

# Recurrent myocardial infarctions and premature coronary atherosclerosis in a 23-year-old man with antiphospholipid syndrome

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A 23-year-old man with primary antiphospholipid syndrome (APLS) was admitted for new onset angina on exertion. He had a history of an anterior ST-elevation myocardial infarction (STEMI) one year ago while he was in a developing country, which was managed conservatively without thrombolysis or cardiac catheterisation. He had no conventional cardiovascular risk factors, and denied any substance abuse. Coronary angiography revealed a filling defect in the mid left anterior descending (LAD) artery (► Figure 1A). Intracoronary optical coherence tomography (OCT) imaging (C7-XR, St. Jude Medical, St. Paul, MN, USA) showed a "honeycomb-like" mass with multiple holes of different sizes separated by smooth, high-backscattering septa, consistent with organized and recanalised thrombus (► Figure 1B). Proximal to the thrombotic lesion, an eccentric atherosclerotic plaque was identified (► Figure 1C). The lesion was treated with bare metal stent with good stent expansion and apposition. Two years later, the patient experienced a new episode of deep-vein thrombosis (DVT) while he

was on aspirin and warfarin (INR: 3.4). At that time, lupus anticoagulant was positive, anti-cardiolipin IgM antibodies were elevated (22.2 MPL; normal, <15 MPL), and anti-cardiolipin IgG antibodies were markedly elevated (>150 GPL; normal, <15 GPL). One and half year later, he was readmitted with a diagnosis of non-STEMI, while on aspirin (81 mg/day) and rivaroxaban (20 mg/day), and underwent aspiration thrombectomy in the first diagonal (D1) without stenting. The patient was discharged on aspirin (81 mg/day), clopidogrel (75 mg/day), and enoxaparin (70 mg twice/day), with recommendation to continue triple therapy indefinitely. However, the patient discontinued clopidogrel shortly after discharge. Three months later, he was readmitted with a diagnosis of STEMI. Coronary angiography showed a filling defect inside the stent and a hazy lesion at the bifurcation to D1 (► Figure 2A). OCT in the LAD showed a platelet-rich, white thrombus overlying a homogeneous neointima with interspersed microchannels (► Figure 2B-D). Aspiration thrombectomy was performed in D1, and two drug-eluting stents were implanted in the LAD and D1. The patient was discharged on aspirin (81 mg/day), prasugrel (10 mg/day), and enoxaparin (70 mg twice/day), to be continued indefinitely.

APLS is a prothrombotic disorder causing venous and arterial thrombosis, associated with specific autoantibodies [i.e. anti-cardiolipin, anti- $\beta$ 2-glycoprotein I ( $\beta$ 2GPI), lupus anticoagulant] (1). Several mechanisms contribute to the prothrombotic state in APLS, including increased oxidative stress, enhanced activation of platelet, endothelial and monocyte receptors by anti- $\beta$ 2GPI antibodies, and increased expression of tissue factor (1). In the present case, the use of high-resolution OCT imaging enabled a detailed assessment of coronary artery morphology

showing the presence of premature atherosclerotic disease in a very young patient with APLS despite the absence of conventional cardiovascular risk factors. This observation is interesting in that it is the first *in vivo* assessment of coronary findings in APLS using OCT, and supports the growing evidence from experimental studies suggesting the development of early atherosclerotic lesions in APLS (2). Second, OCT was useful to understand the nature of the filling defect, which is a critical piece of information to guide targeted therapy. Since an organised thrombus with partial recanalisation was the culprit lesion, thrombolysis or antithrombotic therapy would not have worked well. Therefore, on the basis of the OCT imaging, it was decided to proceed with stenting. During the second admission, OCT showed platelet-rich thrombus rather than fibrin/erythrocyte-rich thrombus. Therefore, a more potent P2Y<sub>12</sub> inhibitor, prasugrel, was chosen instead of less potent clopidogrel. Third, OCT was useful to guide optimal stent sizing and deployment, which is particularly important as stent underexpansion and irregular protrusion between stent struts are known predictors for future adverse cardiac events (3). The management of APLS patients with recurrent thrombotic events is challenging, and strong evidence deriving from randomised controlled trials is lacking (4). Several therapeutic approaches have been proposed by expert consensus guidelines, including high-intensity anticoagulation therapy with a target INR 3.0–4.0, antiplatelet therapy alone, or the combination of antiplatelet and anticoagulation therapies (5). In the present case, the patient developed a DVT despite being on low-dose aspirin plus warfarin, which was then switched to rivaroxaban. The potential role of new direct oral anticoagulants, such as inhibitors of factor Xa (e.g., rivaroxaban, apixaban) or direct thrombin

