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CASE REPORT

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Positron emission tomography rubidium-82 myocardial perfusion imaging in diagnosing uncommon paediatric acute coronary syndrome: a case report

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Abstract

Background Acute coronary syndrome (ACS) is uncommon among the paediatric population with no guideline in the management in this age group up to this date. This case report aims to introduce the Positron Emission Tomography Rubidium-82 (PET Rb-82 MPI) as one of the non-invasive diagnostic tools in paediatric acute coronary syndrome.

Case presentation Patient is an 11-year-old boy with underlying Nephrotic syndrome who was referred to our hospital with the chief complaint of chest pain. This was associated with raised cardiac enzyme and S–T depression on the posterior leads of electrocardiogram. On his arrival, we noted raised lipid profile as well as proteinuria and hypoalbuminaemia. He had frequent relapse of Nephrotic syndrome with the latest episode was three months ago. He has a strong family history of ischaemic heart disease whom his father had an episode of myocardial infarction at the age of 40 as well as a strong family history of hypercholesterolaemia. His father and paternal uncle were diagnosed with hypercholesterolaemia at their early age. He was arranged for Coronary Computed Tomography Angiography which subsequently followed by PET Rb-82 MPI. The PET Rb-82 MPI demonstrated a large area of stress induced ischaemia in the left anterior descending, left circumflex and right coronary artery territories. The left ventricular size is normal with good systolic function and normal wall motion. Global coronary flow reserve was still preserved at 2.07. Following the multi-disciplinary meeting, diagnosis of ACS was established. Patient was treated with dual anti-platelets, and he was then arranged for coronary angiography. The coronary angiography showed complete occlusion of the left circumflex artery from the proximal segment. There was a mild disease at mid segment of the diagonal artery with myocardial bridging. There was also a moderate disease from proximal segment of the dominant right coronary artery. Paclitaxel drug coated balloons were inserted into the diagonal and left circumflex arteries.

Conclusions This rare case report on paediatric ACS highlights the diagnostic value of PET Rb-82 MPI as one of the non-invasive imaging tools in diagnosing paediatric acute coronary syndrome.

Keywords Paediatric, Acute coronary syndrome, PET Rubidium-82

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Background

Acute coronary syndrome (ACS) in paediatric is uncommon that most of the information related to this are gained from case reports. A population databased study conducted by Mahle et al. [1] estimated that risk of myocardial infarction (MI) in adolescent is 6.6 per 1 million-patient years. The study also demonstrated that male, smoker, and history of substance abuse are statistically significant to paediatric MI when compared to the population of similar age. Unlike the adult ACS, there is a wider range of the pathophysiology related to the paediatric ACS [1]. This case report aims to introduce the Positron Emission Tomography Rubidium-82 (PET Rb-82 MPI) as one of the non-invasive diagnostic tools in paediatric acute coronary syndrome.

Case presentation

History of presentation

Patient is an 11-year-old boy with underlying Nephrotic syndrome who was referred to our hospital with the chief complaint of chest pain. This was associated with raised cardiac enzyme and S–T depression on the posterior leads of electrocardiogram (ECG). On his arrival, we noted raised lipid profile as well as proteinuria and hypalbuminaemia. Patient had frequent relapse of Nephrotic syndrome with the latest episode was three months ago. He has a strong family history of ischaemic heart disease whom his father had an episode of myocardial infarction at the age of 40 and strong family history of hypercholesterolaemia. His father and paternal uncle were diagnosed with hypercholesterolaemia at their early age.

Investigations

He was then arranged for Coronary Computed Tomography Angiography (CCTA) which demonstrated moderate to severe stenosis at mid segment of first diagonal artery (Fig. 1) with total occlusion at the mid segment of left circumflex artery (Fig. 2). Otherwise, the right coronary artery was normal.

Subsequently, he underwent myocardial perfusion scan with Discovery 710 MIDR GE Healthcare Positron Emission Tomography Rubidium-82 Myocardial Perfusion Imaging (PET Rb-82 MPI). The body mass index of the young patient was 18.8 kg/m^2. The imaging protocol was initially acquired with low dose non-contrasted gated computed tomography (CT) scan from carina to the base of the heart for attenuation correction. It was then followed by rest imaging PET acquisition with the patient in supine position for approximately 6 min following the intravenous injection of 20.0 mCi of Rb-82. Successively, it was followed by PET acquisition for pharmacological stress imaging using adenosine. The infusion adenosine was given intravenously at 140mcg/kg/min for a total duration of 6 min with 20.0 mCi of Rb-82 injected intravenously at 3 min during the adenosine infusion. The patient's heart rate increased from 68 to 115 bpm at peak stress. The patient's blood pressure at rest was 103/71 mmHg and decreased to 93/54 mmHg at peak stress procedure. Baseline ECG was sinus rhythm and subsequently we noted S–T elevation at lead II, III and aVF with reciprocal changes at lead V2–V3 at third minute into the stress study (Fig. 3). Otherwise, patient was asymptomatic throughout the procedure. The stress-rest study completed in approximately 20 min.

The images were then processed and displayed using the GE workstation. There was a large area of stress induced ischaemia in the left anterior descending, left circumflex and right coronary artery territories (Fig. 4) on the PET Rb-82 MPI. The transient ischaemic dilatation ratio is 1.00 (Fig. 5). The left ventricular (LV) size is normal with good systolic function (Stress Ejection Fraction:65%; Rest Ejection Fraction:56%) and normal wall motion (Fig. 6). Despite the myocardial flow reserve of left circumflex artery is 1.03 the global coronary flow reserve (CFR) was still preserved at 2.07 (normal > 2.0) (Fig. 7).

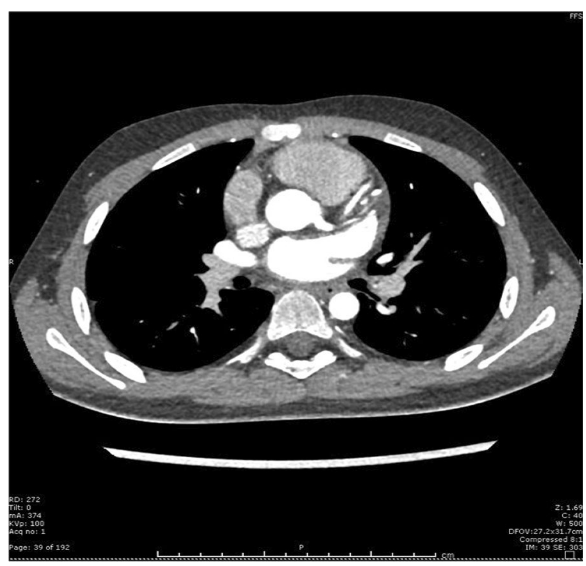

Fig. 1 CCTA of left anterior descending (LAD) coronary artery. The LAD coronary artery is a normal-size vessel, which reaches the apex. There is no luminal stenosis at the proximal or mid segments of the LAD coronary artery. It gives rise to a moderately sized diagonal branch with moderate to severe (50–80%) stenosis at the mid segment. The distal vessel is normal and ends at the apex

