A CASE REPORT OF PITUITARY TUMOR PRESENTING AS FORBES-ALBRIGHT SYNDROME: DETERMINATION OF PITUITARY PROLACTIN CONTENT

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SYNOPSIS

The patient is a 29 years old Japanese female. She got married at 21. Her periods started at 13, but her menstruation had stopped at 17. She had complained of severe headache and right side hemianopsia in 1959 (age 22), and had been diagnosed as pituitary tumor, and the pituitary was removed subcapsularly at the Tokyo University Hospital. The tumor was constructed with polygonal chromophobe cells. After the first operation, her menstruation reappeared several times until her first pregnancy (age 23). Her puerperium had been well, but her lactation had failed to stop, and persisted with amenorrhea for about 5 years up to present time. Physical examination and the laboratory data showed slight obesity with hirsutism and oily skin. The urinary excretion of GTH was less than normal. The urinary excretion of 17-KS and 17-OHCS and Estrogens was a little more than the patients with usual chromophobe adenoma. The thyroid and adrenal function remained within normal limits. Her pituitary adenoma grew again in 1965, and right side hemianopsia appeared with severe headache. Reoperation was performed, and the tumor showed the same histological characteristics as in the first operation. Forbes and Albright suggested that the patients with these syndrome might have overproduction of prolactin in the pituitary. The prolactin content of this tumor tissue was measured by the pigeon crop sac test, and showed remarkably higher value than that of the control pituitary tissues which was obtained from another patient with usual chromophobe adenoma.

Forbes et al. (1954) presented the findings in fifteen non-acromegalic women who had persistent lactation and amenorrhea associated with low urinary FSH excretion. Seven of them had pituitary tumors, and in three cases, chromophobe adenoma was proved by biopsy. They suggested that the patients with these syndrome might manifest overproduction of prolactin in the pituitary.

The findings in a case of pituitary tumor with typical Forbes-Albright syndrome were presented in this study, and were compared with that of five cases with non functioning pituitary chromophobe adenoma. An attempt was made to clarify the mechanisms of the overproduction of prolactin in the pituitary of this case.

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CASE REPORT

The patient is 29 years old Japanese female. Her previous history and family history showed nothing peculiar (Fig. 1). Her periods started throughout the pregnancy and puerperium. She delivered a healthy female baby. But after normal nursing, her lactation failed to stop, and persisted with amenorrhea for about 5 years until present time. She consulted doctors several times with this complaint. The patient was treated with estrogen and progesterone, and uterine hemorrhage was observed during therapy but still the lactation continued as well as before.

In July 1965 her pituitary adenoma grew again, and left side hemianopsia appeared resulting severe headache, nausea, anorexia and general malaise. She was admitted at National Cancer Center Hospital. She was diagnosed as recurrence of pituitary tumor with Forbes-Albright syndrome. In September 1965, subcapsular removal of pituitary was performed at Tokyo University Hospital. The tumor size was about $2.5 \times 2.5 \times 2.0$ cm and histological findings were same as in the first operation. She has been well until present time after the operation, but amenorrhea and slight lactation have persisted continuously.

**Physical examinations:**

The physical examinations showed she was a rather obese young woman, a ruddy lustrous skin, seborrheic dermatitis of the face, clear consciousness, and any other acute distress was not observed. The oral temperature was 36.5°C,
the plus rate 80 beats per minute (regular), and the blood pressure 130/80mmHg. Any notable change suggesting acromegaly was not found in the features, hands and feet. Acral growth, soft tissue growth, prognathism and visceromegaly were not observed. From pelvic examination, the uterus was observed to be normal and ovaries were not palpable. The pertinent findings were as follows; (1) severe headache with nausea. (2) bitemporal hemianopsia. (3) amenorrhea. (4) persistent lactation. (associated neither with a recent pregnancy nor with acromegaly) 5) slight obesity. (6) oily skin. (7) slight hirsutism. (8) postoperative enlargement of sella turcica.

