ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Myocardial Infarction in Young Adults: Diagnosis Begins Through Inspection

Genç Yetişkinlerde Miyokard Enfarktüsü: Teşhis Muayene ile Başlar

ABSTRACT

Spontaneous coronary artery dissection (SCAD) is an atypical cause of myocardial infarction, predominantly seen in women. Among various predisposing factors, genetic vasculopathies such as connective tissue diseases significantly contribute to SCAD. This report discusses a 36-year-old male diagnosed with vascular type Ehlers-Danlos syndrome following an anterior myocardial infarction and explores relevant literature.

Keywords: Acute coronary syndromes, connective tissue disease, premature myocardial infarction, spontaneous coronary artery dissection, vascular Ehler-Danlos syndrome

ÖZET

Spontan koroner arter diseksiyonu (SKAD), genellikle orta yaşlı kadınları etkileyen nadir bir akut koroner sendrom formudur. Genetik vaskülopatiler de dahil olmak üzere bağ dokusu hastalıkları SCAD'ye yol açan önemli predispozan durumlardan biridir. Bu yazıda, anterior miyokard enfarktüsü geçiren ve vasküler tip Ehler-Danlos sendromu tanısı alan 36 yaşında bir erkek hasta sunulmuş ve literatür gözden geçirilmiştir.

Anahtar Kelimeler: Akut koroner sendromlar, bağ dokusu hastalığı, prematüre miyokard enfarktüsü, spontan koroner arter diseksiyonu, vasküler Ehler-Danlos sendromu

CASE REPORT
OLGU SUNUMU

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Received: November 30, 2022
Accepted: August 16, 2023

Cite this article as: Kumral Z, Çolak A, Özpelit ME, Özpelit E. Myocardial infarction in young adults: Diagnosis begins through inspection. *Turk Kardiyol Dern Ars.* 2024;52(4):293-297.

DOI:10.5543/tkda.2023.52578

Myocardial infarction (MI) is more commonly observed in older individuals, but it also affects younger people under 45 years, referred to as premature or young adult MI. Conventional risk factors account for approximately 80% to 85% of these cases, while the remaining 15% to 20% are linked to non-atherosclerotic risk factors that promote thrombosis and/or inflammation.[1]

Several factors can contribute to young adult MI, including coronary artery abnormalities (congenital conditions like aortic coarctation or acquired issues such as coronary artery vasculitis), genetic disorders (such as familial hypercholesterolemia or hypertrophic cardiomyopathy), substance abuse (especially cocaine or amphetamines), smoking, diabetes, stress, and obesity.[2]

It is critical to investigate additional other etiologies beyond the typical risk factors in these younger patients. In this report, we discuss the case of a young patient diagnosed with a genetic vasculopathy following an acute MI.

Case Report

A 36-year-old man without any prior history of hypertension, diabetes, hyperlipidemia, smoking, or family coronary artery disease presented at another hospital's emergency unit with retrosternal chest pain lasting for two hours. His vital signs at presentation included a blood pressure of 135/85 mmHg, respiratory rate of 22 breaths per minute, and heart rate of 104 bpm. His initial electrocardiogram showed sinus rhythm with ST segment elevations in anterior leads, indicative of an anterior MI (Figure 1). The coronary angiogram revealed a subtotal dissected lesion with Thrombolysis in Myocardial

