Radiology Case Reports 18 (2023) 4374–4379

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Severe familial coronary artery spasm in 2 siblings: About 2 cases ☆,☆☆,★,★★

Oualid Kerrouani, MD[a,b], Raid Faraj, MD[a,b,], Abderrahmane Bouchaala, MD[a,b], Hassan Dib, MD[a,b], Nouhaila Lahmouch, MD[a,b], Iness Bargach, MD[a,b], Ouassima Kihoul, MD[a,b], Jamila Zarzur, PhD[a,b], Mohamed Cherti, PhD[a,b]*

[a] *Mohammed V University, Rabat, Morocco*
[b] *Cardiology B Department, Ibn Sina University Hospital center, Rabat, Morocco*

ARTICLE INFO

Article history:
Received 19 August 2023
Revised 26 August 2023
Accepted 1 September 2023

Keywords:
Coronary artery spasm
Familial spasm
Coronary angiography

ABSTRACT

Vasospastic angina is the spasm of coronary arteries causing transient myocardial ischemia. VSA is commonly managed with antispasmodic medications including calcium-channel blockers and nitrates. When vasospasm is refractory to conventional medications, unconventional treatment modalities may be used for symptomatic relief. Coronary artery spasm was observed in 2 sisters. Neither of them had significant atheromatous stenosis in the coronary arteries. The 22-year younger sister presented with rest angina in the early morning. The 32-year-old elder sister complained of rest and effort angina. Their coronary angiogram showed spontaneous spasm in the proximal segment of the left anterior descending coronary artery. The youngest one had resistant and recurrent coronary vasospasm involving different segments of the coronary tree causing myocardial infarction with total occlusion of the proximal segment in the left anterior descending coronary artery. Our patients presented with a lesser-known phenomenon called refractory VSA, where intermittent vasospasm continues despite being on a combination of 2 medications. The familial appearance of coronary artery spasm had been previously reported. Although it is not well understood, the underlying mechanism appears to involve a combination of endothelial

Abbreviations: CAD, coronary artery disease; CAS, coronary artery spasm; CCB, calcium-channel blockers; cTnI, cardiac troponin I; ECG, electrocardiogram; eNOS, endothelial nitric oxide synthase; HLA, human leukocyte antigen; ISDN, isosorbide dinitrate; LAD, Left descending artery; MRI, magnetic resonance imaging; TTE, thransthoracic echocardiogram; VSA, vasospastic angina.

☆ Acknowledgments: None.

☆☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

★ Availability of Data and Materials: Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

★★ Provenance and Peer Review: Not commissioned, externally peer-reviewed.

* *Corresponding author.*
E-mail address: farajraid95@gmail.com (R. Faraj).

https://doi.org/10.1016/j.radcr.2023.09.005

damage and vasoactive mediators. Genetic factors such as human leucocyte antigen contribute to susceptibility to coronary spasm in some patients with VSA. Treatment for VSA is well documented; however, little data is available for refractory VSA.

Introduction

Coronary artery spasm has been identified as a pathogenic factor in the entire spectrum of ischemic heart disease, including vasospastic angina, acute coronary syndrome, and sudden cardiac arrest [1]. The underlying mechanisms that contribute to its development are still not fully understood and are likely multifactorial, involving disturbance of the autonomic nervous system, endothelial dysfunction, and hypercontractility of smooth muscle cells [2]. Both genetic and environmental factors are known to play a role in the development of various diseases, including coronary artery disease, and previous research has highlighted the significance of genetic mutations and polymorphisms in the development of coronary artery spasm. Although coronary artery vasospasm in the general population has been described in several publications, there has been limited research conducted on familial spastic angina. Here, we report a case of 2 young sisters who had severe, resistant, and recurrent coronary vasospasm involving different segments of the coronary tree, which made their management delicate and challenging.

Our paper was written according to the CARE guidelines [3].

