



## Severe Delayed Postoperative Hyponatremia in a Case of TSH-secreting Pituitary Adenoma: A Case Report

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### Abstract

Transsphenoidal resection has been well accepted as the most suitable treatment for TSH-secreting pituitary adenomas. However, due to its rare incidence, appropriate clinical practice for the post-surgical management remains to be accumulated. We report here a case of a 53-year-old male patient diagnosed to have a Thyroid-Stimulating Hormone (TSH)-secreting pituitary adenoma. The tumor was successfully removed by transsphenoidal resection, and the histological examination elucidated a pituitary adenoma with TSH positive staining. The serum level of TSH restored to normal after 3 months and eMRI detection demonstrated no sign of recurrence 12 months after the surgery. Serum levels of T3, T4, FT3, FT4 and TSH were all normal during a 42-month follow-up. While notably, 8 days after the surgery, the patient underwent severe hyponatremia (lowest to 113 mmol/l Na<sup>+</sup>) with lethargy, and the serum level of Na<sup>+</sup> was recovered to 134 mmol/l on day 11 after emergent treatment of hypertonic saline and high salt food. This case reveals the risk of postoperative hyponatremia for thyrotrophinoma patients even with a successful resection of the tumor, which emphasized the significance of combination treatments, including 1-2 weeks prolonged hospitalization, to avoid the severe threats to patients' lives after transsphenoidal resection.

**Keywords:** TSH-secreting pituitary adenomas; Transsphenoidal resection; Hyponatremia

### Introduction

Among pituitary adenomas, the incidence of Thyroid-Stimulating Hormone (TSH)-secreting pituitary adenoma, which is diagnosed by abnormal secretion of TSH and resistance of thyroid hormone, represents only 0.5% to 3% of all pituitary adenomas [1-5]. However, the diagnosis and management of these rare tumors have been improved considerably in the last two decades, due to the spread of the concept of inappropriate secretion of TSH, ultrasensitive methods for TSH measurement, the improvement in pituitary imaging, all of which lead to a better recognition of pituitary microadenomas [6-9]. Treatment of TSH-secreting pituitary adenomas commonly includes transsphenoidal surgery, medical therapy of somatostatin analogs and radiotherapy [9-11]. Once a diagnosis of a pituitary macroadenoma is confirmed, transsphenoidal surgery is usually the best approach for initial surgical management due to its thorough removal of the tumor, maximal preservation of normal pituitary function, and a quick recovery conferred by minimally invasive injury [12,13]. However, although patients with transsphenoidal surgery normally can be discharged from the hospital within 4-5 days, some of these patients developed different complications such as malignant hyperthermia syndrome, Cerebrospinal Fluid (CSF) leaks, various degrees of pituitary dysfunctions and delayed hypernatremia [14]. So a suitable post-surgical management protocol remains to be established to prevent severe complications. Herein, we report the clinical diagnosis, surgical resection and follow-up features of TSH-secreting pituitary adenomas in a patient, who showed overt hyponatremia after the transsphenoidal surgery, emphasizing the importance of prolonged hospitalization to avoid severe complications.

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**Table 1:** Thyroid function tests during diagnosis, surgery and postoperative follow-up.

	FT4 (pmol/L)	T4 (nmol/L)	FT3 (pmol/L)	T3 (nmol/L)	TSH (μIU/mL)
Reference	11.48-22.70	58.1-140.6	3.5-6.5	0.92-2.79	0.55-4.78
2015.7.20	24.24	195.4	7.78	2.74	3.34
2015.7.24	26.29	180.8	9.24	2.82	3.2
	FT4 (ng/dl)	T4 (μg/dl)	FT3 (pg/ml)	T3 (ng/ml)	TSH (μIU/mL)
Reference	0.81-1.89	4.3-12.5	1.8-4.1	0.66-1.92	0.38-4.34
2015.8.4	2.02	13.24	5.23	1.71	2.66
2015.8.5	1.86	12.49	4.38	1.41	0.62
2015.8.6	1.62	10.86	3.83	1.12	0.26
2015.8.7	1.67	12	3.38	1.08	0.2
2015.10.27	1.13	7.97	1.92	0.69	0.07
2015.11.5	0.94	6.82	1.62	0.56	0.02
2016.1.18	1.03	8.91	2.6	1.12	1.72
2016.5.13	1.07	8.9	2.9	1.17	2.51
2016.11.2	1.13	9.4	2.84	0.93	1.97
2017.11.7	1.17	9.62	2.9	1.18	2.09
2019.4.23	1.09	7.5	2.57	0.83	2.27
	FT4 (pmol/L)	T4 (nmol/L)	FT3 (pmol/L)	T3 (nmol/L)	TSH (μIU/mL)
Reference	7.64-16.03	69.97-152.52	3.28-6.47	1.01-2.48	0.49-4.91
2018.9.3	9.74	117.84	4.85	1.43	1.67

The thyroid function tests were conducted for several times in different hospitals and at multiple time points from the primary diagnosis in 2015 to postoperative follow-up until 2019, discrepancy in the reference range cannot be avoided.