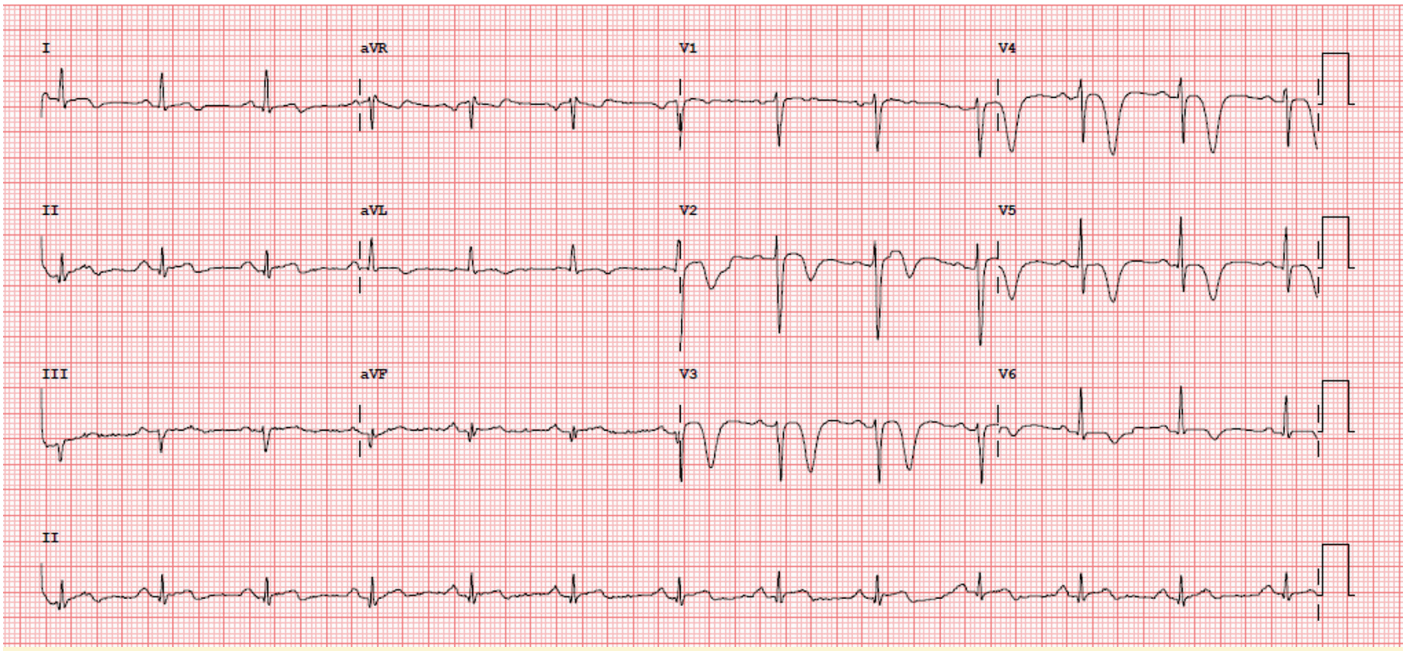

Figure 1. Electrocardiography two weeks after anterior acute myocardial infarction.

Infarction-2 (TIMI-2) flow in the left anterior descending (LAD) artery, while the circumflex and right coronary arteries showed no significant stenosis. Drug-coated stents (2.75 x 33 mm and 3.0 x 22 mm) were implanted, achieving a final TIMI-3 flow (Figure 2). Post-procedure, the patient underwent evaluation for typical cardiovascular risk factors. He was screened for undiagnosed hypertension or diabetes mellitus; however, his blood pressure and fasting blood glucose levels were within normal limits, as was his HbA1c. His lipid profile revealed low-density lipoprotein cholesterol at 123 mg/dl, triglycerides at 194 mg/dl, total cholesterol at 108 mg/dl, and high-density lipoprotein cholesterol at 49 mg/dl. Echocardiography showed a normal ejection fraction of 60% with no significant valvular abnormalities. Upon discharge, he was prescribed acetylsalicylic acid 100 mg daily (QD), ticagrelor 90 mg twice daily, metoprolol 50 mg daily, ramipril 5 mg daily, and atorvastatin 80 mg daily.

Following his discharge, the patient visited our cardiology outpatient clinic. With no conventional cardiovascular risk factors identified, further investigations were undertaken to explore other potential causes of premature MI. Thrombophilia tests were conducted, revealing no Factor V Leiden or prothrombin gene mutations. Levels of lipoprotein A, homocysteine, and anticardiolipin were also found to be within the normal range.

A comprehensive physical examination of the patient revealed several remarkable findings, such as micrognathia, curvature of the fifth phalanx, flat feet, and a high palate (Figure 3). Further exploration of the patient's medical history uncovered three instances of stillbirth among siblings and a history of vision loss in his mother. These familial occurrences, combined with the patient's physical anomalies, prompted an investigation into inherited vasculopathies using a genetic panel.

