

Case Report

## A Case Report of Efficacy of Growth Height and Peak-Luteinizing Hormone Level Suppression on Idiopathic Gonadotropin-Dependent Precocious Puberty Patient Using Herbal Remedy, *Aesopjiyoun-tang*

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The purpose of this report is to evaluate effect of Korean medical treatment on idiopathic gonadotropin-dependent precocious puberty (G-DPP) patient received herbal medicine. We administered *Aesopjiyoun-tang* remedy to idiopathic G-DPP and analyzed the delay effect by hormonal value and radiographs; the height growth effect by measurement of height. After Korean medical treatment, suppression effect to peak- Luteinizing Hormone level (LHL) is 14.39IU/L to 10.9IU/L for 13month, growth effect to height value is 11cm/13month; and change of mean growth velocity (MGV) is 6.08cm/year to 10.06cm/year. The gain in height by treatment is 3.98cm/year. The result suggests *Aesopjiyoun-tang* can be an effective treatment for G-DPP. Herbal medicine can be used as an alternative treatment in place of the GnRH treatment.

**Key Words** : Precocious puberty, Herbal medicine, Growth height, *Aesopjiyoun-tang*, GnRH treatment

### Introduction

Precocious puberty (PP) is defined as the onset of secondary sexual characteristics development more than 2.5 to 3 standard deviations earlier than their same-age cohort<sup>1,2</sup>. Thus the puberty development begins younger than the age of eight years in girls or nine years in boys<sup>3</sup>. The etiology of PP is classified by the underlying pathogenesis into three categories: G-DPP, gonadotropin-independent PP (G-IPP), and incomplete PP. Although more than 80 percent of PP

patients are idiopathic G-DPP<sup>4</sup>. G-DPP can be distinguished from G-IPP by measuring LHL<sup>5</sup>. In G-DPP, the peak-LHL has over 5IU/L diagnostic limit responded to gonadotropin releasing hormone (GnRH) stimulation<sup>6</sup>.

As the latest trend of earlier and growing, more and more patients with PP visit hospitals and clinics for treatment<sup>4</sup>. GnRH agonist is most commonly used for PP in order to lower sex hormone level. However, some patients were hesitant about GnRH treatment for adverse effects<sup>7,8</sup>.

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Several researches reported that herbal medicine prescribed for those children suffering from PP has a certain effect on their symptoms<sup>9,10</sup>. However, reports are problematic in that there were no peak-LHL evaluation and made a simple comparison with breast buds or estradiol values of before and after taking the medicine. Serum estradiol values are highly variable and have a low sensitivity for the diagnosis of PP in girls. The criterion for diagnosis is the peak-LHL after stimulation by GnRH<sup>1</sup>.

This case study evaluated LHL, MGTV duration of both herbal treatment and after cessation of treatment. It was to report to obtain significant results through the patient with G-DPP who were visited hospital of Korean Medicine for herbal treatment.

### Case presentation

An 8-year-old girl was diagnosed with GDPP on Sep. 2014 in OO hospital near home. The pediatrician recommended GnRH treatment, but guardian refused due to anxiety about the adverse effect. They moved to our hospital right after diagnosis and wanted to get Korean Medicine treatment.

Her medical history is unremarkable and pulse pattern is sunken with rough. The parents are below average height, and at physical examination, the girl is 135.2cm tall (in the 90~97<sup>th</sup> percentile for her age), weight 25kg, and has a body-mass index 13.7. On set of breast development is 7.7 years and at time of the clinic breast development is classified as Tanner stage 2. Her peak-LHL was 14.39IU/L and bone age (BA) was 9.7 years. Her Korean medicinal pattern of identification was syndrome of stagnant of *qi* (氣鬱). The general features and distribution of the subject are listed on Table 1.

As they desired to get herbal treatment, *Aesopjiyoun-tang* was prescribed for delay sexual development and growth height. Remedy has been made with ten or so herbal medicine ingredients

**Table 1.** Demographic Characteristic of Participant

| Parameters                           |                |
|--------------------------------------|----------------|
| Gender                               | Female         |
| Chronological age (years)            | 8.2            |
| Bone age (years)                     | 9.7            |
| Height (cm)                          | 135.2          |
| Contrast to same age group (cm)      | +7.8           |
| Weight (kg)                          | 25             |
| Contrast to same age group (kg)      | -1.2           |
| MPH (cm)                             | 154            |
| On set of breast development (years) | 7.7            |
| Date of the first visit              | Sep. 6th, 2014 |
| breast stage                         | 2              |
| breast pain                          | -              |
| menstruation sign                    | -              |

Bone age: Assessment according to TW3

MPH: Mid Parental Height

Breast stage: Rating according to Tanner Stage

including *Cyperus rotundus* (20%), *Angelica gigas* (15%), *Paeonia japonica* (15%), *Atractylodes japonica* (7%), *Astragalus membranaceus* (7%), *Paeonia suffruticosa* Andrews (7%), *Cnidium officinale* Makino (7%), *Citrus unshiu* Markovich (7%), *Cinnamomum cassia* (7%), *Glycyrrhiza uralensis* (5%), *Zingiber officinale*, *Zizyphus jujuba*. The medicines were prescribed every 15 days for three months (Sep. 13th, 2014 ~ Dec. 20th, 2014). The dose is two times a day (morning and evening) with 80cc.

