

# A Rare Autoimmune Quartet: Immune Thrombocytopenia in a Patient with Autoimmune Polyglandular Syndrome Type 3

Otoimmün Poliglandüler Sendrom Tip 3'lü Bir Hastada İmmün Trombositopeni: Nadir Bir Otoimmün Dörtlü

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## To the Editor,

Autoimmune polyglandular syndrome (APS) constitutes a group of disorders characterized by the autoimmune-mediated dysfunction of multiple endocrine glands. Key endocrine pathologies include hypoparathyroidism, adrenal insufficiency, type 1 diabetes mellitus (DM), and hypothyroidism. Non-endocrine manifestations such as mucocutaneous candidiasis, alopecia, vitiligo, celiac disease, and autoimmune gastritis (pernicious anemia) are also observed [1,2]. However, the coexistence of hematological autoimmune conditions, such as immune thrombocytopenia or autoimmune hemolytic anemia, is exceedingly rare within the APS spectrum [3]. APS is currently categorized into four main types (Table 1) [1,2]. APS type 3 is defined by the presence of autoimmune thyroid disease in association with another organ-specific autoimmune condition, excluding adrenal insufficiency and hypoparathyroidism. We report a unique case of APS type 3 in a young woman with a history of immune thrombocytopenia, type 1 DM, Hashimoto's thyroiditis, and myasthenia gravis (MG). In addition to the endocrine-based classification, this constellation is also consistent with multiple autoimmune syndrome (MAS) type 3, a category that closely parallels APS type 3 in the literature [4].

A 25-year-old woman presented for routine follow-up of immune thrombocytopenia. She had been diagnosed two years earlier and was initially treated with corticosteroids. One year ago, during the first month postpartum, she experienced a relapse and received intravenous immunoglobulin (IVIG) along with steroids. Three months after discontinuation of the steroids, the patient experienced a relapse requiring retreatment. After breastfeeding cessation, a subsequent relapse necessitated four doses of rituximab (375 mg/m<sup>2</sup>/week). Further review of her medical history revealed that she had been diagnosed with type 1 DM and Hashimoto's thyroiditis at the age of 18. Additionally, a diagnosis of MG had been established three years ago based

on typical clinical findings and compatible electromyographic results, and she was subsequently treated with steroids and IVIG. She remained asymptomatic for MG during rituximab therapy, achieved a complete response for immune thrombocytopenia (platelet count of >100x10<sup>9</sup>/L at last follow-up), and continued maintenance therapy for MG thereafter. Her current medications include insulin, levothyroxine, and pyridostigmine. Physical examination was unremarkable and laboratory findings showed no signs of thrombocytopenia or anemia. The combination of autoimmune thyroiditis, type 1 DM (type 3a), and MG (type 3c) satisfies the diagnostic criteria for APS type 3. Taken together, these findings also place the patient within the expanded framework of MAS type 3. Although rare, her concurrent diagnosis of immune thrombocytopenia requiring second-line therapy further highlights the complexity of her autoimmune profile.

Immune thrombocytopenia, usually considered a primary hematological disorder, can also develop due to identifiable secondary causes such as infections, medications, or systemic disorders, including autoimmune diseases [5]. In this context, the coexistence of immune thrombocytopenia with APS, though rare, is a relevant consideration, especially in young patients with multiple autoimmune features. Immune thrombocytopenia accompanying Graves' disease, which does not meet the definition of APS, has been reported rarely [6,7]. A previously reported case fulfilling the definition of APS included autoimmune hyperthyroidism and type 1 DM, along with both immune thrombocytopenia and heparin-induced thrombocytopenia [3]. However, our literature search did not identify any previous reports describing the specific combination of type 1 DM, MG, Hashimoto's thyroiditis, and immune thrombocytopenia.

Interestingly, our patient, who had type 1 DM (type 3a component), MG (type 3c component without vitiligo), and autoimmune thyroiditis in the absence of adrenal insufficiency, also had a history of immune thrombocytopenia that required

**Table 1. Classification of autoimmune polyglandular syndrome [1,2].**

APS type 1 (APECED)*	Chronic mucocutaneous candidiasis, hypoparathyroidism, autoimmune adrenal insufficiency
APS type 2 (Schmidt syndrome)**	Autoimmune adrenal insufficiency, autoimmune thyroid disease, type 1 diabetes mellitus
APS type 3***	Autoimmune thyroid disease, other autoimmune diseases (excluding autoimmune adrenal disease and hypoparathyroidism)
APS type 4****	≥2 organ-specific autoimmune diseases not meeting the criteria for type 1, type 2, and type 3

\*: Diagnosis requires two components. Type 1A diabetes, primary hypogonadism, pernicious anemia, autoimmune hepatitis, ovarian failure, pure red cell aplasia, alopecia, and vitiligo may also be present.

\*\* : Diagnosis requires autoimmune thyroid diseases and/or type 1 diabetes mellitus in addition to the presence of autoimmune adrenal insufficiency. Primary hypogonadism, myasthenia gravis, and celiac disease are also commonly observed.

\*\*\*: APS type 3 was defined as the association between one of the clinical entities of the autoimmune thyroid diseases (Hashimoto's thyroiditis, idiopathic myxedema, symptomless autoimmune thyroiditis, Graves' disease, endocrine ophthalmopathy) and one or more of other autoimmune diseases including type 1 diabetes mellitus for type 3a APS; atrophic gastritis or pernicious anemia for type 3b APS; vitiligo, alopecia, or myasthenia gravis for type 3c APS; and systemic autoimmune connective tissue diseases such as systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, systemic sclerosis, antiphospholipid syndrome, or vasculitis for type 3d APS.

\*\*\*\*: Combination of autoimmune diseases that do not satisfy the criteria for type 1, type 2, or type 3.

APS: Autoimmune polyglandular syndrome; APECED: autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy.

second-line treatment. APS-3 and MAS-3 share considerable overlap, although MAS generally encompasses a wider range of non-endocrine autoimmune conditions [4]. This constellation fulfills the diagnostic criteria for APS type 3 (3a + 3c) and, given the coexistence of additional autoimmune disorders such as immune thrombocytopenia, can also be classified within the spectrum of MAS type 3. Despite its rarity, clinicians should maintain a high index of suspicion for underlying endocrinopathies in patients with immune thrombocytopenia, as it may represent a component of APS or MAS.

**Keywords:** Autoimmune polyglandular syndromes, Immune thrombocytopenia, Hashimoto's thyroiditis, Type 1 diabetes mellitus, Myasthenia gravis

**Anahtar Sözcükler:** Otoimmün poliglandüler sendromlar, İmmün trombositopeni, Hashimoto tiroiditi, Tip 1 diabetes mellitus, Miyastenia gravis

## Ethics

**Informed Consent:** Informed consent was not obtained as the report does not include any identifiable patient information.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: Ü.A.; Concept: Ü.A., H.D.; Design: Ü.A., H.D.; Data Collection and Processing: Ü.A.; Analysis or Interpretation: Ü.A., H.D.; Literature Search: Ü.A., H.D.; Writing: Ü.A., H.D.

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