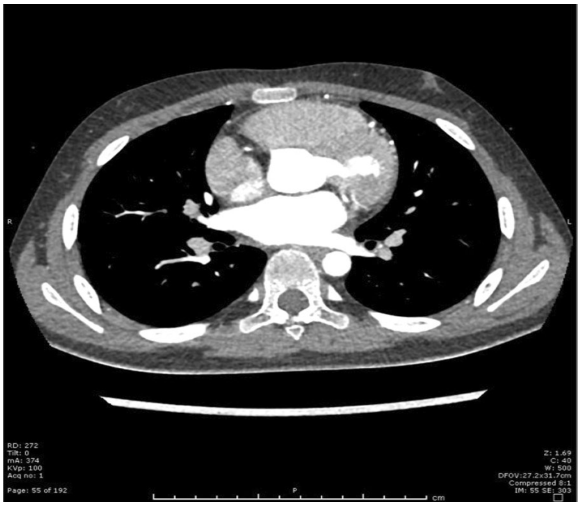

Fig. 2 CCTA of left circumflex coronary artery (LCX). The left circumflex coronary artery is a non-dominant vessel divide into a small-sized postero-lateral branch. There is total (100%) occlusion at the mid segment in the artery

Management

During the multi-disciplinary team meeting, we agreed that this young patient would benefit from the coronary angiography which demonstrated complete occlusion of the left circumflex artery from proximal segment and mild disease at mid segment of the diagonal artery with myocardial bridging (Figs. 8 and 9). There was also moderate disease from proximal segment of the dominant right coronary artery (Fig. 10). Otherwise, the left main stem was normal. Paclitaxel drug coated balloon (DCB) were then inserted into both diagonal and left circumflex arteries. The young patient was asymptomatic post procedure, and he was discharged home with tablet Ezetimibe 10 mg once daily, tablet Rosuvastatin 20 mg once night, tablet Cardiprin 100 mg once daily, tablet Clopidogrel 75 mg once daily and tablet Prednisolone 60 mg once daily (on tapering dosage).

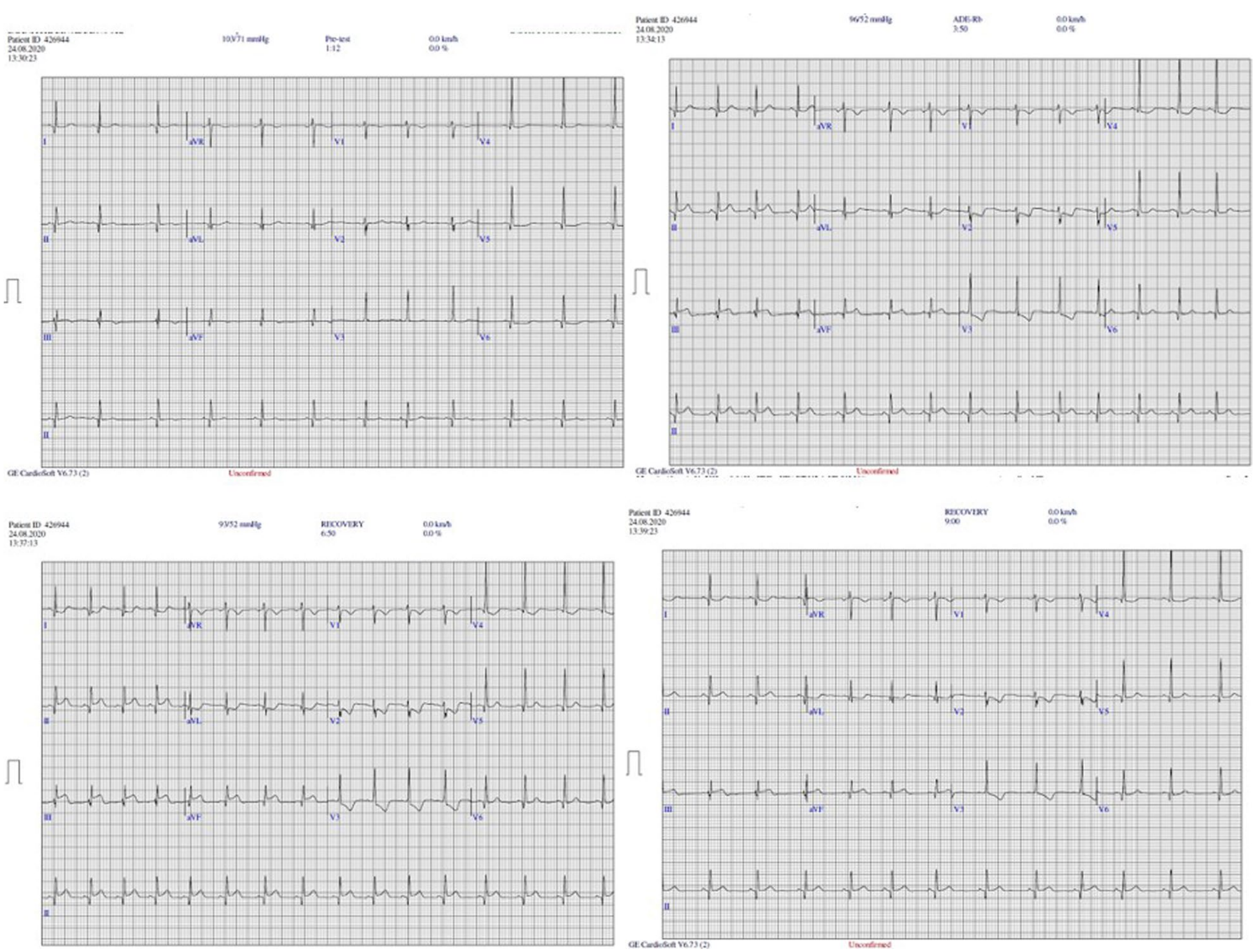

Fig. 3 Serial ECG during stress protocol. Taken at pre-test, 3-min, 6-min and during recovery period showing S-T elevation at the inferior leads with reciprocal changes at lead V2-V3

