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First presentation of Graves' thyroid storm complicated by catastrophic antiphospholipid antibody syndrome: A case report

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Abstract

Catastrophic antiphospholipid antibody syndrome is a rare and severe subtype of antiphospholipid syndrome with multisystemic organ failure due to thromboembolic events, resulting in high mortality rates. The association between catastrophic antiphospholipid antibody syndrome and autoimmune thyroid diseases is rarely reported in the literature. We report a case of a 35-year-old previously healthy female with Graves' thyroid storm, positive lupus antibodies, and probable catastrophic antiphospholipid antibody syndrome. Her hospital course was complicated by extensive venous thromboembolism, superior vena cava syndrome, thromboembolic strokes, and Takotsubo cardiomyopathy. Eventually, this led to an unfortunate death secondary to profound shock after 8 days despite emergent treatment. Our case report discusses the link between autoimmune thyroid disorders and catastrophic antiphospholipid antibody syndrome. We emphasize the difficulty in diagnosing catastrophic antiphospholipid antibody syndrome in extremely ill patients and stress the significance of considering it as a possible cause in thyrotoxicosis patients with multiple organ failure and hypercoagulability. Early recognition and prompt management are crucial in improving outcomes in these patients.

Keywords

SLE, systemic lupus erythematosus, thyroid storm, thyrotoxicosis, graves' disease, antiphospholipid syndrome, catastrophic antiphospholipid syndrome, superior vena cava syndrome

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Introduction

Antiphospholipid syndrome (APS) is an autoimmune disease associated with arterial or venous thrombosis and/or pregnancy complications with persistently positive antiphospholipid antibodies (aPL). APS can be a primary diagnosis or part of an underlying systemic autoimmune disease.[1] Catastrophic antiphospholipid antibody syndrome (CAPS), an accelerated subtype of the disease with multisystemic organ failure, is considered to be a diagnostic challenge with a high mortality rate.[2] Thyrotoxicosis is known to cause hypercoagulability through multiple pathways.[3] The association between autoimmune thyroid disease and CAPS is rarely reported in the literature.[4] We report a case of Graves' thyroid storm with probable CAPS in a previously healthy patient with rapid progressive deterioration that led to unfortunate outcomes despite emergent management.

Case report

A previously healthy 35-year-old Filipino female presented to the emergency department with a 1-day history of palpitations associated with a 2-day history of abdominal pain, subjective fever, insomnia, and dizziness. She experienced a similar episode 15 days before the presentation, which resolved spontaneously. Additionally, she reported noticing a swelling in her neck that was gradually increasing in size and an unintentional weight loss of 6 kg over the past year.

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Her review of systems was negative for any joint pains, rashes, photosensitivity, eye symptoms, mouth or genital ulcers, Raynaud's and sicca symptoms. She had no history of previous miscarraiges or gestational morbidity. There was no family history of any autoimmune diseases. She denied any alcohol consumption or smoking history.

On presentation, the patient was febrile with a temperature of 38.3° Celsius, blood pressure of 134/99 mmHg, pulse rate of 152 beats/min, respiratory rate of 20 breaths/min, and oxygen saturation of 99% in room air. Physical examination revealed an anxious woman with a Glasgow Coma Scale score of 15,[5] a moderately diffusely enlarged, non-tender thyroid gland without ophthalmopathy. Neurological examination was remarkable for generalized hyperreflexia and proximal muscle weakness. Abdominal examination was unremarkable, with a soft, non-tender abdomen and no organomegaly. Cardiovascular examination revealed regular fast-pounding peripheral pulses.

Initial laboratory studies (Table 1) showed a thyroid panel in keeping with hyperthyroidism. Additionally, there was evidence of mild anemia, thrombocytopenia, and mild transaminitis. An electrocardiogram showed sinus tachycardia with diffuse T-wave inversion, and an initial echocardiogram was unremarkable.

She was admitted to the high-dependency unit as a case of thyroid storm with a Burch-Wartofsky Point Scale score of 60 (temperature 38.3° Celsius, 15 points, mild agitation, 10 points, pulse rate of 152 beats/min, 25 points, with a precipitating event, 10 points)[6] and was started on propranolol and carbimazole. A thyroid ultrasound showed bilaterally enlarged thyroid lobes with a mixed echoic nodule measuring $3.6 \times 2.6 \times 3.4$ cm with internal cystic degeneration and echogenic calcific foci in the right lobe (Thyroid Imaging Reporting and Data System TI-RADS 4), and an incidental finding of right internal jugular vein thrombosis.

Four days into admission, the patient developed tachypnoea with facial and right upper extremity swelling, and sustained a cardiac arrest. Return of spontaneous circulation was achieved within 5 min of resuscitation following the advanced cardiac life support protocol. She was intubated and transferred to the intensive care unit.