Due to her clinical improvement, breast buds were not palpable (Nov. 2014) and peak-LHL was suppressed 14.39 to 13.8 (Dec. 2014) (Tab. 2). Height value has increased by 2.5cm for the same period. The MGTV increase was from 6.08 to 10.43

**Table 2.** LH, FSH Level After GnRH Stimulation

| DATE    | Item | Basal | 30min | 60min | 90min |
|---------|------|-------|-------|-------|-------|
| 2014-09 | FSH  | 0.39  | 7.95  | 9.74  | 8.83  |
|         | LH   | 0.02  | 14.39 | 14.18 | 9.82  |
| 2014-12 | LH   | 0.4   | 13.8  | 11.0  | 8.5   |
| 2015-10 | LH   | 1.6   | 10.9  | 7.9   | 5.8   |

Unit: mIU/ml

**Table 3.** Increment Height and Weight Value After Treatment

| DATE    | Height (cm) | Weight (kg) | MGV (cm/year) |
|---------|-------------|-------------|---------------|
| 2014-09 | 135.2       | 25          |               |
| 2014-10 | 135.9       | 25.7        | 6.08          |
| 2014-12 | 137.7       | 26.8        | 10.43         |
| 2015-06 | 143.4       | 28.5        | 10.95         |
| 2015-10 | 146.1       | 30.2        | 10.06         |

MGV: Mean growth velocity, 365/days x height  
All measurements were progressed 9:00AM~10:30AM

**Table 4.** Increment Predicted Height After Treatment

| DATE    | Height (cm) | BA    | Prediction Height(cm) |
|---------|-------------|-------|-----------------------|
| 2014-09 | 135.2       | 9.74  | 164.4                 |
| 2015-03 | 139.6       | 10.41 | 164.9                 |
| 2015-10 | 146.1       | 10.81 | 168.2                 |

PH: Prediction Height  
BA, PH: Assessment according to TW3 method

(Tab. 3). So we decided to discontinue the herbal treatment and recommend a follow-up evaluation every three months. Suppression effective on LHL was maintained, as a result 10.9 IU/L was shown at the latest test (Oct. 2015) (Tab. 2). Follow-up radiographs of patient dated on Oct. 2015 (BA 10.8year) showed no time interval change compared to the initial radiograph in Sep. 2014 and  $\Delta BA/\Delta CA$  value was less than 1 (Fig 1). And her prediction height calculated by RUS is increased 164.4cm to 168.2cm (Tab 4)<sup>11</sup>.

## Discussion

The primary purpose of treatment for G-DPP is to induce a child to grow to a normal adult height<sup>12,13,14</sup>. Treatment effect of PP patient was evaluated by LH suppression effective<sup>15,16</sup>. In this case, basal-LHL was elevated 0.02 to 1.6 and peak-LHL was suppressed 14.39 to 10.9. After 2nd round treatment, it was seen that breast buds had been disappeared. Other previous report, "Kim et al." gained almost identical clinical effect<sup>10</sup>. However, it is hard to

acknowledge medicinal effect. Because it is very often for early adolescence that the breast buds had disappear without receiving any treatment.

