

# Lateral ST-elevation myocardial infarction after donation of COVID-19 convalescent plasma in a naïve donor

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## SUMMARY

A 34-year-old man presented with central chest pain heralded by bilateral arm numbness, tingling and pain soon after donation of 1000 mL of COVID-19 convalescent plasma (CP). ECG showed ST-elevation in lateral leads and coronary angiogram showed large thrombus in diagonal branch of the left anterior descending artery. The patient underwent successful thrombus aspiration and percutaneous coronary intervention of diagonal branch. In this report, we describe a case of coronary thrombosis leading to ST-elevation myocardial infarction in a naïve plasma donor after donation of COVID-19 CP.

## BACKGROUND

With growing evidence on mortality benefit of convalescent plasma (CP) in COVID-19 illness, plasma donations have scaled up worldwide. Side effects of plasmapheresis of COVID-19 CP are assumed to be the same as for any apheresis. The American Red Cross hemovigilance report in 2006 on side effects of blood donation had reported no acute myocardial infarction (AMI).<sup>1</sup> Additionally, a review of 19 736 apheresis procedures did not demonstrate relationship between platelet donation and development of AMI.<sup>2</sup>

The Kuopio Ischaemic Heart Disease Risk Factor Study from 1998 showed reduced risk of myocardial infarction associated with frequent voluntary blood donations in middle-aged men.<sup>3</sup> However, a prospective study of 139 176 person-years found no association between number of blood donations and risk of myocardial infarction.<sup>4</sup> In this case, we report a middle-aged man presenting with ST-elevation myocardial infarction (STEMI) soon after donation of COVID-19 CP.

## CASE PRESENTATION

A 34-year-old man presented with complains of jaw and bilateral arm pain along with numbness and tingling sensation which started 1 hour after donation of 1000 mL of COVID-19 CP. Over the next 3 hours, his symptoms progressed into central chest heaviness along with nausea, vomiting and trepidation. The patient presented with an ongoing chest pain with blood pressure of 150/80 mmHg, heart rate of 85 beats/min, respiratory rate of 17 breaths/min and oxygen saturation of 98% on room air. Cardiovascular and respiratory examination was unremarkable. He was obese, active smoker and hypertensive. He had a history of mild

COVID-19 illness 4 months ago. The patient had no active symptoms of influenza, fever or body aches. His recent COVID-19 PCR was negative and COVID-19 antibodies were positive.

ECG on arrival showed ST-segment elevation in lead I, aVL, V5 and V6 with subtle reciprocal changes in inferior leads (figure 1). The patient was managed with loading dose of aspirin and clopidogrel along with intravenous unfractionated heparin. Cardiac catheterisation lab was activated, and the patient was rushed for coronary angiogram.

Left heart catheterisation was done via right femoral access which showed significant lesion in ostial-proximal diagonal branch of the left anterior descending artery (LAD) along with a large thrombus resulting into Thrombolysis in Myocardial Infarction (TIMI II) flow (figure 2). The left main artery was engaged and diagonal branch was wired with Balance Middle Weight (BMW). A semi-compliant Sapphire 2.0\*10 mm was inflated in the ostium of diagonal artery. Aspiration thrombectomy was performed and SeQuent Please (drug-coated balloon) size of 2.5 mm\*10 mm was expanded in the ostium of diagonal artery with resultant TIMI III flow (video 1).

Post-procedure, the patient remained haemodynamically stable and pain free. Post-angioplasty, ECG showed resolution of ST-elevations and T wave inversions in leads I and aVL (figure 3). Echocardiogram was done which showed normal ejection fraction and valves. The patient was thereafter managed with dual antiplatelets, statins and beta-blockers. Laboratory investigations revealed troponin-I of 0.2 ng/mL (cut-off <0.04 ng/mL), haemoglobin of 162 g/L, platelets of  $376 \times 10^9/L$ , prothrombin time (PT) of 11.9 s and activated partial thrombin time of 22.9 s. His HbA1C was 5.6% (38 mmol/mol) with normal renal and hepatic profile.

## OUTCOME AND FOLLOW-UP

The patient was discharged home after an uneventful coronary care unit stay of 3 days. He was followed up in outpatient clinic for 2 weeks with no active complains. Lifestyle modification was reinforced.

