Dear editor,

Thanks very much for reviewing our manuscript.
We have replied the questions from reviewers below this short reply in this document.
The manuscript was revised according to suggestions from reviewers and the requirement of your journal.
Our revised manuscript was polished by Charlesworth again.

Thanks very much and best wishes!

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Reviewer #1:

A nice case however, there are a few points to discuss.

Why not add a part on the proposed pathophysiology of ectasia would be nice.

Reply 1:

Thanks very much!
We added some contents about pathophysiology of ectasia in this manuscript.
Please see the introduction part: It was characterized by extensive destruction of the musculoelastic elements in the coronary wall with an unknown manner.

The use of ticagrelor is the routine for all acute coronary syndromes unless contraindicated, why did the patient initially receive clopidogrel?

Reply 2:

Thanks very much! Your advice was very important.
The current guideline recommended ticagrelor and aspirin as the first dual anti-platelet agents for acute coronary syndromes. This patient was observed since four years ago (form the year 2017), ticagrelor was not universally accepted as one of the dual anti-platelet agents in that time. Even until present a portion of patients with acute coronary syndromes were still received the treatment of clopidogrel and aspirin because of the concern of bleeding of ticagrelor in practice.

Why did the patient have the coronary angiography on the third day which is not according to guidelines?

Reply 3:

Usually the acute myocardial infarction should be underwent coronary angiography as soon as possible especially the time from onset to admission was within 12 hours. For this patient, the chest pain had become aggravated over the past three days before his admission on our hospital. Emergency electrocardiogram (ECG) showed the Q waves

were clear in lead III and lead avF, the chest pain was appeared and lasted for three days before his admission for medical treatment and it was relieved after the usage of anti-thrombotic therapy after admission, thus a delayed coronary angiography was selected after discussion.

How did you reduce the dose of ticagrelor to 45 mg as the only concentrations present are 90 and 60 mg?

Reply 4:

Thanks very much! Usually after at least 12 months of acute myocardial infarction (AMI), dual anti-platelet therapy (DAPT) would be changed into single anti-platelet therapy according to current guideline. For this patient, the first AMI was appeared in the starting time point of this research, the second AMI was appeared in the fifth observing month of this research, after the 17^{th} month of the observing, the application of ticagrelor was lasted 12 months since the second AMI and it could be considered to be reduced or stopped, thus in the 18^{th} month we reduced the dosages of ticagrelor.

It is really not a standard practice for the dosage of 45 mg ticagrelor twice per day. We known that 60 mg twice per day was a standard usage of ticagrelor. In China only the 90 mg package was available, the 60 mg was not available and it should be cut by patient themself with a unreliable manner, thus for convenience of the such patients, we sometime use the 45 mg by cutting one 90 mg tablet into two parts with each of 45 mg. In future clinical practice we would remember that the standard usage of ticagrelor. Thanks very much for your advice!

Since 2015 whenever a NSTEMI patient has a high thrombotic risk we can add low dose rivaroxaban and this was not highlighted by you.

Reply 5:

Thanks very much for your advice! We known the guideline and your suggestion and we would have a try in future. Our suggestion was that the anticoagulant could be considered if single-platelet therapy/dual failed to provide adequate protection to the recurrence of acute coronary syndromes, especially in CAE patients who did not have other obvious stenotic lesions. Here the warfarin would be as the first choice.

The rivaroxaban usually was not applied out of the medicine instruction. In practice the indications for rivaroxaban from the medicine instruction was: 1) Elective hip or knee replacement surgery in adult patients to prevent venous thrombosis (VTE). 2) Adult deep venous thrombosis (DVT) and pulmonary embolism (PE). 3) adult non valvular atrial fibrillation patients with one or more risk factors (e.g. congestive heart failure, hypertension, age over 75 years, diabetes, stroke or transient ischemic attack).

Reviewer #2:

In the paper “Anti-thrombosis strategy for coronary artery ectasia patients with acute myocardial infarction: A case report and literature review” authors describe an interesting case of dynamic observation on a single patient affected where a DAPT therapy with clopidogrel was not able to prevent events conversely ticagrelor was.

A very interesting point which should be better discussed in the discussion is the fact that after shifting from clopidogrel to ticagrelor, during the follow up, every time the ticagrelor dosage was reduced the patients started to be symptomatic again for chest pain (micro-embolisms?).