Case presentation

Case presentation 1: A 22-year-old woman presented to our institution in January 2016 due to severe rest angina occurring mainly in the morning, lasting for a few minutes to several hours 2 weeks previously. The pain was not pleuritic in character. She had no cardiovascular risk factors particularly smoking nor diabetes mellitus, or a family history of premature coronary artery disease. She was also afflicted by episodes of vascular headaches of pulsatile character and hemi cranial location; in most cases, these were not related to the time of presentation with the chest pain attacks. She never presented arterial hypertension during the migraine complaints or chest pain. Clinical examination was unremarkable. Initial electrocardiography (ECG) showed a sinus rhythm with QS complex, slight ST elevation in anteroseptal leads with poor R-wave progression in the other chest leads (Fig. 1). Cardiac troponin I (cTnI) level was not elevated. The glucose and lipid test was normal. Transthoracic echocardiogram (TTE) showed akinesis interesting the apex and the anterior wall, the ejection fraction was 45% using the biplane Simpson method. There was no evidence of thrombus or pericardial effusion. Coronary angiography revealed diffuse spasm both in the left main artery, the proximal segment of the left anterior descending coronary artery, and the mild circumflex coronary artery. The spasm was spontaneous; therefore, no provocative test was performed. After intracoronary administration of isosorbide dinitrate (ISDN), the spasm disappeared mostly. No atheromatous coronary occlusive lesions were seen (Fig. 2). Therefore, the diagnosis of vasospastic angina was confirmed, and was treated with a calcium channel blocker and Nitroglycerin spray. She was discharged from hospital with a very poor follow-up. In November 2022, she came to the emergency department of our hospital with a similar chest pain episode; she had not been taking medications for about one week. The ECG and echocardiography remained identical. A repeat coronary angiography revealed total occlusion of the proximal segment in the left anterior descending coronary artery, not resolved after intracoronary nitrates injection. The right coronary artery had severe ostial spasm which promptly resolved after nitroglycerin injection (Fig. 3). Cardiac magnetic resonance imaging (MRI) found late enhancement in the anterior wall, the septum, and the apex, consistent with infarcted and no viable myocardium. The LV ejection fraction was decreased at 38% and no intracavitary thrombi were noted. Therefore, Isosorbide dinitrate and nicorandil were added. Considering the patient's young age and severity of the disease, thrombophilia and autoimmune panel tests were performed and were negative. Despite being on optimal medical therapy, the patient continued to experience angina symptoms during evolution, therefore, the possibility of performing preventive angioplasty of the proximal LAD was discussed.

Case presentation 2: The patient mentioned during this hospitalization that her sister who is 37 years old also had exertional angina for 6 months. She had no risk factor either. Her ECG (Fig. 4) and TTE at rest were normal. A coronary angiography was performed and found a subocclusion of the mid-left anterior descending artery (LAD) with an ipsilateral and contralateral circulation that was not resolved after intracoronary administration of isosorbide dinitrate (Fig. 5). The patient was discharged with a treatment consisting of calcium channel blocker, Isosorbide dinitrate, and Nicorandil.

Discussion

VSA is an important functional cardiac disorder, which was first described as a "variant angina" by Prinzmetal et al. [1]. It is characterized by transitory myocardial ischemia induced by spasm of the epicardial coronary arteries, and angina attacks typically happen while at rest. It can be associated with life-threatening events including myocardial infarction, as we presented in our case. VSA is more common in Asia, and new reports suggest that Asian and Caucasian populations may potentially have similar prevalence rates [1]. It can affect vessels with underlying coronary disease and also those with normal coronary arteries, as in our patient's case. Yasue et al. reported