During this period, the patient also underwent examinations for other organ involvement, which could suggest a genetic vasculopathy. The evaluations identified an aneurysm in the right iliac artery and right internal carotid artery, as well as diffuse tortuosity in the celiac truncus (Figure 4). Genetic testing confirmed the presence of a heterozygous pathogenic variant, pGly1074Arg mutations in the *COL3A1* gene, leading to a diagnosis of vascular Ehlers-Danlos syndrome (VEDS).

Discussion

This report details a patient with VEDS, diagnosed following a spontaneous coronary artery dissection (SCAD) in the LAD artery that led to an acute anterior MI. The case underscores the importance of thorough physical examination and detailed family history in the evaluation of young patients presenting with MI.

VEDS is a rare genetic disorder characterized by alterations in connective tissue and follows an autosomal dominant inheritance pattern. The condition is driven by mutations in the *COL3A1* gene, which is responsible for the synthesis of type III procollagen.[3] The diagnosis of VEDS requires molecular genetic testing; however, VEDS should be suspected in patients with idiopathic sigmoid colon perforation or spontaneous pneumothorax, particularly when accompanied by other characteristics consistent with VEDS, or in patients who experience arterial dissection or rupture before the age of 40.[4]

ABBREVIATIONS

ACEI	Angiotensin-converting enzyme inhibitor
LAD	Left anterior descending
MI	Myocardial infarction
SCAD	Spontaneous coronary artery dissection
TIMI-2	Thrombolysis in Myocardial Infarction-2
VEDS	Vascular Ehlers-Danlos syndrome

