Clinical Case Report

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A case report of ^{131}I therapy for Graves' disease patient with hemiagenesis

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Abstract

Rationale: Thyroid hemiagenesis is a rare congenital dysplasia, whereas a variety of pathological changes may occur in residual thyroid lobe. The most frequently described pathology in residual thyroid lobe is Graves' hyperthyroidism. Although ^{131}I therapy has been generally recommended as the preferred treatment for Graves' disease (GD), subjects relating to hemiagenesis are very limited, especially in China.

Patient concerns: A 43-year-old female patient presented to our hospital on November 2014, with a 1-year history of palpitation, fatigue, and hand tremor. Her situation was getting worse within 2 months.

Diagnosis: The thyroid function tests were suggestive of thyrotoxicosis. The technetium thyroid scintigraphy only showed an enlarged right lobe with increased tracer uptake. Then, the agenesis of left lobe and isthmus was confirmed by ultrasound and magnetic resonance imaging (MRI). Thus, a diagnosis of GD with hemiageneis of the left lobe and isthmus of thyroid was made.

Interventions: Thiamazole was discontinued because of drug-induced hepatic injury. According to our procedures, the patient was treated by ^{131}I.

Outcomes: Hypothyroidism was observed 3 months after ^{131}I therapy. After replacement therapy with L-thyroxine (LT4), the state of euthyroid maintained.

Lessons: Once hypothyroidism occurs, regular application of LT4 and review of thyroid function is very important. Thus, patients' compliance needs to be strengthened. Besides, we could not convince the family members of our patient to undergo ultrasonographic examination. The genetic factor of the agenesis could not be proved in this case.

Abbreviations: ^{131}I = radioactive iodine 131, ALP = alkaline phosphatase, ALT = alanine aminotransferase, ATD = anti-thyroid drug, CT = computed tomography, FT3 = free triiodothyroinine, FT4 = free thyroxine, GD = Graves' disease, GGT = glutamyl transpeptadase, LT4 = L-thyroxine, mAST = mitochondrial aspartate aminotransferase, MRI = magnetic resonance imaging, SPECT = single-photon emission computed tomography, TBIL = total bilirubin, TPOAb = anti-thyroid peroxidase antibody, TRAb = thyrotrophin receptor antibody, TSH = thyroid-stimulating hormone.

Keywords: Graves' disease, radioactive iodine 131, thyroid hemiagenesis

1. Introduction

Thyroid hemiagenesis is a rare congenital dysplasia, in which one of the thyroidal lobes fails to develop, and was first described by Handfield-Jones in 1866.[1] Most patients with hemiagenesis are euthyroid, accompanying no clinical symptoms.[2] As a result, thyroid hemiagenesis is usually found incidentally during investigating concomitant abnormalities of thyroid function or suspected structural abnormality. It has been previously reported that a variety of pathological changes may occur in residual thyroid lobe.[3] The most frequently described pathology, concomitant with thyroid hemiagenesis, is Graves' hyperthyroidism.[4]

For patients of Graves' disease (GD) with hemiagenesis, therapy of anti-thyroid drug (ATD) is a common choice, whereas cases concerning the treatment of radioactive iodine 131 (^{131}I) is seldom documented. We report such a patient treated by ^{131}I therapy in China.

2. Ethic

The institutional review board and ethic committee of Tianjin Third Center approved the ethical, methodological, and protocol aspects of this investigation. The ethical approval number was IRB2018-004-01. We confirm that all methods in the present

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study were carried out in accordance with the relevant guidelines and regulations. Informed written consent was obtained from the patient for publication of this case report and accompanying images.

3. Case report

A 43-year-old female patient presented to our hospital on November 2014, with a 1-year history of palpitation, fatigue, and hand tremor. Her situation was getting worse within 2 months. There was no family history of thyroid disease. On examination, grade 2 goiter was presented, on the right side. The left lobe of thyroid was not palpable. Moist skin, hand tremor, and tachycardia (110/min) were presented as well. The rest of the physical examination was unremarkable.

