〈Case Report〉

Case report on a coronary artery bypass graft for a patient with antiphospholipid antibody syndrome associated with systemic lupus erythematosus

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ABSTRACT Antiphospholipid antibody syndrome (APS) is an immune disease in which antiphospholipid antibodies cause hypercoagulability and thromboembolic complications. We experienced APS cases associated with systemic lupus erythematosus with three-vessel lesions of the coronary artery. After a below knee amputation on a 60-year-old woman with APS, she complained of chest pain at rest. An electrocardiogram showed an ST depression and a coronary angiography showed complicated three-vessel disease, as a result she was referred to the cardiac surgery department. A coronary artery bypass with arterial grafts was performed along with postoperative anticoagulant and antiplatelet therapy, and the short-term graft patency was good. Case reports of coronary artery bypass grafts for secondary APS are rare, so we report here on our case and our strategy to treat thromboembolic complications.

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BACKGROUND

Antiphospholipid antibody syndrome (APS) is an immune disease in which antiphospholipid antibodies cause hypercoagulability and thromboembolic complications. Patients with APS suffer systemic disorders including cardiovascular disease[1－4]. There are some reports on cardiovascular surgery for APS patients which showed higher operation risks due to perioperative thromboembolic complications[5－8]. There are two types of APS, idiopathic and secondary. Most published reports have been about cardiac surgery for idiopathic APS, with only a few case reports on secondary APS[1, 5－8].

We experienced a case of on-pump beating-heart coronary artery bypass grafting (CABG)

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for a patient with secondary APS associated with systemic lupus erythematosus (SLE). Case reports on CABG for secondary APS are rare, so we report here on our case and our strategy to treat thromboembolic complications.

CASE REPORT

A 60-year-old female presented with chest pain at rest. She had a long history of medical problems prior to this complaint. In her 30s, she was diagnosed with proteinuria. Later, after two miscarriages, she was diagnosed with both SLE and APS. She had a history of taking high doses of prednisolone to treat her SLE. When she was referred to our department, her SLE was kept under control with 3 mg of prednisolone. Although she had undergone repeated intravascular interventions for arteriosclerosis obliterans (ASO), at the age of 57, her stenotic lesions became much worse. She eventually had a below knee amputation and she complicated of chest pain at rest on the sixth day after the operation. After an electrocardiogram (ECG) showed an ST depression, an echocardiogram revealed anterior and lateral wall motion asynergy, and a coronary angiography showed complicated three-vessel disease, she was referred to our cardiac surgery department.

She had an internal shunt in her left forearm for analgesics and even narcotics due to the severe pain in her extremities after her amputation. A blood test showed anemia due to renal failure. Additional tests showed hemoglobin: 6.6 g/dL, creatinine: 6.69 mg/dL, urea nitrogen: 37 mg/dL, brain natriuretic peptide: 1893.3 pg/mL, lupus anticoagulant: 1.49 (standard value [SD]: < 1.3), anticardiolipin IgG antibody (Ab): 19 U/mL, anti-ss DNA IgG Ab: < 10 AU/mL, anti-ds DNA IgG Ab: < 10 IU/mL, C3: 110 mg/dL (SD: 86-160), C4: 30 mg/dL (SD: 17-45).

In another detailed examination of the condition of the heart, an ECG showed an ST depression in leads V4-V6. Transthoracic echocardiography showed anterior and lateral wall motion asynergy associated with left ventricular diameters of 61 mm (diastolic) and 48 mm (systolic), a left ventricular ejection fraction of 52%, an E/A ratio of 0.7, an e/e' ratio of 15.1 and a deceleration time of 62 ms. There was no specific valvular disease. A coronary angiography showed stenotic lesions. Fig. 1 shows stenitic segment 1 (90%) and segment 4 (99%). Fig. 2 shows totally occluded segment 11 and good

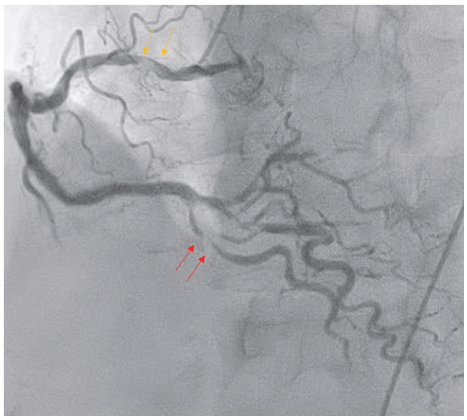

Fig. 1. Coronary angiography (CAG) showing the right coronary artery (RCA). The RCA was severely stenosed at the proximal (yellow arrows) and posterior descending branches(red arrows).

