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Anomalous Coronary Artery Presented with Typical Chest Pain: What is Define The Malignant from Benign Anomalous Coronary Artery (A Case Series)

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Klíčová slova:
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Maligní varianta anomální koronární tepny s odstupem z protilehlého sinu
Vrozené anomálie koronárních tepen

SOUHRN

Kontext: Vrozené anomálie koronárních tepen (congenital coronary anomaly, CCA) představují významnou příčinu morbidity a mortality v souvislosti s anginou pectoris nebo s náhlou srdeční smrtí. Fenomén CCA se dělí na dvě skupiny podle odstupu a průběhu dané koronární tepny. Termínem maligní CCA se označují tepny s ektopickým odstupem z protilehlé strany srdce a s následným interarteriálním průběhem.
Souhrn: Popisujeme dvě naprosto rozdílné varianty anomálií koronárních tepen s typickými projevy bolesti na hrudi. Fyzikální vyšetření obou pacientů přineslo fyziologické výsledky a neprokázalo žádné známky ischemie. V prvním případě prokázala CT koronarografie maligní variantu anomální pravé věnčité tepny z protilehlého sinu (right anomalous coronary artery from the opposite sinus, R-ACAOS) s interarteriálním průběhem. V druhém případě se jednalo o typický znak nestability plátu s tzv. napkin-ring sign, přítomnost smíšené formy plátů a postižení jedné koronární tepny po benigní variantě r. circumflexus a. coronaria sinistra s anomálií v podobě odstupu ze sinu pravé koronární tepny. U obou pacientů sice existovaly různé mechanismy vzniku anginy pectoris, avšak u obou bylo přítomno vysoké riziko fatální srdeční příhody. Vyšší riziko akutního koronárního syndromu a náhlé srdeční smrti bylo popsáno u pacientů s tzv. napkin-ring sign, což v druhém případě bylo pravděpodobně důsledkem ostrého úhlu odstupu, který pro interarteriální průběh ukazoval na označení „maligní", a to i přes přítomnost několika dalších charakteristik.
Závěry: ACAOS je vzácná vrozená anomálie a z klinického hlediska není významná, i když někteří pacienti mohou vykazovat závažné symptomy. Námi popsaný případ ukazuje, že některé abnormality by mohly předefinovat termín „maligní" i v případě takzvaně benigního ACAOS. Kromě optimální farmakoterapie by pro snížení rizika fatálních srdečních příhod a náhlé srdeční smrti bylo možno uvažovat o chirurgickém řešení.

Keywords:
Anomalous coronary artery
Benign ACAOS
Congenital coronary anomalies
Inter-arterial course
Malignant ACAOS
Malignant anomalous coronary artery arising from opposite sinus

ABSTRACT

Background: Congenital coronary anomalies (CCA) are the important causes of morbidity and mortality associated with angina or SCD. CCA divided into two groups, depending on the origin and course of the coronary artery. Malignant CCA comprises arteries with ectopic origin from the contralateral side of the heart followed by an inter-arterial course.
Case summary: We presented two distinct characteristics of coronary anomalies with typical chest pain presentation. Both patients had a normal physical examination and no ischemia sign. Coronary CT-angiography showed a malignant type of right anomalous coronary artery from the opposite sinus (R-ACAOS) with an inter-arterial course in case 1. A napkin-ring sign mixed plaque single vessel disease following benign type LCx originating from right coronary sinus anomaly found in case 2. Both patients have different mechanisms causing angina presentation, but both are at high risk of fatal cardiac events. A higher acute coronary syndrome risk and sudden cardiac death were found in patients with the napkin-ring sign, which in case 2 were possibly caused by acute take-off angle features. These supported the term "malignant" caused by inter-arterial course features but followed by several other features.
Conclusions: ACAOS is a rare congenital abnormality and not clinically significant, but some have potentially severe symptoms. From the case presented, we could learn that some abnormalities could redefine the terms malignantly even in the so-called benign ACAOS. Surgery could be performed besides OMT in reducing the risk of fatal cardiac events and SCD.

