

# Antiphospholipid syndrome combined with acute coronary syndrome

## Case report

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### Abstract

**Rationale:** Antiphospholipid syndrome (APS) combined with acute coronary syndrome (ACS) is rarely reported.

**Patient concerns:** One male patient with APS was admitted to our hospital, who had recent unstable angina (UA).

**Diagnosis:** The preliminary diagnosis of ACS and UA (BraunwaldIB) was then made.

**Interventions:** This patient received secondary preventative therapy for coronary heart disease (CHD) in combination with percutaneous transluminal coronary angioplasty (PTCA) and implantation of NeoVas Bioresorbable Coronary Scaffold.

**Outcomes:** The patient was followed up, without new UA episodes were observed at 6 months, 1 year, and 2 year after surgery, respectively.

**Lessons:** It was thus concluded that percutaneous coronary intervention (PCI) is effective for APS patients and NeoVas scaffold implantation is presumed safe.

**Abbreviations:** ACS = acute coronary syndrome, APS = antiphospholipid syndrome, CHD = coronary heart disease, CTA = computed tomography angiography, LCX = left circumflex artery, PCI = percutaneous coronary intervention, PTCA = percutaneous transluminal coronary angioplasty, UA = unstable angina.

**Keywords:** acute coronary syndrome, antiphospholipid syndrome, bioresorbable scaffold, coronary angiography, unstable angina

## 1. Introduction

Antiphospholipid syndrome (APS) is an autoimmune disease, with antiphospholipid antibody (APL) and usually presents recurrent arterial and venous thrombosis, spontaneous abortion, thrombocytopenia, and positive serum APL.<sup>[1]</sup> Besides thrombosis and pathological pregnancy, APS can also induce severe cardiovascular diseases. Acute coronary syndrome (ACS) refers to a group of symptoms caused by rupture or invasion of coronary atherosclerotic plaques with secondary partially or completely occlusive thrombi. ACS consists of acute ST-segment

elevation myocardial infarction, acute non-ST-segment elevation myocardial infarction, and unstable angina (UA). Recent studies have demonstrated a correlation between APS and ACS. For example, Djokovic et al<sup>[2]</sup> reported cardiovascular diseases in 101 out of 374 patients with APS, including 36 patients with UA. Several cases who received percutaneous coronary intervention (PCI) for APS combined with acute myocardial infarction have been reported.<sup>[3–7]</sup> In this study, we reported a Chinese case of APS combined with ACS.

## 2. Case presentation

The 70-year-old male patient was admitted to hospital on January 25th, 2016 due to chest pain for 20 days. This patient had dull pain behind the sternum and backache. The symptoms were relieved spontaneously after 2 to 3 minutes and did not affect daily activities and sleep. Chest pain recurred in the morning 5 days ago, and the patient received creatine kinase isoenzyme (CK-MB) test and electrocardiogram at the outpatient clinic 3 days ago and the results were normal. However, computed tomography angiography (CTA) indicated 90% stenosis of the proximal right coronary artery. The patient was prescribed with aspirin, Clopidogrel, pitavastatin, and admitted to hospital for further examinations. This patient had a history of type 2 diabetes for over 20 years and had blood glucose properly controlled through insulin injection. He had a history of hypertension for 10 years with the maximum blood pressure of 150/90 mmHg. He generally achieved a proper blood pressure control. Other personal medical histories included diagnoses of immune thrombocytopenic purpura for 8 months and APS for 7 months as well as being a hepatitis B virus carrier for over 20 years. The patient had a history of allergy to sulfonamides without history of smoking and alcohol consumption. He

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received a transfusion of 2 units of platelets in March 2015. Family history of coronary heart disease (CHD) was negative. Physical examinations upon admission revealed: body temperature of 36.3°C, pulse rate 62 beats/min, respiratory rate 16 breaths/min, blood pressure 134/71 mmHg, BMI 21.3 kg/m<sup>2</sup>. The patient had a clear consciousness without carotid bruits. Breathing sounds were clear in bilateral lungs, and dry or moist rales were not detected. The area of cardiac dullness was not enlarged upon percussion. The heart rate was 62 beats/min, with regular rhythm and powerful heart sounds, P2 < A2. Murmurs were not observed in the auscultatory valve areas. The abdomen was soft, and liver and spleen were not palpable below the rib. Meanwhile, there was no edema in the 4 limbs. The preliminary diagnosis of ACS and UA (BraunwaldiB) was then made. The patient took aspirin and ticagrelor for anti-platelet therapy, rosuvastatin for lipid-lowering therapy and plaque stabilization, and low-molecular-weight heparin for anticoagulant therapy.

