Doi: https://doi.org/10.3329/ewmcj.v13i2.79312

Case Report

AUTOIMMUNE POLYENDOCRINE SYNDROME TYPE 3: A CASE REPORT

Haque F[1], Dey G[2], Paul N[3], Ahmed A[4]

Article history:
Received: 1st January 2025
Accepted: 10th February 2025

Key words:
Autoimmune Polyendocirne Syndrome, Multiple Autoimmune Syndrome, APS Type 3. MAS Type 3, Idiopathic Thrombocytopenic Purpura, Hashimoto's Thyroiditis, Sjogren Syndrome, Autoimmune Diseases, Bangladesh

Abstract:

Idiopathic thrombocytopenic purpura (ITP) is a condition characterized by a low platelet count, leading to an increased risk of bleeding. Despite having a shared autoimmune aetiology, documented cases of ITP alongside other autoimmune diseases are scarce. Here, we describe the case of a 55-year-old Bangladeshi woman who presented with bleeding symptoms and generalized weakness. On query, she gave a history of dry eye and dry mouth. She was a known case of hypothyroidism and ischaemic heart disease. After comprehensive evaluation, she was diagnosed with Autoimmune Polyendocrine Syndrome (APS)/Multiple Autoimmune Syndrome (MAS) Type 3, which included acute idiopathic thrombocytopenic purpura, Sjogren's syndrome, Hashimoto's thyroiditis, an old antero-septal myocardial infarction, dyslipidemia, and grade I fatty liver disease. Treatment involved a combination of immunosuppressive therapy, thrombopoietin receptor agonists (TPO-RA) - eltrombopag, platelet transfusion, levothyroxine, and supportive measures leading to successful management. This case highlights the challenge of addressing multiple autoimmune conditions concurrently and stresses the importance of comprehensive evaluation and multidisciplinary care to diagnose and manage these complex presentations accurately. Notably, patients with a autoimmune disease may harbour other undiagnosed autoimmune conditions and face an elevated risk of malignancy in the future. Despite this, in Bangladesh, the prevalence of autoimmune diseases, including APS/MAS, remains poorly understood. Further research is crucial to elucidate the epidemiology and clinical characteristics of autoimmune diseases associated with APS/MAS in this population, enhancing our ability to provide effective care and public health interventions.

EWMCJ Vol. 13, No. 2, July 2025: 152-158

Introduction

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by immune-mediated destruction of platelets, leading to thrombocytopenia and an increased risk of bleeding.[1] While the exact aetiology of ITP remains unclear, it is believed to involve the production of autoantibodies against platelet surface antigens, leading to their destruction by the reticuloendothelial system.[1,2]

Autoimmune diseases are characterized by an abnormal immune response against self-antigens, resulting in tissue damage and dysfunction. They often coexist within individuals, suggesting shared pathogenic mechanisms.[3] There is also an increased risk of cancer in patients with primary ITP.[9] The coexistence of multiple autoimmune diseases poses diagnostic and therapeutic challenges due to overlapping clinical features and potential treatment interactions.

Case Report:

A 55-year-old, normotensive, non-diabetic, Bangladeshi female presented with a history of bleeding manifestations and generalized weakness and was brought to Shaheed Suhrawardy Medical College Hospital in February 2024. She had complaints of bleeding manifestations for the

1. Dr. Fahim Haque, Honorary Medical Officer, Department of Medicine, Shaheed Suhrawardy Medical College Hospital
2. Dr. Gourab Dey, Assistant Registrar, Department of Medicine, Shaheed Suhrawardy Medical College Hospital
3. Dr. Nandita Paul, Associate Professor, Department of Medicine, Shaheed Suhrawardy Medical College Hospital
4. Dr. Akhlak Ahmed, Assistant Professor, Department of Medicine, Shaheed Suhrawardy Medical College Hospital