The galactorrhea persisted for about 5 years after first delivery, and the squeezed secretion of milk were 185cc/day from right side mamma and 190cc/day from left. By the administration of estradiol 0.2mg and progesterone 5mg for ten days, the lactation was depressed remarkably and uterine hemorrhage appeared slightly. But slight galactorrhea persisted during the hormone treatment and also after second operation of pituitary gland until present time.

**Laboratory studies:**

On the renngenologic examination, chest was normal, mammography showed a lactating picture, and right side cerebral angiography showed a slight internal hydrocephalus without tumor shadow in pituitary fossa. Any sign of acromegaly was not found from the bone X-ray film. Any sign of stasis papillaris was not found by the ocular fundus examination, but slight retinopathy was observed. On the EEG awaked, a waves decreased in all leads, and high voltage R waves were observed sporadically without focal sign. Findings by ECG was within normal limits except counter-clockwise rotation. The following tests were normal; the examination of feces, urinolysis, sedimentation rate, serological studies, total serum protein, total serum bilirubin, serum alkaline and acid phosphatases, SGOT, LDH and ICD. By additional laboratory studies, the following values were obtained; Kunkel 15.3u, thymol turbidity 1.5u, cephalin flocculation slight positive, bromsulphalein retention 5.5% after 45 mins., serum cholesterol 210mg/100ml, ester form 85%, serum phospholipids 190mg/100ml, serum Cl 104mEq/L, Na 140mEq/L, K 4.0 mEq/L, Ca 4.7mEq/L, and P 3.2mg/100ml. Complete blood cell count showed almost normal except relative lymphopenia (Lymphocytes 17%, Neutrophiles juvenile 4.0%, segmented 77.5%).

**Endocrinological findings:**

The endocrinological laboratory examinations were performed at the preoperative stage in

<table>
<thead>
<tr>
<th>Endocrinol. Examinations</th>
<th>Present Case</th>
<th>Control*</th>
<th>Methods of Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.M.R.</td>
<td>-6%</td>
<td>-14%</td>
<td></td>
</tr>
<tr>
<td>P.B.I.</td>
<td>5.5μg/100ml</td>
<td>4.7(±0.3)</td>
<td></td>
</tr>
<tr>
<td>1131 uptake</td>
<td>41.9%</td>
<td>14.9(±4.9)</td>
<td></td>
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<tr>
<td>Urinary 17-KS</td>
<td>8.8mg/day</td>
<td>4.2(±2.1)</td>
<td></td>
</tr>
<tr>
<td>Urinary 17-OHCS</td>
<td>6.9mg/day</td>
<td>4.3(±0.7)</td>
<td></td>
</tr>
<tr>
<td>Serum 17-OHCS</td>
<td>12.6μg/100ml</td>
<td>9.9(±4.2)</td>
<td></td>
</tr>
<tr>
<td>Urinary Estrogens</td>
<td>27.6μg/day</td>
<td>7.5(±3.2)</td>
<td></td>
</tr>
<tr>
<td>Urinary GTH</td>
<td>2u./day</td>
<td>4(±2)</td>
<td></td>
</tr>
<tr>
<td>Prolactin content of pituitary tumor tissues</td>
<td>744I.U./g**</td>
<td>186(±42)</td>
<td>Extraction: Li (1961)</td>
</tr>
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<td></td>
<td></td>
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<td>Bioassay: Lyons and Page (1935)</td>
</tr>
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* mean value (S.D.) in 5 patients with non-functioning chromophobe adenoma.

** Based on dried extraction.
1965, and the results were compared with respective values of other 5 non-functioning pituitary chromophobe adenoma. The methods of assay of hormone activity and these results were showed in Table 1. It was noticed that:

1) The findings on PBI, I\(^{131}\) uptake and Triosorb test (28.2\%) suggested that the thyroidal function was within normal. However, in comparison with control (mean value on that of another 5 patients with non-functioning chromophobe adenoma), the thyroid function was rather higher. Scincigram of thyroid glands was normal. Serum TSH was not detected by the level of Mackenzie's method (Mackenzie, 1958).