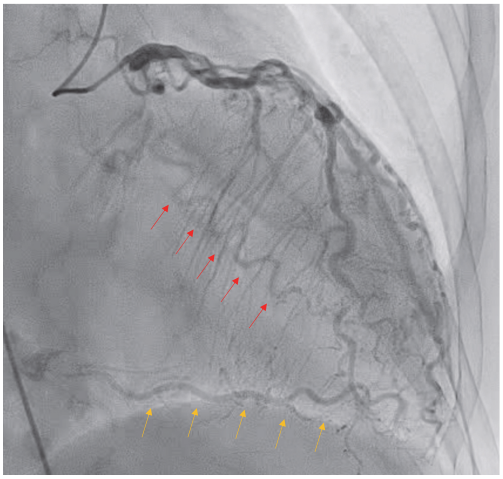

Fig. 2. CAG showing the LCx which was occluded proximally and had collateral flow from the LAD. Red arrows shows high lateral branch, and yellow arrows shows posterior lateral branch. Those are perfused by collateral flow from LAD.

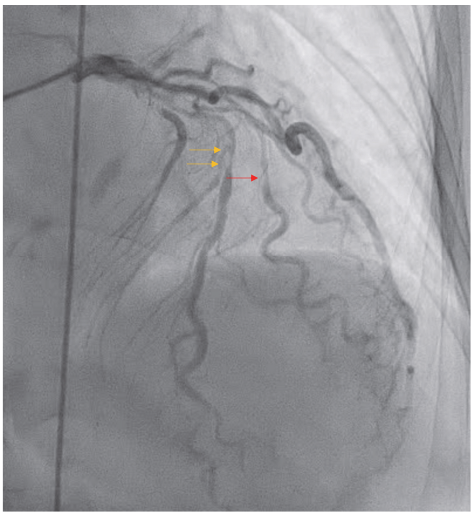

Fig. 3. CAG showing the proximal LAD was diffusely stenosed (yellow arrows) and the diagonal branch was also severely stenosed (red arrow).

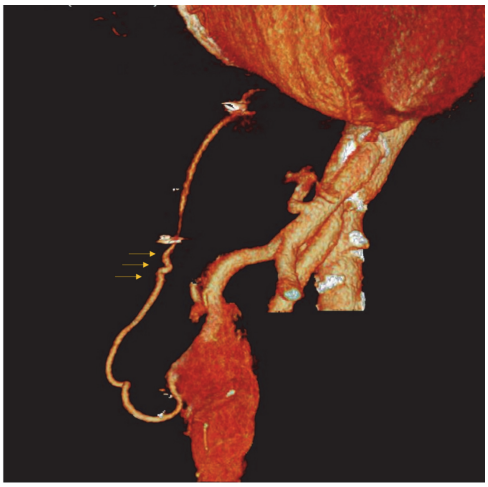

Fig. 4. Postoperative CT angiography showing the RGEA graft. The RGEA graft had a coil-like stenosed section (yellow arrow). The RGEA was not occluded, but there was less blood flow past the stenotic area.

collateral flow from the left anterior descending artery (LAD). Fig. 3 shows stenotic segment 5 (50%), segments 6-7 (diffusely 90%), segment 8 (90%) and segment 9 (90%).

