JACC: CASE REPORTS VOL. 4, NO. 14, 2022

CASE REPORT

ADVANCED

CLINICAL CASE: SURGERY AND INTERVENTIONS

Spontaneous Coronary Artery Dissection and Papillary Muscle Rupture in Patient With Undiagnosed Vascular Ehler-Danlos Syndrome

Johan Hopfgarten, MD,[a,b] Christina Christersson, MD, PhD,[a,b] Johan Forsblad, MD,[a] Eva-Lena Stattin, MD, PhD,[c,d] Anders Albåge, MD, PhD[e,f]

ABSTRACT

We present the case of a woman with acute coronary syndrome on the basis of spontaneous coronary artery dissection causing a papillary muscle rupture with severe mitral regurgitation and acute heart failure. The patient subsequently underwent successful emergent surgery of both the mitral and tricuspid valves. Postoperatively, the patient was diagnosed with vascular Ehlers-Danlos syndrome. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:902–905) © 2022 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 61-year-old woman presented to the emergency department with retrosternal chest pain that had subsided on arrival. The initial work-up was unremarkable, with normal electrocardiogram and laboratory test results. Computed tomography ruled out proximal aortic dissection but showed a dissection of the right renal artery. She developed recurrent chest pain with anterior ST-segment depressions consistent with posterior ST-segment elevation myocardial infarction. Coronary angiography showed a spontaneous coronary artery dissection (SCAD) in an obtuse marginal branch of the left circumflex artery, which was treated conservatively without intervention (Video 1, **Figure 1**). During angiography, she developed hypotension and pulmonary edema but was stabilized on diuretic agents and noninvasive positive pressure ventilation. A transthoracic echocardiogram was done with poor image quality, unable to diagnose the patient's condition. She was moved to a cardiac intensive care unit with persistent shortness of breath and hypotension and was treated with antibiotics

LEARNING OBJECTIVES

- To highlight the specific risk factor profile of patients with SCAD.
- To understand the role of vEDS in cardiac disease and the difficulties in surgical management of these patients because of tissue fragility.

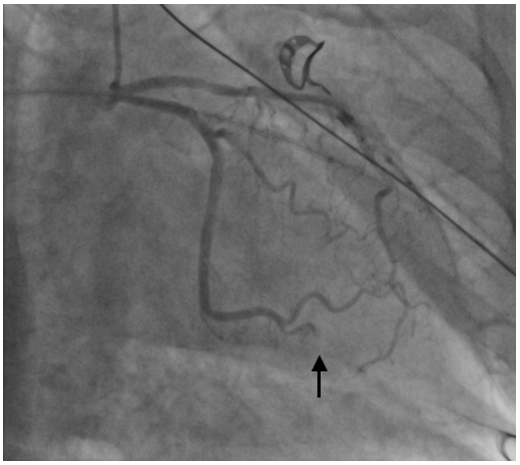
From the [a]Department of Cardiology, Uppsala University Hospital, Uppsala, Sweden; [b]Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [c]Department of Clinical Genetics, Uppsala University Hospital, Uppsala, Sweden; [d]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden; [e]Department of Cardiothoracic Surgery and Anesthesiology, Uppsala University Hospital, Uppsala, Sweden; and the [f]Department of Surgical Sciences, Uppsala University, Uppsala, Sweden.

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 Author Center.

Manuscript received April 13, 2022; accepted May 2, 2022.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2022.05.004

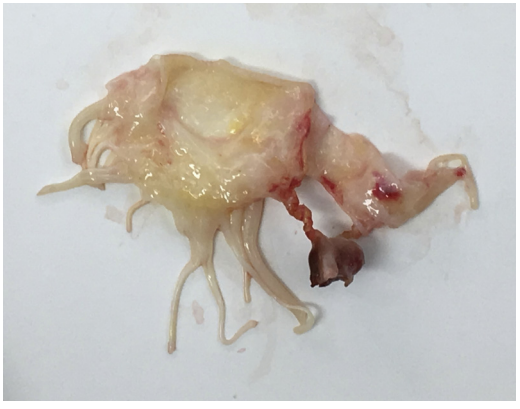
FIGURE 1 Coronary Angiogram



Coronary angiogram showing a spontaneous coronary artery dissection in the obtuse marginal branch of the left circumflex artery **(arrow)**.

because of suspicion of pneumonia and intermittent noninvasive positive pressure ventilation for a total of 10 days before she started to deteriorate with worsening hypotension. A renewed echocardiogram now gave the diagnosis of posteromedial papillary muscle rupture with severe mitral regurgitation, most likely caused by the dissected obtuse marginal branch (Videos 2 to 4). The patient was accepted for emergent mitral valve surgery the following day.

