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IDENTIFICATION OF AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 3 IN PATIENT WITH HYPOTHYROIDISM : A CASE REPORT

Diabetology

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ABSTRACT

Autoimmune polyglandular syndromes (APS) are characterized by sequential or simultaneous deficiencies in the function of several endocrine glands that have a common cause. Etiology is most often autoimmune.We report a case of a 40-year-old female with diabetes who presented with diabetic ketoacidosis (DKA) and was later diagnosed with T1D. The patient has had a history of hypothyroidism. The presence of vitiligo was an incidental finding.Laboratory investigations showed low C peptide level, glutamic acid decarboxylase (GAD) 65 antibodies positive, thyroid peroxidase antibodies (TPO) positive, parietal cell antibody positive, and weakly positive antinuclear antibody (ANA), amid normal corticotropin(ACTH), parathyroid hormone (PTH) , vitamin B 12 levels, and a negative intrinsic factor antibody. The patient had a history of hypothyroidism, subsequently developed T1D, and had vitiligobut was overlooked. The case highlights the notable absence of recognizing the need to investigate this patient who presented with more than two endocrine diseases for measurement of hormone levels, autoantibodies against affected endocrine glands and recognition of related symptoms and signs, and hence the significance of history taking, observation, and maintaining a high degree of suspicion.

KEYWORDS

Autoimmune thyroid disease (AITD), type 1 diabetes mellitus (T1D), vitiligo

INTRODUCTION

Autoimmune polyglandular syndromes (APS) are a group of disorders characterized by a wide range of autoimmune diseases that affect both endocrine and non-endocrine organs. If the autoimmune mechanism has caused damage to at least two organs, PAS may be diagnosed [1].APS can be classified into four subgroupsbased on the organs that are affected [2]. Chronic mucocutaneous candidiasis, hypoparathyroidism, and primary adrenal insufficiency are all symptoms of APS1. A homozygous inactivating mutation in the autoimmune regulator gene AIRE is to blame[3].Both APS2 and APS3 are caused by mutations in the HLA DQ/DR regions, which control antigen presentation to T-cell receptors; APS2 is characterized by T1DM, Addison disease, and hypothyroidism[4], while APS3 is similar but does not include Addison disease. These entities, like other autoimmune disorders, are more common in women, whereas APS1 has no gender preference.[1,5]. The deficiencies do not always appear at the same time and may require years to manifest; in such cases, they do not follow a specific sequence. This paper reports the case of APS type 3.

Case

A 40-year-old homemaker with signs of fatigue, insomnia, and weight gain has been diagnosed with hypothyroidism for the past seven years, taking 125 mcg of L-thyroxine daily. She also was diagnosed to have diabetes mellitus at age of 34 years evaluated for osmotic signs, and weight loss. She was initiated on oral antihyperglycemic agents(OHAs). Since then the patient has had a couple of more admissions for raised blood sugar values stabilized and discharged on insulin and OHAs. She was not investigated for autoimmunity and beta cell functions. On this occasion, she complained of breathlessness, nausea, vomiting, and generalized weakness and was brought to the emergency room. Her capillary blood glucose was 'HI' (more than 600mg/dl) measured using One Touch Verio Flex blood glucose monitor (Life scan, Inc), and the same was also confirmed in venous plasma glucose sample (RBG) on an autoanalyzer at the time of admission. The reason for patient being in DKA was decrease in her insulin dose and increase in the dose of OHAs . Her arterial blood gas analysis showed acidosis (pH -7.048, CO_2 –14.2 mmHg, and HCO3 - 3.8mEq/L). Her plasma beta-hydroxybutyrate was more than 3nmol/l and urine for ketones was > 3 + positive. Her blood pressure recorded was 100/60 mmHg in the right arm supine position with a mercury sphygmomanometer(Diamond Deluxe BP Apparatus). She had Kussmaul breathing. There was pallor . She did not have any goiter. She had acrofacial hypopigmented patches suggestive of vitiligo(Figure 1) .

Figure 1 Acrofacial Hypopigmented patches of vitiligo

She was treated with intravenous insulin and stabilized for DKA and later shifted to basal-bolus insulin therapy. Her L-thyroxine dose was reduced to 100mcg per day based on her thyroid function test. Anemia was confirmed in her laboratory tests (Table 1), as well as a peripheral smear indicating microcytic hypochromic anemia. The patient had antibodies positive to thyroid peroxidase or anti -microsomal antibodies, GAD-65 antibodies, parietal cell antibody, and anti-nuclear antibodywith negativity for intrinsic factor autoantibodies and tissue transglutaminase of IgA class. Ultrasonography of the abdomen revealed no significant abnormalities. Fundus examination revealed no diabetic retinopathy. She was diagnosed with APS type 3syndrome based on her medical history, physical examination, and records.

