Clinical Case Report

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Clinical case report

A case of Turner syndrome with Graves' disease

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Abstract

Introduction: The incidence of Hashimoto's thyroiditis among patients who have Turner syndrome (TS) has increased, but Graves' disease (GD) in patients with TS is rarely reported. Here we report a rare case of TS with GD accompanied by hypogonadotropic hypogonadism.

Patient concerns: We report the case of a 16-year-old girl who complained nervousness, fatigue, marasmus, heat intolerance, sweating, palpitation, and tremor lasting for more than a month. She had no medical history.

Diagnosis: TS was diagnosed of the results of karyotyping demonstrated a gene karyotype of 46, X, i (X)(q10). GD was also diagnosed in this patient following the detection of thyroid function analysis.

Interventions: Methimazole was administered after identification of GD. Due to the absence of secondary sex characteristics, the patient was given a conjugated estrogen preparation for 1 year, followed by the addition of estradiol cyproterone tablets for the onset of menstruation.

Outcomes: The hyperthyroidism symptoms of the patient had improved both clinically and laboratory tests after methimazole therapy. She was treated with estrogen and estradiol cyproterone, and the uterus and secondary sexual characteristics of the patient developed during 1 year follow-up.

Conclusion: TS generally presents as hypergonadotropic hypogonadism. However, hypogonadotropic hypogonadism cannot completely exclude TS. The diagnosis of this disease depends on chromosomal examination. The disease should be detected and treated as early as possible to improve life quality of the patient.

Abbreviations: GD = Graves' disease, HT = Hashimoto's thyroiditis, MRI = magnetic resonance imaging, TS = Turner syndrome, TSH = thyroid-stimulating hormone, US = ultrasonography.

Keywords: Graves' disease, hypogonadotropic hypogonadism, Turner syndrome

1. Introduction

It is well known that Turner syndrome (TS) is among the most common chromosomal abnormalities resulted from structural or numeric abnormalities in the X chromosome.[1–3] It is found in 1/2000 to 1/3000 live-born females.[4] Characteristic physical abnormalities include a short stature, broad chest, webbed neck, kidney abnormalities, cubitus valgus, edema of the hands or feet, cardiac anomalies, gonadal dysgenesis, and delayed puberty.[1,5]

Patients with TS suffer from an increasing risk of autoimmune thyroid disorders, celiac disease, vitiligo, psoriasis, type 1 diabetes, adrenocortical insufficiency, juvenile idiopathic arthritis, and inflammatory bowel disease.[6–9] Hashimoto's thyroiditis (HT) is more frequent in patients who have TS.[10,11] From perspectives of pathogenic mechanism in autoimmune thyroiditis, a higher incidence of Graves' disease (GD) might also be expected in TS patients. However, the connection between GD and this syndrome is significantly more infrequent than expected.[3,12] The aim of our study was to report a case of TS with GD.

2. Case presentation

This study was approved by the ethics committee of the First People's Hospital of Chongqing Liang Jiang New Area. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

In 2017, a 16-year-old girl first visited our hospital and complained nervousness, fatigue, marasmus, heat intolerance, sweating, palpitation, and tremor lasting for more than a month. Physical examination revealed smooth, moist, and warm skin; mild exorbitism, and diffused thyroid gland enlargement. Fine finger tremor was not detected. The patient's heart rate was 148

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Informed written consent was obtained from the patient's guardians for publication of this case report and accompanying images.

The authors have no conflicts of interest to disclose.

