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Preoperative and Postoperative Pituitary Function in Patients with Tuberculum Sellae Meningioma -Based on Pituitary Provocation Tests-

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Abstract

Given the anatomical proximity of tuberculum sellae meningioma (TSM) to the hypothalamo-pituitary system, pituitary function impairments are of great concern. We retrospectively investigated pituitary function changes following surgery in patients with TSM using pituitary provocation tests (PPTs). Thirty-one patients (27 females and 4 males) with TSM underwent initial transcranial surgery (29 patients) or transsphenoidal surgery (two patients); surgeries were performed carefully to avoid injuring the pituitary stalk. In 24 patients, the PPTs were performed via a triple bolus injection with regular insulin, thyrotropin-releasing hormone (TRH), and luteinizing hormone releasing hormone (LH-RH). Seven patients underwent a quadruple test (growth-hormone-releasing factor, corticotrophin-releasing hormone, TRH, and LH-RH). The preoperative and postoperative target hormone levels of the anterior pituitary were normal in 93.5% and 96.8% of patients, respectively. At least one hormonal axis demonstrated impaired PPT responses in two patients (6.5%) preoperatively and in one patient (3.2%) postoperatively. The growth hormone (GH) response was also well preserved. A compromised GH peak level was only observed in one patient (3.2%) preoperatively. Postoperatively, transient diabetes insipidus and transient hyponatremia were observed in four (12.9%) and eight (25.8%) patients, respectively. No patients needed permanent postoperative hormone replacement. The preoperative pituitary function was well preserved in most patients, including those with large tumors pushing against the pituitary stalk considerably or embedded in it. After careful surgery to avoid damaging the pituitary stalk, pituitary function was preserved. However, transient postoperative hyponatremia occurred in 25.8% of patients; thus, surgeons should pay careful attention to this issue.

Key words: hyponatremia, pituitary function, pituitary provoking test, tuberculum sellae meningioma

Introduction

Tuberculum sellae meningioma (TSM) is a collective term that refers to meningiomas arising from the tuberculum sellae, limbus sphenoidale, chiasmatic sulcus, and diaphragma sellae. TSM accounts for 5–10% of all intracranial meningiomas.[1–5] According to the Brain Tumor Registry of Japan, 5.6% of all meningiomas are located in the tuberculum sellae,[6] and TSM comprised 3.6% (36/1011) of all sellar and parasellar tumors that were surgically treated at Kagoshima University and its affiliated hospitals over the last 10 years.

Such tumors commonly impinge on the optic nerve and chiasm causing visual symptoms. In addition, due to the anatomical proximity of TSM to the hypothalamic-pituitary system, hypothalamo-pituitary function is a great concern. The reported incidence of preoperative endocrinologic symptoms widely ranges from 0–42%.[7] However, few of the existing studies focused on the function of the entire

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hypothalamo-anterior pituitary system and many often lacked assessments of hormonal reserve, which can only be elicited by pituitary provocation tests, gold standard analysis of anterior pituitary function.[8] An exceptional report on anterior pituitary provocation test was provided by Fahlbusch et al.,[9] but it was not complete set for comprehensive analysis of anterior pituitary function. Especially, secretory function of growth hormone (GH), the most vulnerable among anterior hormones but essential for keeping good physical and mental condition even in adults,[10,11] can be evaluated solely by provocation test.[8]

Therefore, the primary aim of this study was to identify the changes in anterior pituitary function on the basis of anterior pituitary provocation tests following surgery in patients with TSM. And the incidence and degree of postoperative derangement of electrolyte-water balance, rarely investigated until now, were also our important concern in this study.

Materials and Methods

Patients

The subjects included 31 patients (4 men and 27 women), with previously untreated TSM. Patients underwent either total or subtotal removal of the tumors at Kagoshima University Hospital or Hiroshima University Hospital over the last 15 years under the supervision of senior authors (K.A. and K.K.). The surgical approach was transcranial in 29 patients and transsphenoidal in two patients. The transcranial removal was performed through interhemispheric route in 25, subfrontal route in 3, and trans-Sylvian route in 1. The mean (± standard deviation [SD]) age of the patients was 57.5 ± 9.9 years (range: 36 to 74 years). The maximum tumor diameter ranged from 17 to 60 mm with a mean diameter of 30.0 ± 11.8 mm.

