

Combined Nasal Endoscopic and Subfrontal Craniotomy for Resection Tumors of Anterior Skull Base

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1. Abstract

1.1. Objective: Sinonasal tumors invading anterior skull base is difficult to treat in Otorhinolaryngology and Neurosurgery. Treatment requires the collaboration of ENT and neurosurgeon to remove the tumor completely. This study was to evaluate the outcome of combined technique nasal endoscopic and sub frontal approach in case of Sinonasal tumors involving anterior skull base.

1.2. Methods: retrospective cross - sectional study.

1.3. Result: The study was a cross sectional study that had taken place at Otorhinolaryngology and Neurosurgery department of Cho Ray hospital (CRH), Vietnam. All 45 patients were enrolled and underwent the surgery. 71.1% of these cases were malignant tumors. The ratio of Sino nasal malignant tumor is squamous cell carcinoma and esthesioneuroblastoma were 24.4% and 11.1%, respectively. All the cases were diagnosed as sinonasal

tumor invading anterior skull base and successfully removed by combining nasal endoscopic approach with subfrontal craniotomy.

1.4. Conclusion: The combined nasal endoscopic with subfrontal craniotomy for resection nasoethmoid tumor invading the brain show a good result. This technique is an important adjunct that contribute to the treatment of anterior skull base tumor involving the brain.

2. Introduction

Sinonasal tumors invading the skull base is often seen in ENT and neurosurgery departments. Traditionally, we used the frontal craniotomy combined with a transfacial approach of Ketcham et al to resect the nasoethmoid tumors, paranasal sinus tumors involving anterior cranial base and the brain [1, 7, 21]. However, the transfacial approach has many disadvantages to facial development and causes facial deformity. Development of

endoscopy, endoscopic technique and equipment make the surgery to resect the anterior skull base tumor safe and efficient. Currently, endoscopic surgery has been widely used to treat lesions at anterior skull base, and nasosinus tumor invading skull base. In this study, we used a combined nasal endoscopic and subfrontal approach to treat the sinonasal tumors and anterior skull base tumors invading the brain.

3. Material and Methods

3.1. Patients

All of the patients were diagnosed as anterior skull base tumors invading the brain and underwent surgery at Cho Ray hospital.

3.1.1. Inclusion Criteria:

- Diagnosed with anterior skull base tumors invading the brain
- Underwent combined nasal endoscopic with sub-frontal approach at Cho Ray hospital (CHR), Viet Nam

Indication for the Surgery:

- + Benign or malignant tumors invaded meningeal or adjacent structures that need to resect more than 2cm of meningeal;
- + Nasoethmoidal tumors invaded meningeal and brain;
- + Tumors invade posterior table or recess of frontal sinus

3.1.2. Exclusion Criteria: [9, 14]

- + Tumors invaded palatine bone, nasal bone, lacrimal bone
- + Tumors invaded orbital cavity on both side
- + Tumors invaded cavernous sinus
- + Tumors invaded posterior cranial fossa;
- + Tumors invaded ICA;
- + Metastatic tumors;
- + Patients with internal disease or elderly patients who could not be operated on.

3.1.3. Research Time:

- The present study was conducted over 8 years (between 2010 - 2018). During this study, we had enrolled all 45 cases with anterior skull base tumors.

3.2. Steps to Conduct Surgery: [5, 6, 17, 22]

3.2.1. Step 1: Preoperative Preparation:

- + Clinical assessment;
- + CT-Scan/ MRI for sinuses, skull base and brain;
- + ± Biopsy before operation;
- + Consultation: methods of treatment and surgery;
- + Explain to the patients the risks.

3.2.2. Step 2: Operation

- + Choose appropriate antibiotics;
- + Lumbar drainage;
- + Using nasoseptal flap.

+ General anesthesia.

+ Preparing the patients: supine position, with the head fixed in three pin Mayfield head holder.

Surgical Technique: [7, 5, 13, 3, 9, 21]

* Nasal endoscopic technique to remove nasal tumor mass

- Step 1: debulking of the space - occupying of the tumor
- Step 2: ethmoidectomy and sphenoidectomy
- Step 3: sphenoidectomy (posterior limit).
- Step 4: opening frontal recess/ Lothrop technique (anterior limit).
- Step 5: superior septectomy (the tumor invaded)
- Step 6: Resect the bone of anterior skull base by using Citelli/ drill
- Step 7: Identify anterior and posterior ethmoidal artery
- Step 8: Identify the point of invasion at meningeal and periorbital sheath (cold biopsy)

* Sub Frontal Approach to Remove the Intracranial Tumor:

- Step 1: Bilateral frontotemporal skin incision.
- Step 2: Prepare Galea flap
- Step 3: Craniotomy
- Step 4: Ligation of superior sagittal sinus + resection of meningeal
- Step 5: En bloc resection of tumor, bone, and invaded meningeal (malignant tumor) - marginal cold biopsy
- Step 6: ENT surgeon and neurosurgeon remove the tumor at nasosinus cavity and at the brain at the same time
- Step 7: Reconstruction of the skull base and meningeal by using multilayer techniques (3 layers).

