Cerebrovascular infarct associated with intracoronary adenosine: a possible rare fractional flow reserve complication

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Singapore Med J 2021, 1–5
https://doi.org/10.11622/smedj.2021085
Published ahead of print: 18 June 2021

Online version can be found at
http://www.smj.org.sg/online-first
Dear Sir,

Over the past 20 years, fractional flow reserve (FFR) has emerged as a safe and dynamic modality to assess the haemodynamic significance of angiographically intermediate coronary lesions in order to guide appropriate management. Adequate induction of hyperaemia remains a crucial step in the accurate measurement of FFR. Intracoronary adenosine has been well described as a reasonable alternative to intravenous adenosine infusion to induce hyperaemia, with no noticeable increase in conduction delay or other procedural complications.\(^{(1,2)}\) We report a rare case of stroke that occurred after the induction of hyperaemia with intracoronary adenosine.

A 59-year-old male smoker with a history of pulmonary silicosis and rheumatoid arthritis was admitted for evaluation of worsening dyspnoea. His cardiovascular physical examination was unremarkable. Resting electrocardiogram showed sinus rhythm with nonspecific T wave inversions, and two sets of cardiac troponins were within normal limits. Resting transthoracic echocardiogram revealed a mildly depressed left ventricular systolic function of 44%, with regional wall motion abnormalities. Myocardial perfusion imaging (MPI) demonstrated a moderate-sized non-transmural infarct in the distal to basal inferolateral walls.

The patient underwent diagnostic coronary angiography via the right radial approach. This showed a left dominant system with a borderline lesion in the mid-left anterior descending artery (LAD) segment, as well as a subtotally occluded obtuse marginal artery. FFR of the mid-LAD lesion was performed using a 6-French Ikari left 3.5-cm guider with a PressureWire\textsuperscript{TM} X guidewire system (St Jude Medical, St Paul, MN, USA). Prior to FFR, 6,000 units of intracoronary heparin was administered, followed by sequential boluses of 150 mcg and 200 mcg of intracoronary adenosine to induce hyperaemia. The patient developed a brief period of
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asystole immediately after 200 mcg of intracoronary adenosine was administered. FFR of the mid-LAD was haemodynamically insignificant. Immediately after the 200-mcg dose of intracoronary adenosine, the patient developed slurring of speech and left-sided weakness. He remained clinically stable with a Glasgow Coma Scale score of 15/15. A neurological examination showed left dysmetria, with 4/5 power over the left upper and lower limbs. The clinical impression was that of left ataxic hemiparesis, likely due to a cerebrovascular accident. Urgent computed tomography of the brain and cerebral angiography did not show any intracranial haemorrhage or large vessel occlusion. Emergent thrombolysis was deferred, as the overall National Institutes of Health Stroke Scale was low and there were concerns of potential haemorrhagic conversion since the patient had just received intracoronary heparin.

The patient recovered rapidly over the next two days and had minimal neurological deficit. The presence of an acute non-haemorrhagic infarct in the right frontoparietal region was confirmed on magnetic resonance (MR) imaging of the brain, while the MR angiogram sequence showed focal stenosis of a small right M2/M3 middle cerebral artery branch near the region of the infarct. Telemetry monitoring did not reveal any atrial fibrillation and no left ventricular thrombus was seen on cardiac MR imaging.

Considering the temporal sequence of events and imaging findings, we opined that the most likely mechanism of stroke was transient hypoperfusion during the induction of hyperaemia in the presence of a pre-existing M2/M3 significant stenosis. In the medical literature, the only case of a stroke being precipitated by adenosine was that of a 69-year-old woman who underwent MPI in 1997, and the authors had similarly postulated that adenosine-mediated hypoperfusion of a compromised cerebral artery was the likely mechanism.(3)

One of the challenges of performing FFR is achieving maximal hyperaemia to ensure the validity of FFR results. In our laboratory, both intravenous adenosine and intracoronary adenosine are used for the measurement of FFR. In this case, intracoronary adenosine was
chosen for its ease of administration. Dosing for intracoronary adenosine is highly variable, with doses of 40–600 mcg described in the literature.\(^{(1)}\) In our practice, the use of ‘high-dose’ adenosine is more prevalent, as there is concern that significant lesions may be missed with a ‘low-dose’ protocol. Moreover, the occurrence of brief periods (typically 2–3 seconds) of asystole during the administration of an intracoronary adenosine bolus is not infrequent. Nevertheless, as these episodes were typically brief, self-terminating, and deemed to be of no clinical significance, we had previously no reservations about administering ‘high-dose’ intracoronary adenosine boluses during FFR measurement. In our opinion, the current case may highlight a potentially rare but serious limitation of this technique. Moving forward, newer modalities such as quantitative flow ratio and instantaneous wave-free ratio, which correlate well with FFR and have the advantage of avoiding the need for hyperaemic agents, may help to reduce such complications.

Yours sincerely,

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REFERENCES


FIGURES

![Coronary angiography image](image_url)

**Fig. 1** Coronary angiography image of the left coronary artery in anteroposterior cranial view shows a borderline mid-left anterior descending artery lesion (white arrow) and a partially visualised subtotally occluded obtuse marginal branch (black arrow) originating from the distal left circumflex.
Fig. 2 Diffusion-weighted MR image of the brain shows an acute non-haemorrhagic infarct in the right frontoparietal region.