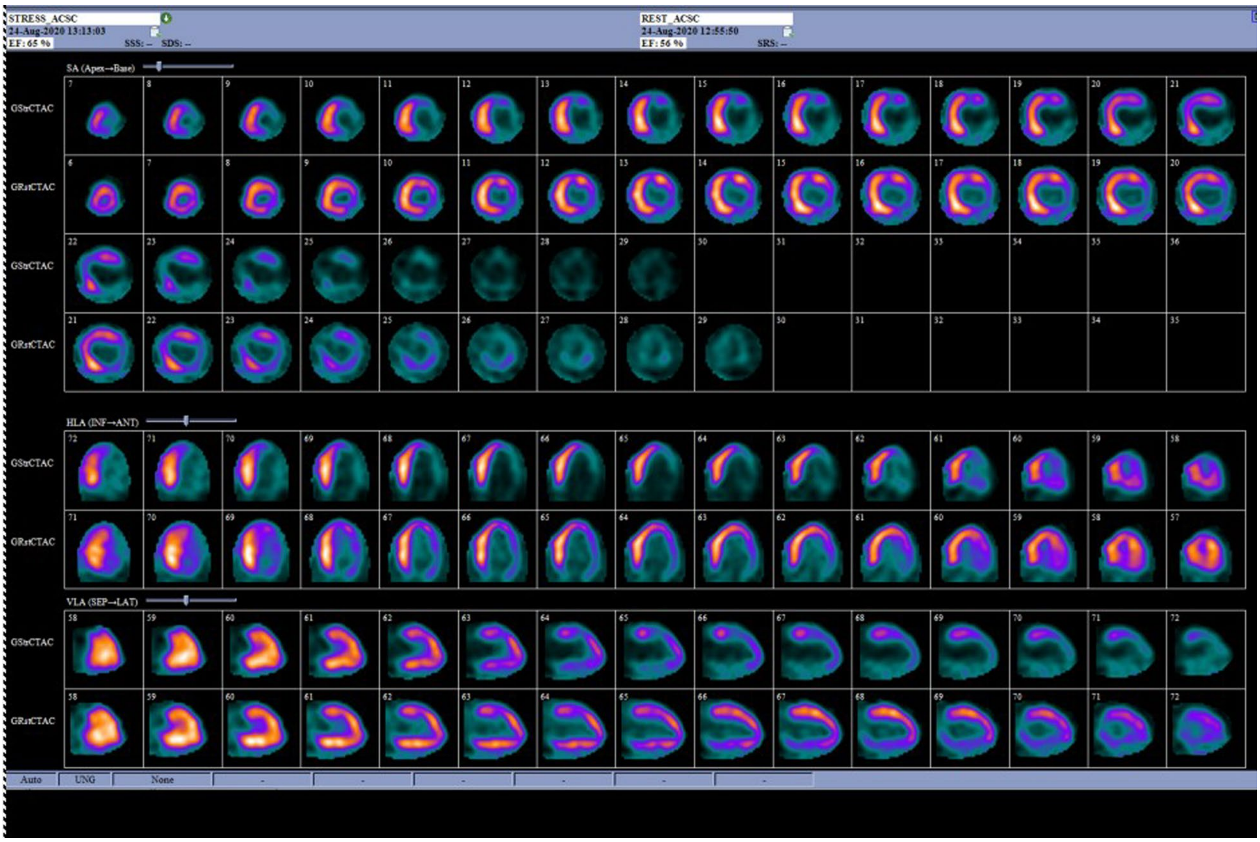

Fig. 4 PET Rb-82 MPI LV myocardial perfusion defect. There is a large area of completely reversible and reduced tracer uptake in the apical to basal anterior, apical lateral, mid to basal anterolateral and apical to basal inferior segments. There is another area of partially reversible and reduced tracer uptake in the mid to basal inferolateral segments

Discussion

We believe that the underlying uncontrolled Nephrotic syndrome combined with hypercholesterolaemia are the two main risk factors of ACS in our patient. There is one similar case reported on acute anterior myocardial infarction in a 22-year-old uncontrolled nephrotic syndrome patient with underlying familial hyperlipidaemia [2]. Patient with Nephrotic syndrome is known to be in a hypercoagulable state, which resulted in high prevalence of thrombus formation due to the alteration in the activity and concentration of the coagulation factors [3]. Hypercholesterolaemia is also known to commonly associated in this group of patients [3]. As there is no controlled trial to guide early treatment of ACS in this age group, the current management of this medical condition is mainly adapted from the adult ACS [3]. In our case report, our patient was decided for both anatomical and functional non-invasive imaging before the coronary angiography. The CCTA allows us to assess the coronary artery stenosis, whereas the PET Rb-82 MPI allows us to evaluate the perfusion status as well as the coronary flow reserve.

We had decided to follow our department protocol for adult PET Rb-82 MPI as well as adapting the article on the role of myocardial perfusion Single Photon Emission Computed Tomography (SPECT) into our practice of this paediatric case [4]. For patient preparation, motionless acquisition remains the greatest concern during a myocardial perfusion imaging. This is possible with intravenous midazolam (0.1mg/kg body weight; maximum dose up to 0.5 mg/kg body weight) or phenobarbital in children younger than 5 years of age [4]. As our patient is a young teenager who can perfectly follow our command, no sedation was required for the imaging. He was advised for caffeinated free drink for 24 hours and his newly started vasodilator (dipyridamole) was withheld to ensure he would be sufficiently augmented during the stress study. Other conventional preparations; fasting for at least 6 hours and securing a patient IV line were also instructed to the primary team.

