RANIOPHARYNGIOMAS grow from remnants of the Rathke pouch. They can be located inside the sella turcica and from there may grow above it, with symmetrical or asymmetrical suprasellar expansion. Exclusively suprasellar tumors involve the infundibulum and the suprasellar cisterns or may be found solely in the third ventricle. Approximately one third of all craniopharyngiomas reported in the literature involve the pituitary fossa.3,6,24,28,29,31,33,36,37,43 When this neoplasm is located either completely or partially within an enlarged sella, TSS is usually performed.13,15,19,21,23,24,28,31–33,42 Recently, however, modified transsphenoidal approaches that make use of a presellar or transsellar route have been proposed in the treatment of craniopharyngiomas located entirely in the suprasellar area, despite a normal sella turcica.10,25,26,30,31,39 In this paper we report the surgical indications for, and the results obtained by, using TSS for the resection of craniopharyngiomas.

Clinical Material and Methods

Table 1 features data regarding tumor localization in 57 patients with craniopharyngiomas treated primarily surgically by using the transsphenoidal approach. Twenty-nine patients were female and 28 were male, with ages ranging from 12 to 79 years (mean 35 years); only five patients were younger than 15 years. Clinical follow up ranged from 2 to 20 years. Clinical follow up ranged from 2 to 20 years (mean 6 years); in 12 patients, it ranged from 10 to 20 years. None of these patients had previously undergone surgery or radiotherapy.

Neuroimaging Evaluation

Preoperative MR imaging of the brain was performed in all patients. Follow-up MR imaging studies were obtained from 3 to 6 months postoperatively and then yearly thereafter.

Surgical Procedure

In all patients in whom the sella turcica was enlarged, because of either an exclusively intrasellar tumor (11 patients) or a tumor with a symmetrical intrasellar and suprasellar development (37 patients), the standard transsphenoidal approach was used, thus achieving a wide opening of the sella as far as the carotid artery laterally and the tuberculum sellae superiorly. When the tumor was characterized by a large intracranial expansion, a wider superior opening together with removal of the tuberculum sellae was performed to achieve a greater control of the suprasellar capsule, thus facilitating an easier dissection from the suprasellar structures.
After widely opening the dura mater, the anterior pituitary gland was often seen anteriorly within the sella turcica and needed to be incised and displaced to reach the tumor. The capsule of the craniopharyngioma was then recognized behind the pituitary gland and was opened. After intracapsular debulking to achieve complete tumor removal, the capsule was gently dissected from the walls of the cavernous sinuses, from the pituitary gland, from the pituitary stalk, from the diaphragma sellae, and, in cases with suprasellar expansion, from the chiasm and hypothalamus.

In nine cases of craniopharyngioma located entirely above the sella and the diaphragma, we made two different modifications in the standard TSS. In seven patients in whom the tumor was in contact with the planum sphenoidale (Fig. 1 left), the surgical route was situated anterior to the sella, and the tumor was reached by opening the floor and anterior wall of the sella, and by removing the bone of the tuberculum sellae and the posterior portion of the planum sphenoidale (transsphenoidal presellar approach). The dura mater overlying this portion of the skull base was opened, with obliteration of the anterior intercavernous sinus if necessary, thus obtaining access to the suprasellar cisterns. The indications for this approach were related both to the severe visual alterations and serious general conditions in the patients, contraindicating a classic intracranial removal, and to the large portion of the tumor in contact with the planum sphenoidale. In those patients, the surgical route was anterior to the sella, its origin is likely to be intrasellar, below the diaphragma. If the diaphragma sellae was congenitally deficient or absent or enlarged by the tumor or if the transsphenoidal route was used to approach a suprasellar tumor, then an intraoperative CSF leakage could occur. In such cases, the sellar cavity was filled with Gelfoam and closed using a fragment of nasal bone placed epidurally and glued to the boundaries of the sella to reconstruct its floor. We have used this method in more than 1000 cases of pituitary adenomas, and we have never observed visual complications related to a postoperative empty sella turcica. The cleaning of the sellar cavity due to the resorption of the Gelfoam permitted better verification of sellar content during follow up.