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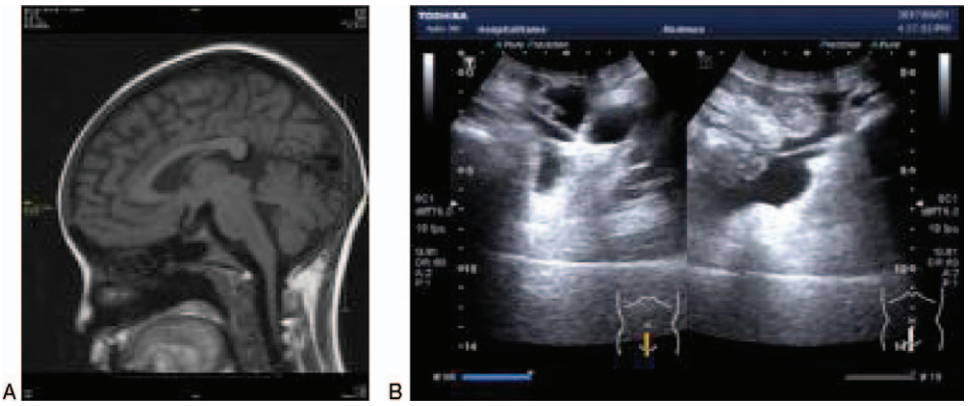

Figure 1. (A) Pituitary MRI revealed partial empty sella. (B) The uterus and both ovaries could not be identified by pelvis ultrasonography. MRI = magnetic resonance imaging.

beats/minutes, the blood pressure was 112/66 mm Hg, and precordial systolic murmur of grade 1 was detected. Her height was 132 cm, the weight was 22 kg, and body mass index was 12.6 kg/m^2. The patient's external genitalia were juvenile, with a pubertal state of A1M1P1 (Tanner staging). Hormonal assays, chromosomal karyotyping, X-ray analysis of bone age, abdominal and pelvic ultrasound, echocardiography, pelvic magnetic resonance imaging (MRI), and pituitary MRI were performed. Her bone age was 12 years old. The results of bone marrow puncture suggested iron deficiency anemia. Pituitary MRI revealed partial empty sella (Fig. 1A). The results of karyotyping demonstrated a gene karyotype of 46, X, i (X)(q10), indicating TS.

Thyroid function analysis presented that the thyroid-stimulating hormone (TSH) level was 0.01 μIU/mL (normal range, 0.38–5.57 μIU/mL), the free (f) T4 level 3.16 ng/dL (normal range, 0.78–1.86 ng/dL), the free T3 level 6.46 pg/mL (normal range, 1.8–3.8 pg/mL), the antithyroglobulin antibody level 2321.7 IU/mL (normal range, 0.00–95.00 IU/mL), the antithyroid peroxidase antibody level 10,000 IU/mL (normal range, 0.00–25.00 IU/mL), and the TSH receptor antibody level >300 IU/L (normal range, 0.00–1.50 IU/L). GD was indicated by the results above, and methimazole was provided. The dose of methimazole was adjusted according to thyroid hormone levels.

Other hormonal tests demonstrated that the prolactin level was 3.10 ng/mL (reference range, 4.1–28.9 ng/mL) and the testosterone level was 8.95 ng/mL (reference range, 9.81–82.1 ng/mL). The patient's estradiol level was less than 25.00 pg/mL (reference range, 40.7–424.6 pg/mL), the luteinizing hormone level was less than 0.2 mIU/mL, and the level of follicle-stimulating hormone was less than 1.0 mIU/mL. The ovaries and uterus failed to be detected by pelvis ultrasonography (US) (Fig. 1B), MRI, or computed tomography. Due to the absence of secondary sex characteristics, the patient was given a conjugated estrogen preparation for 1 year, followed by the addition of estradiol cyproterone tablets for the onset of menstruation. At the latest follow-up (17 years old), the patient's breasts had developed to Tanner stage 2. The patient's bone age was 13.5, and pituitary-enhanced MRI indicated that she still had partially empty sella (Fig. 2A). Neither ovary could be detected by pelvis US; however, a small uterus was identified (Fig. 2B).

