CASE REPORT

Multiple Autoimmune Syndrome (Graves' Disease, Autoimmune Hepatitis, SLE) in Young Male with ASD Secundum: A Rare Case

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ABSTRACT

Multiple autoimmune syndrome (MAS) is characterized by the presence of at least three autoimmune diseases, presenting complex clinical challenges due to overlapping conditions and varied manifestations. Multiple autoimmune syndrome is rarely reported in men, particularly with the combination of Graves' disease, systemic lupus erythematosus (SLE), and autoimmune hepatitis (AIH). We report a case of a 22-year-old male who presented with symptoms of jaundice, significant weight loss, and classic signs of hyperthyroidism, including palpitations and tremors. Physical examination revealed jaundice, exophthalmos, and an enlarged thyroid gland, and he was diagnosed with Graves' disease, SLE, and AIH. Additional findings included stasis dermatitis and an atrial septal defect (ASD) with a moderate risk of pulmonary hypertension. The patient received thiamazole, propranolol, and corticosteroids, leading to clinical stabilization and symptom resolution. This rare MAS case with concurrent Graves' disease, SLE, and AIH highlights the need for accurate diagnosis and individualized management. The immunological interplay among these diseases contributes to diverse clinical manifestations, requiring a multidisciplinary approach. Our patient's management strategy effectively controlled hyperthyroidism, mitigated hepatic inflammation, and stabilized cardiac function, illustrating the effectiveness of comprehensive therapy. In young patients presenting with multiple autoimmune symptoms, MAS should be considered, especially with unusual combinations. Early detection and tailored treatment approaches, along with interdisciplinary collaboration, are essential to manage MAS and its associated complications.

Keywords: Multiple autoimmune syndromes, Graves' disease, *autoimmune hepatitis*, SLE, *atrial septal defect secundum*

INTRODUCTION

Autoimmune diseases (AIDs) have an estimated global prevalence ranging from 3% to 9.4%. In most cases, AIDs manifests as a single disease (mono autoimmunity). However, clinical observations suggest that some patients may develop additional autoimmune conditions over time or simultaneously experience multiple AIDs, a phenomenon known as polyautoimmunity. The global prevalence of polyautoimmunity is estimated at 0.5%, meaning that approximately 4.4% of individuals with autoimmune diseases are affected by more than one AID.[1]

Multiple autoimmune syndrome (MAS), characterized by the presence of at least three distinct autoimmune conditions and creating complex clinical manifestations, is a rare condition. MAS diagnosis and therapy are challenging due to the overlapping conditions and diverse manifestations. Diagnosing MAS needs a physician's accuracy and depends on the age when the first autoimmune disease appears.[2] Based on the frequency of their association, MAS is categorized into three types.[3] This classification helps in predicting the likelihood of additional autoimmune diseases in patients already diagnosed with two AIDs, offering insights into the underlying pathophysiology of autoimmune disorders.[4]

1. Type I: Myasthenia Gravis, Thymoma, Polymyositis, and Giant Cell Myocarditis;
2. Type II: Sjögren's Syndrome, Rheumatoid Arthritis, Primary Biliary Cirrhosis, Scleroderma, and Autoimmune Thyroid Disease (AITD);
3. Type III: Autoimmune Thyroid Disease, Myasthenia Gravis and/or Thymoma, Sjögren's Syndrome, Pernicious Anemia, Idiopathic Thrombocytopenic Purpura, Addison's Disease, Type 1 Diabetes Mellitus, Vitiligo, Autoimmune Hemolytic Anemia, Systemic Lupus Erythematosus, and Dermatitis Herpetiformis.[3]

This paper aims to describe a rare case with an unusual combination of MAS (Graves' disease, systemic autoimmune disease (SLE), and autoimun hepatitis (AIH)) in a male patient. This case involves a 22-year-old male diagnosed with Graves' disease. Epidemiological data show it occurs more frequently in women than men.[5-7] Studies indicate a 3% risk in women and a 0.5% risk in men, with a peak onset age between 20 and 50.[5,6]

CASE ILLUSTRATION

A 22-year-old man presented with jaundice and notable weight loss over the past month. He reported yellow discoloration of his body starting with his nails and eyes, eventually spreading to his entire body, worsening over the past week. He also noted bloating and early satiety over the last month, along with a 10-20 kg weight loss within the past three months. Additional complaints included epigastric pain, palpitations for the past month, excessive sweating, cold intolerance, and frequent hand tremors. He felt easily fatigued and experienced shortness of breath with activity. He reported dark patches on both lower legs for the last seven months. There was no history of alcohol use, nor any family history of autoimmune, liver, or cardiac disease.

