Time to Revive the Value of the Pseudocapsule in Endoscopic Endonasal Transsphenoidal Surgery for Growth Hormone Adenomas

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■ OBJECTIVE: **To investigate the role of endoscopic endonasal transsphenoidal surgery and the pseudocapsule in the treatment of growth hormone adenomas.**

■ METHODS: **The study included 43 patients (age range, 21–64 years) with growth hormone adenomas treated with an endoscopic endonasal approach. We compared the tumor characteristics and surgical outcomes of cases with (group A, 21 cases, from November 2013 to January 2015) and without (group B, 22 cases, from October 2011 to October 2013) extra-pseudocapsule resection.**

■ RESULTS: **The preoperative demographics, tumor characteristics, and surgical complications were not significantly different between groups A and B. Postoperative remission without adjuvant therapy was achieved in 18 of 21 cases (85.7%) in group A, which was significantly greater than that observed in group B (12 of 22 cases [54.4%]). In group A, the pseudocapsules were verified by endoscopy and histopathology. The pseudocapsule was removed en bloc with the whole adenoma in only 5 cases (23.8%). For the remaining 16 patients (76.2%), following extra-pseudocapsule dissection, incomplete pseudocapsule removals with intracapsule procedures were achieved.**

■ CONCLUSIONS: **The combination of extra-pseudocapsule resection and endoscopy led to a high rate of gross total tumor resection and endocrinologicl remission in acromegalic patients compared with the group with intracapsular resection. Extra-pseudocapsule resection resulted in no additional postoperative complications.**

INTRODUCTION

Although the presence of histologic pseudocapsules around pituitary adenomas was noted in 1936,[1] most pituitary surgeons do not pay sufficient attention to this small and delicate structure, possibly because the histologic origin and characteristics of the pseudocapsule have not been clarified. Different definitions have been applied to this fibrous capsule in the literature.[2] Another reason for the neglect of this structure is that previously used techniques lacked sufficiently clear and bright views of this peritumoral structure. However, many authors have insisted on this promising pseudocapsule. In particular, Oldfield described the histology of the pseudocapsule quite elegantly and advocated using this pseudocapsule as a surgical capsule for pituitary adenoma.[3] Refinements in endoscopic image quality and dedicated instrumentation greatly facilitate endoscopic pituitary surgery.[4] Regarding cures for acromegaly, which are heavily dependent on pituitary surgery, any attempt to improve the remission rate is worth a try. In the present study, we introduce endoscopic extra-pseudocapsule resection and compare the remission rates and complications of acromegaly between subjects with and without extra-pseudocapsule resection.

Key words
- Acromegaly
- Endoscopic pituitary surgery
- Pituitary adenoma
- Pseudocapsule

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
GH: Growth hormone
IGF-I: Insulin-like growth factor I
MRI: Magnetic resonance imaging

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MATERIALS AND METHODS

The data collection for this study was approved by the institutional review board of the Zhongshan Hospital, Fudan University. We performed a retrospective analysis of all patients with growth hormone (GH)—secreting pituitary adenomas who were treated via the endoscopic endonasal approach at the Zhongshan Hospital from October 2011 to January 2015. The inclusion criteria were as follows: clinical diagnosis compatible with acromegaly (i.e., GH >1 mU/L and an insulin-like growth factor I (IGF-I) level greater than the normal age-adjusted and sex-adjusted level), the presence of a GH-secreting pituitary adenoma, and a tumor positive for the GH marker on histologic examination. Among the identified patients, the data for 43 patients were sufficient for the analysis. Since November 2013, we have performed extra-pseudocapsular resections as described subsequently for 21 GH adenomas (group A). The patients treated before this time period (from October 2011 to October 2013) were categorized into group B.

All patients underwent neurologic, endocrinologic, ophthalmologic, blood sugar, and heart function evaluations before and after surgery. The maximal tumor diameter was measured on preoperative imaging studies and taken as the largest measurement in the coronal, axial, or sagittal plane. The tumors were categorized as microadenomas (<10 mm) or macroadenomas (>10 mm) and based on evidence of suprasellar/parasellar extension according to the Hardy-Wilson classification based on coronal T1-weighted contrast magnetic resonance imaging (MRI). Remission was defined as a normal IGF-I level and either a reduction of GH to <0.4 ng/mL during an oral glucose tolerance test or a random GH <1.0 ng/mL.[5] A tumor was considered to be totally removed when the surgeon's observation and the MRI examination documented no residual tumor. Resection was considered subtotal when part of the tumor remained in situ. Follow-up MRI and endocrinologic studies were performed 3 months after surgery and every 6 months thereafter.