Further laboratory studies revealed a positive high titer antinuclear antibody, double-stranded DNA antibody (dsDNA), extractable nuclear antigens, anti-smith, and SMRNP antibodies with low complement levels. Thyroid antibodies were in keeping with Graves' disease with a high TSH receptor antibodies (TRAb) of 206.5 IU/L and TPO antibodies of 206.5 KIU/L. A thrombophilia screen showed a positive lupus anticoagulant (LA) but negative anticardiolipin and B-2 glycoprotein (Table 1). Human immunodeficiency virus and hepatitis screen were negative. All cultures were negative. There were no signs of hemolysis with a normal Lactate dehydrogenase (LDH), haptoglobin, bilirubin, and no schistocytes on the blood film. Initial coagulation panel was within normal limits.

Table 1. Laboratory test results on admission.

Variable	Reference range	Result
Hemoglobin (g/dl)	11.6–14.8	10.6
White blood cell count (per μl)	4.5–11.0	9.1×10^9/L
Neutrophils (%)	0.0–2.5	69.4
Lymphocytes (%)	16.5–49.5	20.1
Monocytes (%)	2.0–10.0	10.3
Eosinophil (%)	0.0–8.5	0.10
Platelet count (per μl)	140,000–400,000	28,000
AST (IU/L)	<32	48
ALT (IU/L)	<33	19
Albumin (g/L)	25–52	14
Sodium (mmol/L)	135–145	129
Potassium (mmol/L)	3.6–4.8	4.5
Chloride (mmol/L)	101–108	95
Creatinine (micromol/L)	61–106	34
Urea nitrogen (mmol/L)	2.80–8.10	4
C-reactive protein (mg/dl)	<5	7.27
Procalcitonin (ng/ml)	<0.50	4.62
pH VBG	7.35–7.45	7.40
pCO2 VBG (mmHg)	35.0–45.0	40.4
pO2 VBG (mmHg)	25.0–40.0	24.8
HCO3 VBG (mmol/L)	22–26	25
Lactic acid VBG (mmol/L)	0.5–2.2	2.8
TSH (milli IU/L)	0.270–4.200	0.005
Free T3 (pmol/L)	3.10–6.80	10.40
Free T4 (pmol/L)	12.0–22.0	59.8
TRAb (IU/L)	<1.75	14.90
Anti-TPO	<28 KIU/L	206.5
ANA	<1:80	1:1280
DsDNA	<26.9 IU/mL	423
ENA	<20 CU	429.4 CU
Anti-smith	Negative	Positive
Anti-SMRNP	Negative	Positive
C3	0.9–1.8 g/L	0.27
C4	0.1–0.4 g/L	0.02
Lupus anticoagulant (LA)	Negative	Positive
B-2 glycoprotein IgM	<20 CU	1.1
B-2 glycoprotein IgG	<20 CU	13.1
Anticardiolipin IgM	<20 CU	2.1
Anticardiolipin IgG	<20 CU	6.7

ANA: Antinuclear antibody; AST: Aspartate aminotransferase; ALT: Alanine transaminase; dsDNA: Double-stranded DNA Antibody; ENA: Extractable nuclear antigens; VBG: Venous Blood Gas; TRAb: TSH receptor antibodies; TSH: Thyroid Stimulating Hormone; Anti-TPO: Anti-Thyroid Peroxidase; Anti-SMRNP: Anti-Smith and Anti Ribonucleoprotein.

A neck/chest/abdomen/pelvis computed tomography with contrast revealed a large thrombus in proximal superior vena cava (SVC) suggestive of SVC syndrome (Figure 1(a)), along with extensive occlusive thrombosis involving the right internal jugular vein (Figure 1(b)), subclavian vein, right brachiocephalic vein. Also, there was evidence of bilateral pleural effusions (Figure 1(c)) and external compression from a large necrotic right thyroid nodule (Figure 1(d)).