On admission, the patient was alert with vital signs showing blood pressure of 108/91 mmHg, heart rate of 92 beats per minute, respiratory rate of 20 breaths per minute, temperature of 36.8°C, SpO2 of 100% on room air, and a Visual Analog Scale (VAS) pain score of 2 in the abdominal region. His body mass index was 23.0 kg/m^2 (normal weight). The Framingham score included two major and one minor criterion, and Wayne index scored 22, indicating hyperthyroidism. Examination revealed jaundice, exophthalmos, scleral icterus, and a palpable, smooth, mobile thyroid nodule (1 cm^3) in the right thyroid lobe without tenderness. Cardiac examination revealed an increased caudolateral impulse, a fixed split second heart sound, and a grade 2 tricuspid murmur. Abdominal examination indicated tenderness in the epigastrium and right hypochondrium. Extremities showed dark lesions on both lower legs and a bilateral hand tremor.

Laboratory results included elevated total bilirubin (13.51 mg/dL), direct bilirubin (2.5

mg/dL), indirect bilirubin (0.3 mg/dL), gamma-glutamyl transferase (GGT, 59 U/L), alkaline phosphatase (ALP, 185 U/L), and free thyroxine (FT4 93.04 pmol/L), supporting the diagnosis of jaundice. ANA immunofluorescence testing was positive for both dsDNA and DFS70 antibodies, with an ANA titer of 1:100. Complete blood count, aspartate aminotransferase (AST), and renal function were normal. Tests for viral hepatitis and antimitochondrial antibody (AMA) M2 were negative.

The patient exhibited thrombocytopenia with a platelet count of 80 $\times 10^3/\mu L$, a common hematologic manifestation of SLE, which may be attributed to immune-mediated destruction or bone marrow suppression. Additionally, an elevated INR (2.36) raised concerns about potential coagulopathy, which could be secondary to AIH-related liver dysfunction or lupus-associated antiphospholipid syndrome.

Imaging included chest x-ray showing cardiomegaly with pulmonary edema, abdominal ultrasound revealing ascites, cystitis, and bilateral pleural effusion. MRCP indicated iron overload (R2* values 50.1-132.9 s^{-1}) and grade 1 hepatic steatosis. Thyroid ultrasound revealed bilaterally increased echogenicity and a right-sided thyroid nodule with prominent vascularization, suggesting thyroiditis or Graves' disease.

Electrocardiogram revealed sinus tachycardia with a heart rate of 115 beats per minute, normal axis, transition zone at V3, and complete right bundle branch block (RBBB). Echocardiography showed an atrial septal defect (ASD) with an intermediate risk of pulmonary hypertension (PH). NT-proBNP level was elevated at 1003 pg/mL (normal <49.00 pg/mL).

Histopathological examination of the liver biopsy showed polygonal hepatocytes, inflammatory cell infiltration, erythrocytes, and eosinophils (7 cells/40 high-power fields), with no malignant cells detected, consistent with autoimmune hepatitis. Skin biopsy from the foot revealed hyperkeratosis, mild spongiosis in the epidermis, and dermal fibrosis with hyalinization, confirming stasis dermatitis.

The patient was diagnosed with Graves' disease, systemic lupus erythematosus (SLE), and AIH. Treatment was initiated with thiamazole (20mg-0-20mg), propranolol (20 mg three times daily), methylprednisolone (31.25 mg every 12 hours), and vitamin D3 (5000 IU daily). Conservative management included compression therapy and topical steroids to manage stasis dermatitis. Five days after admission, the patient showed significant improvement; laboratory results revealed normalized bilirubin and thyroid function, prompting a tapering of steroids. ASD closure was scheduled to prevent potential right ventricular volume overload. At a follow-up 28 days post-discharge, the patient continued to show clinical stability and no signs of autoimmune or hepatic complications. Physical examination revealed no jaundice or recurrence of palpitations. Laboratory values remained within normal ranges, and thyroid function was stable. A multidisciplinary approach involving cardiology, dermatology, and endocrinology ensured continued monitoring of potential new autoimmune manifestations. The ASD closure plan remained in place, considering the ongoing pulmonary hypertension risk.