The thyroid function tests were suggestive of thyrotoxicosis, with free triiodothyroinine (FT3) of 24.1 pmol/L (3.1–6.8), free thyroxine (FT4) of 60.6 pmol/L (12–22), and thyroid-stimulating hormone (TSH) of <0.005 mIU/L (0.27–4.2). Antithyroid peroxidase antibody (TPOAb) and thyrotrophin receptor antibody (TRAb) were both positive, with titers of 99.57 IU/mL (<34) and 13.37 IU/L (<1.75), respectively. The hepatic and renal function as well as routine blood tests were all within the normal ranges. The technetium thyroid scintigraphy (SYMBIA T2, SIEMENS, Germany) was carried out, which showed the absence of left lobe and isthmus as well as an enlarged right lobe of thyroid with increased tracer uptake with uniform distribution. Besides, no ectopic thyroid gland was discovered (Fig. 1A). An ultrasound of thyroid (IU-22, PHILIPS, Holland) was done, which confirmed the absence of left lobe and isthmus, whereas the right lobe of thyroid was swelling and plenty of blood flow (Fig. 1B). Cervical magnetic resonance imaging (MRI, MRI-VERIO 3.0t, SIEMENS SONATA, Germany) was undergone, further confirming the thyroid agenesis of left lobe and isthmus (Fig. 1C).

Based on the clinical details above, the diagnosis of GD with hemiageneis of the left lobe and isthmus of thyroid was made. Then the patient took antithyroid drug therapy (ATD) with thiamazole(2×10 mg/d). After 4 weeks, the hepatic function and routine blood test were evaluated again, which revealed an abnormally increased level of alanine aminotransferase (ALT) of 90 (7–40 U/L), whereas other parameters such as mitochondrial aspartate aminotransferase (mAST), glutamyl transpeptadase (GGT), alkaline phosphatase (ALP), total bilirubin (TBIL), akaryocyte, leucocyte, and plastocyte disclosed no abnormalities. Hence, due to the consideration of drug-induced hepatic injury, thiamazole was discontinued immediately.

Two weeks after withdrawal of ATD, the treatment of ^{131}I was applied according to our procedures. ^{131}I uptake was 75.8% in 24 hours and 88.8% in maximum. The effective half time was 3.8 days. The mass of thyroid evaluated by single-photon emission computed tomography (SPECT) was 21 g. A dosage of 148 MBq (dose of ^{131}I ($\times$37 MBq) = mass of thyroid (g) $\times$ absorbed dose of unit thyroid tissue (Gy $\times$ g^{-1}) $\times$ 0.67/[maximum rate of thyroid iodine uptake (%) $\times$ effective half-life (d)[5]] of ^{131}I was taken orally. Three months after ^{131}I administration, hypothyroidism

