International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Cangrelor – A Potential Bridge for Percutaneous Coronary Intervention in Acute Coronary Syndrome with Concomittant Intracranial Haemorrhage – Case Study

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Citation: *Yagna Munesh Gali, Varsha Kiron, Subba Reddy K, Alok Ranjan. Cangrelor – A Potential Bridge for Percutaneous Coronary Intervention in Acute Coronary Syndrome with Concomittant Intracranial Haemorrhage – Case Study. Int Clinc Med Case Rep Jour. 2023;2(18):1-11.*

Received Date: 15 December, 2023**; Accepted Date:** 18 December, 2023**; Published Date:** 20 December, 2023

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ABSTRACT

Acute coronary syndrome (ACS) is a rare fatal consequence in a patient of intracranial haemorrhage (ICH). The complexity in devising a management strategy in such scenario is a considerable challenge to the clinician. The dire need for anticoagulation in the peri-procedural period once percutaneous coronary intervention (PCI) is planned to treat ACS is an absolute contraindication in a case of ICH. We present a plausible management strategy in such scenario thorough this case report of a 43 year old gentleman who presented with ICH and ACS. The beneficial role of cangrelor as a potential bridge for PCI in ACS complicating a case of ICH is highlighted.

Keywords: Cangrelor; Intracranial haemorrhage; Acute coronary syndrome; Percutaneous coronary intervention

INTRODUCTION

Acute coronary syndrome (ACS) is rare, but dreaded complication in a patient with intracranial haemorrhage (ICH). The incidence of serious cardiovascular complications in a patient of ICH is 4 percent.[1] Cardiovascular complications in ICH patient ranges from non ST and ST segment elevated myocardial infarction (STEMI), unstable angina, takotsubo's cardiomyopathy, cardiac arrhythmias and heart failure. Salvaging a patient with ICH and concomitant STEMI with percutaneous coronary intervention (PCI) is quite challenging with regards to managing the thrombotic risk vs bleeding risk. The need for antithrombotic therapy during and after PCI may prove devastating in a patient with ICH. The problem with existing oral antiplatelet agents are, late onset of action, prolonged offset time (3 to 7 days), poor oral bioavailability in hemodynamically unstable patients and non

availability of an effective antidote. Cangrelor and elinogrel are the only available intravenous platelet P2Y12 receptor inhibitors.[2] Cangrelor is a potent reversible antagonist of adenosine diphosphate induced platelet aggregatiaon. It has rapid onset time of 2 – 3 minutes and short offset with platelet function returning to normal in 30 - 60 minutes.[3] This predictable pharmacokinetics with short onset and offset of action makes cangrelor a potentially desirable option as a bridging therapy in a patient of ICH requiring PCI for ACS.

CASE DESCRIPTION

A 43-year-old gentleman, with no prior comorbidities was admitted elsewhere with right hemiparesis three days earlier. Computed tomography (CT) of brain showed an intra-parenchymal haemorrhage with mild perilesional oedema involving left fronto – parietal region in paramedian location extending into lateral ventricle causing mass effect (Figure 1A, 1B). On second day, he complained of chest pain and ECG showed ST elevations in anterior chest leads suggestive of an anterior wall STEMI (Figure 1C). Subsequently he was brought to us for further management. On examination patient was conscious, coherent and oriented with Glasgow coma score of 15 (ICH score of 2/6 implying 26 percent risk of mortality). His vitals parameters were blood pressure of 190/110 mm Hg, heart rate of 98 beats/minute, regular and oxygen saturation of 97 % (on room air). He had medical research council (MRC) grade of 2/5 power in both upper and lower limbs on the right side. His echocardiography showed moderate left ventricular dysfunction, ejection fraction of 35% and severe hypokinesia of apex, mid and distal septum with positive qualitative troponin T test (card test). Hypertension was managed with intravenous labetalol, oral cilnidipine and telmisartan. Hypertonic saline was given for perilesional oedema to target serum sodium over 145meq/l. Since, there was no neurological progression and a plan was made to check cerebral angiogram to look for a potential aneurysm/ bleeder, he was taken up for a simultaneous coronary angiogram. In view of a new worsening of LV dysfunction and progression of ischemic changes on ECG (Sclarovsky – Birnbaum grade I to II), (Figure 1C, Figure 1D) with ongoing chest pain, he was considered a candidate for revascularization. Coronary revascularization was carried out via percutaneous balloon angioplasty using semi - complaint balloon followed by a sirolimus eluting balloon (Magic touch 3 x 20 mm Drug Eluting Balloon (DEB) at 8 atm for 60 seconds). Intravenous Heparin 2500 IU was given peri - procedure (activated coagulation time was 114s). Thrombolysis in myocardial infarction (TIMI) grade III flow was achieved along LAD with borderline thrombotic plaque (Figure 2A – 2E). He was started on intravenous cangrelor at a dose of 0.75mcg/kg/min to prevent re-thrombosis for 48 hours. CT brain repeated, 48 hours after coronary revascularization showed no increase in size of the ICH. The patient was then started on ecospirin 75 mg and intravenous cangrelor was stopped. He was also maintained on beta blocker, diuretic, angiotensin receptor neprilysin inhibitor and ivabradine to improve heart function. The patient was observed for further 48 hours. There was no worsening of neurological deficit or drop in GCS through out the course of hospital stay. Echocardiograph repeated before discharge showed left ventricular ejection fraction of 40 – 45 % with regional wall motion abnormality in distal LAD territory. The patient was followed up after one week with mild improvement in the weakness of right upper and lower limb.