Twenty-five patients were treated due to visual symptoms, while the other six patients were asymptomatic, but underwent treatment to prevent future visual disturbances. None of the patients showed any apparent symptoms of pituitary deficiency. None had thyroid hormone replacement or sexual steroid replacement before surgery.

Assessments

The position of the pituitary stalk and pituitary gland were investigated on pre- and postoperative magnetic resonance images (MRIs).

In order to assess anterior pituitary hormone function, we performed a triple bolus injection that consisted of 0.1–0.12 units/kg of regular insulin, thyrotropin-releasing hormone (TRH, 500 μg), and luteinizing hormone releasing hormone (LH-RH, 100 μg) in 24 patients. For the seven patients who were over 70 years of age, had a past history of chest pain suggesting angina, or had fasting hyperglycemia, we utilized a quadruple bolus injection consisting of GH-releasing factor (100 μg), corticotrophin-releasing hormone (100 μg), TRH (500 μg), and LH-RH (100 μg). We collected blood samples before and 30, 60, and 90 min after the injection to measure the blood levels of the anterior pituitary hormones and target hormones. These provocation tests were performed preoperatively and postoperatively. Postoperative tests were performed 2–6 months after surgery in 73.3% (22/30) of patients. In one patient, the postoperative provocation test was not performed. The GH and adrenocorticotropic hormone (ACTH)-cortisol secretory reserves were assessed only in those patients who underwent triple bolus injection and had sufficient hypoglycemia (<50 mg/dL).

In this study, the criteria for intact secretory function of the pituitary hormones were determined according to Melmed and Kleinberg's criteria.[8] For GH, the peak level was >3 ng/mL. For ACTH-cortisol, the peak cortisol level was >18 μg/dL or an increase of 7 μg/dL from the basal level. For thyroid-stimulating hormone (TSH), the peak value was >2.5-fold of the basal level or >6 mU/L. For prolactin, the peak value was >2.5-fold of the basal level. For LH, the peak value was >3-fold of the basal level or a 10 IU/L increase from the basal. For follicle stimulating hormone (FSH), the peak value was >2-fold of the basal level or a 2 IU/L increase from the basal level. The raw insulin-like growth factor 1 (IGF-1) values were assessed according to the IGF-1 SD scores (IGF-1-SD-scores), which were calculated based on the standard IGF-1 values for each gender and age group in the Japanese population.[12]

Peri-surgical empirical steroid coverage was administered to all patients as follows: 100 mg of hydrocortisone intravenously at anesthetic induction and 100 mg intravenously upon returning to the ward after surgery followed by 10–20 mg of oral hydrocortisone for 2 days. The need for chronic cortisol replacement was determined based on the morning level of blood cortisol at 5–7 days after surgery.

Hormone assay

The assay method, assay kit, sensitivity, and coefficient of variation are presented in Table 1.

Statistical analyses

Data were compared using paired Student's *t*-tests, Mann–Whitney U tests, Fisher's exact tests, and chi-squared tests according to the characteristics of the data sets. Data were analyzed with the Statflex version 6.0 software program (Artech Co., Ltd., Osaka, Japan). A *P* value of <0.05 was considered statistically significant.

Compliance with ethical standards

This retrospective study was approved by the Kagoshima University Hospital Ethical Committee (reference H26-465). The authors certify that this study, which involved human subjects, was conducted in accordance with the Declaration of Helsinki (2013). The data collected here are routinely obtained and are essential for the adequate management of tumors in the sellar and parasellar regions. The data were analyzed anonymously in a linkable fashion to protect the patients' privacy.

Results

Extent of tumor removal

Gross total removal and subtotal removal were achieved in 26 and five patients, respectively. Decompression of the optic nerves and chiasm was possible in all patients. The residual part of the tumor in patients who underwent subtotal removal was near the anterior communicating artery in two patients, beneath the optic chiasm in one, and in the optic canal in two patients.

The pituitary stalk and pituitary gland on MRIs

The pituitary gland was identified on MRIs as a well-enhanced clump in the sella turcica or as being infero-posterior to the tumor in all patients. The pituitary stalk was identified as a well-enhanced cord on the posterior surface of the tumor and was pushed backward in 24 (77.4%) of the 31 patients. Among these 24 patients, 18 stalks were on the midline and six stalks were slightly off the midline. In three (9.7%) patients, the cord-like enhancement was not observed on the surface, but instead seemed to be embedded in the tumor. In four (12.9%) patients, the pituitary stalk was located in its normal position and was not impinged upon by the tumor.