We planned an all arterial graft bypass in case of acute venous graft occlusion due to the APS. We harvested the internal thoracic arteries and right gastroepiploic artery (RGEA). The RGEA had a stenotic section shaped like a coil, but an ultrasonic flow meter showed that distal perfusion was not restricted. A cardiopulmonary bypass (CPB) was established with blood supply to the ascending aorta and bicaval venous drainage. The anastomoses were performed under beating-heart conditions. We anastomosed the right intrathoracic artery (RITA) to the LAD, followed by the diagonal branch. The left intrathoracic artery (LITA) was anastomosed to the obtuse marginal (OM) branch. The RGEA was anastomosed to the posterior descending branch (PD) and the posterolateral branch (PL). Graft flows were measured with an ultrasonic flow meter and were deemed acceptable. The graft flow for RITA-LAD-D was 20 ml/min with a pulsatility index (PI) of 2.8, the LITA-OM flow was 16 ml/min with PI

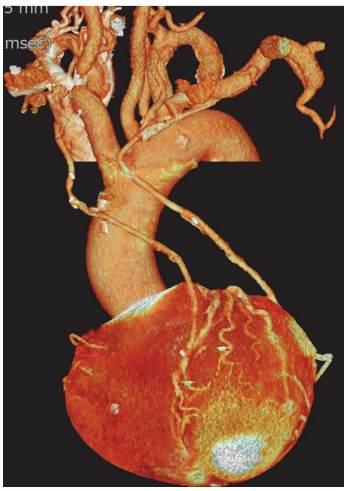

Fig. 5. Postoperative CT angiography showing the patent bilateral ITA grafts.

3.0 and the GEA-PD-PL flow was 31 ml/min with PI 2.5. After the anastomoses, circulation was easily weaned off the CPB. A half dose of protamine was administered, but it took some time to achieve hemostasis because the activated clotting time (ACT) was > 150 seconds. Fig.4 and Fig.5 showed postoperative CT angiography.

Three hours after the operation, a heparin infusion was started and an antiplatelet was also given via

a nasogastric tube. Although her hemodynamics was stable, there was bleeding. Thus, we used a blood transfusion for her anemia. Nafamostat was used in addition to the heparin, because a previous report have shown that some patients with APS had complications with heparin induced thrombocytopenia (HIT)[6]. An oral antiplatelet was begun on postoperative day (POD) 1, and hemodiafiltration was started on POD 2. We maintained her sinus rhythm with a β-blocker and antiarrhythmic drugs. Her bleeding ceased on POD 3. From POD 4, she took two oral antiplatelets and two anticoagulants, warfarin and nafamostat. After the prothrombin time / international normalized ratio (PT-INR) was prolonged enough, we prescribed just two antiplatelets and warfarin. Though it took time to cure an infection in her superficial wound, she had no perioperative thromboembolic complications. After her wound healed, she was transferred to another hospital to continue her rehabilitation for her artificial leg.

Microscopic examination showed that the excised internal thoracic artery had myxomatous degeneration in the tunica intima and tunica media, and that the gastroepiploic artery had some myxomatous degeneration.

DISCUSSION

In the general population, just 1-5% of people test positive for antiphospholipid antibodies. Only a few of that small group will eventually develop antiphospholipid syndrome[1, 2]. There are thought to be 40-50 APS patients per 100,000 people. There are several ways APS can express: carriers who have the antibody without any symptoms, "classic" APS with refractory thrombosis, APS causing refractory miscarriage and catastrophic APS with acute systemic organ dysfunction due to micro-embolisms[1-4].Classification criteria for antophospholipid antibody syndrome was addressed at a preconference workshop, preceding the Eleventh International Congress on antiphospholipid antibodies. The classification includes clinical and laboratory section. Clinical criteria includes vascular thrombosis and pregnancy morbidity, laboratory criteria includes positivity of Lupus anticoagulant, anticardiolipin antibody and anti-β_2 glycoprotein antibody[5]. In our case, the patient had refractory arteriosclerosis obliterans and was on hemodialysis due to lupus nephritis. She also had a medical history of refractory miscarriages and stroke, but there was no history of thromboembolisms except for superficial veins. She had taken warfarin to prevent thromboembolisms and three antiplatelets for repeated ASO restenosis.

There are two types of APS, primary and secondary. Primary APS does not have any associated diseases, and secondary APS has associated immune diseases like SLE and systemic sclerosis. In this case, we believe that our patient has secondary APS which is associated with her SLE[1].

Hedge *et al*. reported on a series of nine APS patients who underwent cardiac surgery. Three cases had thromboembolic complications, two had HIT and one had graft occlusions which necessitated a reoperation[8]. Though the perioperative risk was high, our case here had a good postoperative course without any major APS-specific adverse events other than a superficial incision infection. Most patients with APS are older and so they are usually given vein grafts for their CABG. In this case, we only used arterial grafts to prevent graft occlusion[8]. Her ITAs and RGEA had no specific findings of arteritis pathologically, however her RGEA had a coil-like stenosed section. There are currently no published reports on long-term arterial graft patency for APS patients, therefore long-term follow-up of this patient will be important.

