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CASE REPORT

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Primary hyperaldosteronism associated with type 3 autoimmune polyendocrine syndrome: A rare case report

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Key Clinical Message

Primary hyperaldosteronism with type 3 autoimmune polyendocrine syndrome was a rare combination of both hyper- and hypoendocrine gland function. Comprehensive treatment including surgery and replacement therapy might be an effective strategy.

Abstract

Primary aldosteronism (PA) is a common cause of secondary hypertension originating from hormones. Type 3 autoimmune polyendocrine syndrome (APS-3) is characterized by the simultaneous or subsequent occurrence of autoimmune-mediated endocrine gland damage, except for Addison disease. Here we reported an extremely rare case of a 63-year-old woman with PA and APS-3 who initially presented with hypertension (HT). The APS-3 of this patient mainly exhibited type 1 diabetes mellitus (T1DM) and Hashimoto's thyroiditis. She underwent the adrenal adenoma resection with a histopathologic diagnosis of adrenal cortical adenoma. After surgery, the HT of this patient was immediately reversed, and the concentration of serum potassium went back to normal. Then, this patient was administered with replacement therapy of insulin and levothyroxine sodium tablets (L-T4).

KEYWORDS

Hashimoto's thyroiditis, primary aldosteronism, type 1 diabetes mellitus, type 3 autoimmune polyendocrine syndrome

1 | INTRODUCTION

Primary hyperaldosteronism (PA) is the most common endocrine cause for secondary hypertension, which is due to the excessive secretion of aldosterone. Autoimmune polyendocrine syndrome (APS) is an autoimmune disorder characterized by the coexistence of at least two endocrine gland insufficiencies. APS type 3 (APS-3) includes immune-mediated diabetes and autoimmune thyroid diseases but does not comprise the defect of adrenal cortex. A recent study demonstrated an interaction of glucose metabolism with mineralocorticoid excess, which provided novel insight into the mechanisms of pathophysiology linking PA and diabetes.[1] Besides, an increased relationship between Hashimoto's thyroiditis and PA was reported.[2] However, an underlying association between PA and APS is not clearly understood. Here, we reported an extremely rare case of PA associated with APS-3 in which type 1 diabetes and autoimmune thyroiditis were observed.

2 | CASE HISTORY/EXAMINATION

A 63-year-old woman presented to our hospital for further evaluation and management of HT, with complaints of polydipsia and aversion to coldness. She was diagnosed with HT for 20 years and did not receive long-term medications. The monitored blood pressure was approximately 170/100 mmHg with headache. No aberrant signs were observed in the neurological examination. There was no family history of HT, stroke or diabetes. She had a history of repair of ventricular septal defect (VSD). Then, we performed a series of examinations to comprehensively evaluate the condition of this patient. Electrolyte analysis revealed a potassium concentration of 3.0 mmol/L in the blood and a synchronous potassium concentration of 41 mmol/day in the 24-h urine. The baseline ratio of aldosterone-to-renin activity (ARR) was 78. Captopril challenge test (CCT) results were positive (Table 1). Cortisol circadian rhythm was normal and overnight dexamethasone suppression test (ODST) was negative. No abnormal results of catecholamine concentration were observed in neither blood nor urine. Color Doppler ultrasonography indicated a normal resistance index and blood flow of the renal artery. Contrast-enhanced computed tomography (CT) unraveled a benign nodule (9 mm × 7 mm) in the right adrenal (Figure 1A). Thyroid ultrasonography unraveled diffusely decreased echogenicity (Figure 1B). A significant hyperglycemia and insulin deficiency were detected either. TGAb, GADA, ICA, and IAA were all positive, which suggested diagnosis of Hashimoto's thyroiditis and type 1 diabetes (Table 2).

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS AND TREATMENT)

This patient was diagnosis as PA associated with APS-3, but it needs to be differentiated from pheochromocytoma, Cushing's syndrome and renal artery stenosis. After surgical resection of the adrenal lesion, the HT was immediately reversed and potassium concentration went back to normal. The histopathologic diagnosis was an adrenal cortical adenoma. She received insulin and levothyroxine sodium (L-T4) replacement meantime.

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

During follow-up, the potassium concentration and blood pressure were normal, thyroid function was improved, and blood sugar was appropriate.

5 | DISCUSSION

Given that the coexistence of PA and APS-3 is an extremely rare combination of endocrine disease, the causal association between PA and APS-3 needs to be urgently addressed. An emerging view is that there was a close interplay of PA with the immune system.[3] Chang et al unveiled that plasma aldosterone level, ARR and blood sodium level were positively related to TCR clonotypes, implying T cell may play a crucial role in the progression of PA.[4] A study reported that aldosterone can promote CD8+ T-cell activation and the T helper 17 (Th17) polarization of CD4+ T-cell via interacting with dendritic cells (DCs).[5] Importantly, Herrada et al uncovered that aldosterone can directly promote CD4+ T cells polarization towards Th17, resulting in the development of many organ-specific autoimmune diseases.[6] Hence, PA is related to genetic alteration and immune imbalance, which may serve as a modulator for autoimmune diseases. A research found that patients with PA had an increased risk for a variety of incident new-onset autoimmune diseases (NOAD) and the NOAD incidence of PA patients who underwent adrenalectomy and took mineralocorticoid receptor antagonist still increased.[7] Krysiak and colleagues reported that surgical removal of the tumor in the PA patient may suppress the cell-mediated immune response and PA may lead to

TABLE 1 Captopril challenge test results.