Intraoperative findings

After removing the major part of the tumor that was compressing the optic nerves and chiasm, the pituitary stalk was intently searched behind the posterior aspect of the tumor capsule under the orientation of the acquired preoperative MRIs. In general, the pituitary stalk, which was covered by a thin arachnoid membrane, was separated from the tumor capsule. The pituitary stalks were well preserved in all patients, and the pituitary glands located under the diaphragm sellae were generally untouched.

Postoperative visual function

Preoperatively, 25 patients had visual field impairment with or without decreased visual acuity. Among these patients, visual function improved in 15 patients (60%), was unchanged in eight (32%), and deteriorated in two (8%). Six patients had no preoperative visual disturbances. New visual field deficits appeared in one (16.7%) of these six patients.

Postoperative morbidity

Postoperative morbidities other than visual dysfunction were observed in four (12.9%) patients. The morbidities included chronic subdural hematoma needing irrigation in two patients (6.5%), transient

Table 1 Blood hormone measurements

Hormone	Kit	Assay	Sensitivity	Intra-assay CV (%)
ACTH	Elecsys ACTH Roche	ECLIA	1 pg/mL	0.78
GH	Elecsys hGH Roche	ECLIA	0.03 ng/mL	1.46
TSH	Elecsys TSH Roche	ECLIA	0.005 mIU/mL	1.66
PRL	Elecsys Prolactin III Roche	ECLIA	0.047 ng/mL	1.42
LH	Elecsys LH Roche	ECLIA	0.1 mIU/mL	2.61
FSH	Elecsys FSH II Roche	ECLIA	0.1 mIU/mL	1.70
fT4	Elecsys FT4 II Roche	ECLIA	0.025 ng/dL	1.86
Testosterone	Elecsys Testosterone II Roche	ECLIA	0.025 ng/mL	2.16
IGF-1	IGF-1 IRMA "Daiichi"	IRMA	10 ng/mL	1.80

ACTH: adrenocorticotropic hormone, CV: coefficient of variation, ECLIA: electrochemiluminescence immunoassay, FSH: follicle stimulation hormone, GH: growth hormone, IGF-1: insulin-like growth factor I, IRMA: immunoradiometric assay, LH: luteinizing hormone, PRL: prolactin, TSH: thyroid stimulation hormone.

mild hemiparesis in one (3.2%), and cerebrospinal fluid rhinorrhea needing repair in one patient (3.2%).

Hormones of target organs of the anterior pituitary

Preoperatively, the IGF-1-SD-scores were above the lower normal limit (-2 SD) in 29 (93.5%) of the 31 patients (Fig. 1b). The blood cortisol and fT4 levels were above the lower normal limits at 4 µg/dL and 0.9 ng/mL, respectively, in all patients (Figs. 1c, and 1d). In the four men, the blood testosterone level ranged from 2.3 to 4.9 ng/mL, and was above the lower normal limit (2.0 ng/mL) in all. In the four premenopausal women who were under the age of 47, the estradiol level ranged from 44 to 288 pg/mL, and was above the lower normal limit for both the luteal and follicular phases.

Postoperatively, the IGF-1-SD-scores were above the lower normal limit in all patients. The blood levels of cortisol and fT4 were below the lower normal limit in one patient, but the hormone levels in this patient recovered over time.

Analyses with Student's *t*-tests demonstrated no statistical differences between the pre- and postoperative levels of these target hormones (Fig. 1) (P = 0.89 for IGF-1, 0.97 for IGF-1-SD-score, 0.13 for cortisol, and 0.12 for fT4).

Prolactin level

Preoperatively, two patients showed mild hyperprolactinemia, with levels at 35.4 and 48.6 ng/mL. One of them became normoprolactinemic postoperatively.

Assessment of anterior pituitary function by the pituitary provocation test

For GH and ACTH-cortisol, the peak level assessments with provocation tests were limited to the 21 patients who underwent triple (insulin, TRH, and LH-RH) bolus injection and had sufficient hypoglycemia (<50 mg/dL).

At least one function of the anterior pituitary was judged to be impaired in two patients (6.5%). The peak TSH, prolactin, LH, and FSH values did not reach the criteria for normal responses in one patient. In another, the peak GH level was 2.9 ng/mL, which is slightly lower than the lower limit of the normal response (3 ng/mL) (Fig. 2a).

