Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.4123-19
Intern Med 59: 1457-1460, 2020
http://internmed.jp

【 CASE REPORT 】

Sudden Cardiac Arrest as the First Manifestation in a Patient with Catastrophic Antiphospholipid Syndrome

Yuki Sahashi, Tatsuma Serge Yanagimoto, Susumu Endo,
Hiroaki Ushikoshi and Hiroyuki Okura

Abstract:

We herein report a 26-year-old woman with sudden cardiac arrest who had no remarkable medical history. While resuscitation was successfully performed with adrenalin administration and extracorporeal membrane oxygenation, the cause of cardiac arrest could not be determined for over two weeks. Given the presence of autoimmune disease along with the findings of refractory renal insufficiency and thrombocytopenia, a kidney biopsy and blood examinations, including lupus anticoagulant testing, were performed, which proved the presence of antiphospholipid syndrome. The patient was successfully treated with steroid pulse therapy. This drastic case scenario highlighted the fact that autoimmune disease can be the cause of sudden cardiac arrest.

Key words: sudden cardiac arrest, catastrophic antiphospholipid syndrome, antiphospholipid syndrome, intensive care

(Intern Med 59: 1457-1460, 2020)
(DOI: 10.2169/internalmedicine.4123-19)

Introduction

Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by venous and/or arterial thrombosis and accompanied by positive levels of antiphospholipid antibodies. In addition to these characteristics, catastrophic antiphospholipid syndrome (CAPS) is defined when the manifestations of APS develop in multiple organs simultaneously or in less than one week. As thromboembolic events related to CAPS develop in multiple organs, the syndrome itself can manifest in a variety of ways (1).

We herein report a young woman who survived sudden cardiac arrest due to CAPS.

Case Report

A 26-year-old woman with no remarkable medical history visited her general practitioner due to chest discomfort with the following vital signs: pulse rate 130 beats per minute (regular rhythm) and respiratory rate of 30 per minute. An electrocardiogram performed by the general practitioner showed sinus tachycardia with no evidence of ST elevation or hypertrophy (Fig. 1). Peripheral oxygen saturation could not be measured due to systemic cyanosis. Furthermore, chest X-ray revealed bilateral pulmonary edema, and echocardiography showed a significantly impaired left ventricular systolic function with an ejection fraction of 20.3%. The patient was therefore transferred to our tertiary medical center to receive intensive care.

Since she suffered cardiopulmonary arrest [initial rhythm: pulseless electrical activity (PEA)] refractory to resuscitation just before her arrival at our facility, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was performed immediately after arrival. Initial blood testing showed multiple organ failure, including acute kidney injury (Cre: 7.00 mg/dL), elevation of liver enzymes [alanine aminotransferase (ALT): 473 U/L, aspartate aminotransferase (AST): 324 U/L], disseminated intravascular coagulation [platelet count: 25,000/μL, fibrinogen degradation product (FDP): 18.5 μg/mL], metabolic acidosis (pH: 6.71, base excess: -29.7 mmol/L, HCO^{3-}: 3.4 mmol/L, lactate: 186 mg/dL), elevated brain natriuretic peptide (BNP; 6,839 pg/mL), and elevated troponin I (5.43 ng/mL). The results of a blood examination performed in the emergency department are shown in Table 1.

Department of Cardiology, Gifu University, Graduate School of Medicine, Japan
Received: November 4, 2019; Accepted: January 20, 2020; Advance Publication by J-STAGE: March 12, 2020
Correspondence to Dr. Yuki Sahashi, mourinho384@yahoo.co.jp

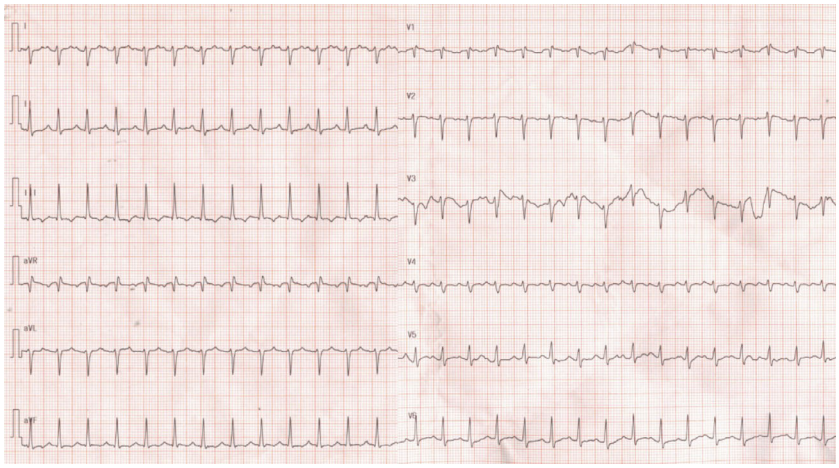

Figure 1. **The 12-lead electrocardiogram examined by the general practitioner.**

