CASE REPORT

Hot and cold: coexistent Graves' disease and Hashimoto's thyroiditis in a patient with Schmidt's syndrome

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Accepted 8 May 2014

SUMMARY

A 37-year-old housewife presented with generalised fatigue, palpitations and weight loss over the past 3 months. Physical examination revealed signs of hyperthyroidism. Thyroid function tests confirmed the presence of thyrotoxicosis. Pertechnetate radionuclide imaging of the thyroid showed diffusely increased radiotracer uptake consistent with Graves' disease and a cold nodule in the right lobe. Needle aspiration from the nodule yielded evidence of Hashimoto's thyroiditis. The patient also tested strongly positive for antithyroid peroxidase antibodies. Simultaneous laboratory evaluation revealed primary adrenal failure and probable pernicious anaemia, thus producing a diagnosis of Schmidt's syndrome. The patient was initiated on appropriate medical therapy for endocrinopathy. Graves' disease was treated with radioablation.

BACKGROUND

Graves' disease and chronic autoimmune thyroiditis, better known as Hashimoto's thyroiditis, represent two forms of autoimmune thyroid disease with diametrically opposite clinical manifestations of hyperthyroidism and hypothyroidism, respectively. Both these disorders have been associated with type 2 polyglandular autoimmune syndrome also known as Schmidt's syndrome, although the association is somewhat stronger for Hashimoto's thyroiditis.[1] This report describes a patient with autoimmune thyroid disease on a background of Schmidt's syndrome. Unlike previously reported cases, however, this patient was ultimately diagnosed with an unusual mosaic pattern of Graves' disease and Hashimoto's thyroiditis affecting discrete portions of the thyroid gland. The presence of clinically silent Hashimoto's thyroiditis in a patient with overt signs of Graves' disease raises questions regarding whether a proportion of patients currently diagnosed with Graves' disease, might actually represent such mosaic disease, and which form of therapy might be best suitable for this subset of patients.

CASE PRESENTATION

A 37-year-old housewife presented with generalised fatigue, palpitations and weight loss over the past 3 months. She had been seen at a local health centre, diagnosed with anaemia and prescribed oral haematinics. When her symptoms failed to respond, she was referred to our hospital. There was no significant medical history. Menstrual history revealed associated oligomenorrhoea. She denied any history of substance abuse.

On general physical examination, she was found to have regular tachycardia with a heart rate of 130 bpm, warm moist peripheries and moderate conjunctival pallor. Blood pressure was normal (116/74 mm Hg) with no postural variation. Obvious signs of hyperthyroidism in the form of fine tremors, bilateral lid retraction and a diffuse goitre were also noted. Systemic examination was normal barring a faint systolic murmur in the pulmonary area.

INVESTIGATIONS

Routine laboratory tests showed macrocytic anaemia (haemoglobin 8.3 mg/dL, mean corpuscular volume 117 mmoL), with normal leucocyte and platelet counts (5400 and 283 000 cells/μL, respectively). Erythrocyte sedimentation rate was normal (35 mm/h). Peripheral blood smear confirmed macrocytosis. Fasting blood glucose was 92 mg/dL. Renal and liver function tests and serum electrolytes were within normal limits. Thyroid function tests confirmed thyrotoxicosis (serum T3 4.63 ng/mL, serum T4 19.54 μg/dL, serum thyroid stimulating hormone <0.005 μIU/mL).

Tc-99 m pertechnetate radionuclide imaging of the thyroid showed diffusely increased radiotracer uptake consistent with Graves' disease and a cold nodule in the right lobe. A fine-needle aspiration was performed under ultrasonic guidance to rule out malignancy. It revealed features suggestive of Hashimoto's thyroiditis, including lymphoid tangles, colloid ingested macrophages, histiocytic lymphocytic clusters and multinucleated giant cells. Antithyroid peroxidase antibodies were assayed and were strongly positive (323 IU/mL).

Evaluation of anaemia yielded a diagnosis of vitamin B_{12} deficiency (serum B_{12} 115.2 pg/mL). Gastric biopsy showed evidence of atrophic gastritis. Screening for other endocrinopathies showed low serum cortisol level (8:00 2.04 μg/dL). Adrenocorticotropic hormone stimulation test was consistent with primary adrenal failure.

DIFFERENTIAL DIAGNOSIS

- Concomitant Graves' disease with Hashimoto's thyroiditis, associated with type 2 polyglandular autoimmune syndrome (Schmidt's syndrome).
- Hashitoxicosis was ruled out by the presence of diffusely increased radiotracer uptake on radionuclide imaging.

To cite: Dasari S, Naha K, Hande M, *et al*. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2013-010432

TREATMENT

The patient was treated initially with carbimazole (10 mg orally q8 h) followed by I-131 radioablation of the thyroid. Adrenal failure was managed with glucocorticoid replacement therapy (7.5 mg orally once daily of prednisolone). She was also treated with parenteral vitamin B_{12} supplementation.

