Spontaneous Resolution of Diabetes Insipidus After Pituitary Stalk Sectioning During Surgery for Large Craniopharyngioma
—Endocrinological Evaluation and Clinical Implications for Surgical Strategy—

Shigeru NISHIZAWA, Seiji OHTA, and Yutaka OKI*

Departments of Neurosurgery and *Internal Medicine, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka

Abstract

The mechanism of spontaneous resolution of diabetes insipidus (DI) was investigated after surgery for large craniopharyngioma. Twenty-two adult patients (mean age 48.9 years old), who underwent surgery via the anterior interhemispheric trans-lamina terminalis approach, were divided into three groups: Group I, the entire pituitary stalk was preserved (n = 2); Group II, the stalk was dissected distally from the tumor but ultimately sacrificed (n = 9); Group III, the stalk was not identified and was sacrificed (n = 11). All patients were discharged without neurological deficits 1 month after surgery. Four patients underwent gamma-knife treatment for residual tumor or recurrence. Postoperative endocrinological functions were normal in Group I, and no replacement therapy was required. Hormonal replacement for pan-hypopituitarism and DI was necessary in Groups II and III (mean follow-up period 5.9 years). DI resolved at 2.7 ± 1.3 years after surgery in four patients in Group II, and a hypertonic saline infusion test revealed production of small amounts of intrinsic antidiuretic hormone (ADH). Urine osmolarity was high in the morning, and a significant increase in urinary osmolarity was noted after Pitressin injection. These results indicate induction of hypersensitivity of the distal renal tubules to small amounts of intrinsic ADH, resulting in decreased urinary output. Recovery from DI can be expected, despite permanent impairment of anterior pituitary function, if the pituitary stalk is dissected as distally as possible.

Key words: craniopharyngioma, diabetes insipidus, endocrinology, pituitary stalk, surgery

Introduction

Craniopharyngioma has been the subject of several large surgical treatment series.1,6,10,11,15-17,19,22-24,27-29,31,34-42,44,45) The surgical strategies, surgical outcome, efficacy of multi-modality treatment, long-term prognosis, pre- and postoperative neurological and neurocognitive functions, hormonal disturbances, and so on, have been evaluated in children and/or adults. The treatment outcomes vary markedly between series, pediatric and adult cases, and adamantinomatous and squamous histologies.1,38,39,45) The long-term outcome of surgery for relatively small craniopharyngiomas is favorable in terms of complete removal, recurrence rate, and neurological and endocrinological functions, regardless of the surgical approach. However, the surgical outcomes for large craniopharyngiomas remain controversial.1,6,10,11,15-17,19,22-24,27-29,31,34-42,44,45) Furthermore, most reports on craniopharyngioma have focused primarily on children10,15-17,22,27,41,42) or mixed series,1,19,23,24,31,34,36,38-40,45) and studies of only adults are limited.6)

The postoperative endocrinological state of patients treated for craniopharyngioma is critical to the quality of life. Hypothalamic-pituitary dysfunctions may occur in patients with craniopharyngioma, especially diabetes insipidus (DI), before and after surgery.17,19,22-24,31,36,38-42,45) However, DI is rare after pituitary stalk sectioning for craniopharyngioma surgery.

We surgically treated 22 adults with large craniopharyngiomas via the anterior interhemispheric trans-lamina terminalis approach. Postopera-
tive hypothalamic-posterior pituitary lobe function was evaluated to clarify the mechanism of spontaneous resolution of DI after pituitary stalk sectioning.

Clinical Materials and Methods

I. Patient population

Twenty-two adult patients, 15 males and seven females aged 32–65 years (mean ± standard deviation [SD] 48.9 ± 16.5 years), with large craniopharyngiomas, i.e. occupying the suprasellar cistern and the entire third ventricle, were treated via the anterior interhemispheric trans-lamina terminalis approach. The endocrinological states of these 22 patients were analyzed. The follow-up period was 1.5–8 years (mean ± SD 5.9 ± 2.1 years) after surgery.

The tumors averaged 5.5–7.2 cm (mean 6.3 cm) in anteroposterior diameter, 3.2–3.8 cm (mean 3.5 cm) in width, and 4.3–5.1 cm (mean 4.8 cm) in height. The suprasellar cistern was completely occupied by the tumor. The tumor was located in the third ventricle in all cases, as confirmed during surgery.

