet system can achieve safe and optimum removal without vascular damage.^[44]

An endoscope holder can be useful when another expert endoscopic surgeon is not available to assist. This allows both hands to be free.^[45] The management of intradural bleeding can be done with the use of a thrombin–gelatin haemostatic matrix.^[46] A high definition (HD) camera is much superior to standard three-chip camera. Improved resolution, color information, and larger viewing field are some of the advantages of HD.^[47] Three-dimensional endoscopic trans-sphenoidal pituitary surgery with improved depth perception^[48] and Video endoscopic endonasal pituitary surgery could prove to be an excellent method in coming years.^[49]

Hypothalamic-pituitary-adrenal function is usually preserved in non-functioning pituitary macroadenoma. Peri-operative steroid treatment should be given only in patients with hypocortisolism.^[50]

Indications

Endoscopic endonasal trans-sphenoidal surgery is indicated in sellar^[51] and suprasellar tumors.^[25,26]

Staged^[52] or combined endoscopic trans-sphenoidal-transventricular approach^[2,53-55] for resection of a giant pituitary adenoma with ventricular extension can achieve a gross total removal. Endoscopic endonasal transposition of the pituitary gland and its stalk can provide a valuable corridor to the retroinfundibular tumor.^[27] Pituitary tumors with invasion in the internal carotid artery and cavernous sinus could be managed by EETS.^[56,57] Recurrent and residual tumor,^[58] and patients with pituitary apoplexy^[59,60] could be treated by EETS. Chiasmopathy for empty sella syndrome with post-operative visual deterioration^[61] can be effectively performed by EETS [Table 1].

Result of Endoscopic Endonasal Trans-Sphenoid Surgery and Comparison with Microscopic Approach

Endoscopic intracranial surgeries are increasingly used in various conditions.^[62-64] Endoscopic surgery is a better technique in removal of a suprasellar tumor

Table 1: Showing indications, advantages, limitations, complications and complication avoidance of endoscopic endonasal trans-sphenoid surgery for pituitary

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|---|--|
| Indications | Sellar, suprasellar, intraventricular, retro-infundibular, invasive, recurrent and residual tumors, pituitary apoplexy and chiasmopathy for empty sella syndrome. |
| Result of endoscopic endonasal trans-sphenoid surgery (EETS) and a comparison with a microscopic approach | Most recent reports favor EETS in terms of safety, better quality of life, less nasal symptoms, less blood loss, less operating time, more tumor resection, shorter hospital stay, better endocrinological and visual outcome as compared to microscopic technique. |
| Limitations | Sinusitis is considered a relative contraindication to trans-sphenoidal approach because of possible transcranial spread of infection. Absence of pneumatization of sphenoid sinus and very close position of carotid artery could pose difficulties. Significant suprasellar extension with small hiatus of diaphragmatic sella, lateral extension, retrosellar extension, brain invasion with edema, firm tumor consistency, involvement or vasospasm of circle of Willis arteries, and encasement or invasion of the optic apparatus and the optic foramina. |
| Complications | Steep learning curve and relatively difficult transition from microsurgery to EETS. Cerebrospinal fluid leaks, endocrinological complications (anterior lobe insufficiency and diabetes insipidus), delayed nasal bleeding, sinusitis, meningitis, intrasellar-suprasellar hematoma, intracapsular hematoma, pontine hematoma, empty sella syndrome, carotid artery injury |
| Complication avoidance | Proper pre-operative study of CT and MRI scans and per operative endoscopic visualization for detailed information about the anatomy of sphenoid sinus, sellar floor, para-nasal sinuses, tuberculum sellae, clivus, position of carotid artery, optic pathways and infundibulum Use of Neuronavigation techniques and Open low-field intraoperative MRI could add to the safety Proper planning of various naso-septal flaps and other technique of CSF leak repair could help reduce CSF leak and better reconstruct skull base. Complication rate can be further reduced after achieving the learning curve, good understanding of limitations with proper patient selection, proper post-operative care of endocrine function, team concept of neurosurgeon/otolaryngologist, attending hands on cadaveric dissection, practice on models and observation of live surgeries, establishing pituitary center of excellence, conversion to a microscopic or endoscopic-assisted approach and more focused residency and endoscopic fellowship training programs. Multi-modality treatment could be safer than more aggressive surgery in selected patients with giant and invasive tumors |

than the microscopic approach due to the better visualization.^[65] The avoidance of craniotomy, brain retraction, and reduced neurovascular manipulation with less morbidity are potential advantages.^[66] Endoscopic pituitary surgery was found to be safe.^[51,67-69] The quality of life was better in terms of patient discomfort and pain perception^[70-73] as compared to conventional microscopic technique. Operating time,^[71,74-77] hospital stay,^[71,72,74,76-78] and blood loss^[72-74,77] was less in the endoscopic technique as compared to the microscopic technique.

