Pituitary Stalk Interruption Syndrome in a 54-year Adult Male

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ABSTRACT
Pituitary stalk interruption syndrome (PSIS) is a rare disease with isolated growth hormone deficiency or multiple anterior pituitary hormone deficiencies; and is characterised by a thin or absent pituitary stalk, hypoplasia of the adenohypophysis, and ectopic neurohypophysis. The literature have reported primarily on cases of infants and young people, and there are few reports in adults. A case is presented here of a 54-year male, who reported dizziness accompanied by fatigue and anorexia for more than 20 days; and the results from the blood tests showed a general decline in growth hormone, thyrotropin, and sex hormone levels. On the basis of the medical history, laboratory and imaging examination, a diagnosis of PSIS was made. After treatment, the patient’s condition as well as laboratory results returned to normal. In summary, PSIS can also occur in adults. In the suspected cases, magnetic resonance imaging should be done in time to diagnose and manage it appropriately early in the course of the disease.

Key Words: Pituitary stalk interruption syndrome, Pituitary hormone deficiency, Adults.


INTRODUCTION
Pituitary stalk interruption syndrome (PSIS) is a rare clinical disease, which is characterised by a thin or absent pituitary stalk, hypoplasia of the adenohypophysis, and ectopic neurohypophysis. The hormones secreted by the hypothalamus cannot be transported to the pituitary by the pituitary stalk, resulting in clinical symptoms. Fujisawa et al. first reported the disease in 1987. The pituitary magnetic resonance imaging (MRI) is the most important and direct means of examination for the diagnosis of this disease. The MRI imaging is helpful in correlating the severity of pituitary target hormone deficiencies and can even predict the occurrence and phenotype of PSIS.

In recent years, reports on PSIS cases and on the process of diagnosis and treatment have increased. The understanding of the disease has improved, but research has primarily concentrated on infants and young people, and little information is available on adults with this disease. We, herein, present a case of a 54-year male with this syndrome and review the relevant literature.
anterior lobe was more obvious, and the posterior lobe showed
a high signal. An enhanced scan showed uniform enhancement
of the pituitary and there was no abnormally low enhancement
signal shadow. The middle of the pituitary stalk was found and
showed no obvious thickening. The absence of signal in the
middle appeared to be dotted along the T1 signal shadow. How-
ever, the enhanced scan did not indicate any obvious
enhancement.

Table I: Serum hormones levels.

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Patient’s Result</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma cortisol</td>
<td>1.06 ug/dl (8am)</td>
<td>5.0-25.0 ug/dl</td>
</tr>
<tr>
<td></td>
<td>1.05 ug/dl (4pm)</td>
<td></td>
</tr>
<tr>
<td>Serum adrenocorticotropic hormone</td>
<td>10.9 pg/mL (8am)</td>
<td>0.0-46.0 pg/mL</td>
</tr>
<tr>
<td></td>
<td>11.60 pg/mL (4 PM)</td>
<td></td>
</tr>
<tr>
<td>Serum estradiol</td>
<td>24.2 pg/mL</td>
<td>0.0-56.0 pg/mL</td>
</tr>
<tr>
<td>Follicular hormone</td>
<td>0.2 mIU/mL</td>
<td>0.7-11.1 mIU/mL</td>
</tr>
<tr>
<td>Luteinizing hormone</td>
<td>0.3 mIU/mL</td>
<td>0.8-7.6 mIU/mL</td>
</tr>
<tr>
<td>Prolactin</td>
<td>41.0 ng/mL</td>
<td>2.5-17.0 ng/mL</td>
</tr>
<tr>
<td>Progesterone</td>
<td>&lt;0.20 ng/mL</td>
<td>0.27-0.90 ng/mL</td>
</tr>
<tr>
<td>Human growth hormone</td>
<td>1.22 ng/ml</td>
<td>0.00-0.80 ng/ml</td>
</tr>
<tr>
<td>Serum total thyroxine</td>
<td>29.30 nmol/L</td>
<td>55.47-161.25 nmol/L</td>
</tr>
<tr>
<td>Total triiodothyronine</td>
<td>0.60 nmol/L</td>
<td>1.02-2.96 nmol/L</td>
</tr>
<tr>
<td>Third generation thyrotropin</td>
<td>0.292 mIU/L</td>
<td>0.380-4.340 mIU/L</td>
</tr>
<tr>
<td>Free thyroxine</td>
<td>7.81 pmol/L</td>
<td>10.45-24.38 pmol/L</td>
</tr>
<tr>
<td>Free triiodothyronine</td>
<td>1.86 pmol/L</td>
<td>2.77-6.31 pmol/L</td>
</tr>
</tbody>
</table>

According to MRI report, the patient was considered to have
partial vacuolar sella, shrinkage of the pituitary volume with an
absence of signal in the middle of the pituitary stalk, and possible
disruption (Figures 1 and 2). Thyroid B-mode ultrasonography
indicated 0.6×0.3 cm hypoechoic nodules in the right thyroid.
The diagnosis, based on relevant examination and clinical symp-
toms, was made of PSIS and hypothyroidism.

