CASE REPORT

A 38-year-old female was brought to our emergency department due to fever, general weakness and days of poor appetite. She had come to our hospital for the first time in August, 1989 due to progressively enlarged zygomatic arch for 3 months. After studies, bitemporal hemianopia was also noted by visual field examination. The basal hormone data showed that growth hormone was 2.13 ng/mL (reference range: less than 5 ng/mL; Table 1). The serum cortisol level was undetectable. Intravenous hydrocortisone was administered after the diagnosis of acute adrenal insufficiency. The patient improved physically after treatment, but social withdrawal and inappropriate affect persisted. We present the case and review the relevant literature to impress on physicians that the cognitive disorders in hypopituitarism can result from not only hormone deficiency, but also the influences of pituitary tumor surgery and radiotherapy on neuropsychological functions.
mography (CT) revealed a pituitary tumor with perisellar extension. The patient first received an operation of trans-sphenoid adenomectomy on September 1st, 1989. The pathology report proved an acidophil adenoma. However, visual field defects did not improve after the operation. The follow-up serum concentration of growth hormone was still high. Brain CT revealed that superior part of the pituitary adenoma was not completely removed, with compression of the optic chiasma. In the same year, she received subsequent postoperative radiotherapy with a total dosage of 6000 cGy during 6 weeks by 10 MV x-ray from bilateral opposed parallel ports. Unfortunately, follow-up magnetic resonance imaging (MRI) of sella in 1990 demonstrated residual tumor tissue, and random serum growth hormone concentration was 5.81 ng/mL. The highest serum growth hormone after oral glucose suppression was 4.71 ng/mL. Therefore, a secondary operation by transfrontal craniostomy was decided on and the pathology result showed residual acidophil adenoma with fibro-adipose tissue. The immunohistochemical staining of the adenoma was positive to both growth hormone and prolactin. After the two operations and one course of radiotherapy, a panhypopituitarism state progressively developed and thyroid, glucocorticoid and estrogen combined with the progesterational agent were given for hormone replacement therapy. However, the patient’s family first noted that she suffered from a per sonal ity change and unstable emotions. She had visited our psy chi a try out pa tient de part ment in 1991 and an organic mood disorder was noted. The thyroid function test was normal at that time. There af ter, the patient had not had regular follow-up at our hos pital for about 9 years until this admission.

### Table 1. The levels of hormones before and after operation and radiotherapy

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Before operation (normal range)</th>
<th>After operation (normal range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone</td>
<td>2.13a (&lt; 5 ng/mL)</td>
<td>&lt; 0.1b (&lt; 5 ng/mL)</td>
</tr>
<tr>
<td>Prolactin</td>
<td>301a (&lt; 600 uIU/mL)</td>
<td>1.1b (3.0 - 20.0 ng/mL)</td>
</tr>
<tr>
<td>ACTH</td>
<td>12.3a (&lt; 46 pg/mL)</td>
<td>12.3b (5 - 25 pg/mL)</td>
</tr>
<tr>
<td>Cortisol</td>
<td>219a (50 - 250 ng/mL)</td>
<td>&lt; 1.0b (0.4 - 4.0 uIU/mL)</td>
</tr>
<tr>
<td>TSH</td>
<td>2.11a (&lt; 6.2 uU/mL)</td>
<td>0.36b (0.4 - 4.0 uIU/mL)</td>
</tr>
<tr>
<td>T4</td>
<td>5.84a (6.0 - 12.0 ug/dL)</td>
<td>&lt; 3.0b (1 - 30 mIU/mL)</td>
</tr>
<tr>
<td>FSH</td>
<td>12.41a (1 - 30 mIU/mL)</td>
<td>7.19b (1 - 30 mIU/mL)</td>
</tr>
<tr>
<td>LH</td>
<td>7.19a (1 - 30 mIU/mL)</td>
<td>7.19b (1 - 30 mIU/mL)</td>
</tr>
</tbody>
</table>

*a measured by RIA; b measured by Immunometric assay.

At the emergency department, the physical examination showed that blood pressure was 82/46 mmHg and body temperature was 38.9°C. In addition, mild memory impairment, unstable mood, social withdrawal and perseverative thoughts were also noted, but there was no disorientation to time, persons or places, and other physical examination findings were essentially normal. The patient’s mental state was regu lar and she was not ed for her sex hormone replacement after the operation. Laboratory analysis revealed a white blood cell count of 9600/mm³, plasma glucose level of 68 mg/dL, serum sodium level of 138 mEq/L, and serum potassium level of 4.3 mEq/L. Lumbar puncture was performed to rule out central nervous system infection, and the result was normal. The serum free thyroxine level was 9.4 pg/mL (reference range: 7 - 19 pg/mL), and ACTH level was 12.3 pg/mL (normal range 0 - 46 pg/mL), with an undetectable serum cortisol that also did not show any increase after a 1 mg dexamethasone suppression injection. The growth hormone concentration was not detectable, and prolactin was only 1.1 ng/mL (reference range: 3.0 - 20.0 ng/mL). Based on the patient’s past history, clinical mani festation and laboratory examination results, acute adrenal crisis was diagnosed at first, and intravenous hydrocortisone was administrated immediately. After hydrocortisone treatment, the serum cortisol concentration was up to 12.6 µg/dL. The fever, poor appetite, and general weakness subsided and her condition improved, but her psychological symptoms still persisted during hospitalization. Brain injury-induced affective disorder and false cognitive function were diagnosed by a psychologist consultant. The MRI of the brain demonstrated no obvious brain damage, except empty change at the sellar area was
noted with out any re sid ual tu mor tis sues (Fig. 1).

