Apixaban for massive intracoronary thrombosis: A case series

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Introduction

The common pathophysiology of acute coronary syndrome is usually thrombus formation after rupture or erosion of the coronary artery plaque. The key goal of treatment is to resolve ischemia by early revascularization and prevent complications, such as death, re-infarction, or life-threatening arrhythmias (1). Coronary thrombus burden is a significant factor affecting the success of percutaneous coronary intervention (PCI) during revascularization. Failure of recanalization, distal embolization, no reflow and impaired myocardial perfusion and function, stent malapposition, and stent thrombosis are frequently encountered complications during PCI of patients with massive thrombus (2-4). Thrombus burden can be reduced by pharmacological or mechanical methods, as a bail-out choice, to increase the success of the procedure. The recommended pharmacological treatment options are intravenous or intracoronary fibrinolytic agents or antiplatelet agents, such as glycoprotein GP IIb/IIIa inhibitors, in addition to the standard antiplatelet procedure. In this case series, we presented two patients with acute coronary syndrome and severe thrombus burden in the ectatic coronary arteries, resolved by apixaban treatment as a novel approach, in addition to the dual antiplatelet therapy.

Figure 1. a: A marked ectasia and dense thrombus appearance in the proximal segment of left anterior descending artery. b: The large thrombus image in the proximal segment of LAD persisted but has decreased slightly following tirofiban infusion. c: The thrombus in the proximal segment of LAD had completely resolved after apixaban plus dual antiplatelet therapy for 1 month.

Case Reports

Case Report 1

A 38-year-old man presented with a pressure-like chest pain and shortness of breath that started three hours prior to presentation. His blood pressure was 110/65 mm Hg, pulse rate was 85 bpm, and he was hemodynamically stable. He had no known chronic diseases. There was a history of smoking and a positive family history for cardiovascular disease. There was no obvious sign of ischemia in the electrocardiogram (ECG) and no wall motion defects in the echocardiographic evaluation. The highly sensitive troponin T level was elevated (250 pg/mL). The patient was admitted to the coronary angiography laboratory with a diagnosis of myocardial infarction with non-ST segment elevation (NSTEMI). Marked ectasia and dense thrombus appearance in the proximal segment of the left anterior descending artery (LAD) was detected in coronary angiography, as well as ectasia formation accompanied by noncritical stenosis in circumflex artery (Cx) and right coronary artery (RCA) (Fig. 1a). The diameter of the proximal segment of LAD was measured above 5 cm. Control angiography was planned following intravenous tirofiban infusion for 24 hours. In control angiography, the large thrombus image in the proximal segment of LAD persisted but had decreased slightly (Fig. 1b). Therefore, it was planned to prescribe apixaban 5 mg twice a day for one month as an off-label treatment in addition to dual antiplatelet therapy. The patient had no inherited coagulation tendency checked by the laboratory parameters. In the angiography performed at the end of the first month, it was observed that the thrombus in the proximal segment of LAD had completely resolved (Fig. 1c). The medical treatment of the patient was continued with clopidogrel 75 mg once a day and apixaban 5 mg twice a day for six months.

Case Report 2

A 60-year-old male patient was admitted to the emergency department with a complaint of epigastric pain that started after...
meals, which radiated to his chest. His blood pressure was 135/65 mm Hg, pulse rate was 80 bpm, and he was hemodynamically stable. He had been followed up for a 4-cm ascending aortic aneurysm and had no known additional cardiovascular risk factors. There was minimal ST segment depression at the inferior derivations of ECG and mild hypokinesia at basal and middle segments of the inferior wall on echocardiographic evaluation. The high sensitive troponin T level was elevated (850 pg/mL). The patient was admitted to the coronary angiography laboratory with a diagnosis of NSTEMI. Coronary angiography revealed marked diffuse ectasia and dissection at the proximal segment till the crux of the RCA, and thrombus formation was observed in both lumen. Thrombus formation was also observed at the posterior descending artery (PDA) and posterolateral (PL) branches (Fig. 2a, Video 1). Following intravenous tirofiban infusion for 24 hours, control coronary angiography was performed, which showed that the dissection and massive thrombus image in the RCA was still present, although the size of the thrombus had decreased slightly following tirofiban infusion. The original huge ectatic vascular structure of the RCA was restored after apixaban plus dual antiplatelet therapy for 1 month.