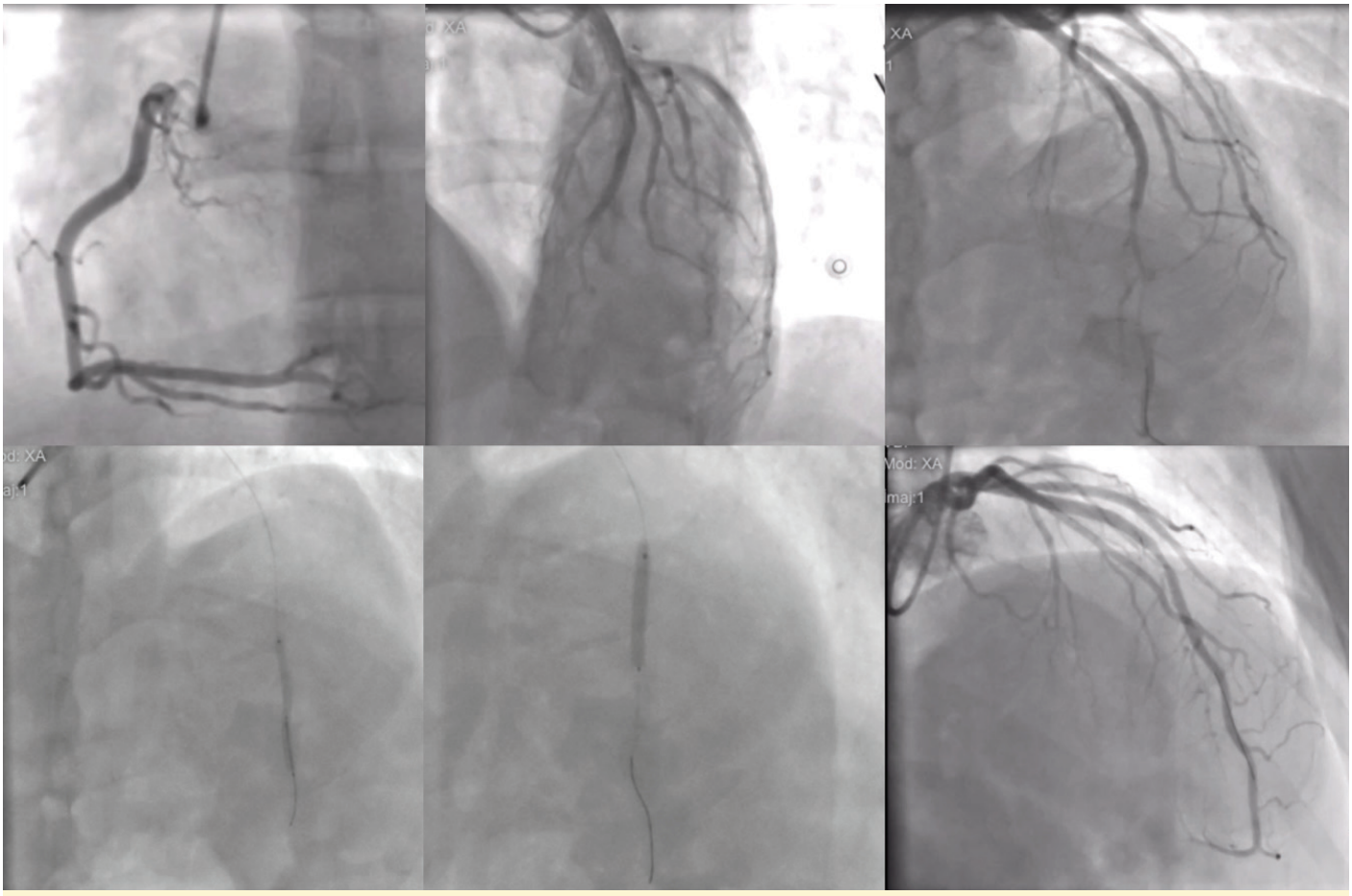

Figure 2. Coronary angiographic images showing percutaneous coronary intervention in the LAD.

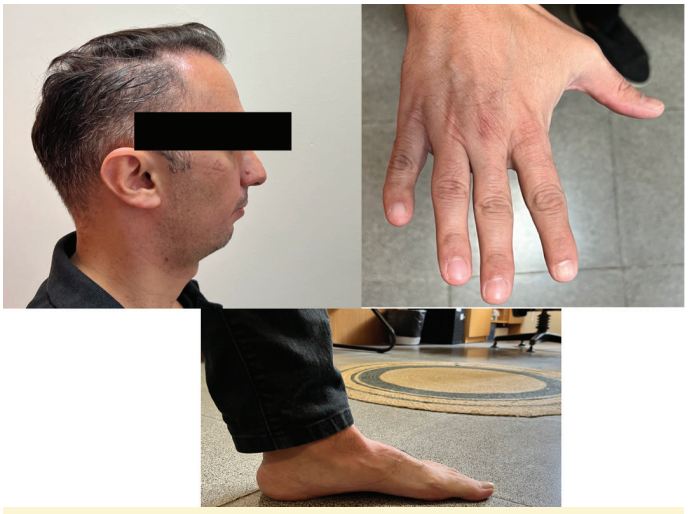

Figure 3. Physical examination findings (micrognathia, a narrow nose, prominent eyes, and acrogeria).

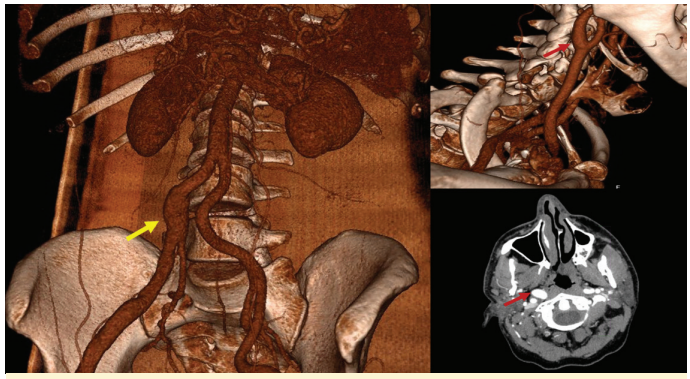

Figure 4. Imaging findings (an aneurysm in the right iliac artery and right internal carotid artery, and diffuse tortuosity in the celiac trunk).

