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Are ovarian cysts a coincidence after treatment for Van Wyk-Grumbach syndrome?

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Key words: *ovarian cyst; precocious puberty; Van Wyk-Grumbach syndrome*

Van Wyk-Grumbach syndrome, summarised and named by Van Wyk and Grumbach in 1960 [1], is primarily characterised by hypothyroidism, paradoxical precocious puberty, and ovarian cysts. Patients often have short stature. More than 100 cases have been reported worldwide, but reports are few and inconclusive on the use of medications other than thyroid hormone to improve the adult height of patients, especially older adolescents.

A female patient aged 13 years and 3 months was admitted to the hospital for examination due to the onset of menstruation for 2 months but with short stature. Her height had increased less than 5 cm in the past 3 years. She was usually quiet and suffered from constipation, without symptoms of increased intracranial pressure such as headache. There were no abnormalities in her birth history or family history. The parents' heights were 165 cm and 156 cm, respectively, with a genetic height of 154 cm ± 5 cm.

Physical examination: height 134.6 cm [< –3 standard deviation (SD)], weight 28.2 kg (< –3 SD), dry hair, rough skin, no thyroid enlargement, breast development at stage B4, no pubic hair or axillary hair. Considering the child's short stature, relevant examinations were performed, and the laboratory test results are shown in Table 1.

Imaging examination (bone age: 10+ years). Pituitary magnetic resonance imaging (MRI): a 16 mm × 14 mm isointense soft tissue shadow in the anterior lobe of the pituitary, with clear boundaries, and slight upward pressure on the pituitary stalk and optic chiasm (Fig. 1A).

Pelvic ultrasound-: The size of the uterus is about 34 × 26 × 37 mm, the left ovary is 26 × 13 × 14 cm, the right ovary is 24 × 14 × 13 mm, multiple follicles can be seen in both ovaries, with the largest diameter being 5 mm (Fig. 2A).

Table 1. *Laboratory test results*

Laboratory test	Initial diagnosis	After 3 months of treatment	After 17 months of treatment (after 4 months of adding GnRHa treatment)	Reference range
TSH [mIU/L]	> 150	2.45	0.09	5.18
FT4 [pmol/L]	4.09	17.66	1.87	7.64–16.03
TT4 [nmol/L]	3.30	118.62	13.15	69.97–152.52
TPOAb [IU/mL]	> 1300.0	328.52	294.1	< 9.0
Tgab [IU/mL]	339.8	101.70	7.5	< 4.0
LH [mIU/mL]	1.60	8.14	2.2*	2.0–12.0
FSH [mIU/mL]	7.45	6.03	9.07*	3.3–7.9
E2 [pmol/L]	164.27	86.0	18.35	< 121.0
PRL [ng/mL]	72.57	7.65	20.0	3.34–26.72

GnRHa — gonadotropin-releasing hormone agonist; TSH — thyroid-stimulating hormone; FT3 — free triiodothyronine; FT4 — free thyroxine; TT4 — total thyroxine; TPOAb — thyroid peroxidase antibodies; Tgab — thyroglobulin antibodies; LH — luteinising hormone; FSH — follicle-stimulating hormone; E2 — serum oestradiol; PRL — serum prolactin; *Serum LH, FSH after injection of GnRHa for 1 hour

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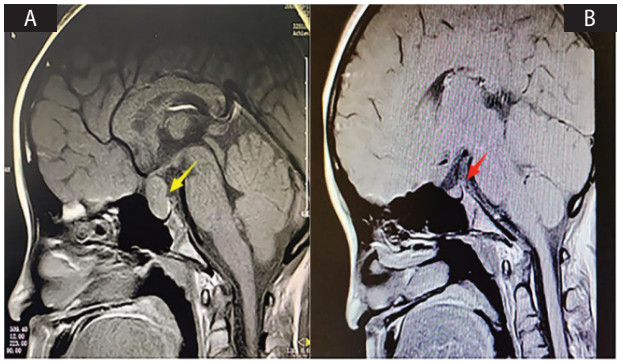

Figure 1. *Pituitary magnetic resonance imaging (MRI): at the initial diagnosis, there was a gourd-shaped occupancy in the anterior lobe of the pituitary, with slight upward pressure on the pituitary stalk and optic chiasm (***A***) (yellow arrow). After 3 months of thyroid hormone replacement therapy, the pituitary returned to normal (***B***) (red arrow)*