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Introduction

Coronary arteries are the blood vessels that supply the heart muscle to maintain myocardial hemostasis and function. Anomalies of the coronary artery may present as a result of coronary development disruption during embryogenesis. These anomalies can affect the cardiovascular system by causing shunting and ischemia, thus resulted in hemodynamic impairment. Congenital coronary artery anomalies are rare and usually an incidental finding during elective coronary angiography. The incidence of coronary anomalies was reported to be 0.64–1.3% in a large registry of patients undergoing coronary angiogram, with a composition of 0.15% of the left coronary arteries originates in the right coronary sinus and 0.92% of the right coronary artery (RCA) originates from the left coronary sinus.[1–4]

Most of the anomalous coronary artery arising from opposite sinus (ACAOS) is not clinically significant, but some have potentially severe symptoms. Left ACAOS (L--ACAOS) describing take-off of the left coronary artery from the right coronary sinus of Valsalva, Right ACAOS (R-ACAOS) is when the right coronary artery originating from the left coronary sinus of Valsalva. Differentiating coronary anomalies based on anatomical consideration seems to be an essential matter. R-ACAOS that travels between the aorta and pulmonary artery, a relatively rare congenital, is a malignant RCA anomaly. The disruption of blood flow due to coronary artery anomalies could lead to cardiac events or death through several mechanisms such as reduced coronary flow by acute kinking of the acute take-off or slit-like ostium, compression between aorta and pulmonary artery, intramural course under strenuous physical activity or exercise especially in young athletes. We present a case series of patients showing typical chest pain with different coronary anomalies origin characteristics.[2]

Case presentation

Case 1

A 60-year-old woman came to an outpatient unit with a complaint of typical chest pain that is often felt with moderate-to-heavy activity for the last five years. Chest pain was relieved by resting and sublingual nitrate administration. The previous history of diseases, such as diabetes mellitus (DM), hypertension (HT), dyslipidemia, and stroke was refuted. From the vital examination, blood pressure (BP) was 130/80 mmHg, a regular heart rate (HR) of 80 bpm, respiratory rate (RR) of 20 breaths per minute, and peripheral saturation (SpO_2) of 99% with free oxygen. Physical examination status was within normal limits. From the electrocardiography (ECG), the sinus rhythm 80 bpm and left atrial abnormalities were obtained. There were no signs of ischemia on the ECG. Chest X-ray (CXR) was within normal limits with a CTR of 50%. Laboratory tests were within normal limits. From echocardiography examination, the valves did not appear abnormal. The dimensions of the heart chambers were normal. It was found normal left ventricular (LV) systolic function with ejection fraction by Teich 68% normokinetic LV segmental analysis.

Further workup was needed to determine the underlying diagnosis since ECG, CXR, and echocardiography were within normal limits without a sign of ischemia. In addition, the pretest probability (PTP) of coronary artery disease (CAD) was 58%, which indicated for undergoing exercise stress test (EST). However, the patient refused to undergo an EST for personal reasons; thus, a cardiac computed tomography angiography (CCTA) examination was performed in the non-invasive unit.

From the evaluation of CCTA, we found no stenosis (Fig. 1), calcium score 0, with anomalous origin of right coronary artery (RCA) from left coronary sinus with subsequent coursing between the aorta and pulmonary trunk (Fig. 2).

The patient was given education about the diagnosis of rare congenital disorders. Management of the disease includes conservative strategies, intervention to surgery, and the disease's prognosis, where sudden death can occur during activity. However, patients still chose conservative therapy. She was given 5mg isosorbide dinitrate (ISDN) three times daily and bisoprolol 2.5 mg twice a day orally.

