Original Article

Endoscopic Approach to Remove Intra-extracranial Tumors in Various Skull Base Regions: 10-year Experience of a Single Center

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Abstract

Background: Some problems have been found in the usually adopted combined approach for the removal of intra-extracranial tumors in skull base. Herein, we described a pure endoscopic transnasal or transoral approach (ETA) for the removal of intra-extracranial tumors in various skull base regions.

Methods: Retrospectively, clinical data, major surgical complications, pre- and postoperative images, and follow-up information of a series of 85 patients with intra-extracranial tumors in various skull base regions who were treated by surgery via ETA in our skull base center during the past 10 years were reviewed and analyzed.

Results: Gross total tumor removal was achieved in 80/85 cases (94.1%) in this study. All 37 cases with tumors in anterior skull base and all 14 cases with tumors in jugular foramen received total tumor removal. Thirteen and three cases with tumors in clivus received total and subtotal tumor removal, respectively. Total and subtotal tumor removal was performed for 16 cases and 2 cases in lateral skull base, respectively. The complications in this study included: cerebrospinal fluid leakage ($n = 3$), meningitis ($n = 3$), and new cranial nerve deficits ($n = 3$; recovered in 3 months after surgery). In the follow-up period of 40–151 months (median: 77 months), seven patients (8.8%) out of the 80 cases of total tumor removal experienced recurrence.

Conclusions: Complete resection of intra-extracranial growing tumors in various skull base regions can be achieved via the pure ETA in one stage in selected cases. Surgical procedure for radical removal of tumors is feasible and safe.

Key words: Endoscopy; Intra-extracranial Growth; Neoplasm; Skull Base; Surgery

Introduction

The main method of management for intra-extracranial growing tumors in the skull base is surgical removal. However, complete tumor resection is very difficult given that tumors can grow to an enormous size and may be either intradural or extradural. Conventionally, a combined intra- and extracranial approach is considered the best option.[1-6] However, risks and problems such as brain retraction, secondary cerebral edema, and damage to the cranial nerves cannot be thoroughly resolved. Some authors[7-9] have recommended excising the dumbbell-shaped tumors with intra- and extracranial extension in two stages by removing the intracranial part of the tumor using variations of the transcranial approach during the first stage and removing the extracranial part of the tumor using an extracranial approach at a later stage if it becomes symptomatic. In fact, the extracranial component usually remains. Based on our early experiences using endoscopic approaches to remove meningioma and schwannoma with intra-extradural growth,[10-12] here we present our findings from 10 years of experience by using a purely endoscopic transnasal or transoral approach (ETA) for intra-extracranial

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growing tumors in various skull base regions to demonstrate the outcome and evaluate feasibility and safety of this method.

Methods

Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Ethical Committee of Xuanwu Hospital, Capital Medical University. All patients gave informed consent for the present study.

Patients

From November 2004 to March 2014, 85 patients with intra-extracranial tumors were treated with surgery using a purely endoscopic approach in Xuanwu Hospital. There were 44 males and 41 females, aged 8–71 years old (median: 42 years old). Tumors were located in the anterior skull base in 37 cases (male/female [M/F]: 23/14), in the clivus in 16 cases (M/F: 9/7), in the lateral skull base in 18 cases (M/F: 7/11), and in the jugular foramen in 14 cases (M/F: 5/9). The tumor pathology was as follows: schwannoma (n = 24), chordoma (n = 16), meningioma (n = 14), esthesioneuroblastoma (n = 13), carcinoma (n = 6), neuroendocrine carcinoma (n = 5), adenocarcinoma (n = 3), chondrosarcoma (n = 2), angiofibroma (n = 1), and rhabdomyosarcoma (n = 1). Detailed symptoms and signs were not shown. All patients underwent preoperative protocol including computed tomography and contrast-enhanced magnetic resonance imaging (MRI). A preoperative angiography with balloon occlusion test was performed for each patient whose tumor involved the cavernous sinus and internal carotid artery (ICA).

Surgical technique

The operative techniques have been previously described in detail both by us and others in the field.[10-15]

In this study, certain points were emphasized. In almost all ETA procedures on the skull base, especially in resections of tumors with intra- and extracranial involvement, the bimanual binarial technique, also known as the "three- or four-handed technique", was mandatory.