The postoperative pituitary provocation test showed that the responses of these two patients returned to normal. However, in another patient, the peak cortisol value was 15 µg/dL, which did not reach the lower normal limit (18 ng/mL) or the minimum increase of >7 µg/dL from the basal level (Fig. 2b).

In total, none of the patients needed permanent postoperative hormone replacement. Thus, in general, anterior pituitary function was well preserved pre- or postoperatively in more than 90% of cases.

Changes in the basal and peak hormone levels

Student's *t*-tests were performed to compare the hormone levels obtained during the provocation tests between the pre- and postoperative periods. The results showed slight but significant postoperative decreases in the peak cortisol level

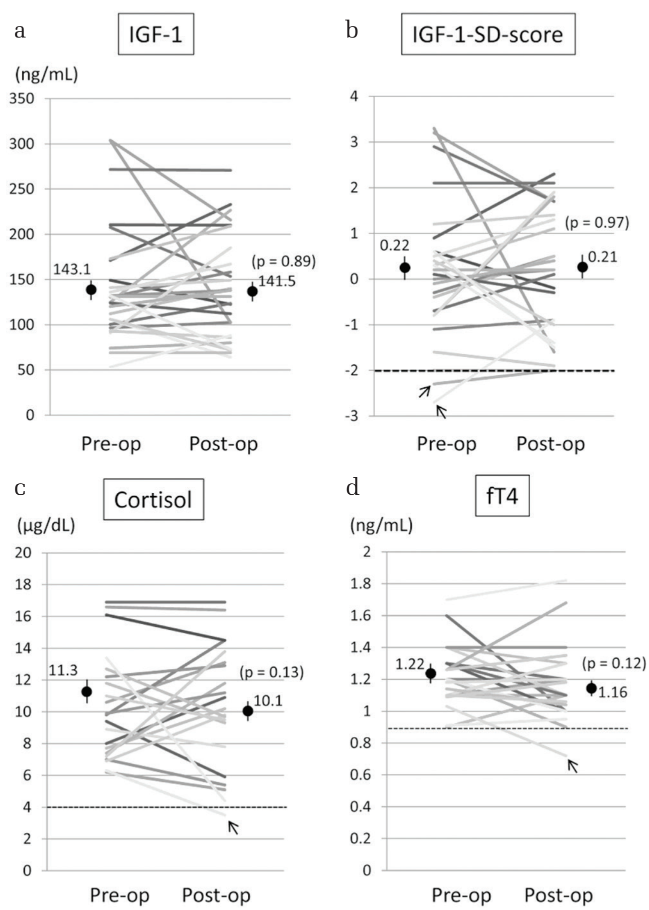

Fig. 1 Blood concentrations of target hormones in the anterior pituitary. (a) Insulin like growth factor-1 (IGF-1). (b) IGF-1-SD (standard deviation)-score. The preoperative IGF-1-SD-score was under the normal limit in two (6.5%) of the 31 patients (*arrow*). The *dotted line* indicates the lower normal limit. (c) Cortisol. The postoperative fasting blood level of cortisol was under the normal limit in one patient (3.2%) (*arrow*). The *dotted line* indicates the lower normal limit. (d) fT4. The postoperative blood level of fT4 was under the normal limit in one patient (3.2%) (*arrow*). The *dotted line* indicates the lower normal limit. Pre-op: preoperative, Post-op: postoperative. Closed circles with bars indicate the mean ± standard error. Numerals in parentheses show the *P* value for the paired Student's *t*-test.

(from 24.3 to 22.5 μg/dL, $P = 0.04$; Fig. 2b) and in the basal LH level (from 20.8 to 18.3 mIU/mL, $P = 0.03$; Fig. 2e). As for the other hormones, no changes in the basal or peak levels were observed during the provocation tests (Figs. 2a, 2c, 2d, and 2f).

Water and electrolyte balance

Transient diabetes insipidus was observed in four patients (12.9%). Hyponatremia (Na <135 mEq/L) was observed in eight (25.8%) patients after surgery. The lowest Na level ranged from 133 to 114 mEq/L, with a mean (± SD) value of 121.8 ± 5.8 mEq/L. In seven patients, the lowest level was <125 mEq/L. The lowest levels were recorded 4 to 12 days after surgery, with a mean of 8.6 ± 2.6 days and median of 9 days. Three of the eight patients with hyponatremia had preceding diabetes insipidus. Five of these eight patients presented with symptoms of hyponatremia including nausea, appetite loss, and lethargy. The hyponatremia was successfully controlled within several days without sequelae by fluid restriction and oral sodium loading with/without mineral corticoid tablets.