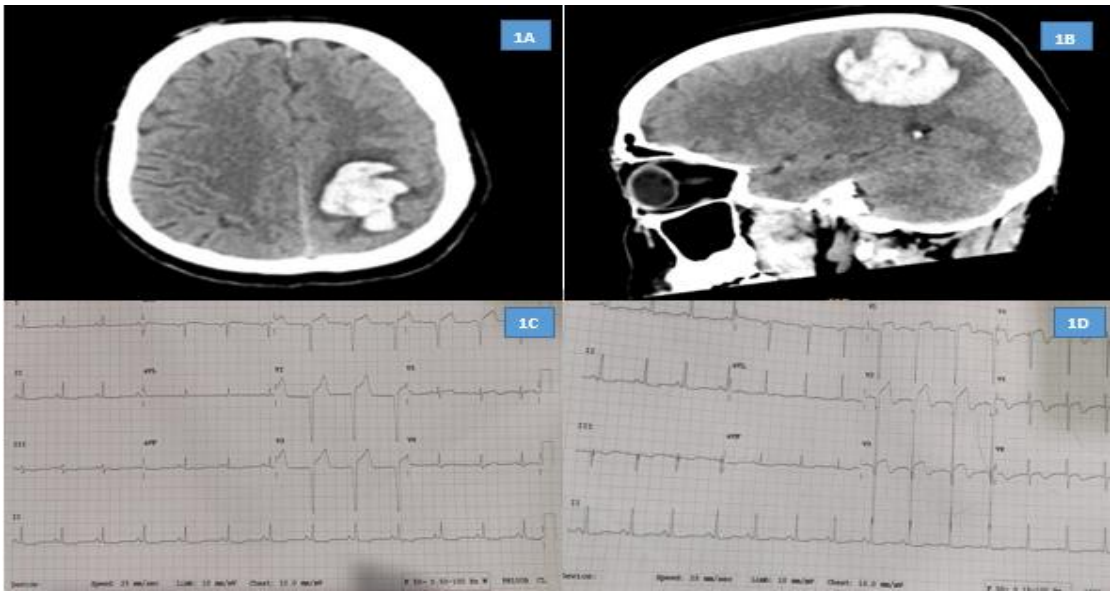

Figure 1A : CT Brain axial section showing left parietal ICH

Figure 1B: CT Brain sagittal section showing left fronto – parietal ICH

Figure 1C: 12 lead ECG showing hyperacute T waves with ST segment elevations in anterior leads.

Figure 1D: ECG showing progression of ischaemic changes with loss of R wave, ST segment elevations and T wave inversions in anterior leads