Address of Correspondence: Dr. Fahim Haque, Honorary Medical Officer, Department of Medicine, Shaheed Suhrawardy Medical College Hospital. fahim.haque.02@gmail.com

last 7 days and multiple purplish rashes for 1 month and generalized weakness for 2 years. She recounted 2 episodes of epistaxis, which were spontaneous, unprovoked, and resolved after applying pressure to the nasal bridge. At the same time, there was also spontaneous gum bleeding, without gum hypertrophy. She also complained of multiple ecchymoses and purpura throughout her body for the past month. These began as multiple red petechiae on both legs and gradually spread to the rest of the body. The rashes were of various sizes, non-itchy, not photosensitive, painless, non-blanchable, and non-palpable. There was no history of trauma, respiratory distress, allergy, oral ulcers or any new drugs. On query, there was a history of fever 15 days back. She also complained of weakness for about 2 years. There was no swelling, fatigability with diurnal variation, or any heat/cold intolerance. She gave no history of weight gain or loss, and her appetite was normal. Her bladder and bowel habits were normals. There was no history of taking any steroids. She gave a history of occasionally itchy, gritty, and foreign body sensations in both her eyes for the last 2 months associated with a dry mouth for the same duration. Additionally, she had no features of polyarthritis, Raynaud's phenomenon, skin tightening, thickening, or induration, hyper or hypopigmentation, frothy or high-coloured urination, palpitation, seizure, or loss of consciousness. She had a known case of hypothyroidism (2 years) and previously had a myocardial infarction (2012) and a spontaneous abortion (2000). She was already on treatment with Levothyroxine, antiplatelet and lipid-lowering agents. Although she was diagnosed with primary hypothyroidism, autoantibodies had not been previously tested.

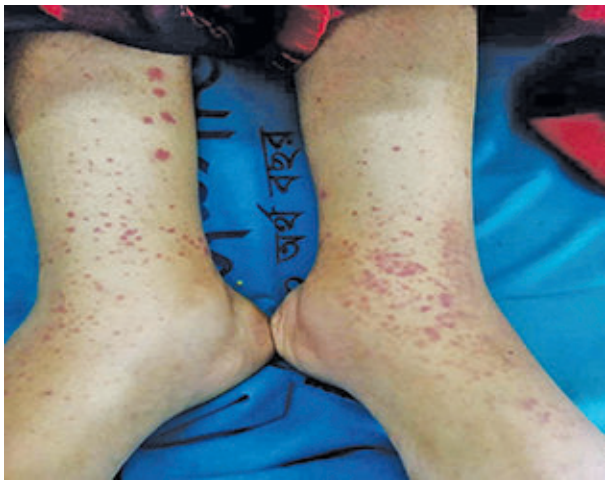

Figure 1: *Petechial rash on legs*

Systemic examination revealed that blood pressure was 110/60 mmHg without postural drop, radial pulse was 88 bpm and regular, respiratory rate was 14 breaths/min, SpO2 was 96% on air, and temperature was 98 F. The patient was mildly anaemic and had non-pitting oedema. There were no palpable lymph nodes or bony tenderness. Skin survey revelaed bleeding spots on the gum & palate, as well as multiple purpuric rashes across the arms, legs, back and trunk. Schirmer's Test was positive in both eyes. Fundoscopy was normal.

Investigations revealed haemoglobin 11.2 gm/dl, total white cells 7970/cmm, platelet <5000/cmm, erythrocyte sedimentation rate 83 mm/1st hour, TSH 17.10 µIU/ml, FT4 1.11 ng/dL, Anti-TPO Ab 149.48 IU/ml (positive), total cholesterol 292.1 mg/dl, triglycerides 261.8 mg/dl, HDL Cholesterol 33.9 mg/dl, LDL Cholesterol 205.84 mg/dl. Peripheral blood film showed gross thrombocytopenia. All other routine investigations, including c-reactive protein, serum creatinine, serum electrolytes, uric acid, serum creatinine phosphokinase, SGPT, serum albumin, random blood sugar, serum calcium, serum inorganic phosphates, prothrombin time, and APTT were within normal limits. Chest X-ray, Urine RME, and Blood cultures were normal. ECG showed old anteroseptal myocardial infarction, ultrasonography of the whole abdomen showed fatty liver disease (grade I); ultrasonography of the thyroid gland showed a small isoechoic nodule in the left lobe of the thyroid and small lymph nodes in both submandibular regions. Dengue and viral hepatitis serology were negative. Coomb's Test was negative. Autoimmune profile showed ANA 11.40 U/ml, Anti dsDNA 8.50 IU/ml, ENA profile showed positive SS-A/Ro60KD, SS-A/Ro52KD, SS-B/La and PM-Scl. Additionally, Complement 3 (C3) 1.64 g/L, Complement 4 (C4) 0.14 g/L, 24hr UTP 0.17g/24hr, Lupus Anticoagulant, Anti-Cardiolipin IgM & IgG were negative.