Discussion

In patients with myocardial infarction with NSTEMI, 50% to 70% also exhibit a substantial thrombus burden in the culprit vessel (5). Angiographic no reflow rates range from 15% to 40%, depending on the thrombus burden, and reperfusion results are suboptimal in the vast majority of these patients (6). Medical therapies acting on thrombocytes and coagulation cascade, mechanical flow restoration, or extraction of the thrombus should be used systematically in these thrombotic lesions to increase procedural success (7).

During PCI of severe thrombotic lesions, stent malapposition possibly because of inappropriate size, increased risk of stent thrombosis, distal embolization, no reflow, and suboptimal thrombolysis in myocardial infarction (TIMI) flow are the most challenging entities (1). In our first case, the proximal LAD segment was ectatic, and the lesion diameter was approximately over 5 mm. Similarly, in the second case, RCA was diffusely ectatic. Although it was more pronounced in the second case, both the patients had a significant thrombus burden in the culprit coronary arteries associated with NSTEMI. The balloon-stent technique was not preferred owing to high risk of no reflow related to crush of intense thrombus burden and high risk of malapposition in such marked ectatic coronaries.

Thrombectomy is another method used to increase the success of the intervention in thrombotic lesions. In the TATORT study conducted in 440 patients with NSTEMI, there was no difference in the primary outcome (prevalence of late microvascular obstruction) between conventional PCI and manual thrombectomy (6). The finding of TASTE and TOTAL studies in patients with STEMI also do not support the routine use of thrombectomy; however, it can be beneficial in selected cases (8, 9). In our cases, because of the large vessel diameter and high thrombus burden increasing the risk of procedure related cerebrovascular accident, thrombectomy was not performed.

In addition to the use of periprocedural dual antiplatelet agents and heparin, interrupting the coagulation cascade with GP IIb/IIIa inhibitors or lysing the existing thrombus by intracoronary thrombolytic agents are the pharmacological methods that increase the effectiveness of intervention and preserve distal flow (10, 11). In our cases, we preferred to give GP IIb/IIIa inhibitor in addition to the anti-aggregant treatment. Although the thrombi size had decreased slightly in 24th hour control angiographies, they still persisted. Owing to the ectatic nature of the vessels, we decided to add apixaban to the dual antiplatelet regimen as a new approach.
Apixaban is a direct oral anticoagulant, used for protection from cerebrovascular events in atrial fibrillation, venous thromboembolism, and pulmonary embolism (12, 13). However, their use in intracardiac thrombus and in cerebral venous bed is included in the literature on a case-by-case basis (14, 15). Although there is no specific reason for preferring apixaban, the usage of apixaban in addition to dual antiplatelet therapy in one of the triple treatment arms of the AUGUSTUS study conducted with a 2*2 factorial design, motivated us to prefer apixaban in such a clinical situation (16). As far as we searched the literature, there is no use of DOACs in the coronary arterial system. Coronary ectasia can produce sluggish blood flow and predispose to thrombus formation and acute myocardial infarction, even without obstructed coronary arteries. There have been successful results in the literature with the use of warfarin in ectatic coronary arteries (17, 18). Although no specific ranges have been clarified for the use of warfarin in patients with coronary artery ectasia, effective doses have been preferred as in the prevention of stroke because of atrial fibrillation. Therefore, it was thought that the use of standard doses of apixaban would be more appropriate in patients with acute coronary syndrome because of coronary artery ectasia associated with huge thrombus formation, as in atrial fibrillation. In both our patients, apixaban was used instead of warfarin, as a novel approach, and it was observed that the thrombus had resolved successfully in the control angiographies performed at the end of the first month.

**Conclusion**

In these two patients with ectatic coronary arteries and severe thrombus burden, apixaban was administered in addition to the dual antiplatelet therapy, following GP IIb/IIIa inhibitor infusion. At the end of the first month, thrombus had resolved, and TIMI 3 flow was restored in the culprit coronary arteries. In the future, through large-sized clinical trials assessing long-term outcomes, it may be possible to prescribe DOACs for the treatment of high intracoronary thrombus burden.

**Informed consent:** An informed consent was obtained from the patients.

**Video 1.** Marked diffuse ectasia and dissection at the proximal segment till the crux of RCA and huge thrombus formation in both lumen.

**Video 2.** The dissection and massive thrombus image in the RCA was still present, although the size of the thrombus had slightly decreased following tirofiban infusion.

**Video 3.** The original huge ectatic vascular structure of the RCA was restored after apixaban plus dual antiplatelet therapy for one month.

**References**


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