II. Anterior interhemispheric trans-lamina terminalis approach

After making a coronal skin incision and a bifrontal craniotomy, the distal interhemispheric fissure was opened under a microscope. When the optic chiasm was post-fixed and an adequate surgical field was available over the pre-chiasmatic cistern, the cistern was opened and the tumor dissected from the bilateral optic nerves and chiasm, and identification of the pituitary stalk attempted before opening the lamina terminalis. However, identification succeeded in only a few cases. The lamina terminalis was sharply incised to open the third ventricle. First, the tumor in the third ventricle was internally decompressed as much as possible. The tumor capsule was then dissected from the hypothalamus and gently pulled away from the lateral wall of the third ventricle. Removal of the tumor component in the third ventricle was confirmed to reveal the entire anterior surface of the brain stem and aqueduct, and the lateral walls of the third ventricle. The tumor in and around the chiasmatic cistern was then exposed and dissected from the surrounding structures. The pituitary stalk was identified during this procedure. The tumor capsule was strongly attached to the pituitary stalk and below the optic chiasm. The tumor capsule was sharply dissected from the pituitary stalk, proximally to distally as much as possible, but sometimes had to be cut to remove the entire tumor. After dissection of the tumor capsule from the inferior surface of the chiasm, the entire tumor was removed, and a microsurgical mirror was used to confirm the absence of residual tumor tissue under the chiasm.

III. Preoperative hormonal work-up

Provocation tests consisting of simultaneous intravenous injection of regular insulin (0.1 unit/kg), thyrotropin-releasing hormone (TRH) (500 μg), and luteinizing hormone-releasing hormone (LH-RH) (100 μg) were performed to evaluate the preoperative hypothalamic-anterior pituitary axis function in all patients. A venous blood sample was collected before the injections, and at 15, 30, 60, 90, and 120 minutes after the injections. Serum glucose, growth hormone (GH), cortisol, adrenal corticotrophic hormone (ACTH), thyroid-stimulating hormone (TSH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin levels were determined. A provocation test with GH-releasing hormone (GRH) (100 μg) was also done in patients with insufficient GH response. The GH response in the provocation test was considered to be normal if the GH level was higher than 10 ng/ml, and as impaired if the GH level was lower than 5 ng/ml. If the cortisol, ACTH, and TSH responses were higher than twice the basal levels, those responses were considered to be normal. The LH and FSH responses were judged to be normal or impaired based on consideration of the patient’s age and whether female patients were pre- or post-menopausal.

The basal antidiuretic hormone (ADH) level was measured sporadically, and total 24-hour urine volume, and the specific gravity and osmolarity of the total 24-hour urine specimen were measured daily after admission to evaluate hypothalamic-posterior pituitary axis function.

IV. Postoperative work-up

Postoperative magnetic resonance (MR) imaging was performed in every patient to confirm complete removal of the tumor.

Postoperatively, a dose of 24 mg of betamethasone a day was administered to all patients, which was withdrawn within 2 weeks. Thereafter, 10 mg of cortisol was orally prescribed to all patients until hormonal provocation tests were performed. One month after surgery, just before discharge, hormonal provocation tests using simultaneous intravenous injection of corticotropin-releasing hormone (CRH) (100 μg), TRH (500 μg), GRH (100 μg), and LH-RH (100 μg) were performed just before oral administration of 10 mg of cortisol early in the morning. Based on the results, it was decided whether continuation of cortisol replacement therapy was necessary, and whether replacement of thyroid hormone was required. If the patient
suffered from DI, replacement therapy with desmopressin was started, and specific tests to evaluate hypothalamic-posterior pituitary function were not performed. In patients with spontaneous resolution of DI at any time after surgery (described later), specific tests to evaluate posterior pituitary function, the hypertonic saline (5.0%) infusion test and the Pitressin test, were performed when needed.

Results

I. Pre- and postoperative neurological states, and neurocognitive function

Twenty-one of the 22 patients presented with headache as the chief complaint. One patient visited the hospital because of severe recent memory disturbance. Neurological examination disclosed decreased visual acuity and visual field deficits in all patients. The deficits varied between the patients, for example, unilateral or bilateral decreases in visual acuity, and bitemporal or homonymous hemianopsia. Deficit type and severity depended on the extent of the tumor in the chiasmatic cistern. All but one patient had normal neurocognitive functions.