If a postoperative CSF fistula was observed, a lumbar drain, maintained for 72 hours, was usually able to stop the leakage in most cases. Among these cases, a second surgical repair of the sellar floor was necessary in only one case. If a tumor was only partially removed, an intracranial approach was planned as a second surgical step to be performed a few weeks or months later.

Additional Surgical Procedures

Nine patients underwent more than one operation, because of incomplete decompression of visual pathways (two patients) or tumor regrowth (seven patients). Two patients were submitted to a secondary TSS, whereas seven patients, because of a totally suprasellar regrowth of the tumor, needed to undergo a transcranial approach. One of these patients underwent a total of four transcranial surgical procedures.

Evaluation of Tumor Removal

In addition to the evaluation conducted by the surgeon, the extent of tumor resection was analyzed on MR imaging enhanced with Gd diethylenetriamine pentaacetic acid, which was performed 3 to 6 months after surgery. Tumor removal was considered to be total when the lesion together with its capsule was completely resected, subtotal when small fragments of the capsule were left attached to important structures, and partial when parts of the tumor remained

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>No. of Tumors (%)</th>
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<tbody>
<tr>
<td>purely intrasellar</td>
<td>11 (19)</td>
</tr>
<tr>
<td>intrasellar &amp; suprasellar</td>
<td>37 (65)</td>
</tr>
<tr>
<td>purely suprasellar</td>
<td>9 (16)</td>
</tr>
</tbody>
</table>

Table 1: Localization of craniopharyngiomas in 57 patients

Fig. 2. Preoperative (left) and postoperative (right) sagittal T1-weighted Gd-enhanced MR images. The exclusively intrasellar craniopharyngioma is located behind the pituitary gland. The follow up in this case was 10 years.
in situ with the capsule. Magnetic resonance imaging was repeated yearly in the follow-up period.

**Hormone Study**

Complete pre- and postoperative hormone studies were performed. The modalities of sample collection and radioimmunoassay used for hormone determination have been reported in our previous articles.2,9 Immediate postoperative and long-term evaluations were performed in this study.

**Clinical Outcome**

Surgical outcome was considered to be good if the patient, although requiring hormone replacement therapy, had resumed a normal life and was able to work or to go to school without mnemonic, psychological, or hypothalamic problems. His or her condition was considered to be fair if the patient, once a normal life had been resumed, exhibited mild neurological or psychological problems. The patient's condition was considered to be poor if he or she had severe neurological problems or compromised consciousness.

**External Radiotherapy**

Two patients received adjunctive external radiotherapy.

**Results**

**Surgical Results**

In 11 patients, the craniopharyngioma was exclusively intrasellar. Complete excision of the tumor together with preservation of the normal pituitary gland and stalk was possible in 10 patients (91%; Figs. 2 and 3). In one patient, a small fragment of the capsule was left attached to the pituitary stalk. Six years later, a regrown tumor, completely filling the pituitary fossa, was totally removed through TSS.

In 37 patients, the tumor was intrasellar and suprasellar. Complete radical removal of the tumor was achieved in 20 cases (54%; Figs. 4 and 5). In seven patients, tumor removal was subtotal. In one of these patients, tumor regrowth was observed 12 years postsurgery and was then totally removed through TSS. In 10 patients, partial tumor removal was accomplished. In two of these patients, a second intracranial surgical step, because of insufficient tumor removal, was performed a few months later. In the other two patients 4 years later, an intracranial removal was necessary because of tumor regrowth (complete removal in one, subtotal removal in one, and partial removal in two). Vision improved in eight of 10 patients whose sight had been previously compromised.