*Skull Base Reconstruction: [12, 13]

- Step 1: suture the temporal fascia/galeal to defective meningeal
- Step 2: Cover the pedicled galeal, suture to the horizontal part of sphenoid bone (sphenoidale planum).
- Step 3: Place the titanium plate over galeal flap and below resected meningeal.
- Step 4: closing skull base, suture skin and drainage.
- Step 5: Inside the nasal cavity: cover the dural defect by using pedicled nasoseptal flap + gelfoam

3.3.3. Step 3: Post operation:

- Medication.
- Mental status and neurologic monitoring.
- Post-operative CT-Scan within 24 hours (had defective dural)
- Packing (merocel) is removed on postoperative day 2 or 4.
- Lumbar drainage is removed 5 days after surgery.
- 7 - 10 days after surgery: mental status stable, normal neurological condition, no CSF leakage. Patient can discharge.

3.3.4. Step 4: Follow up and assessment:

- Clinical symptoms:
- Nasal endoscopy examination after discharge: 1 week, 2 weeks, 4

weeks, 8 weeks, every 3 months in the first year, every 3-6 months in the second year, every six months in third year. After 5 years, once a year.

- MRI/ CT-Scan: 3-6 months in the first year, every 6 months in the second year, once a year after 3 year

3.4 Statistical Analysis:

All data analyses were performed by IBM SPSS software, with a P value of <0.05 considered statistically significant.

4. Results:

4.1. Gender: this study consisted of 22 males (48.9%), 23 females (51.1%)

4.2. Age: average age is 48,2 ± 15

4.3. Clinical symptoms: most common symptoms include headache (78%), congestion (73%), decrease sense of smell (62%), loss sense of smell (47%), epistaxis (44%), running nose (42%), exophthalmos (33%)

4.4. Type of tumor:

	Frequency	Ratio(%)
Squamous cell carcinoma	11	24,4
Adenocarcinoma	3	6,7
Neuroendocrine tumor	3	6,7
Rhabdomyosarcoma	3	6,7
Esthesioneuroblastoma	5	11,1
Chordoma	1	2,2
Chondrosarcoma	3	6,7
Osteosarcoma	3	6,7
Olfactory groove meningioma	5	11,1
Ossifying fibroma	3	6,7
Osteoma	2	4,4
Inverted papilloma	1	2,2
Neurofibromatosis	2	4,4

4.5. Stage:

Stage of disease	Frequency	Ratio (%)
<i>Staging of esthesioneuroblastoma according to Kadish [13] (n=5)</i>		
Stage A/ B/ C	0/ 1/ 4	0/ 20%/ 80%
<i>Staging of inverted papilloma according to Krouse[14] (n=4)</i>		
- IP 1/ IP2/ IP3/ IP4	0/ 0/ 1/ 3	0/ 0/ 25%/ 75%
<i>Staging of tumor according to TNM [18] (n=27)</i>		
T2/T3/ T4a/ T4b	1/7/13/6	3,7%/25,9%/48,2%/22,2%

According to TNM, 32 patients (71.1%) were presented with malignant tumors, T3 and T4 accounted for 96.3%. Referring to the staging system of Kadish, the majority of patients with esthesioneuroblastoma (80%) were diagnosed with stage C.

4.6. Recurrence rate and mortality rate over time:

Table 3. Recurrence rate and mortality rate of benign and malignant tumor

Characteristics	0 year	1 year	2 year	3 year	4 year	5 year
Recurrence rate	0%	4,4%	18,4%	28,1%	41,4%	41,4%
Mortality rate	0%	2,2%	9,6%	18,4%	18,4%	45,6%

5. Discussion

5.1. Clinical Symptoms

Most common clinical symptoms of anterior skull base tumor are sinonasal symptoms, including headache, nasal congestion, decrease sense of smell with ratio 78%, 73%, and 62% respectively. Following are the symptoms of the eye which was compressed by tumor: bulging eye, blurred vision. Meanwhile, epistaxis (56.3%) and nasal congestion (84.4%) are commonly seen in malignant tumors rather than benign tumors with ratios of 15.4% and 46.2% respectively (p < 0.05).