Case 2

A 60-year-old man, an active smoker with a CAD family history, presented to an outpatient unit with a chief complaint of typical chest pain. The pain was episodic and felt two years ago, precipitated with moderate-to-heavy activity, and relieved by rest. He had taken nitrate sublingual ever since to control his symptoms. There were no complaints of shortness of breath or palpitations during chest pain. He had a history of uncontrolled hypertension with a history of changing therapeutic prescriptions due to his remaining symptoms. He came to our clinic for a second opinion since previous medical records had only shown HT without any sign of heart ischemia. BP was 150/80 mmHg from vital sign examination, a regular

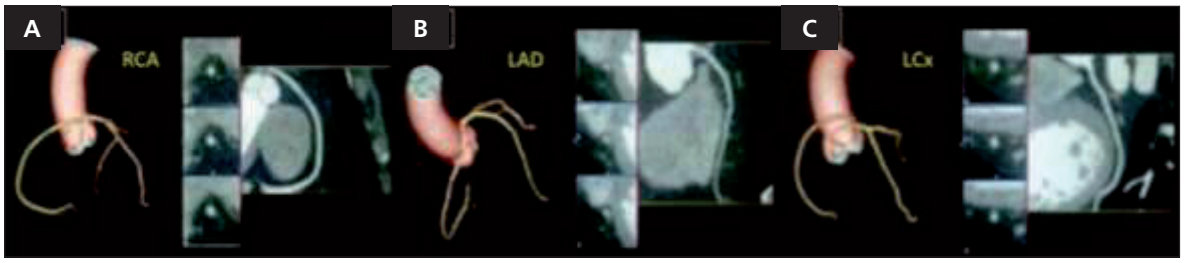

Fig. 1 – The CCTA showed no stenosis in (A) RCA, (B) left anterior descendent (LAD), (C) left circumflex (LCx).

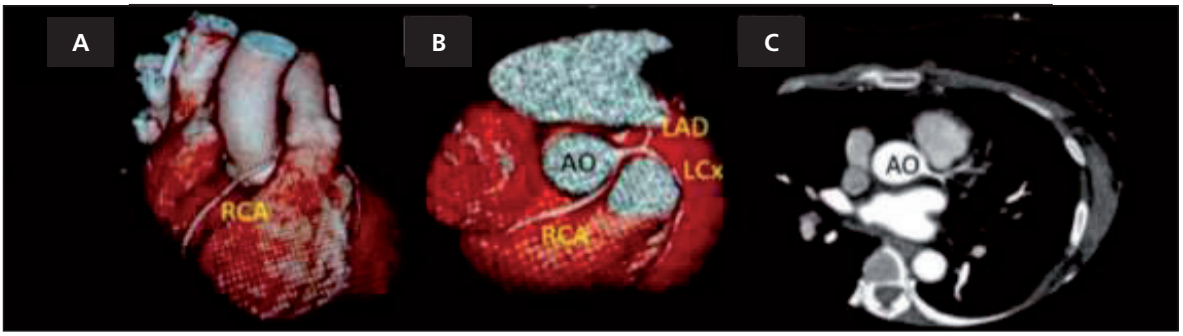

Fig. 2 – The 3D reconstruction CT showed (A) an anomalous origin of RCA from left coronary sinus (CS) with (B) subsequent coursing between the aorta and pulmonary trunk. (C) Multi-planar CT showed the anomalous origin of RCA from left CS with inter-aortic course.

HR of 90 bpm, RR of 20 breaths per minute, and SpO_2 of 99% with free oxygen. Physical examination status was within normal limits. ECG showed a normal sinus rhythm 90 bpm. Chest X-ray was within normal limits with a CTR of 50%. Laboratory tests were within normal limits. Echocardiography examination showed a normal cardiac chamber with normal left ventricular ejection fraction (LVEF) (Teich 68%). The PTP score was 84%. Hence non-invasive imaging should be done. He was then referred to a non-invasive examination, and a CCTA examination was performed.

The CCTA (Fig. 3) showed RCA dominant with CAD single vessel disease (SVD) mixed plaque 50% at proximal RCA and mixed plaque 50% with "napkin ring sign" at distal RCA. It also showed minor disease at LAD as mixed plaque 30% in proximal LAD with the aneurysmatic part. The coronary characteristic is complicated by anomalous LCx origin from right coronary cusps (RCC) (Fig. 4).