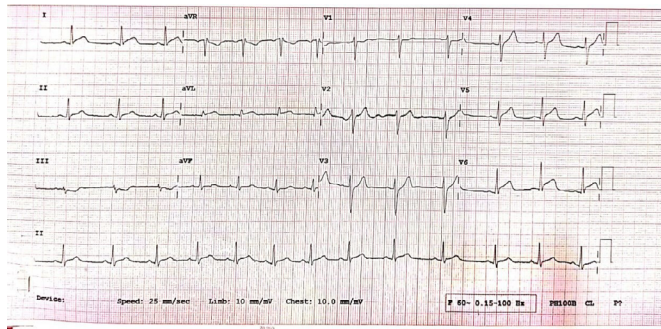
## DISCUSSION

A meta-analysis of randomised controlled trials have proven to reduce COVID-19 mortality after administration of high-titre CP.<sup>5</sup> Plasmapheresis refers to selective extracorporeal removal of plasma from patient's blood. Cardiovascular effects of plasmapheresis in a healthy donor have been



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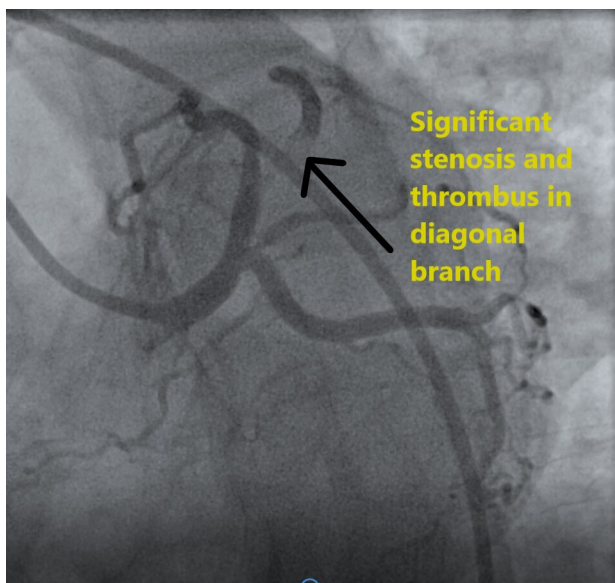


**Figure 1** ECG on arrival showing ST-segment elevation in lead I, aVL, V5 and V6 with subtle reciprocal changes in inferior leads.

studied and include short-term increased blood pressure variability.<sup>6</sup> Additionally, low-density lipoprotein apheresis is being used in patients with refractory hypercholesterolaemia.<sup>7,8</sup> It is also being studied as a novel therapy in patients with dilated cardiomyopathy.<sup>9</sup>

There is controversial evidence about the effect of plasmapheresis on donor's hypercoagulability. This procoagulant effect was studied in 54 donors and it was found that in comparison to pre-plasmapheresis sample, post-plasmapheresis sample showed significant reduction of PT, increased clot growth velocity and increased endogenous thrombin generation turning normocoagulant plasma into a hypercoagulant one.<sup>10</sup> On the other hand, Akay *et al* showed plateletpheresis did not induce hypercoagulability in healthy donors.<sup>11</sup>

Venous thrombosis following plasmapheresis has been reported in upper extremity veins.<sup>12–14</sup> Intracranial arterial thrombosis leading to stroke is reported in two cases with underlying prothrombin gene mutation and raised Von Willebrand antigen and C-reactive Protein (CRP).<sup>15</sup> This indicates that presence of underlying coagulation pathway defects increases the risk of thrombosis following plasma donation. Large volume apheresis leading to cerebral infarction has also been reported but with underlying inherited thrombophilia.<sup>16</sup>



**Figure 2** Left main artery is engaged via femoral approach showing a significant lesion in ostial-proximal diagonal branch of the left anterior descending artery along with a large thrombus resulting into Thrombolysis in Myocardial Infarction (TIMI II) flow.



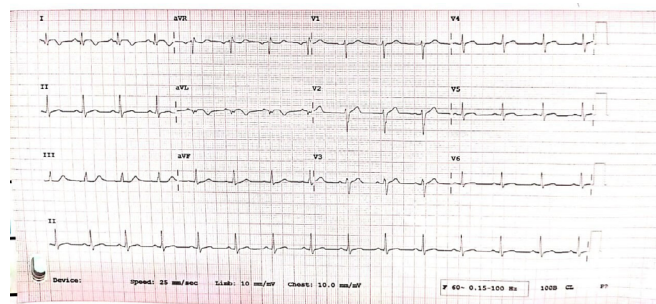
Diagonal branch and LAD are wired with BMW wire.