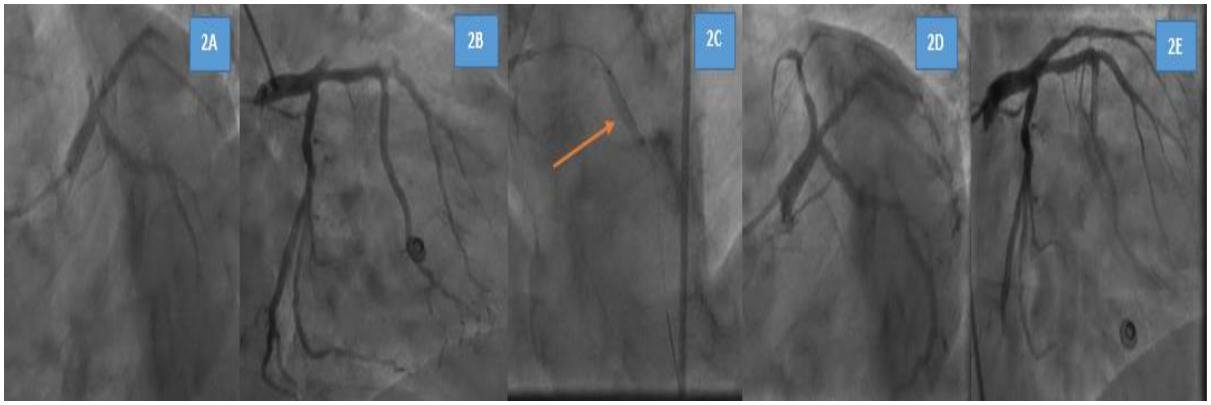

Figure 2: Selective coronary angiogram showing left coronary artery system

Figure 2A: Left anterior oblique caudal view showing occluded proximal left anterior descending artery

Figure 2B: Right anterior oblique caudal view showing occluded proximal left anterior descending artery

Figure 2C: Plain old balloon angioplasty (POBA) with drug eluting balloon (Magic touch 3 x 20 mm)

Figure 2D: Left anterior oblique caudal view showing post POBA – TIMI III distal flow

Figure 2E: Right anterior oblique caudal view showing post POBA – TIMI III distal flow

DISCUSSION

Anticoagulation in a patient with hypertensive ICH and concomitant acute coronary syndrome holds an extensive risk of worsening of ICH. Furthermore, in case of emergency decompressive craniectomy, reversal of antiplatelet

effect is an arduous task. Considering the risks and benefits of antithrombotic agents in this scenario, there is a need for a suitable agent which helps the heart with minimal risk to brain. The available oral antiplatelet agents in case of a PCI are ecospirin, clopidogrel, prasugrel and ticagrelor. Reversal of ecospirin and clopidogrel requires administration of platelets which can cause volume overload on already dysfunctional heart causing congestive cardiac failure and various transfusion related complications. There is no reversal agent for prasugrel and the newly identified antibody based antidote bentracimab for ticagrelor is not commercially available4. Unfractionated heparin is another choice where reversal is possible by protamine with a risk of intracoronary thrombus.[5] Cangrelor is an attractive choice in this scenario owing to its short onset time of action and rapid offset following discontinuation. It is traditionally used in acute MI with cardiogenic shock as oral antiplatelet agents are poorly absorbed in the gut and acute MI with severe triple vessel coronary disease requiring early coronary artery bypass graft. The infusion dose of 0.75mcg/kg/min is good enough to yield a platelet inhibition of more than 60 percent[6] with significant reduction in ischemic events during PCI when compared to clopidogrel. [7] In case of increase in ICH, cangrelor can be discontinued and because of its rapid offset without any reversal is advantageous with regain of platelet function in 30 minutes.

Restoration of TIMI III flow is of paramount importance in managing STEMI to prevent irreversible myocardial injury. PCI with a Drug eluting stent (DES) is the current 1st line of management in a patient with STEMI.[8] DES implantation however, commits patients to a prolonged course of dual antiplatelet therapy. There are numerous studies demonstrating abbreviated DAPT, however that still requires 4-6 weeks of therapy.[9] POBA has a restenosis rate of approximately 30 % of patients within six months following a successful procedure.[10] Therefore, it is not preferred as a stand-alone therapy during PCI. Use of DEB in STEMI is an off-label indication However, it was a viable option in our case where implantation of stent was contraindicated as the patient could not receive necessary antiplatelet loading doses.[11] Deferred stenting strategy did show a role in avoiding unnecessary stent placements in patients with STEMI who only have a minor atheromatous lesion to begin with.[12] This justifies the use of DEB to restore TIMI III flow and do an interval PCI at a later date.

We did plan on repeating the coronary angiogram after 4-6 weeks, once the patient improved neurologically and was cleared for prolonged antiplatelet therapy to consider a stent placement if needed. However, the patient was lost to follow up and we could not follow up the angiographic outcome of DEB intervention. Cangrelor although is widely available in pharmacies, it is not regularly used. This case provides a strong testimony to the utility of cangrelor where the short duration of onset and offset of action is of paramount importance.

CONCLUSION

Cangrelor offers a plausible solution as an excellent bridging therapy in patients of ICH complicated by ACS requiring PCI. The role of DEB as an alternative to DES implantation during PCI needs further research.

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