There were no statistical differences in the clinical factors, including age, sex, tumor size, surgical approach, degree of tumor removal (Simpson's grade), and postoperative endocrine dysfunction, between cases with postoperative hyponatremia and those without hyponatremia, but postoperative diabetes insipidus was significantly more frequent in patients with hyponatremia than it was in those without hyponatremia ($P = 0.04$) (Table 2).

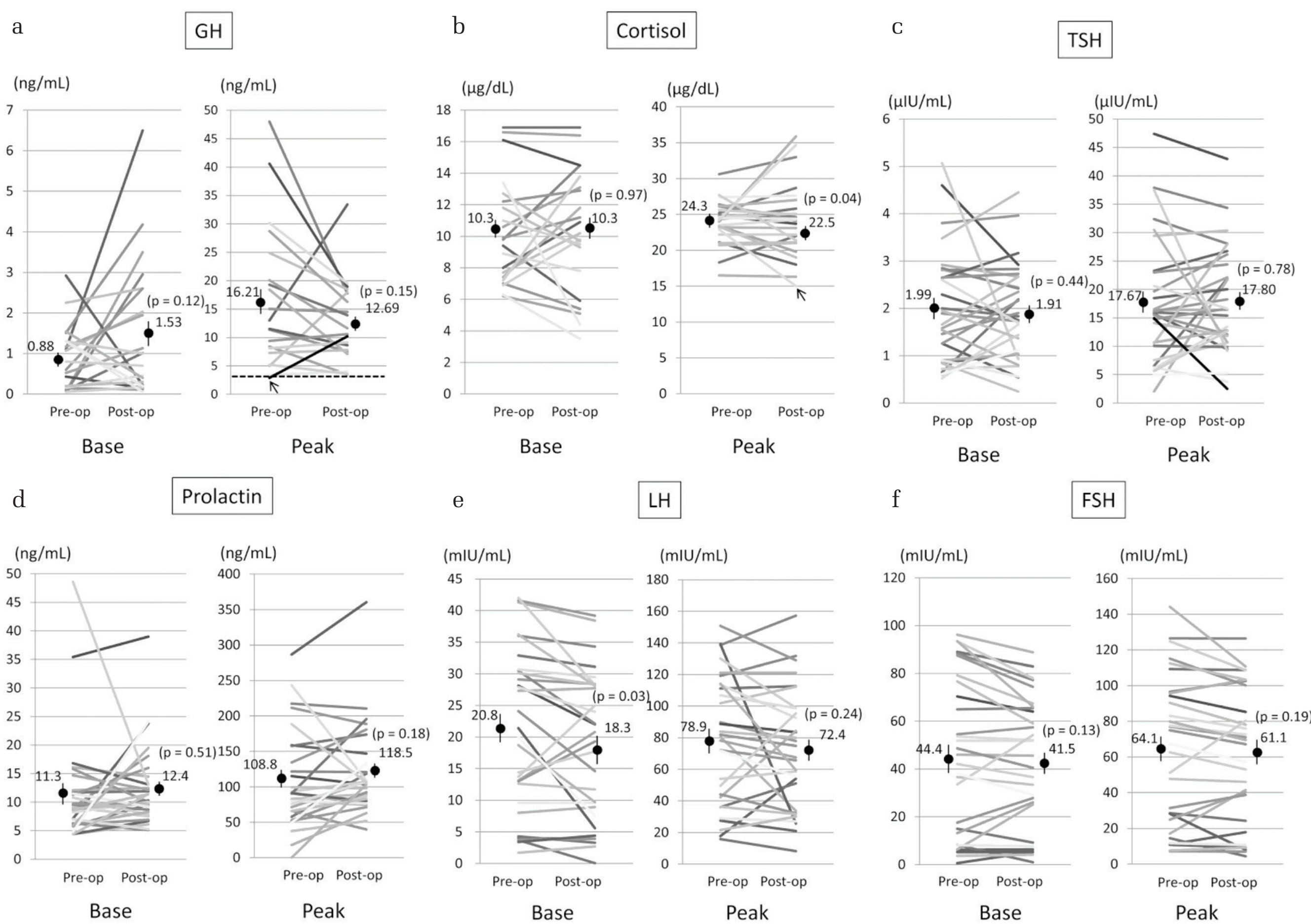

Fig. 2 Results of the pituitary provocation tests. (a) Growth hormone (GH). The preoperative peak level did not reach the normal limit in one case (*arrow*). The *dotted line* indicates the lower normal limit of the peak GH level. (b) Cortisol. The postoperative peak level did not reach the normal limit in one patient (*arrow*). The postoperative peak values of cortisol were significantly lower than the preoperative levels. (c) Thyroid stimulating hormone (TSH). (d) Prolactin. (e) Luteinizing hormone (LH). The postoperative basal values of LH were significantly lower than the preoperative values. (f) Follicle stimulating hormone (FSH). Pre-op: preoperative, Post-op: postoperative. Closed circles with bars indicate the mean ± standard error. Numerals in parentheses show the *P* value for paired Student's *t* test.

Table 2 Comparison of the clinical factors between cases with postoperative hyponatremia and cases without hyponatremia

	Mean (SD)		
	Hyponatremia	No hyponatremia	*P* value
Age (years)	52.5 ± 8.3	59.2 ± 10.0	0.10[a]
Sex (male/female)	0/8	4/19	0.32[b]
Tumor size (mm)	24.0 ± 8.3	28.6 ± 9.6	0.14[a]