In nine patients, a huge tumor causing severe visual deterioration was located entirely above the sella and the diaphragma. In seven patients in whom the tumor was in contact with the planum sphenoidale, we used a transsphenoidal presellar approach (Figs. 6 and 7). In the two remaining patients in whom the tumor was retrochiasmatic, we used a transellar–transdiaphragmatic approach (Fig. 8). In two patients total tumor removal was achieved; in two the removal was subtotal; in four the tumor was partially removed; and in one, because of the very solid consistency of the tumor mass, only a simple biopsy could be realized. Vision improved in eight of these nine patients. One year later in one patient in whom the resection had been partial (Fig. 6), we observed regrowth of the residual mass in the suprasellar cisterns. Complete removal was achieved using an intracranial approach. Despite the fact that the surgical
evaluation results and postoperative MR images indicated total removal, 6 years later we observed signs of tumor recurrence and the patient underwent radiosurgical treatment.

**Overall Results**

A total removal of the craniopharyngioma was achieved in 32 patients (56%). In another four, a complete removal was accomplished after a second approach, thus reaching a radical removal rate of 63%. If we consider only the 48 patients with sellar involvement, the use of TSS allowed for total removal in 30 cases (63%; 33 cases after a second approach, 69%). All patients had good clinical follow up, regardless of the extent of tumor expansion and removal.

Eighteen patients needed hormone substitute therapy, and 14 of these underwent surgery for suspected panhypopituitarism. In eight patients, diabetes insipidus appeared after surgery. Gonadotropic functions in four patients and prolactin levels in three patients became normal, but this last result could be interpreted as a consequence of additional damage to lactotrophic cells. Sixteen of 19 patients with visual disturbances experienced a significant improvement and the three remaining patients’ conditions remained unchanged. Postoperative CSF leakage occurred in 10 patients (Table 2). In nine patients, this leak was successfully treated through continuous lumbar drainage, which was maintained for 48 to 72 hours. One patient required a repeated operation and sellar repair with photo-activated glue. None of the patients with CSF leakage experienced meningitis.

The mortality rate caused by later complications was 3.5% (two patients). One patient died several months after surgery, because of diencephalic insufficiency (he had undergone abdominal surgery at another institution, with interruption of hormone replacement therapy). The other patient died of progression of the disease notwithstanding one TSS procedure, conventional external radiotherapy, and four intracranial operations.

The anatomical and surgical findings are featured in Table 3.

**Recurrences, Regrowths, and Secondary Operations**

In our series, cases of tumor recurrence or regrowth numbered eight (14% of all patients; Table 4). Seven of these patient underwent a second surgery, with good clinical results in all patients and total tumor removal in four. One patient received radiosurgery and another underwent conventional external radiotherapy.

**Discussion**

The main purpose of this retrospective study was to analyze the results obtained in a group of patients with craniopharyngioma who had undergone transsphenoidal surgery. In general, we used TSS in treating the majority of craniopharyngiomas (57 of 92 patients; 62%), assuming that this route was less traumatic than the intracranial approach. In our study, 52% of all craniopharyngiomas involved the sella turcica, similar to the data collected by Laws.
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Fig. 8. A transsellar–transdiaphragmatic approach was used to treat a suprasellar retrochiasmatic craniopharyngioma. Sagittal T₁-weighted postcontrast MR images obtained preoperatively (left) and after subtotal resection (right). The follow up in this case was 2 years.