Table 1. **Blood Findings and the Results of a Rapid Influenza Check on Admission.**

Biochemistry		Peripheral blood	
Alb	2.5 g/dL	RBC	3.05×10^6 /μL
CK	265 U/L	WBC	10,170 /μL
CK-MB	54 IU/L	Hb	7.9 g/dL
AST	473 U/L	Hct	26.6 %
ALT	324 U/L	Plt	25,000 /μL
LDH	1,832 U/L	FDP	18.5 μg/mL
Cre	7.00 mg/dL	Fibrinogen	240 mg/dL
eGFR	6.7 mL/min/1.73m^2		
BUN	53.4 mg/dL	Arterial blood gas test on arrival at Emergency department	
		FiO2	100 %
Na	133 mmol/L	pH	6.71 mmHg
K	8.0 mmol/L	PaCO2	27.8 mmHg
Cl	98 mmol/L	PaO2	135.0 mmol/L
		HCO^{3-}	3.4 mmol/L
Troponin I	5.43 ng/mL	Base Excess	-29.7 mEq/L
BNP	6,839 pg/mL	Anion gap	26.8 mg/dL
CRP	1.86 mg/dL	Lactate	186
		Rapid influenza check	
		negative result	

Table 2. **Laboratory Findings of Immunological Testing.**

		*Normal range
Antinuclear antibody	56.2	(~40)
Anti DNA antibody	6.70 IU/mL	(~6.0 IU/mL)
Anti ds-DNA antibody	14 IU/mL	(~10 IU/mL)
Anti Sm antibody	10.2 U/mL	(~10 U/mL)
Anti cardiolipin antibody	33 U/mL	(~10 U/mL)
Lupus anticoagulant	2.35	(~1.3)
IgG	822 mg/dL	
IgA	199 mg/dL	
IgM	58 mg/dL	
CH50	<10.0 U/mL	
C3	54 mg/dL	
C4	4 mg/dL	
PR3-ANCA	<1.0 U/mL	
MPO-ANCA	<1.0 U/mL	

ADAMTS-13 inhibitor activity : negative result

The multiple organ failure was initially attributed to either fulminant myocarditis or acute myocardial infarction; however, the latter was denied due to coronary angiography showing no evidence of occlusion.

Cardiopulmonary support with VA-ECMO was terminated two days after admission based on the finding of slight improvement in her left ventricular ejection fraction. However, intermittent renal replacement therapy (IRRT) and blood transfusion with platelet concentrates were continued for over two weeks due to sustained kidney injury and severe thrombocytopenia, respectively. Autoimmune disease was suspected because of the sustained kidney dysfunction and severe thrombocytopenia despite the stabilization of the systemic condition, and blood testing on the 20th day of admission showed positive results for lupus anticoagulant (Table 2).

A renal biopsy was then performed, which demonstrated

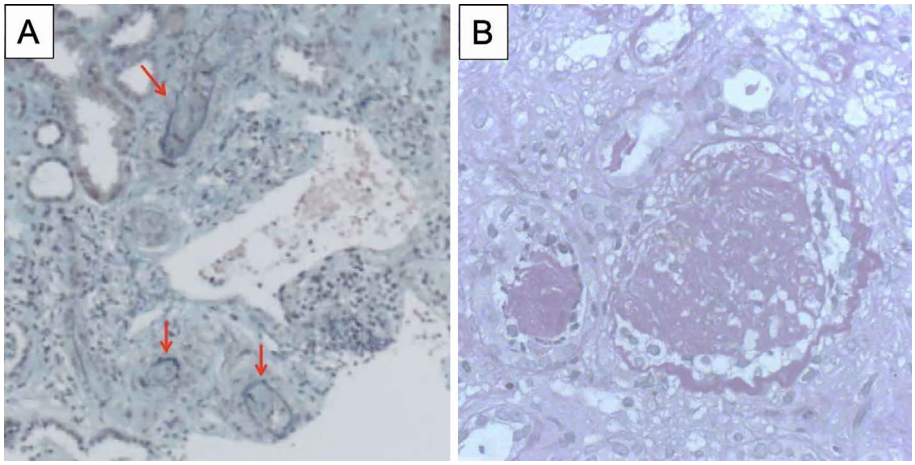

Figure 2. **The evaluation of a kidney specimen revealed renal artery thromboembolism (Left: red arrows, Elastica-Masson staining; 100×) and segmental glomerulosclerosis (Right: periodic acid-Schiff staining; 400×).**