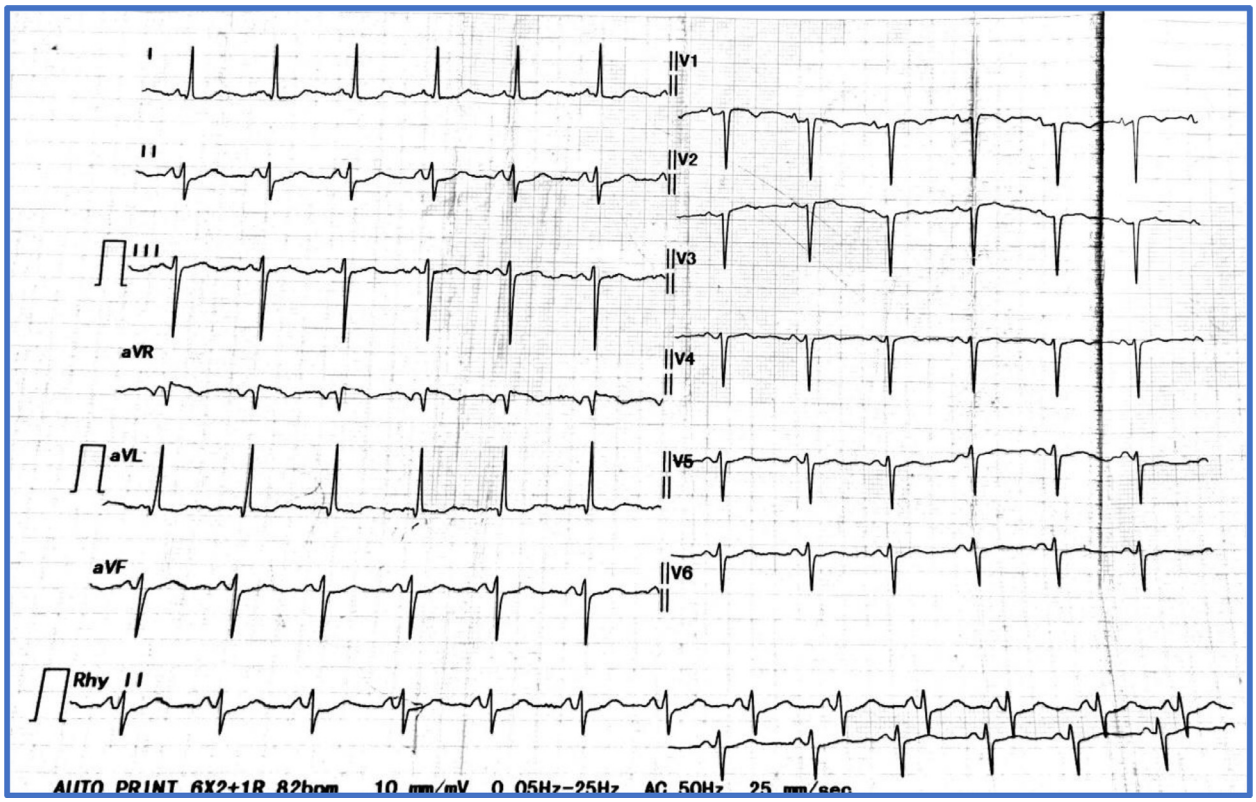

Fig. 1 – ECG findings of case 1: sinus rhythm with QS complex, slight ST elevation in anteroseptal leads with poor R-wave progression in the other chest leads.

