



Prevalence of myocardial infarction with non-obstructive coronary arteries (MINOCA) amongst acute coronary syndrome in patients with antiphospholipid syndrome

Himali Gandhi ^{*}, Navid Ahmed, Daniel M. Spevack

Division of Cardiology, Department of Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, United States of America

ARTICLE INFO

Article history:

Received 3 November 2018

Received in revised form 24 December 2018

Accepted 27 December 2018

Available online 1 February 2019

ABSTRACT

Antiphospholipid antibody syndrome (APLS) is well known to cause thrombotic events and premature atherosclerosis leading to coronary artery occlusion. The association of non-thrombotic acute myocardial infarctions (AMI) with APLS is not as clearly delineated. The objective of this study was to determine the relative prevalence of myocardial infarction with non obstructive coronary arteries (MINOCA) compared to MI from vaso-occlusive disease amongst patients with known APLS at our institution. Out of 575 patients with positive antiphospholipid antibodies, cardiac catheterizations were performed in 40 patients presented with AMI and had cardiac catheterizations. MINOCA was found in 8 patients. We found that MINOCA is common in patients with APLS presenting with ACS and that spasm may also play a role in AMI in patients with APLS.

© 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Antiphospholipid antibody syndrome (APLS) is well known to cause thrombotic events and premature atherosclerosis leading to coronary artery occlusion [1]. The association of non-thrombotic acute myocardial infarctions (AMI) with APLS is not as clearly delineated. Our group has previously reported individual cases of AMI with non-obstructive coronary arteries (MINOCA) in this population.

MINOCA has gained increasing recognition in the medical literature and accounts for approximately 6% of AMI presentations [2]. Based on our anecdotal experience, we hypothesize that there is a greater prevalence of MINOCA in patients with APLS. Potential underlying mechanisms of MINOCA include coronary spasm, coronary microvascular dysfunction, takotsubo cardiomyopathy, and myocardial disorders including myopericarditis [3]. Paradoxically, thrombophilia states are relatively common in those presenting with MINOCA [4]. The objective of this study was to determine the relative prevalence of MINOCA compared to MI from vaso-occlusive disease amongst patients with known APLS at our institution.

2. Methods

Our institutional database was queried for all patients testing positive for antiphospholipid antibodies (n = 575) between 2000 and 2012. APLS syndrome was defined in patients who met one or more clinical or laboratory criteria. Clinical criteria include (a) vascular thrombosis (arterial, venous, or small-vessel thrombus in any organ) or (b) complication of pregnancy. Laboratory criteria includes (a) anticardiolipin antibodies positive on two or more occasions at least six weeks apart (b) lupus anticoagulant antibodies positive on two or more occasions at least six weeks apart [5]. From this sample, we identified 46 patients having cardiac catheterization. Of these total patients, six were excluded since they received cardiac catheterization for reasons other than ACS. ACS was defined based on ischemic symptoms with elevation of troponin (troponin I > 0.1 mg/dL) with or without electrocardiographic (ECG) changes, per the universal definition of MI [6]. Cardiac angiography reports were analyzed for these 40 patients. The diagnosis of MINOCA was made if the patient had (a) signs and symptoms of a myocardial infarction according to the universal definition of AMI [7] (b) the exclusion of obstructive CAD (obstructive CAD is typically defined as ≥50% stenosis in the major vessels) and (c) no other overt cause of the AMI [5]. Table 1 shows the selection of patients.

^{*} Corresponding author at: Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467, United States of America.

E-mail address: hgandhi@montefiore.org (H. Gandhi).

Table 1
Characteristics of patients presenting with APLS and MINOCA.

	Nonthrombotic (n = 8)
Age, mean (STD)	41 ± 8
Female (%)	5 (63)
Race/ethnicity	
White	0
Black	6 (75)
Hispanic	2 (25)
Other	0
Coronary risk factors	
HTN	8 (100)
HLD	7 (88)
DM	4 (50)
CKD	3 (38)
CVA	5 (63)
TIA	1 (13)
APLS Ab	
aCL IgM	3 (38)
aCL IgG	3 (38)
aCL IgA	1 (13)
aB2 GPI IgM	0 (0)
aB2 GPI IgG	2 (25)
aB2GPI IgA	0 (0)
aLA	5 (63)
Peak troponin	0.36 (IQR:0.17–0.53)
Echo findings	
Normal LVEF and wall motion	6 (75)
Other	2 (25)
INR (n = 6)	2.35 (IQR:1.9–2.65)

2.1. Statistical analysis

We studied the baseline characteristics in APLS patients with non-obstructive CAD using descriptive statistical analysis techniques. The variability of continuous measures was represented as means and standard deviations when they followed a normal distribution and with medians and interquartile ranges when they followed a non-normal distribution.