Nasal symptoms

The nasal outcome was better in the endoscopic group as compared to microscopic group. Post-operative nasal packing is not necessary and post-operative discomfort is minimal.^[77,79,80] On the other hand, the overall nasal symptoms did not show any significant change in the earlier study.^[81]

Tumor resection

Amount of tumor resection was better in the endoscopic technique compared to microscopic technique.^[73,75-78,82-87] In other study, the extent of tumor resection was same in the endoscopic and microsurgery technique.^[71]

Visual outcome

Ophthalmological recovery was better in the endoscopic group as compared to the microscopic group.^[87] On the other hand, the visual outcomes of microscopic and endoscopic techniques were the same.^[76,88]

Endocrinological outcome

The endocrinological outcome of endoscopic technique was superior to traditional microsurgical technique.^[73,76,77,84,85,87,89,90] In one earlier study, similar results were observed in both the techniques.^[71]

Non functional pituitary tumors

The amount of tumor resections, endocrinological outcome of anterior pituitary function and ophthalmological recovery were significantly better in endoscopic group as compared to microscopic group. There was no significant difference in morbidity in two groups.^[87]

Functional tumor

Controls of tumor growth and endocrinopathy was better and complications were less in EETS as compared to other treatment modalities.^[91]

Growth hormone secreting tumors

A majority of the EETS series reported a high rate of gross-total tumor resection and endocrinological remission in acromegaly patients.^[84,85] Factors affecting the success of the endoscopic surgery were lesion size, suprasellar/parasellar extension, and the degree of sella

floor erosion.^[92] Trans-sphenoidal surgery in longstanding acromegaly frequently poses greater challenges than other tumors.^[93] On the other hand, similar clinical outcome was reported after EETS and the microsurgical technique in growth hormone secreting tumor.^[94]

Cushing disease

Trans-sphenoidal pituitary surgery is the primary therapy for Cushing disease because of its potential to produce lasting remission without the need for long-term drug or hormone replacement therapy. It is also safe.^[95-99] The EETS led to shorter anesthesia time, less blood loss, and shorter hospital stay compared to the sub-labial trans-septal approach. On the other hand, there was no difference between the two surgical procedures with respect to cure or complications in other study.^[100]

Thyroid-stimulating hormone secreting pituitary tumor

The diagnosis of thyroid stimulating hormone secreting pituitary lesions is often delayed. The clinical picture is heterogeneous and it is difficult to treat. A trans-sphenoid approach can effectively treat such cases.^[101]

Prolactinoma

Most of the prolactinomas now can be managed by medical therapy. Medical therapy-resistant prolactinomas need surgery. Endoscopic techniques are found to be better than the microscopic technique. The advantages of extended endonasal approaches are most profound in tumors with suprasellar extension and cavernous sinus invasion.^[96,98,99] Endoscopic trans-sphenoidal surgery offers better removal of the adenoma from the medial cavernous sinus wall as compared to transcranial surgery. Gamma Knife surgery and medical therapy should be supplementary treatment options after endoscopic trans-sphenoidal surgery especially with gross cavernous sinus involvement lateral to carotid artery.^[102]

Limitations

Sinusitis is considered a contraindication to trans-sphenoidal approach because of possible transcranial spread of infection. Now there are reports of the concurrent trans-sphenoidal approach and endoscopic sinus surgery in selected patients with chronic rhinosinusitis and pituitary adenoma.^[103] The absence of pneumatization of sphenoid sinus and very close position of carotid artery could pose difficulties in EETS.

Significant suprasellar extensions with small hiatus of diaphragmatic sella, lateral extension, retrosellar extension, brain invasion with edema are some of the limitations of EETS. Firm tumor consistency, involvement or vasospasms of the circle of Willis arteries, and

encasement or invasion of the optic apparatus are also some of the limitations of endoscopic trans-sphenoid surgery. Presence of these findings increases risk of trans-sphenoid surgery even in the expert hands. Open craniotomy as the initial operation should be performed in such cases.^[104] Although significant suprasellar extensions, lesions with intraventricular spread and retro-infundibular lesions can be managed by the endoscopic approach after gaining sufficient experience, it carries more complications in the initial learning curve.