## Case Presentation

On July 20 of 2015, a 53-year-old male patient, suffering from insomnia, marasmus and agitation, was referred to hospital for physical examinations. The thyroid function tests showed elevated levels of serum-T3, T4, FT3, FT4 and normal serum TSH (Table 1), indicating the potential occurrence of hyperthyroidism. Color Doppler examination of thyroid was conducted and showed normal results (Figure 1A). The detection of Thyroid Stimulating Hormone Receptor Antibody (TRAb), Thyroglobulin Antibody (TGAb), Thyroid Peroxidase Antibody (TPOAb) and Thyroglobulin (Tg) excluded autoimmune thyroid diseases (Table 2). The levels of LH, cortisol, estradiol, GH, testosterone and FSH were normal, while slight upregulation of PRL was observed (Table 3). Based on the elevated thyroid hormones but normal TSH, Gd-DTPA enhanced MRI was conducted, showing enlarged sella and pituitary gland with suprasellar extension, with a size of about 1.5 cm × 1.1 cm × 1.3 cm (Figure 1B). The pituitary stalk was skewed to the right and displaced upward. To further investigate the subtype of the pituitary adenoma, the patient was subcutaneously treated with somatostatin (0.1 mg Q8h). Thyroid function tests were performed 12 h, 24 h, 48 h, and 72 h later and showed typical sensitivities with thyroid hormones recovering to normal levels (Table 1). Based on these clinical evaluations, the patient was primarily diagnosed with TSH-secreting pituitary adenoma and resection of the tumor mass was planned. Before surgery, the patient was injected with 20 mg Sandostatin LAR once a month for 3 months to decrease thyroid crisis and improve the complete resection of the tumor mass. On October 26<sup>th</sup> of 2015, the patient underwent transsphenoidal adenomectomy. The tumor was dissected from the pituitary stalk without mechanical injury. Bilateral cavernous sinus had complete medial wall and sellar septum, and no gross invasion was observed. A small amount of cerebrospinal

**Table 2:** Main thyroid antigens before and after surgery.

	Reference	2015.7.20	2018.9.3
TRAb (IU/L)	0-1.75	<0.3	<0.3
TGAb (IU/ml)	0-115	12.75	10.50
TPOAb (IU/ml)	0-34	8.60	12.87
Tg (ng/ml)	3.5-77	12.05	-

fluid leakage was found during the operation, which was repaired with the thigh fascia. Immunohistochemical staining revealed that the tumor was positive for TSH (Figure 1C). On postoperative day 6, serum sodium level was decreased to 127 mmol/L and the patient was treated with timely electrolytic therapy (Table 4). However, the serum sodium level further decreased to 113 mmol/L and the patient fell into coma on POD 8, demonstrating a definite symptom of hyponatremia. Antiemetic combined with high-salt food was administered to correct electrolyte balance and the normal level of serum sodium (134 mmol/L) was achieved 3 days later. Without sign of hyponatremia, the patient was discharged from the hospital on POD 12. The thyroid hormones were restored to normal levels at 3-month follow-up evaluation and remained in the reference ranges 6 and 12 months after the surgery (Table 1). The eMRI of hypothalamic-pituitary region revealed no evidence of tumor recurrence (Figure 1D and E). At 24-month and 36-month follow-up evaluations, the levels of thyroid hormones, main thyroid antigens and pituitary hormones were all in the normal ranges (Table 1-3). The last 42-month follow-up test showed normal levels of TSH, T3, T4, FT3 and FT4 (Table 1), indicating the success of this treatment.

