Pituitary Tumor Surgery: Review of 3004 Cases

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Key words
- Cushing disease
- Endoscopy
- Growth hormone–secreting pituitary adenoma
- Nelson syndrome
- Pituitary neoplasm
- Prolactinoma
- Retrospective studies
- Transsphenoidal surgery

Abbreviations and Acronyms
ACTH: Adrenocorticotropic hormone
GH: Growth hormone

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OBJECTIVE: **To report the efficacy, safety, and outcomes through time of the biggest series to our knowledge of pituitary surgery using transcranial, transsphenoidal, and endoscopic techniques.**

METHODS: **An observational, retrospective, and descriptive review was performed of 3004 patients surgically treated by the senior author from 1973 to June 2011 in Mexico City. A sublabial approach was used in 3000 patients, and a transnasal approach was used in the remaining 4 patients. Tumors were classified according to size as microadenomas or macroadenomas.**

RESULTS: **During the time period of this study, 3004 patients were surgically treated; there were 510 prolactinomas, 822 growth hormone adenomas, 62 adrenocorticotropic hormone–producing adenomas, 8 tumors that produced Nelson syndrome, and 1562 adenomas that were not biologically active. The cure rate of prolactinoma was 82% for microadenomas and 9% for macroadenomas. Gender distribution showed a male predominance of 57.1%. Cure rate for growth hormone adenomas was 87%. Adrenocorticotropic hormone adenomas showed no cure rate; surgery simply aided pharmacologic control. Global mortality rate was 1.6%. The main complications were cerebrospinal fluid fistula, diabetes insipidus, and meningitis.**

CONCLUSIONS: **The sum of this 38-year experience of managing pituitary pathology and its surgical treatment shows the importance of working together with other specialists such as endocrinologists, ophthalmologists, and radiologists. The correct treatment approach for each case must be individually selected. Transsphenoidal surgery is an effective and safe treatment for most patients with pituitary adenoma and could be considered the first-choice therapy in all cases except for prolactinomas that respond to pharmacologic therapy (dopamine agonist).**

INTRODUCTION

Pituitary adenomas represent nearly 15% of intracranial neoplasms, making them the third most common intracranial tumor after meningiomas and gliomas. The first surgical treatment for this pathology was performed in 1887 by Horsley; since then, different approaches have been described. We present a review of all cases of transsphenoidal pituitary surgery performed by the senior author (M.L.-V.) over 38 years, including hypophysectomy for breast cancer, prostate cancer, and proliferative neuropathy. We analyze the results of the experience of the senior author and his collaborators in the treatment of various pituitary tumors, including results of both medical and surgical treatment and the use of radiosurgery and radiotherapy.

BACKGROUND AND HISTORY

In 1887, Horsley performed the first pituitary surgery when he operated on a pituitary adenoma through a subtemporal craniotomy (15). In 1906, Schloffer and Von Eiselberg described the transsphenoidal approach (11); in 1910, Kanavel and Hirsh initiated the first series of transsphenoidal approaches (8). From 1910–1928, Cushing, the father of modern American neurosurgery, performed 64% of operations on microadenomas by this approach; morbidity and mortality were high compared with the transcranial approach because of technologic limitations (21). McOmish Dott and Guiot continued with this technique and together with Hardy introduced the image intensifier in 1961, assisted by the surgical microscope and the developing design of microsurgery-specific tools for this approach (7, 17, 18). The contribution of tumor classification by Hardy and Vezina is still a cornerstone in the patient approach (6, 17, 18). Hardy's description of secretory microadenomas and in some cases plurihormonal tumors, with and without response to medical treatment, was another great breakthrough (6). Several neurosurgeons, including Wilson, Laws, Landolt, Falbush, Basso, and Marino (1, 4, 9, 10), published their series, formally initiating the era of transsphenoidal surgery for pituitary tumors. Various transsphenoidal approaches have been described. Griffit, Veerapen, Jankowski, Sethi, Pillay, Jho, and Carrau initiated transnasal endoscopic surgery for pituitary tumors a decade ago, in some cases using a neuronavigation system (3, 14, 16, 19, 20). The beginning of the twenty-first century witnessed major ad-