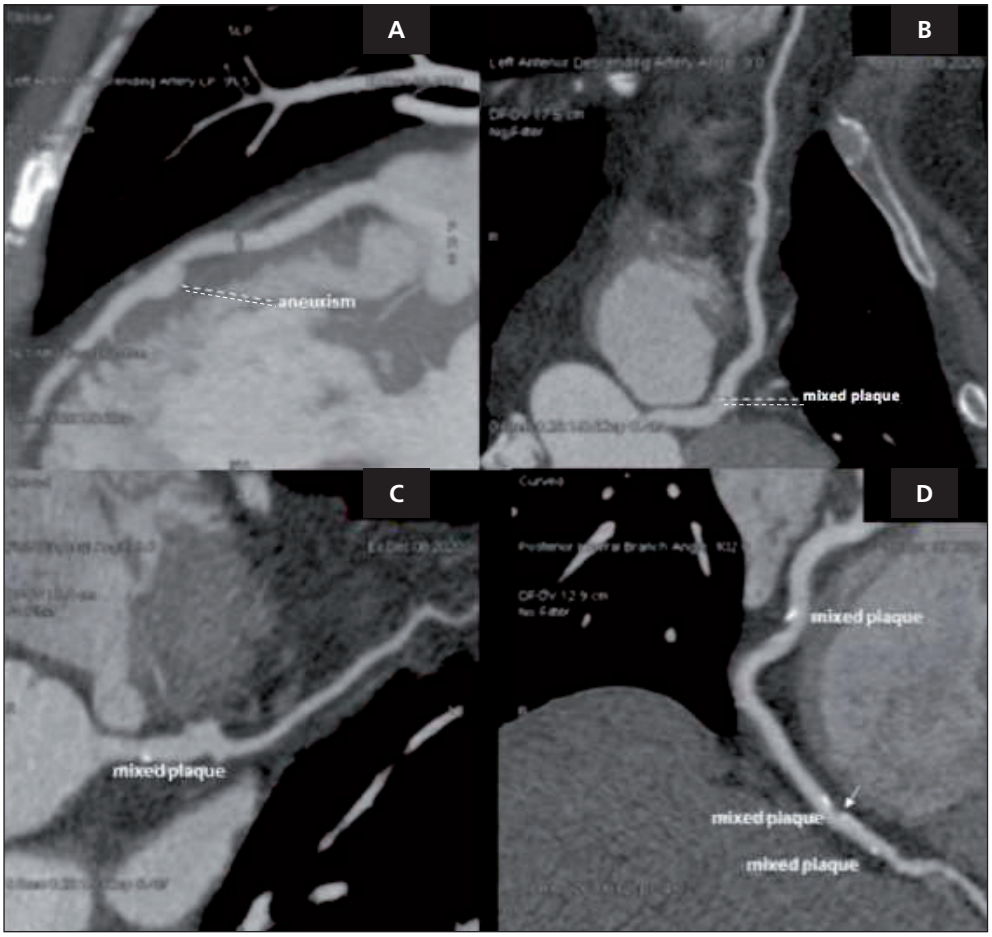

Fig. 3 – The CCTA imaging of the patient presented with (A) aneurysmatic part of the proximal LAD, (B) mixed plaque 30% in proximal LAD, (C) mixed plaque 50% in proximal RCA, and (D) mixed plaque 50% with the presence of "napkin ring sign" (white arrow) at distal RCA.