The patient had normal results of routine blood test, kidney, and liver function test, as well as CK-MB evaluation after admission, but relatively higher level of anti-beta2 glycoprotein I ( $\beta$ 2GPI)-IgG level which was 36.8 RU/mL (reference range 0.0–20.0) and negative ACL-IgG level which was 3.0 RU/mL (reference range 0.0–12.0). Coronary angiography indicated right predominance of coronary artery distribution and no apparent stenosis in the left main coronary artery (LM). Linear shadow was observed in the proximal and middle section of the left anterior descending artery (LAD) (Fig. 1) with 80% stenosis. For the first diagonal branch (D1), 50% stenosis was observed and the distal lumen was irregular. For the left circumflex artery (LCX), 50% stenosis was observed in the middle and distal section. No apparent stenosis was observed in OM1 (first obtuse marginal branch); 90% stenosis in the proximal right coronary artery (Fig. 2); no stenosis in PD, and 50% stenosis in PL. One NeoVas Bioresorbable Coronary Scaffold (3.0 × 24 mm) was implanted to proximal right coronary artery (RCA). Dilation was performed with a balloon (Quantum 3.5 × 12 mm with 20 atm). Another scaffold (2.5 × 24 mm) was implanted to the proximal



**Figure 1.** Coronary angiography analysis of LAD. LAD: RAO caudal view: 80% stenosis in the proximal and middle section, with a linear shadow observed locally; 50% D1 stenosis, with irregularity of distal lumen, D1=first diagonal branch; LAD=left anterior descending artery; RAO=right anterior oblique.



**Figure 2.** Coronary angiography analysis of RCA. RCA: LAO view, with 90% proximal stenosis and no stenosis in PD. LAO=left anterior oblique; PD=posterior descending branch; RCA=right coronary artery.

and middle section of LAD. Dilation was performed with a balloon (Quantum 2.75 × 12 mm with 18 atm). The patient was recommended to receive dual antiplatelet therapy with aspirin 100 mg daily plus ticagrelor 90 mg twice daily for at least 1 year and aspirin 100 mg daily indefinitely for life.

No new UA episodes were reported during the follow-up at 6 months, 1 year, and 2 years after discharge, respectively.

### 3. Discussion

Typically, APS has 3 major presentations: arterial and venous thrombosis; pregnancy loss; thrombocytopenia. Typical changes in laboratory indicators include lupus antibody (LA) in plasma for  $\geq 2$  times, with a time interval  $\geq 12$  weeks; moderate-to-high titer IgG/M anticardiolipin (ACL) in serum by standard enzyme linked immunosorbent assay (ELISA) for  $\geq 2$  times, with a time interval  $\geq 12$  weeks; IgG/M anti- $\beta$ 2 GPI in serum for  $\geq 2$  times by standard ELISA, with a time interval  $\geq 12$  weeks. APS is diagnosed if the patient has one of the above presentations and meets the standard on 1 laboratory indicator. Clinically, APS patients are divided into 4 types: type I, positive for at least one laboratory indicator; type IIa, only positive for LA; type IIb, only positive for ACL; type IIc, only positive for anti- $\beta$ 2-GPI antibody.<sup>[1]</sup>