The degree of bone removal of the cranial base is dependent on the pathology, size, and location of the lesions. The bone of the medial orbital walls and skull base adjacent to the lesion should be drilled and removed to acquire a safe resection margin for malignancy. When undertaking resection of a tumor in the clivus, the clival bone removal by drill needs careful attention because the dura behind the clivus is very thin and usually adheres to the clival bone. Care should be taken to protect the integrity of the dura to prevent possible intracranial infection. Partial condyle should be drilled (if necessary) with a high-speed diamond drill to expose and open the hypoglossal canal as well as the jugular foramen for the removal of tumors in the jugular foramen.

After intra- and extracranial lesions were completely removed, multilayered reconstruction of the skull base was performed to repair the dural defect in the skull base. An inlay autogenous fascia lata graft harvested from the lateral thigh was used to reconstruct the arachnoid barrier. A layer of autogenous muscle graft harvested from the same thigh as that used for the fascia lata graft was placed extradurally (in an outlay manner) to cover the dural and bone edges. A thin layer of Ethisorb Dura Patches (Johnson and Johnson, Belgium) was applied to cover the muscle graft. Finally, the operative area was packed with Surgicel® (Johnson and Johnson, one layer) and iodoform gauze for 7 days. The Ethisorb Dura Patches and iodoform gauze helped to prevent graft migration. The iodoform gauze provided appropriate and constant pressure to the multilayered dura graft. More recently, we have used a vascularized septal mucosal flap to reconstruct a large skull base defect (>3 cm in diameter), which was prepared during the exposure, as described by Hadad *et al*.[16]

Results

The removal of a tumor was considered complete when no tumor components remained in intraoperative endoscopic view, verified by comparing pre- and postoperative volumetric data of contrast-enhanced MR images. The comparisons were performed by two independent neuroradiologists with 14 and 20 years of experience, respectively. In this series, complete resection of tumors with intra- and extracranial involvement was achieved in 94.1% of patients (80 out of 85 people) using ETA, including total tumor removal in all 37 cases in the anterior skull base; total tumor removal in 13 cases and subtotal tumor removal in 3 cases in the clivus; total tumor removal in 16 cases and subtotal tumor removal in 2 cases in the lateral skull base; and total tumor removal in all 14 cases in the jugular foramen. All patients with carcinoma, esthesioneuroblastoma, and neuroendocrine carcinoma were given postoperative radiotherapy. Complications included cerebrospinal fluid (CSF) leakage (3 cases), meningitis (3 cases), and new cranial nerve deficits (3 cases, recovered 3 months after surgery). No patient experienced other complications. Only 3.5% of patients (3 out of 85 people) experienced postoperative CSF leak, then went on to develop delayed meningitis that responded to antibiotic therapy. CSF leak was successfully treated using an endoscopic endonasal approach. In the follow-up period (40–151 months), seven out of 80 patients (8.8%) who received total tumor removal experienced recurrence, including 5 cases with chordoma in the clivus, one case with esthesioneuroblastoma, and one case with adenocarcinoma in the anterior skull base. Two patients with chordoma died from tumor aggression and two patients with esthesioneuroblastoma died from metastasis. One patient with schwannoma and one patient with chordoma who received subtotal tumor removal underwent a second surgery, and one patient with chordoma continued to live with the disease. There were no operative

or perioperative deaths. The duration of hospital stay varied from 10 to 23 days (median: 12 days). Prolonged hospitalization was due to the initial attempt to treat the complications of three cases with CSF leak and meningitis.

Illustrative cases

Patient 1: An esthesioneuroblastoma with intra-extracranial growth in the anterior skull base

A 42-year-old woman presented with nasal obstruction and anosmia for 6 years, aggravated with swelling on the right eye and diplopia for 2 months. Histopathological examination 3 weeks before the operation revealed that the lesion was an esthesioneuroblastoma. There were no other neurological deficits. A giant enhanced intra- and extracranial lesion extended from the frontal recess and posterior table of the frontal sinus to the tuberculum sellae with no surrounding edema was seen on MR images [Figure 1a-1c]. Gross total removal of the esthesioneuroblastoma was achieved using a pure ETA on July 25, 2012 [Figure 2]. The period of all surgical procedures took a total of 3 h. The volume of intraoperative bleeding was 900 ml. Complete tumor removal was seen on the postoperative enhanced sagittal, coronal, and axial MR images 20 days after surgery [Figure 1d-1f]. The swelling on the right eye and diplopia disappeared on the first day after surgery. The lesion was revealed to be an esthesioneuroblastoma by postoperative histopathological examination. The patient was discharged 12 days after surgery. There were no new neurological deficits or intra- and postoperative complications. At the time of the 60-month follow-up evaluation, there was no evidence of recurrence.