SCAD is characterized by the spontaneous separation of the coronary artery wall layers without any external force, with more than 90% of cases occurring in females. Connective tissue disorders, including fibromuscular dysplasia, Marfan syndrome, and VEDS, are known predisposing factors for SCAD, though they are reported in only 1% to 2% of cases.[5] The pathophysiology of SCAD is understood through two primary mechanisms. The first, the intimal rupture hypothesis, involves the formation of an intramural hematoma due to a tear in the intima, leading to the separation of the vessel wall. The second, the medial hemorrhage hypothesis, posits that spontaneous perforation of the vasa vasorum leads to hemorrhage within the vessel wall, causing separation of the arterial wall.[5]

Table 1. Clinical Characteristics of Patients with Vascular Ehlers-Danlos Syndrome Associated with Spontaneous Coronary Artery Dissection

No	Authors	Published date	COUNTRYC (country)	Age & sex	HIstory	Symptoms	Complications	Diagnosis	Vessel	Treatment	Outcome
1	L. N. Cupo et al.[6]	December, 1981	United States	30-year-old female	Joint hypermobility, lung disease, aneurysms of the sinuses of Valsalva	Chest pain	Myocardial infarction, ventricular fibrillation	NSTEMI-SCAD	LAD	Conservative	Died
2	T. Kitazono et al.[7]	June, 1989	Japan	30-year-old female	None	Chest pain	Myocardial infarction	NSTEMI- SCAD	Not reported	Conservative	Survived
3	L. C. Adès et al.[8]	August, 1995	Australia	16-year-old male	Prominent eyes, a pinched nose, joint hypermobility	Chest pain, nausea	Myocardial infarction	NSTEMI- SCAD	LAD	Conservative	Survived
4	V. Catanese et al.[9]	October, 1995	United States	33-year-old male	Family history	Chest pain	Myocardial infarction	NSTEMI-SCAD	LM, LAD, CX	Conservative	Died
5	A. M. Athanassiou et al.[10]	April, 1996	United States	30-year-old female	30 weeks pregnant, mother died at 42 during labor	Chest pain	Myocardial infarction	NSTEMI- SCAD	Not reported	Conservative	Died
6	Y. Nishiyama et al.[11]	January, 2001	Japan	43-year-old male	Splenic artery rupture, bilateral hip dislocations, equinovarus deformity, sudden deaths in 3 family members	Chest pain	Myocardial infarction, pneumothorax	Inferior STEMI-SCAD	No occlusive stenosis	Conservative	Died
7	Robert S. Dieter et al.[12]	December, 2003	United States	78-year-old male	Abdominal aortic aneurysm, pulmonary artery aneurysm, joint mobility, chronic, conjunctivitis, pectus excavatum	Chest pain	Myocardial infarction	NSTEMI-Coronary arteriomegaly	No occlusive stenosis, coronary arteriomegaly in major proximal vessels	Conservative	Survived
8	Emma R. Gilchrist et al.[15]	January, 2005	United States	30-year-old female	None	Chest pain	Myocardial infarction, cardiac tamponade, myocardial rupture	NSTEMI-SCAD	LAD	Surgery	Died
9	Michinari Nakamura et al.[14]	June, 2009	United States	33-year-old female	Rupture of a splenic artery aneurysm after cesarean section	Chest pain	Myocardial infarction, ventricular fibrillation	NSTEMI-SCAD	LAD, CX, RCA	PCI	Survived
10	Yoshiaki Ohyama et al.[15]	February, 2011	Japan	45-year-old female	Transarterial embolization for right carotid-cavernous fistula	Chest pain	Myocardial infarction, cardiac tamponade	Inferolateral STEMI, SCAD	CX and RCA	Pericardiocentesis, conservative treatment for SCAD	Survived
11	Andres E. Carmona-Rubio et al.[16]	October, 2015	United States	53-year-old female	Skin paleness, pseudoaneurysms involving the right vertebral artery, splenic artery, and common hepatic artery	Chest pain	Anterior STEMI, dissection in LAD and LIMA-LAD CABG	NSTEMI-SCAD	CX and RCA	Conservative	Survived
12	Zeid Nesheiwat et al.[17]	February, 2019	United States	38-year-old female	Hypothyroidism, hypertension	Chest pain	Myocardial infarction	NSTEMI-SCAD	CX-OM	Conservative	Survived
13	Qiao Li et al.	August, 2022	China	39-year-old male	Splenectomy due to splenic rupture, subcutaneous ecchymosis, protruding eyes, thin skin, increased skin elasticity	Chest pain	Myocardial infarction	Anterior STEMI-SCAD	LM, LAD, CX	PCI	Survived

