CASE REPORT

Thyrotoxicosis in patients with hypothyroidism is not just overtreatment

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SUMMARY

A 62-year-old Caucasian woman presented with hypothyroid symptoms and biochemical thyrotoxic picture. Previously, she underwent right-sided subtotal thyroidectomy and left partial thyroid lobectomy for thyroid lumps, and treated with thyroxine replacement for hypothyroidism. Although there were no significant findings on clinical examination, investigations confirmed thyrotoxicosis with positive autoimmunity against thyroid gland all in line with a diagnosis of Graves' hyperthyroidism. We would like to highlight atypical presentations of thyroid dysfunction and conversion of underactive to overactive thyroid status with this case. Early recognition, diagnosis and intervention are essential to prevent and/or reduce associated morbidity and mortality. When encountered with such clinical conundrums, we recommend seeking opinion from an experienced endocrinologist while interpreting such situation.

BACKGROUND

Postlobectomy hypothyroidism is a common complication. However, many may recover with their preoperative thyroid-stimulating hormone (TSH) forming an independent predictor.¹ There are cases described of latent and/or overt hyperthyroidism and clinical thyrotoxicosis after several years of thyroxine treatment for such hypothyroidism.² Also, in the presence of autoimmunity, such patients may manifest conversion from hypothyroid to hyperthyroid due to a shift in the balance between stimulating and inhibiting thyroid autoantibodies. If left untreated, hyperthyroidism with continued thyroid supplementation may contribute to several comorbidities such as atrial fibrillation, osteopenia, osteoporosis and stroke.³ We describe one such case to highlight the importance of systematically evaluating thyrotoxicosis noted while treating a patient with hypothyroidism.

CASE PRESENTATION

A 62-year-old Caucasian woman was referred by her general practitioner in February 2016 in view of hypothyroid symptoms but with biochemical thyrotoxic picture. She did have a right-sided subtotal thyroidectomy in March 1989 (histology: colloid goitre with marked fibrosis; thyroglobulin antibodies—1:640; thyroid microsomes antibodies—1:400) and left partial thyroid lobectomy in November 1993 (histology: cystic thyroid adenoma) for thyroid lumps. Patient reported no

thyrotoxic state presurgery and, currently, there are no biochemical results available to confirm this. Postsurgery, she was commenced on thyroxine replacement (levothyroxine 150 µg once daily) for postoperative hypothyroidism. This was continued until November 2015 when it was stopped in view of the thyrotoxic biochemistry. Apart from thyroidectomies, she had cholecystectomy and hysterectomy in the 1970s; otherwise, she did not have any significant medical history. There is no report of thyroid disorder in the family. She never smoked and was a teetotaler with healthy lifestyle all her life.

During review in February 2016, she described symptoms of lethargy, dry skin and weight gain. On examination, she appeared clinically euthyroid. There were no features of goitre or any other swelling on neck examination. The thyroidectomy scar was well healed and there were no obvious keloid formations or any goitre. There is no evidence of thyroid eye disease. She was clinically in sinus rhythm.

INVESTIGATIONS

Her thyroid function test indicated thyrotoxic picture. Interestingly, patient had nearly undetectable TSH with raised free T4 for over a decade of monitoring at primary care; free T3 was not routinely monitored during this period (see figure 1A–C). Anti-TSH receptor antibodies (TRAb) were 12.3 U/L (0.0–0.9 U/L); antithyroid peroxidase antibody test was negative.

Ultrasound of thyroid: There was a 10×7 mm hypoechoic tissue within the right thyroid bed (probable residual thyroid tissue). The left thyroid lobe measured 32×17×13 mm. An 8×8 mm heterogeneous solid nodule was noted within the lower pole of the left thyroid lobe. Further, there was a 48×38×32 mm heterogeneous mass within the suprasternal notch with echo characteristics of a thyroid tissue indicating a suspicion of ectopic thyroid tissue (see figure 2A). Re-examination of the patient confirmed this finding. There was no obvious cervical lymphadenopathy. Thyroid technetium uptake scan confirmed hyperfunctional left lobe of thyroid which is larger than the right lobe and also increased tracer uptake in the suprasternal notch corresponding to the lesion identified on ultrasound (see figure 2B). These imaging results were interesting due to the fact that she has had thyroidectomies, initially right sided, and later left sided.