5.2. Pathology of Tumor

The malignant tumors (71.1%) consist of squamous cell carcinoma (24%), esthesioneuroblastoma (11.1%), neuroendocrine tumors (6.7%). Benign tumors (28.9%) includes olfactory groove meningioma (11.1%), ossifying fibroma, osteoma (6.7%). According to Abuzayed (2011) [2], in 27 cases of anterior skull base tumor, 77.8% was malignant. Buchmann et al [8] found the majority of malignant tumors were squamous cell carcinoma (33%), esthesioneuroblastoma (23%), adenocarcinoma (15%), other types of carcinoma accounted for less. Eloy and colleagues also observed that the frequency of histopathology of squamous cell carcinoma (37.9%) was the most common, esthesioneuroblastoma and adenocarcinoma were 21.2% and 16.7% respectively. Conclusively, the tumors of anterior skull base are very diverse, both benign and malignant tumors could originate from sinonasal cavity, skull base or intracranial structures. Meanwhile, malignant tumor (71.1%) is the most common that could originate from nasal cavity or paranasal sinuses.

5.3. Staging Classification

In our study, all 27 patients were classified according to TNM of AJCC: stage II (T2, N0, M0) and stage III (T3N0M0) were 3,7%, 25,9% respectively, stage IV accounted for 70.4% (IVa: 48,2%; IVb: 22,2%). A study on 31 patients with anterior skull base by Batra [4] showed that malignant tumors (80.6%) consisted of 14 cases (56%) were T3N0M0 and T4N0M0, 11 cases (46%) were other malignant tumors, most of patients were treated at late stage of cancer. 17 cases of malignant tumor in Dave’s study [11] were classified according to the Kadish system, that consisted of 5 cases (55%) were stage A, 2 cases (22%) were stage B, and 10 cases (22%) were stage C. 7 cases were classified according to TNM (AJCC 2002), there were 2 cases (29%) with T1, 1 case with T2 (14%), 2 cases with T3 (29%), and 2 cases with T4 (29%).

The majority of patients were diagnosed with late stage cancer (esthesioneuroblastoma stage B and stage C were 20% and 80% respectively, stage III and IV accounted for 96.3%). Therefore, treatment for these patients was difficult and a combination of

techniques were needed to prolong the patient's life and improve the quality of life of the patients.

5.4. Surgical Technique

When the tumor invaded the periorbital sheath, orbital structures, anterior table or lateral recess of frontal sinus, or invades intracranially > 2cm, the traditional nasal endoscopic surgery will be limited. To ensure the complete removal of the tumor by using combined nasal endoscopic surgery and other techniques, we need to identify the limit of infiltration of tumor into the supraorbital meningeal, brain tissues preoperative and during operation [18, 19]. Paolo and colleagues [10, 9] reported that the nasal endoscopic surgery combined with frontal craniotomy is an alternative to the traditional transfacial technique. Also, this combined technique allows the resection of the anterior skull base tumor completely and efficiently.

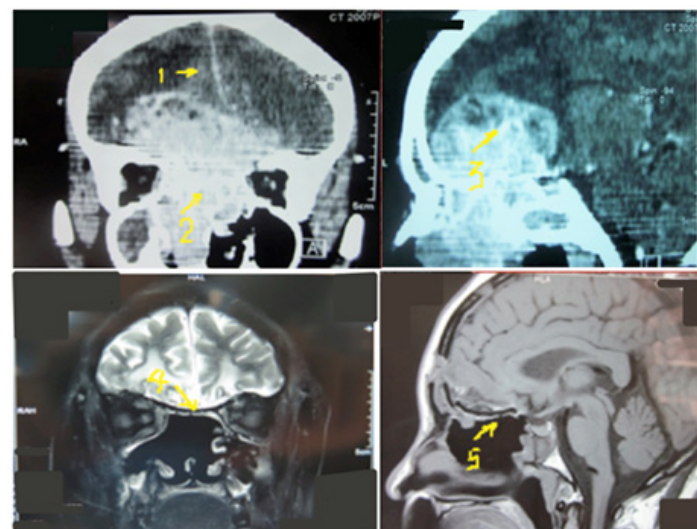


Figure 1: Esthesioneuroblastoma invades into anterior skull base, brain (1) Brain edema surrounded tumor, (2) dislocation of middle line, (3) tumor compress optic chiasma, (4) tumor is completely removed, (5) anterior skull base was reconstructed by multiple layer

In our study, most cases of tumor infiltrated the meningeal into the brain, invading laterally and over optic nerve or compressed the optic nerve and destroyed the roof of ethmoid and infiltrated into the supraorbital cerebral tissue. In these cases, the use of nasal endoscopy will be limited, surgeons will not be able to remove tumors completely and preserve the important neural blood vessel structures [18]. Therefore, it is necessary to combine with subfrontal craniotomy to remove these tumors. Our study noted the correlation between surgical techniques and the invasion or spread of the tumor into the meninges on MRI images ($p < 0.05$ which is statistically significant). In cases with the tumors invaded into the meninges or brain on MRI images that required combined technique to remove tumor, malignant tumor accounted for 40.6%, tumor invaded meningeal, brain with compressed optic nerve

(7/32) accounted for 91.7%, surrounded brain edema was 15.4% and meningeal defect > 2cm due to invasive tumor, it is necessary to have wide resection to achieve safe margin. Benign tumors were 69.2%, infiltrated through meningeal into the brain 100%, with compressed optic nerve, optic chiasm or brain edema 38.5%, defective meningeal > 2 cm.

