



Inherent Tumor Characteristics That Limit Effective and Safe Resection of Giant Nonfunctioning Pituitary Adenomas

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BACKGROUND: Surgical treatment of giant pituitary adenomas is sometimes challenging. We present our surgical series of giant nonfunctioning adenomas to shed light on the limitations of effective and safe tumor resection.

METHODS: The preoperative tumor characteristics, surgical approaches, outcome, and histology of giant nonfunctioning adenoma (>40 mm) in 128 consecutive surgical patients are reviewed. The follow-up period ranged from 19 to 113 months (mean 62.2 months).

RESULTS: A transsphenoidal approach was used in the treatment of 109 patients and a combined transsphenoidal transcranial approach in 19 patients. A total of 93 patients (72.7%) underwent total resection or subtotal resection apart from the cavernous sinus (CS). The degree of tumor resection, excluding the marked CS invasion, was lower in tumors that were larger ($P = 0.0107$), showed massive intracranial extension ($P = 0.0352$), and had an irregular configuration ($P = 0.0016$). Permanent surgical complications developed in 28 patients (22.0%). Long-term tumor control was achieved in all patients by single surgery, including 43 patients with adjuvant radiotherapy. Most tumors were histologically benign, with a low MIB-1 index (<3.0%) beside a few tumors mainly silent adenomas of pituitary-specific transcription factor lineage.

CONCLUSIONS: Irrespective of the surgical approach, massive intracranial extension, an irregular configuration, and marked CS invasion are inherent factors that

independently limit effective resection. These high-risk tumors require an individualized therapeutic strategy.

INTRODUCTION

Transsphenoidal surgery (TSS) has been the gold standard operative approach for nonfunctioning pituitary adenomas for decades. With the recent evolution of surgical techniques and instruments, including the endoscope, complete and safe resection is possible for many adenomas, and the ability to resect complex adenoma is evolving dramatically. However, several inherent tumor characteristics still limit effective and safe resection.¹⁻⁵ Giant adenomas, usually defined as those with a maximum diameter >40 mm, may occasionally remain a therapeutic challenge because of their size, invasiveness, and irregular extrasellar extensions. Radical removal of giant adenomas has been achieved in fewer than one half of the cases described in the literature.^{2,6-9} Complex adenomas are not only difficult to resect but also have a greater risk of complications. Currently most pituitary surgeons favor endoscopic TSS in the surgical management of giant adenomas, although some tumors require an individualized surgical approach.^{6,8,10} Most giant adenomas are slow-growing and histologically benign tumors despite giant in size and troublesome to manage.¹¹⁻¹⁴ Here, we review the surgical outcome and histology of a large consecutive series of giant nonfunctioning adenomas to elucidate the factors that limit effective and safe resection. We also discuss current therapeutic strategies.

Key words

- Combined approach
- Giant
- Intracranial extension index
- Nonfunctioning
- Pituitary adenoma
- Transsphenoidal surgery

Abbreviations and Acronyms

- ACTH:** Adrenocorticotrophic hormone
CS: Cavernous sinus
GH: Growth hormone
MRI: Magnetic resonance imaging
Pit-1: Pituitary-specific transcription factor 1

TS: Transsphenoidal

TSS: Transsphenoidal surgery

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Citation: *World Neurosurg.* (2017) 106:645-652.
<http://dx.doi.org/10.1016/j.wneu.2017.07.043>

