

Reviewer A

Comment 1: This case report involves an individual presenting with acute coronary syndrome (ACS) caused by a calcified nodule. A well-known cause of stent failure. The authors show that at seven months post-procedure which included placement of a covered stent following perforation of the artery during PCI showed relatively minimal calcification at or around the lesion and no restenosis. Typically, significant sheet calcification surrounds calcified nodules, yet this was not prominently observed nor does the rest of the artery show severe calcification this case. Also, the lumen is not severely narrowed. It would be beneficial if the authors had performed OCT which has very characteristic nodules. The reviewer believes that there may have been necrotic core that ruptures and the plaque shows presence of surface calcification.

This case report is unlikely to represent calcified nodules (CN) the IVUS is not convincing, and the authors should have done OCT.

Reply 1:

- Culprit lesion exhibited a convex shape of the luminal surface, convex shape of the luminal side of calcium, an irregular luminal surface, and an irregular leading edge of calcium on IVUS imaging. These features were consistent with the definition of IVUS-derived calcified nodule (Am J Cardiol. 2011;108:1547-51.). According to the classification of calcified nodule on IVUS (PLoS One. 2020;15:e0241836.), culprit lesion in our case was considered as a type 1 calcified nodule which was defined as an eccentric calcified nodule without superficial calcification at the opposite site of calcified nodule (PLoS One. 2020;15:e0241836.).
- As the reviewer mentioned, OCT imaging is better to evaluate calcified nodule. However, in our case, IVUS was used for the guidance of PCI according to the operator's discretion.

Changes in the text: In the revised manuscript, we change the sentence on page 8, lines 113-116 as follows;

IVUS imaging prior to PCI revealed *a convex shape of the luminal surface, convex shape of the luminal side of calcium, an irregular luminal surface, and an irregular leading edge of calcium* at his culprit lesion, suggesting the presence of *type 1 eccentric* CN (Figure 1-B, Video-1).

Reviewer B

Comment: Authors described a calcified nodule case which showed good clinical course with covered stent. I feel the volume of calcified nodule is not that big. That could be one reason why it was successful. There would be many opinions in treating calcified nodule like this case. Nevertheless, it is clinically important to have this kind of case report. Overall, the manuscript is well written and well discussed.

Reply: We appreciate for the reviewer's thoughtful comment.

Changes in the text: We do not change the manuscript.

Reviewer C

Comment 1: Regarding the culprit lesion of STEMI, there seems to be no evidence of thrombus at the site of calcified nodule that can be observed by IVUS, and there is a finding of relatively low-intensity unstable plaque more proximal to the lesion. Based on the findings of ST-segment elevation on electrocardiogram and decreased left ventricular wall motion on echocardiography, is this the site of the culprit lesion? It would be good to present the findings of left coronary angiography as well. Also, did treatment of this site result in ST-segment elevation of the ECG and improvement of symptoms?

Reply 1:

- According to the reviewer's suggestion, we presented a supplementary movie which showed left coronary angiography in this case. There were two intermediate stenosis at the middle segments of his left anterior descending artery and left circumflex artery, respectively. In addition, his left circumflex artery was small. His posterolateral region was mainly supplied by his right

coronary artery. Therefore, we considered a severe stenosis in his right coronary artery as a culprit lesion in this case.

- After the completion of PCI, his chest symptom was resolved, accompanied by the resolution of ST-segment depression.

Changes in the text: As reviewer recommended, we add some angiographical finding. We add some sentence on page 8, lines 109-112 as follows;

Coronary angiogram revealed one severe stenosis at the middle segment of his right coronary artery (RCA) (Figure 1-A), moderate stenosis at middle segment of left anterior descending artery and middle segment of left circumflex artery (Supplementary video-1,2).

As reviewer recommended, we add two supplementary videos which demonstrated angiography of his LCA.

Supplementary Video 1. Coronary angiography of his LCA (cranial view)

LCA=left coronary artery

Supplementary Video 2. Coronary angiography of his LCA (caudal view)

LCA=left coronary artery

As reviewer recommended, we described change in symptom, and change in the electrocardiogram after the PCI on page 10, lines 138-139 as follows;

Because of successful PCI, his symptom was recovered and ST segment elevation at electrocardiogram was resolved.

Comment 2: In fact, eruptive calcified nodules have been reported to respond well to balloon dilatation and stent dilatation is relatively good, while noneruptive calcified nodules are reported to have somewhat worse stent dilatation. Was adequate dilation of the lesion actually observed with balloon dilation prior to stenting? Please present the balloon response prior to stenting and any IVUS findings after balloon dilation. If a noneruptive calcified nodule was expected, then poor stent dilation could have been expected, the risk of perforation on subsequent post-dilation would have been higher, the re-protrusion rate of the calcified nodule would have been lower, and the rate of revascularization would not have been higher. Discussion on this point is warranted.

Reply 2: We did not conduct OCT imaging at the PCI. Therefore, intravascular imaging did not detect whether the fibrous cap was disrupted or not. On angiogram, balloon and DES were well dilated (Figure 1-C). By the favourable balloon and DES response, this calcified nodule might be the eruptive calcified nodule. We consider the possibility that the coronary artery perforation occurred because the CN forced by the DES exerted pressure on the adventitia of the coronary artery.

Changes in the text: According to the reviewer's recommend, we add some sentence in the discussion section on page 12, lines 171-174 as follows:

We did not conduct OCT imaging at PCI. Therefore, we did not detect whether the fibrous cap was disrupted or not. However, balloon and DES was well dilated. By the favourable balloon and DES response, this calcified nodule might be the eruptive calcified nodule.