Table 1. Laboratory Results on the 1st Day of Admission

Parameter	Result	Unit	Normal Value
Hematology			
Hemoglobin	11.1	g/dL	13,5 - 17,5
Hematocrit	30	%	33 - 45
Leucocyte	6.3	$10^3/\mu L$	4,5 - 11,0
Platelets	80	$10^3/\mu L$	150 - 400
Erythrocyte	3.59	$10^6/\mu L$	4,5 - 5,9
MCV	83.7	fL	70 - 96

Parameter	Result	Unit	Normal Value
MCH	30.9	pg	28,0 - 33,0
MCHC	36.9	g/dL	33,0 - 36,0
Eosinophil	1.70	%	2-4
Basophil	0.60	%	0,0- 2,0
Neutrophil	52.60	%	55,0-80,0
Lymphocyte	35.70	%	22,0-44,0
Monosite	9.40	%	0,0-7,0
PT	30.3	seconds	10-15
APTT	39.8	seconds	20-40
INR	2.360	seconds	
Chemistry			
SGOT	55	u/l	<35
SGPT	40	u/l	<45
Albumin	2.5	g/dl	3.5-5.2
Creatinin	0.3	mg/dL	0,6 - 1,2
Ureum	23	mg/dl	>50
Blood Natrium	133	mmol/l	136-145
Blood Potassium	3.7	mmol/l	3.3-5.1
Blood Chloride	109	mmol/l	98-106

Table 2. Monitoring of Total Bilirubin, TSH, and FT4

Laboratory Examination	Results (2024)						Reference	Unit
	24 Apr	29 Apr	17 May	24 May	31 May	24 July		
Total Bilirubin	13,51	15,83	12,54	4,22	2,11	1,25	0.00-1.00	mg/dl
TSH	0,01			0,01		0,07	0.40-4.20	ulU/ml
FT4	93,04		77,22		24,57	14,68	10.30-34.70	pmol/l

Tabel 3. Simplified AIH Criteria.[30]

Variable	Score
ANA or SMA/F-actin	
≥1:40	+1
≥1:80 or	+2
LKM ≥ 1:40 or	+2
SLA (+)	+2
IgG serum	
> Upper normal limit	+1
>1.1 × Upper normal limit	+2
Histological findings	
Compatible AIH	+1
Typical AIH	+2
Negative viral hepatitis markers	+2

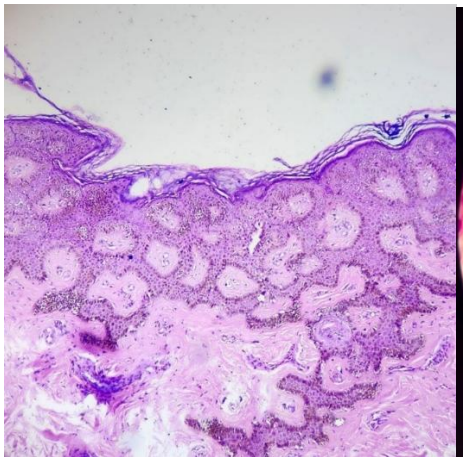

Figure 1. Skin Biopsy Showed Epidermal Hyperkeratosis and Dermal Hyalinizing Fibrosis

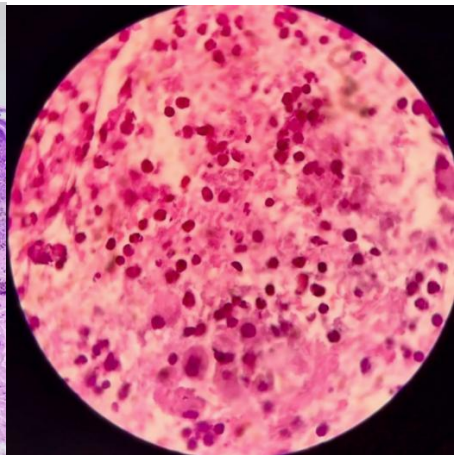

Figure 2. Liver Biopsy Showed Hepatocyte Rosette, Emperipolesis, and Plasma Infiltration

Referee: 2405170111 SLO Test: Ana Profile3 plus DFS70
Results from: 20/05/2024 Strip Number: 287-68

