Historical movements in transsphenoidal surgery

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Over the past century pituitary surgery has undergone multiple revolutions in surgical technique and technological advancements that have resulted in what is now recognized as modern transsphenoidal surgery. Although the procedure is well established in the current neurosurgical literature, the historical maze that led to its development continues to be of interest because it allows us to appreciate better the unique contributions made by the pioneers of the technique as well as the innovative spirit that continues to fuel neurosurgery. The early events in the history of transsphenoidal surgery have already been well documented. Therefore, the authors summarize the major early transitions along the timeline and then further describe more recent advancements in transsphenoidal surgery such as the surgical microscope, fluoroscopy, endoscopy, intraoperative neuroimaging, frameless image guidance, and radioimmunoassay. The story of these innovations is unique because each was developed as a response to certain needs of the surgeon. An understanding of these more recent contributions coupled with the early history provides a more complete perspective on modern transsphenoidal surgery.

KEY WORDS • pituitary • transsphenoidal surgery • hypophysectomy • neurosurgical history

The evolution of transsphenoidal surgery is a complex tale of innovative leaps in ideology coupled with periods of extensive surgical experimentation and even complete rejection of the technique. The historical movements that resulted in its adoption as the preferred approach to tumors of the hypophysis have already been well documented. Within this history, however, there exist some significant revolutions in technique and technology that have further advanced the utility of this operation and merit further study. The first of these revolutions, regarding surgical technique, was initiated with the introduction of sublabial and transnasal approaches to the pituitary gland. With the introduction of intraoperative image intensification by Guiot, et al.,¹¹ in 1958 and the surgical microscope by Hardy¹⁴ in 1967, many of the technical difficulties that had been faced by pioneers such as Harvey Cushing could then be circumvented. These modalities laid the foundation for the advances that now shape modern transsphenoidal surgery, including the use of endoscopy, intraoperative imaging, frameless guidance, and radioimmunoassay.

EVOLUTION OF TRANSPHENOIDAL TECHNIQUES

The movements that have influenced the last 50 years in pituitary surgery were set into motion almost a century earlier by the 1886 report of Marie²⁶ in which he introduced the term *acromegaly*. In this landmark paper the author described two new patients and reviewed five previously published reports of patients in whom similar findings were demonstrated. Marie's publication ushered in a period in which there was renewed interest in pituitary function; likewise, it led to intense debate between those advocating transsphenoidal and those advocating transcranial

approaches to the pituitary gland in the early part of the next century. Although he did not report his findings until 1906, Horsley¹⁹ performed the first transcranial pituitary operation in 1889 but his success was limited because of what was later determined to be forceful retraction of the frontal lobe. Subsequently, surgeons such as Kiliani,²⁴ Frazier,⁸ and Cushing⁶ improved on the technique and outcomes. In 1893 Canton and Paul¹ performed a pituitary resection via a temporal approach, which was suggested to them by Horsley, and they are often cited as having been the first to utilize the transcranial approach. The first attempt at transsphenoidal surgery was undertaken soon thereafter in 1907 by Schloffer³² in Innsbruck. He performed a lateral rhinotomy, turning the entire nose toward the right side, and removed the nasal septum, turbinates, medial wall of the orbit, and maxillary sinus. Postoperatively, the patient suffered from a brief period of cerebrospinal fluid rhinorrhea and died 2 months later of acute intracranial hypertension. An autopsy examination revealed that a majority of the tumor remained, occluding the foramen of Monro. Neither preoperative neurological examination nor skull radiographs demonstrated the true magnitude of the lesion, and unfortunately it would not be until 1919 when Dandy introduced pneumoencephalography, that imaging modalities became capable of the level of accuracy that Schloffer required.