Patient 2: A chordoma with intra-extracranial growth in the clivus

An 8-year-old boy presented with a history of 2 months of cervicomedullary compression including neck pain, vertigo, instability of gait, and nasal obstruction. The preoperative MRI demonstrated an inhomogeneous enhanced intra- and extracranial lesion that extended from the sellar floor, the clivus to the cervical vertebrae, and compressed the brainstem [Figure 3a and 3b]. Gross total removal of the tumor with intra-extracranial growth was achieved using pure ETA on March 14, 2008 [Figure 4]. The postoperative MRI at 1 month after surgery showed that the tumor had been completely removed [Figure 3c and 3d]. Histopathological examination revealed that the lesion was a chordoma. The patient was discharged 12 days after surgery. There were no postoperative complications such as CSF leak, meningitis, cerebrovascular events, intracranial hemorrhage, or new neurological deficits. At the time of the 112-month follow-up evaluation, there was no evidence of recurrence.

Patient 3: A schwannoma with intra-extracranial growth in the jugular foramen

A 16-year-old girl presented with a 3-month history of progressive left-sided hearing loss, left-sided facial paralysis, and deviation of the tongue to the left on protrusion. Neurologic examination showed left-sided hearing loss (50–60 dB, 500–4000 Hz), left-sided facial paralysis (Grade 3 according to the House-Brackmann classification), and deviation of the tongue to the left on

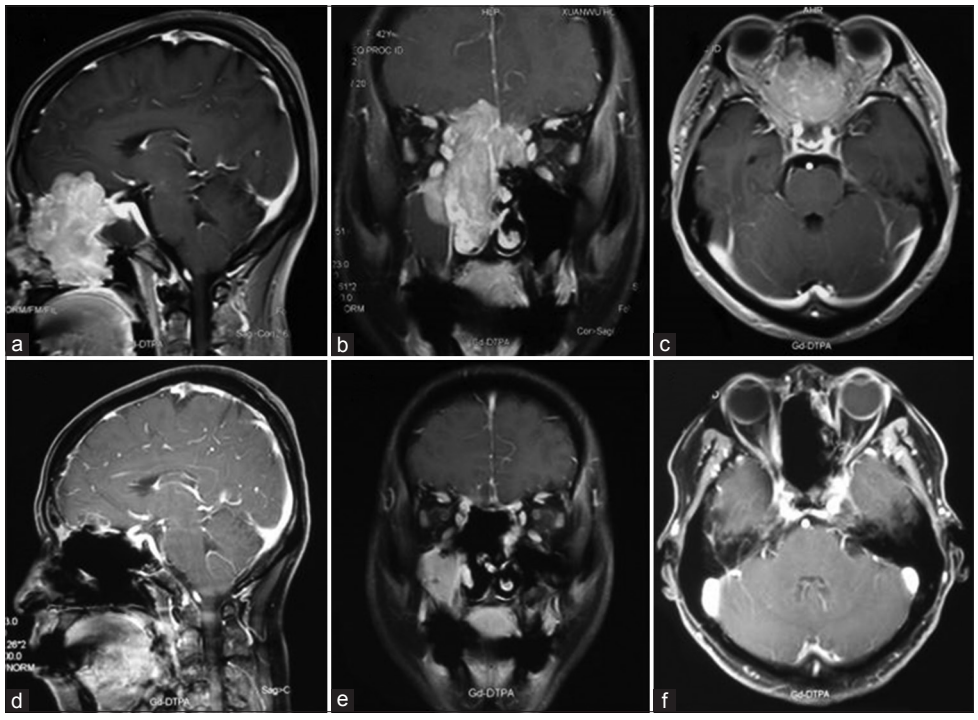

Figure 1: Preoperative sagittal (a), coronal (b), and axial (c) enhanced MRI demonstrated a giant enhanced intra- and extracranial lesion which extended from the frontal recess and posterior table of the frontal sinus to the tuberculum sellae with no surrounding edema. Postoperative sagittal (d), coronal (e), and axial (f) enhanced MRI at 20 days after surgery showed that the tumor had been completely removed. MRI: Magnetic resonance imaging.