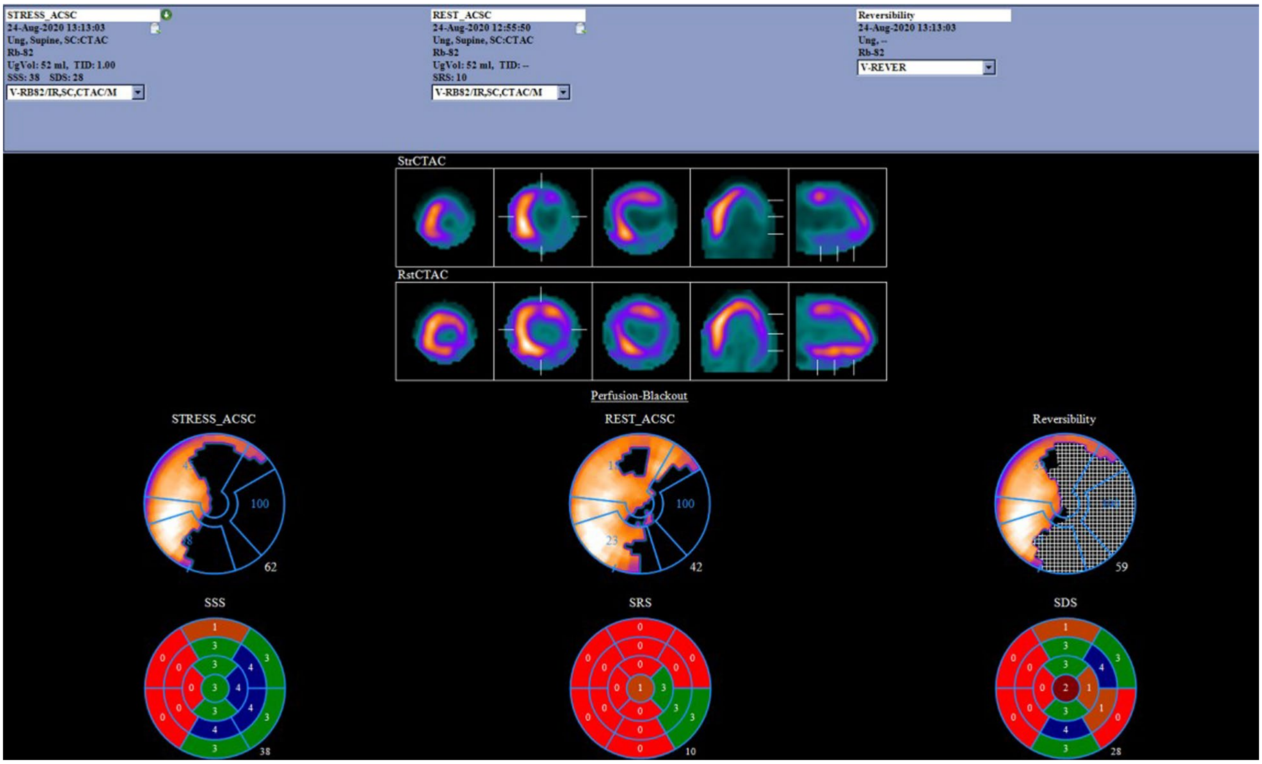

Fig. 5 PET Rb-82 MPI. Transient ischaemic dilatation ratio was 1.00 (Normal value: < 1.15)

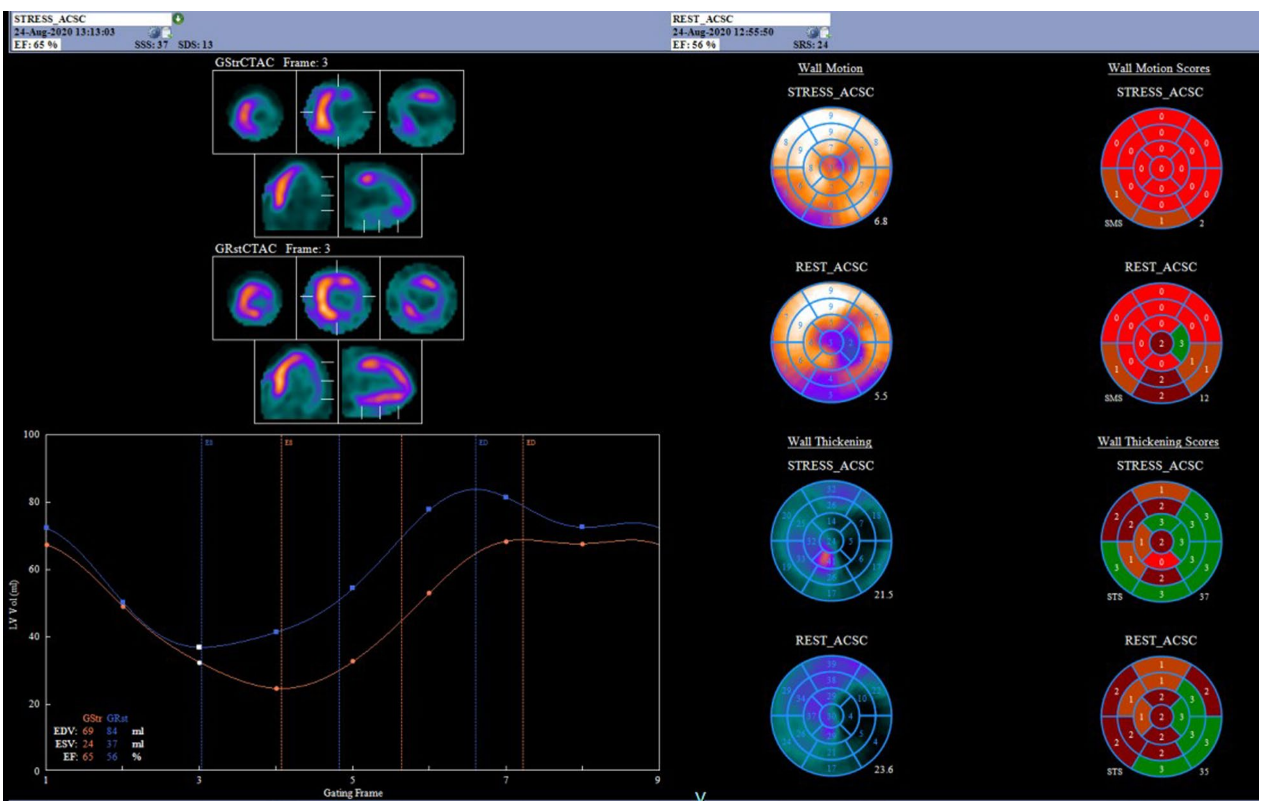

Fig. 6 PET Rb-82 MPI Stress vs Rest. Ejection fraction: 65% versus 56% ED volume: 69 mL versus 84 mL ES volume: 24 mL versus 37 mL. LV global function: good. LV volume: normal. LV regional function: normal LV wall motion

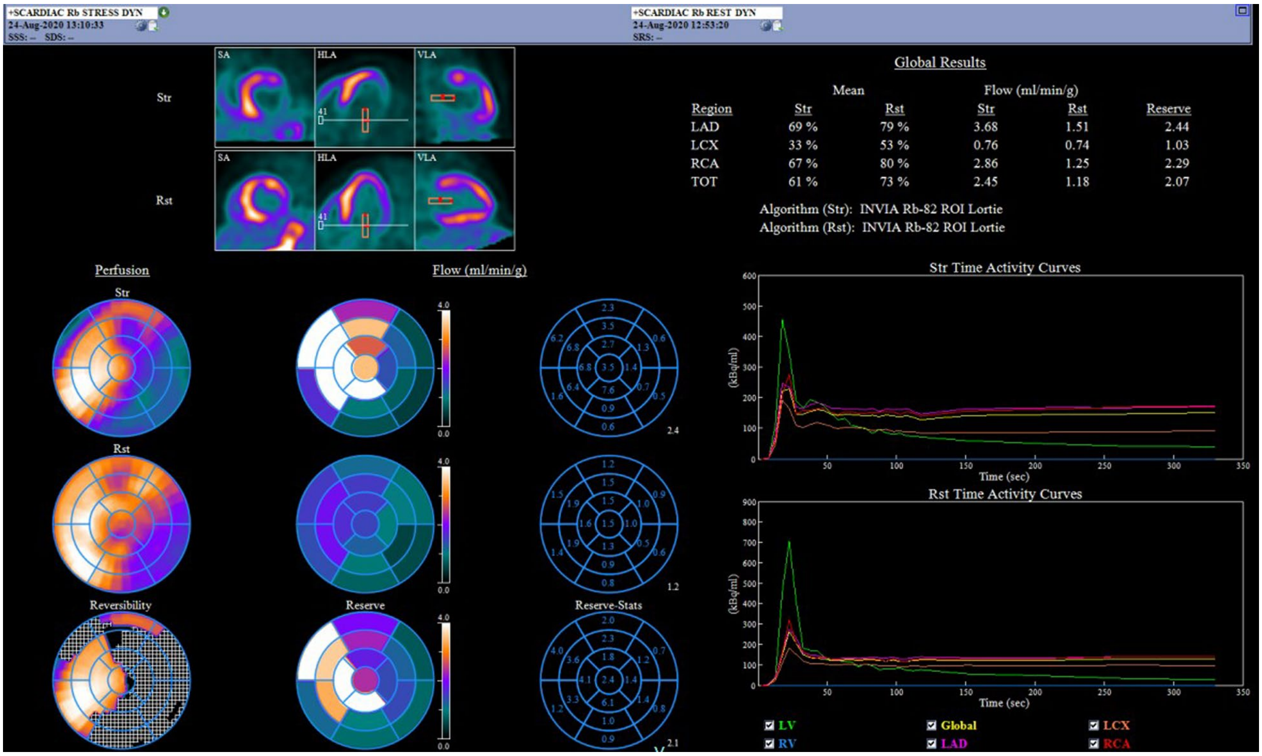

Fig. 7 PET Rb-82 MPI. Normal global flow reserve at 2.07, with reduced regional coronary flow reserve of 1.03 at the LCX

