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MINI-FOCUS ISSUE: CORONARIES

BEGINNER

CASE REPORT: CLINICAL CASE

Cardiac Arrest in the Setting of Diffuse Coronary Ectasia

Perspectives on a Unique Ischemic Insult

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ABSTRACT

A 69-year-old man with a history of coronary artery ectasia, potentially resulting from an underlying heritable connective tissue disorder, presented with ventricular fibrillation. Despite medical management of ischemia, he developed recurrent ventricular tachycardia with poor neurological recovery. We highlight challenges in the management of coronary artery ectasia. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:1662–6) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 69-year-old male with a history of non-ST-segment elevation myocardial infarction (NSTEMI) and coronary artery ectasia (CAE) presented following a cardiac arrest at home. The patient had reported indigestion shortly before he was discovered unresponsive by his spouse. She immediately initiated cardiopulmonary resuscitation and called emergency medical services, who arrived 20 min later and found the patient in ventricular fibrillation (VF). He was defibrillated, with return of spontaneous circulation, but he had 3 additional episodes of cardiac arrest en route to the hospital (polymorphic ventricular tachycardia [VT], pulseless electrical activity, and VF). On arrival to the intensive care unit, the patient was intubated and sedated, but he had intact pupillary reflexes. He was febrile (38.4°C), bradycardic, with a regular heart rhythm, and he had no murmurs. He had a normal jugular venous pressure with warm extremities and no peripheral edema, but he required norepinephrine to maintain adequate mean arterial pressure.

LEARNING OBJECTIVES

- To heighten awareness of various causes of coronary artery ectasia.
- To develop an approach to management of acute coronary syndromes in patients with coronary artery ectasia.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

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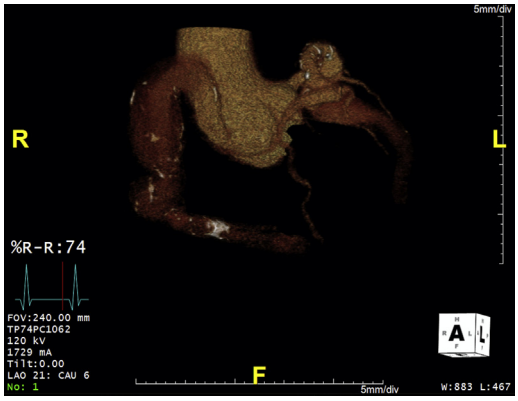
FIGURE 1 Coronary Computed Tomography Angiography 1 Year Before Presentation



The image demonstrates aneurysmal dilation of all coronary arteries with limited opacification of distal vasculature, suggesting slow flow versus thrombus. A = anterior; CAU = caudal; F = foot; FIV = field of view; L = lateral (and also left); LAO = left anterior oblique; R = right.

PAST MEDICAL HISTORY

The patient first received a diagnosis of CAE in 2004 after he presented with NSTEMI at an outside institution. Coronary angiography at the time revealed aneurysmal, ectactic coronary vasculature, concerning for vasculitis or Kawasaki disease, and he was referred to our institution.

He informed us that his biological brother had also recently been given a diagnosis of CAE, and his father underwent surgery for abdominal aneurysms. The patient was subsequently evaluated for and received a diagnosis of thoracic aortic aneurysm and iliac artery aneurysms. He was transitioned to aspirin and warfarin and was referred to a geneticist.

Given his family history and the distribution of vascular involvement, vasculitis was believed to be an unlikely cause of his presentation, and limited genetic testing for mutations in matrix metalloproteinase proteins and tissue inhibitor of metalloproteinases-1 genes was ordered, but it did not identify a pathogenic variant. The patient was clinically stable on medical therapy consisting of aspirin and warfarin (international normalized ratio [INR] goal 2.0 to 3.0) for many years and had intermittent surveillance with coronary computed tomography angiography (**Figure 1**).