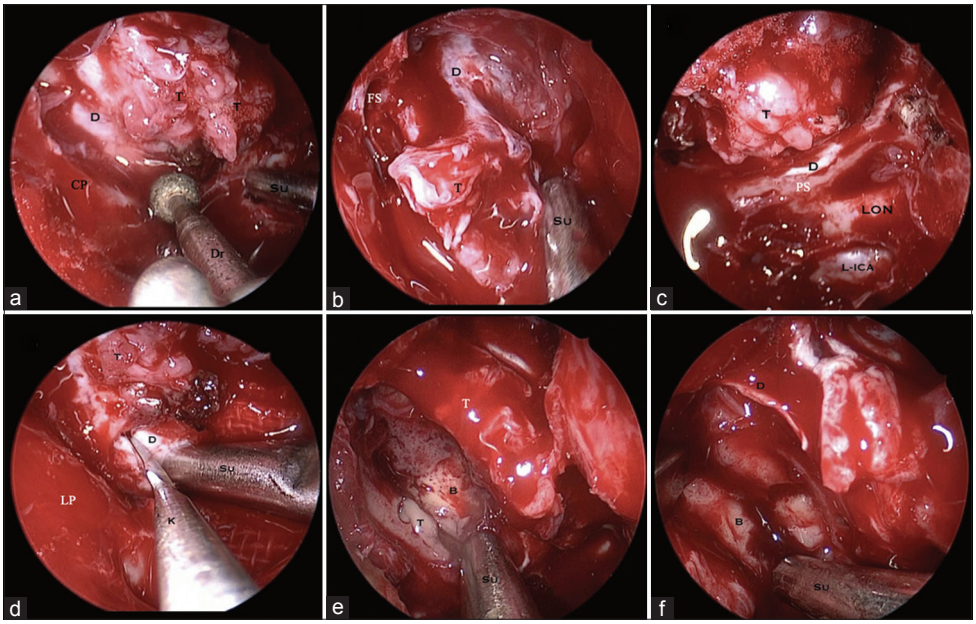

Figure 2: Intraoperative endoscopic view showing: (a) The bone of the anterior skull base was removed with a high-speed diamond drill during debulking of the extradural tumor; (b) the dura of the anterior skull base surrounding the tumor margin was exposed after removal of the bone of the anterior skull base; (c) The posterior margin of the tumor, left optic nerve, and left internal carotid artery was exposed after removal of the extradural tumor; (d) Incising the dura of the anterior skull base along the tumor margin; (e) Endoscopic endonasal view of the surface of the brain and intradural residual tumor during removal of the intradural tumor; (f) The brain descended after complete removal of the intradural tumor. T: Tumor; D: Dura; Su: Suction; LON: Left optic nerve; L-ICA: Left-internal carotid artery; K: Knife; B: Brain; CP: Cribriform plate: Dr: Drill; PS: Planum sphenoidale; LP: Lamina papyracea; FS: Frontal sinus.

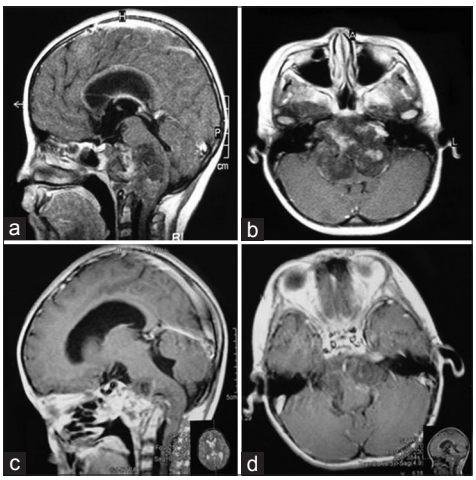

Figure 3: Preoperative sagittal (a) and axial (b) MRI demonstrated an inhomogeneous intra- and extracranial lesion that extends from the sellae, the clivus to the cervical vertebrae, and compressed the brainstem; postoperative sagittal (c) and axial (d) enhanced MRI at 1 month after the surgery showing that the tumor had been completely removed. MRI: Magnetic resonance imaging.

protrusion with left hemiatrophy of the tongue, without deficits of other cranial nerves. The preoperative MRI demonstrated a solitary inhomogeneous enhanced intra- and extracranial lesion (5.6 cm × 3.4 cm × 3.2 cm) that extended from the left side cerebellopontine angle to the infratemporal fossa, with a low T1-weighted signal and an inhomogeneous high T2-weighted/fluid-attenuated inversion recovery signal [Figure 5a-5c]. Gross total removal was achieved using a pure ETA on January 20, 2011 [Figure 6]. The entire surgical procedure took 5 h; intraoperative bleeding was 700 ml. The patient was discharged 10 days after surgery. The MRI 1 week after surgery showed that the tumor had been removed completely [Figure 5d-5f]. Histopathological examination revealed that the lesion was a schwannoma. Postoperatively, the patient experienced hoarseness for about 3 months due to a temporary left vagus palsy. The patient had presented with Grade 3 facial palsy before surgery and recovered approximately 3 months after surgery to Grade 2. She had presented with hearing loss before surgery and recovered to normal (10–15 dB, 500–4000 Hz) after surgery. At this time, lingual motor function was restored but hemiatrophy of the tongue was still detectable. At the time of the 78-month follow-up evaluation, there was no evidence of recurrence.