Surgical approach (TC/TS)	6/2	23/0	0.06[b]
Simpson's grade (I/II/III/IV/V)	2/4/0/2/0	3/17/0/3/0	0.82[c]
Postoperative DI (yes/no)	3/5	1/22	0.04[b]
Postoperative pituitary dysfunction (yes/no)	0/8	2/21	0.60[b]

[a]Mann-Whitney *U* test, [b]Fisher's exact test, [c]Chi-squared test, DI: diabetes insipidus, SD: standard deviation, TC: transcranial, TS: transsphenoidal.

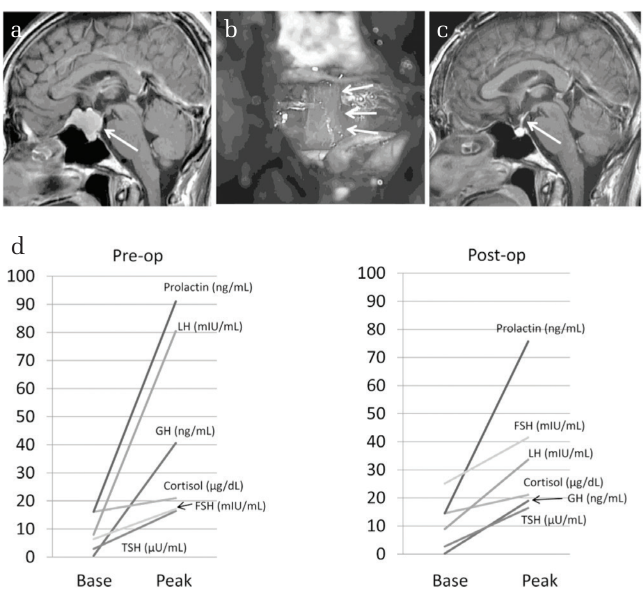

Fig. 3 A 47-year-old woman with tuberculum sellae meningioma. (a) Preoperative sagittal magnetic resonance image (MRI) shows a suprasellar tumor pushing the pituitary stalk backward (*arrow*). (b) Intraoperative photo acquired after the tumor was removed shows that the pituitary stalk is well preserved (*arrows*). (c) Postoperative MRI also shows the intact pituitary stalk (*arrow*). (d) Results of the pre- and postoperative triple bolus injection in this patient. The secretory functions of all hormones were well preserved. Pre-op: preoperative, Post-op: postoperative.

Representative cases

Case 1: A 47-year-old woman with TSM who presented with bitemporal hemianopia and decreased eyesight in her right eye underwent tumor removal through the interhemispheric approach. Preoperative MRIs showed that the tumor had pushed the pituitary stalk backward considerably (Fig. 3a). The stalk was separated from the tumor capsule and was well preserved during the transcranial surgery (Fig. 3b). Postoperative MRIs revealed the total removal of the tumor and an intact pituitary stalk (Fig. 3c). Pre- and postoperative anterior provocation tests showed normal basal and peak hormone values (Fig. 3d).