3. Discussion

TS has a high incidence of autoimmune diseases, including HT, celiac disease, diabetes mellitus, inflammatory bowel disease, GD, and adrenocortical insufficiency, in girls.[13,14] Excess autoimmune antibodies likely result from X chromosome

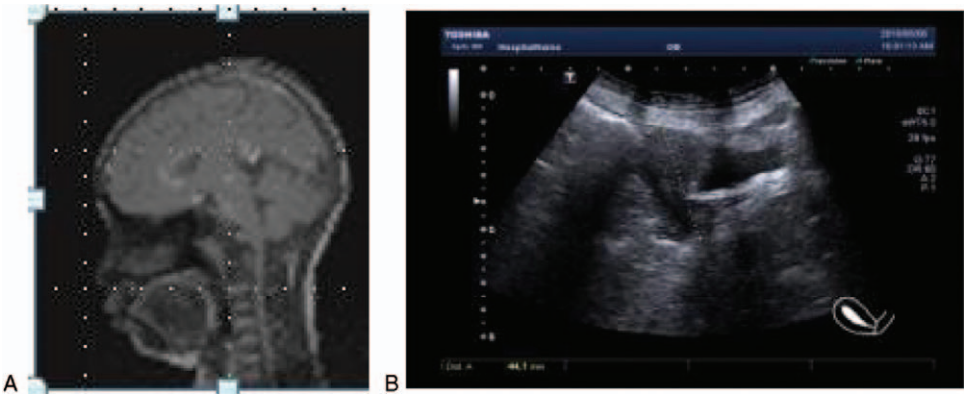

Figure 2. (A) Pituitary-enhanced MRI indicated partially empty sella. (B) A small uterus was detected, and both ovaries could not be identified on pelvis ultrasonograph.MRI = magnetic resonance imaging.

defects.[15,16] Haploinsufficiency of more than 10 genes located on the X chromosome was related to the immune regulating process, influenced the regulation of the immune response and led to altered immune tolerance.[15,17] Another mechanism suggested the upregulation of pro-inflammatory cytokines contributed to the increasing susceptibility of girls with TS to Autoimmune thyroid disease.[18] The reasons why the thyroid gland was an autoimmune target in TS patients have not yet been clearly identified, but the predilection could be elucidated based on the close connection between the thyroid autoimmunity and female gender.[19]

The present patient exhibited a diffused thyroid gland and thyrotoxicosis longer than approximately 1 month. The result of serum analysis was highly positive for antithyroid antibodies.[12,20] In contrast to the well-recognized combination of TS and HT, the combination of TS and GD is rather rare.[21,22] The next issue is why TS accompanied by hyperthyroidism is rare, compared with TS with HT.[3,23] This may be elucidated if typical GD and HT involve different autoimmune processes.[24,25] Since TS belongs to sex chromosome disorder, it is likely that the combination of these 2 disorders is attributed to a specific gene.[26,27] Considering the high susceptibility of patients with TS to autoimmune disease, human leukocyte antigen genes analysis is of vital importance.[6,28] To date, there has been no clear explanation to explain this problem. In conclusion, the connection between GD and TS is far from elucidated, and we cannot exclude that the 2 diseases are just related by chance.[29] In our patient, treatment with thiamazole was continued and the thyroid function has stayed within normal ranges.

TS generally presents as hypergonadotropic hypogonadism,[30] but this patient presented with hypogonadotropic hypogonadism. This may be related to the patient's vacuolar sella turcica, which can compress the pituitary tissue and displace the pituitary stalk, thus leading to a decline in hypophysis function; in addition, this may be related to the patient's malnutrition. The patient was given successively estrogen and estradiol cyproterone treatment to develop the uterus and secondary sexual characteristics.

4. Conclusion

Vigilance for TS is required when young girls exhibit hyperthyroidism accompanied by growth retardation and gonadal dysplasia. A decrease in the gonadotropin expression cannot completely exclude TS. The diagnosis of this disease depends on chromosomal examination. The disease should be detected and treated as early as possible to improve the short-term and even long-term life quality of the patient.

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