Discussion

The goal of modern skull base surgery is to decrease the perioperative complications and preserve the cranial nerve function while achieving radical resection and decreasing the risk of recurrence. A purely endoscopic approach provides an angled and magnified view and a clear surgical field. The expanded endoscopic approach has been used in skull base surgery over the last decade.[10-15] The feasibility of this approach for removing lesions in the skull base and its advantages of preventing surgical retraction of the brain and improving cranial nerve function have gradually been recognized by more and more neurosurgeons.

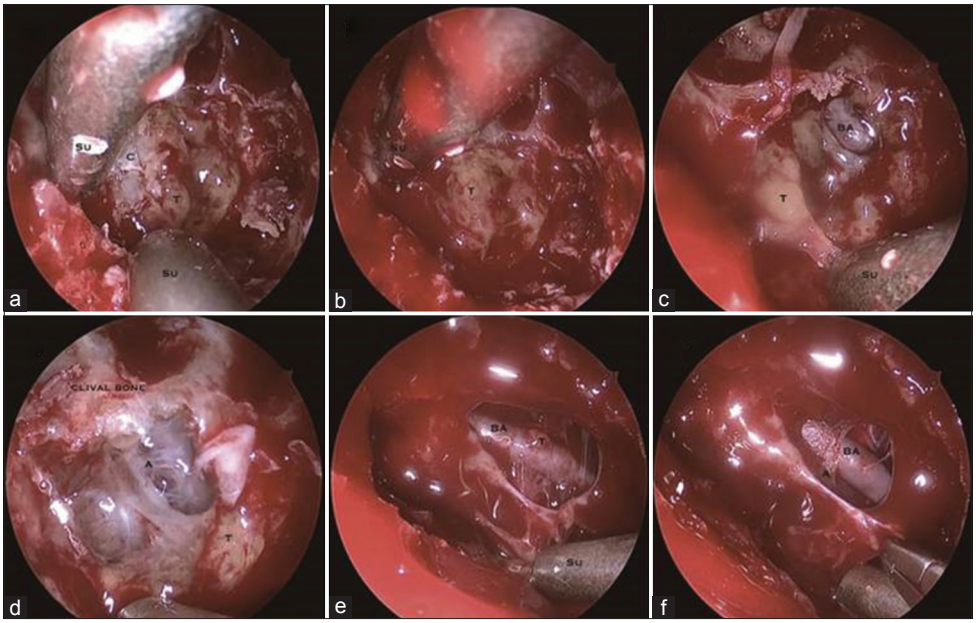

Figure 4: Illustrative case 2, intraoperative endoscopic view showing: (a) The bone overlying the clivus was removed to expose the dura of the sellae, clivus, and the intra-extradural part of the tumor after complete removal of the extracranial part of the tumor; (b) exposing the intradural part of the tumor after removal of the bone of the clivus; (c and d) removal of the tumor covering the basilar artery; (e) removal of the residual tumor on the surface of the basilar artery; (f) the arachnoid membrane, basilar artery, and brainstem were demonstrated after complete removal of the tumor. T: Tumor; C: Clivus; Su: Suction; A: Arachnoid membrane; BA: Basilar artery.