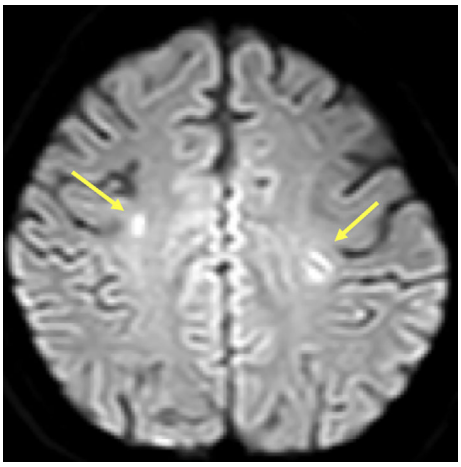

Figure 3. **Findings of brain magnetic resonance imaging (diffusion-weighted imaging) indicate multiple thromboembolisms (yellow arrows).**

the presence of a small renal artery thromboembolism and segmental glomerulosclerosis (Fig. 2). CAPS was therefore diagnosed based on positive lupus anticoagulant findings, the rapid development of manifestations, pathological findings of the renal biopsy, and diffusion-weighted imaging of brain magnetic resonance imaging (MRI) showing multiple thromboembolic cerebral infarctions (Fig. 3). Concurrent systemic lupus erythematosus (SLE) was also diagnosed based on the established criteria (Systematic Lupus Erythematosus Disease Activity Index score of 21 points) (2).

After the diagnosis, the patient was treated with warfarin [target PT-INR (prothrombin time internal normalized ratio): 2.0-3.0], intravenous methylprednisolone pulse therapy (1,000 mg/day for 3 days), and subsequent oral prednisolone therapy (1 mg/kg/day). As shown in the clinical time course in Fig. 4, the severe kidney dysfunction and thrombocytopenia normalized after methylprednisolone pulse therapy. Finally, hemodialysis therapy was able to be terminated. In addition, the patient's reduced motor function due to long-term bed rest was significantly improved with daily cardiac rehabilitation, and her subsequent clinical course was uneventful after being transferred to the general ward. Both the clinical cardiac status and echocardiogram findings were nearly normalized.

Discussion

CAPS, systemic autoimmune disorder characterized by venous and/or arterial thrombosis, includes many symptoms because of micro-thromboembolic event-related multiple organ failure. In addition, the diagnosis of CAPS is challenging in patients who suffer cardiopulmonary arrest as the first manifestation of CAPS, as in the present case. The mortality of CAPS remains high despite combination therapy with corticosteroids, intravenous immunoglobulin, plasma exchange, and anticoagulants, which makes the early diagnosis all the more crucial (3).

Regarding the etiology of CAPS-related acute cardiac failure, a number of different causes have been described, including macrovascular (4) or microvascular coronary artery embolization (5), valve involvement (6), fulminant myocarditis (7), and severe hypoxemia. In the present case, we failed to confirm the presence of microvascular coronary artery embolization or myocarditis since a cardiac biopsy or gadolinium-enhanced cardiac MRI could not be performed due to the patient's severe thrombocytopenia and kidney dysfunction. However, the persistent severe thrombocytopenia and kidney dysfunction despite dialysis therapy, blood transfusion, and improvement of other symptoms were key features suggesting the presence of autoimmune disorder.

Steroid pulse therapy drastically improved the general condition and led to the complete recovery of this patient with CAPS. However, the suitability of steroids as an empirical therapy for cryptogenic cardiac arrest is still being