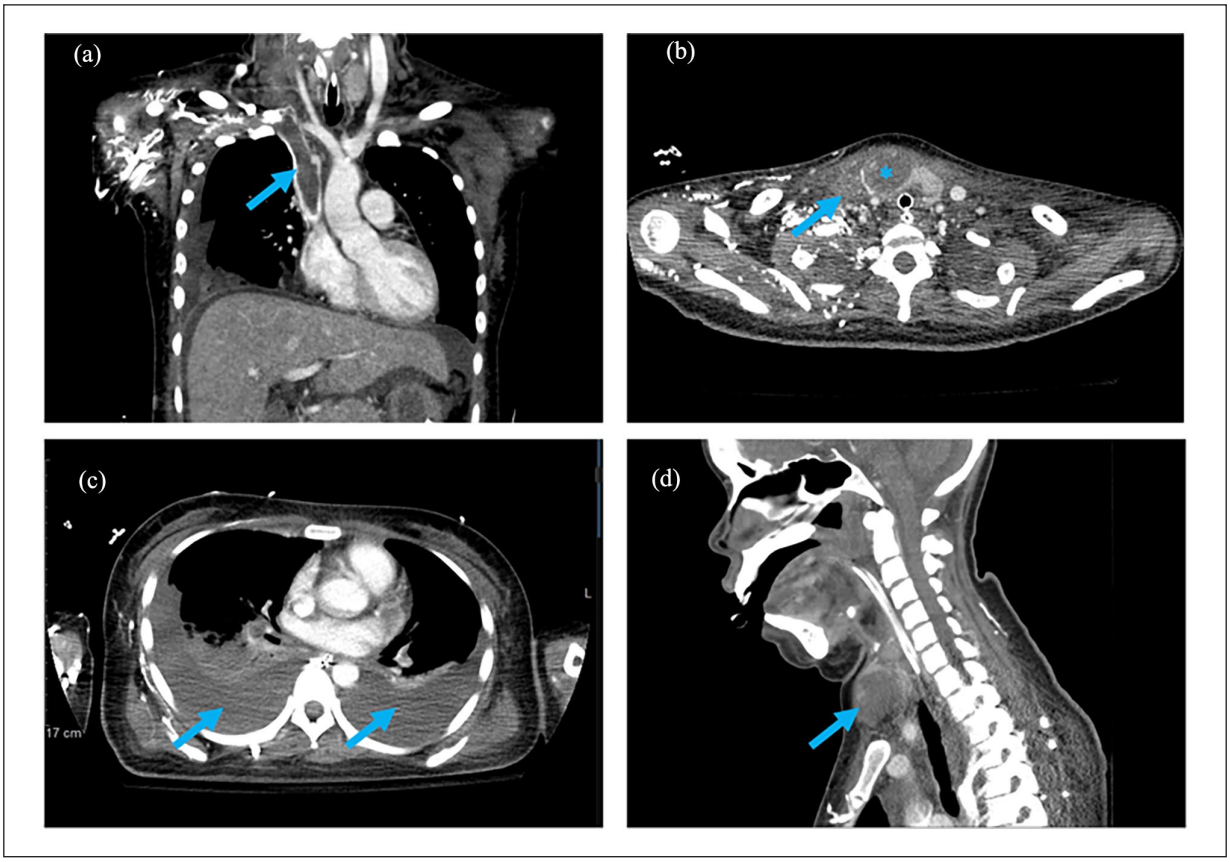

Figure 1. Neck/chest/abdomen/pelvis computed tomography with contrast. Coronal section of neck and chest showing a large thrombus in proximal Superior vena cava (SVC) suggestive of SVC syndrome (arrow) (a). Transverse section of neck showing extensive occlusive thrombosis involving the right internal jugular (arrow) with compression from a large necrotic right thyroid nodule (*, asterisk) (b). Transverse section of chest showing bilateral pleural effusions (arrow) (c). Sagittal section of neck showing a large necrotic right thyroid nodule (arrow) (d).

Furthermore, it showed bilateral pulmonary emboli without signs of ventricular strain, occlusive thrombus in the distal left common iliac vein extending to the external iliac vein and left common femoral vein, and nonocclusive thrombus involving the proximal right common iliac vein were seen.

The SVC obstruction in our patient was a Grade 1 Category Mild with head & neck edema according to "A Proposed Classification System and Algorithm for Management" published in 2008.[7] Given the extensive thrombosis and positive antibodies, she was treated as probable CAPS with intravenous steroids and intravenous immunoglobulins (IVIG) with a dose of 400 mg/kg daily for 5 days. Anticoagulation was not initiated due to the risk of bleeding with the profound thrombocytopenia. There was no improvement in the platelet count after treatment with steroids and IVIG.

Repeated echocardiogram showed significant changes with apical wall motion abnormality, reduced left ventricular ejection fraction to 30%–35%, and apical ballooning suggestive of Takotsubo cardiomyopathy (TC).

Due to multiple episodes of possible seizure activity, a magnetic resonance imaging of the brain was done. It showed multiple acute embolic infarcts at the bilateral centrum semiovale, body of the right caudate nucleus, bilateral high parietal lobes, and right cerebellum. Electroencephalogram showed moderate to severe diffuse encephalopathy with no epileptic waves.

