Premature Menarche Associated with Hashimoto Thyroiditis at 2 years 9 months: Case Report

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Abstract

Primary hypothyroidism is frequently associated with delayed puberty. However, precocious puberty is known to occur in some rare cases of hypothyroidism untreated for a long time.

A female patient with Down syndrome aged 2 years and 9 months was referred with the symptom of vaginal bleeding continuing for 1 week. In her history, there were no symptoms suggesting trauma, foreign body, urinary tract infection or intracranial mass. She exhibited the phenotypic features of Down syndrome. Breast development was at Tanner stage 3 bilaterally, and she had no axillary or pubic hairs. Suprapubic ultrasonography revealed cystic lesions in the right lower quadrant and left adnexial region. She was diagnosed with Hashimoto thyroiditis as result of the tests and was started on Na I-thyroxine replacement therapy, and all examination findings relevant to precocious puberty and laboratory parameters returned to normal in the 6th month of the treatment.

Keywords: Premature Menarche; Hashimoto Thyroiditis; Primary Hypothyroidism; Precocious puberty; Suprapubic ultrasonography

Introduction

The association between Down’s syndrome and thyroid disorders is well recognized. Patients with Down syndrome have an increased prevalence of both congenital hypothyroidism and acquired thyroid dysfunction [1,3]. Hypothyroidism is frequently associated with delayed puberty. However, precocious puberty is known to develop in some rare cases with hypothyroidism untreated for a long time [4]. Van Wyk and Grumbach have reported 3 cases with hypothyroidism developing galactorrhea, retarded bone age and early menarche in 1960 [5]. Then in 1963, Hubble and his colleagues reported a mongoloid child with precocious menstruation [6]. In precocious puberty associated with hypothyroidism, thelarche with or without galactorrhea occurs characteristically followed by menarche without pubic and axillary hairs. Differently from the cases suffering from precocious puberty due to other causes, linear growth and bone age are retarded in children developing precocious puberty associated with hypothyroidism [4]. In addition to these findings, hyperprolactinemia, elevated gonadotropin levels, ovarian growth, multiple abdominopelvic cysts were frequently observed in previously reported cases [7-9]. On the other hand, macroorchidism without virilization has been reported in boys with prolonged hypothyroidism [10]. There are no definite data about the incidence of precocious puberty associated with hypothyroidism [11]. Knowledge about the long term follow-up of these patients is still limited [12].

Case Report

2-year 9-month old female patient with Down syndrome was referred to our clinic from an outer center because of vaginal bleeding lasting for 7 days. Her history revealed that she was diagnosed with Down syndrome when she was 2 months old, was last seen at the hospital when she was 3 months old and was not brought to the recommended control visits since then. Her history did not include any symptoms suggesting trauma, foreign body, urinary tract infection or central nervous system pathologies. Vaginal bleeding started approximately 7 days before and was in small amounts and in the form of spotting. She had typical phenotypic features of Down syndrome such as flattened nasal bridge, hypertelorism, bilateral Simian lines and her height was 77.1 cm (5%-25% percentile) and weight was 10.7 kg (25%-50% percentile). Her heart rate was 80 per minute and blood pressure was 80/50 mmHg. She had excessively dry skin and her hair was very sparse. Her telarche was Tanner stage 3 and she had no axillary and pubic hairs. Her abdomen appeared distended but she had no organomegaly. Her genital examination did not reveal any foreign body, tumor or signs suggesting trauma. Laboratory work up was as follows: Hb:11.5 g/dL (9.6-13.7 g/dL), TSH:>150 µIU/mL (0.5-6.5 µIU/mL) free t4 (ft4) :0.38 ng/dL (0.9-2.1 ng/dL), FSH:3.56 mIU/mL (0.67-3.3 mIU/mL) LH:<0.07 mIU/mL (0.9-1.9 mIU/mL), E2:40.67 pg/mL (0.1-18 pg/mL), prolactin :106.6 ng/mL (19.2-25 ng/mL), anti-thyroid peroxidase (anti-TPO) antibodies:1600 IU/mL (0-35 IU/mL). Her bone age was compatible with 6 months. In thyroid ultrasonography, thyroid volume (tv: 1.4 cm³) was within the reference range for her age and parenchyma of both lobes had heterogeneous appearances compatible with thyroiditis. Her thyroid scintigraphy revealed images compatible with a minimally suppressed thyroid gland of normal size. In suprapubic ultrasonography, there was a cystic mass
in the right lower quadrant with its largest diameter being 3.4 cm and a mass measuring 20x14 mm between this mass and uterus compatible with the right ovary and a septated cystic lesion measuring 43x17x33 mm in the left adnexal region. Bone scintigraphy was carried out to rule out Mc-Cune Albright syndrome and findings were within normal limits in all bone structures.

The patient was started on 2 µg/kg/day Na l-thyroxine therapy. The dose was raised to 4 µg/kg/day on the 5th day of treatment. Vaginal bleeding stopped on the 4th day of treatment and did not recur in the follow-up. Thyroid function tests and other hormonal values were seen to be within normal levels for her age in the 3rd month of follow-up (TSH: 2.1 µIU/mL, st4:1.72 ng/dL, FSH < 3 mIU/mL, LH<0.07 mIU/mL, E2:11.8 pg/mL). In the 6th month of her treatment, breast development regressed to Tanner stage 1 and suprapubic ultrasonography revealed that previously noted cystic structures totally disappeared. In the 8th month of her follow-up, growth rate reached a high level of 9.9 cm/8 months and percentile of height reached 50%-75%.

Discussion

Primary hypothyroidism is frequently associated with delayed puberty [4]. However, in precocious puberty associated with hypothyroidism untreated for a long time as in our case, telarche with or without galactorrhea followed by menarche seen without auxiliary and pubic hairs is characteristic [13]. In fact, our patient had Tanner stage 3 breast development and did not have axillary and pubic hairs at presentation. Another important clinical clue in favor of primary hypothyroidism is linear growth and pause in bone age observed in patients with hypothyroidism which is different from many disorders causing precocious puberty. At presentation, height of our case was in the 5%-25% percentile adjusted for children with Down syndrome and her bone age was compatible with 6 months when her calendar age was 2 years 6 months. This finding suggests that pathologic changes started around 6 months. Furthermore, her breast development regressed to Tanner stage 1 in the 6th month of her treatment for hypothyroidism and her growth rate was noted to be 9.9 cm/8 months. Other findings noted in cases of precocious puberty associated with hypothyroidism are hyperprolactinemia, increased gonadotropin levels but hyperprolactinemia was not noted. These findings suggest that not only one but a combination of the mentioned theories can explain the clinical, laboratory and radiologic findings noted in our patient.

Hypothyroidism is common in childhood due to many reasons like congenital hypothyroidism and autoimmune lymphocytic thyroiditis. However, premature menarche is a rarely seen clinical presentation of hypothyroidism. Contrary to the other cases of precocious puberty due to other reasons, linear growth is stunted and bone age is retarded. This knowledge alone is enough to draw attention once more to the importance of monitoring the growth curves of children and evaluating tiroid function in all endocrinologic problems.

References