She was treated with methylprednisolone (500mg) for 3 days followed by prednisolone (50mg) orally, eltrombopag (50mg), pilocarpine (15mg), carboxymethylcellulose eye drops, rosuvastatin (10mg), bisoprolol (2.5mg), omeprazole (20mg), and levothyroxine (100mcg). Eltrombopag was stopped following advice from Rheumatology. 3 units of platelets were transfused. All bleeding manifestations resolved after two days of the initiation of a high-dose steroid. After 3 days of treatment, the platelet count was

Investigation	Result	Normal Range
Haemoglobin	11.2 gm/dL	13.0 -17.0 g/dL
Total White Cells	7970/cmm	4000 - 10000/cmm
Platelet Count	<5000/cmm	150000-400000/cmm
Erythrocyte Sedimentation Rate (ESR)	83 mm/1st hour	<20 mm/1st hour
TSH	17.10 µIU/mL	0.3 - 5.50 µIU/mL
FT4	1.11 ng/dL	0.71 - 1.85 ng/dL
Anti-TPO Ab	149.48 IU/mL	< 5.61 IU/mL
Total Cholesterol	292.1 mg/dL	130 - 200 mg/dL
Triglycerides	261.8 mg/dL	50 - 150 mg/dL
HDL Cholesterol	33.9 mg/dL	>35 mg/dL
LDL Cholesterol	205.84 mg/dL	<100 mg/dL
Peripheral Blood Film	Gross thrombocytopenia	-
C-reactive Protein	3.0 mg/dL	< 5.0 mg/dL
Serum Creatinine	0.96 mg/dL	0.5 - 0.9 mg/dL
Serum Electrolytes	Within normal limits	-
Uric Acid	5.0 mg/dL	2.4 - 5.7 mg/dL
Creatinine Phosphokinase (CPK)	23 U/L	30 - 135 U/L
ALT (SGPT)	23 U/L	<40 U/L
Serum Albumin	3.9 g/dL	3.4 - 5.4 g/dL
Random Blood Sugar	6.3 mmol/L	< 7.8 mmol/L
Serum Calcium	9.11 mg/dL	8.80 - 10.60 mg/dL
Serum Inorganic Phosphates	3.1 mg/dL	2.5 - 4.5 mg/dL
Parathyroid Hormone(PTH)	76.10 pg/mL	9 - 80 pg/mL
Prothrombin Time and APTT	Normal	-
Chest X-ray	Normal	-
Urine RME	Normal	-
Blood Cultures	No Growth	-
ECG	Old anteroseptal myocardial infarction	-
Ultrasonography (whole abdomen)	Fatty liver disease (grade I)	-
Ultrasonography (thyroid gland)	Small isoechoic nodule in left lobe; Small lymph nodes in both submandibular regions	-
Dengue Serology	Dengue IgM - Negative Dengue IgG - Negative	-
Viral Hepatitis Serology	HBsAg - Negative Anti-HCV - Negative	-
Coomb's Test (Direct)	Negative	-
Anti-Nuclear Ab(ANA)	11.40 U/ml	Negative: < 1.0 U/ml Borderline: 1.0-1.2 U/ml Positive: > 1.2 U/ml
Anti-ds DNA	8.50 IU/ml	Negative: < 20 IU/ml Equivocal: 20-25 IU/ml Positive: > 25 IU/ml
ENA Profile	Positive: SS-A/Ro60KD SS-A/Ro52KD SS-B/La PM-Scl	-
Complement 3 (C3)	1.64 g/L	0.90 - 1.80
Complement 4 (C4)	0.14 g/L	0.10 - 0.40
24hr UTP	0.17 g/24 hours	<0.15 g/24 hours
Lupus Anticoagulant	Negative	-
Anti-Cardiolipin IgMAnti-Cardiolipin IgG	Negative	-
Peripheral Blood Film	Gross Thrombocytopaenia	-
Bone Marrow Biopsy(on Day 10 of therapy)	Normal Active Marrow	-

15,000/cmm, at 2 weeks 75,000/cmm, and 160,000/cmm at 3 weeks. A repeat peripheral blood film showed only mild thrombocytopaenia. A bone marrow biopsy was carried out after 10 days of treatment and showed normal marrow activity. While Anti-Platelet Antibody could not be tested due to limited availability, the rapid improvement to steroids suggested a clinical diagnosis of immune-mediated thrombocytopenia. This was diagnosed as a case of Autoimmune Polyendocrine Syndrome (APS)/Multiple Autoimmune Syndrome (MAS) Type 3 (comprising Acute Idiopathic Thrombocytic Purpura, Sjogren's syndrome, Hashimoto's Thyroiditis), Old Antero-Septal Myocardial Infarction, Dyslipidemia, and Fatty Liver Disease (Grade I).