OUTCOME AND FOLLOW-UP

The patient tolerated radioablation and remains euthyroid 6 months after ablation.

DISCUSSION

Graves' disease and Hashimoto's thyroiditis share a number of pathogenetic features including T-cell-mediated autoimmunity, human leucocyte antigen linkage[2] and the presence of autoantibodies such as antithyroid peroxidase antibodies[3]; it is therefore not surprising that both these disorders can run together in families.[4] The close link between autoimmune thyroiditis and Graves' disease is further demonstrated by the development of autoimmune hypothyroidism in up to 15% of patients with Graves' disease, 10–15 years after the index illness,[5] and the more infrequent transition of autoimmune thyroiditis into Graves' disease.[6]

At a very basic level, Graves' disease arises directly from the action of thyroid-stimulating antibodies on thyrotropin receptors, while autoimmune hypothyroidism is characterised by the development of antithyrotropin receptor antibodies that block the action of thyrotropin. Indeed, blocking antibodies can coexist with stimulating antibodies in persons with Graves' disease, where they can mitigate the clinical severity of hyperthyroidism. The simultaneous presence of functionally antagonistic autoantibodies also explains the frequency with which either of these forms of autoimmune thyroid disease can evolve into the other, depending on the relatively predominant form of circulating autoantibody. This phenomenon is also responsible for hypothyroid Graves' disease—a subtype of Graves' disease presenting with features of hypothyroidism.[7]

When the weight of epidemiological and pathological evidence connecting these clinically contrasting disorders is considered, it is somewhat surprising to note that their simultaneous occurrence has been reported only infrequently in medical literature, in the form of hypothyroid Graves' disease.[7] It is possible that the intrinsically opposing manifestations of these conditions result in complete masking of one by the other, such as was seen in our patient, who presented with features of hyperthyroidism alone. Only the chance demonstration of a cold nodule on radionuclide imaging in this instance, showed concurrent Hashimoto's thyroiditis. However, unlike the cases of hypothyroid Graves' described before, our patient had distinct and discrete histopathological and radiological features of Hashimoto's and Graves' diseases, respectively. Therefore, this case report also raises the intriguing possibility that a proportion of patients currently diagnosed with one form of autoimmune thyroid disease, might actually represent a mosaic form of disease, with hyperactive and hypoactive regions in different parts of the thyroid. The reason behind why different regions of the thyroid gland responded variably in this case to the same milieu of autoantibodies is unclear. Possibly, this phenomenon reflects localised activation of cytotoxic T cells in circumscribed discrete areas within the thyroid, resulting in histopathological features of thyroiditis.

Practicing medical professionals should be aware of the possibility of concurrent Hashimoto's thyroiditis in patients with Graves' disease. Demonstration of a 'cold' nodule in a 'hot' thyroid on radionuclide imaging would appear to be the best indicator of such concurrence. The relative benefits of currently employed therapeutic strategies including antithyroid drug therapy and radio-iodine ablation can be determined when further cases of such mosaic disease are identified.

Learning points

- Graves' disease and Hashimoto's thyroiditis can coexist in the same individual, reflecting their common autoimmune origin.
- Simultaneous occurrence of Graves' disease and Hashimoto's thyroiditis can result in clinical masking of one disorder by the other.
- Demonstration of a 'cold' nodule in a 'hot' thyroid on radionuclide imaging appears to be the best indicator of concurrent Graves' disease and Hashimoto's thyroiditis.

Contributors SD, KN and GV were involved in the concept, design, definition of intellectual content, literature, preparation, editing and review of the manuscript. SD and KN were involved in data acquisition. SD and MH were involved in clinical care of the patient. MH was in addition involved in the concept, design, editing and review.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Wiebolt J, Achterbergh R, den Boer A, *et al*. Clustering of additional autoimmunity behaves differently in Hashimoto's patients compared with Graves' patients. *Eur J Endocrinol* 2011;164:789–94.
2 Jacobson EM, Tomer Y. The genetic basis of thyroid autoimmunity. *Thyroid* 2007;17:949–61.
3 Weetman AP. Graves' disease. *N Engl J Med* 2000;343:1236–48.
4 Dayan CM, Daniels GH. Chronic autoimmune thyroiditis. *N Engl J Med* 1996;335:99–107.
5 Umar H, Muallima N, Adam JM, *et al*. Hashimoto's thyroiditis following Graves' disease. *Acta Med Indones* 2010;42:31–5.
6 Wasniewska M, Corrias A, Arrigo T, *et al*. Frequency of Hashimoto's thyroiditis antecedents in the history of children and adolescents with graves' disease. *Horm Res Paediatr* 2010;73:473–6.
7 Starrenburg-Razenberg AJ, Castro-Cabezas M, Gan IM, *et al*. Four patients with hypothyroid Graves' disease. *Neth J Med* 2010;68:178–80.