Learning curve

EETS like every other surgical technique do have a learning curve. Results are poor in the beginning of the learning curve. This also explains why complications were higher in some endoscopic series as compared to other series. These complications are significantly reduced after achieving this learning curve which could vary between 17 surgeries in O'Malley *et al.* series and 50 surgeries in Leach *et al.* series.^[105,106] Attending workshops, hands on cadaveric dissection, practice on models, and observation of live surgeries can reduce the learning curve. A training model using a skull and eggs is useful to improve surgical techniques in EETS.^[107]

Transition from microsurgery to endoscopic trans-sphenoidal pituitary neurosurgery

Transition from microsurgery to EETS requires steep learning curve. The collaboration between otolaryngologists and neurosurgeons, attending live workshops, hands on cadaveric dissection, training on models and a controlled, supervised residency training programs could improve the learning curve.^[108]

Complications and its Avoidance

Complication rates were low in most endoscopy group as compared to the microscopic technique.^[71,75,76,91] On the other hand, comparable complications were reported in both the groups.^[78] Gondim *et al.* observed 26.9% complications in their series. Post-operative CSF leaks, delayed nasal bleeding, sphenoid sinusitis, carotid artery injury, and meningitis occurred in 2.6%, 1.9%, 1.6%, 0.9%, and 0.6%, respectively. Endocrinological complications were observed in 17.9% cases out of which anterior lobe insufficiency was seen in 11.6% and diabetes insipidus in 6.3% cases.^[109] Empty sella syndrome, diabetes insipidus, CSF rhinorrhea, post-operative intracapsular hematoma were also reported in other studies.^[17,61,110-115]

CSF leak

Intraoperative CSF leaks were classified as grade zero when there was no intraoperative CSF leak. Grades 1 and 2 were classified based on the degree of CSF

leakage (low or high output) and size of the opening in the arachnoid membrane (<5 or ≥5 mm).^[116] A higher incidence of post-operative CSF leak was noted in the endoscopic approach as compared to the microscopic technique.^[73,77,89] The higher incidence of complication in the endoscopic group could be due to large lesions with higher proportions of suprasellar tumors and also due to initial learning curve in the endoscopy group. On the other hand, low CSF leak was also reported in the endoscopic group.^[117] CSF leak can be prevented or reduced by the multi-layered repair and the dural suture technique with a fascia lata graft.^[14-19,118]

Nasal complications

Nasal complications occurred in 29.6% of the operated cases. The most common complications were prolonged nasal crusting (10.4%), synechia formation (8.8%), and septal deviation (3.7%).^[119] Rhinosinusitis/mucocele occurs in about 6% cases.^[120,121] The most frequent sinusitis complication was sphenoiditis followed by ethmoid sinusitis and maxillary sinusitis.^[121]

Visual deterioration

Visual deterioration though rare could be seen in cases requiring more dissection to the under surface of optic apparatus such as in giant invasive pituitary tumor and craniopharyngioma.^[122]

Olfactory changes

Although the transnasal endoscopic approach to the sella removes structures known to contribute to olfactory function, it has no clinically significant effect on olfaction.^[123]

Conversion from endoscopic endonasal trans-sphenoid surgery to microscopic or endoscopic assisted microsurgery

Although EETS provides superior visualization in most patients, conversion to a microscopic or endoscopic-assisted approach could be essential in selected patients for the safety of the patient. Reasons of conversion to microscopic technique in Zada *et al.* series were reoperations with scarring along with loss of anatomic landmarks especially in Cushing's disease and acromegaly. Atypical nasal and sphenoid anatomy, desire for binocular vision, difficulty visualizing sella/midline and bleeding were also reasons of conversion.^[124] Significant invasion of cavernous sinus especially lateral to carotid artery could be indication for conversion.^[125] Intraoperative bleeding can be controlled by clip or haemostatic agent.^[46,126]

Pituitary centre

Strategies to improve patient outcome and to reduce complications include establishing centers of excellence

for pituitary tumor. More focused residency and fellowship training in EETS could also improve outcome.^[96,127]

Multi-modality treatment for giant and aggressive invasive tumors

Very aggressive surgical treatment in some giant and invasive tumor could increase complications. Multi-modality treatment could improve clinical outcome and reduce complications [Table 1]. Close collaboration of neurosurgeons with endocrinologists and radiation oncologists is essential for optimal treatment of patients with these challenging tumors.^[128] Multimodality therapy such as Gamma knife, stereotactic radiotherapy, medical management, apart from endoscopic surgery, could be required for optimal tumor control.^[32,102,129,130] The octreotide long-acting release and lanreotide Autogel are used in acromegaly patients and were found to have similar efficacy for biochemical cure and tumor shrinkage as compared to surgery.^[131]

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How to cite this article: Yadav YR, Sachdev S, Parihar V, Namdev H, Bhatele PR. Endoscopic endonasal trans-sphenoid surgery of pituitary adenoma. *J Neurosci Rural Pract* 2012;3:328-37.
Source of Support: Nil. **Conflict of Interest:** None declared.