FIGURE 2 Excised Anterior Leaflet



Excised anterior leaflet of the mitral valve with a ruptured papillary muscle head.

PAST MEDICAL HISTORY

The patient had no known risk factors for coronary artery disease. Her past medical history included hypothyroidism, fibromyalgia and longstanding problems with pain from joints and muscles, and a history of bruising easily. She had no children of her own.

DIFFERENTIAL DIAGNOSIS

The patient presented with acute coronary syndrome (ACS) on the basis of SCAD, which is an underrecognized but important cause of ACS, particularly among women with a low prevalence of traditional cardiovascular risk factors. The true prevalence is uncertain, but recent studies suggest SCAD may be the cause of 1% to 4% of all ACSs and up to 35% of ACSs in women ≤50 years of age.[1] Numerous conditions have been associated with SCAD, the most common being fibromuscular dysplasia. Other inherited disorders associated with arterial fragility and dissection, such as vascular Ehlers-Danlos syndrome (vEDS), Marfan syndrome, and Loeys-Dietz syndrome, have also been implicated as risk factors for SCAD, although these are rare and underlie no more than 5% of all cases.[1]

Papillary muscle rupture is a rare but life-threatening condition most often associated with ACS. Nonischemic ruptures are more infrequent but have been reported in conditions such as myocarditis, endocarditis, EDS, takotsubo cardiomyopathy, and mitral annular calcification.[2]

MANAGEMENT

Before surgery and induction of anesthesia, the patient was hypotensive with clinical pulmonary edema. Surgery was performed through a median sternotomy, and upon entry, 1,500 mL of pleural fluid was evacuated. The patient was cannulated in the ascending aorta and separately in both venae cavae. At this point, there was an obvious increased fragility of the right atrial tissue because it partly ruptured upon cannulation. Cardiopulmonary bypass was started, and cardioplegia, both antegrade and retrograde, was administered. The left atrium was opened in the interatrial groove, and the mitral valve diagnosis was confirmed, showing a flail head of a papillary muscle in the A2-A3 region with entangled chordae (**Figure 2**). The valve was deemed irrepairable because of the excessive tissue fragility. The anterior mitral leaflet was entirely excised, and a mechanical mitral valve (ATS Medical Open Pivot 29 mm,

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

SCAD = spontaneous coronary artery dissection

vEDS = vascular Ehlers-Danlos syndrome

JACC: CASE REPORTS, VOL. 4, NO. 14, 2022
JULY 20, 2022:902–905

Medtronic) was implanted. In addition, a tricuspid ring annuloplasty (CE Physio Tricuspid 32 mm, Edwards Lifesciences) was performed. Weaning from cardiopulmonary bypass, decannulation, and administration of protamine sulfate was uneventful, but in the final stage of the operation, there was a sudden and spontaneous rupture of the large brachiocephalic vein in the cephalad portion of the wound cavity with profuse bleeding requiring multiple sutures.

The postoperative period was complicated with atrial fibrillation, the need for permanent pacemaker implantation, pneumothorax treatment, and prolonged antibiotic therapy. The patient required 5 days in the intensive care unit and was finally discharged 23 days after surgery in good condition.

INVESTIGATIONS

Preoperative transthoracic and transesophageal echocardiography confirmed a hyperdynamically contracting left ventricle and a severe mitral regurgitation on the basis of a flail anterior mitral leaflet with a 1.5-cm mass on the atrial side representing the papillary muscle head (Videos 5 and 6). In addition, systolic right ventricular pressure was 85 mm Hg, and a severe tricuspid regurgitation was present, necessitating double valve surgery. Postoperative echocardiography showed normal left ventricular function, a well-functioning mitral prosthesis, and remaining mild tricuspid regurgitation.