Reply 6:

Thanks very much! The application of ticagrelor was lasted 12 months since the second AMI and it could be considered to be reduced or stopped, thus in the 18th month we reduced the dosages of ticagrelor. We did not known what was happened for this patients when the chest pain recurred after the reduction of ticagrelor. But as the chest pain usually was an indicator for the unstable condition in coronary for patients with for coronary heart disease, thus it was possible that the micro-embolisms was appeared. We did not perform coronary angiography again after the reduction of ticagrelor because the patients already received 4 times coronary angiography. We would add some discussion about the possibilities in this manuscript.

“Thus CAE is likely to be a thrombotic disease”: authors could not define CAE as a “thrombotic disease” because it is a pathology involving the vessel wall ……conversely the could say that CAE may expose to thrombotic complications or similar concepts.

Reply 7:

Thanks very much! The CAE was a similar to coronary heart disease and it was with a the possibility of thrombosis.

There are minor spelling errors like: “angiotonin receptor” “stalbe” “dura antiplatelet agents” “the 12 monthes”

Reply 8:

Thanks very much! We would make those revisions.

Thank you for the opportunity to review the paper.

Reviewer #3:

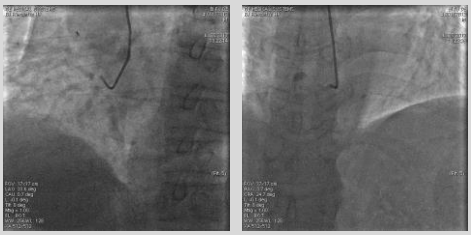
The paper is interesting; however some improvements are necessary.

Images included at the end of the article need a better / higher resolution. I hope authors will be able to submit these (since embedding images in the word document might blur them).

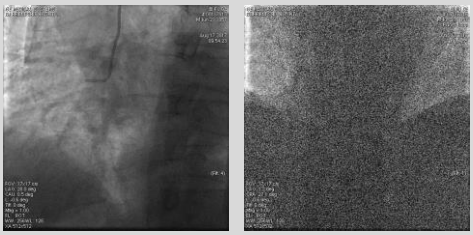
Reply 9:

Thanks very much.
The images in this manuscript were captured from the video of coronary angiography (CAG). The uncompressed original images would be submitted in separate files instead of embedding into the manuscript as we did before. For this CAE patients we have totally performed four times of CAG, the original videos also could be submitted into the supplemented material.

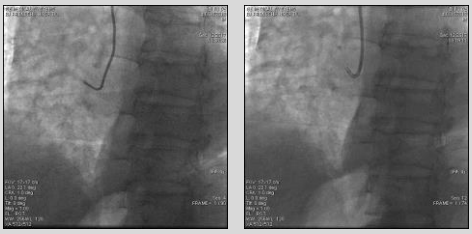
Here were parts of the typical videos for browsing selected four times of coronary angiographies, please double-click the picture then it would play automatically.



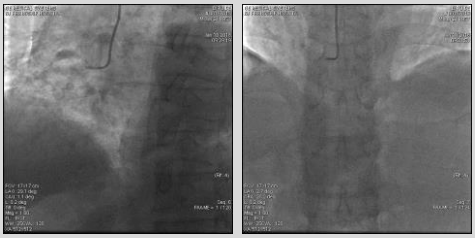
First coronary angiography. Compressed video.
Click the picture to play the vedio



Second coronary angiography. Compressed video.
Click the picture to play the vedio



Third coronary angiography. Compressed video.
Click the picture to play the vedio



Fourth coronary angiography. Compressed video.
Click the picture to play the vedio

Authors are concentrated on non-surgical / conservative treatment. It is a must to discuss cardiosurgical options as well (aneurysmectomy; stent; angioplasty....). Please consult relevant sources and add some of importance to the references.

Reply 10：

Thanks very much.
Surgical treatment was very important for CAE patients with AMI, it should be cooperated with non-surgical treatment.Most of proposals for treating CAE were based on the treatment for CHD at present because most of CAE patients were accompanied with CHD and the exact etiology and pathogenesis of CAE were not fully understood, and it was also lack of enough clinical evidences to testify varieties treatment. We have searched from Pubmed and other source to find the relevant references about the CAE, we have added those related contents into the main text (introduction part, the paragraph 1 in discussion part) and the reference of the manuscript in the following process.