The data were analyzed using 9.3.1 SAS software (SAS Institute, Inc., Cary, North Carolina, USA) and are presented as mean ± SD for continuous variables. Non—normally distributed data are presented as the median (quartile 1—quartile 3). The categorical data are presented as the numbers of subjects (*n*) and percentages (%). The statistical analyses of the categorical variables were performed using χ^2 tests and Fisher exact tests as appropriate. The statistics for the means were performed with unpaired Student *t* tests, but the IGF-I and GH data were log normally distributed; therefore, we examined the longitudinal changes in the log (GH), log (IGF-I), and log (oral glucose tolerance test) by group using linear mixed-effects models that included fixed effects for groups and random effects for the intercept and slope for time. A *P* value < 0.05 was considered statistically significant.

A standard binostril endoscopic transsphenoidal approach was routinely used. Wide exposure of the entire sella was necessary. In cases in which the cavernous sinus was involved, a more lateral exposure was achieved by carefully and completely exposing the anterior wall of the cavernous sinus. In the early stages, angled curettes and suction were used to resect the adenomas region by region after the membranes of the floor of the sella were incised. After November 2013, the concept of extra-pseudocapsule dissection throughout the process of resection was implemented. Following the exposure of the sellar dura mater, a No. 15 scalpel was used to incise the dura mater, while leaving the underlying pituitary capsule intact (Figure 1). In the key step, blunt microdissection was patiently applied to develop a plane around the pseudocapsule after cutting the pituitary capsule (macroadenomas) or the pituitary capsule and pituitary adenohypophysis (microadenomas) (Figure 2). When the adenoma was too large for integral enucleation, internal debulking was typically required. When the pseudocapsule was too soft for integral enucleation, piecemeal resection after extra-pseudocapsule dissection was also typically employed. When the GH adenoma invaded nearby structures, such as the cavernous sinus, upper clivus, sellar floor dura, and bone, the pseudocapsule was no longer present. In these cases, more extensive surgical resection was applied. The closures were performed in a multilayer fashion.

RESULTS

Patients and Tumor Characteristics

Of the 43 patients, 21 (48.8%) were men. The mean age of patients was 48.52 years (range, 21—64 years). The most common presenting symptom, with the exception of acromegaly, was headache (46.5%). There were 39 patients with macroadenomas and 4 with microadenomas with a mean size of 19.675 mm (range, 7—54 mm). The Hardy-Wilson classification was used to indicate the degrees of suprasellar and parasellar extension and sellar floor erosion. Regarding suprasellar and parasellar extension, 23 patients (53.5%) were stages A and B, and 20 (46.5%) were stages C—E. Regarding sellar floor destruction, 34 patients (79.1%) were grades I and II, and 9 (20.9%) were grades III and IV. Only 5 patients (11.6%) had undergone prior Gamma Knife or transsphenoidal approach procedures. The mean preoperative random GH value was 25.9 ng/mL (range, 11.7—40 ng/mL), and the mean preoperative IGF-I level was 896 ng/mL (range, 746—1129 ng/mL). The preoperative demographics and tumor characteristics were not significantly different between groups A and B (Table 1).

Surgical Outcomes and Remission

Radiographically, 30 patients (69.8%) achieved gross total resection, 12 patients (27.9%) achieved subtotal resection, and 1 (2.3%) patient achieved partial resection. The patients who underwent extra-pseudocapsule resection exhibited a higher resection rate than the patients who underwent intracapsule resection (85.7% vs. 54.5%, $P < 0.05$). Regarding the 3-month to 1-year follow-up examinations, we analyzed the biochemical remission rates according to surgery only. Similarly, the patients who underwent extra-pseudocapsule resection exhibited a significantly higher remission rate than patients who underwent intracapsule resection ($P = 0.028$, $P < 0.05$) (Table 2). In group A, 1 patient with a subtotal resection who did not exhibit biochemical remission was treated with Gamma Knife radiosurgery. In group B, 2 patients were treated with Gamma Knife radiosurgery, 1 patient was treated with repeat surgery, and 2 patients were treated with medical therapy (somatostatin). However, 3 of these patients exhibited poor control of the excess GH.

Complications

Although the technology for the reconstruction of the skull base has developed substantially, cerebrospinal fluid (CSF) rhinorrhea