Table 4. Brain edema, compressing surrounding structures on MRI image

Characteristics	Malignant (n=32)	Benign (n=13)	Total (n= 45)
Brain edema surrounded tumor	4 (12,5%)	1 (7,7%)	5 (11,1%)
Compress optic nerve, optic chiasm	17 (53,1%)	4 (30,8%)	21 (46,7%)
Compress ICA	3 (9,4%)	1 (7,7%)	4 (8,9%)

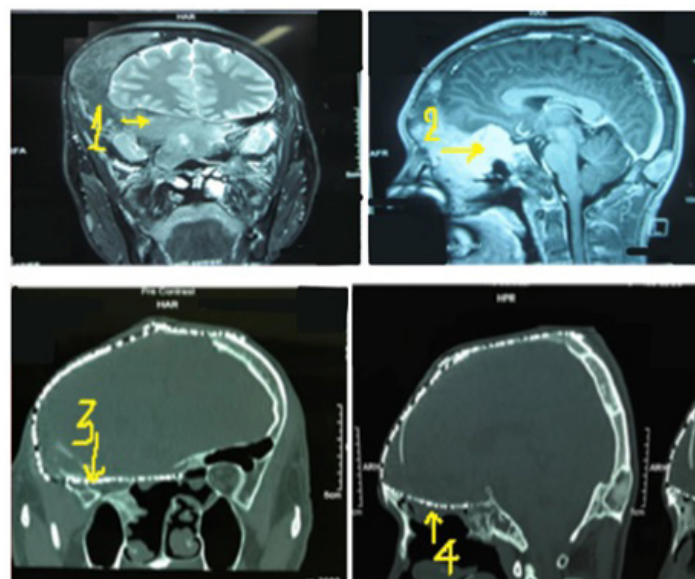


Figure 2: (1) ossifying fibroma invades skull base, sphenoid bone and compress right optic nerve, (2) tumor invade total anterior skull base bone and partial of temporal bone, (3) tumor is completely removed, (4) skull base defect was reconstructed by multiple layer (titanium mesh and 2 pedicle flaps)

5.5. Recurrent Rate and Overall Survival Over Time

In our study, patients' deaths related to malignant tumors and correlated with recurrence after surgery ($p < 0.05$). Meanwhile, recurrence cases comprised of squamous cell carcinoma (25%), and neuroendocrine tumor, esthesioneuroblastoma, chondrosarcoma (16.7%).

Table 3.4. Recurrence rate and mortality of benign and malignant tumors

	Malignant (n=32)	Benign (n=13)	p value (long -rank)
Death/ mortality	8 (25%)	0 (0%)	0,069
Recurrence rate	12 (37,5%)	0 (0%)	0,025

Our study reported 45 cases of nasal tumor invaded anterior skull base and brain, in which, 32 cases were malignant and 13 cases were benign. All 12 recurrence cases were malignant. After 5 years, there were 8 deaths, in which 6 cases were due to

recurrence, 2 cases were not due to recurrence. Recurrence rate and mortality rate after 5 years were 41.4% and 45.6 respectively, commonly seen in stage T4a, T4b. Conclusively, all recurrence and death cases were malignant or were treated at a late stage. There was correlation between mortality and recurrence rate ($p < 0.05$). Batra's study showed the overall survival after 5 years was 51.7% for stage T4 tumors.

In previous decades, most tumors seen invading into the brain from the nasal cavity required two operations. One from a neurosurgeon, performing a craniotomy to remove the part of tumors inside the brain space and followed by the guidance of an ENT surgeon to remove the part of tumor inside nasal cavity. Division of the operation was to avoid disruption between the nasal cavity and the brain space to decrease meningitis rate. However, this approach causes a delay in subsequent supportive treatment such as radiation therapy in cases where tumors are malignant and reoccurrence is likely.

6. Conclusion

Over 45 cases of nasal tumors invaded anterior skull base and into the brain that were treated by using nasal endoscopic surgery combined with subfrontal approach to resect the tumor. By conducting this study, we have gained more experience in approaching skull base surgery to treat patients with late stage tumors while decreasing mortality. This approach presents another method to treat patients with sinonasal tumors invading anterior skull base efficiently.

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