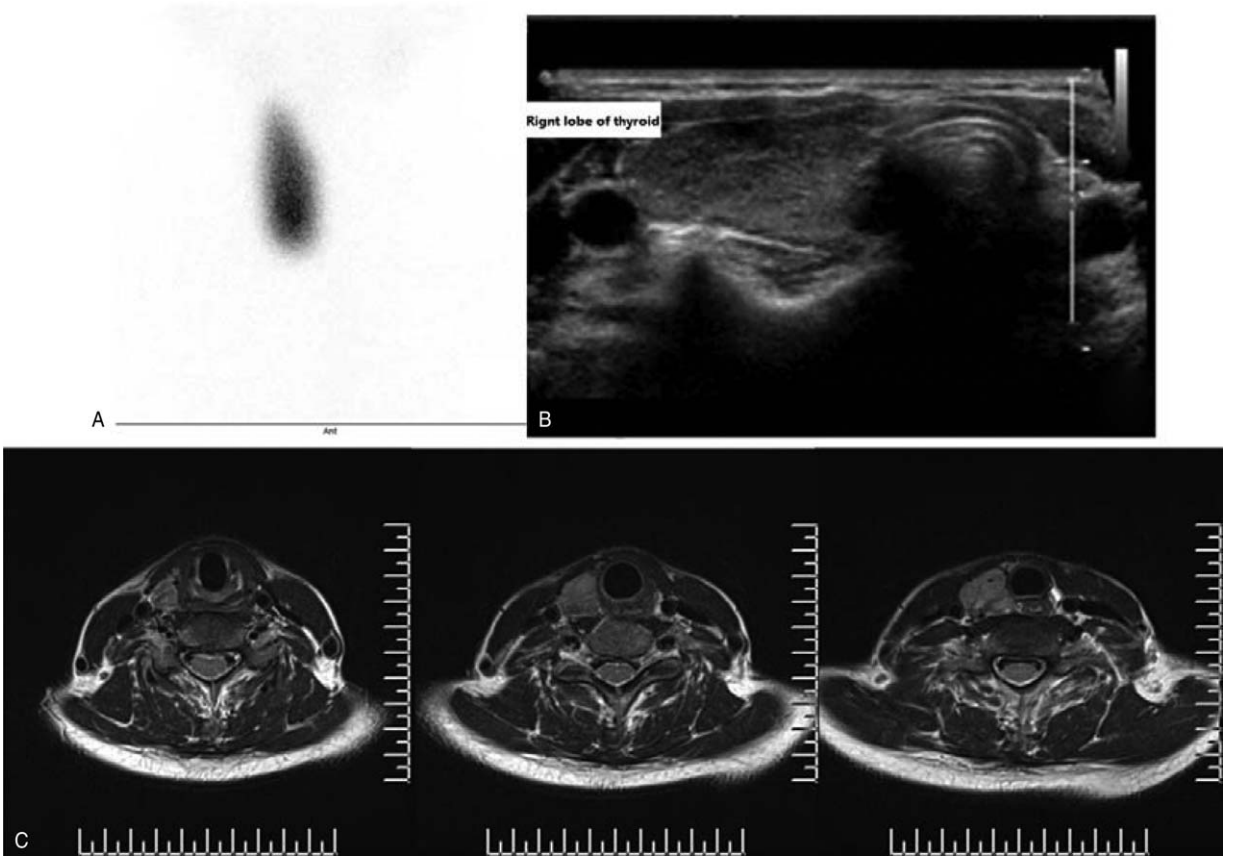

Figure 1. The first technetium thyroid scintigraphy (A) showed the absence of left lobe and isthmus as well as the enlarged right lobe of thyroid with increased tracer uptake with uniform distribution. The ultrasound of thyroid (B) and cervical magnetic resonance imaging (C) both showed the enlarged right lobe of thyroid and agenesis of left lobe and isthmus.

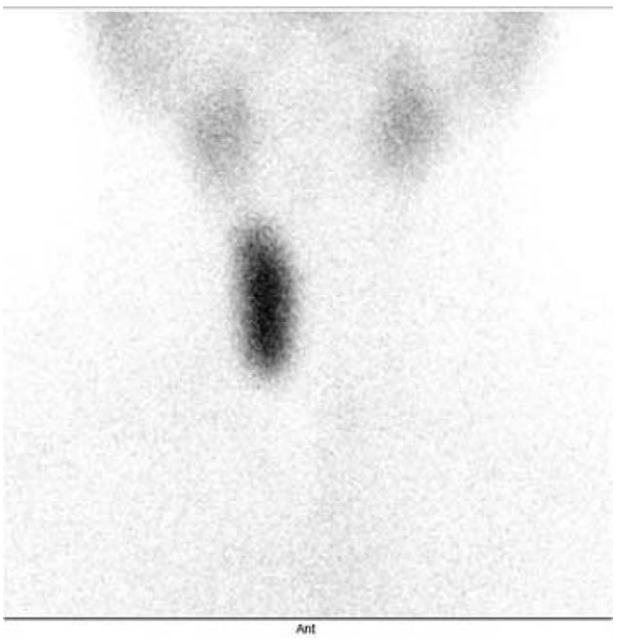

Figure 2. The second technetium thyroid scintigraphy showed obviously decrease in size and tracer uptake degree of right lobe of thyroid than the former.

was observed, with FT3 of 1.08 pmol/L (3.1–6.8), FT4 of 2.23 pmol/L (12–22), and TSH of 54.84 mIU/L (0.27–4.2). Thus, replacement therapy with L-thyroxine (LT4, 50 μg/d) was introduced. In the meantime, the hepatic function recovered. Six months later, the state of euthyroid was achieved.

The check-up examination was performed 30 months after ^{131}I therapy. During the period, the patient did not take LT4 as prescribed for a while. Thus, hypothyroidism occurred again. Once LT4 was taken regularly, thyroid function of the patient gradually returned to normal. The technetium thyroid scintigraphy was carried out 24 months after ^{131}I therapy (Fig. 2). The evaluated mass of thyroid reduced to 9.8 g.

