CASE REPORT

Generalised pruritus as a presentation of Grave's disease

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Abstract

Pruritus is a lesser known symptom of hyperthyroidism, particularly in autoimmune thyroid disorders. This is a case report of a 27-year-old woman who presented with generalised pruritus at a primary care clinic. Incidental findings of tachycardia and a goiter led to the investigations of her thyroid status. The thyroid function test revealed elevated serum free T4 and suppressed thyroid stimulating hormone levels. The anti-thyroid antibodies were positive. She was diagnosed with Graves' disease and treated with carbimazole until her symptoms subsided. Graves' disease should be considered as an underlying cause for patients presenting with pruritus. A thorough history and complete physical examination are crucial in making an accurate diagnosis. Underlying causes must be determined before treating the symptoms.

Background

Pruritus is a common presenting complaint in the primary care setting. Besides dermatological conditions, systemic diseases are known to cause pruritus. In one study, systemic diseases were the main cause of chronic pruritus in 13.3% of the cases.[1] Metabolic disorders, haematological diseases, malignancies and drugs were the main culprits.[1] However, pruritus is an uncommon presentation of hyperthyroidism. In Malaysia, only 6.9% of hyperthyroid patients are diagnosed with pruritus.[2] This case illustrates the importance of proper diagnosis in establishing the diagnosis of Grave's disease.

Case presentation

A 27-year-old woman presented to a primary care clinic with generalised itch lasting three days. There was no skin rash. She was constantly scratching which affected her sleep. There were no precipitating factors such as food or fabric allergies, though she complained that warm weather worsened the itch.

She had a similar episode one and a half years ago where the itch lasted for one year despite being treated with antihistamines and alternative therapies. The itch disappeared completely when she conceived.

She had a history of allergic rhinitis but no bronchial asthma or eczema. There was no history of food allergies or medication intolerances. There was no significant past medical history.

On examination, she did not look jaundiced or pale. Her blood pressure was 140/70 mmHg; her pulse rate was 120 beats per minute with regular rhythm. Apart from superficial scratch marks on her limbs and trunk, there were neither skin eruptions, burrows, vesicles nor scaly lesions to suggest scabies or fungal infection. Her nails, hair and scalp appeared normal.

On examination of her hands, there was fine tremor but the temperature was normal. On examination of her eyes, she was found to have mild exophthalmos but there was no lid lag on ophthalmoplegia. Upon removing her headscarf, there was a diffuse goitre, measuring 2 x 4 cm, which was soft and non-tender. There was no bruit detected over the goitre. Her reflexes were normal. Cardio-respiratory examination was normal.

The clinical findings prompted further investigation focusing on symptoms of thyroid disorders. She did not experience any palpitations, increased appetite, weight loss or menstrual cycle disturbances. She did not have a family history of goitre or thyroid disorders. She was given oral loratadine 10mg daily as well as chlorpheniramine 4mg at night pending further investigation. She returned two weeks later with no improvement of symptoms despite the antihistamines.

Investigations confirmed an elevated free T4 level (see Table 1) and her anti-thyroid globulin and anti-thyroid peroxidase levels were high. However, anti-TSH receptor antibody level was not tested. The patient's renal profile and liver functions were normal and her ECG showed no atrial fibrillation. She was administered carbimazole 30mg orally as well as propranolol 40mg twice daily. She was also cautioned of the adverse effects of carbimazole such as Stevens-Johnson Syndrome, agranulocytosis and skin rash.

Two months later, the patient reported a decrease in tremors and her itch had subsided completely. She gained 3kg of weight and her free T4 level dropped from 77.22 pmol/L to 36.2 pmol/L. Another two months later, her free T4 level dropped to 19.57 pmol/L and the carbimazole dosage was reduced to 20mg daily. The patient was also referred to the endocrine clinic for definitive treatment of Graves' disease as she was keen on radioactive iodine therapy. Pruritus did not recur following her treatment of hyperthyroidism.