Between 1907 and 1912 many general, ENT, and neurosurgeons attempted to develop innovative approaches to the pituitary gland from below while trying to minimize the incidence of meningitis and maximize the preservation of vision. General surgeons in Europe were among the first to approach the pituitary gland transnasally. Because of their inexperience with illumination and depth of field in such a restricted surgical space, however, they created unnecessarily large external nasal openings. This approach was soon replaced in favor of those involving less invasive procedures. One of the first steps toward reduc-

Abbreviations used in this paper: CT = computerized tomography; ENT = ear, nose, throat; MR = magnetic resonance.

ing invasiveness was taken in 1912 by Chiari⁴ who performed a superior transthemoidal approach via the medial aspect of the orbit. This route provided a much shallower surgical cavity; however, because of the risk of damage to the anterior ethmoidal artery and the carotid siphon, this approach was abandoned except by a few ENT surgeons of the time.

In 1909 and 1910 multiple variations of inferior transnasal exposures of the pituitary gland were simultaneously being developed in America and Europe. Kanavel²³ and Halstead¹³ first introduced an infranasal approach and subsequently a gingival approach that was quickly adopted by Cushing⁵ in Baltimore. Cushing performed his first pituitary operation in 1909 and over the next 30 years, in an era before the development of steroidal agents and antibiotic medications, was able to sustain a remarkable mortality rate of 5.6%.¹⁷ Contemporaneously, Hirsch,¹⁸ a Viennese ENT surgeon, introduced the technique that is still in use today in a modified form. He incised the columella between the nares, and using a nasal speculum to keep the operative field open, he performed a submucosal resection of the entire nasal septum and opened the sphenoid sinus, resecting the sphenoid septum and finally perforating the sella floor and the basal dura. Hirsch performed hundreds of these operations, first in Vienna until 1938 and then for another 20 years in Boston. Cushing's sublabial approach and Hirsch's transnasal approach became the two most popular methods of transsphenoidal surgery. After gaining operative experience in both transcranial and sphenoidal approaches, however, Cushing⁶ gradually began to favor the former technique; by 1929 he had completely abandoned the transsphenoidal approach.³¹ His rationale was that reoperation in cases in which surgery was performed via a transsphenoidal route was more difficult than that in cases in which a transcranial approach was used; additionally transcranial operations were associated with a higher rate of visual restoration.⁶ He also found that many of the pituitary lesions were in fact not adenomas or were adenomas with significant suprasellar extension, which were easier to treat transcranially under direct vision. There remains considerable debate as to the true statistical validity of Cushing's findings, but at the time, a majority of neurosurgeons followed his example, abandoning the transsphenoidal approach.

For the next 25 years the transsphenoidal approach remained essentially forgotten except by a few of neurosurgeons. Among these was Norman Dott, a pupil of Cushing, who in turn taught the technique to Guiot in Paris in 1956, and thus began to revive interest in transnasal pituitary surgery that quickly spread abroad. For many years the sublabial transsphenoidal approach that Cushing had once taught was the preferred inferior nasal approach. Over the last few decades the transnasal approach, similar to the Hirsch method has once again regained its popularity.

FLUOROSCOPY AND THE MICROSCOPE

Numerous innovations introduced in the 1950s served as catalysts for new interest in transsphenoidal surgery. With the introduction of cortisone and antibiotic therapy, total hypophysectomy was widely performed with significantly reduced mortality rates and long-term success. Additionally, soon after undertaking his first transnasal

resection, Guiot introduced the techniques of intraoperative image intensification and fluoroscopy, allowing the surgeon for the first time to visualize the depth and positioning of surgical instruments intraoperatively. On fluoroscopy, Hardy¹⁵ has recently remarked, "...the major advantage of fluoroscopy was the monitoring of the instrumental maneuvers on the television screen while removing large pituitary tumors with suprasellar extension. Intermittent views during the progressive descent of the tumor dome, monitored by air injection through the lumbar route or by direct visualization with contrast solution perfusion, afford immediate intraoperative live imaging of the tumor removal...." This modality of real-time visualization revolutionized the technical aspects of pituitary surgery and set the stage for subsequent innovations in intraoperative image guidance.