3. Results

MINOCA was found in eight patients with APLS presenting with ACS (Table 1). Five of these patients were female and the mean age for these patients was 41 ± 8 years. All eight patients had history of prior arterial (stroke n = 5) or venous thrombosis (n = 4). Median troponin-I was 0.36 mg/dL [range 0.17, 0.53]. One patient was found to have diffuse coronary artery spasm, which reversed following administration of intra-coronary nitroglycerine. Six patients had a normal ejection fraction (EF). One patient had an EF of 30% with moderate anterolateral wall hypokinesis and inferoposterior wall akinesis. Another patient had global ventricular dysfunction with an EF of 40%. Six of the patients were on long term anticoagulation with warfarin for APLS with an INR between 1.7 and 3.2 at the time of presentation. Four of the six patients had a therapeutic INR (INR ≥ 2).

4. Discussion

The main finding of our study is that MINOCA is common in patients with APLS presenting with ACS. Most of the infarctions were small, spasm played a role in two cases, and none of the cases had takotsubo-like pattern (apical ballooning) on echocardiography.

The findings of this report helped us to characterize and compare features of patients with APLS who present with MINOCA compared to the general population presenting with AMI. In our population,

8 out of 40 patients with APLS presented with MINOCA. While our study sample is not large, this number is suggestive that MINOCA is higher in APLS compared with the 6% MINOCA rate in non-APLS populations. [2] The mean age of our population with APLS presenting with AMI was 41 ± 8 years compared to the typical average age of patients presenting with AMI, which is generally most common in the 7th decade.

Our observation also suggest that spasm may play a role in AMI in patients with APLS. To our knowledge, coronary vasospasm has not been previously associated with APLS. The fact that both vasospasm and APLS, two uncommon findings were present in two of our eight patients raises the possibility that these two entities are related. The etiology of MINOCA in the remaining six patients in whom spasm was not demonstrated is not known. None displayed the characteristic apical ballooning appearance of takotsubo cardiomyopathy. It is certainly plausible that spasm had been present in these patients but had resolved prior to angiography. It is also possible that the patients actually had myocarditis, which was confused for AMI. Without cardiac MRI, this possibility cannot be ruled out.

5. Limitations

To our knowledge, this is the first study of MINOCA in a population with diagnosed APLS. Although the subjects were all from a single center and constituted a relatively sample, we feel that these data are an important contribution and begin to shed some insights into the mechanism of disease in subjects with APLS. That being said, a larger sample taken from multiple centers would improve the precision of our prevalence estimates for MINOCA in subjects with APLS. It would also help to improve the generalizability of the results to the general population.

6. Conclusion

A large relative prevalence of MINOCA was seen amongst patients with APLS presenting with AMI. Further studies describing the mechanism of MINOCA in APS patients is necessary to help guide optimal treatment for these patients.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

References

- [1] B. Lagana, L. Baratta, L. Tubani, et al., Myocardial infarction with normal coronary arteries in a patient with primary antiphospholipid syndrome, *Angiology* 52 (11) (2001).
- [2] S. Pasupathy, T. Air, R. Dreyer, et al., Systematic review of patients presenting with suspected myocardial infarction and non-obstructive coronary arteries, *Circulation* 131 (10) (2015) 861–870.
- [3] S. Pasupathy, R. Tavella, J.F. Beltrame, Myocardial infarction with nonobstructive coronary arteries (MINOCA): the past, present, and future management, *Circulation* 135 (16) (2017) 1490–1493.
- [4] S. Pasupathy, R. Tavella, S. McRae, et al., Myocardial infarction with non-obstructive coronary arteries- diagnosis and management, *Eur. Cardiol. Rev.* 10 (2) (2015) 79–82.
- [5] J.S. Levine, L. Branch, J. Rauch, The antiphospholipid syndrome, *N. Engl. J. Med.* 346 (10) (2002) 752–763.
- [6] K. Thygesen, J.S. Alpert, H.D. White, Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction, Universal definition of myocardial infarction, *Circulation* 116 (2007) 2634–2653.
- [7] S. Agewall, J.F. Beltrame, H.R. Reynolds, et al., ESC working group position paper on myocardial infarction with non-obstructive arteries, *Eur. Heart J.* 38 (3) (2017) 143–153.