Discussion:

The presented case illustrates a complex clinical scenario involving the coexistence of idiopathic thrombocytopenic purpura with multiple autoimmune diseases. The patient's history, clinical presentation, and laboratory findings are consistent with acute ITP, Sjogren syndrome, Hashimoto's thyroiditis, old antero-septal myocardial infarction, dyslipidemia, and grade I fatty liver disease.

Idiopathic thrombocytopenic purpura is a serious acquired autoimmune disorder characterized by a low platelet count (thrombocytopenia) and mucocutaneous bleeding.[1,2] It is commonly assumed that ITP results from autoantibodies causing accelerated platelet destruction. Recent data suggest that autoantibodies may also inhibit platelet production.[13] ITP is traditionally divided into acute and chronic forms, based on the duration of thrombocytopenia (i.e., less than 6 months for acute and more than 6 months for chronic). ITP is generally acute in young children and typically, occurs a few days to a few weeks after an infection (e.g., varicella zoster virus, viral cold). ITP in children is thought to be a benign and self-limiting disorder with an excellent prognosis. In contrast, ITP in adults is primarily chronic, and the onset is often asymptomatic. The disease is more prevalent in females than males. The diagnosis of ITP is clinical and is very often based on the exclusion of other causes of thrombocytopenia.[12] There are no standard tests to diagnose ITP, with anti-platelet antibodies having low sensitivity (53%) but high specificity (>90%). A positive autoantibody test can be useful for ruling in ITP, but a negative test does not rule out ITP.[15]

The association between ITP and other autoimmune conditions has been documented in the literature.[4] Sjogren syndrome, characterized by lymphocytic infiltration of exocrine glands leading to dry eyes and mouth[5], frequently coexists with ITP. Similarly, Hashimoto's thyroiditis, an autoimmune disorder affecting the thyroid gland, has been reported in patients with ITP. The underlying mechanisms linking these autoimmune diseases remain poorly understood but likely involve shared genetic predisposition and dysregulation of immune responses. Prevalence of ITP has been reported to range from 7% to 30% in systemic lupus erythematosus (SLE) patients, and several groups have studied the clinical characteristics of ITP in SLE patients. However, clinical characteristics of ITP in other autoimmune diseases such as Sjogren syndrome (SS) and the difference between ITP associated with different autoimmune diseases are still not very clear.[14]

Similar cases of ITP coexisting with multiple autoimmune diseases have been reported globally. In Spain, cases of ITP with concurrent autoimmune thyroiditis and Sjogren syndrome were documented, mirroring our patient's presentation. In Western countries, associations between ITP and systemic lupus erythematosus, rheumatoid arthritis, and autoimmune hepatitis have been described, highlighting the diverse spectrum of autoimmune comorbidities in patients with ITP.[5] There is also the possibility of developing pernicious anaemia in patients suffering from chronic ITP.[8] Furthermore, all the diagnosed autoimmune conditions confer a higher risk of cancer, particularly haematological malignancies.[9,10,11]

Sjögren's syndrome is relatively often classified as a part of autoimmune syndromes.[16] Sjögren's syndrome is probably the most frequent disease of connective tissue associated with AITD, especially with Hashimoto's disease.[17] During more than 10 years of examination, Lazarus et al. found that in a cohort of 114 patients with SS, c. 40% of patients had another autoimmune disease and AITD patients comprised the largest group (16%).[18] The most common manifestation of AITD in SS was hypothyroidism. In most cases it was diagnosed before SS. Similar results were obtained by Ramos-Casals et al. in a group of patients with SS 20% of the them had AITD and 16% had non-AITD. This confirms that more than 1/3 of the patients with SS also suffered from thyroid diseases, the most frequent manifestation of which

Table-I

First classification of PGAD or APS according to Neufeld and Blizzard (1980)