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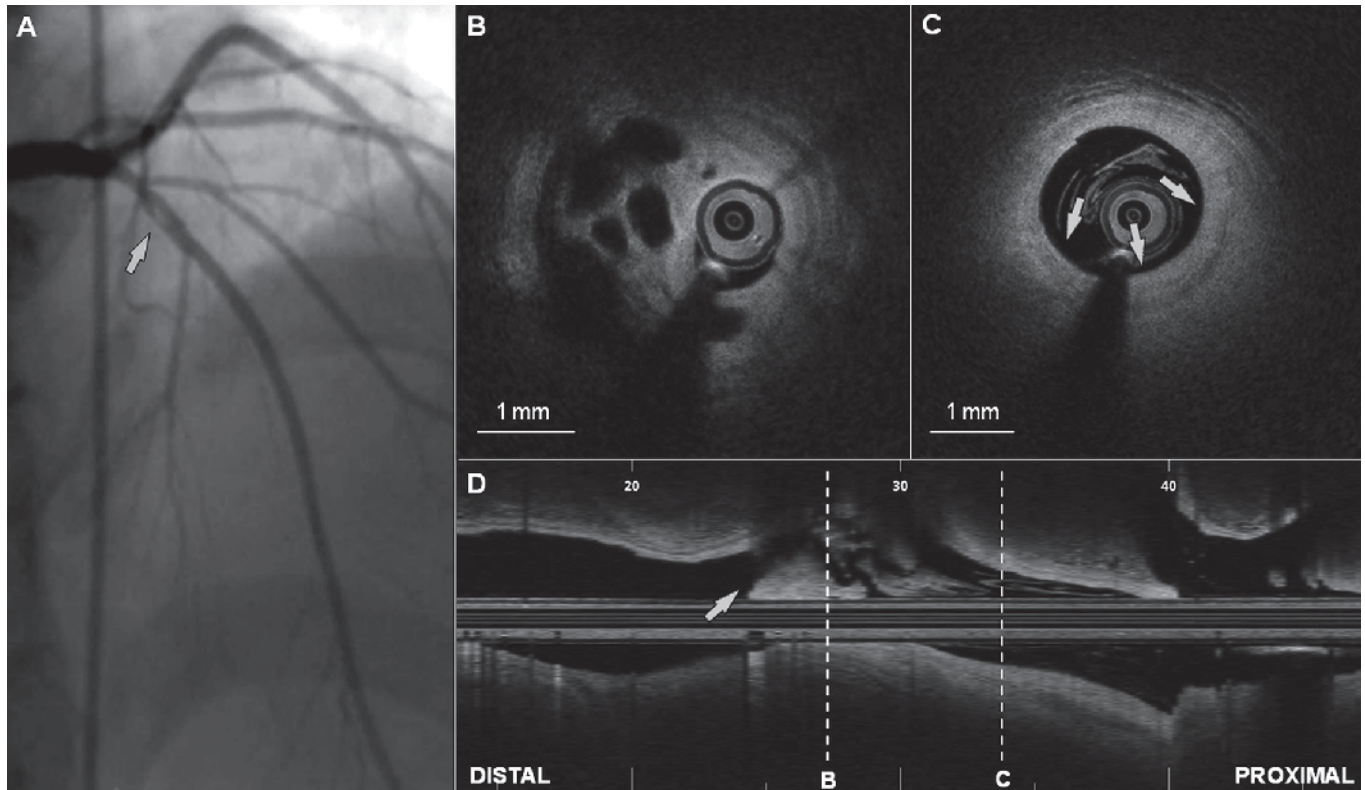
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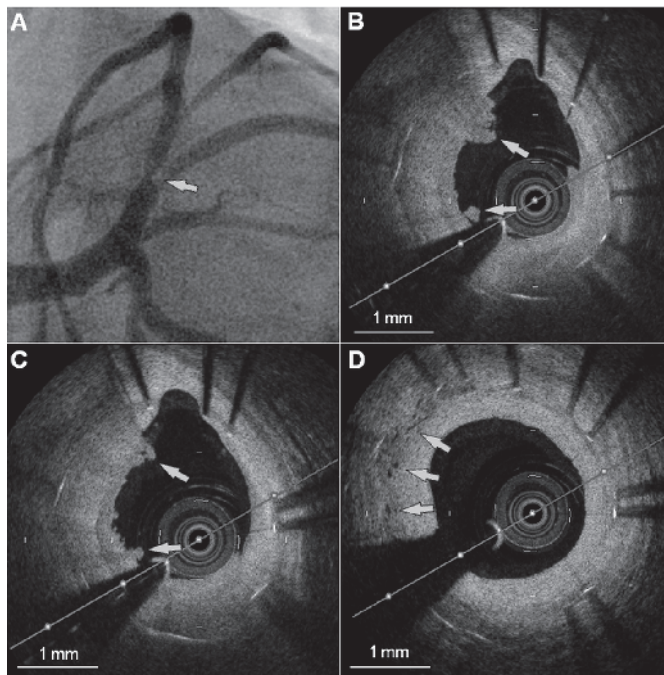
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**Figure 1: Baseline angiographic and OCT findings in a 23-year-old patient with APLS with angina on exertion.** A) Coronary angiography of the left coronary system showing a filling defect (arrow) in the mid left anterior descending artery. B) OCT cross-sectional image showing a "honeycomb-

