Recurrent spontaneous coronary artery dissection as the cause of repeated myocardial infarctions

Arnon Møldrup Knudsen[1], Nicolaj Støtrup[2], Henrik Hager[1], Henning Mølgaard[2], and Christina Stilling[1]

[1]Aarhus University Hospital Department of Pathology
[2]Aarhus University Hospital Department of Cardiology

September 20, 2024

Recurrent spontaneous coronary artery dissection as the cause of repeated myocardial infarctions

Arnon Møldrup Knudsen* (1), Nicolaj Brejnholt Støtrup (2), Henrik Hager (1), Henning Mølgaard (2), Christina Stilling (1).

1. Department of Pathology, Aarhus University Hospital, Aarhus Denmark.

2. Department of Cardiology, Aarhus University Hospital, Aarhus Denmark.

*Corresponding author:

Arnon Møldrup Knudsen

Department of Pathology, Aarhus University Hospital, Aarhus Denmark.

Mail: arnknu@rm.dk

Key words: Spontaneous coronary artery dissection, myocardial infarction, myocardial reperfusion injury, infarction sequels

Author contributions

Data generation and interpretation: AMK, NBS, HH, HM, CS

Drafting of manuscript: AMK

All authors have read and approved the final manuscript

Abstract

Spontaneous coronary artery dissection (SCAD) is characterized by intramural hematoma in a coronary artery leading to partial or complete vessel obstruction. A 51-year-old female was hospitalized with acute myocardial infarction and cardiogenic shock. She was diagnosed with severe SCAD, affecting the proximal left coronary artery. A complex percutaneous coronary intervention, complicated by cardiac arrest and need for cardio pulmonary support, succeeded with stent insertion and revascularization. In the following days the patient developed severe heart failure due to extensive cardiac reperfusion injury, and subsequently experienced multiple organ failure, ultimately resulting in death. The patient had previously been acutely hospitalized twice with myocardial infarctions and was both times also diagnosed with SCAD affecting the left coronary artery. This case highlights an unfortunate patient outcome due to recurrent SCAD, and

serves as an important reminder to consider SCAD differential diagnostically in younger female patients with myocardial infarction.

Key clinical message

Spontaneous coronary artery dissection is a relatively rare cause of myocardial infarction among the general population, but is an important differential diagnosis in younger female patients without cardiovascular risk factors, and pregnant individuals, presenting with acute coronary syndrome.

Introduction

Spontaneous coronary artery dissection (SCAD) is an intramural loosening and bleeding of the tunica media within a coronary artery wall that can lead to reduced blood flow or complete luminal arterial obstruction. The clinical presentation varies from short-term chest discomfort to severe chest pain and acute coronary syndrome with risk of myocardial infarction [1]. The prevalence of SCAD among all patients hospitalized with acute coronary syndrome is approximately 4% [2], while up to 90% of all SCAD cases are seen among younger females aged 43-57 with no prior cardiovascular risk factors [3]. SCAD most commonly affects the left anterior descending (LAD) coronary artery [4]. The etiology is multifactorial and known predisposing factors include underlying vessel- or connective tissue diseases such as fibromuscular dysplasia, various genetic syndromes such as Marfan- Ehlers-Danlos, Loeys-Dietz and Alport syndromes, as well as hormonal fluctuations including pregnancy, hypertension and systemic inflammatory conditions. In predisposed individuals, SCAD can be triggered and manifest after physical- or emotional stress [5].

Methods (Differential diagnosis, investigations and treatment)

A complicated percutaneous coronary intervention was performed, during which the patient experienced renewed ventricular fibrillation after formation of a spontaneous embolus in the circumflex artery. The patient was connected to an extra corporal membrane oxygenation (ECMO) system for circulatory support, and stents were successfully inserted into the left coronary artery and LAD, resulting in restoration of TIMI-3 blood flow (Figure 1B). Later, the ejection fraction was estimated to approximately 10% and Troponin I measured to >1.5 million ng/l.

In the following days, the patient had unchanged severe heart failure with an ejection fraction remaining at 10% leading to insufficient organ perfusion and accumulation of lactic acid. The patient eventually developed multi-organ failure despite maximum treatment efforts, and ultimately the treatment was ceased, with the patient passing away shortly thereafter.

Conclusion and results

An autopsy was performed, and in the heart the left ventricular wall was hypertrophic. The myocardium in the antero-lateral part of the left ventricle and the anterior 2/3 of septum was characterized by severe transmural reperfusion injury (Figure 2A). In the same region, fibrotic tissue was identified, indicating previous infarction. In the left main coronary artery and LAD, the SCAD changes were located and confirmed (Figure 2B). In all coronary arteries, only mild atherosclerotic changes in the form of fatty streaks were identified. The patient had previously at age 39 been admitted to emergency care with a Non-ST-elevation myocardial infarction, where a coronary angiography showed SCAD in a branch of LAD resulting in 50% stenosis. At age 48, she was again acutely hospitalized with severe chest pain, and was diagnosed with an ST-elevation myocardial infarction. Coronary angiography showed SCAD from the middle part of LAD involving the distal half of the artery. The patient was treated conservatively at both occasions, due to spontaneous symptom remission. Following the event, the patient was genetically tested for potential pathogenic gene variants related to aortic vascular disease. This was performed due to possible familiar disposition given a twin-sister

also diagnosed with SCAD, and her father and paternal aunt both having aortic aneurisms. However, no pathogenic genetic variants were identified. Post-mortem, supplementary more extensive genetic testing of 106 genes involved in hereditary cardiomyopathies and familial hypercholesterolemia was performed; The testing among others, included the genes *ACTC1, MYBPC3, MYH7, MYL2, MYL3, TNNI3* and *TNNT2* involved in hypertrophic cardiomyopathy [6], *DSP, LDB3, LMNA, PLN, RBM20, SCN5A* and *TTN* involved in dilated cardiomyopathy [7], as well as *APOB, LDLR* and *PCSK9* involved in familiar hypercholesterolemia [8]. No pathogenic or likely pathogenic variants were identified.