Type	Features
1	Candidiasis, hypoparathyroidism, Addison's disease (two or three present)
2	Addison's disease + Thyroid autoimmune diseases and/or type 1 diabetes mellitus
3	Thyroid autoimmune diseases + (3A) Type 1 diabetes mellitus (3B) Pernicious anemia (3C) Vitiligo, alopecia, and/or other organ-specific autoimmune diseases
4	Two or more organ-specific autoimmune diseases not falling into types 1, 2, or 3 PGAD polyglandular autoimmune diseases, APS autoimmune polyglandular syndromes

was subclinical hypothyroidism.[19] Hashimoto's coexistence with SS is relatively well documented. Additionally, it is interesting that both disorders share similar symptoms and even nonspecific antibodies (e.g. anti-nuclear antibodies, rheumatoid factor – RF). Symptoms such as keratoconjunctivitis and xerostomia are reported by as many as 30% of the patients with autoimmune thyroid disease. Positive anti-nuclear antibodies are present in as many as 20–55% of patients with AITD; therefore, they have to be monitored due to a high risk of development of other autoimmune diseases, including SS.[20]

Autoimmune Polyendocrine Syndromes (APSs), also called polyglandular autoimmune syndromes (PGASs), are a group of autoimmune diseases mainly involving the endocrine organs, but also frequently affecting the skin and musculoskeletal system. Neufeld & Blizzard first described the syndrome in 1980 when only two forms of APS were proposed.[24] Since then there have been several developments, including the discovery of the autoimmune regulator gene (AIRE) gene thought to be responsible for APS.[22-25] When the majority of the autoimmune conditions are rheumatological or dermatological, they are often referred to as Multiple Autoimmune Syndrome (MAS) instead.[21,26-27]

Autoimmune Polyendocrine Syndrome (APS) is classified into three main types:

- APS Type 1: Typically manifests in childhood with features like chronic mucocutaneous candidiasis, hypoparathyroidism, and Addison's disease.
- APS Type 2: Usually appears in adulthood and includes Addison's disease, autoimmune thyroid disease, and type 1 diabetes.
- APS Type 3: Characterized by autoimmune thyroiditis with other autoimmune diseases, excluding Addison's disease.

APS Type 3 is further subdivided into 4 types:

Autoimmune thyroid diseases (AITD) and

- APS (3a): Other autoimmune endocrine diseases(excluding Addison's disease)
- APS (3b): Other autoimmune gastrointestinal, hepatic, or pancreatic diseases
- APS (3c): Other autoimmune diseases of the skin, central nervous system, or hematopoietic system
- APS (3d): Other autoimmune rheumatic and cardiovascular diseases or vasculitis

There are also other types of APS:

- PEX Syndrome: This X-linked recessive disorder is caused by mutations in the FOXP3 gene and primarily affects males. It can lead to severe autoimmune activity against multiple organs
- POEMS Syndrome: Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes

Multiple Autoimmune Syndrome (MAS) was first defined by Cojocaru et al. in 2010 as when an individual has three or more autoimmune diseases.[21] It was initially classified as:

- Type 1 MAS: Includes myasthenia gravis, thymoma, polymyositis, and giant cell myocarditis.
- Type 2 MAS: Includes Sjögren's syndrome, rheumatoid arthritis (RA), primary biliary cirrhosis

(PBC), scleroderma, and autoimmune thyroid disease.

- Type 3 MAS: Groups autoimmune thyroid disease with conditions like myasthenia gravis, Sjögren's syndrome, pernicious anaemia, ITP, Addison's disease, type 1 diabetes mellitus, vitiligo, autoimmune hemolytic anaemia (AIHA), systemic lupus erythematosus (SLE), and dermatitis herpetiformis.

However, since then, Autoimmune Polyendocrine Syndrome (APS) and Multiple Autoimmune Syndrome (MAS) have often been used interchangeably.[26] Subsequent research into the genetics of multiple autoimmune patients has yielded similar involvement of HLA haplotypes and alleles, suggesting that the two are indeed the same condition.[28,29] A further fourth type, Type 4 APS/MAS, has been proposed to fit any other autoimmune disease combination not included in the previous classifications.[26]

The management of patients with multiple autoimmune diseases necessitates a multidisciplinary approach involving haematologists, rheumatologists, endocrinologists, and other specialists. Treatment strategies aim to suppress immune-mediated inflammation while addressing organ-specific manifestations and complications. Corticosteroids, immunomodulators, cytotoxic and biologic agents may be employed, tailored to individual patient needs and disease severity.[6] Specific treatments for ITP also include thrombopoietin receptor agonists(TPO-RA) namely eltrombopag and romiplostim, biologics (rituximab) and splenectomy in refractory cases.[1] Interestingly, case series have shown that the number of autoimmune conditions does not correlate with the severity of the disease; in fact, most patients only have mild clinical features relative to the number of autoimmune conditions.[30]