By the late 1950s the basic operative techniques necessary to perform transsphenoidal surgery had been well established. Advances in our ability to visualize the operative field and tumor bed were required to improve patient outcomes and expand the versatility of the technique. Inadequate illumination of the operative field had always limited the transsphenoidal method. Cushing had used a headlight, ENT surgeons such as Hirsch had operated using the ENT mirror, and Dott had tried to improve illumination by attaching small light bulbs near the tip of the blade.²⁵ Although ENT surgeons had used the operating microscope since the 1920s when performing ear-related surgery, its applications to transsphenoidal surgery were pioneered by Hardy¹⁴ in Montreal many years later. In 1965 he first used the operating microscope while performing a total hypophysectomy for breast cancer as well as while undertaking a selective anterior hypophysectomy for diabetic retinopathy.³⁴ The microscope and the specialized new instruments were inserted through a midline oronasal approach. Not only did this strategy improve illumination, it also added intraoperative magnification and stereoscopic visualization. The microscope and instruments were quickly adopted and have become an essential part of transsphenoidal approaches to the pituitary gland.

ENDOSCOPY

The use of fluoroscopy and the operative microscope greatly expanded the versatility of the transsphenoidal approach; the growing need for even greater accuracy and visualization was clearly demonstrated. More recently, there has been considerable debate over the use of endoscopy in pituitary surgery. Although introduced to neurosurgery almost a century ago, until recently the use of endoscopy had been primarily limited to intraventricular procedures. In 1963, Guiot¹² was the first to report the use of an endoscope during sublabial transsphenoidal surgery. Additionally, the endonasal route first used by Hirsch in 1909 was reintroduced by Griffith and Veerapen¹⁰ in 1987, opening the door for endoscopic pituitary surgery. Even with the operating microscope, visualization during pituitary surgery was limited to the straight and narrow view at the sella. During the mid-1990s, endoscopy as an adjunct to the microscope was described in multiple studies as a way to provide improved visualization of the pituitary gland and surrounding structures, via a small operative opening, and the authors describing this adjunctive endoscopy claimed that it facilitated better dissection of the

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tumor away from the normal pituitary.^{9,16,21} Supporters of the technique went also one step further by using endoscopy, without an accompanying microscope, for the removal of pituitary tumors. In 1992 Jankowski, et al.,²⁰ reported the first of these operations in three patients with pituitary adenomas in whom surgery was performed via a middle turbinectomy approach. Although the approach was later replaced by a conventional transseptal method, the use of endoscopy as a stand-alone instrument in pituitary surgery is becoming increasingly popular.^{3,22} Endoscopy may also have applications in the excision of recurrent and residual sellar masses where the anatomy is distorted by the first operation or by radiotherapy.² Currently, endoscopy is often used as an adjunct to the microscope, expanding the field of vision, rather than as a replacement. The advocates of the method point to such advantages as the endoscope's angled telescopes, which allow for visualization of otherwise blind corners and the ability to change perspectives between close-up and panoramic settings. The lack of binocular viewing, the subsequent lack of depth of field, the difficulty with intraoperative bleeding, and the large learning curve for neurosurgeons already trained in microsurgery, however, continue to be points of debate and have hampered the universal adoption of endoscopy in pituitary surgery.

INTRAOPERATIVE IMAGING AND FRAMELESS GUIDANCE

In addition to the challenges of illumination, pioneers of pituitary surgery also faced significant difficulties in obtaining adequate images of the region. Schloffer,³² using only plain lateral skull x-ray films, attempted the first transsphenoidal operation in 1907; however, the results were with disappointing because he was unable to assess the gross extent of the tumor. The use of pneumoencephalography, first introduced in 1919, partially addressed the need for better imaging and was in use until modern sectional imaging methods of CT and MR imaging became available in the 1970s. These newer modalities offered the neurosurgeon unprecedented visualization of the pituitary gland, allowing for more accurate preoperative planning as well as postoperative follow-up evaluation. Over the past decade further advancements in radiological protocols have allowed for the use of intraoperative imaging techniques that may potentially replace radiofluoroscopy in the coming years. Radiofluoroscopy, an established standard in pituitary surgery, when combined with the injection of contrast medium, can demonstrate the shape and size of the sella as well as outline the suprasellar extension of the tumor mass in the lateral view. It is unable to demonstrate adequately the lateral extension of the tumor, however, and fails to define essential topographical relationships of adjacent structures such as the carotid artery and the optic chiasm. The authors of numerous recent studies have indicated that intraoperative CT and MR imaging provide as the solutions to the shortcomings of radiofluoroscopy.²⁷⁻²⁹ Theoretically, by being able to obtain serial images of the operative region intraoperatively, a more complete resection is possible. Despite the possible advantages of these modalities, however, their popularity remains limited because of the high cost and specialized operating suites required for their implementation, as well as the additional operating time required to