Table 1 Laboratory work-up

Test	Observed Value	Normal range
Hemoglobin	8.2	11-15 g/dl
MCV	56.1	fl 76-96
Reticulocyte count	1.4	Upto 1.0 %
GAD65 Antibodies	79.53	Negative < 17
C-Peptide level	< 0.10	0.9- 7.1 ng/ml

HbA1c	8.1	< 5.7%
Free T4	1.93	0.93-1.7 ng/dl
TSH	0.141	0.4-5.3uIu/ml
Anti TPO Antibodies	545.7	0- 5.61 IU/ml
ACTH	8.33	7.2- 63.6 pg/ml
PTH	38.8	15- 65 pg/dl
Calcium	8.5	8.4-11 mg/dl
Ionized Calcium	4.92	4.5-5.3 mg/dl
Vitamin B12	692	197-771 pg/ml
Intrinsic factor antibody	Negative	Negative
Parietal cell antibody	Positive	Negative
ANA	Weak Positive, Speckled	Negative

Abbreviations: MCV – Mean corpuscular volume, GAD – Glutamic acid decarboxylase, HbA1c – glycated hemoglobin, T4 – thyroxine, TSH – thyrotropin, TPO – thyroid peroxidase, ACTH – corticotropin, PTH – parathyroid hormone, ANA – anti nuclear antibody.

DISCUSSION:

APS is a set of disorders that cause the death or dysfunction of multiple endocrine glands, as well as other organs and tissues. Immune-mediated infiltrative cellular destruction caused by multiple genetic defects, or a combination of these factors, maybe the pathogenesis. The APS polyendocrinopathies are the most common characterized by a lack of immune tolerance to self-antigens, resulting in autoimmune destruction of endocrine glands and other tissues.Thyroid autoimmune diseases (TADs) are the most common autoimmune diseases in the world, appearing in the majority of cases as spontaneous hypothyroidism and affecting 4–21% of females. Around 15% of TAD patients have another clinical autoimmune disease [6], and another 15% of those with seemingly isolated TADs can test positive for organ and non-organ-specific autoantibodies if screened. TADs are more often associated with another autoimmune disorder in APS-3 patients, with the most common associations being chronic atrophic gastritis [7] and T1D [8,9]. Our patient had auto-immune thyroid disease and autoimmune gastritis was detected on further work-up. T1D has a trimodal presentation, with the first peak occurring between the ages of 3-6 years, the second during puberty, and the third round 35-40 years of age.The absence of DKA at the presentation in approximately 1/3rd to 2/3rd of patients is due to early detection of disease (presence of residual beta-cell function) and variability in the rate of destruction of beta-cells. Destruction of 90% beta- cells is required to manifest as DKA. A similar presentation was seen in our patient. Age of onset and duration of disease determines the presence or absence of a particular autoantibody in a patient with T1D. The autoantibodies of importance in T1D include anti-GAD 65 antibodies, islet-cell autoantibody, insulinoma–associated antigen 2 antibodies, anti-insulin antibody, and anti-zinc transporter antibody. Our being a charitable institute, the patient was screened for only one antibody. Autoimmune polyendocrine syndrome type 3 (excluding Addison's) is characterized by autoimmune thyroid disease and T1D (type 3A), with the presence of chronic atrophic gastritis or pernicious anemia (type 3B), and in presence of vitiligo, alopecia, or myasthenia gravis (Type 3C). Thus the term APS is insufficient since it is often used to describe not only cases of multiple autoimmune endocrine diseases such as TADs and T1D, but also associations between endocrine and non-endocrine autoimmune diseases such as T1D and celiac disease or TADs and gastric autoimmunity, or associations between non-endocrine autoimmune diseases such as vitiligo[10], Sjogren's disease, autoimmune hepatitis, and myasthenia gravis.

CONCLUSION

Although APS is a rare disorder, the clinical presentation is salient and hardly misinterpreted. In this case, type 1 diabetes mellitus was misdiagnosed as type 2 and was treated with OHA. This case highlights the need to be vigilant, as diagnosis and treatment will prevent the patient from impending complications due to morbidity and/or mortality.

Ethics Approval: Not applicable

Consent Publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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