In Bangladesh, the prevalence of autoimmune diseases, including APS/MAS, needs to be better studied. Limited epidemiological data hinder our understanding of the true burden of autoimmune disorders in the population. During our literature review, we found only a handful of publications on APS/MAS in Bangladeshi adults and none any similar publications involving ITP and other autoimmune disorders. This case underscores the importance of conducting further research to elucidate the epidemiology and clinical characteristics of autoimmune diseases in Bangladesh.[7]

Conclusion:

In conclusion, this case highlights the complexity of autoimmune disorders and the challenges associated with managing multiple autoimmune conditions concurrently. The presence of one autoimmune disease should alert the physician to investigate for additional autoimmune conditions because a high degree of clinical suspicion is needed to diagnose multiple coexisting autoimmune disorders. Comprehensive evaluation, accurate diagnosis, and multidisciplinary care are essential for optimising patient outcomes in such cases.

We report a case of adult idiopathic thrombocytopenic purpura with multiple autoimmune diseases, diagnosed as Autoimmune Polyendocrine Syndrome (APS) Type 3, including Sjogren syndrome and Hashimoto's thyroiditis. This case highlights the complexity of managing multiple autoimmune conditions concurrently and underscores the importance of a thorough evaluation and a multidisciplinary approach. Further research is needed to elucidate the underlying mechanisms and optimal management strategies for patients with concurrent autoimmune diseases.

Acknowledgement

This case was previously presented as a poster at a conference, and its abstract was published as a supplement to the conference journal.

Haque, F., Dey, G., Paul, N., & Ahmed, A. (2024). Exploring the Autoimmune Spectrum: A Case Study. Bangladesh Journal of Medicine, 35(20), 180. https://doi.org/10.3329/bjm.v35i20.73476"

References:

1. Neunert C, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019;3(23):3829-3866.
2. Audia S, et al. Pathogenesis of immune thrombocytopenia. Autoimmun Rev. 2017;16(6):620-632.
3. Janeway CA Jr, Travers P, Walport M, et al. Immunobiology: The Immune System in Health and Disease. 5th edition. New York: Garland Science; 2001.
4. Díaz-Polo, L. , Pujol-Moix, N. , Jiménez, B. , Canals, C. , Barranco-Charris, E. , Muñiz-Díaz, E. and Souto, J. (2016) Shared Autoimmunity: A Case Series of 56 Patients with Immune Thrombocytopenia (ITP) Associated with Other Autoimmune Disorders. Open Access Library Journal, 3, 1-9.
5. Negrini, S., Emmi, G., Greco, M., Borro, M., Sardanelli, F., Murdaca, G., Indiveri, F., & Puppo, F. (2022). Sjögren's

syndrome: a systemic autoimmune disease. Clinical and experimental medicine, 22(1), 9–25.