One year before cardiac arrest, he presented with NSTEMI. At the time of that admission, his INR was 1.8, cardiac troponin T (cTnT) level peaked at 1.38 ng/ml (upper reference limit 0.1 ng/ml), and the electrocardiogram was notable for sinus bradycardia, an early precordial R-wave transition, a premature ventricular contraction, and nonspecific T-wave changes (**Figure 2A**). He underwent coronary angiography (**Figure 3**, Videos 1, 2, 3, and 4), which revealed diffuse CAE with Thrombolysis In Myocardial Infarction flow grade 1 to 2. An echocardiogram demonstrated a newly reduced left ventricular ejection fraction of 45% with regional hypocontractility in the inferior, posterior, and apical walls. Given the subtherapeutic INR on presentation, the risks and benefits of direct oral anticoagulant therapy were discussed with the patient, and he was transitioned to apixaban 5 mg twice daily. One month later, he again presented with NSTEMI. He was conservatively managed and transitioned back to warfarin with a higher INR goal (2.5 to 3.5). Genetic testing was revisited, and sequencing for a 48-gene panel assessing for heritable disorders of connective tissue was ordered (including genes for Marfan syndrome [MFS] and Loeys-Dietz syndrome).

ABBREVIATIONS AND ACRONYMS

CAE = coronary artery ectasia
cTnT = cardiac troponin T
INR = international normalized ratio
MFS = Marfan syndrome
NSTEMI = non-ST-segment elevation myocardial infarction
TGFβ = transforming growth factor-beta (gene)
VF = ventricular fibrillation
VT = ventricular tachycardia

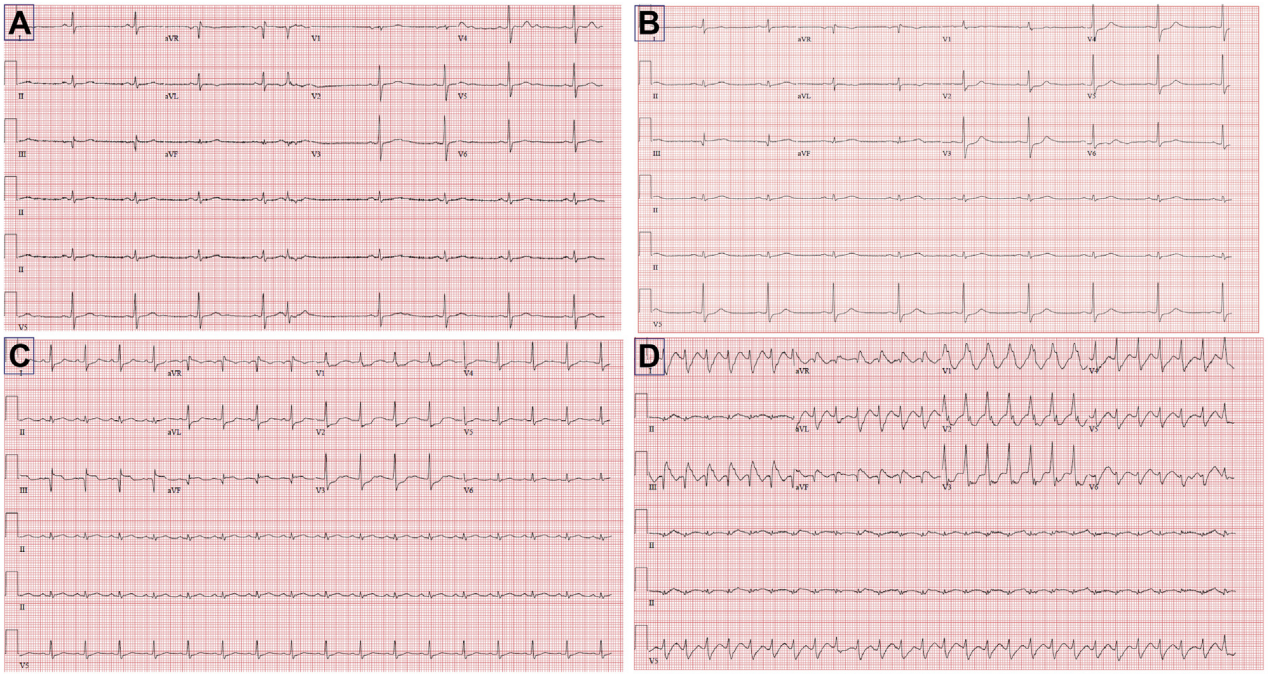
DIFFERENTIAL DIAGNOSIS

In the context of known CAE and multiple previous NSTEMIs, the patient was presumed to have experienced an ischemic VT or VF arrest. However, coronary artery dissection or rupture, VT or VF related to underlying cardiomyopathy, electrolyte abnormalities, and sepsis were also considered.