Several kinds of anticoagulants and antiplatelets were used due to previous reports on postoperative thromboembolic complications. Some APS patients

in those reports had a longer preoperative ACT and activated partial thrombin time (APTT) than usual. Matsuyama *et al*. reported on an APS patient with an elongated ACT which was controlled with a higher ACT target and who went on to avoid any thromboembolic complications[6]. In our case, both the preoperative ACT and APTT were in the normal range, so we used our institution's usual ACT standard of < 400 seconds. HIT was also reported as a postoperative complication of APS, therefore nafamostat was used along with heparin during and after the operation. The operation was successfully concluded without any thrombus occurring in the cardiopulmonary circuit.

After circulation was weaned off the CPB, we could not achieve hemostasis without protamine administration. A half dose of protamine brought the patient into hemostasis and ACT was considered controlled at < 150 sec. There was no bleeding from the anastomoses, but there was considerable amount of bleeding from connective tissues and from the bone marrow of the sternum. A transfusion of red blood cells was necessitated perioperatively, but we did not transfuse fresh frozen plasma or platelets and the bleeding ceased on POD 3. We believe that if there was no major bleeding necessitating surgical repair, bleeding would cease even while taking several kinds of antiplatelets and anticoagulants due to the postoperative hypercoagulative phase. We also believe that APS patients have an increased risk of acute graft thrombosis without enough antiplatelets and anticoagulants during the postoperative hypercoagulative phase.

Though there was more hemorrhaging than usual due to the combination use of antiplatelets and anticoagulants, the patient had no thromboembolic complications. We believe that post cardiac surgery care for APS patient should be focused on coping with potential thromboembolic complications.

CONFLICTS OF INTEREST

The authors declare no conflict of interest associated with this manuscript.

REFERENCES

1) Cervera R: Antiphospholipid syndrome. Thrombosis Research. 2017; 151: S43-S47. doi: 10.1016/S0049-3848(17)30066-X.

2) Linnemann B. Antiphospholipid syndrome – an update. Vasa.2018; 47: 451-464. doi: 10.1024/0301-1526/a000723.

3) Cervera R, Asherson RA, Acevedo ML, *et al.*: Antiphospholipid syndrome associated with infections: clinical and microbiological characteristics of 100 patients. Ann Rheum Dis. 2004; 63: 1312-1317. doi: 10.1136/ard.2003.014175.

4) Gómez-Puerta JA, Cervera R, Espinosa G, Aguiló S, Bucciarelli S, Ramos-Casals M, Ingelmo M, Asherson RA, Font J: Antiphospholipid antibodies associated with malignancies: clinical and pathological characteristics of 120 patients. Semin Arthritis Rheum. 2006; 35: 322-332. doi: 10.1016/j.semarthrit.2005.07.003.

5) Miyakis S, Lockshin MD, Atsumi T, *et al.*: International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost.2006; 4: 295-306. doi: 10.1111/j.1538-7836.2006.01753.x.

6) Matsuyama S, Suenaga E, Sato M, Koga S: A case of left ventricular reconstruction in a patient with systemic lupus erythematosus and antiphospholipid syndrome. Jpn. J. Cardiovasc. Surg. 2008; 37: 116-119. doi: 10.4326/jjcvs.37.116. (Article in Japanese).

7) Berkun Y, Elami A, Meir K, Mevorach D, Naparstek Y: Increased morbidity and mortality in patients with antiphospholipid syndrome undergoing valve replacement surgery. J Thorac Cardiovasc Surg. 2004; 127: 414-420. doi: 10.1016/j.jtcvs.2003.07.016.

8) Hedge VA, Vivas Y, Shah H, Haybron D, Srinivasan V, Dua A, Gradman A: Cardiovascular surgical outcomes in patients with the antiphospholipid syndrome – a case-series. Heart Lung Circ. 2007; 16: 423-427. doi: 10.1016/j.hlc.2007.03.010.