In the late 1970s Rougerie and Garcia-Uria affirmed that TSS is not suitable for the radical removal of craniopharyngioma. In fact, Yaşargil used this approach in only 9.7% of his cases. More recently, Van Effenterre, et al., followed this concept and proposed the use of a frontotemporal intracranial approach in cases involving the sella turcica. In that series 44% of tumors involved the sella, but TSS was used in only 8% of cases. On the contrary, we have favored TSS and chose to use it in all 48 cases in which the tumor was entirely or partially located in the sella, thus achieving complete tumor removal in 30 cases (63% rate of complete removal on the first attempt and 69% rate on the second attempt) and a good clinical outcome in all patients, with only minor morbidity and no perioperative death regardless of the extent of suprasellar expansion. The rate of total removal on the first operation was 91% (10 of 11 cases) in patients with purely intrasellar tumors (100% after a second operation) and 54% (20 of 37 cases) in those with intrasellar and suprasellar tumors (22 [59%] of 37 cases after a second operation). The pituitary stalk was preserved in all cases. In the majority of previously affected patients, visual disturbances improved and none experienced a worsening of vision. Similar data are reported by other authors, particularly those skilled in transsphenoidal surgery.

Craniohypophysealomas involving the sella turcica—different from the infundibular craniohypophysealoma, which is more often calcified, or for the intraventricular craniohypophysealoma, which is usually solid with no cysts—are often cystic or friable, making intracapsular debulking easier. Such tumors usually do not infiltrate surrounding structures, and dissection of the capsule from the optic chiasm, hypothalamus, and pituitary stalk can be carefully performed. In only two patients with huge tumors was TSS unable to reach a satisfactory decompression of the optic chiasm, and a second intracranial procedure had to be planned as an additional surgical step.

Transsphenoidal surgery has traditionally been restricted to the removal of tumors involving the pituitary sella and to the suprasellar extension of such tumors if the sella appears enlarged. Craniohypophysealomas located entirely within the suprasellar area together with a normal-sized sella turcica have generally been considered to be not manageable by TSS. In such cases, either pterional or frontotemporal craniotomy has been used for a more complete removal. Recently, however, two modified transsphenoidal approaches, despite the presence of a normal pituitary fossa, have been proposed for treatment of these craniohypophysealomas. A transsellar–transdiaphragmatic method of approaching the suprasellar cisterns has been reported in the excision of both craniohypophysealomas and pituitary adenomas, with splitting and displacement of the pituitary gland. We have used this approach in two cases of entirely suprasellar retrochiasmatic craniohypophysealomas, in which a total removal was thought to be difficult to achieve using an intracranial approach.

Alternatively, the transsphenoidal route was also used to realize a presellar–transtuberculum approach, through a widening of the surgical field obtainable with the standard procedure. In this technique, bone was removed from the sellar floor, tuberculum sellae, and posterior part of the planum sphenoidale, thus permitting a prediaphragmatic view of the contents of the basal cisterns. This exposure takes advantage of the direct access to supradianaphragmatic lesions adjacent or anterior to the pituitary stalk, without resecting the pituitary gland. In 1995 in a surgical series of craniohypophysealomas, we reported two cases of huge suprasellar tumors treated using this approach. In the present paper we report on seven patients who underwent a similar approach. These approaches to the suprasellar cisterns provide midline exposure, allowing dissection in the space around the optic nerves, avoiding brain retraction and some of the disadvantages of transcranial surgery, and realizing a less traumatizing and time-consuming surgery. It has proved to be useful for not only small but also huge craniohypophysealomas.

Analysis of our data indicates that the use of TSS for the primary removal of craniohypophysealomas does not significantly increase the potential for complications, compared with standard transsphenoidal procedures, except for CSF leakage. Only the rate of postoperative CSF rhinorrhea was higher than the rate previously reported, reaching 19% in patients with craniohypophysealomas with sellar and suprasellar...

TABLE 2
Postoperative CSF leakage in 10 patients*

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>No. of Leaks (%)</th>
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<tr>
<td>purely intrasellar</td>
<td>NA</td>
</tr>
<tr>
<td>intrasellar &amp; suprasellar</td>
<td>7 of 37 (19)</td>
</tr>
<tr>
<td>suprasellar</td>
<td>3 of 9 (33)</td>
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* NA = not applicable.