Table 1. Blood investigation results

Test	Results	Normal range
Thyroid stimulating hormone (TSH)	0.01 mIU/mL	0.32 - 5.00 mIU/mL
Free thyroxine (fT4)	77.22 pmol/L	9.1 – 23.8 pmol/L
Anti-thyroid globulin	2736 IU/mL	0.0 – 40.0 IU/mL
Anti-thyroid peroxidise	>1000 IU/mL	0.0 – 35.0 IU/mL
Anti-nuclear antibody	Negative	-
Rheumatoid factor	Negative	-
Alanine transaminase (ALT)	107 mmol/L	< 44 mmol/L

Discussion

Graves' disease is an autoimmune thyroid disorder which accounts for 60 to 80% of cases presenting with hyperthyroidism.[3] It is eight times more common in women, with the incidence rate of 0.5 per 1000 women.[3] In Grave's disease, thyroid-stimulating antibodies stimulate thyrotropin receptors, resulting in an increased production of thyroid hormone. The distinguishing features of Graves' disease are the presence of ophthalmopathy and dermopathy (pretibial myxoedema).

Pruritus is an uncommon but recognised feature of autoimmune thyroid disorders. Although this condition had been noted since 1935, there are very few cases reported in the literature.[4] In a Malaysian study of 236 patients with hyperthyroidism, up to 6.4% of

patients with hyperthyroidism had symptoms of pruritus.[2] In two of the cases, the patients presented with pruritus alone which resulted in a delay in making the diagnosis of Graves' disease.[2]

The pathophysiology of generalised pruritus in autoimmune thyroid disorders is still unclear. Neither the levels of free T4 nor auto-antibody correlate well with the presentation of pruritus.[5,6] Therefore, it is postulated that pruritus in autoimmune thyroid disorders is a manifestation of cell-mediated immunity, which lowers the mast cell threshold for the release of histamine.[5] However, this does not adequately explain the non-response to antihistamines.[4,7,9]

This patient sought medical help for pruritus but the diagnosis was not apparent from history-taking alone. She had few symptoms of hyperthyroidism, which did not cause her distress as much as the pruritus. Thus, the clinical diagnosis of Graves' disease was made only after discovering that she had tachycardia and other clinical signs of hyperthyroidism. This is in contrast with other cases where symptoms and signs of hyperthyroidism are more obvious.[7]

Other systemic causes of pruritus should be considered and they include: hepatobiliary conditions (e.g. cholestasis and primary biliary cirrhosis), haematological disorders (polycythaemia rubra vera and lymphoma), paraneoplastic syndromes and uraemia.[8] The patient did not have any of these conditions. Studies have found that pruritus does not respond to conventional antihistamines and can only be resolved with treatment of hyperthyroidism.[4,7,9]

Anti-thyroid antibodies such as anti-thyroid peroxidase and anti-thyroglobulin antibody are non-specific for Grave's disease, but are indicative of the presence of autoimmunity in this patient. An association between autoimmune thyroid diseases with pruritus and urticaria has been suggested.[6] It is interesting to note that patient's symptoms that developed prior to the conception of her first child abated during her pregnancy. It recurred during the post-partum period. This is a common feature of autoimmune thyroid disorders such as Graves' disease and Hashimoto's thyroiditis.[10] Human chorionic gonadotrophins (HCG) have thyrotropic properties due to their structural similarities to TSH. In early pregnancy, raised HCG levels exacerbate Graves' disease .[11,12] However, the symptoms usually abate as the pregnancy progresses primarily because pregnancy causes a immunosuppressed state in the patient resulting in reduced levels of auto-antibodies.[11,12] Secondly, as a result of alterations in the levels of thyroid-binding globulin, free thyroxine levels drop.[11] Lastly, iodine consumed by pregnant mothers is also absorbed by the foetus, resulting in relative maternal iodine deficiency, which limits maternal thyroid hormone synthesis.[11]

In conclusion, underlying thyroid disorders should be considered in patients presenting with pruritus who do not respond to conventional anti-pruritic agents. This case also highlights the importance of a complete physical examination in arriving at an accurate diagnosis.

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