Postoperatively, decreased visual acuity and visual field deficits normalized in eight patients, and recovered but normalized in nine patients. There was no improvement of visual function in five patients. The extent of visual function recovery seems to depend on the duration of visual impairment.

One patient who had had no preoperative deficit in neurocognitive function showed severe recent memory disturbance postoperatively for 3 months, then gradually recovered to the preoperative level and currently works as an executive at an architectural company. One patient had severe recent memory disturbance before surgery, which persisted after surgery for 2 years postoperatively, although some improvement was seen.

All patients were discharged 1 month after surgery (mean ± SD 30 ± 2.5 days after surgery) without neurological deficits related to the surgery. All patients were followed up in the outpatient clinic once a month with or without hormonal replacement. All patients returned to their previous lives, and none required assistance.

II. Pre- and postoperative hypothalamic-pituitary hormonal evaluation

Preoperative hypothalamic-pituitary function: The preoperative provocation tests showed normal responses in four patients. A low GH response to insulin-induced hypoglycemia was observed in 18 patients, but the GRH test was normal in all these 18 patients, indicating that the low GH responses were of hypothalamic origin. Limited responses to the ACTH and cortisol provocation tests, and to TSH based on our criteria, were observed in seven and eight patients, respectively. Low LH and FSH responses to LH-RH test were detected in 12 patients. Hyperprolactinemia was observed in 12 patients (87–122 ng/ml).

The total urine volume of all patients was in the 1800–2300 ml/day range, and the specific gravity and osmolarity of the urine were 1.010–1.025 and 297–320 mOsm/l, respectively. The serum ADH level was within normal limits. Therefore, none of our patients had impaired function of the hypothalamic-posterior pituitary axis.

Postoperative hypothalamic-pituitary function: The 22 patients were classified into three groups according to the condition of the pituitary stalk: in Group I, the pituitary stalk was completely preserved (n = 2); in Group II, the pituitary stalk was identified during surgery and dissected from the tumor, but ultimately sacrificed because of tight adhesion of the tumor to the stalk (n = 9); in Group III, the pituitary stalk was not identified during surgery and was sacrificed, as confirmed by the lack of anatomical continuity between the floor of the third ventricle and the diaphragm sellae during surgery (n = 11).

Provocation tests were performed 1 month after surgery, just before discharge. All anterior pituitary hormonal responses were the same as those measured preoperatively in Group I. One of the two patients had a low GH response before and after surgery. However, the low ACTH, cortisol, and TSH responses normalized after surgery. Prolactin levels also normalized (<20 ng/ml). No temporary DI occurred, and no hormonal replacement therapy was needed during the follow-up period (3.5 and 6 years). No anterior pituitary hormone responses to provocation tests were observed in Groups II and III, so 10–20 mg cortisol was continued and 50–75 μg thyroid hormone replacement therapy was started. The postoperative prolactin levels remained at preoperative levels. Several hours after surgery, urine volume increased markedly in these 20 patients, and urinary specific gravity was 1.002–1.005. Control was achieved by nasal administration of desmopressin.

The hormonal conditions of our patients were evaluated on an outpatient basis after discharge. In Group I, the basal levels of pituitary hormones were within normal limits, there was no DI, and the patients were followed up without hormonal replacement. In Groups II and III, basal pituitary
hormone levels were measured once a month. The basal cortisol and thyroid hormone levels were within the normal range, due to the replacement therapy. Provocation tests were performed once a year after admission to the hospital. Cortisol and thyroid hormone replacement was stopped for a week, and provocation tests with CRH, GRH, TRH, and LH-RH were performed. Blood samples were collected before and at 15, 30, 60, 90, and 120 minutes after simultaneous intravenous injection of CRH, GRH, TRH, and LH-RH, and pituitary hormones were measured. Since no anterior lobe pituitary hormone responses were obtained in any of the 20 patients in Groups II and III, replacement therapy was continued. However, four patients in Group II were allowed to self-administer desmopressin because they had noticed decreased daily urine volume or facial edema in the morning after administration of desmopressin. Ultimately, all four patients decided to stop using desmopressin. The interval between surgery and final use of desmopressin was 2.7 ± 1.3 years. A hypertonic saline (5.0%) infusion test and a Pitressin test were performed in these four patients to evaluate hypothalamic-posterior pituitary axis function.26) These tests were performed only once because of continued resolution of DI.

