

A rare simultaneous manifestation of polyglandular autoimmune syndrome type II

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Summary

Polyglandular autoimmune syndrome type II is a rare condition defined by the presence of autoimmune primary adrenal insufficiency along with autoimmune thyroid disease and/or type-I diabetes. Onset of these conditions will usually be separated by several years, though in rare instances it can occur simultaneously. This syndrome can also be associated with various non-endocrine autoimmune diseases, such as vitiligo and alopecia. Coeliac disease is less commonly associated with polyglandular autoimmune syndrome type II and is more commonly associated with polyglandular autoimmune syndrome type III. Here we describe an interesting case of a young male presenting with simultaneous manifestation of Addison's disease and Graves, with coincident asymptomatic coeliac disease, as a rare manifestation of polyglandular autoimmune syndrome type II.

Learning points:

- Polyglandular autoimmune syndrome type II is rare, has female predominance, and peak onset in the third and fourth decades of life.
- Onset of Addison's disease will usually precede or follow onset of type-I diabetes or autoimmune thyroid disease by several years in this syndrome.
- Simultaneous onset can occur, as in this case.
- Coeliac disease is uncommonly associated with this syndrome.
- Coeliac disease is more commonly associated with polyglandular autoimmune syndrome type III.
- Coeliac disease should be screened for in patients with associated autoimmune conditions, such as type-I diabetes or autoimmune thyroid disease.

Background

Polyglandular autoimmune syndrome type II is a rare condition with an approximate prevalence of 1:20 000 (1). It shows female predominance, with peak onset in the third and fourth decades of life (2). It is defined by autoimmune failure of at least two endocrine glands, with primary adrenal insufficiency being the central manifestation, along with type-I diabetes, and/or autoimmune thyroid disease (AITD) – 'Schmidt's syndrome' (1, 2). It may also be associated with non-endocrine autoimmune diseases (1, 3).

While the manifestation of one autoimmune condition increases the chance of developing others, the time between onset of the different syndromes varies greatly, often with many years between diagnoses of the first and second disorders (1, 3).

Here we describe a young man presenting with simultaneous manifestation of Graves and Addison's disease, along with asymptomatic coeliac disease as a rare manifestation of polyglandular autoimmune syndrome type II.



Case presentation

A usually fit and well 27-year-old male presented with a 3-day history of worsening postural dizziness, flushing and fatigue. Family history was strongly linked to autoimmune conditions. His mother, brother, and sister have Graves disease. His mother also has type-I diabetes.

Examination revealed noticeable tanning, oral pigmentation, and pigmented knees. There was a symptomatic postural sinus tachycardia to 150 b.p.m, and he was feeling hot and light-headed, without an associated postural blood pressure drop.

Investigation

Significant initial investigations included normal potassium: 4.6 (3.5–5.2 mmol/L), TSH: 0.07 (0.27–4.20 mU/L), free-T4: 37 (12–22 pmol/L), free-T3: 16.0 (3.9–6.8 pmol/L), early morning cortisol: 63 (170–500 nmol/L), ACTH: 561 (2–11 pmol/L), renin: 2630 (4–46 mU/L), and aldosterone: 90 (60–1000 pmol/L). These results indicated hyperthyroidism and primary adrenal insufficiency. A short synacthen test showed no increase in basal serum cortisol (basal: 71 nmol/L, peak: 70 nmol/L), also diagnostic of primary adrenal insufficiency.

Serum TSH receptor antibodies (TSHR-ab) were negative – 1.3 (<1.75 IU/L), thyroid peroxidase antibodies (anti-TPO) positive – 133 (<34 IU/mL) in keeping with non-specific AITD. A scintiscan was performed demonstrating diffuse increased uptake of 9.6% ($n < 2.2\%$) consistent with TSHR-ab negative Graves disease (4).

Autoimmune screening investigations showed a weakly positive tissue transglutaminase (tTG) 29 (<4 U/mL) and deaminated gliadin peptide (DGP) 21 (<20 U). He had no clinical symptoms of coeliac disease. Gastroscopy and duodenal biopsy revealed partial villous atrophy and intraepithelial lymphocytosis, consistent with coeliac disease. Diabetes screening antibodies for GAD and IA-2 were negative, as were parietal cell, smooth muscle, and mitochondrial autoantibodies.

Treatment

He was initially started on oral hydrocortisone 20 mg mane/10 mg nocte, oral fludrocortisone 0.1 mg daily, and oral carbimazole 15 mg twice daily. Doses were adjusted according to clinical and biochemical response.

Outcome and follow-up

He is currently well and maintained on a gluten-free diet, hydrocortisone 15 mg mane/5 mg nocte,

and fludrocortisone 0.1 mg daily. Carbimazole was discontinued after 6 months of therapy, with remission of hyperthyroidism maintained at 1 year off treatment.

Discussion

Polyglandular autoimmune syndrome type II is a genetically complex multifactorial syndrome associated with certain alleles of HLA genes, particularly HLA-DR3 and HLA-DR4 (1, 3). While the time between onset of associated conditions shows significant variability and recent data is lacking, historical data suggest adrenal insufficiency is the initial presentation in roughly 50% of patients, occurs simultaneously with AITD or diabetes in 20%, and subsequently in the remaining 30% (1, 3, 5). In hyperthyroidism, cortisol is metabolised and removed from plasma more rapidly than normal. In our patient, AITD may well have contributed to an earlier manifestation of Addison's disease than would have been observed in the absence of AITD.

While polyglandular autoimmune syndrome type II can be associated with a range of other endocrine and non-endocrine autoimmune syndromes, including primary hypogonadism, vitiligo, and alopecia, coeliac disease is rarely described in this setting (1, 2, 6, 7). Coeliac disease is more commonly associated with polyglandular autoimmune syndrome type III, defined as the presence of AITD and another autoimmune condition, excluding Addison's (1, 2, 8, 9, 10). In this setting, it is closely associated with type-I diabetes (1, 8). Because of its association with numerous autoimmune conditions including type-I diabetes and AITD, serological screening for coeliac disease is indicated in patients with associated autoimmune conditions (8, 9).

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Patient consent

Written informed consent for publication of their clinical details was obtained from the patient.

Author contribution statement

Michael Dick was responsible for obtaining patient consent, collating case information, reviewing literature, and writing the original draft and final



versions of this report. Michael Croxson is the patient's lead physician. He provided specialist advice, reviewed draft manuscripts, suggested alterations to draft manuscripts, and agreed with the final version of this report.

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