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Autoimmune Polyglandular Syndrome Type 3-D: A Case Report

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ABSTRACT

Background: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease characterized by the presence of autoantibodies against cell nuclei and involves many organ systems in the body. The etiopathology of SLE is thought to involve complex and multifactorial interactions between genetic variation and environmental factors. Hyperthyroidism is a disease due to increased thyroid hormone function followed by signs and symptoms that affect the body's metabolic system. Graves' disease is an autoimmune disease characterized by the presence of antibodies to TSHR (TRAb). Several coexisting autoimmune diseases have been classified under different syndromes.
Case Presentation: A woman, 29 years-old, came to office with complaint of chest palpitation. Patient had history of fever, joint pain, hair loss, and malar rash. Patient had been diagnosed with hyperthyroidism for 4 years and regularly taking propylthiouracil 100 mg and propranolol 10 mg. Titer ANA Test 1/100, Anti ds-DNA 68.08, C3-Complement 93 (N: 83-193), C4-Complement 11.2 (N: 15-57), Free T3 7.79 (N: 1.71-3.71), Free -T4 2.50 (N: 0.70-1.48), TSHs 0.0001 (N: 0.350-4.94), TRAb 3.38 (N: < 1.75). Patient was diagnosed with systemic lupus erythematosus (SLE) and graves' disease. Patient treated with methimazole 10 mg, propranolol 10 mg, myfortic 360 mg, and methylprednisolone 4 mg.
Conclusion: Autoimmune Polyendocrine Syndromes (APS) was at first characterized as different endocrine organ diseases related to an immune system disease in a subject. Hence, affiliation between illnesses in APS was noted not to be irregular but in specific combinations in which a few non-endocrine immune system diseases were moreover portion of the disorders.

Keywords: Autoimmune polyglandular syndrome, systemic lupus erythematosus, Graves' disease.

1 Background

Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease characterized by the presence of autoantibodies against cell nuclei and involves many organ systems in the body. Etiopathology of SLE is thought involving complex and multifactorial interactions between genetic variation and environmental factors. Genetic factors are thought to play an important role in predisposing this disease. In cases of SLE

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that occur sporadically without the identification of genetic factors, various environmental factors are thought to be involved. [1,2,3].

Hyperthyroidism is a disease due to increased thyroid hormone function followed by signs and symptoms that affect the body's metabolic system. Graves' disease is an autoimmune disease characterized by the presence of antibodies to TSHR (TRAb) [2,4,5].

Most autoimmune diseases stand alone. However, several coexisting autoimmune diseases have been classified in different syndromes. Autoimmune Polyglandular Syndrome (PGAS), also known as autoimmune polyendocrinopathies syndrome (APS) is a heterogeneous group of rare genetically caused diseases of the immune system that cause inflammatory damage of various endocrine glands resulting in their malfunction. In addition, autoimmune diseases of non-endocrine organs can also be found [5].

2 Case Presentation

A woman, 29 years-old, came to the office with complaints of chest palpitations and fatigue. patient also complains of fever, joint aches, hair loss, and malar rash. History of hyperthyroidism in the patient's father. Patient has been diagnosed with hyperthyroidism since 2017 and regularly consumes propylthiouracil 100 mg. On physical examination found exophthalmos, malar rash, alopecia areata, palpable goiter in the neck, heart rate 110x/minutes. Other physical examinations within normal limits.

Laboratory examination showed the results of ANA Test titer 1/100, Anti ds-DNA 68.08, C3-Complement 93 (N: 83-193), C4-Complement 11.2 (N: 15-57), Free T3 7.79 (N: 1.71- 3.71), Free-T4 2.50 (N: 0.70-1.48), TSHs 0.0001 (N: 0.350-4.94), TRAb 3.38 (N: < 1.75).

With 2019 EULAR scoring for SLE of 13 and a Wayne index scoring 25, patient was diagnosed with graves' disease with systemic lupus erythematosus (SLE), which is part of the polyglandular autoimmune syndrome type 3-D. The patient was treated with methimazole 10 mg, propranolol 10 mg, myfortic 360 mg, and methylprednisolone 4 mg.

3 Discussion

Autoimmune polyglandular syndrome (PAS), also known as autoimmune polyendocrinopathies syndrome (APS), is a heterogeneous group of rare genetically caused diseases of the immune system that cause inflammatory damage of various endocrine glands resulting in malfunction. In addition, autoimmune diseases of non-endocrine organs can also be found [5].

APS-3, unlike APS-1 and APS-2, does not involve abnormalities in the adrenal cortex. In APS-3 autoimmune thyroid disease occurs in association with other organ-specific autoimmune diseases, but this syndrome is not classified into SPA-1 and SPA-2. Like other autoimmune diseases, the pathophysiology of SPA-3 and SPA-4 can occur due to the involvement of genetic and environmental factors. Some researchers state that environmental factors can trigger and play a role in the incidence of polyglandular syndromes, such as viral infections, peptides, and others [6-9].