Fig. 8 Pre and post Paclitaxel drug coated balloon (DCB) at the complete occlusion from proximal segment of left circumflex artery

Our young patient body mass index is 18.8 kg/m^2. Therefore, based on our department Rb-82 dose protocol he was given 20.0 mci of Rb-82 during both rest and stress study. During stress study, he was given IV infusion of adenosine at 140 mcg/kg/min for 6 min duration. According to the review article, the adenosine is suggested to be infused at a dose of 140 mcg/kg body weight per minute like the adult dosing by an infusion pump for

Fig. 9 Pre and post DCB at mild disease of mid segment of diagonal artery

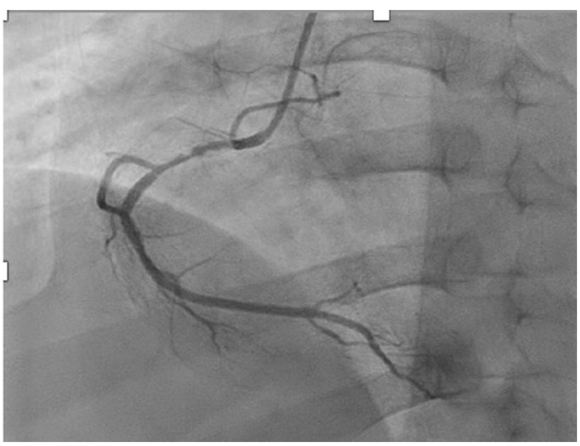

Fig. 10 Moderate disease from proximal segment of the dominant right coronary artery

4–6 min with total amount of 0.56–0.84 mg/kg [4]. Similar dose of adenosine was also documented given to all ten patients who undergone SPECT myocardial perfusion scan in a study of paediatric patients after arterial switch operation [5]. Our patient heart rate was successfully increased by 69% from the basal heart rate while his ECG showed ST elevation at lead II, III and aVF with reciprocal changes at lead V2–V3 during the stress study. The PET-Rb 82 perfusion study was completed with no side effects and complications (Fig. 11).

The results of non-invasive imaging; CCTA and PET Rb-82 perfusion study are compared to the invasive coronary angiography in Table 1. Each modality has its own strength in giving us information of the coronary artery status [6]. CCTA was able to identify the stenosis at the level of branching artery (diagonal artery) accurately

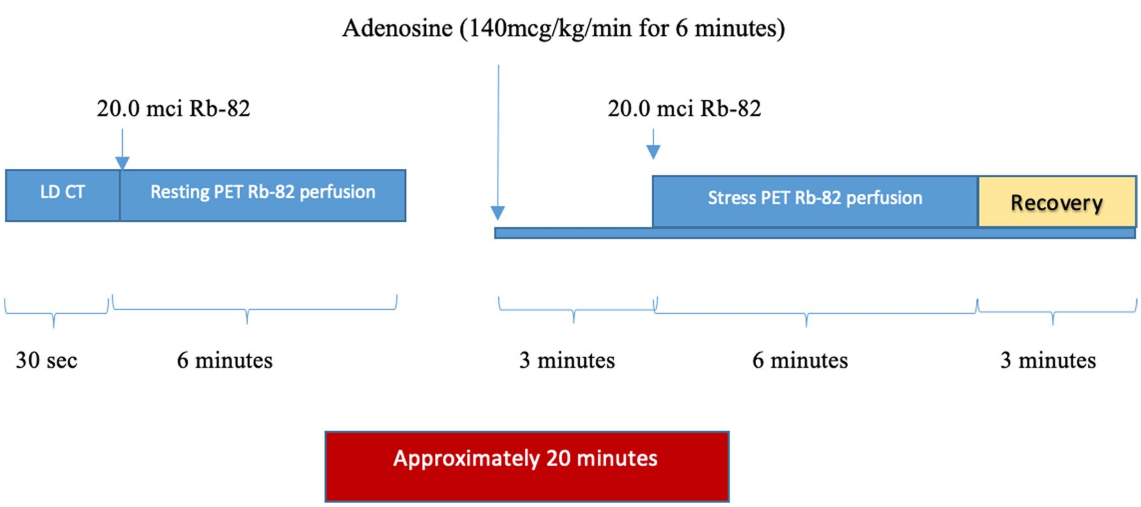

Fig. 11 Schematic illustration of the PET Rb-82 perfusion study. Low dose CT (LD CT)

Table 1 Comparison of the findings between CCTA, PET Rb-82 perfusion scan and Coronary Angiography

	CCTA	**PET Rb-82 MPI**	**Coronary Angiography**
Left Anterior Descending Artery (LAD)	No luminal stenosis at the proximal or mid segments of the LAD coronary artery. A moderately sized diagonal branch with moderate to severe (50- 80%) stenosis at the mid segment. The distal vessel is normal and ends at the apex	Area of completely reversible and reduced tracer uptake in the apical to basal anterior, apical lateral and apical inferior indicating as stress induced ischaemia in the LAD territory LAD myocardial flow reserve of 2.44	Mild disease at mid segment of the diagonal artery with myocardial bridging
Left Circumflex Artery (LCX)	Total (100%) occlusion at the mid segment in the artery	Area of completely reversible and reduced tracer uptake at mid to basal anterolateral with another area of partially reversible and reduced tracer uptake in the mid to basal inferolateral segments indicating as stress induced ischaemia in LCX territory LCX myocardial flow reserve of 1.03	Complete occlusion of the left circumflex artery from proximal segment
Right Coronary Artery (RCA)	Normal artery	Area of completely reversible and reduced tracer uptake at the mid to basal inferior segments indicating as stress induced ischaemia in RCA territory RCA myocardial flow reserve of 2.29	Moderate disease from proximal segment of the dominant right coronary artery

as per coronary angiography. On the other hand, PET Rb-82 gave us information on the perfusion status of the LAD territory. Based on the PET Rb-82 MPI, there is a large area of completely reversible perfusion defect indicating stress induced ischaemia in the LAD territory. CCTA also accurately identified the total occlusion of LCX as per documented by the coronary angiography. PET Rb-82 perfusion study reported area of partially reversible and reduced tracer uptake indicating stress induced ischaemia at the LCX territory. Superiorly, PET Rb-82 MPI demonstrated stress induced ischaemia at the RCA territory seen as moderate disease from proximal segment of the dominant right coronary artery on coronary angiography. This finding of RCA was not demonstrated by the CCTA in our young patient. Recent study by Danad I *et al* reported that CCTA and PET had shown similar sensitivity and negative predictive value in diagnosing CAD [6]. However, CCTA had proven to be significantly lower in specificity and positive predictive value when compared to PET in diagnosing CAD [6]. Despite preserved global coronary flow reserve of 2.07 (normal > 2.0), this study had demonstrated severely impaired regional myocardial flow reserve of LCX at 1.03. This finding of severely reduced regional myocardial flow reserve of LCX emphasizes the need of early revascularization of this artery.