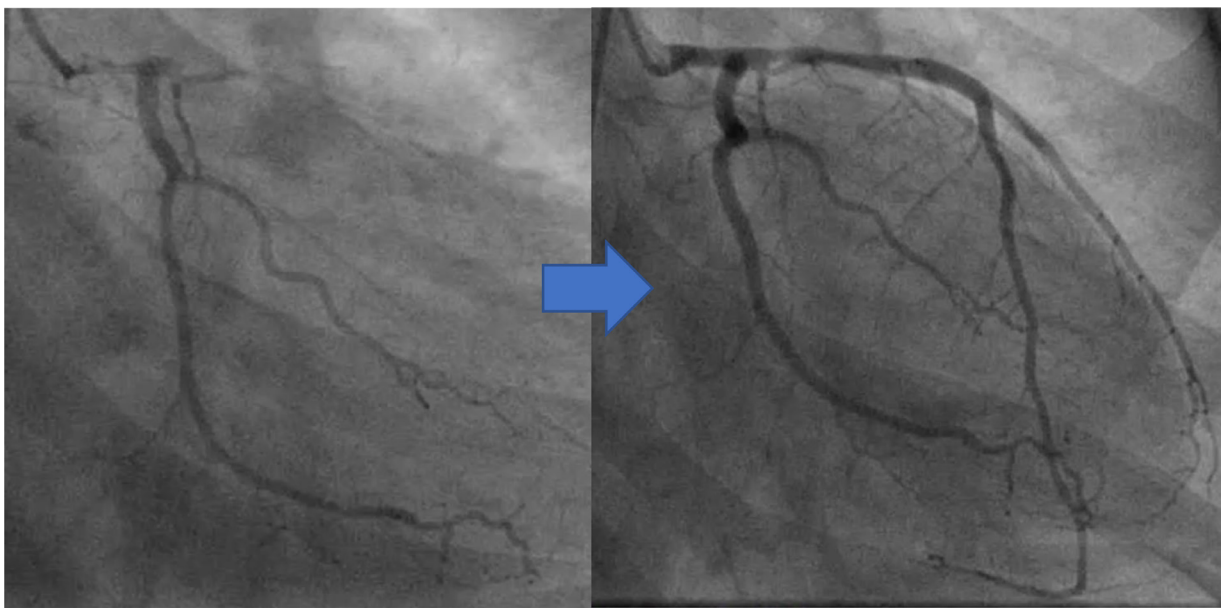

Fig. 2 – First coronary angiography findings of case 1: diffuse spasm both in the left main artery, the proximal segment of the left anterior descending coronary artery, and the mild circumflex coronary artery. After the intracoronary administration of isosorbide dinitrate (ISDN), the spasm disappeared mostly.