4. Discussion

Thyroid hemiagenesis is a rare congenital abnormality. Since the first case was described in 1866,[1] approximately 300 cases have been reported in literatures. A large meta-analysis[6] has estimated a 0.05% prevalence of this abnormality. However, the total number of reported cases probably underestimates the actual incidence of thyroid hemiagenesis because this anomaly was usually clinically euthyroid and detected accidentally during the investigation of accompanying thyroid disease. The true incidence in the general population is difficult to detect. A study in Belgium was conducted by Shabana et al[7] to determine the actual prevalence of this anomaly at an early age. They evaluated 2845 normal school children (aged between 6 and 12 years) during a systematic ultrasound study of thyroid gland volume and found left lobe agenesis in 4 girls and 2 boys. Their study showed that the estimated prevalence of thyroid hemiagenesis is 0.2%. Another similar study in Sicily was conducted by Maiorana et al.[8] They evaluated 24,032 unselected children (aged between 11 and 14 years) by neck ultrasound examination. In this study, left lobe agenesis was identified in 5 girls and 7 boys, with a total prevalence of 0.05%.

Just as our patient, thyroid hemiagenesis is more frequent in left lobe (80%).[1] Besides, the agenesis of isthmus is detected in 44% to 50% of cases.[6] The sex tendency of the anomaly is not clear. There seems to be a greater number of female cases with thyroid hemiagenesis in literatures. However, this may be linked to higher incidence of concomitant thyroid diseases in female group.

The reason of hemiagenesis is undiscovered. Embryologically, the thyroid gland develops from a duct-like invagination of the primitive pharynx endoderm and expands ventrally along the thyroglossal duct line as a spherical thyroid gland primordium. Then the thyroid primordium begins to expand laterally and acquire the characteristic bilobular structure. Researchers attributed the agenesis of a part of the thyroid to the failure of the cells to migrate laterally.[9] It is unknown whether the lobulation defect is due to the interference of environmental factors or to some genetic mutations. Until now, a genetic factor is suggested by the presence of thyroid hemiagenesis among monozygotic twins,[10] among sisters,[11] or together with other thyroid malformations within one family.[12–13] Several genes, such as 3 thyroid transcription factors (TTF-1, TTF-2, and PAX-8), have been found to control thyroid morphogenesis and descent. However, these genes have not been investigated in thyroid hemiagenesis.[14–15] It is regrettable that we could not convince the family members of our patient to undergo ultrasound examination. The genetic factor of the agenesis could not be verified in our patient.

Thyroid hemiagenesis is commonly diagnosed during the investigation of accompanying thyroid disorders. Such disorders include GD, nodular goitor, subacute thyroiditis, hyperfunctioning adenoma, chronic thyroiditis, and carcinoma.[2] Hyperthyroidism was reported to be the major reason for diagnosis.[4] The patients, who were suggestive of thyrotoxicosis, should receive further examinations for differential diagnosis. In diagnostic precedures, thyroid scintigraphy takes up an irreplaceable function, which shows uptake capacity of thyroid tissue. Yet, ultrasound has a clearly superiority over physical examination and scintigraphy in the assessment of thyroid morphology.[16] As in this patient, numerous cases in literatures were accidentally found to be functional hemiagenesis by scintigraphy and finally confirmed by ultrasound. In addition, cervical computed tomography (CT) and cervical MRI could give more detailed descriptions on the relationship between thyroid gland and adjacent organs. But both the techniques are expensive and time consuming.

Although ^{131}I therapy has been generally recommended as the preferred treatment for GD,[17] subjects relating to hemiagenesis are very limited. In our case, a favorable result was achieved through treatment. Similarly, in 2008, Ruchala et al[18] adopted ^{131}I treatment for GD with hemiagenesis instead of method of ATD because of the severe allergic reaction in the form of nettle-rash and granulocytopenia, and finally succeed in treatment. Harisankar et al[19] also approved that ^{131}I ablation was a safe and convenient modality of treatment for GD complicated with structural abnormalities of thyroid gland.

We identify that a small initial thyroid volume (in case of the agenesis of one thyroid lobe) is a predictor for suppressing hyperthyroidism symptoms after a single course of radioiodine treatment, as well as a risk factor for development of early hypothyroidism.[20] Once hypothyroidism occurs, regular application of LT4 and reexamination of thyroid function are very important. Thus, patients' compliance needs to be strengthened.

Author contributions

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Supervision: Zhaowei Meng.
Writing – original draft: Xuehui Liu, Jianping Zhang.
Writing – review and editing: Zhaowei Meng.

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