Discussion

While SCAD is a relatively rare cause of myocardial infarction among the general population, it is estimated to be the cause of up to 35% of infarctions in females younger than 50 years [2]. Further, SCAD is the most common cause of myocardial infarction among pregnant women and in the post-partum period, and should be excluded in case of acute chest pain in this specific patient group [9]. SCAD recurs in approximately 10% of patients, and the recurrence risk increases with untreated or insufficiently treated hypertension [10]. Given the relatively low recurrence risk, a presentation as reported in this case, with multiple recurrences leading to several myocardial infarctions, and ultimately death, is unusual and a reminder of the potential severity of SCAD, which is usually treated conservatively [11]. The reported prevalence of SCAD-patients with simultaneous vascular- and/or connective tissue disease varies significantly, ranging from 30.1-80.7% [2]. When SCAD is diagnosed, genetic testing for potential underlying predisposing diseases should therefore be considered. In patients with underlying vascular- and/or connective tissue disease experiencing symptoms of myocardial infarction, SCAD should be considered as a differential diagnosis. In this case, supplementary comprehensive genetic testing was performed without positive findings, thereby excluding the most well annotated genetic causes of aortic disease, cardiomyopathy and familial hypercholesterolemia. Taken together, SCAD is a relatively rare cause of myocardial infarction among the general population, however, in younger and predisposed females <50 years old, SCAD is an important differential diagnosis as the cause of myocardial infarction.

References

[1] R.A. Byrne, X. Rossello, J.J. Coughlan, E. Barbato, C. Berry, A. Chieffo, M.J. Claeys, G.A. Dan, M.R. Dweck, M. Galbraith, M. Gilard, L. Hinterbuchner, E.A. Jankowska, P. Jüni, T. Kimura, V. Kunadian, M. Leosdottir, R. Lorusso, R.F.E. Pedretti, A.G. Rigopoulos, M. Rubini Gimenez, H. Thiele, P. Vranckx, S. Wassmann, N.K. Wenger, B. Ibanez, 2023 ESC Guidelines for the management of acute coronary syndromes, Eur Heart J, 44 (2023) 3720-3826. [2] S.N. Hayes, M.S. Tweet, D. Adlam, E.S.H. Kim, R. Gulati, J.E. Price, C.H. Rose, Spontaneous Coronary Artery Dissection: JACC State-of-the-Art Review, J Am Coll Cardiol, 76 (2020) 961-984. [3] E.S.H. Kim, Spontaneous Coronary-Artery Dissection, N Engl J Med, 383 (2020) 2358-2370. [4] A.S. Lobo, S.M. Cantu, S.W. Sharkey, E.Z. Grey, K. Storey, D. Witt, G. Benson, R.F. Garberich, Y. Kubota, C.N. Bairey Merz, T.D. Henry, Revascularization in Patients With Spontaneous Coronary Artery Dissection and ST-Segment Elevation Myocardial Infarction, J Am Coll Cardiol, 74 (2019) 1290-1300. [5] N. Brunton, P.J.M. Best, K.A. Skelding, E.E. Cendrowski, Spontaneous Coronary Artery Dissection (SCAD) from an Interventionalist Perspective, Curr Cardiol Rep, 26 (2024) 91-96. [6] M.J. Litt, A. Ali, N. Reza, Familial Hypertrophic Cardiomyopathy: Diagnosis And Management, Vasc Health Risk Manag, 2023 Apr 6:19:211-221. [7] C. Horvat, R. Johnson, L. Lam, J. Munro, F. Mazzarotto, A. M. Roberts, D.S. Herman, M. Parfenov, A. Haghighi, B. Mcdonough, S.R. DePalma, A.M. Keogh, P.S. Macdonald, C.S. Hayward, A. Roberts, P.J.R. Barton, L.E. Felkin, E. Giannoulatou, S.A. Cook, J.G. Seidman, C.E. Seidman, D. Fatkin, A Gene-centric Strategy For Identifying Disease-causing Rare Variants In Dilated Cardiomyopathy, Genet Med, 2019 Jan;21(1):133-143. [8] V.E. Bouhairie, A.C. Goldberg, Familial Hypercholesterolemia, Cardiol Clin, 2015 May;33(2):169-79. [9] A.M.G. Aishat F Mustapha, Bryan J Wells, Sex and Gender Differences in Cardiovascular Disease: A Review of Spontaneous Coronary Artery Dissection, US Cardiology Review

2023;17:e15. [10] J. Saw, K. Humphries, E. Aymong, T. Sedlak, R. Prakash, A. Starovoytov, G.B.J. Mancini, Spontaneous Coronary Artery Dissection: Clinical Outcomes and Risk of Recurrence, J Am Coll Cardiol, 70 (2017) 1148-1158. [11] N. Pristera, P. Chaudhury, E.H. Van Iterson, L.S. Cho, Spontaneous coronary artery dissection: Principles of management, Cleve Clin J Med, 88 (2021) 623-630.