The patient was married at the age of 23 years, and his spouse
was reportedly healthy. They had one son and one daughter. The
parents and children were all healthy, and the height and weight
of the family members were normal. The patient had no history of
relevant medical or surgical illnesses. In addition, the patient had
no history of food and drug allergies, surgery, trauma, blood
transfusion, or poisoning.

In the treatment, hydrocortisone tablets with doses of 20 mg (8
AM) and 10 mg (4 PM) were given once per day orally, and levothy-
roxine at a dose of 25 μg was given once per day orally. After one
week of treatment, the symptoms improved, the patient’s sense
of well-being and diet improved, the dizziness disappeared, and
he showed no nausea and vomiting or other discomforts. On one
month follow-up, the adrenocortical function and thyroid func-
tion were normal. After six months of follow-up, the patient had a
good appetite, no obvious discomfort, an overall weight gain of
10 pounds, and the laboratory examinations were normal.

DISCUSSION

PSIS is a rare disease with isolated growth hormone deficiency or
multiple anterior pituitary hormone deficiencies. It is charac-
terised by a thin or absent pituitary stalk, hypoplasia of adeno-
hypophysis, and ectopic neurohypophysis.

To date, the underlying mechanisms involved in PSIS ontogen-
esis have remained unclear. Some investigators have reported
that PSIS is associated with perinatal abnormalities (breech presentation, cesarean section, preterm birth, and postpartum asphyxia) or craniocerebral trauma.\(^6\)

The recent studies suggest that gene mutations during early embryogenesis may be the cause of PSIS. Genes such as PIT1, PROPI, LHX3/LHX4, PROKR2, OTX2, TGIF, and HESX1 may be affected, thus contributing to the disease.\(^2,7\) Mutations in these genes affect the Wnt, Notch, and sonic hedgehog signalling pathways and the Prokineticin pathway. Reynaud et al.\(^8\) have analysed the features of 83 patients with PSIS from 80 pedigrees and screened the HESX1, LHX4, OTX2, and SOX3 genes. In that study, the authors found a novel HESX1 causative mutation in a consanguineous family, as well as two LHX4 mutations present in familial PSIS. In 2015, a mutation in the CDON gene was first reported to be associated with PSIS.\(^9\) Ender Karaca et al.\(^10\) have identified a homozygous GPR161 mutation in a family with PSIS. Both GPR161 and CDON genes are involved in the sonic hedgehog signalling pathway, which has been implicated in hypothalamic-pituitary development.

Pituitary MRI is the most important and direct means of examination for the diagnosis of PSIS.\(^4\) The typical MRI manifestations of PSIS are as follows: the pituitary stalk is absent or thinner; the hypophyseal lobe disappears and is ectopic to the middle of the recess of the third ventricle funnel, a characteristic sign of this disease; and the anterior pituitary shows dysplasia.\(^5\) Whenever there is clinical suspicion of PSIS, MRI should be ordered in time to make its diagnosis early.

For patients with PSIS, the injured pituitary stalk cannot be recovered through treatment with drugs or surgery. Hormone replacement therapy is the only effective method.\(^1\) For patients with a deficiency in adenocortical hormone and thyroxine, corticosteroids should be replaced first or replaced with thyroxine together to avoid acute adenocortical dysfunction. In this case, oral administration of hydrocortisone tablets and oral levothyroxine tablets were administered in a timely manner, which improved the patient's condition and achieved satisfactory results.

In summary, PSIS not only affects children and adolescents but can also occur in adults. Adults with isolated growth hormone deficiency or multiple anterior pituitary hormone deficiencies should be promptly evaluated by MRI to diagnose the disease early, and start timely hormone therapy.

**PATIENT’S CONSENT:**
The patient has provided informed consent for publication of the case.

**CONFLICT OF INTEREST:**
The authors declared no conflict of interest.

**AUTHORS’ CONTRIBUTION:**
WWL: Data collection, literature search, and manuscript writing.
XF: Data collection.
GY: Data collection, literature search.
GLW: Supervised to write case report.

**REFERENCES**