In the morning, the patient rested in bed for 30 minutes, and 5.0% hypertonic saline was intravenously infused at 0.05 ml/kg/min. Plasma osmolarity, sodium, and ADH were measured before the infusion and at 30, 60, 90, and 120 minutes after starting the infusion. The results are shown in Table 1, and the relationship between plasma osmolarity and ADH levels in Fig. 1

Urine was collected in the morning to measure osmolarity, and a blood sample was collected to measure plasma atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP). Pitressin (10 units) was subcutaneously injected, and urine was collected 1 hour later to measure osmolarity. The results are shown in Table 2.

III. Postoperative MR imaging findings
Postoperative MR imaging showed residual tumor tissue on the left hypothalamic surface in one patient, and under the optic chiasm in another. Postoperative gamma-knife treatment was performed in both these patients. Recurrence of the tumor under the optic chiasm was detected in another two patients at 6 months and 1 year, respectively, after surgery. Both also underwent gamma-knife treatment. The tumors were well controlled in all four patients. No tumor recurrence was detected in the other 18 patients (follow-up period: range 1.5–8 years, mean ± SD 5.9 ± 2.1 years).

Fig. 1 Relationship between plasma antidiuretic hormone (ADH) levels and plasma osmolarity measured by the hypertonic saline infusion test in four patients whose diabetes insipidus resolved after surgery for large craniopharyngiomas occupying the entire third ventricle and suprasellar cistern. shaded area: normal response zone, ○: Case 1, □: Case 2, ●: Case 3, ■: Case 4.
Table 2  Urine osmolarity (Osm), plasma atrial natriuretic peptide (pANP), and plasma brain natriuretic peptide (pBNP) obtained by the Pitressin test

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Urine Osm (mOsm/l)*</th>
<th>pANP (pg/ml)</th>
<th>pBNP (fmol/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>453</td>
<td>523</td>
<td>10.1</td>
</tr>
<tr>
<td>2</td>
<td>562</td>
<td>739</td>
<td>11.4</td>
</tr>
<tr>
<td>3</td>
<td>305</td>
<td>483</td>
<td>11.5</td>
</tr>
<tr>
<td>4</td>
<td>410</td>
<td>595</td>
<td>11.3</td>
</tr>
</tbody>
</table>

*Before: urine osmolarity before Pitressin administration, after: urine osmolarity after Pitressin administration.

Fig. 2  Case 3. Preoperative T₁-weighted magnetic resonance images with contrast medium showing a large craniopharyngioma occupying the entire third ventricle and suprasellar cistern.

Fig. 3  Case 3. Postoperative T₁-weighted magnetic resonance images with contrast medium demonstrating total removal of the tumor.

Representative Case

Case 3 (in Tables 1 and 2): A 36-year-old man came to our university hospital complaining of morning headaches for 3 weeks. Neurological examination revealed bitemporal hemianopsia. MR imaging showed a partially cystic, mostly solid tumor occupying the entire third ventricle and suprasellar cistern (Fig. 2). The diagnosis was craniopharyngioma. Preoperative endocrinological examination was normal except for a low GH response. There was no evidence of DI. Surgery was performed via an anterior interhemispheric trans-lamina terminalis approach, and the intraventricular part of the tumor was totally removed through the window of the lamina terminalis. The suprasellar part of the tumor was then dissected from the surrounding structures and the pituitary stalk. However, since the tumor was highly adherent to the pituitary stalk, the stalk was cut close to the diaphragma sellae, and the entire tumor was removed. Histological examination showed squamous cell type of craniopharyngioma.

Postoperatively, the patient was awake and alert, but had severe recent memory disturbance. On the day after surgery, urine volume increased to 5000 ml, with specific gravity of less than 1.005, indicating DI. Urine volume was maintained between 2000–3000 ml by nasal administration of desmopressin. Postoperative MR imaging confirmed total removal of the tumor (Fig. 3). The patient was discharged from the hospital 1 month after surgery and then followed up in the outpatient clinic once a month. One month after surgery, just before discharge, postoperative endocrinological examination revealed pan-hypopituitarism, so replacement
therapy with 10 mg of cortisol was started and 75 μg of thyroid hormone was started. The recent memory disturbance gradually improved and he had returned to his preoperative condition by 3 months after surgery. He currently works as an executive and is asymptomatic. The bitemporal hemianopsia improved remarkably, but most lateral portions of the visual field were bilaterally defective.