Antigen	Class	o	(+)	+	++	+++
RNP/Sm (RNP/Sm)	o					
Sm (Sm)	o					
SS-A native (60 kDa) (SSA)	o					
Ro-52 recombinant (52)	o					
SS-B (SSB)	o					
Scl-70 (Scl)	o					
PM-Scl100 (PM100)	o					
Jo-1 (Jo)	o					
Centromere B (CB)	o					
PCNA (PCNA)	o					
dsDNA (DNA)	(+)					
Nucleosomes (NUC)	o					
Histones (HI)	o					
Ribosomal Protein (RIB)	o					
AMA-M2 (M2)	o					
DFS70 (DFS70)	+					
Control (Ko)	+++					
Label (ET)						

Figure 3. ANA Profile Results

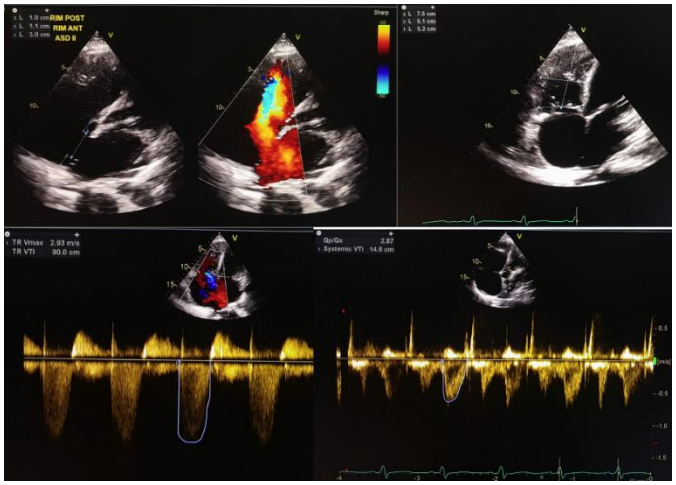

Figure 4. Echocardiography (ASD II L To R shunt, LV Concentric Remodeling with good LV Contractility EF 65 % (Simpson 62 %), Grade I Diastolik Dysfunction, TR dan MR Moderate dan PR Mild, Intermediate Probability of PH)

