

Detailed Responses to Reviewers

Title: Relationship between coronary artery ectasia, cocaine abuse and acute coronary syndromes.

ESPS manuscript NO: 24030

Response to Reviewer (code: 00227470)

Egregious reviewer,

Thank you for your suggestions. All the recommended changes have been made.

1. As required we have added in the manuscript the missing angiographic informations such as the size of catheter and the dose of contrast medium per each injection. We have also reported in the figure legend the maximum coronary artery diameter at CAE on right and left coronary arteries, which result clearly ectatic (left anterior descending artery and circumflex coronary artery with maximum diameter of 5,8mm and right coronary artery with a maximum diameter of 5.6mm).
2. It is known that coronary artery ectasia can be caused by long lasting hypertension, but it is also known that the cocaine abuse may determines CAE (*Satran, et al. Increased prevalence of coronary artery aneurysms among cocaine users. Circulation. 2005 May 17;111(19):2424-9*). In this case the patient did not reported to suffer from hypertension and his young age and lack of familiarity for hypertension does not support the hypothesis that CAE may be only secondary to a possible persistent hypertension. Moreover to exclude this hypothesis and on the basis of the echocardiography view of concentric hypertrophy (most likely due to cocaine abuse with a consequent left ventricular pressure overload) we also investigated possible causes of secondary hypertension but all the exams resulted negative. No others conditions (except cocaine abuse) were present to exclude other causes of CAE.

3. Of course not only the presence of CAE may cause ACS. In the text we have reported the other possible causes of ACS such as coronary thrombosis or coronary spasm. In this case, to exclude a possible role of a coronary spasm in the genesis of the ACS, an hyperventilation testing and an intracoronary injection of acetylcholine (with incremental doses of 20 and 50µg into the right coronary artery and of 20, 50, and 100µg into the left coronary artery over 20 seconds and with at least a 3-minute interval between injections) were performed and were negative. Furthermore, to exclude a thrombophilic diathesis, a thrombophilia testing was also performed and was negative.
4. As required we have provided the normal range of matrix metalloproteinases plasma concentrations and of their tissue inhibitors.

The manuscript has been read and approved by all of the Authors.

Yours sincerely

Gregory Dendramis MD, FACC

Response to Reviewer (code: 24030)

Egregious reviewer,

Thank you for your suggestions. All the recommended changes have been made.

1. As required we have provided the normal range of matrix metalloproteinases plasma concentrations and of their tissue inhibitors.
2. To exclude a thrombophilic diathesis, a thrombophilia testing was performed and was negative (we added this information in the text).

The manuscript has been read and approved by all of the Authors.

Yours sincerely

Gregory Dendramis MD, FACC

Response to Reviewer (code: 00227470)

Egregious reviewer,

Thank you for your suggestions. All the recommended changes have been made.

1. Of course this is only a case report without a control group. We do not want to draw any strong conclusions from our case report. For this reason in the text we specify that patients with CAE **appear to be** at increased risk of angina and acute myocardial infarct as reported by *Satran, et al. Increased prevalence of coronary artery aneurysms among cocaine users. Circulation. 2005 May 17;111:2424-9*). For this reason we added in the text this sentence: “further studies that can strengthen this hypothesis would be useful to deepen and better analyze this interesting association”.
2. As required we have provided the normal range of matrix metalloproteinases plasma concentrations and of their tissue inhibitors.

The manuscript has been read and approved by all of the Authors.

Yours sincerely

Gregory Dendramis MD, FACC