Eighteen months after discharge, the patient noticed a more marked decrease in daily urine volume with continuous usage of desmopressin, and facial edema every morning. The patient reduced the dose and ultimately stopped using desmopressin, but the urine volume did not increase and nocturnal micturition did not occur. Hypothalamic-pituitary function was tested at that time, and anterior pituitary gland provocation tests still showed panhypopituitarism. The hypertonic saline infusion test showed an increase in plasma ADH from 0.6 to 1.5 pg/ml and a change in plasma osmolarity from 306 to 326 mOsm/l. The diagnosis was partial DI. Urine osmolarity in the morning was measured as 305 mOsm/l, and increased to 483 mOsm/l after Pitressin injection. Apparently the sensitivity of the distal renal tubules had increased to the endogenous plasma ADH level, resulting in resolution of the DI. The patient was followed up with replacement of cortisol and thyroid hormone, without desmopressin.

Discussion

I. Surgical results

Our fundamental treatment policy for patients with craniopharyngioma is to perform total removal whenever possible, and to remove as much of the tumor as possible when total removal is not an option. Relatively small tumors located in the chiasmatic cistern with extension only into the anterior part of the third ventricle, or with lateral extension, are treated via the unilateralpterional approach. A tumor arising from the intrasellar region with suprasellar extension is treated by transphenoidal surgery. Very large tumors, for example, occupying the entire third ventricle and suprasellar cistern, have been treated via the anterior interhemispheric trans-lamina terminalis approach since 1992. A pediatric large craniopharyngioma would be surgically treated via the unilateralpterional approach. However, we have treated too few such patients for analysis.

Postoperative outcomes after surgical removal, as well as neurological and neurocognitive functions, were favorable in our 22 adult patients with craniopharyngioma occupying the entire third ventricle and suprasellar cistern. Since the olfactory nerves were not exposed during surgery, none of our patients experienced postoperative impairment of olfactory function. All patients returned to their original lives. Postoperative gamma-knife treatment was required in only four patients. Based on our surgical outcomes, the anterior interhemispheric trans-lamina terminalis approach is one of the most advantageous approaches for the treatment of large craniopharyngiomas occupying the entire third ventricle and suprasellar cistern.

II. Postoperative endocrinological function

Management of hypotalamic-pituitary function is extremely important for the quality of life after surgery for craniopharyngioma. The pituitary stalk is sometimes very difficult to preserve during surgery for large craniopharyngiomas, and may be sacrificed for total removal of the tumor. The resultant hypothalamic-pituitary hypofunction may require cortisol and thyroid hormone replacement therapy. Patients may also develop DI and thus require nasal administration of desmopressin.

In our series, the pituitary stalk was completely preserved by surgery via the anterior interhemispheric trans-lamina terminalis approach in two (Group I) of 22 patients with large craniopharyngiomas, neither of whom required postoperative hormonal replacement. The pituitary stalk was sacrificed in the other 20 patients (Groups II and III), all of whom required hormonal replacement with cortisol, thyroid hormone, and desmopressin. Evaluation of postoperative hormonal function in these patients showed no recovery from panhypopituitarism. On the other hand, DI resolved spontaneously in four patients in Group II, at 2.7 ± 1.3 years after surgery.

The hypothalamic-posterior pituitary function was further evaluated by a hypertonic saline infusion test and a Pitressin test in these four patients to determine the mechanism of spontaneous resolution of DI. These tests showed the intrinsic production of plasma ADH was still low even after resolution of DI, and the ADH response to hypertonic saline infusion was modest, with plasma ADH increasing 0.9 ± 0.1 pg/ml. These results were considered evidence of partial DI. On the other hand, the urine osmolarity of these patients was sufficiently high in the morning, and increased significantly after subcutaneous Pitressin injection. Since both plasma ANP and BNP levels in these patients were within normal range, these four patients were considered not to be dehydrated. The results of these tests indicated that the distal renal tubules
had become hypersensitive to even a slight increase in intrinsic production of plasma ADH,7.8.13.25) which resulted in production of sufficiently concentrated urine and decreased 24-hour urine volume. The natural sequelae of hypothalamic-pituitary posterior lobe axis function after surgery for craniopharyngioma is unclear, but we suggest that evaluating function by provocation tests is very worthwhile.