like" structure consistent with organized and recanalized thrombus. C) OCT cross-sectional image showing an eccentric atherosclerotic plaque (arrows) proximal to the thrombotic lesion. D) Longitudinal OCT view showing the thrombotic mass in LAD.



**Figure 2: Angiographic and OCT findings at the time of recurrent myocardial infarction.** A) Coronary angiography showing a filling defect in the previously stented LAD and a hazy lesion at the bifurcation to the first diagonal branch. B-D) OCT images of the LAD showing platelet-rich, white thrombus (arrows) overlying neointimal tissue (B and C) with multiple microchannels (D, arrows).

inhibitors (e.g. dabigatran) for prophylaxis of thrombotic events in patients with APLS is under investigation in randomised controlled trials (6). The rationale behind these studies is that, unlike oral vitamin K antagonists, novel oral anticoagulant drugs may provide a more predictable pharmacologic effect, without interfering with the activity of the physiological anticoagulant protein C/S system, and without requiring systematic anticoagulation monitoring. However, high-risk patients (such as those with arterial thrombotic events or high antibody titres) may be less protected with these drugs, as suggested by our report and recent case series (7). After the first recurrent coronary event, the patient was put on aspirin, clopidogrel and enoxaparin, but a recurrent event occurred few months after discharge due to non-compliance with clopidogrel. After stenting, he was again discharged on dual antiplatelet therapy (DAPT) plus anticoagulation with enoxaparin to be continued indefinitely. Our

case highlights the difficulty of managing patients with APLS and acute coronary syndrome, and suggests that inhibition of both coagulation cascade and platelet pathway is important in cases like this, due to the risk of both DVT and coronary platelet-rich thrombus formation. The recurrent myocardial infarctions occurred after thienopyridine was discontinued, while the patient was on aspirin and anticoagulant therapy only. It is likely that, in addition to anticoagulation, a more prolonged DAPT after stenting, as proposed by the recent DAPT trial (8), might be of particular benefit in patients with prothrombotic disorders such as APLS. Laboratory measures of therapeutic efficacy, such as the assessment of coagulation cascade activation and the measurements of platelet reactivity, may further aid the management of these

patients with the final goal of preventing future events.

#### Conflicts of interest

Dr. Jang received grant support and consulting fees from LightLab Imaging/St. Jude Medical. Other authors have no relevant conflicts of interest to disclose.

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