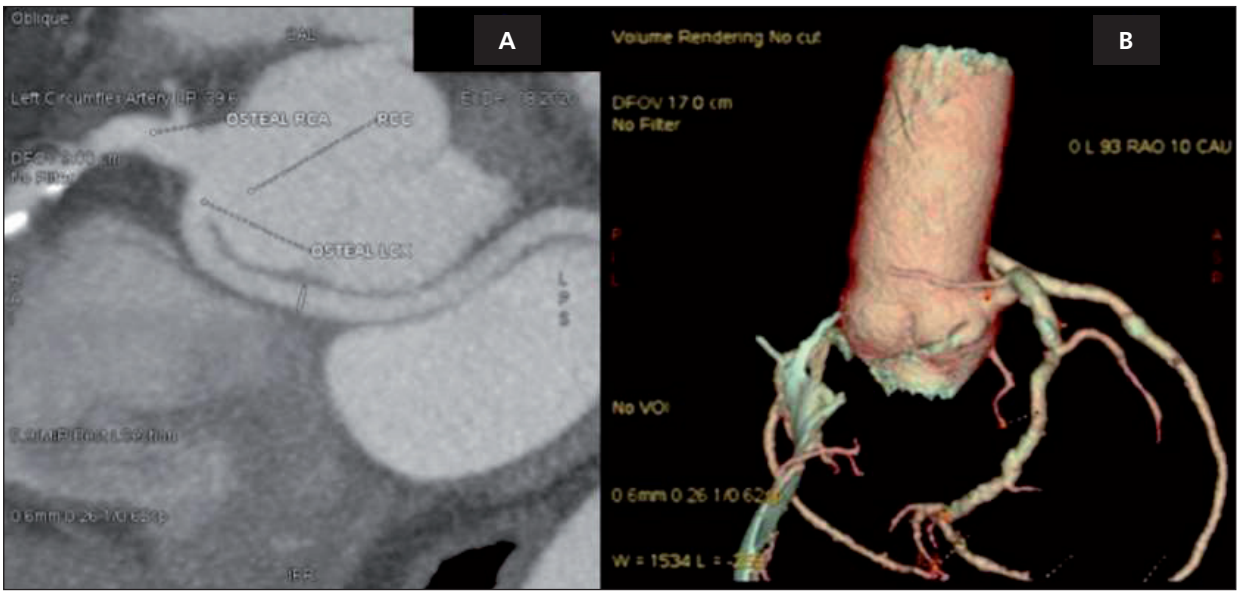

Fig. 4 – The CCTA showed (A) an anomalous origin of LCx from RCC (double ostium). (B) The 3D reconstruction CT.

The patient was given education about the diagnosis of atherosclerotic disease concomitant with his congenital disorder. Management of the disease includes revascularization through a heart-team discussion, whether by performing percutaneous coronary intervention or surgical procedure. However, patients still consider both options with the understanding of SCD risk. Routine atherosclerotic coronary therapies were given, i.e., double antiplatelets, ACE inhibitors, and statins. He was also given 5 mg ISDN three times daily and bisoprolol 5 mg once a day orally to control his symptoms.

Discussion

Intact coronary circulation is essential for myocardial hemostasis and function, enabling the rest of the body to function. A normal coronary artery is characterized by the LAD and LCx artery originating from an aortic aorta above the upper third of the left posterior sinus (left CS). In contrast, RCA originates from the upper third right CS. The anomalous coronary artery can affect hemodynamic status through disruption in the coronary circulation. The effect can be benign, even lethal. Therefore, the anatomical characteristic is one of the important factors affecting the outcomes of the patient. Multidetector CT (MDCT) is a diagnostic tool that is usually used to detect a coronary artery's anomalous origin and course. CT angiography has a higher advantage over catheter angiography in detecting coronary artery abnormalities.[3,5,6]

Recent classification of the coronary anomalies is based on anatomical consideration, recognizing three categories, i.e., anomalies of the origin and course, anomalies of the intrinsic coronary artery anatomy, and anomalies of the termination. In the setting of ACAOS, the proximal anomalous coronary artery may run anterior to the pulmonary trunk (pre-pulmonic), posterior to the aorta (retro-aortic), septal (subpulmonic), or between the aorta and pulmonary artery itself (inter-arterial). Between these characteristics, the inter-arterial type is regarded as a malignant condition at an increased risk of ischemia, arrhythmia, syncope, and even sudden cardiac death (SCD). Therefore, clinical guidelines recommend surgical correction for this type of anomaly.[7,8]

Among all coronary artery abnormalities, anomalous origin of the LCx from the right coronary sinus (RCC) is the most common coronary anomaly reported, accounting for 0.37–0.7% of all patients. This anomaly is thought to be benign, even though several cases show the increased risk of ischemia due to accelerated atherosclerosis. The coronary angiography characteristic in this group consists of LCx originating from the left sinus Valsalva (55.5%), RCA (36.9%), and right sinus Valsalva (25.9%).[2–4]