The effect of experimental pituitary stalk sectioning and endocrinological function sequelae have been extensively studied in rhesus monkeys,2) dogs,21) and rats.9) Regeneration of the proximal stump with reconstitution of a “new” neurohypophysis occurred as early as 3 weeks after the operation, illustrating the remarkable regenerative capacity of the system.2,9,21) This remarkable regenerative capacity was confirmed by the disappearance of DI in rhesus monkeys and rats.2) The degree of cell loss in the hypothalamic nuclei due to degeneration was greater if the nerve tract in the stalk was severed at a higher level. Damage to the median eminence in dogs may be associated with a marked loss of cells in hypothalamic nuclei.21) Similar results have been reported after palliative sectioning of the pituitary stalk in patients with breast cancer.14,32,33) Disappearance of DI has occurred in patients with malignant tumors, and degeneration and regeneration of the hypothalamic nuclei were found at autopsy at 3 days to 32 months after surgery.14,32,33) However, the degree of regeneration was modest in humans compared with experimental animals. Regeneration of nerve fibers and resolution of DI also occurred in patients who survived for 540 days after stalk sectioning.14) The level of hypophyseal stalk sectioning influenced the degree of cell loss in the hypothalamic nuclei, i.e. more proximal sectioning was associated with more extensive cell loss.14,32,33)

Recovery from DI is unlikely if the pituitary stalk is cut close to the median eminence. The reported period of recovery from DI after pituitary stalk sectioning in humans is similar to that in our series. Based on these results, the pituitary stalk should be dissected as distally as possible to preserve endocrinological function as far as possible. The hypothalamic nuclei may then regenerate and produce ADH. Even modest production of ADH will decrease daily urinary volume because of the hypersensitivity of the distal renal tubules. Therefore, resolution of DI can be expected.8,13)

III. Pseudo-posterior lobe after sectioning of the pituitary stalk

T1-weighted MR imaging has demonstrated a high intensity spot after sectioning of the pituitary stalk, which was described as a pseudo-posterior lobe due to storage with re-production of ADH from the hypothalamus.12,18,20) Follow-up T1-weighted MR imaging of our four patients did not show such a high intensity spot in the sella or stump of the pituitary stalk even after resolution of DI. All our four patients still had partial DI, and the accumulation of ADH may have been very small. This may explain why high intensity spots were not observed on the MR images.

IV. Conclusions

Large craniopharyngioma occupying the whole suprasellar cistern and third ventricle can be totally removed via the anterior interhemispheric transfalamina terminalis approach. The pituitary stalk should be sectioned as distally as possible to preserve ADH production and allow recovery from DI, despite permanent impairment of anterior pituitary function.

References

9) Billenstien DC, Leveque RG: The reorganization of
the neurohypophyseal stalk following hypophysectomy in the rat. Endocrinology 56: 704–717, 1955


21) Hare K: Degeneration of the supra-optic nucleus following hypophysectomy in the dog. Am J Physiol 119: 326–327, 1937


40) Shirane R, Su CC, Kusaka Y, Yokura H, Yoshimoto T: Surgical outcomes in 31 patients with craniopharyngiomas extending outside the suprasellar cistern: an

Address reprint requests to: S. Nishizawa, M.D., Department of Neurosurgery, Hamamatsu University School of Medicine, 1–20–1 Handayama, Hamamatsu, Shizuoka 431–3192, Japan.
e-mail: nisizawa@hama-med.ac.jp

Commentary

I totally agree with the first part of the “Conclusion” of this important interdisciplinary publication, that “large craniopharyngioma occupying the whole suprasellar cistern and third ventricle can be totally removed via the anterior interhemispheric translaminar approach.” It is also my experience that giant (< 4 cm in diameter) craniopharyngiomas can be resected in about 90% of resectable cases as described by the authors and by their preferred approach, but I would add only if no contraindication for major surgery like permanent hypothalamic disturbance is present.