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Figure 1 Timeline of significant events and biochemical changes in (A) thyroid-stimulating hormone (TSH), (B) free thyroxine and (C) free triiodothyronine over the years.

TREATMENT

To summarise, the patient had biochemical thyrotoxicosis, positive TRAb, and toxic left lobe of thyroid all in line with a diagnosis of Graves' hyperthyroidism. The results were discussed with the patient and antithyroid medication (carbimazole 5 mg once daily) was temporarily initiated and later radioactive iodine (RAI) (555 MBq) was administered in September 2016.

OUTCOME AND FOLLOW-UP

Four weeks post-RAI, patient presented with worsening tiredness. Biochemical tests indicated thyrotoxicosis (see figure 1). Following evaluation, she was diagnosed with probable radioiodine-induced thyroiditis and an observing approach was adopted after discussing the findings and results with the patient.

Three months post-RAI, patient continued to have persistent tiredness and had now developed clinical features of thyrotoxicosis with tremors on outstretched hands. Her repeat

Figure 2 Thyroid ultrasound scan (A) showed the heterogeneous solid nodule within the lower pole of the left thyroid lobe and a heterogeneous mass within the suprasternal notch (SSN). Thyroid technetium uptake scan (B) confirmed hyperfunctional left lobe of thyroid and increased tracer uptake in the SSN.

biochemistry confirmed a persistent thyrotoxic state and hence suggested failed radioiodine treatment. Patient was restarted on carbimazole and advised about potential side effects and complication. A review 6 weeks after carbimazole initiation indicated clinical and biochemical euthyroidism. Patient received second dose of RAI (650 MBq) as a definitive treatment for the relapsed hyperthyroidism. She has now achieved optimal outcome of clinical and biochemical hypothyroidism and is on levothyroxine therapy.

DISCUSSION

We describe an atypical case of thyroid dysfunction conversion and clinical manifestation. Although initially treated for hypothyroidism, the patient eventually developed biochemical thyrotoxicosis but exhibited symptoms traditionally associated with hypothyroidism. This can be very confusing to an inexperienced healthcare professional. Several scientific reports dating as early as 1931 have reported atypical hyperthyroid symptoms; sometimes, these manifestations are much closer to those noted in hypothyroidism.^{4,5}

The first case of hypothyroid patient converting to hyperthyroidism was reported by Joplin and Fraser in 1959. Since then, several similar cases have been reported worldwide.^{1,2} Several mechanisms have been postulated to explain the phenomenon. Presence of both stimulating and blocking antibodies to thyroid receptors and their cyclical expression was postulated to explain a push-pull phenomenon of thyroid dysfunction where the same patient can manifest with both Hashimoto's and Grave's disease.⁶ Another theory postulates imbalance in the recovery of thyroid tissue and hence overactivity after destruction from initial autoimmune tissue damage—a phenomenon described as hashitoxicosis.^{7,8} In vitro, Rapoport *et al* demonstrated a production of a non-immunoglobulin thyroid stimulator by human lymphocytes during mixed culture with human thyroid cells resulting in thyroid hyperplasia and thyrotoxicosis.⁹

In summary, atypical presentation of thyroid dysfunction and conversion of underactive to overactive thyroid features are not uncommon. Early recognition, diagnosis and intervention are essential to prevent and/or reduce associated morbidity and mortality. When encountered with such clinical conundrums, we

recommend seeking opinion from an experienced endocrinologist while interpreting such situation.

Learning points

- ▶ Hyperthyroidism can sometimes manifest atypically with symptoms of hypothyroidism.
- ▶ Conversion of hypothyroidism to hyperthyroidism and thyrotoxicosis is not an uncommon phenomenon.
- ▶ Presence of clinical or biochemical thyrotoxicosis in treated hypothyroid patients should not be glossed over as an adverse effect of thyroid hormone supplementation.
- ▶ Care should be taken to routinely monitor thyroid function test and further probed if thyrotoxicosis persists despite discontinuing thyroid supplementation.

Contributors PK prepared the first draft of the case report and AUK did overall supervision. Both were involved in the management of the case.

Competing interests None declared.

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