Case 2: A 60-year-old woman with incidentally found TSM (Fig. 4a) underwent endoscopic transsphenoidal surgery. Postoperative MRIs showed total removal of the tumor and an intact pituitary stalk (Fig. 4b). Preoperative and postoperative pituitary provocation tests revealed normal anterior pituitary function. Transient diabetes insipidus was observed on postoperative day 3. On postoperative days 5 to 8, the patient was lethargic and showed appetite loss. At this point, the blood Na level was the lowest at 125 mEq/L (Fig. 4c). Fluid restriction and oral salt loading provided normalization of the Na level and the patient was discharged on postoperative day 16 without sequelae.

Discussion

This is the first reported series of TSM, in which comprehensive analysis of anterior pituitary function was conducted. Due to impingement of the pituitary stalk by the tumor, there is a reasonable concern for hypothalamo-pituitary disorders in patients with TSM. In most of the patients we examined, the pituitary stalk was largely pushed backward on preoperative MRIs. In some, it was unidentified due to encasement by the tumor. However, pre- and postoperative pituitary provocation tests showed well-maintained anterior pituitary function in almost all patients in the present study.

In a review by Bassiouni et al., preoperative hypopituitarism varied widely from 0 to 42%.[7] According to the review by Dusick et al.,[13] hypo-

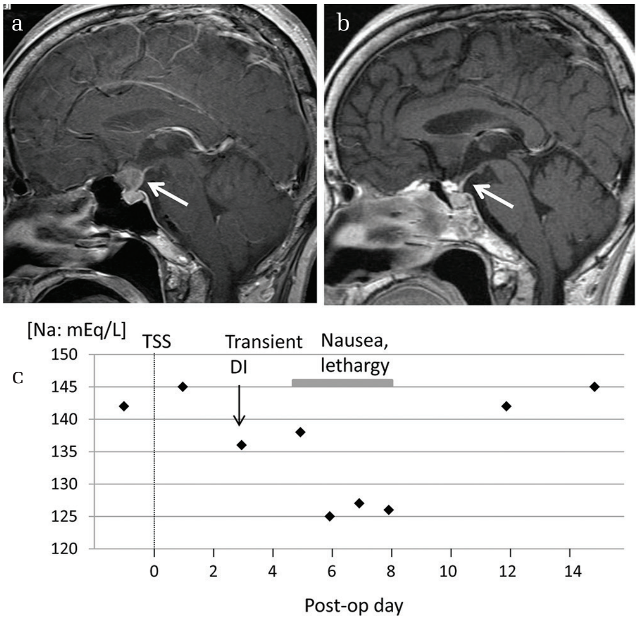

Fig. 4 A 60-year-old woman with tuberculum sellae meningioma. (a) Preoperative magnetic resonance image (MRI) shows a suprasellar tumor, which slightly compressed the pituitary stalk (*arrow*). (b) Postoperative MRI shows total removal of the tumor and the intact pituitary stalk (*arrow*). (c) Peri-operative changes in the blood Na level, which hit the lowest point (125 mEq/L) 6 days after surgery. TSS: transsphenoidal surgery, DI: diabetes insipidus.

pituitarism was noted in 7–14.5% of patients. The variety seems to be due to the different modalities used to assess anterior pituitary function. Moreover, many of the studies did not perform the pituitary provocation tests that are essential for evaluating the pituitary reserve. Although Fahlbusch and Schott[9)] reported the results of pituitary stimulation with a combination of ACTH, gonadotropin-releasing hormone, and TRH, this combination stimulation still could not precisely evaluate ACTH-cortisol and GH secretion.

Here, we performed a triple bolus injection, which served as a comprehensive assessment of anterior pituitary function. A quadruple bolus injection was performed in the other seven patients who were unsuitable for the triple bolus injection. These seven patients were omitted from the assessments for the GH or ACTH-cortisol response but were included in the assessments for the other hormones.

Preoperatively, two patients (6.5%) had impaired responses in at least one of the six anterior pituitary axes. The low rates of anterior pituitary dysfunction in our patients with TSM are in marked contrast to the high rate of pituitary deficiency in patients with nonfunctioning pituitary adenoma, with more than 50% of those patients exhibiting anterior pituitary hormone deficiency.[14-17)] The main cause of the hypopituitarism in pituitary adenoma is likely direct compression of the pituitary tissue by the adenoma, which arises within the anterior pituitary gland. In contrast, TSM rarely compresses the pituitary gland itself; it generally compresses the pituitary stalk considerably. However, the arachnoid membrane between the pituitary stalk and tumor surface may serve as good protection against derangement of the pituitary portal system.