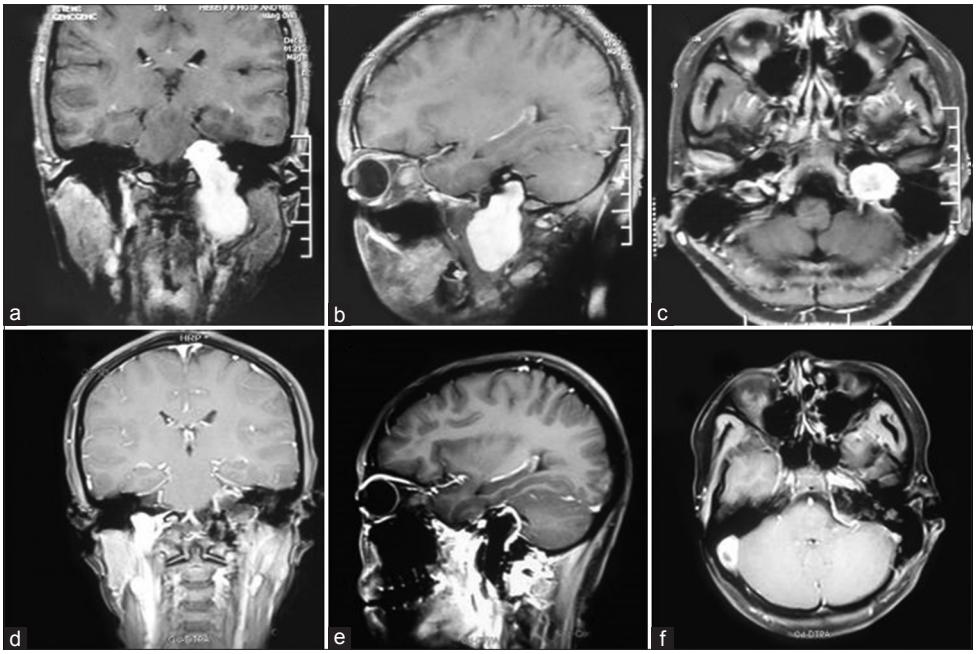

Figure 5: Illustrative case 3, preoperative coronal (a), sagittal (b), and axial (c) gadolinium-enhanced MRI demonstrated a dumbbell-shaped schwannoma with intra- and extradural extension through the left-side hypoglossal canal and the jugular foramen. Postoperative coronal (d), sagittal (e), and axial (f) gadolinium-enhanced MRI at 4 days after the surgery demonstrated that the lesion in the left side of the lateral skull base had been completely removed. MRI: Magnetic resonance imaging.

Extent of tumor resection

The extent of tumor resection objectively depends on the location and the pathology type of the tumor, the density of the tumor, and the surgeon's experience in endoscopic skull base surgery. For intra-extracranial tumors in the anterior skull base, the anterior limit of ETA is the frontal sinus, and the posterior limit is the optic chiasm and the anterior communication artery. The lateral boundary is the orbital contents and the optic nerve. Theoretically, tumors within these limits can be managed using ETA. In contrast to conventional transcranial approaches, ETA has the advantage of dealing with lesions in the optic canal, which has been well demonstrated by optic nerve decompression for traumatic optic neuropathy. The