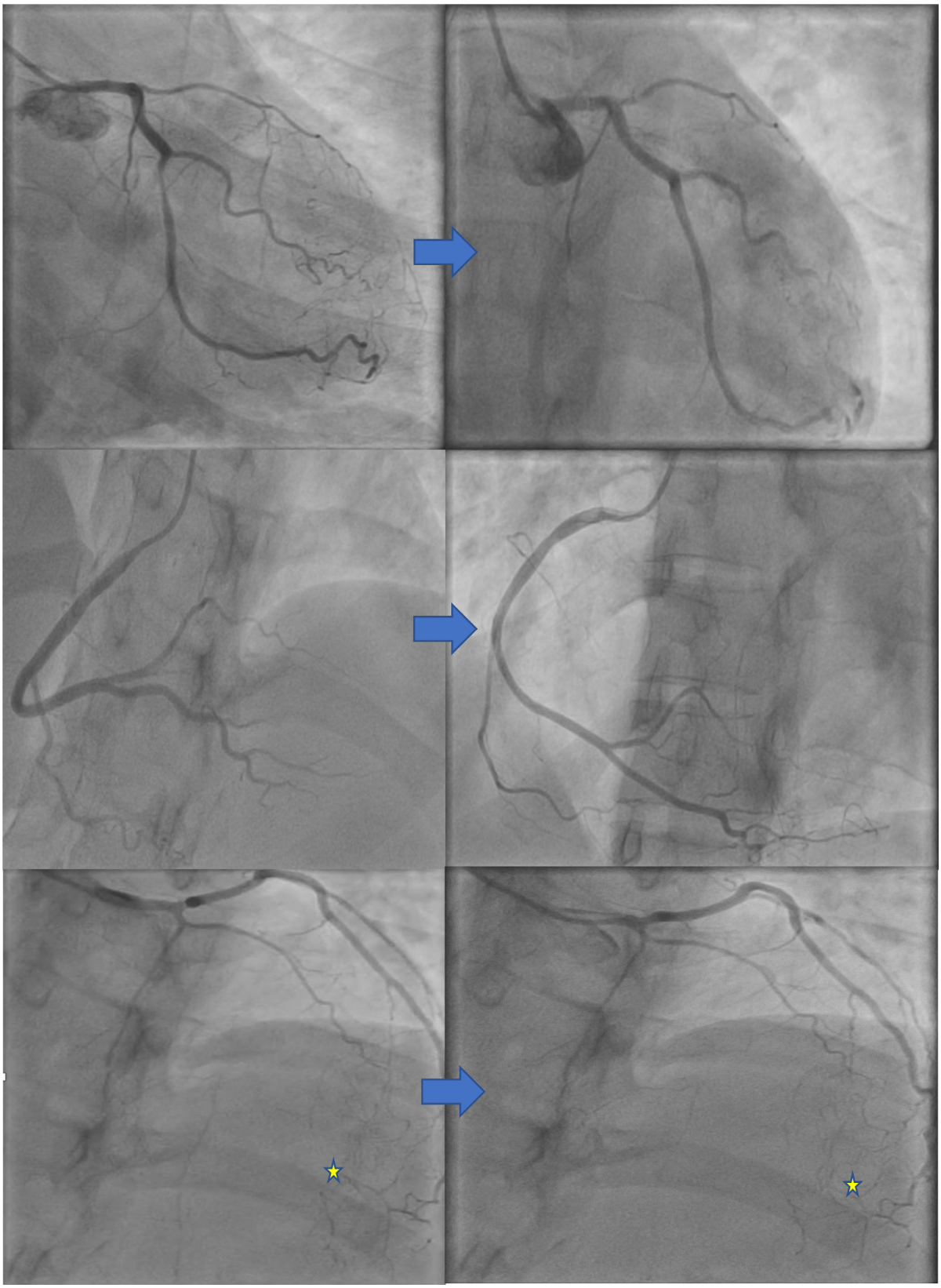

Fig. 3 – Coronary angiography findings of case 1: total occlusion of the proximal segment in the left anterior descending coronary artery with ipsilateral circulation (yellow star), not resolved after intracoronary nitrates injection. Spasm of the mild circumflex coronary artery and the ostial segment of the right coronary artery resolved after nitrates injection.

