A clue to diagnosis in a boy with short stature: Testicular enlargement

To the Editor,

Acquired hypothyroidism is one of the most common endocrine disorders in the childhood, but long-term problems are observed in rare untreated patients. Van Wyk-Grumbach syndrome which is one of these problems was described as juvenile hypothyroidism, delayed bone age and isosexual early puberty in 1960 for the first time (1). This condition is mostly manifested with ovarian cysts, early menstrual bleeding and galactorrhea in girls (1-3), while it is manifested with prominent penile enlargement and increased testicular size without increased testosterone rarely in boys (4, 5). Complete recovery is provided by administering thyroid hormone in both genders (6). In this article, we present an 8 year 9 month-old male patient who presented with short stature in whom increased testicular size found on physical examination directed us to the diagnosis.

An 8 year 9 month-old male patient was referred with deceleration in growth for the last two years and no growth in the last one year. The patient whose neurodevelopmental history was compatible with his age had no familial history of short stature or thyroid disease. On physical examination his height was measured to be 118 cm (Standard deviation score=SDS: -2.33) and weight was found to be 23.2 kg (SDS: -1.25). The patient who had a dry skin had no goitre. His blood pressure was measured to be 90/50 mmHg, his pulse was found to be 64/min and his systemic examination was found to be normal. He had no axillary hair growth, pubic hair growth was found to be Tanner stage I. The left testicle was measured to be 5 cc and the right testicle was measured to be 6 cc. The stretched penile length was measured to be 6 cm.

Biochemical and hormonal values were as follows: AST: 42 U/L (N: 0-35), ALT: 45 U/L (N: 0-45), total cholesterol: 280 mg/dL (N: 0-200), LDL-K: 205 mg/dL (N: 0-130), HDL-K: 55 mg/dL (N>40), TG: 101 mg/dL (N: 0-150), TSH: >500 uIU/mL (N: 0.41-3.45), free T4: 0.45 ng/dL (N: 1.07-1.75), prolactin: 168 ng/mL (N: 4.04-23.3), LH: 0.19 mIU/mL (N: 0.02-0.3), FSH: 1.73 mIU/mL (N: 0.26-3.0), total testosterone <0.08 ng/mL (N<0.2-3.4). The patient's bone age was found to be compatible with 5 years of age. A diagnosis of Van Wyk-Grumbach syndrome was made with the association of short stature, increase in testicular size, hyperlipidemia, hypothyroidism and delayed bone age. Anti-thyroid peroxidase: 144 IU/mL (N: 0-5.61), Anti-thyroglobulin: 194 IU/mL (N: 0-4.11). Hypoplastic and heterogeneous parenchymal appearance which was compatible with chronic thyroiditis was found on thyroid ultrasonography. Low dose thyroid hormone was started and the dose was increased gradually. Euthyroidism was obtained in 2 months and blood lipid levels normalized. The testicles which were firm and swollen started to reduce from the fourth month of treatment and they were each measured to be 3 mm at the 6th month. With treatment annual growth was realized as 10 cm.

Although Van Wyk-Grumbach syndrome which is a rare complication of acquired hypothyroidism has been mostly defined in girls, it has also been reported in boys. Among the causes of early puberty, it is the only condition where delayed bone age and short stature are observed. Penile enlargement and pubic hair growth do not accompany the increase in testicular size observed in boys. In our patient, enlarged testicular size in association with delayed bone age was warning for van Wyk-Grumbach syndrome. Thyroid function tests, presence of autoantibodies and ultrasonographic findings confirmed Hashimoto thyroiditis.

In the pathogenesis of Van Wyk-Grumbach syndrome, it was proposed primarily that low thyroid hormone levels caused to an increase in thyrotropin releasing hormone by disrupting negative feedback. Increased thyrotropin releasing hor-

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mone leads to an increased release of thyroid stimulating hormone (TSH) from the hypophysis as well as an increase in gonadotropins and prolactin (1). One reason of increased prolactin is the fact that hyperplasia of TSH releasing cells in the hypophysis induces prolactin release (6). In our patient, the increased prolactin level at the time of the diagnosis normalized with administration of thyroid hormone. Increased prolactin levels can have an inhibitory effect on pituitary gonadotropins by slowing down the gonadotropin releasing hormone pulse frequency (7). In Van Wyk-Grumbach syndrome, luteinizing hormone levels are low or normal and follicle stimulating hormone levels are increased (3-6). The mechanism of this is based on the interaction of common alpha subunits included in the structures of TSH and follicle stimulating hormone (8). In addition, in vitro studies have shown that excessively increased TSH secondary to untreated hypothyroidism weakly stimulates FSH receptors (9). This may explain the finding that luteinizing hormone and testosterone values are measured to be at prepubertal levels as observed in our patient. Increase in tubular units without marked Leydig cell increase is observed on testicle histology (9).

Conclusively, it should be kept in mind that Van Wyk-Grumbach syndrome can also be observed in boys as an increase in testicular size. Thyroid functions should be absolutely investigated in patients who are found to have short stature and delayed bone age despite findings of early puberty.

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