Because of spontaneous dissections of both the right renal and a coronary artery, the patient was further evaluated for connective tissue disorder after discharge. Genetic analysis showed a variant in *COL3A1*, c.2555G>T, p.(Gly852Val) [NM_000090.3]. To our knowledge, this variant has not been described before in the literature, although another amino acid exchange in the same codon has been defined as pathogenic.[3] The variant was defined as likely pathogenic, and the patient was diagnosed with vEDS.[4]

DISCUSSION

We present the case of a woman with spontaneous dissections in both the right renal artery and a branch of the left circumflex artery, with the latter causing ACS, papillary muscle rupture with severe mitral regurgitation, and acute heart failure. The patient underwent successful surgery of both the mitral and tricuspid valves in a procedure complicated by remarkable tissue fragility. Postoperatively, the patient was diagnosed with vEDS, with genetic analysis showing a novel variant in *COL3A1*.

vEDS is a rare genetic disorder of connective tissue with a prevalence of 1/50,000 to 1/200,000.[2] It is an autosomal dominant disorder caused by pathogenic variants of the *COL3A1* gene, which encodes type III collagen. The diagnosis requires genetic testing, but clinical signs such as easy bruising, early onset of varicose veins, and characteristic facial features can raise the suspicion. It is a potentially life-threatening condition, with increased risk of visceral rupture as well as vascular aneurysm, dissection, and rupture. There is no established medical treatment in vEDS, but studies have suggested that treatment with celiprolol, a cardioselective β1 blocker with a vasodilatory effect, may reduce the frequency of arterial events.[5] The patient had no relatives with known vEDS, but approximately 50% of all patients have a de novo mutation, making it possible that she was the first in her family with vEDS.

There are reports of SCAD in patients with vEDS, although this is a relatively rare complication, with dissections primarily affecting medium to large arteries.[2] There are 2 reported cases of papillary muscle rupture in patients with vEDS; both were nonischemic and presented in the postpartum period.[6,7] The authors found only 1 prior report of successful surgery of the mitral valve in vEDS, with surgical repair being technically challenging because of tissue and vascular fragility.[8] This is, to the best of our knowledge, the first reported case of a patient with vEDS with papillary muscle rupture caused by SCAD undergoing successful surgery of both the mitral and tricuspid valves.

FOLLOW-UP

The patient was started on celiprolol, and follow-up has been uneventful, with no further vascular events.

CONCLUSIONS

The case highlights the importance of considering SCAD in patients with ACS without traditional cardiovascular risk factors. The SCAD in the presented case subsequently caused an ischemic papillary muscle rupture, necessitating emergent surgery of the mitral and tricuspid valves, which proved to be technically challenging because of tissue fragility related to the patient's underlying vEDS. This further highlights the importance of considering disorders of tissue and vascular fragility in patients with spontaneous artery dissections, because this has important implications for surgical management.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Johan Hopfgarten, Akademiska sjukhuset, 751 85, Uppsala, Sweden. E-mail: johan.hopfgarten@medsci.uu.se.

REFERENCES

1. Hayes SN, Kim ESH, Saw J, et al. Spontaneous coronary artery dissection: current state of the science. *Circulation*. 2018;137(19):e523–e557.

2. Byers PH, Belmont J, Black J, et al. Diagnosis, natural history, and management in vascular Ehlers-Danlos syndrome. *Am J Med Genet C Semin Med Genet*. 2017;175(1):40–47.

3. Pepin MG, Schwarze U, Rice KM, Liu M, Leistritz D, Byers PH. Survival is affected by mutation type and molecular mechanism in vascular Ehlers-Danlos syndrome (EDS type IV). *Genet Med*. 2014;16(12):881–888.

4. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants. *Genet Med*. 2015;17(5):405–424.

5. Baderkhan H, Wanhainen A, Stenborg A, Stattin EL, Björck M. Celiprolol treatment in patients with vascular Ehlers-Danlos syndrome. *Eur J Vasc Endovasc Surg*. 2021;61(2):326–331.

6. Sève P, Dubreuil O, Farhat F, Plauchu H, Touboul P, Broussolle C. Acute mitral regurgitation caused by papillary muscle rupture in the immediate postpartum period revealing Ehlers-Danlos syndrome type IV. *J Thorac Cardiovasc Surg*. 2005;129(3):680–681.

7. Hutt E, Santos-Martins C, Aguilera J, Wierup P, Kalahasti V, Tan C. A 27-year-old woman with postpartum papillary muscle rupture. *J Am Coll Cardiol Case Rep*. 2020;2(14):2191–2195.

8. Takano H, Miyamoto Y, Sawa Y, et al. Successful mitral valve replacement in a patient with Ehlers-Danlos syndrome type VI. *Ann Thorac Surg*. 2005;80(1):320–322.

KEY WORDS acute coronary syndrome, dissection, genetic disorders, mitral valve, papillary muscle, valve replacement

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