For decades, SPECT for myocardial perfusion imaging (MPI) has been an established non-invasive imaging tool for assessing suspected coronary artery disease [7]. However, in the recent years PET myocardial perfusion imaging has started to become more prevalent due to its advantages over SPECT. PET MPI can be performed in a shorter time with lower radiation exposure when compared to SPECT MPI [7]. Few radiopharmaceuticals of PET MPI include Nitrogen-13 ammonia, Rubidium-82 and Oxygen-15. Rubidum-82 has become our radiopharmaceutical of choice as there is no in-house cyclotron in our centre. Due to its shorter tracer half-life, PET MPI will prefer pharmacological stress rather than exercise stress test [7]. In view of the tracer property and scanner related factors (PET-CT system for attenuation correction), the image resolution of PET MPI is significantly better than the SPECT MPI [7]. Thus, it explains its higher accuracy in diagnosing coronary artery disease (CAD). There are several studies evaluating the diagnostic accuracy of PET MPI compared to other modalities. One of the recent studies concluded the accuracy of PET MPI when compared to fractionated flow reserve as 85%, statistically significant than the accuracy of CCTA and SPECT in diagnosing CAD [6]. PET MPI also reported the highest sensitivity and specificity in detecting CAD; 87% and 84%, respectively, when compared to the above modalities [6]. Furthermore, PET MPI also proven to carry a high prognostic value. A recent large study with more than 16 000 patients concluded that patient with 5% or more ischaemia burden on PET Rb-82 MPI had improved survival with early revascularisation.

Besides assessment on the relative perfusion, PET MPI also provides us with the assessment of myocardial blood flow at stress and rest as well as the coronary flow reserve. CFR estimates the ratio of total coronary blood flow with maximal hyperaemia (at peak stress) compared to rest flow [7]. Therefore, CFR reflects the burden of CAD of the entire coronary artery and estimates the patient's global status by reflecting the combined effect of disease both in the macro- as well as microcirculation [7]. A recent study has recommended that use of myocardial blood flow or segmental flow reserve values in combination with visual assessment of Rb-82 PET scans in detecting obstructive coronary artery disease [8]. This study has proven its significant diagnostic value compared to global CFR in coronary artery disease patients [8].

One of the advantages of CFR is to assist the diagnosing of left main and multivessel CAD in otherwise normal MPI [7]. These two conditions may lead to a state of balanced ischaemia which may appear as 'normal' MPI thus left undetected on the SPECT images. PET MPI on the other hand, with the complimentary CFR parameter allows us to identify this high-risk patient who present as 'normal' on perfusion study. A study of 120 patients who went for PET MPI concluded that most patients with multivessel CAD had reduced CFR (<2.0) [9]. A more recent study comparing SPECT and PET accuracy also demonstrated out of 21 patients with multivessel disease or left main disease, 4 (19.0%) had normal perfusion results with SPECT, while quantitative PET correctly identified ischaemia in all patients [6].

The other advantage of PET MPI is the ability to diagnose subclinical CAD (endothelial dysfunction or coronary calcification) and microvascular dysfunction in patient with absence of overt CAD or normal findings on coronary angiography [7]. The ability of PET over SPECT in providing CFR parameter allows us to assess the myocardium beyond the epicardial coronary artery [7]. Lastly, PET-derived myocardial blood flow and CFR are strong predicting factors for major adverse cardiac event [7]. Few studies have concluded that besides the known traditional risk factors, these two parameters have proven to give incremental risk stratification [7]. A study by Patel KK *et al* with PET Rb-82 had concluded that coronary flow reserve of 1.8 and lower will significantly benefit from early revascularization [10]. Study has also proven that myocardial blood flow and CFR threshold values