2) Daily urinary excretions of 17-KS and 17-OHCS were within normal, but higher than control. For ACTH test responded normal.

Crystereized lysin-8-vasopressin test showed normal response. Summarized data of author's clinical trial using synthetized lysin-8-vasopressin acting as a corticotropin releasing agent in normal, hypopituitary or pituitary tumor patients were set out in Figure 2. Then adrenal function and pituitary ACTH releasing capacity seemed to be maintained within almost normal level.

3) Daily urinary GTH excretion decreased. However, total estrogens excretion increased slightly (27.6\(\mu\)g/day).

4) Concerning with growth hormone, radioimmunoassay or bioassay was not performed. The results of the glucose tolerance test did not show high levels as acromegaly. (fasting: 71mg/100ml, after administration of 50g glucose; 30 mins., 95mg/100ml; 60 mins, 100; 90 mins, 112; 120 mins, 117; 150 mins, 114; 180 mins, 109) The serum phosphorus level was definitely lower than acromegaly. From these findings and clinical observations, it was doubtful whether the growth hormone secretion increased in this case.

5) From the exterpated pituitary tissue of this case and of control, crude extract of each tissue was prepared by the modified method of C.H.Li (Table 2) and the prolactin contents of these extracts were measured by the minimum crop stimulation method of Lyons. The test sample was necessary to be purified to some extent for this assay, but contamination of ICSH was not eliminated. Growth hormone contamination in this specimen was reactable to this test, but chemical separation of growth hormone from prolactin in human sample was
not perfectly succeeded yet. It was found in our experiment on this assay that minimum dose for perfect positive response was equivalent to 0.3 I.U., and thus the amounts of prolactin in the extracts were expressed as I.U., based on their specific activities. Remarkably higher content of prolactin than control was recognized in the pituitary of this case. (Table 1)

**DISCUSSION**

A case of pituitary adenoma with typical Forbes-Albright syndrome was presented. At first, it is necessary to discuss in this case whether the function of the pituitary adenoma was changed by the course of pregnancy and puerperium. The initial sign of the tumor growth was amenorrhea and slight headache at the age of 17, and it is supposed that secretion of GTH had decreased at that time. But for about 5 years up to the first operation, she had not had any sign of hypothyroidism or hypoadrenocorticism. At the stage before the first operation, it has been written that the urinary excretions of 17-KS and 17-OHCS were both within normal level, but sign of galactorrhea was not recognized. The persistent lactation started clearly after her puerperium, and at this stage all other endocrinological characteristics are supposed to be the same as before the first operation. Then it is difficult to suppose that the function of the pituitary adenoma might be changed by puerperium, and rather, it is conceivable that the latent galactorrhea was not detected in early stage of the illness.

Also, it is supposed that pituitary prolactin content of this patient is remarkably higher than controls. The clinical picture of this syndrome differed from that of acromegaly in which growth hormone was over-produced. In this case, common syndrome of acromegaly, such as acral growth, prognathism, osteoporosis, soft tissue growth or visceromegaly was not found. Although the contamination of growth hormone in the pituitary extracts was not avoided, but it is not the elevating content of growth hormone but the high content of prolactin in this extracts that was suggested by these assay results and by the clinical findings. More directly certification of hypersecretion of prolactin may be achieved by measurement of plasma and urine prolactin concentrations, but these clinical prolactin assays are unsatisfactory to clarify these problems.

**SUMMARY**

A case of pituitary adenoma with typical Forbes-Albright syndrome was presented, and clinical observations with the hormonal basis for this syndrome were studied. Prolactin content in the pituitary gland of the patient was measured, and was found to be remarkably higher than controls.

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**REFERENCES**