acquire the repeated images. A possible alternative, which has only recently been applied to pituitary surgery, is intraoperative ultrasonography.³⁰ Analysis of preliminary studies has suggested that ultrasonography may be especially useful in identifying microadenomas that are not revealed on preoperative MR images.³³ Because blood can cause artifacts that may distort the ultrasonographic image, ultrasonography is currently only recommended for intraoperative localization prior to opening the dura.

In addition to serial intraoperative imaging, multiple image guidance systems are now available and have been applied in transsphenoidal surgery. By registering the preoperative CT or MR images, the systems allow for three-dimensional localization during the surgical approach and resection. As with intraoperative imaging, however, these image guidance systems are expensive, increase operative time, and are still unable to provide true real-time pictures while the suprasellar mass moves into the sella intraoperatively. The eventual utility of these systems probably lies in their application during reoperation or when there is significant destruction of osseous landmarks where the neurosurgeon can no longer rely on traditional localization methods.⁷

RADIOIMMUNOASSAY

When pituitary surgery was first undertaken, the surgery-related indications and the evaluation of surgery-related cure were based only on the patient's clinical presentation. In 1959 Yalow and Berson³⁵ introduced radioimmunoassay for insulin concentrations in biological fluid. Soon after this similar tests for pituitary hormones were developed. By the 1970s radioimmunoassay was widely available and had become an essential adjunct to transsphenoidal surgery. The test provided valuable information regarding the secretory products of pituitary tumors as well the level of tumor-induced compromise of the pituitary gland's normal hormone production. Additionally, in conjunction with new advances in imaging, it was now possible to gauge objectively the efficacy of surgical intervention and detect the early recurrence of the tumor. This provided significant advancement in understanding the secretory function of the pituitary gland, which in turn improved the indication for and the evaluation of the results of surgery.

CONCLUSIONS

Initially transsphenoidal surgery started as a quickly proliferating innovation with a multitude of technical variations, most of which have long been abandoned. During this period, the sublabial and transnasal approaches gained prominence, and the latter eventually became the standard surgical route. The establishment of a single, universally accepted procedure was one of the first major transitions in the development of transsphenoidal surgery. During the revival of the approach in the 1950s, use of radiofluoroscopy and the operating microscope once again quickly allowed for the advancement of the field by greatly improving illumination and the clarity of intraoperative imaging. Innovations in technology soon offered even more advanced methods to visualize the operative field in the form of endoscopy, which was used as an adjunct to the microscope or by itself. Because it allowed surgeons to visualize otherwise blind corners within the operative

field and because it provided a variety of panoramic and close-up views, it became popular during the past decade and its use, as evidenced by reports currently being published in the literature, is being expanded. In conjunction with advances in operative visualization, there have been two major, historically important developments in intraoperative imaging for pituitary surgery. The first is intraoperative neuroimaging (CT and MR imaging) that now offers the surgeon an unprecedented ability to determine the immediate extent of resection and the exact location of important anatomical structures. More recently, the allure of real-time intraoperative imaging has led to the wide popularity of frameless guidance systems that can allow for exact instrument placement and anatomical localization throughout the operation. The use of radioimmunoassay has also significantly contributed to the current success of transsphenoidal surgery by providing a more objective gauge by which to undertake surgical intervention and to assess cure. Each of these major historical transitions has helped to define modern transsphenoidal surgery. The surgical technique itself has been concretely established, although some debate remains with regard to the true utility and applications of the more recent technological innovations. Instead of stifling the growth of these advances, this debate will undoubtedly fuel the same innovative spirit that first drove the pioneers in our specialty and will lead to new revolutions in transsphenoidal surgery.

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