Parameters	Supine position	Upright position	Captopril stimulation	Reference
Angiotensin I, pg/mL	106	104	103	Supine: 25–129 Upright: 49–252
Aldosterone, pg/mL	106	134	136	Supine: 10–160 Upright: 40–310
Plasma renin activity, pg/mL	1.27	1.72	1.16	Supine: 4–24 Upright: 4–38
ARR	83	78	117	0–38

Abbreviation: ARR, Ratio of aldosterone-to-renin activity.

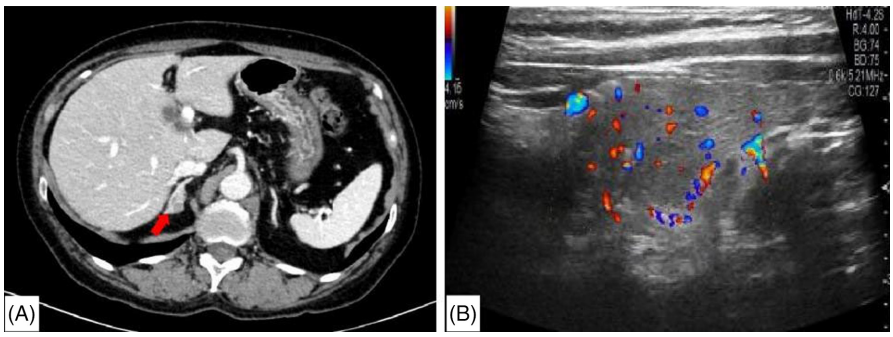

FIGURE 1 Images of adrenal contrast-enhanced CT and thyroid ultrasonography. (A) a benign nodule in the right adrenal (9 mm × 7 mm) was observed, implying the possibility of adrenal adenoma. (B) Diffusely decreased echogenicity in the whole thyroid was detected, indicating the possibility of Hashimoto's thyroiditis.

TABLE 2 Diabetes and thyroiditis-related laboratory data.

Diabetes-related	Value 1	Thyroiditis-related	Value 2
FPG (3.9–6.1 mmol/L)	17.0	FT3 (3–7 pmol/L)	3
HbA1c (4%–6%)	11	FT4 (12–22 pmol/L)	15
IAA (Negative)	Positive	TT3 (1–3 nmol/L)	1
ICA (Negative)	Positive	TT4 (66–181 nmol/L)	80
GADA (<10 IU/mL)	151	TSH (0–4 μIU/mL)	5
Fasting insulin (2.6–24.9 μU/mL)	1.8	TPO-Ab (<34 KIU/L)	<9
Fasting C-peptide (1.1–4.4 ng/mL)	0.3	TgAb (0–115 KIU/L)	144

Abbreviations: FPG, fasting plasma glucose; FT3, free serum triiodothyronine; FT4, free serum tetraiodothyronine; GADA, glutamic acid decarboxylase antibodies; HbA1c, hemoglobin A1c; IAA, insulin autoantibodies; ICA, islet cell antibodies; TgAb, antithyroglobulin antibodies; TPOAb, antithyroid peroxidase antibodies; TRAB, thyrotropin receptor antibodies, TSH, thyroid stimulating hormone; TT3, total serum triiodothyronine; TT4, total serum tetraiodothyronine.

the exacerbation of the clinical course of Hashimoto's thyroiditis.[8] The Human Leukocyte Antigen (HLA) complex served as the most influential genetic determinant of T1DM, contributing to 40%–60% of the inheritable risk.[9] For example, IAA are associated with HLA-DQ8 and GADA are related to HLA-DQ2.[10] In addition, the non-HLA gene *PTPN22* R620W allele was linked to the risk of islet autoimmunity and *IL2RA* was strongly associated with T1DM in IAA-positive patients.[11,12] Besides, HLA and *PTPN22* also played a crucial role in immune modulation and the generation of thyroid autoantigens in Hashimoto's thyroiditis.[13]

The final goal of treatment for patients with PA is to prevent mortality associated with HT, hypokalemia, renal toxicity, and cardiovascular damage. Treatment for PA mainly includes surgery, medication and ablation therapy, while surgery is the preferred treatment if patients exhibit a well-tolerated operation. The latest research found that compared to medical therapy for PA, surgery is associated with lower all-cause mortality and major adverse cardiovascular outcomes.[14]

In summary, PA with APS-3 was a rare combination of both hyper- and hypoendocrine gland function, and its further pathogenesis was still unclear yet, however, overactivated aldosterone might be an important trigger for autoimmune endocrine gland damage. Comprehensive treatment including surgery and replacement therapy might be an effective strategy.

AUTHOR CONTRIBUTIONS

Xuesong Li: Conceptualization; resources; visualization; writing – original draft; writing – review and editing. **Liangbiao Gu:** Data curation; investigation; validation. **Wenhui Zhao:** Methodology. **Jianzhong Xiao:** Project administration. **Chenxiang Cao:** Funding acquisition.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study can be available for review upon reasonable request.

ETHICAL APPROVAL

This article is a practice-oriented case study description that made extensive use of secondary information sources

and also drew upon the professional knowledge of the co-authors. As such, the creation of this case study article did not involve any formal research study, nor did it involve human participation in a research study. As such, IRB review was not required for this article.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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