We presented serial cases showing two distinct characteristics of coronary artery abnormalities with angina presentation. Both patients were seen normal during ECG, chest X-ray, and echocardiography examination. No sign of ischemia was found, so that further evaluation using CT angiography was performed. Patient in case 1 showed no stenosis and malignant feature of anomaly origin of RCA from left CS with an inter-aortic course. In contrast, in case 2, the CCTA showed mixed plaque 50% SVD and benign feature of anomalous origin of LCx from right CS.

Typical angina could be presented among patients with coronary artery abnormality as an effect of numerous ischemia mechanism, i.e., (1) compression of the anomalous segment coursing inter-arterial during increased cardiac output (CO) and expansion of the great vessel; (2) acute angle take-off of the anomalous segment with further stretch during exercise, possibly accounting for a flap-like closure of the coronary ostium; (3) spasm or kinking of the abnormal vessels; and (4) the course within an aortic wall (intramural) of the proximal segment of the anomalous vessel.

From both cases, we found no sign of ischemia during echocardiography examination supported by Molajo et al.[9] Only significant stenosis in the aberrant artery could impair myocardial perfusion. However, even in the pre-

sence of patent arteries, fatal cases have been reported. Interaortic course, which is presented in case 1, is at the highest risk for SCD. The increased risk of a fatal cardiac event of inter-arterial course is decreased coronary flow due to pressure between aorta and pulmonary trunk caused by increased CO. A fatal cardiac event in benign type, as presented in case 2, could be caused by repeated compression of the anomalous artery by unusual angle as a result of retro-aortic course of the LCx, which can compress the coronary ostium and restrict blood flow.[3,10]

Although only 20% of coronary artery abnormalities have life-threatening symptoms, a comprehensive evaluation should be performed. Even in benign type, LCx abnormalities originating from the right sinus could have a high ischemic risk. The increased risk of SCD can be due to a slit-like ostium, a bend with acute take-off angles of the aberrant coronary arteries, or arterial compression between the aorta and pulmonary trunk when there is increased blood flow through the vessel with exercise and stress.[5,6]

LCx abnormalities alone can become symptomatic and cause myocardial infarction in the sixth decade later in life. In the research comparing LCx abnormalities originating from RCC, those with retro-aortic course appeared to be the most predisposed to selective atherosclerosis. Case 2 showed a napkin ring sign, known as a predictor of an acute coronary event, including SCD. The napkin ring sign is the presence of a ring of high attenuation around a particular coronary artery plaque. This sign might be caused by both acute take-off angle and retro-aortic course feature in this patient. From several studies, as shown previously, a malignant type is at a higher fatal cardiac event risk, the presence of napkin ring sign in the benign type (case 2) showing an ACS risk of 41%.[11] Understanding the anatomical and pathological reason of coronary artery abnormality feature will redefine the term "benign", as Grani et al. suggested.[12] ACAOS can be considered malignant if inter-arterial course is present, acute take-off angle, intramural course, proximal elliptic vessel/proximal narrowing, anomalous vessel-induced ischemia, and scar.

Both patients were in terms of malignant course, so intervention should be performed besides optimal medical treatment using nitrate and beta-blocker. Exercise stress testing, though commonly employed for diagnosing coronary ischemia, is inadequate in predicting future risk of SCD in patients with anomalous coronaries. Surgical intervention in ACAOS patients is generally performed to prevent SCD and/or ischemia. Surgical recommendation in case of anomalous origin of left main from right coronary sinus and interarterial course is supported by ACC/AHA Guidelines for the management of adult with congenital heart disease.[7,8] It ranges from reimplantation into appropriate coronary sinus, bypass (with/without native vessel ligation), pulmonary artery translocation, proximal coronary artery patch enlargement, and unroofing (in the event of intramural coronary course). The understanding of course and structure are the major determinants of successful intervention. The superiority of surgical intervention over percutaneous coronary intervention lies on higher instent re-stonosis rates, stent thrombosis, stent fractures, and risk of coronary artery dissection/rupture. Another guideline recommendation regarding SCD prevention among ACAOS patients secondary to ventricular arrhythmias is the ICD implantation. However, there are no guidelines for ICD implantation after surgical correction of anomalous coronary vessel, especially in patients with preserved ejection fraction. The option for performing intervertion is listed in Table 1.[2,12,13]