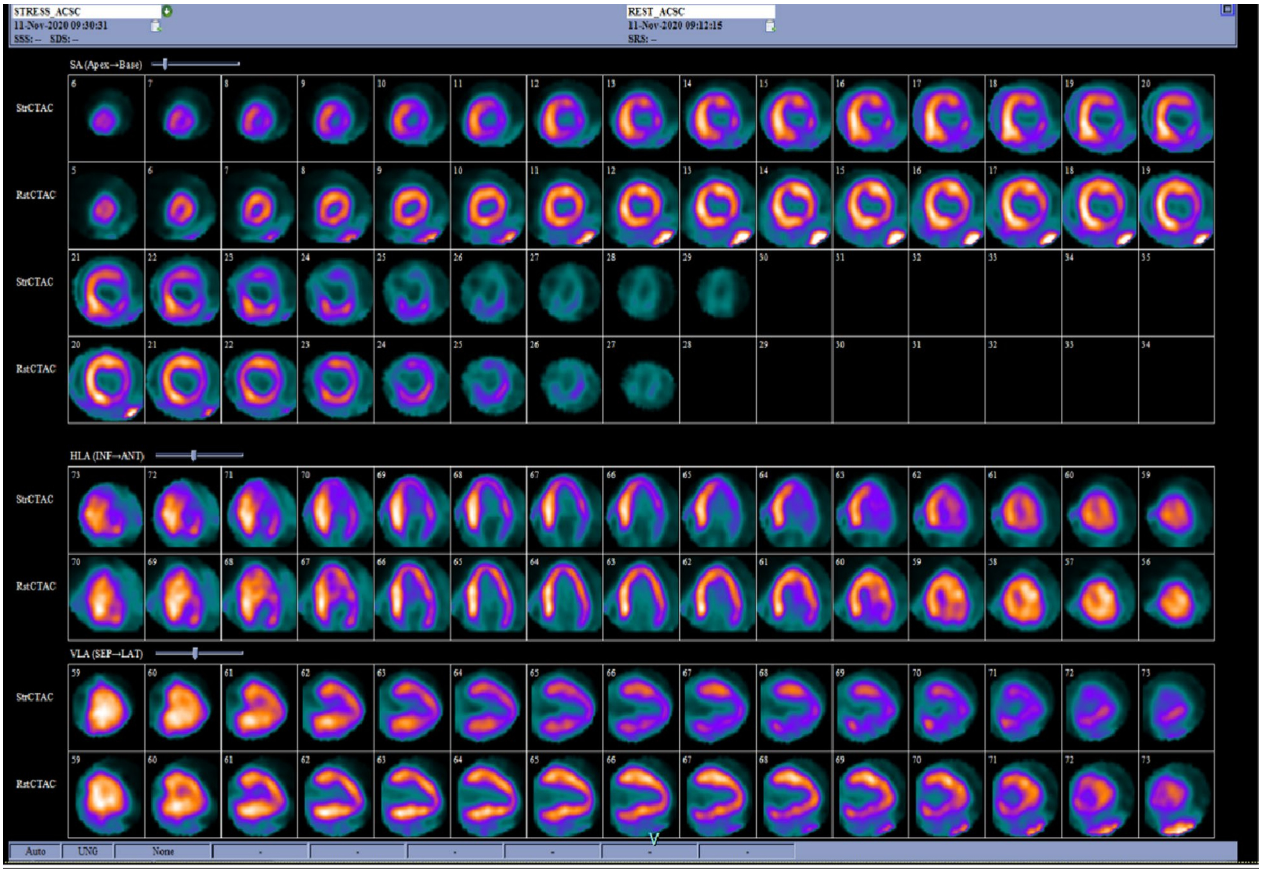

Fig. 12 PET Rb-82 MPI post revascularization. Large area of stress induced ischaemia involving the apex and apical to basal segments of lateral wall (LCX territory)

are highly based on sex and age group in low CAD risk patients, with female demonstrating higher threshold values than male for all age groups [11].

Mentioned above are all the advantages of PET over other modalities in diagnosing CAD but specifically in adult population. Therefore, further exploration into paediatric cases may further extend our understanding into the role of PET in paediatric cardiology. It is also worth to mention, the cut-off points of <2.0 for abnormal CFR in this study is adapted from the understanding of the adult population study. Therefore, the reliability and the significance of this value in paediatric population remains unclear. A study on the impact of the findings on PET MPI on patient management (i.e., medical therapy or percutaneous coronary intervention) will also a potential field to explore to solidify our current understanding in this field.

Follow-up

The patient was scheduled for a PET Rb-82 MPI 3 months later to reassess the myocardial perfusion status post-intervention. Patient was asymptomatic since discharge and the repeated scan shows significant improvement. There is a large area of stress induced ischaemia involving the LCX territory (Figs. 12 and 13). Otherwise, other areas show normal perfusion. The myocardial flow reserve of the three main coronary arteries and global flow reserve are also normal (> 2.0) (Figs. 14 and 15).

Conclusion

This rare case report on paediatric ACS highlights the diagnostic value of PET Rb-82 MPI as one of the non-invasive imaging tools in diagnosing paediatric acute coronary syndrome.

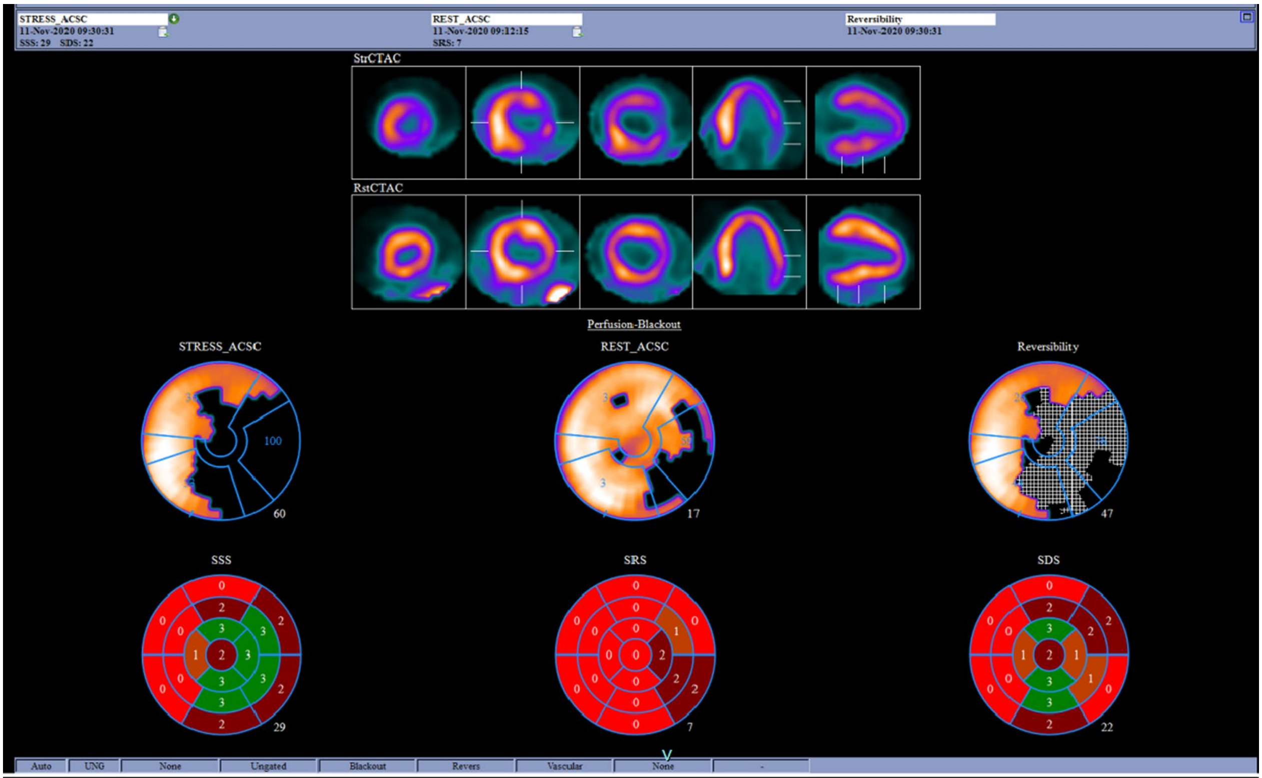

Fig. 13 PET Rb-82 MPI post revascularization. Large area of stress induced ischaemia involving the LCX territory with SDS of 22