Seven days later, she was extubated but remained deconditioned with flaccid quadriparesis, requiring reintubation within 24 h due to hemodynamic instability and multiorgan failure. She developed severe lactic acidosis, which was most likely from abdominal ischemia manifested by melena secondary to ongoing coagulopathy and embolic events. The patient unfortunately developed profound shock and sustained a cardiac arrest. Despite resuscitation, Return of spontaneous circulation (ROSC) was not achieved, and she was declared dead.

Discussion

APS is a systemic autoimmune disease characterized by arterial or venous, micro- or macro-vascular thrombosis, pregnancy morbidity, or nonthrombotic manifestations.[8] According to 2023 ACR/EULAR APS classification criteria, our patient fulfills the entry criteria (positive LA within the

clinical criterion period), clinical criteria (macrovascular arterial/venous thromboembolism, hematological abnormalities with thrombocytopenia), and laboratory criteria (positive LA).[8]

CAPS is a rare form of APS occurring in less than 1% of APS patients, with an incidence of 5 per million in the general population.[9] It is characterized by diffuse, micro, and macrovascular thrombosis affecting multiple organs. Around 50% of the patients diagnosed with APS experience CAPS as their first symptom. Diagnosis is based on clinical judgment with the guidance of the classification proposed by the International Congress on aPL.[2] Our patient falls under the criteria of probable CAPS with rapid involvement of multiple organs over less than 1 week with the presence of LA. Due to the patient's unfortunate outcome, there was no histologic confirmation of small vessel occlusion or repeat aPL antibodies after 12 weeks.[10]

CAPS results in multiorgan failure, with the most common organs involved being kidneys in 74%, brain in 56%, lungs in 55%, and heart in 53%, respectively.[11] It is usually related to a precipitating factor, most frequently infections in 29%, followed by surgeries in 9%, malignancies in 9%, and less often systemic lupus erythematosus)SLE(flares in 2%.[11] CAPS carries a reported mortality rate of 36%.[11] Recommended treatment includes anticoagulation, glucocorticoids, plasma exchange, and/or IVIG. Some emerging therapies, such as rituximab or eculizumab, can be used in refractory cases, although only a few cases have been reported.[11] Our patient had positive anti-dsDNA and anti-SM antibodies and low complement levels, suggesting a probable underlying diagnosis of SLE.

Interestingly, our patient had an additional diagnosis of Graves' thyrotoxicosis. Autoimmunity is one of the several pathogenic mechanisms involved in thyroid dysfunction in SLE. Anti-thyroglobulin and anti-TPO antibodies have been found more often in patients with lupus, ranging from 14% to 68%.[12] However, the association between SLE and Graves' disease has been less often identified, ranging from 0% to 8.9%, with no increased risk in the general population.[13]

Additionally, hyperthyroidism has been implicated as a procoagulant state through multiple mechanisms, including elevated Factor VIII, Factor IX, von Willebrand factor, and fibrinogen levels and lower plasma levels of plasminogen and tissue plasminogen activator and endothelial dysfunction leading to reduced fibrinolytic activity.[2] Few studies have reported the presence of aPL antibodies in autoimmune thyroid diseases and vice versa; however, their clinical association remains limited.[3] Our patient had a thyroid storm and catastrophic APL, suggesting a potential correlation between both presentations.

TC is a reversible type of cardiomyopathy commonly associated with physical or emotional stress.[14] Secondary TC results from a pre-existing medical condition, illness, or surgery that triggers a rise in catecholamines, unlike primary TC where patients present with cardiac symptoms and the cause is usually emotional stress.[15] Thyrotoxicosis has been identified as an infrequent cause of stress-induced cardiomyopathy, with less than 15 cases reported in the literature.[16] The adrenergic and thyroid axes are interrelated; thus, the high levels of thyroid hormones cause an exaggerated inotropic and chronotropic response to catecholamines.[17] In our patient, the initial echocardiogram was unremarkable; however, after persistent thyrotoxicosis and new events of thromboembolism, the patient developed features of TC with apical ballooning on repeat study. Unfortunately, further investigations to confirm the diagnosis of TC such as coronary angiography were not done due to the patient's clinical condition.

Conclusion

This case report highlights the association between autoimmune thyroid disease and CAPS, rarely reported in the literature. The patient presented with Graves' thyroid storm and probable CAPS, which led to unfortunate outcomes despite emergent management. The case emphasizes the importance of considering CAPS in patients with autoimmune thyroid disease who present with multisystemic organ failure and extensive thrombosis. Early recognition and prompt management are crucial in improving outcomes in these patients.

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Author contributions

A.A. contributed to Case presentation, consent, discussion, literature review; N.A. contributed to Discussion, conclusion, literature review, data editing; T.H. contributed to General supervision, literature review, data editing.

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Informed consent

Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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