Figure 5. Clinical Presentation on the 1st Day of Admission

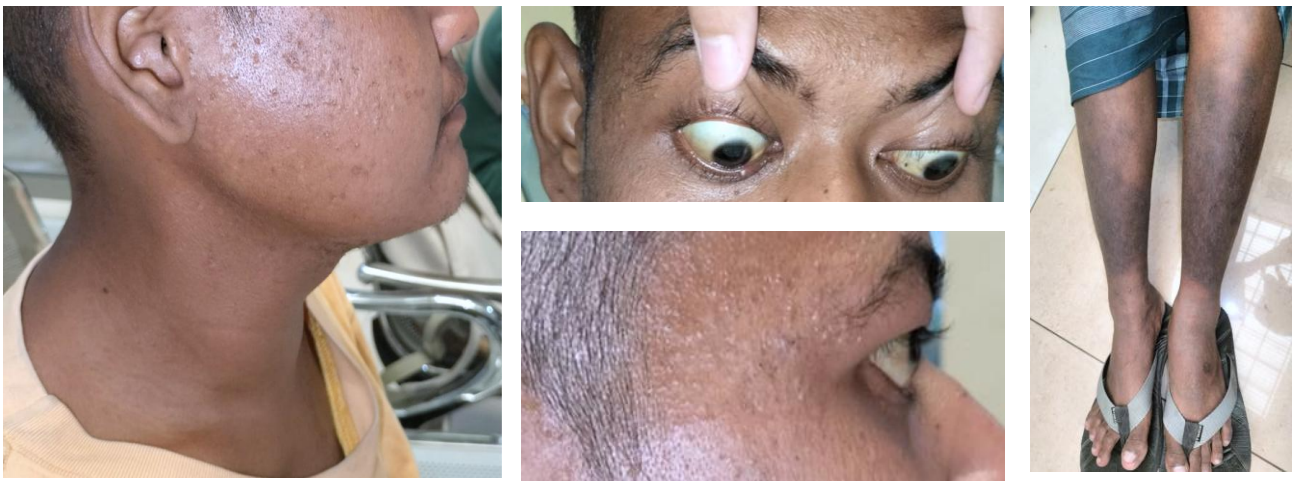

Figure 6. Follow-Up 28 Days After Hospital Discharge

DISCUSSION

This case presented symptoms of autoimmune thyroid disease (Graves' disease), SLE, and AIH, which is classified as an unusual combination of MAS with additional skin involvement to form stasis dermatitis. MAS refers to the coexistence of three or more autoimmune disorders in a patient, classified into types based on the associated diseases. [8] This patient's condition falls into MAS type III, which includes autoimmune thyroid diseases, SLE, and other autoimmune diseases, a group first described by Humbert and Dupond (1988),[3] such as those in this case, share common immunologic and genetic mechanisms that involve the breakdown of immune tolerance, leading the body to attack its tissues. This phenomenon is often termed "autoimmune tautology," describing how these diseases, despite distinct clinical manifestations, may share underlying mechanisms, often presenting in what is called a "kaleidoscope of autoimmunity". Studies show that approximately 25% of patients with one autoimmune disease may develop another, underscoring the importance of monitoring for emerging autoimmune manifestations.[8]

Graves' disease is a disorder with systemic manifestations primarily affecting the heart, skeletal muscles, eyes, skin, bones, and liver. Failure to diagnose Graves' disease promptly can predispose to thyroid storm, leading to high morbidity and mortality in patients. The symptoms of our patient included a 10-20 kg weight loss over the past three months, palpitations for one month even at rest, profuse sweating daily, preference for cold

environments, fatigue during activities, tremors, and consistently sweaty palms. These complaints are classic signs and symptoms of hyperthyroidism.[6,9,10] Physical examination revealed right thyroid enlargement and exophthalmos, known as Graves ophthalmopathy.[11] Thyroid ultrasound can assist in diagnosis, particularly when nodules are detected, as it is susceptible in identifying lesion/nodule size and differentiating solid from simple or complex cystic lesions.[12]

In suspected thyrotoxicosis, additional testing is needed to confirm diagnosis, assess severity, and guide therapy. Investigations include TSH, FT4, T3, and FT3; thyroid isotope uptake; thyroid isotope scanning; thyroid ultrasound; and antithyroid antibodies.[10,13,14] Thyroid function tests in our case indicated hyperthyroid (TSH <0.05 IU/ml; Free T4 93.04). Positive results on TSH-Receptor-Thyrotropin receptor antibody (TRAb) testing strongly support Graves' disease. TRAb testing in our case showed positivity (>40 IU/L), with ANA immunofluorescence positive results for dsDNA and DFS70, while 14 other panels were negative.[12]

The presence of DFS70 antibodies in the ANA profile is noteworthy. Their presence in isolation, without other disease-specific autoantibodies, tends to suggest a lower likelihood of SLE.[15] However, in this case, the co-occurrence of anti-dsDNA positivity alongside thrombocytopenia and systemic symptoms strongly supported an SLE diagnosis, minimizing the potential confounding effect of DFS70 positivity. The clinical relevance of anti-DFS70 antibodies remains a subject of debate.[16] While some studies, such as Mahler et al. (2012), have found no significant differences in clinical or laboratory findings between SLE patients with and without anti-DFS70,[17] other studies, including Dai et al. (2022), suggest an association between anti-DFS70 positivity and a higher frequency of anti-dsDNA antibodies. Additionally, a correlation between anti-DFS70 and anti-dsDNA titers has been reported. This suggests that while DFS70 antibodies alone may not be indicative of SLE, their coexistence with disease-specific autoantibodies, as observed in this patient, warrants careful consideration.[16]

The treatment options for Graves' disease are (1) Iodine-131 therapy; (2) hormone synthesis blockade by antithyroid drugs; and (3) thyroid surgery.[7,10,18] Our patient received thiamazole as an antithyroid drug.[19] Antithyroid drug therapy allows on avoid damage to the thyroid (and parathyroid or nerve), as well as radiation exposure and surgery. The disadvantages of this antithyroid treatment are the need for commitment to comply with the treatment for months or years, increased doctor visits for control, possible side effects of the drugs, and most importantly, a very low rate of permanent remission.[18]

Our case patient received beta-blocker therapy in the form of propranolol and carvedilol. Beta-blockers should be given to most hyperthyroid patients who do not have contraindications to their use. Beta-blockers are relatively or, depending on the severity of the disease, absolutely contraindicated in patients with asthma or chronic obstructive pulmonary disease, severe peripheral vascular disease, Raynaud's phenomenon, bradycardia, second- or third-degree heart block, and diabetics who are susceptible to hypoglycemia. If there are no contraindications, beta blockers can be given immediately after the diagnosis of hyperthyroidism is established, even before a definite diagnosis of the etiology of thyrotoxicosis is obtained. Propranolol is a non-selective beta-1 and beta-2 blocker used in hyperthyroidism and thyroid storms because of its effect on blocking the peripheral conversion of inactive T4 to the active form T3.[20]