INVESTIGATIONS

The admission electrocardiogram (**Figure 2B**) was notable for sinus bradycardia with 0.5-mm ST-segment depressions in the anterior precordial leads, concerning, but not yet meeting criteria, for posterior ST-segment myocardial infarction. Admission laboratory studies included an INR of 1.6, lactate level of 4.7 mmol/l, and cTnT level of 0.88 ng/ml (upper reference limit 0.1 ng/ml). The echocardiogram (Video 5) revealed a left ventricular ejection fraction of 35% with inferior and posterior akinesis. The results of genetic testing were reviewed and were notable for a missense mutation (heterozygous at c.164 G>A, p.Ser55Asn) in the transforming growth factor-beta (*TGFβ3*) gene, with conflicting clinical interpretations, including variant of uncertain significance, benign, and likely benign. In silico data were indeterminate with regard to effect on protein disruption.

FIGURE 2 Electrocardiograms Through the Patient's Clinical Course



(A) On previous admission with non–ST-segment elevation myocardial infarction. **(B)** On admission. **(C)** During transient ST-segment elevation. **(D)** With ventricular tachycardia.

MANAGEMENT

Given the absence of ST-segment elevation and the patient's prolonged resuscitation and tenuous hemodynamic status, coronary angiography was deferred on arrival but was planned pending neurologic recovery (1). The patient was treated medically with dual antiplatelet therapy, unfractionated heparin, amiodarone, targeted temperature management, and ventilatory support. His cTnT level peaked at 8.12 ng/ml. He developed transient inferior-posterior ST-segment elevation (**Figure 2C**), but coronary angiography was deferred because of the perceived low likelihood of successful intervention in the setting of known complex anatomy and evolving evidence of poor neurologic recovery.

He subsequently developed VT storm (**Figure 2D**), which required lidocaine, repeat initiation of sedation, and ultimately stellate ganglion blockade, which only temporarily prevented recurrent VT. Given the patient's poor neurologic prognosis, his family decided to withdraw care.

