Case Report

Autoimmune Polyglandular Syndrome Type III: A Case Report of a Diagnostic Challenge in a Middle-Age Woman

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ABSTRACT

Introduction: Autoimmune Polyglandular Syndrome Type III (APS III) is characterized by the coexistence of autoimmune thyroid disease with other autoimmune disorders, excluding adrenal insufficiency. It remains underdiagnosed due to its variable and often non-specific clinical presentation.

Case Presentation: We report the case of a middle-aged female with a known history of autoimmune hypothyroidism who presented with symptoms of anemia and poor glycemic control. Laboratory investigations revealed positive anti-parietal cell antibodies, elevated intrinsic factor antibodies, and vitamin B12 deficiency consistent with pernicious anemia. She was also diagnosed with latent autoimmune diabetes in adults (LADA), based on positive anti-GAD antibodies and suboptimal glycemic response. These findings fulfilled the criteria for APS Type III. The patient responded well to vitamin B12 supplementation and insulin therapy, with marked improvement in hematological and metabolic parameters.

Conclusion: APS type III can manifest with non-specific or overlapping clinical features, which may contribute to delayed identification. Clinicians should maintain a high level of suspicion in patients with already diagnosed autoimmune disorders.

KEY WORDS: Thyroiditis, Pernicious Anemia, Autoimmune Polyglandular Syndrome Type III, Latent Autoimmune Diabetes in Adults (LADA) , Autoimmune Endocrinopathy.

INTRODUCTION

Autoimmune polyglandular syndromes (APS) are a heterogenous group of disorders characterized by immune-mediated dysfunction of multiple endocrine glands, often associated with other autoimmune disorders, such as vitiligo, chronic atrophic gastritis, pernicious anemia, chronic autoimmune hepatitis, and celiac disease.

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The presence of autoimmune thyroid disease without adrenal involvement is classified as autoimmune polyglandular syndrome type III (APS III), which primarily affects middle-aged women.[3] It frequently presents as a combination of pernicious anemia, type 1 diabetes, or latent autoimmune diabetes of adults (LADA), and autoimmune thyroiditis.

Here we report a rare case of APS IIIB, highlighting its diagnostic complexity and the importance of early recognition to prevent irreversible complications.

Submitted: August 03, 2025 **Revision Received:** November 17, 2025

Accepted for Publication: December 08, 2025

How to cite this: *Ali M, Safdar A, Raja LF, Mahboob M. Autoimmune Polyglandular Syndrome Type III: A Case Report of a Diagnostic Challenge in a Middle-Age Woman. JPES. 2025;2(2):94-97.*

CASE HISTORY

A 47-year-old, Asian female resident of Rawalpindi presented with symptomatic anemia, poor glycemic control, peripheral paresthesia, oral ulcers, and fine tremors. She had a 15-year history of autoimmune hypothyroidism confirmed by elevated positive anti-TPO and anti-thyroglobulin antibodies. She was treated with levothyroxine with stable thyroid function.

She was also diagnosed with diabetes mellitus with an HbA1c of 13% and positive islet-cell antibodies, for which she was receiving insulin therapy. On examination, she appeared pale with Tongue glossitis, hair thinning, dry skin, koilonychia and fine tremors. Detailed history, revealed that she was previously treated for adrenal insufficiency with corticosteroids and iron deficiency anemia. Despite adequate iron replacement, her Hb levels were drastically low. Further workup revealed hyper segmented neutrophils on the peripheral smear, along with borderline vitamin B12 levels. Given her history of autoimmune disorders, a comprehensive autoimmune workup was undertaken. Surprisingly, she tested positive for anti-parietal cell and intrinsic factor antibodies, confirming a diagnosis of pernicious anemia. Her management was optimized with vitamin B12 replacement and insulin adjustment, leading to marked improvement in anemia and glycemic control. The coexistence of autoimmune thyroiditis, type 1 diabetes mellitus, and pernicious anemia confirmed autoimmune polyglandular syndrome type III (APS III). Early recognition and appropriate long-term support are essential to prevent further complications.

The following workup was done during her admission to the hospital.

TESTS	*UNITS*	*RESULTS*	*REFERENCES*
HB	g/dl	8.8	12.0 and 16.0 g/dL
TLC	$\times 10^9$/L	10.04	140-425 ×109/L
PLT	$\times 10^9$/L	334	140000-425000
NEUTROPHILS	%	47	55-70
LYMPHOCYTES	%	30	25-40
MCV	fL	75	82-98
MCHC	g/dL	26	32-36
RDW-CV	%	23	11.5% to 14.5%
EOSINOPHILS	%	14	00-04
PERIPHERAL FILM SMEAR	_	Hyper segmented neutrophils	_
RETICULOCYTE COUNT	%	0.1	0.5-2.0%
URINE MICROALBUMIN	mg/g	<5	<20
Na	mmol/L	139	135-145
K	mmol/L	4.1	Adults: 3.5-5.5
Cl	mmol/L	107	95-110
CREATININE	mg/dL	0.9	0.2-1.3
TOTAL BILIRUBIN	mg/dl	0.2	Adult: 0.2- 1.2
AST(SGOT)	U/L	30	34
ALT(SGPT)	U/L	13	<45
VITAMIN B12	pg/dL	206	187-883
FOLIC ACID	ng/dL	13.1	3.1-20.0
TRIGLYCERIDES	mg/dL	86	<150