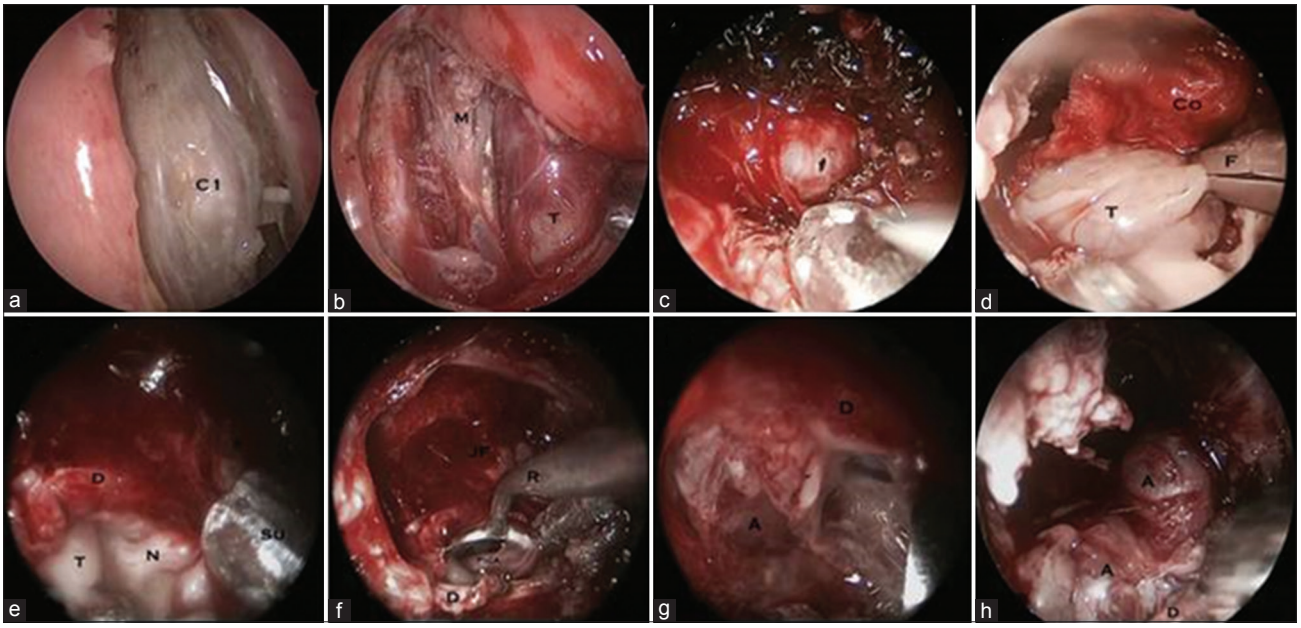

Figure 6: Illustrative case 3, intraoperative endoscopic views showing: (a) Incision was made on the midline of the oropharyngeal membrane using an electric scalpel. The muscle and fascia were separated to the left side; (b) the extracranial part of the tumor in the infratemporal fossa was exposed; (c) the intradural part of the tumor was exposed after radical intracapsular removal of the extracranial part of the tumor; (d) removal of the intradural part of the tumor; (e) removal of the intradural part of the tumor; (f) the posteroinferior cerebellar artery can be identified after partially dissecting and debulking the intradural part of the tumor; (g) exposing the arachnoid membrane over the tumor after removal of the intradural part of the tumor; (h) the arachnoid membrane covering the intradural tumor bulged through the dural defect after complete removal of the tumor. C1: Anterior tubercle of atlas; T: Tumor; M: Muscle; F: Forceps; Co: Cotton; N: Posterior cranial nerve; D: Dura; PICA: Posteroinferior cerebellar artery; R: Rongeur; JF: Jugular foramen; A: Arachnoid membrane.

gross total resection in all of the cases in our series also confirmed the feasibility of ETA in dealing with various anterior skull base tumors with intra- and extracranial growth within these limits. Another factor that may impede total resection is the density of the tumor, but the impediment in the anterior skull base may be less than in other regions of the skull base. In our experience, ETA's contraindications may include tumors that extend to cerebral ventricles, encase the vital vessels (such as the anterior communicating artery and the intracavernous ICA), and subpially diffuse or extend beyond the optic nerves. Another potential limitation for the use of ETA may be patients who present with significant preoperative cerebral edema. In the cases drawn on in this study, the intra-extracranial tumors in the clival region were all chordomas. Gross total removal was achieved in 13 cases and subtotal removal was performed in 3 cases. The gross total removal rate was lower than in the anterior skull base and in the jugular region. Clival chordomas are challenging targets to surgeons because of their critical location, invasive nature, and tendency for aggressive recurrence. Surgical treatment has a definitive role in the management of clival chordomas.[17-19] At present, whether or not radical removal is still controversial. Clival chordomas are particularly difficult to manage because these tumors usually involve not only the intra-extra dura of the clivus, but also the bone of paraclivus, sella, atlas, odontoid process as well as the ICA, cavernous sinus, vertebral artery, basilar artery, and brainstem, *etc*. To achieve a gross total resection, according to our experience, wider bone removal and exposure of the tumor margin should be considered.

In the lateral skull base region, the majority of the tumors had become quite large before being diagnosed. The appearance of symptoms such as facial numbness, headaches, facial sensory disturbance, masticatory muscle atrophy, toothache, hypoplasia, nasal obstruction, hearing loss, or dysosmia indicates tumor enlargement. A CT scan performed at the initial diagnosis usually shows widening of the foramen ovale or the foramen rotundum, and MRI clearly shows the location, shape, size, and extent of the tumor and its relationship with the neighboring structures. Compared with traditional approaches, the greatest advantages of ETA are good visualization of the mass and its adjacent anatomical structures, easy manipulation of vessels and nerves, and decreased morbidity from tissue trauma. Particularly in pediatric patients, it is important to preserve the facial skeleton to avoid disruption of the development of facial symmetry. The ETA can expose tissue from the median line of the sella turcica to the bilateral jugular foramens, as well as the mandibular joints in the horizontal plane. In this series, 16/18 patients with Jefferson's Type D tumors received complete removal using pure ETA. Another two patients whose tumors invaded the cavernous sinus received subtotal removal. There were no obvious intra- or postoperative complications.

In this study, in the jugular foramen region, the pathology of all intra-extracranial tumors was schwannomas. Since

schwannomas are benign tumors, safe removal of the dumbbell-shaped tumors is to be expected with modern skull base approaches. The surgical approach should be well planned to achieve complete surgical removal as repeated operations drastically increase the chance of injury to the lower cranial nerves.[20] However, complete removal of a schwannoma in the jugular foramen region is very difficult due to the tumor's intra- and extradural extension and its intimate anatomical relationship to neurovascular as well as brainstem structures. Despite variations of the transcondylar approach or intradural approach combined with an extradural approach have been used, complete tumor resection was achieved only in 9 (28.1%) out of 32 cases in our own studies and in others studies.[10,21-23] Usually, the extracranial component remained. In this series, complete tumor resection was achieved in all the 14 patients using pure ETA, without creating additional permanent damage to cranial nerve. This minimally invasive approach provided a safe and wide exposure of the lower clivus, anterior rim of the foramen magnum, C1 transverse process, occipital condyle, vertebral artery, posterior inferior cerebellar artery, and even the infratemporal fossa. It also allowed effective control of intraoperative extradural bleeding.