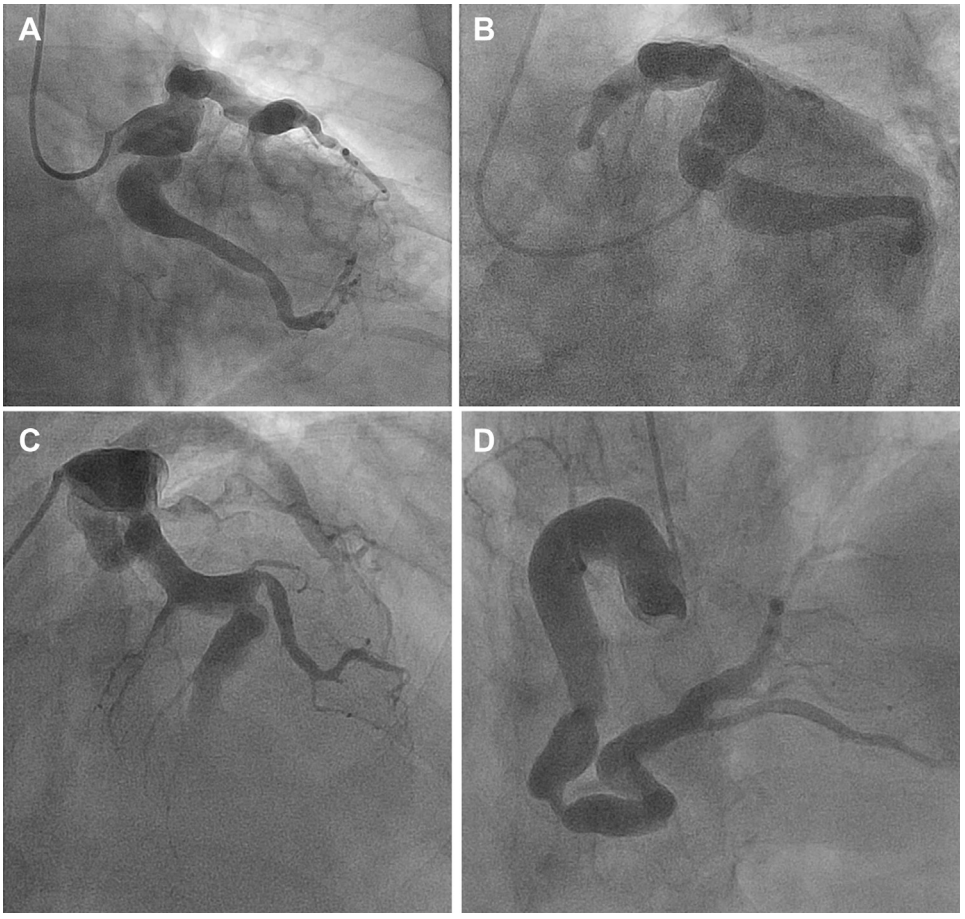
DISCUSSION

CAE, defined as diffuse segments of coronary artery at least 1.5 times that the size of the adjacent normal coronary vasculature, can be found in 1% to 5% of patients presenting for coronary angiography and is most commonly caused by atherosclerosis (2). Less common causes include vasculitis (Kawasaki, Takayasu), infections (mycotic, syphilitic), and genetic connective tissue disorders (MFS) (2).

Mechanisms of ischemia in CAE include: 1) flow alterations along aneurysm segments causing; 2) thrombus formation and/or embolization; 3) concomitant atherosclerosis; and 4) microvascular dysfunction (3,4). Optimal management of stable CAE centers on traditional atherosclerotic risk factor modification. Nitrates, however, have been shown to exacerbate myocardial ischemia and should generally be avoided as antianginal therapy (5).

Acute coronary syndromes in patients with CAE are difficult to manage and are associated with worse outcomes when compared with patients with normal

FIGURE 3 Still Images From Coronary Angiography Demonstrating Diffuse, Severe Coronary Ectasia With Sluggish Flow to Distal Coronary Beds



(A) Right anterior oblique, caudal view, **(B)** left anterior oblique, caudal view, and **(C)** cranial view of the left coronary artery. **(D)** Cranial view of the right coronary artery.

coronary anatomy (4). Percutaneous interventions are technically challenging, but they can include thrombectomy, intracoronary infusion of thrombolytic agents or glycoprotein IIb/IIIa inhibitors, or covered stenting in the appropriate clinical setting, although data are limited (4). Techniques for surgical repair include resection of aneurysmal segments or bypass grafting and are driven by individual patient anatomy (4). Medical management centers on antithrombotic therapy, with an observational analysis of 51 patients demonstrating that patients with CAE who were able to achieve significant (≥60%) time in therapeutic range with warfarin anticoagulation had significant reductions in adverse cardiovascular outcomes over 49-month follow-up (6). No data are currently available on the efficacy of direct oral anticoagulant therapy in this group.

With regard to etiology, the patient's family history and aneurysmal dilations in other vascular beds triggered a genetic evaluation that revealed the patient was a carrier of a missense variant in the *TGFβ3* gene. Variants in *TGFβ3* have been associated with aortic aneurysmal disease with clinical overlap with MFS and Loeys-Dietz syndrome (7), but there remain conflicting interpretations of our patient's variant because of limited available data.

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FOLLOW-UP

Autopsy revealed the following: 1) coronary vasculature with intimal fibrosis, replacement scar, but no evidence of necrosis or healed arteritis; 2) a subacute, large transmural infarct from the posterior septum to the lateral free wall, with evidence of thrombus in the proximal left circumflex artery; and 3) acute thrombus in the distal left main artery. To investigate further whether the identified variant of uncertain significance is pathogenic, we are in the process of contacting family members for genetic evaluation.

CONCLUSIONS

We present a case of ischemic cardiac arrest in the context of diffuse CAE, potentially resulting from an underlying genetic connective tissue disorder, and highlight challenges in the management of these patients.

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KEY WORDS cardiac arrest, connective tissue disease, coronary ectasias, coronary thrombosis

APPENDIX For supplemental videos, please see the online version of this paper.