## Discussion

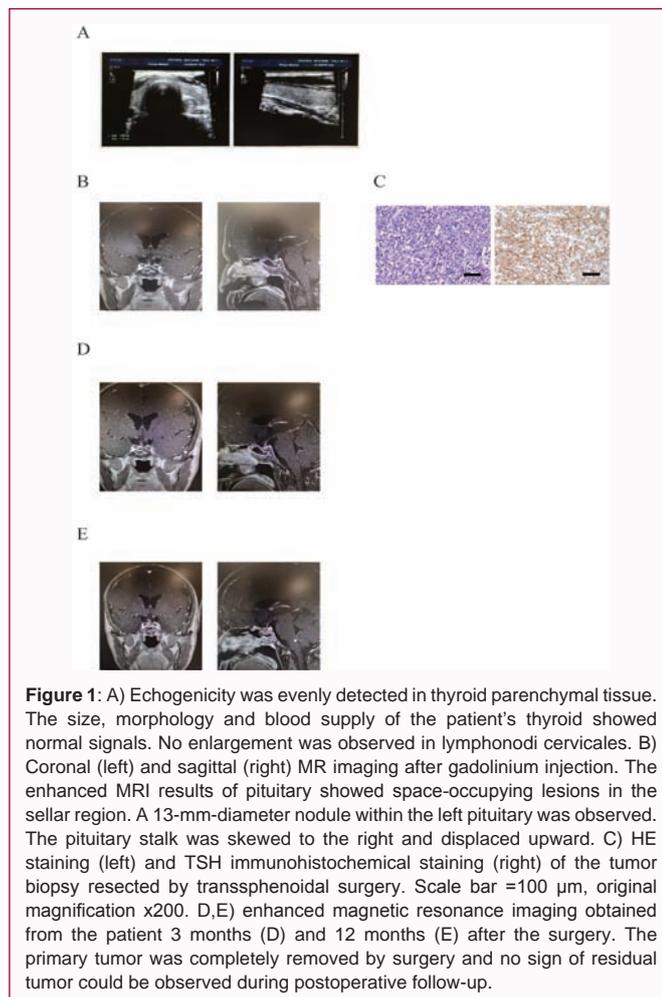
Primary diagnosis of TSH-secreting pituitary adenomas is usually based on the observation of hyperthyroidism with inappropriately

**Table 3:** Hormonal tests before and after surgery.

	Reference	2015.8.4	2017.11.7	2018.9.3	2019.4.23
FSH (mIU/ml)	1.27-19.28	3.29	3.07	3.39	2.72
estradiol (pg/ml)	0-47	-	30.00	32.00	29.00
testosterone (ng/ml)	1.75-7.81	6.98	7.65	8.89	6.98
LH (mIU/ml)	1.24-8.62	1.74	2.74	3.12	2.84
PRL (ng/ml)	2.64-13.13	16.47	5.62	4.97	5.60
GH (ng/ml)	0.03-2.47	0.70	-	-	-
cortisol (µg/dl)	4.4-19.9	9.41	14.97	12.51	-

**Table 4:** Na<sup>+</sup> levels during postoperative course.

	POD 1	POD 2	POD 6	POD 8	POD 11	POD 12
Na <sup>+</sup> (mM) (135-145)	136	141	127	113	134	134



high or normal levels of TSH. Therefore, approximately 30% of TSH-secreting adenomas were misdiagnosed as hyperthyroidism, which were generally followed by thyroid ablative treatment [14-16]. In our case, based on thyroid function tests, color Doppler examination of thyroid and eMRI, TSH-secreting pituitary adenomas was finally determined. So abnormality in thyroid function tests should be seriously carried out, and comprehensive physical examination is also necessary for an accurate diagnosis. Our patient developed acute hyponatremia 8 days after transsphenoidal surgery. Similarly, some other cases demonstrated that patients with transsphenoidal resection of TSH-secreting pituitary adenoma experienced the

risk of hyponatremia [16,17]. Most patients undergoing Delayed Postoperative Hyponatremia (DPH) had no specific symptoms at the beginning but fall into danger finally, so the prediction and prevention of DPH is extremely meaningful to avoid this serious complication. The older age was a predictive factor of DPH and the decline of serum Na<sup>+</sup> levels tended to be greater in patients older than 60 years. In addition, a low BMI was found to be intimately associated with development of DPH. Therefore, prolonged hospitalization with close serum electrolyte level monitoring for 1-2 weeks is absolutely required for patients undergoing transsphenoidal surgeries, especially for older patients with low BMI.

## Conclusion

In conclusion, the present case provides new insight into the clinical research about the safety of surgical resection in patients with TSH-secreting pituitary adenomas. Although the minimally invasive transsphenoidal resection of the primary tumor endows the patients with quick recovery, we strongly recommend additional 1-2 week hospitalization to avoid the occurrence of severe hyponatremia symptom and save lives of DPH patients.

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