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

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METHODS

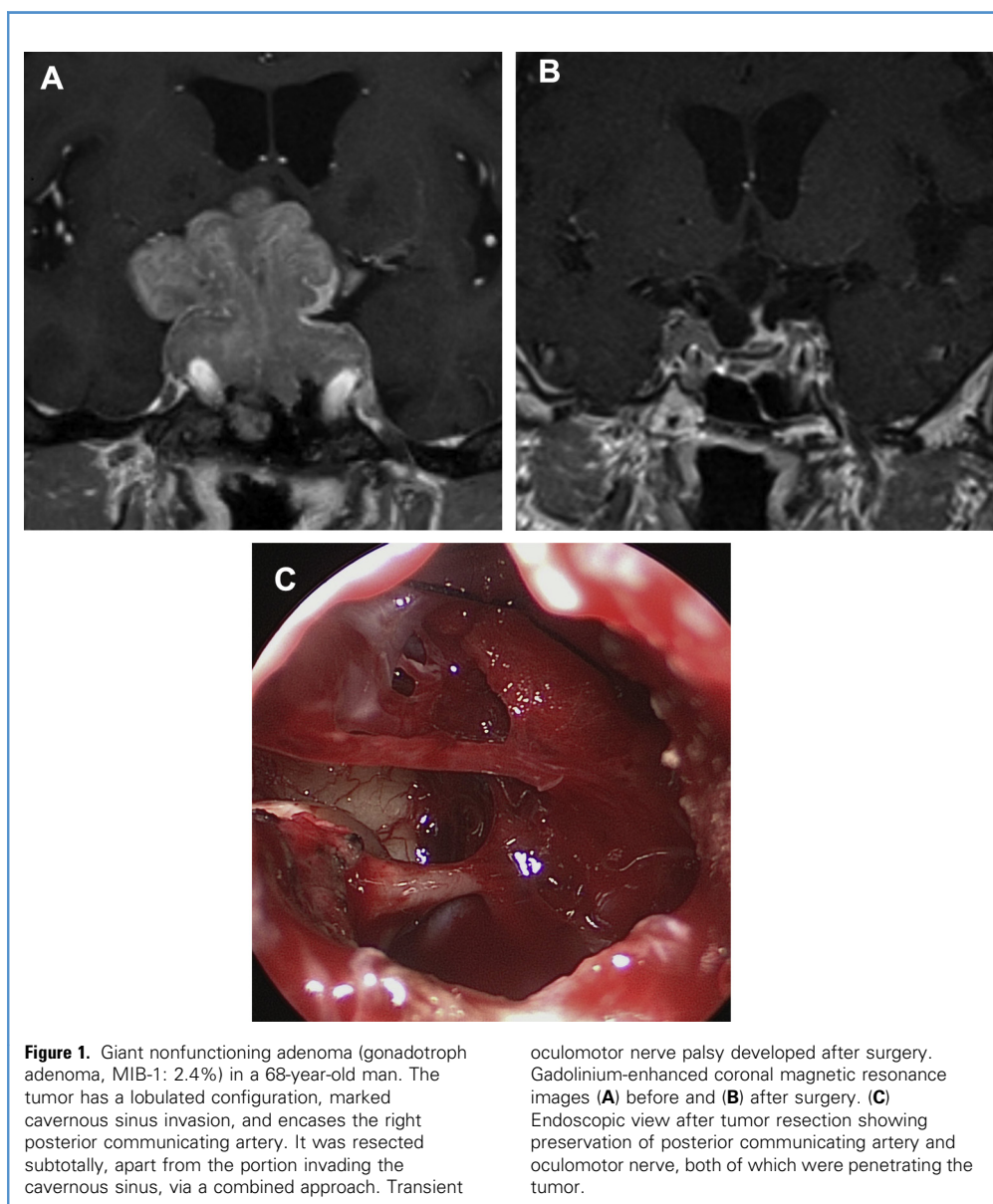
Patients

The cases of 128 consecutive patients with giant nonfunctioning adenoma, defined as tumors measuring ≥ 40 mm in their maximum diameter, surgically treated between 2008 and 2015 are reviewed herein. They made up 12.8% of the 1001 cases of surgical nonfunctioning adenoma managed during this period at our institute. The 71 men and 57 women ranged in age from 27 to 81 years (mean 48.1 years). Surgery was performed for the first time in 91 patients, whereas 37 patients (28.9%) had previously undergone surgical treatment of the tumor, either transsphenoidal (TS; 23 patients), transcranial (10 patients), or both (4 patients), at other hospitals (35 patients) or at our hospital (2 patients).

Samples were collected with informed consent of all individual participants included in the study in accordance with the requirement of the Clinical Research Ethics Committee of Toranomon Hospital.

Magnetic Resonance Imaging (MRI) Investigation

The following parameters were assessed on preoperative MRI: the maximum tumor diameters, the intracranial extension index (defined as the approximate ratio of intracranial to total tumor volume measured by sagittal and coronal images), marked cavernous sinus (CS) invasion (defined as Knosp grade 4 invasion¹⁵), irregular configuration (defined as significant lobulation(s) of the suprasellar portion), and complete encasement of the subarachnoid arteries (**Figure 1A and C**).



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