Beta blockers can also be useful in controlling heart rate in ASD II Left to Right shunt conditions suffered by patients. Previously, the patient denied a history of heart disease. This may be because ASD is the most common congenital heart disease diagnosed in adulthood, accounting for 25-30% of diagnoses. ASD shows a direct connection between the atrial chambers, allowing blood flow between the systemic and pulmonary circulations. A unique feature of ASD is its slow clinical

progression with most children and young adults being asymptomatic, causing a delay in diagnosis.[21]

Patients with ASDs <5 mm often experience spontaneous closure of the defect within the first year of life. Defects >1 cm are more likely to require medical/surgical intervention to close the defect. Other indications for therapy include stroke, significant hemodynamic shunting greater than 1.5:1, and evidence of systemic oxygen desaturation.[22] If the ASD requires closure, options include percutaneous transcatheter and surgical intervention.[21] According to the European Society of Cardiology guidelines, the best treatment outcomes are with ASD repair at age <25 years.[23] When the ASD is closed percutaneously, patients require antiplatelet therapy for the next 6 months.[22]

Transcatheter closure of ASD (tcASD) in patients with pulmonary arterial hypertension (PAH) has been shown to improve PAH severity, enhance cardiac functional capacity, and reduce atrial arrhythmias. However, some patients may experience residual PAH (rPAH) or worsening PAH following ASD closure.[24] Askeer *et al.* (2020) reported a decline in the prevalence of combined PH from 44% at baseline to 18% post-closure, with a follow-up duration ranging from 15 to 60 months.[25] Chronic left-to-right shunting contributes to pulmonary vascular remodeling and increased pulmonary artery pressure, which may persist even after ASD closure. Risk factors for rPAH post-procedure include advanced age and high pulmonary vascular resistance (PVR). Long-term management should emphasize lifelong monitoring for emerging autoimmune conditions and cardiac complications, including pulmonary hypertension, given the risk of persistent pulmonary vascular changes even after ASD closure.[24]

Jaundice (hyperbilirubinemia) serves as an indicator of liver disease.[26] Jaundice in Graves' disease is rare and multifactorial.[7,27] Direct and indirect mechanisms contribute to liver dysfunction in hyperthyroidism, including hepatotoxicity from hormone exposure, hepatocyte anoxia, free radical damage, accelerated decomposition of glycogen, autoimmune, congestive hepatopathy, underlying liver disease, and antithyroid drug-induced hepatotoxicity.[27] The patient's test results (HBsAg non-reactive, anti-HCV non-reactive, anti-HBc total negative) excluded viral hepatitis etiology. Magnetic resonance imaging (MRI) of the whole abdomen with contrast showed hepatomegaly with hyperhidrosis and grade 1 hepatic steatosis, which is useful for identifying iron overload, especially in the liver. Iron overload, though mild, may be associated with chronic liver disease and metabolic syndrome.[28]

Since this patient had no history of antithyroid drug use a liver biopsy was necessary to confirm the diagnosis, which was consistent with AIH. The liver biopsy result was consistent with AIH. AIH is a chronic, immune-mediated liver disease with complex etiology rooted in genetic susceptibility and environmental triggers, such as viral infections and microbiome alterations along the gut-liver axis. These factors contribute to an immune dysregulation that underpins the inflammation of hepatic tissue, evidenced by circulating autoantibodies, elevated IgG, and characteristic histological findings like interface hepatitis and plasma cell infiltration. Untreated AIH carries a significant mortality risk, underscoring the need for prompt intervention, even in asymptomatic cases, to reduce morbidity and mortality.[29] The diagnostic process for AIH is nuanced due to its broad spectrum of clinical manifestations and serological markers. Patients often present with unexplained elevated serum aminotransferase levels, yet about 25-34% are asymptomatic, complicating early diagnosis. Notably, untreated asymptomatic individuals have a markedly lower 10-year survival rate than those who receive timely therapy (67% vs. 90%).[30]