6. Provan D, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115(2):168-186.
7. Hannan, Mohammad & Kamrul Hasan, A.B.M. & Karim, Md & Selim, Shahjada & Stocker, M & Diug, B & Ilic, D & Mustari, Marufa & Haq, Tahniyah & Fariduddin, Md. (2022). Hypothyroidism in Bangladesh: Is Autoimmunity the Next Big Threat?. Mymensingh Medical Journal. 31. 449-457.
8. Juncà J, Flores A, Granada ML, Jiménez O, Sancho JM. The relationship between idiopathic thrombocytopenic purpura and pernicious anaemia. Br J Haematol. 2000 Nov;111(2):513-6.
9. Charlotta Ekstrand, Shahram Bahmanyar, Honar Cherif, Helle Kieler, Marie Linder.Cancer risk in patients with primary immune thrombocytopenia – A Swedish nationwide register study. Cancer Epidemiology, Volume 69, 2020, 101806, ISSN 1877-7821
10. Igoe, Ann, Sali Merjanah, and R. Hal Scofield. "Sjögren syndrome and cancer." Rheumatic Disease Clinics 46, no. 3 (2020): 513-532.
11. Azizi, G., J. M. Keller, M. Lewis, K. Piper, D. Puett, K. M. Rivenbark, and C. D. Malchoff. "Association of Hashimoto's thyroiditis with thyroid cancer." Endocrine-related cancer 21, no. 6 (2014): 845-852.
12. Feudjo-Tepie, M. A., G. Le Roux, K. J. Beach, D. Bennett, and N. J. Robinson. "Comorbidities of idiopathic thrombocytopenic purpura: a population-based study." Advances in hematology 2009 (2009).
13. R. McMillan, L. Wang, A. Tomer, J. Nichol, and J. Pistillo, "Suppression of in vitro megakaryocyte production by antiplatelet autoantibodies from adult patients with chronic ITP," Blood, vol. 103, no. 4, pp. 1364–1369, 2004.
14. Liu, Yuan MDa; Chen, Shiju MDa; Sun, Yuechi MMa; Lin, Qingyan MMa; Liao, Xining MBb; Zhang, Junhui MMb; Luo, Jiao MBb; Qian, Hongyan MMa; Duan, Lihua PhDa; Shi, Guixiu MD, PhD. Clinical characteristics of immune thrombocytopenia associated with autoimmune disease: A retrospective study. Medicine 95(50):p e5565, December 2016.
15. Vrbensky JR, Moore JE, Arnold DM, Smith JW, Kelton JG, Nazy I. The sensitivity and specificity of platelet autoantibody testing in immune thrombocytopenia: a systematic review and meta-analysis of a diagnostic test. J Thromb Haemost 2019; 17: 787–94.
16. Rojas-Villarraga A, Amaya-Amaya J, Rodriguez-Rodriguez A, et al. Introducing polyautoimmunity: secondary autoimmune diseases no longer exist. Autoimmune Dis 2012; 2012: 254319.
17. Bourji K, Gatto M, Cozzi F, et al. Rheumatic and autoimmune thyroid disorders: a causal or casual relationship? Autoimmune Rev 2015; 14: 57–63.
18. Lazarus MN, Isenberg DA. Development of additional autoimmune diseases in a population of patients with primary Sjögren's syndrome. Ann Rheum Dis. 2005; 64: 1062–1064,
19. Ramos-Casals M, García-Carrasco M, Cervera R, et al. Thyroid disease in primary Sjögren syndrome. Study in a series of 160 patients. Medicine (Baltimore) 2000; 79: 103–108,
20. Tektonidou MG. Presence of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med 2010; 123: e23
21. Cojocaru, M., Cojocaru, I. M., & Silosi, I. (2010). Multiple autoimmune syndrome. Maedica, 5(2), 132–134.
22. Betterle C, Zanchetta R, Dotta F, et al. Autoimmune polyendocrine syndromes: type I, II, and III. Endocr Rev. 2002;23(3):377-422.
23. Tani C, Tozzoli R, Buzio C. Autoimmune polyendocrine syndromes: a review. Autoimmune Rev. 2008;7(5):328-334.
24. Neufeld M, Blizzard MR. Polyglandular autoimmune disease. In: Pinchera A, Doniach D, Fenzi GF, Baschieri L, editors. Symposium on autoimmune aspects of endocrine disorders. New York: Academic; 1980.
25. Husebye ES, Anderson MS, Kampe O. Autoimmune polyendocrine syndromes. NEJM.2018;378:1132–41.
26. Polyendocrine Disorders and Endocrine Neoplastic Syndromes. Acta Endocrinol (Buchar). 2021 Jan-Mar;17(1):147–8.
27. Jankowska K, Dudek P, Stasiek M, Suchta K. Autoimmune polyendocrine syndromes associated with autoimmune rheumatic diseases. Reumatologia. 2023;61(4):225-238
28. Anaya JM. The autoimmune tautology. Arthritis Res Ther. 2010;12(6):147. doi: 10.1186/ar3175. Epub 2010
29. Anaya JM, Castiblanco J, Rojas-Villarraga A, Pineda-Tamayo R, Levy RA, Gómez-Puerta J, Dias C, Mantilla RD, Gallo JE, Cervera R, Shoenfeld Y, Arcos-Burgos M. The multiple autoimmune syndromes. A clue for the autoimmune tautology. Clin Rev Allergy Immunol. 2012 Dec;43(3):256-64.
30. Gupta S, Aggarwal S, Chopra D. The kaleidoscope of autoimmunity: A report of 10 cases of multiple autoimmune syndrome. J Med Res Innov. 2023;6(1):22-3.

Peer-Review History:
The peer review history for this paper can be accessed here: https://ewmch.com/review/