APS is usually accompanied by a hypercoagulable state. The main pathogenesis of APL is the immunoglobulin that reacts with various negatively charged phospholipid antigens, including ACL and anti- $\beta$ 2 GPI. APL directly binds to the surface of endothelial cells, activating endothelial cells, inducing upregulation of adhesion molecules in endothelial cells. Moreover, through binding to the endothelial cells, APL inhibits the secretion and release of prostacyclin, leading to increased platelet adhesion and expression of tissue factors by monocytes and vascular endothelial cells. As a result, the protein C anticoagulant pathway is inhibited, which further promotes the release of plasminogen activator inhibitor and subsequent fibrinolytic inhibition. Eventually, thrombosis and vascular intimal hyperplasia may occur.<sup>[8]</sup> The pathology of ACS involves the rupture and

detachment of atherosclerotic plaques, platelet accumulation, and thrombosis. ACS is categorized into UA, ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction. It is hypothesized that the hypercoagulable state resulting from APL contributes to the progression and development of ACS. Evidence has shown that the positive rate of APL and antibody titer were higher in ACS patients than that in normal controls.<sup>[9]</sup> Greco et al<sup>[10]</sup> found that the positive rate and titer of anti-β2GPI antibody were significantly higher in ACS patients compared with controls.

In this study, we reported an APS case combined with diabetes, hypertension, and old age, all of which are risk factors for CHD. Given the fact that the patient suffered from angina in the last month, it was speculated that several factors led to endothelial dysfunction of the coronary artery and atherosclerosis (intimal hyperplasia), which further resulted in ACS. Coronary angiography revealed linear shadow in the proximal and middle section of LAD (Fig. 1). It was reported<sup>[11]</sup> in 2017 that 2 linear defects existed in the coronary lesion in an APS patient combined with ACS. Optical coherence tomography (OCT) detected that the lesion was separated by homogenous hyperintense septum into a central lumen and circumferential small channels, suggesting a recanalized thrombus. Intimal hyperplasia was observed as well. This finding was different from the previous report which indicated similar multiple lumens in honeycomb sign in different patients upon OCT.<sup>[12,13]</sup> We assume this sign may be unique in these patients, but more OCT findings are required to confirm this.

Gurlek et al<sup>[14]</sup> included 80 patients who received PCI for APS combined with CHD. Among them, 30 patients were positive for ACL, and 50 negative for ACL. At 1 year during the follow-up, 40% of ACL-positive patients had restenosis (8/20) versus 14% of ACL-negative patients (6/43) ( $P < .05$ ). According to Perl et al<sup>[15]</sup>, the incidence of post-PCI in-stent restenosis and target vascular reconstruction rate (TVR) was significantly higher among patients with APS combined with CHD than among non-APS patients. Moreover, there was also a significant increase in the post-PCI incidence of adverse vascular events in patients with APS combined with CHD during long-term follow-up (>1 year).

In our case, the reference diameter of affected coronary artery was relatively high, which was 3.0mm at the lesion in right coronary artery and 2.5 mm at the lesion in the middle section of LAD. All of them were simple lesions. This patient was negative for ACL and the expected incidence of in-stent restenosis and thrombosis was low. So NeoVas Bioresorbable Coronary Scaffold was implanted with dilation at high pressure. Dual antiplatelet therapy was administered post-PCI. No new UA episodes were reported at 6 months or 1 year after surgery, suggesting effective treatment with PCI.

A meta-analysis published on *Lancet* in 2017 showed that coronary artery diameter <2.25mm and female sex were independent risk factors for in-stent thrombosis.<sup>[16]</sup> In 2018, Wang et al<sup>[17]</sup> conducted an observation of 31 cases implanted with NeoVas scaffold in PCI over a 1-year period and reported no cardiac death or in-stent thrombosis, except for 1 case who suffered recurrent ischemic events. This finding supports the implantation of NeoVas scaffold as demonstrated in our study.

Given the susceptibility to thrombosis and hypercoagulable state of APS patients, more efforts are needed to develop the optimal individualized therapy for PCI in APS combined with ACS. We still need to extend the follow-up period to assess the prognosis of this patient.

In conclusion, we reported a case of antiphospholipid syndrome combined with acute coronary syndrome and PCI is

effective for APS patients and NeoVas scaffold implantation is presumed safe.

## Author contributions

**Conceptualization:** Yuan Shan, Ping Wang, JingHua Liu.

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