**Video 1** Percutaneous coronary intervention of diagonal branch with a drug-coated balloon.

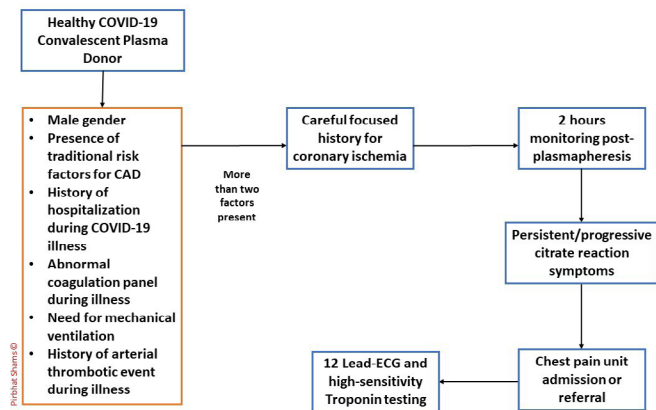
Two case reports have defined occurrence of coronary thrombosis following apheresis, dating back to 2010–2011. In one case report, a 47-year-old man presented with anterior STEMI 12 hours after plasma donation of 724 mL and coronary angiogram revealed thrombotic subocclusion of LAD. However, he had been a regular large volume plasma donor (a total of 21 times and 5 times in the year of presentation with STEMI).<sup>17</sup> Another case report has defined anterolateral STEMI in a 57-year-old man 10 min after plateletpheresis with a volume depletion of 663 mL. This patient also had history of repeated platelet donation (54 times in 9 years).<sup>18</sup> However, our patient presented with STEMI after plasma donation for the first time. The short duration between onset of symptoms and completion of plasmapheresis in our patient points towards possible association of CP donation and ACS.

Plasma donation is generally considered a safe procedure. Patients can commonly develop tingling or numbness around lips, jaw, neck and shortness of breath. Occasionally, profound hypotension and life-threatening arrhythmias can ensue,<sup>19</sup> which can generally confound physicians to be 'citrate reaction'. Citrate is used as a primary anticoagulant during apheresis procedures and makes calcium unavailable for coagulation cascade by chelation. However, physicians should be aware of the possibility of acute coronary syndrome (ACS) after plasmapheresis, as in our case.

With growing use of COVID-19 CP, we might witness similar cases in otherwise healthy plasma donors. We should be mindful of the hypercoagulable state that a recent COVID-19 illness confers to the patient. ACS workup should be done in those with persistent symptoms suggestive of coronary ischaemia or haemodynamic instability, as symptoms of citrate reaction can herald symptoms of ACS, as in our case. As opposed to the other



**Figure 3** Post-angioplasty ECG showing resolution of ST-elevations and T wave inversions in leads I and aVL.



**Figure 4** Algorithm for detecting COVID-19 convalescent plasma donors who are at high risk of thrombotic event following plasmapheresis. CAD, coronary artery disease.

two cases, even a first-time donation can result into significant coronary thrombosis.

To not miss the diagnosis of ACS in COVID-19 CP donors, one should carefully monitor the symptoms of citrate reaction for progression and evolution into typical anginal symptoms. Additionally, one should be mindful of standard risk factors for coronary artery disease (CAD) and a careful focused history for previous anginal symptoms before plasmapheresis can help one in detecting high-risk donors. An otherwise healthy plasma donor, who has traditional risk factors and develops protracted symptoms after plasmapheresis, should have an initial 12-lead ECG and a serial ECG if symptoms persist. As for standard chest pain algorithms, a high sensitivity troponin-I (hs-TnI) in 2–3 hours after onset of symptoms would guide the decision for further observation.

We hereby propose an algorithm that can guide us in detecting COVID-19 CP donors who are at high risk for thrombotic events following plasmapheresis (figure 4). High-risk factors include male gender,<sup>20</sup> traditional risk factors for CAD, history of hospitalisation during COVID-19 illness (intensive or non-intensive care units), requirement for mechanical ventilation (as hypoxia drives endothelial injury leading to hypercoagulability), degree of COVID-19 illness, abnormal coagulation markers<sup>20</sup>

### Learning points

- ▶ Occurrence of coronary thrombosis after plasmapheresis is limited to a few case reports. Physicians should be vigilant about this possibility and ischaemia workup should be done in those with persistent symptoms after donation.
- ▶ COVID-19 illness is associated with hypercoagulability and consequent systemic or organ thrombosis. Plasmapheresis after COVID-19 illness might act synergistically to increase the risk of systemic or organ thrombosis in an otherwise healthy (recovered) donor. This needs further research.
- ▶ If further similar reports continue, there might be a need to prospectively follow up donors of COVID-19 convalescent plasma for future thrombotic events and major adverse cardiovascular events.

during illness (such as high D-dimer, high fibrinogen, thrombocytosis, prolonged PT or prolonged activated partial thromboplastin time) and history of arterial thrombotic events during the illness (such as myocardial infarction, stroke or acute limb ischaemia). Validating this proposed algorithm in COVID-19 CP donors needs further research.

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