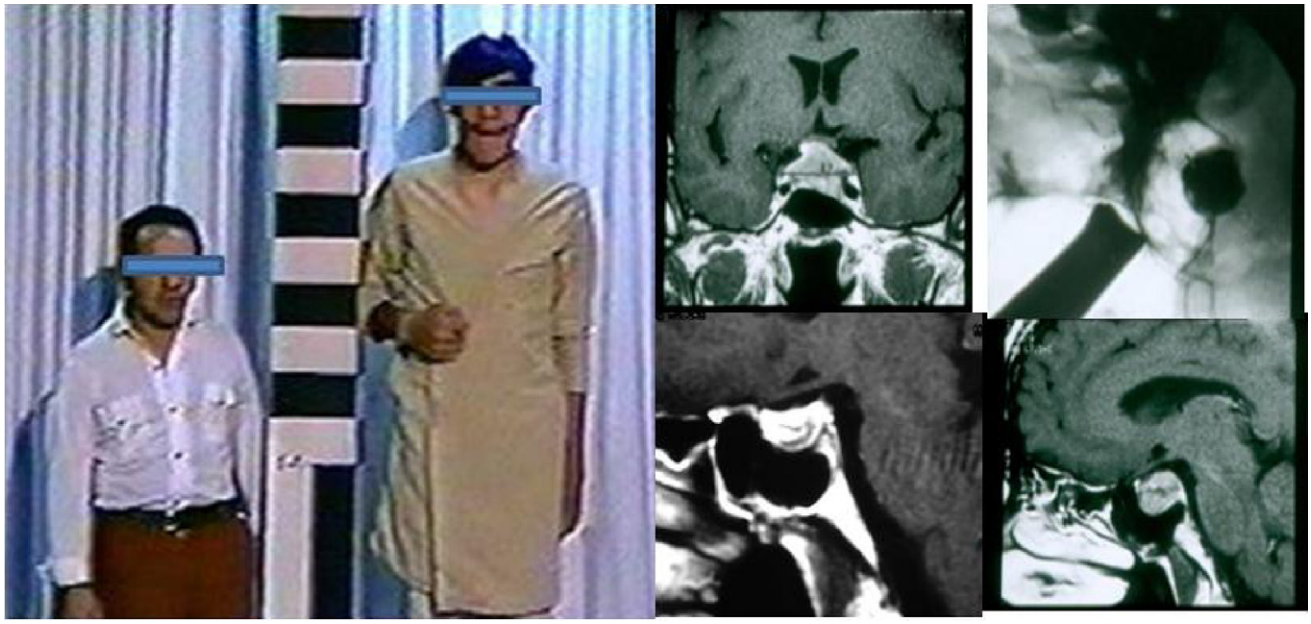

Figure 1. Functional pituitary adenoma producing acromegaly and gigantism with disease control after the surgical treatment. Preoperative sagittal and coronal magnetic resonance imaging (MRI) show a large tumor with important mass effect of the recess of the third ventricle. The postoperative MRI demonstrates gross total resection. Note the malleable instruments improving resection in angle areas, such as, the capsule dome.

vances in this field by Cappabianca, Kassa, Frank, Gentile, and Alancastro, all of whom demonstrated the convenience and safety of the procedure (2).

PERSONAL SERIES

The senior author performed his first sublabial transsphenoidal approach in a growth hormone (GH)–producing tumor in 1973; the last case of the present series was an endoscopic transnasal microscopic approach in a GH-producing tumor, performed in 2011. The major and most significate limitation of this study is lack of follow-up data because most of the files were lost in the earthquake that hit Mexico City in 1985. The introduction of malleable instruments, designed by the senior author in 1982, facilitated resection of the lateral portions or near the cavernous sinus (13). In 1984, he published the article entitled "Combined Supra-infrasellar Approach for Large Pituitary Tumors" (12). In 1986, he published "The Transnasal Approach to the Cavernous Sinus" (5).

Of the 3004 transsphenoidal approaches to pituitary tumors in the present series, the sublabial approach was used in 3000; a total of 510 prolactin-producing tumors, 822 GH-producing tumors, 62 adrenocorticotropic hormone (ACTH)–producing tumors, 8 tumors that produced Nelson syndrome, and 1562 inactive tumors were treated. During the early years of the series, 16 total hypophysectomies cases were conducted for treatment of breast cancer (female patients), 12 cases were performed for prostate cancer treatment, and 8 were performed for proliferative retinopathy; all of these cases were counted as microadenomas for statistical purposes. The final 4 cases of 3004 cases were total hypophysectomies in which the endoscopic transnasal approach was used.

Prolactin-Producing Tumors

A total of 510 prolactinomas cases were treated. Nighty-seven were H&V grade I-A, 73 grade II-A, 183 grade II-B, and 47 grade III-A microadenomas. Macroadenomas accounted for 110 cases: 72 grade III-IV-B, 35 grade III-IV-C, 2 grade III-IV-D, and 1 grade IV-E, resulting in 82% with cured criteria microadenomas and 9% cured macroadenomas.

The results of our series are similar to other international series. Upon close observation of the 510 prolactinomas, we found that some of the flaws in the surgical procedures were due to the fact that sometimes some tumors were plurihormonal. It has been shown that the best results in prolactinomas are obtained with treatment with a dopamine antagonist, like cabergoline, mainly in the normalization of prolactin, the regulation of menstruation, and more feasibility of pregnancy, and we now use the surgical procedure only when there is intolerance to drug treatment or no treatment response.

GH-Producing Tumors

A total of 822 GH-producing tumors were treated; 450 were microadenomas. Twenty-one cases were H&V grade I-A, 273 cases grade II-A, 109 grade II-B, and 47 grade III-A. The rest of this cohort comprised 191 cases with grade IV-B, 180 cases grade IV-C, and 1 case grade IV-D. Clinically, acromegaly was found in 818 cases and 4 gigantism cases; all were surgically treated with good results.

In our experience, we have used different medical treatments in these tumors. Initially, we used somatostatin analogues without obtaining acceptable results. With the advent of cabergoline and lanreotide (Somatuline), we have alternated the regimen with fair results. In some grade III–IV tumors, we began treatment with Somatuline for 2 months and achieved reduction of GH in 50% in some tu-