Ca^{+2}	mg/dL	9	Adults: 8.4-10.2
$Po4^{-3}$	mg/dL	4	Adults: 2.5- 4.8

TESTS	*UNITS*	*RESULTS*	*REFERENCES*
ALBUMIN	g/dL	4.4	14.1-60y: 3.5-5.2
IRON	µg/dL	21	Female: 50170
TIBC	µg/dL	405	250 - 450
TRANSFERRIN SATURATION	%	5.19	
TOTAL T3	ng/mL	0.8	0.6- 1.6
FREE T4	ng/dL	1.1	0.7- 1.5
TSH	µIu/mL	6.4	0.4- 4.5
VITAMIN D	ng/mL	31.9	>30
HbA1c	%	8.5	Excellent: 4.0- 6.0
ANTI-GAD (65) ANTIBODIES	IU/mL	280	Negative: < 17 Positive: >17
SERUM CORTISOL	µg/dL	19.9	4.0-22
ISLET CELL ANTIBODIES	U/m	279	<28
ANTI THYROGLOBULIN ANTIBODIES	IU/mL	7.8	<10
INTRINSIC FACTOR ANTIBODIES	U/mL	22.6	<1.20
ANTI-THYROID PEROXIDASE	IU/mL	>1000	< 34
ANTIBODIES			
ULTRASOUND THYROID	–	Enlarged thyroid with heterogeneous texture hypoechoic micronodules and intervening echogenic septae seen suggestive of Hashimotos thyroiditis	–

DISCUSSION

Thyrogastric condition, also called Autoimmune Polyglandular Syndrome type 3b (APS-3 b), frequently coexists with pernicious anemia and autoimmune thyroid illness. It is believed that this link results from the anatomical and embryologic similarities between thyroid follicular cells and gastric parietal cells, particularly their Na/I symporters and apical microvilli.[4] The most common autoimmune ailment is autoimmune thyroiditis, especially Hashimoto's thyroiditis, which is confirmed by the presence of Thyroid peroxidase (TPO) and anti-thyroglobulin antibodies.

Pernicious anemia (PA), resulting from an immune-mediated loss of parietal cells, impairs intrinsic factor production and vitamin B12 absorption, and is clinically manifested as peripheral neuropathy, macrocytic anemia, and subacute combined degeneration of the spinal cord.[5,6] The persistent anemia, subnormal vitamin B12 level despite adequate iron replacement, and elevated HbA1c of 13% were reflective of underlying autoimmune dysfunction and poor glycemic control in the patient. The treatment of PA includes regular lifelong injections of supplemental cyanocobalamin (1000 mcg weekly for 1-2 weeks, then weekly for approx. 4 weeks till improvement is noted).[7]

LADA, a slowly progressive form of autoimmune diabetes (>30 years of age at time of diagnosis), is the clinical and metabolic combination of both type 1 and type 2 diabetes, requiring delayed need for insulin.[8]

In this patient, the diagnosis was supported by low C-peptide levels and positivity for anti-GAD and islet cell antibodies, requiring initiation of basal-bolus insulin therapy.[9]

The goal of managing APS-3 is to replace hormones while carefully screening for other autoimmune illnesses. The patient was treated with long-acting and short-acting insulin for LADA, thyroxine for hypothyroidism, and an intramuscular injection on alternate days to replenish vitamin B12. It is essential to recognize that IDA and pernicious anemia can coexist, for this reason, both deficiencies should be evaluated to ensure accurate diagnosis and effective management. Additionally, patients with APS 3 should be routinely checked for other possible autoimmune diseases such as vitiligo, autoimmune hepatitis, and celiac disease.

CONCLUSION

This case highlights the importance of maintaining a high index of suspicion for additional autoimmune conditions once a single autoimmune disorder has been identified. Early recognition and timely intervention are crucial to prevent potentially irreversible complications, particularly neurological sequelae related to vitamin B12 deficiency and long-term metabolic consequences of delayed diabetes management. The marked clinical and biochemical improvement following integrated, multidisciplinary treatment emphasizes the need for comprehensive evaluation, regular surveillance, and lifelong follow-up in patients with autoimmune polyglandular syndromes to optimize outcomes and improve quality of life.

Acknowledgments: None.

Conflict of Interest: The authors declare no conflict of interest.

Ethical Approval: Not applicable.

Patient Consent: Written informed consent was obtained from the patient for publication of this case report.

Data Availability: Available upon request from the corresponding author.

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MAA: Clinical input, literature review, conceptualization.
AS: Manuscript writing, Literature review, Formatting.
LFR: Data Assistance.
MM: Supervision, case interpretation, final approval.

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