DISCUSSION

We present a patient with adrenal insufficiency and psychiatric disorders after pituitary tumor surgery and radiotherapy. A state of hypoadrenalism developed after repeated pituitary gland operations and their concomitant radiotherapy. Psychiatric symptoms and signs have long been recognized in patients with adrenocortical insufficiency. Cyclic mood change, such as depression, apathy, delirium or confusion, and memory impairment are common findings in most reported cases. Other less frequent psychiatric presentations include paranoia, schizophrenia or self-mutilation. These psychiatric disorders might even occur as the first manifestation of adrenal hypofunction before the appearance of the well-known symptoms and signs, such as poor appetite, weight loss or constitutional malaise. Under such conditions, the adrenal insufficiency itself was even probably misdiagnosed as primary psychological disorder at first. The high serum ACTH value is thought to be the major cause for the development of psychiatric symptoms in Addison’s disease, though the associated low glucocorticoid state, metabolic disturbance, hypoxemia or hypotension have also been implicated. In the anterior pituitary gland, the ACTH andendorphin come from the same precursor. A hyper-ACTH state might then lead to endorphin overscretion, leading to mental change. Our patient, in contrast to most reported cases of Addison’s disease, suffered from secondary adrenal insufficiency, in which cortisol and ACTH secretions were low. In fact, the ACTH deficiency state has been reported in cases with depressive symptoms or apathy which were improved after ACTH injection. Generally, the psychiatric manifestations were remitted fully or improved significantly soon after the hormone replacement. However, in our patient, the mental disorder persisted in spite of adequate hormone supplementation. The other possible mechanisms, such as organic brain damage after her repeated surgeries and radiotherapy should be taken into consideration.

Cerebral dysfunction has been reported in patients after pituitary tumor surgery or radiotherapy. The damage could result either from the tumor itself, surgical trauma or irradiation. By transfrontal approach during pituitary surgery, the frontal lobe was retracted and damage to small perforating arteries or vasospasm occurred with subsequent nervous ischemic injury, which might be responsible for the frontal destruc tion in our patient, though no obvious brain tissue damage was noted on brain MRI. From the lobe in jury has been shown in several studies to cause memory impairment, mood change or cognition disturbances. This patient, in spite of adequate hormone replacement, had persistent psychiatric symptoms, that could be partly explained by the permanent damage of the frontal lobe.

In addition to surgical injuries, this patient also received radiotherapy, which could be as significant with adverse effects on the balance structures, such as the hypothalamus, frontal and temporal lobes, which could result in so-called delayed cerebral radiation necrosis. In this patient, the postradiation areas had been cared fully examined by MRI and no definite necrosis change was demonstrated. However, microscopic injury by radiotherapy...
could not be ruled out. Further, an ad ditive in jury of ra di other apy on cog ni tive func tion was de mon strated in pa tients who had re ceived pit uit ary tu mor sur gery. Other fac tors which af fect neuropsychologi cal per for -mance, such as sub tle pre vi ous post op er a tive in fec tion, hem or rhage, hy dro cep halus or chronic ill ness state with re peated ad mis sion are all pos si ble rea sons. How ever, es tab lish ing these causes might be clin i cally dif fi cult. Of note, in our patient, the serum con cen tra tion of growth hor mone could not be de ter mined. Re cently, many stud i es have shown that growth hor mone de fi ciency can also cause psy chi atric dis tur bance.

In con clu sion, psy chi atric symp toms can de vel op in pa tients with pit uit ary hor mone de fi ciency or in ju ries from op er a tion and ra di other apy. Af ter hor mone re place ment, they might ei ther get im prove ment or per sist, es pe cially in those with irre vers ible or ganic ner vous tis sue damage.

REFERENCES

8. Ve ith JL, Sand man CA, Ge or ge JM, Kend all JW. The re la tion -ship of en de nous ACTH lev els to vi sual-at ten tional func ti on ing in pa tients with con gen i tal ad re nal hy per plasia. Psy chore neuro endo crino lo gy 1985;10:33-48.
14. Peace KA, Orme SM, Pa day atty SJ, Godfrey HP, Bel chet z PE. Cog ni tive dys func tion in pa tients with pit uit ary tu mor who have been treated with transfrontal or transshenoidal sur gery or med i ca tion. Clin Endocrinol 1998;49:391-6.