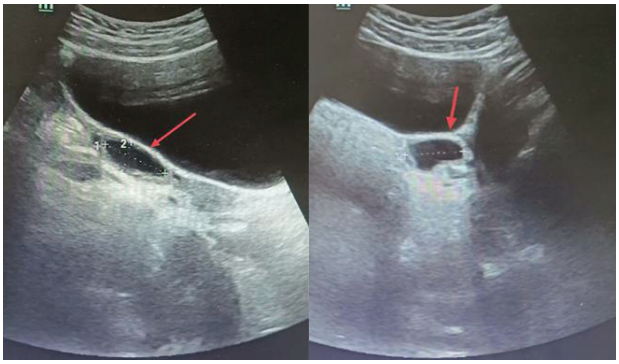

Figure 2. *Ultrasound after 4 months of gonadotropin-releasing hormone agonist (GnRHa treatment): A 3.3 × 1.6 × 2.9 cm cystic echo was seen in the left ovary*

Based on the clinical manifestations and examination results, the child was diagnosed with Van Wyk-Grumbach syndrome and was given levothyroxine sodium tablets for replacement therapy. After 3 months, the pituitary MRI returned to normal (Fig. 2B), and the initial height growth significantly accelerated, but it fell back after 5 months of treatment. After adding growth hormone therapy, the rate of height growth improved. However, at 13 months of treatment, the bone age rapidly progressed to 13.5 years, and combined treatment with gonadotropin-releasing hormone agonist (GnRHa) was given, but there was no significant benefit. By the end of the follow-up, the patient's adult height was 146.0 cm.

It is worth noting that after we added GnRHa treatment for 4 months, the child's thyroid function became abnormal again (Tab. 1), and a cyst in the left ovary was found (Fig. 2). Loris Marin et al. [2] believe that patients with autoimmune thyroid diseases are more likely to develop hypothyroidism when using GnRHa, and our observations seem to support this view. Ryan et al. [3]. High concentrations of TSH can activate the FSH receptor, thereby promoting the development of the uterus and ovaries, even causing ovarian cysts. In addition, long-term hypothyroidism causes a negative feedback increase in TSH-releasing hormone, which has a promoting effect on prolactin (PRL) secretion. High levels of PRL may be a link in the pathogenesis [4, 5].

In summary, the author believes that, for children with Van Wyk-Grumbach syndrome during adolescence and older, who still have unsatisfactory height growth with thyroid hormone treatment alone: 1. Adding growth hormone therapy may allow the child to benefit more in terms of adult height, and more cases need to be explored to support this. 2. Such children may experience bone age catching up after effective L-T4 replacement therapy, which may affect adult height, but before deciding to use combined GnRHa therapy, it is necessary to fully consider the potential adverse effects of GnRHa treatment on the child, such as thyroid dysfunction and ovarian cysts, and more follow-up observations are needed.

Authors' contributions

F.H. conceptualised the study and designed the research. L.H. and W.H. drafted the manuscript and produced the figures. Z.L. revised the manuscript.

Disclosure

The authors have nothing to disclose.

Conflict of interest

None of the authors have any conflict of interest that could be perceived as prejudicing the impartiality of this submission.

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Consent from patient

Obtained.

References

1. Wyk J, Grumbach M. Syndrome of precocious menstruation and galactorrhea in juvenile hypothyroidism: an example of hormonal overlap in pituitary feedback. J Pediatr. 1960; 57(3): 416–435, doi: 10.1016/s0022-3476(60)80250-8.
2. Marin L, Ambrosini G, Noventa M, et al. Thyroid Dysfunction after Gonadotropin-Releasing Hormone Agonist Administration in Women with Thyroid Autoimmunity. Int J Endocrinol. 2022; 2022: 6331657, doi: 10.1155/2022/6331657, indexed in Pubmed: 35465072.
3. Ryan GL, Feng X, d'Alva CB, et al. Evaluating the roles of follicle-stimulating hormone receptor polymorphisms in gonadal hyperstimulation associated with severe juvenile primary hypothyroidism. J Clin Endocrinol Metab. 2007; 92(6): 2312–2317, doi: 10.1210/jc.2006-2086, indexed in Pubmed: 17356048.
4. Bhansali A, Kashyap A, Lodha S, et al. Isosexual precocity: uncommon presentation of a common disorder. Postgrad Med J. 2000; 76(893): 177–178, doi: 10.1136/pmj.76.893.177, indexed in Pubmed: 10684335.
5. Chattopadhyay A, Kumar V, Marulaiah M. Polycystic ovaries, precocious puberty and acquired hypothyroidism: The Van Wyk and Grumbach syndrome. J Pediatr Surg. 2003; 38(9): 1390–1392, doi: 10.1016/s0022-3468(03)00403-2, indexed in Pubmed: 14523827.