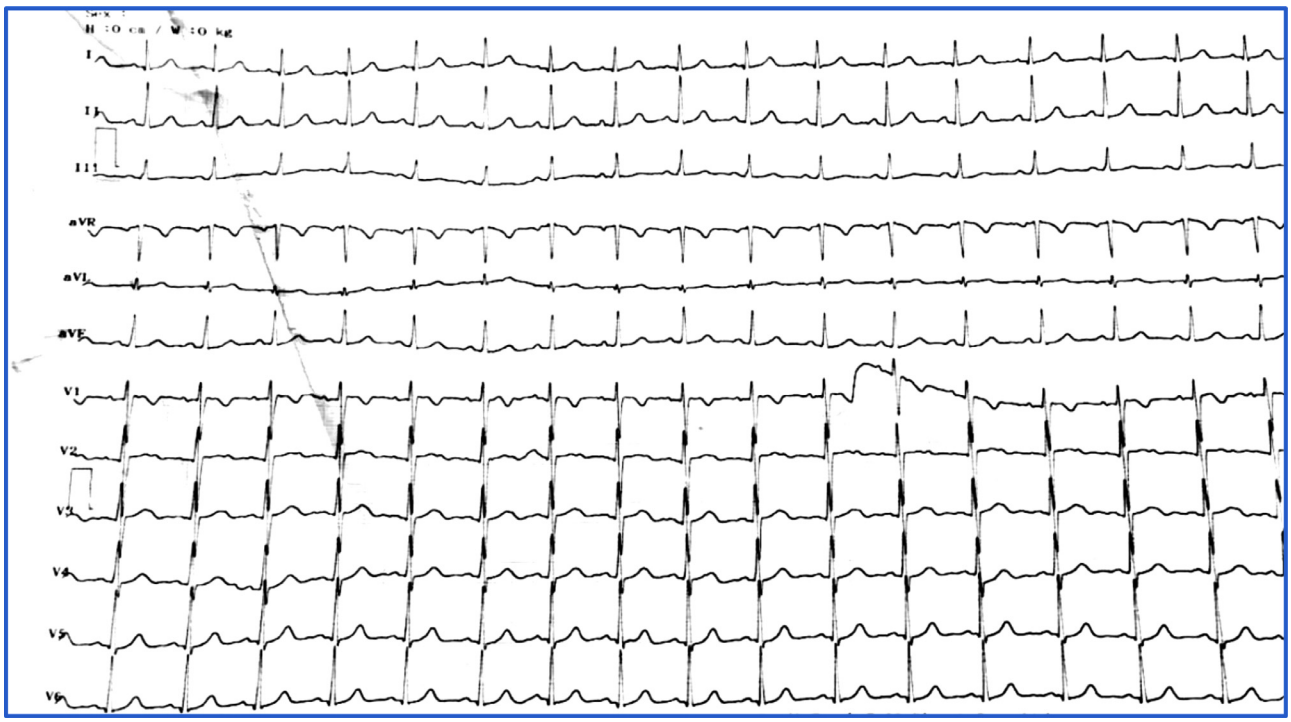

Fig. 4 – ECG findings of case 2 that was unremarkable.

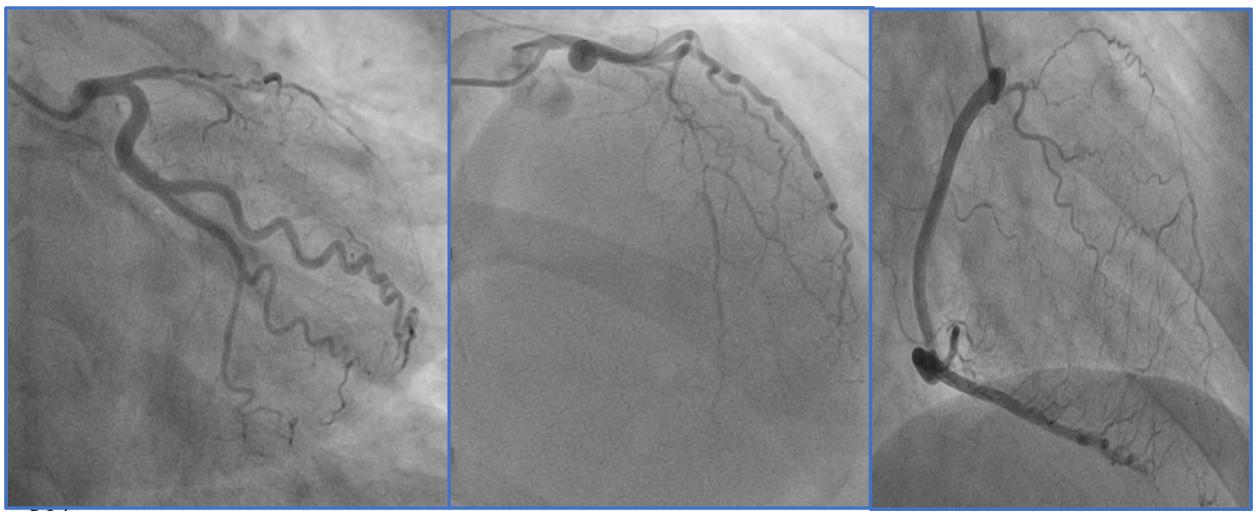

Fig. 5 – Coronary angiography findings of case 2: subocclusion of the mid left anterior descending artery (LAD) with an ipsilateral and contralateral circulation that was not resolved after intracoronary administration of isosorbide dinitrate.