A few cases of VEDS leading to SCAD have been reported (Table 1). The first case in the literature was described by Cupo et al.[6] They detailed the medical history of a 30-year-old female patient who experienced MI alongside joint hypermobility, lung disease, and aneurysms of the sinuses of Valsalva. Early reports in the literature, including this case, were mostly diagnosed postmortem through autopsy. However, today VEDS is well-recognized as a cause of SCAD, a serious and rare cause of MI that primarily affects young to middle-aged women with minimal or no conventional atherosclerotic risk factors. An interesting aspect of our case report is the rarity of SCAD in male patients, with the diagnosis of VEDS being even more unusual among them. Similar to our patient, the diagnosis in previously reported cases was often suspected based on physical examination findings, family history, clinical presentation, and arterial complications and later confirmed by genetic testing.[6-17]

Our patient received dual antiplatelet therapy, beta blockers, an angiotensin-converting enzyme inhibitor (ACEI), and high-dose statin treatment after discharge. There is a general consensus on using beta blockers in SCAD patients as they decrease arterial shear stress.[5,18] However, the use of ACEIs and statins in this setting remains controversial.[5] Rogowski et al.[19] conducted a prospective study in which they prescribed statins to address endothelial dysfunction and reported excellent long-term outcomes in SCAD patients. Conversely, some authors recommend statins only in patients with dyslipidemia or accompanying atherosclerosis.[5,20] Similarly, studies on the use of ACEIs in these patients are scarce in the literature, and ACEIs tend to be recommended for SCAD patients with decreased left ventricular function.[5] A randomized, prospective study is currently underway comparing ramipril plus rosuvastatin versus placebo in patients with SCAD (SAFER-SCAD; Statin and Angiotensin-converting Enzyme Inhibitor on Symptoms in Patients With SCAD). The appropriateness of using ACEIs and statins in our case is uncertain at this time.

Conclusion

This report presents a patient with VEDS, whose initial presentation was an MI, underscoring the importance of maintaining a high level of suspicion for genetic vasculopathies, especially in young patients with SCAD. It also emphasizes the need for a thorough evaluation of comorbidities in young MI patients, including a detailed inquiry into family history, a comprehensive physical examination, and a complete clinical evaluation. Additionally, connective tissue diseases should be considered when assessing patients with SCAD.

Informed Consent: Written informed consent was obtained from the patient for the publication of this case report.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.Ç., E.Ö.; Design – A.Ç., E.Ö.; Supervision – E.Ö.; Resource – M.E.Ö.; Materials – M.E.Ö.; Data Collection and/or Processing – A.Ç.; Analysis and/or Interpretation – Z.K.; Literature Review – Z.K.; Writing – Z.K.; Critical Review – E.Ö.

Use of AI for Writing Assistance: Artificial intelligence was not used in this study.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