The authors concentrate on diabetes insipidus, which should be avoidable, when “the pituitary stalk should be sectioned as distally as possible to preserve ADH production and allow recovery from diabetes insipidus, despite permanent impairment of anterior pituitary function.” The distal resection of the stalk seems to be possible in the majority of cases, but should be orientated to the real origin of the craniopharyngioma, which can also be more proximal. I divided management of stalk preparation in our published earlier series from 1999 (refs. 19 and 23 of this article) into four groups: 1) preserved stalk = no deficits; 2) sacrificed stalk = complete panhypopituitarism in all cases; 3) partially resected stalk = not always complete panhypopituitarism but also partial anterior lobe insufficiency and preservation, with resolution of hypothalamo-posterior lobe function; and 4) not identified or not visible pituitary stalk, which does not mean that complete deficits occur automatically. The results are not as good as in the group with identified and preserved stalk, but better than in the group with partially resected stalk.

Nevertheless I agree that the mechanism of resolution of diabetes insipidus depends mainly on the preserved localization of the storage of the neurosecretory ADH containing granules in the distal stalk area with its regenerative potential, although I personally suppose that individual variations are considerable. I am furthermore convinced that in only exceptional cases craniopharyngiomas are developed within the third ventricle, the described “occupation” of the third ventricle is more a displacement of the ventricle by the tumor mass, which partially can invade or perforate the ventricle wall. Fortunately the hypothalamus, compared with a thumb-nail by Harvey Cushing, is bilaterally developed, otherwise I would have had my doubts also regarding my own results today, if such excellent surgical results — morphologically and functionally — could be obtained, as presented in this paper.

Edward R. Laws, Jr., M.D., F.A.C.S.
Department of Neurosurgery
University of Virginia

Neurol Med Chir (Tokyo) 46, March, 2006
This is a very elegant presentation of removal of large intra-third ventricle craniopharyngiomas through the lamina terminalis approach. From the 22 operated adult cases they were able to preserve the pituitary stalk in only two cases, and this structure had to be sacrificed in the remaining 20 cases, thus showing how difficult these tumors can be for radical removal, and only 4 patients needed radiosurgery for residual lesion. However, the main contribution of the authors was to demonstrate that spontaneous resolution of diabetes insipidus — even in panhypopituitary patients — may occur postoperatively (in 4 patients) over 2 years after the procedure if the stalk is cut more distally. The distal renal tubules with time become hypersensitive to a very slight increase of ADH produced by the remaining median eminence and preserved stalk stump.

Raul Marino, Jr., M.D.
Department of Neurosurgery
University of São Paulo Medical School
Instituto Neurológico de São Paulo
São Paulo, Brazil

This is a remarkable series for many reasons even though it is relatively small. The surgical results are nothing short of spectacular from the neurological point. Given the size of the tumors, and location, it is unusual to see such superb results in regard to memory, cognition, and vision. While many patients presented with visual loss of acuity and fields, no patient was made worse from the manipulation of tumor resection. The surgeons should be congratulated for this.

The preoperative endocrine testing was extensive, yet no diabetes insipidus was seen. This is somewhat unusual with such large craniopharyngiomas and perhaps raises the question as to whether the site of ADH secretion was already in flux. The spontaneous resolution of postoperative diabetes insipidus is interesting. In the days when hypophysectomy was done, we often saw transient diabetes insipidus with the concept that secretion of ADH was assumed in the newly formed bulb at the end of the stalk. The observations in this paper reaffirm that, but now add the dimension of hypersensitivity of the distal renal tubules to small amounts of intrinsic ADH. This is not surprising and is well demonstrated here. It reaffirms the surgical concept of a low stalk section when sacrifice of the stalk is necessary. Often the stalk can be identified, but not followed through its entire course. Dissecting it away from the suprasellar tumor to the lowest point is worthwhile for the possibility of transient, rather than permanent, diabetes insipidus.

It would be very interesting to see long-term follow up with enhanced MRI to see if a high intensity spot develops at the stump of the sectioned stalk.

Again, I congratulate this team on superb surgical results and very interesting observations in regard to the diabetes insipidus.

Kalmon D. Post, M.D.
Mount Sinai School of Medicine
New York, New York, U.S.A.