that coronary spasm is thought to be related to endothelial cell dysfunction, leading to hypercontractility of smooth muscle cells [4]. The rho-kinase system is also involved in the contractility of these cells, which may be extremely important in the etiology of coronary artery spasm. The female population exhibit certain characteristics in this pathology, such as a relatively more severe clinical presentation, multiple spasms, and more frequent microvascular spastic phenomena. The cases that we reported had severe and multiple spasms and had no risk factors. Recently, cases of VSA in families have been reported, and it is thought that a gene deficiency, such as an abnormality of the endothelial nitric oxide synthase (eNOS) gene or the HLA antigen, is responsible for the pathogenesis [5]. Indeed, Numano et al. [6] investigated the relationship between vasospastic angina and human leukocyte antigen (HLA) and suggested that genetic factors in disequilibrium with HLA-B40 or Bw 52 antigen may be linked to the pathophysiology of CAS. In both our cases, HLA type DQw3 was not performed. In Japanese, certain authors have described cases of vasospastic angina in families, including those involving brothers and sisters [7,8]. These findings reinforce the theory that vasospastic angina has a genetic factor. Hereditary

predisposition to coronary vasospasm appears rare because cases similar to ours remain very few. Calcium-channel blockers (CCB) and nitrates are 2 antispasmodic drugs that are frequently used to treat VSA. Unconventional therapies may be employed for symptomatic relief when vasospasm is refractory. These treatment methods include the use of alpha-2-agonists, rho-kinase-inhibitors, statins, and magnesium [9,10]. In addition to pharmacotherapy, angioplasty may be indicated but it is only performed for recurrent focal spasms [11], which is not the case for our patient. Aggressive risk factor modification, such as smoking and alcohol cessation should be recommended. We advised our patients to avoid any emotional or physical triggers of their symptoms. Further research and the sharing of the experiences of managing such perplexing refractory VSA cases should be encouraged to better understand and expand management.

Conclusion

Vasospastic angina is a dangerous but uncommon heart disorder. Although significant progress has been achieved in the diagnosis and treatment of VSA, the condition is still difficult to diagnose and treat because of the disease's wide range of clinical manifestations. Familial cases of vasospastic angina may be somewhat influenced by genetic factors. The search for genetic elements involved in the process of vasospasm has to be given much greater attention.

Patient consent

Written informed consent was obtained from the 2 patients for publication of this study and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

REFERENCES

[1] Prinzmetal M, Kennamer R, Merliss R, Wada T, Bor N. Angina pectoris. I. A variant form of angina pectoris; preliminary report. Am J Med 1959;27:375–88.
[2] Lanza GA, Careri G, Crea F. Mechanisms of coronary artery spasm. Circulation 2011;124(16):1774–82.
[3] Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: explanation and elaboration document. J Clin Epidemiol 2017;89:218–35.
[4] Yasue H. Pathophysiology and treatment of coronary arterial spasm. Chest 1980;78:216–23.
[5] Kawata M, Mizutani T, Shimizu M, Takenaka K, Kobayashi S, Okada T, et al. Endothelial nitric oxide synthase gene mutation and human leukocyte antigen analyzed in three cases of familial vasospastic angina pectoris. Jpn Circ J 2000;64:524–7.
[6] Numano F, Nomura S, Yajima M, Aizawa T, Fujii J, Kishida H, et al. Human leucocyte antigen in variant angina. Int J Cardiol 1987;14:47.
[7] Yoshino F, Sakuma N, Unoki T, Fukugawa K, Miyamoto T, Nishio H, et al. Variant angina in two brothers with left anterior descending coronary artery spasm. Am J Cardiol 1989;63:379.
[8] Fujiwara Y, Yamanaka O, Nakamura T, Yamaguchi H. Coronary spasm in two sisters. Jpn Circ J 1993;57:472.
[9] Frenneaux M, Kaski JC, Brown M, Maseri A. Refractory variant angina relieved by guanethidine and clonidine. Am J Cardiol 1988;62:832–3.
[10] Masumoto A, Mohri M, Shimokawa H, Urakami L, Usui M, Takeshita A. Suppression of coronary artery spasm by the Rho-kinase inhibitor fasudil in patients with vasospastic angina. Circulation 2002;105:1545–7.
[11] Khatri S, Webb JG, Carere RG, Dodek A. Stenting for coronary artery spasm. Catheter Cardiovasc Interv 2002;56:16–20.