Treatment of medicines: 1) antiplatelet and anticoagulant agents were the main

treatments: it was found that patients with CAE had large peripheral blood mean platelet volume (MPV)(1-4), increased MPV indicated increased platelet reactivity index, reflecting the body's thrombus state, the thrombosis risk was greater while MPV was higher, because a large platelet particles was associated a faster speed of collagen aggregation, the more TAX2 generated, and the more Gp I and IIb/ IIIa receptor expressed(5)，thus it was the reason for the recommendation of antiplatelet therapy for CAE(3). Larger coronary aneurysms required more aggressive treatment by combination of antiplatelet and anticoagulant therapy to reduce thrombosis and coronary artery embolism events (6, 7). 2) Angiotensin receptor blockers (ARB): in theory they would be beneficial for CAE patients because connective tissue abnormalities were usually associated with overexpression of TGF- beta and MMPs, which can promote the formation of coronary artery aneurysm, ARB such as losartan can inhibit TGF- beta(8). Ang II might also be related with those aneurysm (9, 10), thus inhibition of RAAS may prevent CAE; 3) statins. statins could regulate collagen metabolism and reduce collagen degradation by inhibiting MMP1/2/3/9 which were derived from macrophage and vascular smooth muscle(6, 11), it also could significantly reduce the level of inflammation indexed by hsCRP, and thereby prevent CAE formation and progression(12). 4) nitrate esters. This kind of medicine such as nitrates and other coronary arteries dilating components, could not improve clinical symptoms for patients with CAE and should be avoided (13-15), it could active MMPs and promote the expansion. 5) calcium channel blockers: the dihydropyridine can prevent coronary artery spasm (one of the complications of CAE). It had not yet found any adverse reactions similar to nitrates(16, 17), but the effect needed to be further investigated; 6) other agents such as beta blockers, trimetazidine, there were no evidences they should be limited, and in theory all of them could be used (18).

For patients with poor effect of medicine, or patients with high-risk acute coronary events such as acute myocardial infarction, besides the methods of thrombolytic therapy, coronary artery bypass graft surgery, coronary artery interventional therapy can also be considered(14, 19). Interventional treatment includes: coronary artery thrombosis aspiration(20), coronary angioplasty, coronary stent implantation and so on. Polytetrafluoroethylene (PTFE) stent, drug-eluting stent (DES), bare metal stent (BMS) and coil embolization could effectively eliminate coronary aneurysm, but there were technical difficulties, especially when coronary artery was with tortuosity or with severe calcification(21). PTFE covered stent was an alternative choice, it can isolate the expansion site, reduce the risk of thromboembolism, Szalat summarized the follow-up of 18 cases of stent implantation in patients with PTFE (22). Of course, there were drawbacks such as blockage of collateral circulation by the stent could induce ischemia events, and the incomplete coverage would also increase the risk of thrombosis, and stent restenosis rate in CAE patients was higher than in CHD patients. In order to overcome the risk of stent migration, self expandible stent (self-expending STENTYS BMS and DES stents) was a feasible choice, it provided a better anatomic fitting, can overcome the loosening and displacement over time, IVUS and OCT can guide the positioning and releasing of the stent, especially when it was adjacent to the

narrow site and expansion site(23). The main purpose of surgery was to prevent coronary artery rupture, to avoid thrombosis and embolism, and to reduce sudden death, the surgery technique including dilated coronary artery resection, folding, transplantation and distal grafts ligation(24-26). It should be noted that, the rate of no reflow phenomenon and the incidence of distal thrombosis were higher in patients with CAE than non-dilated patients after surgery (27-32). Recently it was founded double-layer bare metal stents implantation for patients with localized coronary artery aneurysm complicating with severe stenosis in single vessel is safe and effective(30).

You must as well add an 'abbreviation section' to the paper: there are too many acronyms, and readers might have difficulties to follow the sense.

Reply 11：

Thanks for your advises.

The abbreviations and its original words were listed as following. There were lots of abbreviations in this manuscript and it was uncomfortable for reading and understanding, we would try our best to reduce some of them which were unnecessary and unimportant.

Abbreviations

ACS, acute coronary syndrome; AMI, myocardial infarction; ARB, angiotensin receptor blocker; CAE, coronary artery ectasia; CAG, coronary angiography; CHD, coronary heart disease; DAPT, dual antiplatelet therapy; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LMWH, low molecular weight heparin; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis myocardial infarction.

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