In addition to liver enzymes, diagnosis is further refined through autoimmune markers like *antinuclear antibodies* (ANA), *smooth muscle antibodies* (SMA), *liver/kidney microsomal antibody type 1* (anti-LKM1), and the simplified AIH scoring system, which integrates these

findings with histology to confirm the diagnosis and exclude other liver pathologies. Histology remains indispensable, revealing interface hepatitis, periportal necrosis, and other distinctive changes. Non-invasive imaging modalities, such as elastography and MRI, are valuable for staging fibrosis and assessing inflammatory activity without the need for repeated biopsies. The simplified scoring system requires four variables, namely autoimmune antibodies, hyper-gammaglobulinemia, histology, and exclusion of viral hepatitis. Definite AIH is defined as ≥7 points, and probable AIH is defined as ≥6 points. Although these systems are helpful in excluding AIH in patients with other conditions, they are less sensitive in identifying atypical cases.[29,30]

Management goals in AIH include achieving remission, reversing fibrosis, and preventing disease progression. Induction therapy typically begins with corticosteroids, with prednisolone as the preferred agent due to its potent anti-inflammatory effects, achieving biochemical response within a week in most cases. This rapid response contrasts with alternatives like budesonide, which show slower efficacy, reinforcing prednisolone's utility as a first-line therapy. The common initial dose of prednisolone is 0.5 mg/kgBW. Once remission is reached, azathioprine is introduced for maintenance, reducing the risk of steroid-induced adverse effects. The recommended dose is 1-2 mg/kgBW. Dose adjustments are guided by patient tolerance and metabolite monitoring, especially in those with thiopurine methyltransferase (TPMT) deficiency, who are prone to azathioprine toxicity. In cases resistant to first-line therapy, options include mycophenolate mofetil, inhibitor calcineurin-inhibitor (cyclosporin, tacrolimus), mercaptopurine, and biologic agents (rituximab, infliximab) can be considered.[29,30]

For select patients, long-term therapy may be unnecessary if remission is maintained; approximately 10-20% can eventually discontinue immunosuppressive treatment under close medical supervision. Relapse remains a concern, making gradual tapering essential to sustain remission. Supplementary vitamin D is also beneficial, contributing to improved disease outcomes. AIH may progress to cirrhosis and liver failure, requiring liver transplantation in advanced cases. Though recurrence post-transplant occurs in a notable proportion (8-12% within the first year, 36-68% within five years), outcomes are generally favorable. Close monitoring and individualized treatment approaches are paramount in managing AIH to improve survival and quality of life.[29,30]

Diagnosing Systemic Lupus Erythematosus (SLE) requires clinical evaluation supported by standardized classification criteria, such as the American College of Rheumatology (ACR) 1997, Systemic Lupus International Collaborating Clinics (SLICC) 2012, or the European League Against Rheumatism (EULAR)/ACR 2019 criteria. Assessment of disease activity is critical in guiding treatment, with scoring tools like the SLEDAI and MEX-SLEDAI helping to quantify disease severity and guide therapy. Severe cases of SLE, indicated by SLEDAI scores over 12 or MEX-SLEDAI scores between 10 and 13, require comprehensive evaluations to rule out other potential causes, including infections, given their impact on both morbidity and treatment choices. Management of severe SLE typically involves immunosuppressive therapy, including intravenous methylprednisolone or oral prednisolone (≤1 mg/kg/day). Additionally, vitamin D supplementation has shown benefits in improving SLE-related outcomes.[31]

Our patient received methylprednisolone 31.25 mg every 12 hours. The methylprednisolone dosing was chosen to balance the need for effective immunosuppression in the context of AIH and SLE while mitigating the risks associated with high-dose corticosteroids, such as infection, hyperglycemia, and gastrointestinal bleeding.[32,33] Given the patient's elevated INR, corticosteroid therapy posed an increased risk of gastrointestinal bleeding, necessitating close monitoring and potential gastroprotective

measures such as proton pump inhibitors (PPIs) or H2 receptor antagonists.[34] To mitigate this, our patient received intravenous omeprazole (40 mg every 12 hours).