In our series, new postoperative impairment of anterior pituitary hormones was only observed in 3.2% of patients. No patients needed permanent postoperative hormone replacement. According to Bassiouni et al., new postoperative pituitary dysfunction was found in 21.6% of patients for the adrenal axis.[7)] In our surgeries, we scrupulously scouted for the pituitary stalk after identifying the bilateral optic nerves and chiasm; it was usually found on the midline behind the tumor capsule. The stalk was generally observed to be covered by a thin arachnoid membrane. We carefully separated the tumor capsule from the pituitary stalk, leaving the arachnoid membrane undisrupted whenever possible. We were able to observe the pituitary stalk in all of the patients, including the three patients in whom the pituitary stalk was not identified on preoperative MRIs. Through this "pituitary-oriented surgery," we could recover pituitary function in two patients with preoperatively impaired responses and minimize the rate of new pituitary insufficiency cases.

As GH is the most vulnerable of the six anterior pituitary hormones to a variety of insults, including compression by tumors and radiation therapy,[14,18,19] it can serve as a good indicator of diminutive pituitary dysfunction. We observed only one patient with a compromised preoperative GH peak (2.9 ng/mL), which recovered well after the surgery. None of the patients had severe growth hormone deficiency (GHD) (peak GH <1.8 ng/mL) in either the preoperative or postoperative provocation tests.

However, the comparison of the hormone levels between the preoperative and postoperative periods showed slight but significant decreases in the basal levels of LH and peak cortisol levels. This fact suggested that the impact of the surgical intervention on the hypothalamo-pituitary axis was not negligible. This means reckless or aggressive manipulation of the pituitary stalk may result in permanent impairment of pituitary functions.

Regarding the hypothalamo-posterior pituitary axis, preoperative diabetes insipidus has very rarely been reported.[7,20)] Postoperative diabetes insipidus has been reported in 3–26% of patients.[4,7,20,21] In our study, postoperative diabetes insipidus occurred in 12.9% of patients, and all were transient, concordant with past reports.

In patients with TSM, postoperative hyponatremia has rarely been reported, except for in a study by Symon and Rosenstein,[20] where hyponatremia was observed in five of 101 postoperative patients. In our series, hyponatremia was observed in a quarter of the patients. A number of potential causes of hyponatremia exist in patients who have undergone pituitary surgery. The syndrome of inappropriate antidiuretic hormone secretion is one of the most common causes of postoperative hyponatremia.[22–25] Other potential causes of hyponatremia include hypocortisolemia, volume overload, over administration of desmopressin, and hypothyroidism. If hyponatremia occurs during the early postoperative period, then cortisol deficiency or fluid overload may be surmised as the causes. However, in our patients, a stress dose steroid was administered during the early postoperative period and the nadir of the serum Na occurred 8.6 days after surgery.

Transsphenoidal pituitary surgery or injury of the neurohypophysis can produce a triphasic response of vasopressin release characterized by diabetes insipidus followed by the syndrome of inappropriate antidiuretic hormone secretion.[25] In cases with TSM, the neurohypophysis was rarely manipulated. However, even mild manipulation of the pituitary stalk when attempting to separate it from the tumor capsule may cause the same triphasic secretion of vasopressin and lead to delayed hyponatremia. In our eight patients with hyponatremia, three had precedent diabetes insipidus, as is shown in Table 2. Regardless of the responsible pathophysiologic mechanism, it is important to be aware of the possibility of this postoperative condition, and clinicians should monitor the serum Na level on at least day 8 after surgery for early detection.

Conclusion

In this study, we found that the preoperative hypothalamo-pituitary axis was well preserved in almost all of the patients, even in patients with large tumors that were severely compressing the pituitary stalk. After surgery, the pituitary stalk remained intact and pituitary function was well preserved. However, the possibility of permanent postoperative pituitary dysfunction induced by aggressive manipulation should be heeded. Moreover, clinicians should pay careful attention to transient postoperative hyponatremia.

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Conflicts of Interest Disclosure

We declare that each of us acknowledges that he or she participated sufficiently in the work to take public responsibility for this paper content. Moreover, we declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the paper reported. All authors who are members of The Japan Neurological Society have registered online self-reported COI Disclosure Statement Forms through the JNS member website.

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