TABLE 3
Anatomicosurgical findings in 57 patients with craniohypophysealoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients (%)</th>
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<tr>
<td>pituitary gland anterior to tumor</td>
<td>27 (47)</td>
</tr>
<tr>
<td>thin layer of pituitary gland surrounding tumor</td>
<td>12 (20)</td>
</tr>
<tr>
<td>evidence of tumor capsule</td>
<td>40 (70)</td>
</tr>
<tr>
<td>necrotic material w/ cholesterol</td>
<td>27 (47)</td>
</tr>
<tr>
<td>solid calcified material</td>
<td>21 (36)</td>
</tr>
<tr>
<td>cyst w/ oil</td>
<td>12 (20)</td>
</tr>
<tr>
<td>solid noncalcified material</td>
<td>5 (9)</td>
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lar extension and 33% in patients with purely suprasellar tumors. Nonetheless, no meningitic complications were observed. With the use of TSS, the risks of visual injury are reduced, compared with the risks in craniotomies performed to treat similar lesions.34,33,50 Note that memory deficits, cognitive deteriorations, personality changes, and behavioral problems were irrelevant in our series.

Normal pituitary tissue was recognized anterior to the tumor within the sella turcica in 47% of patients, and in all patients the gland had to be split to reach the craniopharyngioma. This surgical procedure has never provoked serious damage to the gland.

Although our results can be considered to be good, TSS for huge craniopharyngiomas must be considered a difficult surgical procedure and should be exclusively performed in well-selected cases and by surgeons with extensive experience in pituitary surgery.

Craniopharyngiomas have a tendency to recur,46,47 even after apparent total removal.1 According to major literature series,34 the rate of recurrence ranges from 0 to 53% in cases of total removal and from 30 to 100% in cases of subtotal or partial removal. Most recurrences happen in the first 3 years after surgery.11,14,23,27,49 Regardless, some authors33,44,50 have reported no recurrence after primary radical excision.

In our series we observed signs of tumor recurrence 6 years after surgery in only one patient in whom the evaluation by the surgeon, together with MR imaging results, indicated total tumor removal. It is remarkable that in nine patients with total tumor removal, the clinical follow up was between 10 and 20 years. Tumor regrowth was observed in 20% of patients who had experienced subtotal removal (interval between first and second surgery, 4 years) and in 33% of patients who had experienced partial removal (interval between first and second surgery, 1 year).

A new attempt to remove the tumor was undertaken in seven patients. The good results obtained at such a second surgery indicate, as asserted by Carmel5 and Laws,33 that a careful total removal of the lesion even at a late secondary operation does not necessarily cause additional damage to the hypothalamic structures. A policy of radical resection is advocated to prevent tumor recurrence and to improve the patient survival rate. External conventional radiotherapy or radiosurgery was reserved for cases of new recurrences after a first reoperation. Because the endoscopy-assisted TSS was performed in only the last six cases, our experience is too little to be able to predict the future of this procedure in TSS in patients with suprasellar craniopharyngiomas.

Conclusions

The best way to treat craniopharyngiomas is to attempt a complete removal; that is, radical excision, whenever possible, should be the aim of surgery. Our experience indicates that a complete removal of these tumors can be safely achieved in selected cases by using the transsphenoidal approach. Even tumors with large suprasellar expansion can be managed with the aid of this approach. In the majority of patients previously affected, visual disturbances became normal or improved. The main disadvantage of TSS, mainly in huge suprasellar expansion, was the increased risk of CSF leakage. In our opinion, this approach, when used in appropriately located craniopharyngiomas and by neurosurgeons with extensive experience in pituitary surgery, may give excellent results with minor risks.

References


Table 4

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. of Patients (%)</th>
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<tr>
<td>recurrence despite total removal</td>
<td>1 of 32 (3)</td>
</tr>
<tr>
<td>regrowth despite subtotal removal</td>
<td>2 of 10 (20)</td>
</tr>
<tr>
<td>regrowth despite partial removal</td>
<td>5 of 15 (33)</td>
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