Table 1. Classification of Polyglandular Syndromes [13]

	Diseases
PAS-1	Chronic candidiasis, Chronic hypoparathyroidism, Addison's disease
PAS-2	*Addison's disease*(always present) with autoimmune thyroid disease and/or Type 1 Diabetes Mellitus
PAS-3	Autoimmune thyroid disease with other autoimmune diseases (other than Addison's disease and/or hypoparathyroidism)
PAS-4	Other combinations of autoimmune diseases

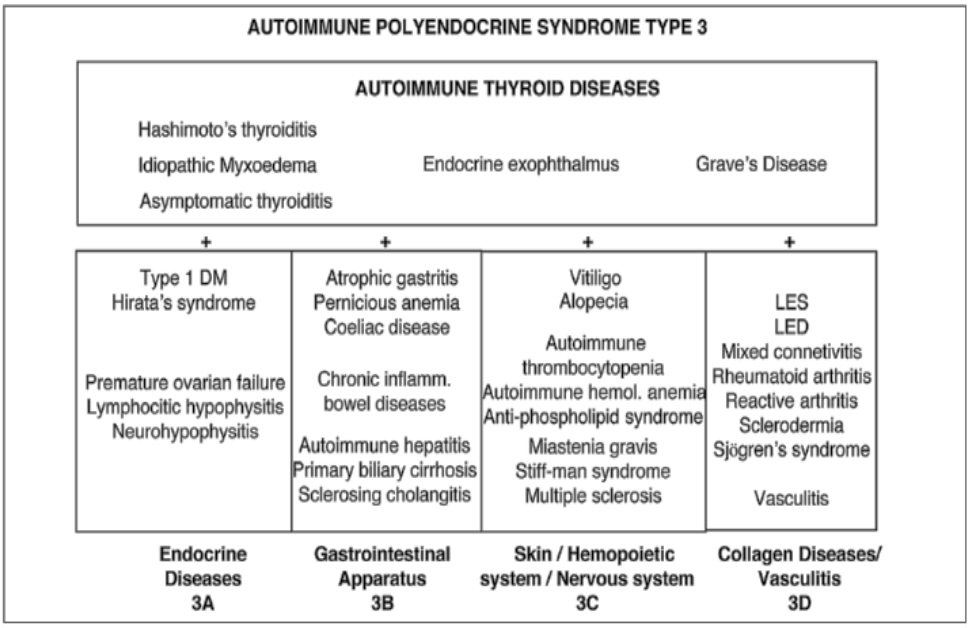
Systemic lupus erythematosus (SLE) is a complex autoimmune disease with a varied clinical picture. Manifestations of SLE are associated with multiple autoantibodies, which are associated with the formation and deposition of immune complexes. In 1971 the committee of the ARA published the initial criteria for

the classification of lupus and revised them in 2019. ARA criteria state that a person can be referred to as a lupus patient if he has at least one clinical criterion and a score of 10 or more [8,9].

SLE is epidemiologically more common in women than men in a 12:1 ratio, with a 25% increased risk in monozygotic twins. Autoantibodies in SLE are generally formed several years before the onset of SLE symptoms. There are 3 phases of autoantibody development in SLE [1,2]:

1. Normal phase is people without symptoms (asymptomatic) and does not have autoantibodies for SLE
2. Benign autoimmunity phase, where autoantibodies have been found without clinical manifestations.
3. Pathogenic autoimmunity phase, where autoantibodies have been formed and clinical manifestations have been present.

Figure 1. Classification of autoimmune polyendocrine syndrome type 3 [13]



Hyperthyroidism is a disease due to increased thyroid hormone function followed by signs and symptoms that affect the body's metabolic system. Graves' disease is an autoimmune disease characterized by the presence of antibodies to TSHR (TRAb). The incidence of Graves' disease in monozygotic twins is higher than in dizygotic twins [1,2,4,5].

Graves' disease occurs due to chronic stimulation of follicular cells to continuously produce thyroid hormone. This long-acting thyroid stimulator is now known as TSH receptor stimulating antibody. In some circumstances, the symptoms and signs of thyrotoxicosis are very clear, namely the presence of a diffuse goiter accompanied by clear toxic signs and symptoms. In general, to diagnose the presence of thyrotoxicosis and determine the cause, a history and physical examination are needed to be assisted by laboratory examinations for TSH and FT4 levels, sometimes total T3. TRAb test can also be performed. TRAb is an antibody against the TSH receptor, and TSAb describes only the stimulating antibody. Thyroid sonography may be considered to determine radioactive uptake in doubtful circumstances [10-13].

Diagnosis requires major criteria and one or more minor criteria [13]. Major criteria: Clinically and/or biochemically hyperthyroidism i.e increased FT4 and/or free T3 (FT3), decreased TSH. Minor criteria: Clinical manifestations of ophthalmopathy and/or dermopathy, positive serum TRAb, Diffuse radioactive iodine uptake [14-16].

Diagnosis of hyperthyroidism is clinically based on physical examination as listed on the Wayne index, biochemically based on hormone levels of T3, T4, and TSH. Patient had Wayne index score of 25 indicating hyperthyroidism and was supported by a high FT4 and low TSH result.

Management of Graves' disease has 3 therapeutic modalities, respectively antithyroid drugs, surgery and radioablation. Antithyroid drugs are a cornerstone of the management of Graves' disease. Antithyroid drugs that are widely used are the thionamide group, namely PTU, imidazole (methimazole, thiamazole, and carbimazole). potential side effects of antithyroid drugs are bone marrow toxicity (agranulocytosis) and hepatotoxicity, both of which can be life-threatening. Several other drugs can also be used in the management of Graves' disease, such as inorganic iodine and beta-adrenergic antagonist drugs. Beta-adrenergic antagonists are often used early in treatment, while waiting for the patient to become euthyroid on antithyroid drugs. Thereafter treatment was continued with antithyroid drugs alone [11-16].

4 Conclusion

Autoimmune Polyendocrine Syndromes (APS) was at first characterized as different endocrine organ diseases related to an immune system illness in a subject. Hence, the affiliation between illnesses in APS was noted not to be irregular but in specific combinations in which a few non-endocrine immune system diseases were moreover portion of the disorders.

5 Declarations

5.1 Ethical Approval

This publication was approved by Ethics Committee of RSUP Dr. Mohammad Hoesin Palembang. (Docket number 156/kepkrsmh/2021).

5.2 Informed Consent

The patient and her parents consented to publish this case report.

5.3 Competing Interests

The authors declared that no conflicts of interest exist in this publication.

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