Table 1 – Options for performing intervention in ACAOS patient

Anatomic feature	Preferably imaging method to detect high-risk feature	Possible mechanism of ischemia	Interventional option
Inter-arterial course	CCTA/CMR>ICA(IVUS)>TTE	Dynamic compression	Re-implantation, pulmonary artery dislocation, unroofing (if intramural segment present)
Slit-like ostium	CCTA>ICA(IVUS)>CMR	Valve-like occlusion	Unroofing (if intramural segment present), re-implantation, potentially PCI
Acute take-off angle	CCTA>CMR>TTE>ICA	Kinking	
Intramural course	ICA(IVUS)>CCTA>CMR>TTE	Dynamic compression	Unroofing re-implantation, potentially PCI
Intramural length	ICA(IVUS)>CCTA>CMR>TTE	Dynamic compression	
Diastolic proximal narrowing/elliptic vessel shape	CCTA/ICA(IVUS)>CMR	Dynamic compression under stress	
Systolic proximal narrowing/elliptic vessel shape	ICA(IVUS)>CCTA>CMR	"Milking" and dynamic compression at rest and stress	
Arrhythmogenic substrate		Recurrent intermittent ischemia leading to myocardial scarring	Unclear, potentially medication (beta-blocker)

CCTA – coronary computed tomography angiography; CMR – cardiovascular magnetic resonance; ICA – invasive coronary angiography; IVUS – intravascular ultrasound; TTE – transthoracic echocardiogram.

Conclusion

ACAOS is a rare congenital abnormality and it is not clinically significant, but some have potentially severe symptoms. Malignant ACAOS was previously described in L--ACAOS and R-ACAOS with an inter-atrial course. We could learn from the cases presented that some abnormality features consisting of acute take-off angle, intramural course, proximal elliptic vessel/proximal narrowing, anomalous vessel-induced ischemia, and scar could increase the risk of fatal cardiac event, thus redefined the terms malignantly even in the so-called benign ACAOS. CCTA is superior non-invasive imaging technique in diagnosing coronary anomalies with high accuracy. It provide precise information regarding orifice location and vessel course. There is no precise consensus and recommendation regarding the intervensive management of ACAOS. Moreover, the procedure of choice is uncertain, and its impact on long-term survival is unknown. The only clinical guidelines for cardiac surgery are in case of anomalous origin of left main from right coronary sinus and interarterial course.

Authors contribution

Louisa Fadjri Kusuma Wardhani: conceptualization: lead; data curation: lead; formal analysis: lead; investigation: lead; methodology: lead; project administration: lead; resources: lead; validation: lead; visualization: lead; writing – original draft: lead; writing – review & editing: lead.
Ivana Purnama Dewi: conceptualization: equal; data curation: equal; formal analysis: equal; investigation: equal; resources: equal; software: equal; validation: equal; visualization: equal; writing – original draft: equal; writing – review & editing: equal.
Arifta Devi Anggraeni: conceptualization: equal; data curation: equal; formal analysis: equal; investigation: equal; resources: equal; software: equal; validation: equal; visualization: equal; writing – original draft: equal; writing – review & editing: equal.
Meity Ardiana: conceptualization: equal; data curation: equal; formal analysis: equal; investigation: equal; resources: equal; software: equal; validation: equal; visualization: equal; writing – original draft: equal; writing – review & editing: equal.

Conflict of interest

None declared.

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Ethics approval and consent to participate

This paper already got ethics approval, and the patient/the family sign the informed consent for publication.

Consent for publication

Written informed consent was taken from the patient to use medical data for academic and research purposes, including publication.

Availability of data and material

The datasets used are available from the corresponding author on reasonable request.

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