Comment 3: Observing IVUS and follow-up OCT after stent placement, it appears that a stent considerably longer than 15 mm was implanted to the proximal right coronary artery, but is this correctly described regarding stent length and area covered?

Reply 3: At the PCI device delivery was difficult due to the coronary artery tortuosity and moderate stenosis at the proximal segment of his RCA. We implanted one DES at proximal segment of his RCA ahead of the intervention of the culprit lesion.

Changes in the text: According to the reviewer's recommend, we add some sentence about procedure on page 8-9, lines 116-120 as follows:

The device delivery was difficult due to the coronary artery tortuosity and moderate stenosis at the proximal segment of his RCA, we implanted one 4.0x15 mm DES (Resolute OnyxTM, Medtronic,

Dublin, Ireland) at the proximal segment of his RCA. And then, we conducted the intervention to the culprit lesion.

Comment 4: Since calcified nodules are commonly observed in dialysis patients, please add a note on risk factors for atherosclerotic disease, including presence of diabetes and renal function and dialysis.

Reply 4: The patient had normal renal function and no risk factors for atherosclerotic disease without hypertension.

Changes in the text: According to the reviewer's recommend, we add some laboratory data on page 8, lines 105-107 as follows:

On laboratory data, his creatinine was 1.02 mg/dL, hemoglobin A1c was 5.9%, low density lipoprotein was 112 mg/dL, and no evidence of elevation of cardiac enzyme at the presentation.

Comment 5: Antiplatelet and anticoagulant therapy is prasugrel and edoxaban, but how long after PCI did you use the two drugs together? You mentioned no TLR until 2 years later, is that two drugs for 2 years?

Reply 5: The patient had prasugrel and edoxaban for 1 year, after then, he discontinued prasugrel.

Changes in the text: According to the reviewer's recommend, we add some sentence on page 10, lines 146 as follows:

One year after the PCI, he discontinued taking 3.75 mg of prasugrel.

Reviewer D

Comment 1: Calcified nodule has different plaque characteristic and pattern which impact long-term outcome (Pengchata P, J of interventional cardiology 2023; ID6456695, doi.org/10.1155/2023/6456695). In this case, it is eccentric calcified nodule.

Reply 1: As reviewer pointed out, this case has calcium arch <180 degree. Therefore, this case was eccentric calcified nodule which associated with worse clinical outcome.

Changes in the text: As reviewer recommended, we add some sentence on page 8, lines 113-116 as follows;

Primary PCI was performed under the guidance of IVUS imaging (AltaView™, Terumo, Tokyo, Japan). IVUS imaging prior to PCI revealed a convex shape of the luminal surface, convex shape of the luminal side of calcium, an irregular luminal surface, and an irregular leading edge of calcium at his culprit lesion, suggesting the presence of type 1 eccentric CN (Figure 1-B, Video-1).

As reviewer recommended, we add some sentence on page 11, lines 161-163 as follows;

Furthermore, this case did not experience any clinically-driven TLR for 2 years after PCI *even in the presence of the eccentric CN which associated with worse clinical outcome (8).*

As reviewer recommended, we add one reference as reference 8.

8.Pengchata P, Pongakasira R, Wongsawangkit N, et al. Characteristics and Pattern of Calcified Nodule and/or Nodular Calcification Detected by Intravascular Ultrasound on the Device-Oriented Composite Endpoint (DoCE) in Patients with Heavily Calcified Lesions Who Underwent Rotational Atherectomy-Assisted Percutaneous Coronary Intervention. J Interv Cardiol. 2023;21:6456695

Comment 2: Case number is very small, only 1 patient. The evidence is not strong enough for support use cover stent for all calcified nodule. Cover stent is usually have higher chance of stent restenosis compare to contemporary DES stent

Reply 2: As reviewer pointed out, this is only one case, and we did not recommend the use of covered stent for all CN lesions.

Changes in the text: According to the reviewer's comment, we add some sentence at limitation section on page 12, lines 178-180 as follows;

This is only one case report. Further clinical follow-up is required to monitor whether the use of covered stent continues to prevent CN-related ISR.

Comment 3,4: In most case of calcified nodule, will have a lot of calcium in adjacent part. This makes difficulty for stent delivery and stent expansion. In this case is very small calcium at calcified nodule and no calcium in adjacent tissue.

Reply 3,4: As reviewer pointed out, the presence of adjacent calcification makes difficult for device delivery and stent expansion. This case had less calcification in the adjacent lesion. It might affect the favourable clinical course.

Changes in the text: According to the reviewer's comment, we add some sentence at limitation section on page 12, lines 174-176 as follows;

In most case of CN, a greater amount of calcification is often recognized at the adjacent lesion. However, this case had less calcification in the adjacent lesion. It might affect the favourable clinical course.

Comment 5: Author should also comment intravascular imaging assessment after immediate PCI such as stent apposition, stent expansion, stent eccentricity which impact the long term outcome.

Reply 5: We did not conduct IVUS imaging after first DES deployment because of coronary artery rupture. Therefore, we could not measure the apposition, stent expansion, or stent eccentricity of the first DES. However, balloon and DES were well dilatated on angiogram. IVUS imaging after post dilatation of covered stent, demonstrated optimal stent apposition and stent expansion. The stent was dilated almost to a regular circle.

Changes in the text: According to the reviewer's comment, we add some sentence on page 10, lines 136-138 as follows;

The IVUS imaging after post dilatation of covered stent, demonstrated optimal stent apposition and stent expansion. The stent was dilated almost to a regular circle.
