



Endonasal endoscopic surgery for giant pituitary neuroendocrine tumor with multimodal support to avoid complications – Clinical management and outcomes

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Introduction:

- The treatment of giant pituitary neuroendocrine tumors (GPitNETs) is challenging.
- It is obviously very difficult to remove all tumors with complicated shapes involving vascular structure and cranial nerves without any damage.
- We present clinical management and outcomes of patients with GPitNETs resected mainly by endoscopic endonasal surgery (EES) using multimodal supports with neuro-navigation, and neuro-monitoring to avoid surgical complications.

Material and Methods:

- Methods: Retrospectively Study
- Objects: patients with PitNETs treated with endoscopic endonasal surgery and/or transcranial surgery at Nara Medical University
- Duration: from November 2008 to October 2021.
- Evaluation: postoperative visual tests (visual acuity and visual fields), endocrinological studies, and clinical examinations, the tumor size, shape, extension, complications

Result:

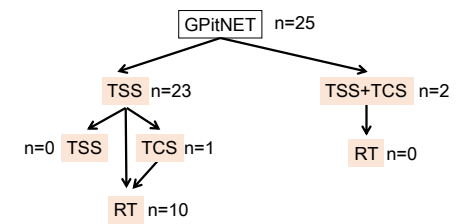
Patient and tumor characteristics

No. of patients	25	Previous surgery, no. (%)	
Age, years	58.12±11.27	Primary	18 (72)
Gender, no. (%)		Recurrent	7 (28)
Female	16 (64)	Extension, no. (%)	
Male	9 (36)	Anterior fossa	5 (20)
Tumor volume, cm ³	44.85 (40-63.2)	Middle fossa	14 (56)
Shape, no. (%)		Posterior fossa	0 (0)
Round	4 (16)	Sphenoid sinus	15 (60)
Dumbbell	4 (16)	Suprasellar region	24 (96)
Multilobular	17 (68)	Intraop tumor consistency, no. (%)	
Knosp, no. (%)		Soft	13 (52)
1	0 (0)	Firm or fibrotic components	12 (48)
2	0 (0)	Ki-67	
3	10 (40)	<1%	14 (56)
4	15 (60)	1-3%	8 (32)
Hormone secretion, no. (%)		>3%	2 (8)
Non functional	23(92)		
Functional	2(8)		
(PRLoma)	1(4)		
(Cushing disease)	1(4)		

Clinical presentation

Clinical presentation	No. of patients (%)
Headache	24 (96.0)
Visual impairment	22 (88.0)
Pituitary insufficiency	10 (40.0)
Apoplexy	3 (12.0)
CN palsy	2 (8.0)
Hydrocephalus	0 (0)
Altered mental status	0 (0)
DI	0 (0)

Selection of approach and adjuvant therapy



Extent of resection

Extent of resection	No. of patients (%)
GTR	6 (24)
NTR (>90%)	9 (36)
PR	10 (40)

Factors with influence on achieving GTR

Variable	GTR	Non-GTR	Univariate OR (95% CI), P-value	Multivariate OR (95% IC), P-value
Shape				
Round	2	2	1.000 (ref)	-
Dumbbell	2	2	1.000 (0.063, 15.988), 0.999	-
Multilobular	2	15	0.133 (0.011, 1.550), 0.107	-
Knosp				
Grade 3	6	4	1.000 (ref)	-
Grade 4	0	15	0.022 (0.001, 0.477), 0.015	-
Extension				
Anterior fossa	2	3	2.667 (0.327, 21.733), 0.360	-
Middle fossa	1	13	0.082 (0.009, 0.973), 0.047	0.092 (0.009, 0.973), 0.047
Sphenoid sinus	2	13	0.231 (0.033, 1.628), 0.141	-
Suprasellar region	18	6	1.054 (0.038, 29.246), 0.975	-
Firm tumor	1	11	0.145 (0.014, 1.498), 0.105	-

Discussion:

- The goal of surgery for GPitNETs is decompression to optic apparatus to get visual improvement, recovery from endocrinological and neurological symptoms, and maximal safe resection.
- To achieve this goal, **multimodal supports were applied to prevent patients with GPitNETs from complication.**
- Cavernous sinus invasion is one of the main limitations that precludes complete tumor resection.
- In our series, univariate analysis revealed **cavernous sinus invasion (Knosp 4)** and **tumors extending to middle fossa** had disturbing factors to achieve GTR ($p = 0.015, 0.047$ respectively), and **multivariate analyses** revealed that **tumors invading into the middle fossa negatively affected the extent of resection**
- With regard to complication, its rate was reported about 10-20% owing to large size, invasiveness, and irregular extension.
- There are several life-threatening complications, such as carotid injury, stroke, post operative pituitary apoplexy, or meningitis.
- To avoid these critical complications, the operators should make deep concentration on dissecting tumor from neurovascular structure, and use the multimodal supports with navigation, monitoring, and doppler to keep safe maneuver. To keep perforators safe, tumors involving vessels may be sometimes intentionally left to avoid injury or vasospasm.

Conclusion:

- Although endonasal endoscopic surgery with multimodal support was safe, and efficient for managing GPitNETs, complications would be severe if apoplexy occurred.
- Therefore, it should be avoided as much as possible to prevent patients with GPitNETs from apoplexy.
- It is important to keep maximal safe resections to achieve decompression for optic apparatus.

Clinical outcomes

Clinical outcomes	No. of patients (%)
Outcome in patients with visual impairment before surgery	
Improved	13 (59)
Stable	8 (36)
Worse	1 (4.5)
Outcome in patients with normal vision before surgery	
Stable	3 (100)
Worse	0 (0)
Oculomotor palsy	
Permanent	1 (4)
Transient	1 (4)
Postoperative bleeding (eTSS)	
	1 (4)
New hypopituitarism	
Permanent DI	7 (28)
Delayed CSF leakage	6 (24)
	1 (4)

Multimodal fusion image

planning

Neuronavigation

anatomical orientation

Doppler

detect the location of the carotid artery

Neuromonitoring

monitor and keep neurofunction

Multimodal support is very useful for the treatment of GPitNETs

Koutourousiou M et al. *J Neurosurg.* 2013;118:621-631.
 de Paiva Neto MA et al. *Clin Endocrinol (Oxf).* 2010;72:512-519.
 Kuo CH et al. *World Neurosurg.* 2016;91:121-128.