In cases of lower extremity lesions, differential diagnoses might include stasis dermatitis, scleroderma, and vasculitis. In this patient, a biopsy confirmed stasis dermatitis, a chronic inflammatory skin disease caused by chronic venous insufficiency (CVI) and frequently affecting the lower extremities of elderly patients. Stasis dermatitis develops when venous plexus dysfunction in the legs causes blood to reflux into the superficial venous system, resulting in venous hypertension, skin inflammation, and potential complications like venous ulcers.[35] The widely accepted CEAP classification system (Clinical, Etiologic, Anatomic, and Pathophysiologic) helps assess the severity of varicose vein-related issues, which often underlie stasis dermatitis.[36]

In this patient, the stasis dermatitis may be related to chronic venous insufficiency secondary to an atrial septal defect (ASD) II with a left-to-right shunt. Normally, systemic and pulmonary circulations handle equal blood volumes (Qp/Qs = 1). However, with a left-to-right shunt, "back-leak" blood flows from systemic to pulmonary circulation, resulting in a higher pulmonary flow (Qp/Qs >1). This pulmonary overload can lead to chronic venous insufficiency, contributing to stasis dermatitis development.[37]

Treatment for stasis dermatitis aims to manage the venous insufficiency, reduce edema, alleviate inflammation (itching and pain), and improve skin lesions or heal ulcers. Initial therapy includes lifestyle modifications, such as exercise, walking, and leg elevation, which are generally effective for mild cases. Compression therapy, a cornerstone of treatment, employs high-pressure wraps or stockings (approximately 60 mmHg) to reduce ambulatory venous pressure and mitigate venous hypertension.[35]

The diagnosis of MAS presents significant challenges due to the need for specialized tests that are not readily available in all hospitals. Although our hospital is a type a facility, certain diagnostic tests, such as TRAb and ANA Profile had to be sent to an external laboratory for confirmation. This highlights the financial and logistical barriers to timely diagnosis. Additionally, the patient, a self-employed person with a lower-middle income, faced economic constraints that made an extensive diagnostic workup difficult. Culturally, the patient also struggled with regular follow-ups due to work obligations and difficulty obtaining leave. Furthermore, he was an orphan, having lost both parents during the COVID-19 pandemic two years ago, which added to his socioeconomic burden and limited access to continuous care.

Initially, the patient believed that his symptoms were purely gastrointestinal in origin, as his primary complaint was jaundice, leading him to seek consultation with a gastroenterologist. He was unaware that he had underlying thyroid dysfunction and multiple autoimmune conditions until further investigations were conducted. After receiving treatment, the patient reported a significant improvement in his overall health and clinical condition. He also acknowledged the complexity of his illness and understood the necessity of long-term follow-up to achieve remission and prevent complications.

During hospitalization, the patient experienced a thyroid storm, a severe and life-threatening complication of Graves' disease. The diagnosis was confirmed using the Burch-Wartofsky score, which indicated a high probability of thyroid storm. The patient was promptly treated with PTU, Lugol's iodine solution, and intravenous methylprednisolone, leading to significant clinical improvement within five days.

The patient's overall prognosis depends on multiple factors, including the control of thyroid disease, autoimmune hepatitis, and SLE. The presence of an ASD further complicates long-term outcomes, as it increases the risk of pulmonary hypertension. While the intermediate probability of pulmonary hypertension was identified in this case, the patient's long-term prognosis will be influenced by the progression

of his autoimmune conditions and cardiovascular status. With adequate management and long-term follow-up, remission and prevention of complications are achievable.

This case demonstrated the complex interplay between multiple autoimmune disorders and congenital cardiac anomalies, providing valuable insight into the management of such rare presentations. However, a key limitation is that the patient should ideally undergo ASD closure to prevent long-term complications, but this procedure was postponed due to the need for stabilization of thyroid metabolism and autoimmune conditions. Additionally, despite medical recommendations, the patient expressed reluctance toward undergoing ASD closure due to fear of the procedure and challenges with regular follow-ups due to work constraints.

CONCLUSION

This case report highlights a rare presentation of MAS in a young male patient with an unusual combination of Graves' disease, SLE, and AIH. The complex, multisystemic manifestations necessitated a comprehensive approach. The patient's jaundice, stasis dermatitis, and cardiac anomaly (ASD) contributed additional challenges to the diagnosis and treatment. The management approach focused on targeted therapies for each autoimmune disorder. Thiamazole successfully controlled hyperthyroidism, while methylprednisolone was effective in reducing the autoimmune response associated with SLE and AIH. Propranolol provided symptomatic relief for hyperthyroid symptoms and mitigated cardiovascular risks associated with ASD. This case underscores the importance of early diagnosis and individualized, multidisciplinary treatment for MAS, as timely intervention can significantly improve outcomes. Continued follow-up is essential, as MAS patients may experience the emergence of new autoimmune manifestations or complications over time. This case report emphasizes the need for vigilance in managing MAS due to its complex nature, particularly in young male patients, where atypical presentations and rare autoimmune combinations may occur.

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