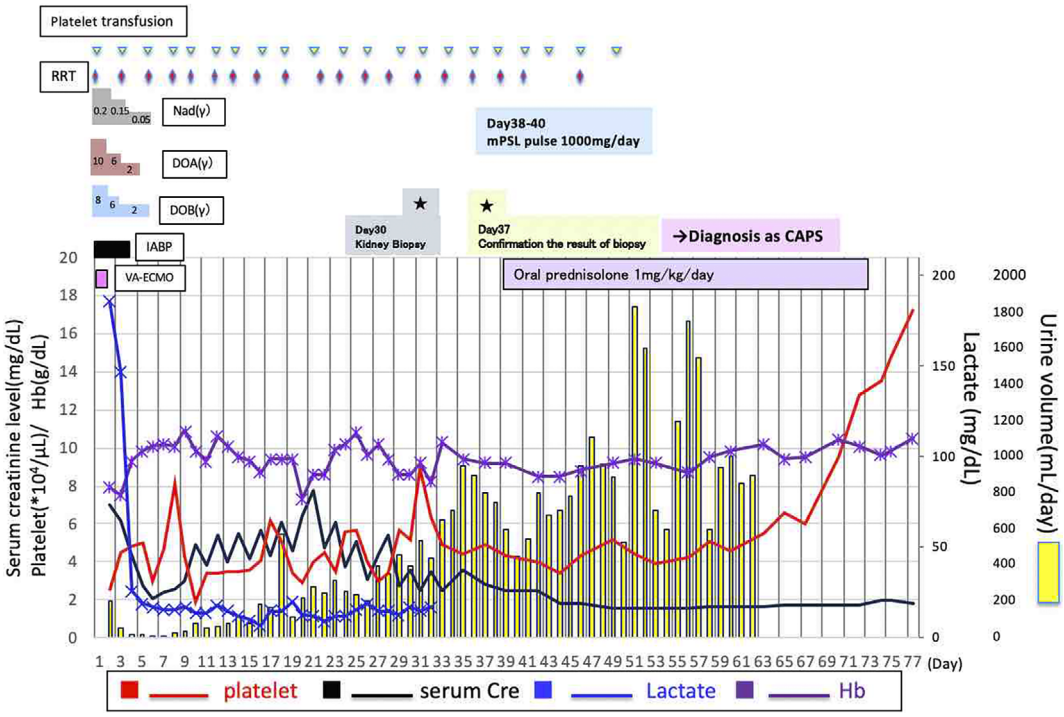

Figure 4. **Clinical time course of the present case, demonstrating changes in creatinine (Cre), urine volume, lactate, hemoglobin (Hb), and thrombocytopenia before and after methylprednisolone therapy. While the serum creatinine and platelet levels did not improve despite every-other-day renal replacement therapy (hemodialysis filtration) and transfusion with platelet concentrate, methylprednisolone pulse therapy led to the improvement of both the renal function and urine output and ultimately resulted in the discontinuation of hemodialysis. All creatinine testing was performed before dialysis therapy. IABP: intraaortic balloon pump, VA-ECMO: veno-arterial extracorporeal membrane oxygenation, RRT: renal replacement therapy, Nad: Noradrenalin, DOA: dopamine, DOB: dobutamine, mPSL: methyl prednisolone**

debated, as steroid therapy can worsen the prognosis of patients with virus-related myocarditis (8-10). The present case highlights the presence of APS as a potential cause of cryptogenic cardiac arrest. While cardiac arrest does not directly suggest APS, it is important for physicians to consider the possibility of APS in the aforementioned clinical scenario, especially if the patient is a young woman.

The authors state that they have no Conflict of Interest (COI).

References

1. Cervera R. Update on the diagnosis, treatment, and prognosis of the catastrophic antiphospholipid syndrome. Curr Rheumatol Rep **12**: 70-76, 2010.
2. Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis **78**: 1151-1159, 2019.
3. Cassyanne L, Aguiar CL, Erkan D. Catastrophic antiphospholipid syndrome: how to diagnose a rare but highly fatal disease. Ther Adv Musculoskelet Dis **5**: 305-314, 2013.
4. Okura H, Tomon M, Nishiyama S, Yoshikawa T. Patent foramen ovale and "catastrophic" antiphospholipid syndrome. Intern Med **39**: 83, 2000.
5. Tulai IM, Penciu OM, Raut R, Rudinskaya A. Catastrophic antiphospholipid syndrome presenting as congestive heart failure in a patient with thrombotic microangiopathy. Tex Heart Inst J **46**: 48-52, 2019.
6. Michel TC, Ali DG, Robert D, et al. Antiphospholipid syndrome role of vascular endothelial cells and implications for risk stratification and targeted therapeutics. J Am Coll Cardiol **69**: 2317-2330, 2017.
7. William JH, Yiannis SC, Michael LS, Gayle L, James MK. Myocardial catastrophe a case of sudden, severe myocardial dysfunction. Circulation **130**: 854-862, 2014.
8. Mason JW, O'Connell JB, Herskowitz A, et al. A clinical trial of immunosuppressive therapy for myocarditis. N Engl J Med **333**: 269-275, 1995.
9. Saito T, Katayama H, Kodani E. Is steroid therapy really banned for lymphocytic myocarditis before excluding viral infection? Eur Heart J **40**: 1014-1015, 2019.
10. Chen HS, Wang W, Wu SN, Liu JP. Corticosteroids for viral myocarditis. Cochrane Database Syst Rev. Forthcoming.