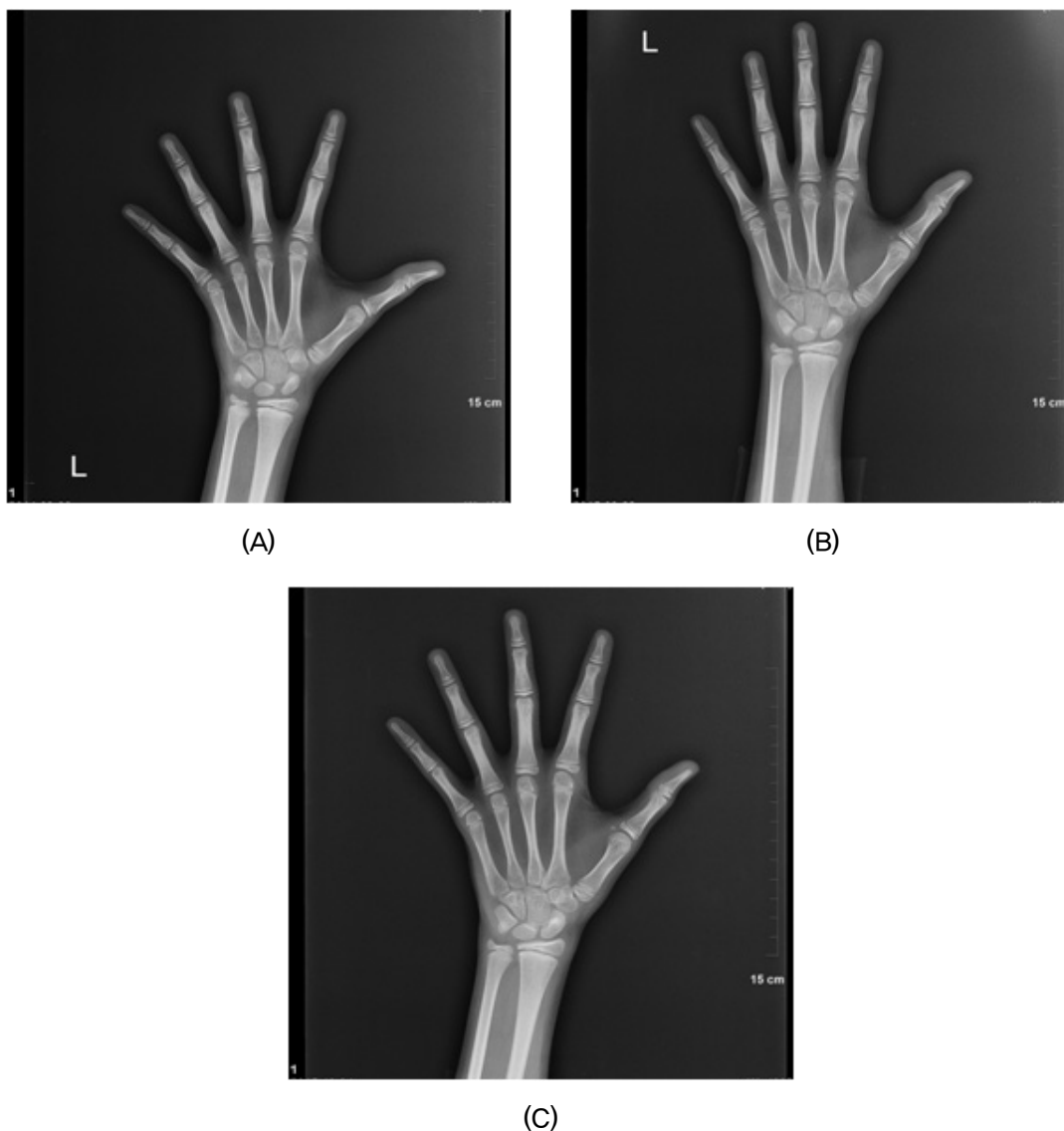
The height growth value for subject was increased to 146.1cm, while that before herbal treatment was 135.2cm. Increment of height growth value has very important meaning to PP patient. Because in not all cases but most advanced bone age may reach short adult height<sup>17,18</sup>.

Patient with PP's BA are more advanced than chronological age. Radiograph of the Sep. 2014, BA is more than 9.5 years old (Fig. 1A). Radiograph of the Mar. 2015, the main point of interest in this case is the sesamoid of thumb. The sesamoid bone was normal in more than 10 year old girls' AP view of the hand but rarely to 8 year old girls (Fig. 1B). Radiograph of the Oct. 2015, it shows no specific change in carpal bone and radius, ulna for 13 months<sup>11</sup> ( $\Delta BA/\Delta CA < 1$ ) (Fig. 1C). These represent the growth plate fusion was delayed.

In Korean medicine, there is no specific term or definition that refers to the current understanding of G-DPP. The pattern of identifications on G-DPP are follows: syndrome of stagnant of *qi* (氣鬱), syndrome of deficiency of *yin* (陰虛), syndrome of damp-heat (濕熱)<sup>19</sup>.

In this case, the patient's pattern of identification was syndrome of stagnant of *qi* (氣鬱). Therefore, we decided to administer *Aesopjiyoun-tang* which has been recommended for PP patients who have identified syndrome of stagnant of *qi* (氣鬱). The remedy consists of circulation meridian system (通經絡), adaptation of *qi* (順氣), releasement of stasis (解鬱) herb such as *Cyperus rotundus*, *Citrus unshiu* Markovich: healthy spleen (健脾) herb such as *Atractylodes japonica*: activation of blood (活血) herb such as *Paeonia japonica*, *Angelica gigas*, *Cnidium officinale* Makin.

This case demonstrates that herbal treatment can have beneficial effects on the symptom of idiopathic G-DPP, including height growth. Although these



**Fig. 1.** Radiographs of the left hand were obtained.

(A) Radiograph of the left hand AP view (2014–09), BA of this radiograph is more than 9.7 years old, (B) Radiograph of the left hand AP view (2015–03), The main point of interest in this case is the sesamoid of thumb, The sesamoid bone was normal in more than 10 year old girls' AP view of the hand but rarely to 8 year old girls, (C) Radiograph of the left hand AP view (2015–10), This radiograph shows no specific change in carpal bone and radius, ulna for 13 months ( $\angle BA/\angle CA < 1$ ). These represent the growth plate's fusion was delayed.

results cannot be extrapolated to patients with all of PP, this case study provides a basic data for the investigation of Korean herbal medicine as a alternative therapy. In future studies, we intend to confirm the efficacy of *Aesopjiyoun-tang* in detail

and the underlying mechanisms with well-controlled clinical trials.

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