Improvement or preservation of cranial nerve function

Eleven patients in our series presented with visual complaints before their operations. As previously stated, the improvement or preservation of vision should be paramount when selecting an approach to resect intra-extracranial growing tumors. Unlike transcranial approaches, ETA has the advantage of providing direct exposure to and early protection of the optic nerve, optic apparatus, and subchiasmatic perforators. In addition, the manipulation and retraction of the optic nerve and the optic chiasm are reduced by adopting a medial-to-lateral trajectory in ETA. The ophthalmic artery and the vascular supply to the optic nerve and the chiasm are also easily dissected and preserved using ETA, which helps to preserve vision. No patient in any of the cases drawn on here experienced an immediate or permanent worsening of vision after surgery. The postoperative visual outcomes were improved in all patients who presented with preoperative visual complaints. Similar to the visual outcome in our series, Gardner *et al*.[13] described resolution or improvement of visual symptoms in all 35 intra-extracranial meningiomas in the anterior cranial base using an ETA, which also strongly demonstrates the advantage of ETA in visual preservation. Of 11 patients in the cases included in our study who presented with cranial nerve VI palsies before the surgery, seven recovered after surgery. Of ten patients who presented with cranial nerve X palsies prior to surgery, five recovered after surgery. One patient who experienced new temporary left vagus palsies after surgery had recovered by the time of the follow-up approximately 3 months after the surgery. One patient who experienced new temporary left hypoglossal palsy after surgery had recovered within a week after surgery. Lower cranial nerve palsy may be due to less intraoperative irritation (such as retracting or dragging) in ETA and less postoperative swelling of soft tissue, which would compress the nerves.

Complications

Due to the limited number of cases drawn on in this study, it is difficult to make direct quantitative comparisons between ETA and open approaches in terms of complications after the resection of tumors with intra- and extracranial involvement. However, it is clear that the rate of complications in these cases was very low. Given that the nasal or oral cavity is never a sterile pathway, postoperative intracranial infections are common. However, only three patients (3.5%) experienced meningitis, which was secondary to a CSF leak. The low rate of infection was due to repeated irrigation with sterilized saline and betadine before the operation and good reconstruction of the skull base, which protected the calvarium from retrograde infection. Pedicled nasoseptal flap was not our primary method of reconstruction in this series although we have used a vascularized septal mucosal flap to reconstruct large skull base defects in more recent cases. We prefer sandwich-like reconstruction, using fascia lata, autogenous muscle, and an Ethisorb Dura patch to repair skull base defects. Our experience showed that the autogenous muscle was reliable in obliterating dead space after the tumor was removed. CSF leaks seem to be another problem after cranial base tumor resection using ETA. In the series of cases drawn on here, only three patients (one case of meningioma in the anterior skull base and two cases of chordomas in the clivus) experienced a postoperative CSF leak. The three patients (3.5%) with CSF leak experienced second repair using ETA. As previously stated, CSF leaks are a manageable complication. All postoperative leaks should be rapidly repaired using ETA when necessary. Moreover, the rate of CSF leaks in our study is similar to that (approximately 5%) when using the pedicled nasoseptal flap method.[16,24,25] In this series, no patient experienced other intra- and postoperative complications such as ICA rupture, cerebrovascular events, intracranial hemorrhage, hydrocephalus, or new permanent cranial nerve deficits. There were no operative or perioperative deaths.

Our experience has suggested that ETA provides better exposure of the structures surrounding a tumor, and excellent visualization and exposure of the endoscope, in selected cases allowing for complete removal of intra- and extradural tumors in one stage. Although the endoscopic approach is not the answer to every problem associated with cranial base surgery, with appropriate preoperative evaluation, careful planning of the perioperative period, and adequate surgical experience, the majority of cranial base tumors with intra- and extracranial involvement in the various regions of the skull base can be successfully dealt with using this approach. The surgical procedure for radical removal of tumors should be feasible, safe, and effective. It should also be emphasized that surgeons should not consider using this approach until sufficient experience has been gained due to the potential risks of endoscopic approaches.

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Conflicts of interest

There are no conflicts of interest.

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