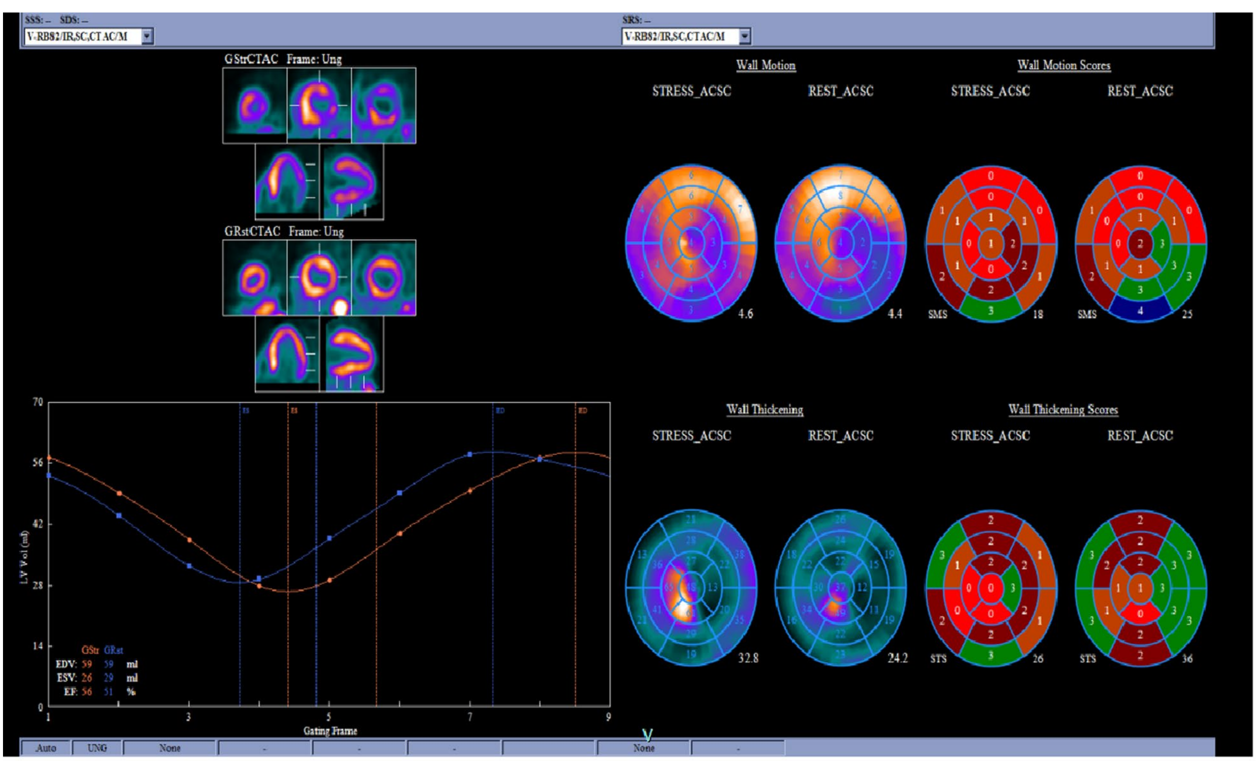

Fig. 14 PET Rb-82 MPI post revascularization. The ejection fraction during stress study is 56% and during rest study is 51%

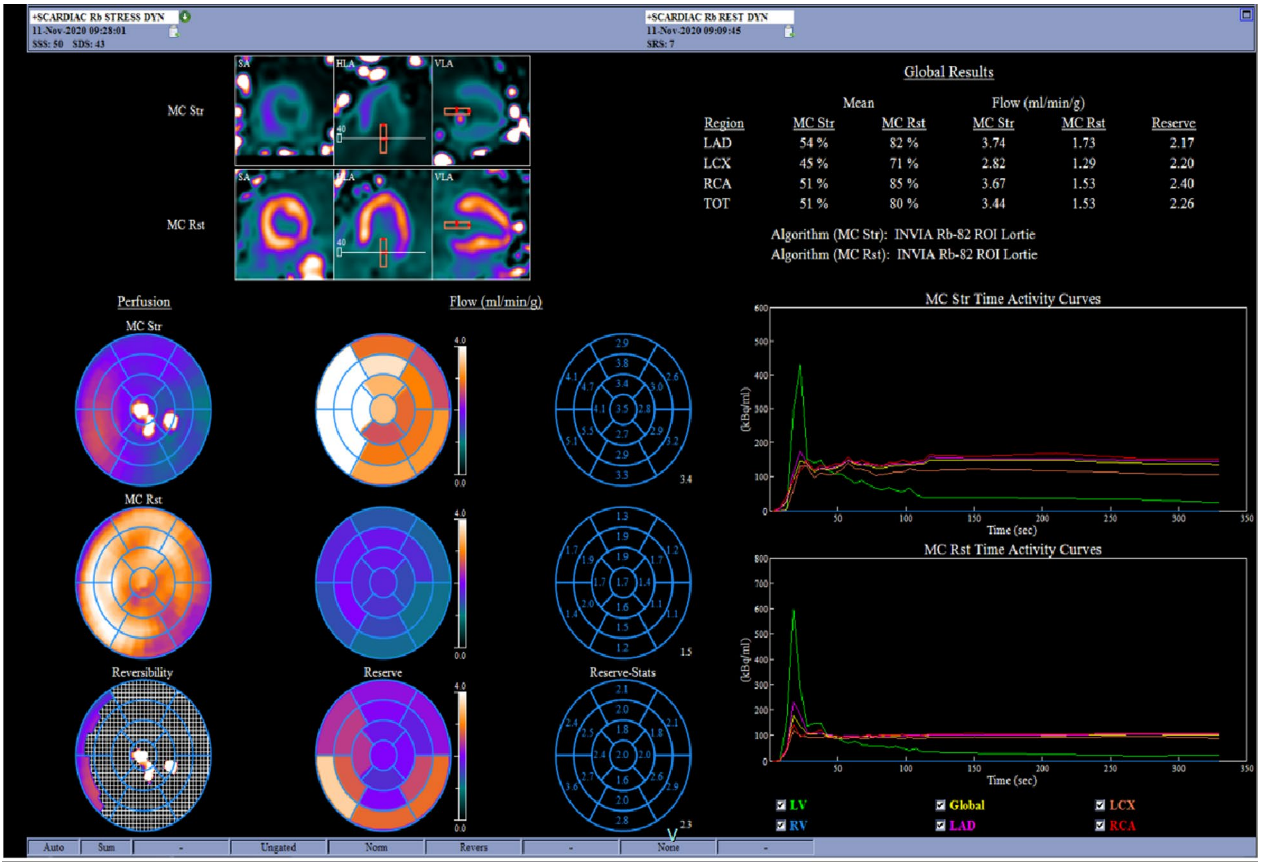

Fig. 15 PET Rb-82 MPI post revascularization. The myocardial flow reserve and global coronary flow reserve are normal

Abbreviations

ACS	Acute coronary syndrome
CT	Computed tomography
CCTA	Coronary computed tomography angiography
CFR	Coronary flow reserve
DCB	Drug coated balloon
ECG	Electrocardiogram
LAD	Left anterior descending
LCX	Left circumflex
LV	Left ventricular
MI	Myocardial infarction
PET Rb-82 MPI	Positron emission tomography rubidium-82 myocardial perfusion imaging
SPECT	Single photon emission computed tomography

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NAR and AKMY were the major contributor of the case report write up with inputs from all authors. Everyone read and agreed with the final manuscript.

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Availability of data and materials
All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
Approved by Hospital.

Consent for publication
Consented by the patient for publication.

Competing interests
The authors declare that they have no competing interests.

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