References

1. Kayikcioglu M, Ozkan HS, Yagmur B. Premature Myocardial Infarction: A Rising Threat. *Balkan Med J*. 2022;39(2):83-95. [CrossRef]
2. J Borges-Rosa, GM Campos, S Martinho, et al. Myocardial infarction in young adults: are the risk profile and mortality outcomes different from older patients? *European Journal of Preventive Cardiology.* 2021;28(Suppl_1):i81. [CrossRef]
3. 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. [CrossRef]
4. Malfait F, Francomano C, Byers P, et al. The 2017 international classification of the Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet*. 2017;175(1):8-26. [CrossRef]
5. Saw J, Mancini GBJ, Humphries KH. Contemporary Review on Spontaneous Coronary Artery Dissection. *J Am Coll Cardiol*. 2016;68(3):297-312. Erratum in: *J Am Coll Cardiol*. 2016;68(14):1606. [CrossRef]
6. Cupo LN, Pyeritz RE, Olson JL, et al. Ehlers-Danlos syndrome with abnormal collagen fibrils, sinus of Valsalva aneurysms, myocardial infarction, panacinar emphysema and cerebral heterotopias. *Am J Med*. 1981;71(6):1051-1058. [CrossRef]
7. Kitazono T, Imaizumi T, Imayama S, Shinkai H, Takeshita A, Nakamura M. Two cases of myocardial infarction in type 4 Ehlers-Danlos syndrome. *Chest*. 1989;95(6):1274-1277. [CrossRef]
8. Adès LC, Waltham RD, Chiodo AA, Bateman JF. Myocardial infarction resulting from coronary artery dissection in an adolescent with Ehlers-Danlos syndrome type IV due to a type III collagen mutation. *Br Heart J*. 1995;74(2):112-116. [CrossRef]
9. Catanese V, Venot P, Lemesle F, Delille F, Runge I, Kuchly B. Myocardial infarction by spontaneous dissection of coronary arteries in a subject with type IV Ehlers-Danlos syndrome. *Presse Med*. 1995;24(29):1345-1347. French.
10. Athanassiou AM, Turrentine MA. Myocardial infarction and coronary artery dissection during pregnancy associated with type IV Ehlers-Danlos syndrome. *Am J Perinatol*. 1996;13(3):181-183. [CrossRef]
11. Nishiyama Y, Nejima J, Watanabe A, et al. Ehlers-Danlos syndrome type IV with a unique point mutation in COL3A1 and familial phenotype of myocardial infarction without organic coronary stenosis. *J Intern Med*. 2001;249(1):103-108. [CrossRef]
12. Dieter RS, Murtaugh T, Black J, Russell DC. Coronary arteriomegaly in a patient with Ehlers-Danlos syndrome and multiple aneurysms--a case report. *Angiology*. 2003;54(6):733-736. [CrossRef]
13. Gilchrist ER, Duflou JA. Incidental myocardial infarction in Ehlers-Danlos syndrome type IV? *J Forensic Sci*. 2005;50(2):461-464. [CrossRef]
14. Nakamura M, Yajima J, Oikawa Y, et al. Vascular Ehlers-Danlos syndrome--all three coronary artery spontaneous dissections. *J Cardiol*. 2009;53(3):458-462. [CrossRef]
15. Ohyama Y, Iso T, Niño ACV, et al. Multiple spontaneous coronary artery ruptures and cardiac tamponade in vascular Ehlers-Danlos syndrome. *J Cardiol Cases*. 2010;3(1):e29-e32. [CrossRef]
16. Carmona-Rubio AE, Narasa M, Lang J, Graham S, Sharma U. Spontaneous triple-vessel coronary artery dissection in a patient with Ehlers-Danlos Type IV. *J Integr Cardiol*. 2015;1(6):229-231. [CrossRef]
17. Nesheiwat Z, Mangi MA, Kosinski D. Spontaneous Coronary Artery Dissection in a Patient with Undiagnosed Ehlers-Danlos Syndrome. *Cureus*. 2019;11(2):e4065. [CrossRef]
18. Nienaber CA, Powell JT. Management of acute aortic syndromes. *Eur Heart J*. 2012;33(1):26-35b. [CrossRef]
19. Rogowski S, Maeder MT, Weilenmann D, et al. Spontaneous Coronary Artery Dissection: Angiographic Follow-Up and Long-Term Clinical Outcome in a Predominantly Medically Treated Population. *Catheter Cardiovasc Interv*. 2017;89(1):59-68. [CrossRef]
20. Saw J. Spontaneous coronary artery dissection. *Can J Cardiol*. 2013;29(9):1027-1033. [CrossRef]