# Infective Endocarditis of a Coronary Artery Fistula With Aortic Valve Involvement



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## INTRODUCTION

Coronary artery fistula (CAF) is a rare congenital coronary artery anomaly, and infective endocarditis (IE) is an uncommon complication associated with a high mortality rate. We describe the case of a patient with a giant CAF complicated by IE of the fistula, extending to and involving the aortic valve (AV). The initial diagnosis was considered after transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE) with three-dimensional (3D) modality and cardiac computed tomography (CCT) were subsequently used to accurately identify the CAF, its origin, course, drainage site, and vegetation.

## CASE PRESENTATION

A 37-year-old woman was referred to our hospital for echocardiography because of dyspnea on exertion (New York Heart Association functional class II) and chest pain. The patient's symptoms began approximately 5 months prior, following a dental procedure (tooth extraction). During this period, the patient experienced intermittent fever, weakness, fatigue, loss of appetite, and significant weight loss (12 kg). Upon physical examination, the patient's blood pressure was 90/40 mm Hg, and there was tachycardia (110 beats/min), with no fever at presentation. A continuous murmur was detected at the right parasternal border, along with a diastolic murmur over the aortic area. The remainder of the physical examination was unremarkable.

Laboratory data revealed a total white blood cell count of 9,000/mL (neutrophils, 77.6%), normochromic normocytic anemia (hemoglobin 8.6 g/dL), an elevated erythrocyte sedimentation rate of 77 mm/h (normal range, <22 mm/h), and C-reactive protein of 2.24 mg/dL (normal range, <0.5 mg/dL). Before being referred to our center, the patient had been receiving care from various general physicians as an outpatient for 5 months and had been prescribed empirical antibiotics for brief periods, without a definitive diagnosis. Consequently, upon admission to our hospital, the patient's blood culture was negative. Serologic testing for *Coxiella burnetii*, *Bartonella*, and *Brucella* was also negative. Chest radiography revealed clear lung fields with cardiomegaly. Electrocardiography exhibited sinus tachycardia without signs of ischemia or atrioventricular block.

TTE demonstrated a dilated left ventricular cavity with preserved global systolic function, moderate secondary mitral regurgitation, a dilated right ventricular cavity with reduced systolic function, and moderate secondary tricuspid regurgitation (Table 1). A grossly abnormal trileaflet AV with suspected vegetative mass and severe aortic regurgitation (AR) was also seen. Additionally, an echo-free space (16 mm in diameter) on the anteromedial side of the aortic root at the right coronary artery (RCA) orifice site was observed, accompanied by significant continuous turbulent flow in the right atrium (RA), indicative of a large CAF from the RCA to the RA. A mobile, filamentous mass at the RCA origin was also noted as a probable vegetation. TEE was performed to improve diagnosis and assessment of the extent of involvement (Figures 1 and 2, Videos 1-5). Real-time 3D TEE revealed a large CAF from the RCA to the roof of the RA near the superior vena cava junction (Figure 3, Videos 6-9). Multiple vegetations were observed at the fistula origin (10 × 5 mm), within the fistula, at the fistula drainage site (20 × 3 mm), and at the jet effect site in the RA, as well as on the tip of the noncoronary cusp of the AV (11 × 7 mm). The AV was also damaged, resulting in severe AR. CCT demonstrated a giant fistula connecting the proximal RCA to the RA at the cavoatrial junction, with suspicious filamentous particles observed at the drainage site (Figure 4).

The patient received partial, but incomplete, treatment for acute endocarditis initially that likely contributed to the negative blood cultures. Nonetheless, the history of a dental procedure before the onset of constitutional symptoms, along with left-shift leukocytosis, anemia, elevated erythrocyte sedimentation rate, C-reactive protein, and ultimately the discovery of a CAF and multiple vegetations at various sites on echocardiography all pointed toward a diagnosis of IE. The patient underwent urgent surgery following a brief period (3 days) of antibiotic therapy. During surgical exploration, a giant aneurysmal RCA with a fistula draining into the RA near the superior vena cava was identified, with the RCA ostium measuring approximately 15 to 20 mm. The RCA aneurysm was opened longitudinally, and a saphenous vein graft was attached to a large right ventricular branch.

The RCA ostium was closed using a pericardial patch, and the fistula foramen was closed within the RA. The vegetations at the orifice and drainage site of the fistula in the RA were completely resected. The eroded AV was removed, and a mechanical bileaflet prosthetic AV was implanted. The excised vegetations were sent for pathologic

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## VIDEO HIGHLIGHTS

**Video 1:** TEE, midesophageal long-axis (113°) view, demonstrates the vegetation on the noncoronary cusp of the damaged trileaflet AV and an echo-free space on the anteromedial side of the aortic root at the RCA ostium, representing the origin of the CAF with a vegetation visible within it.

**Video 2:** TEE, midesophageal simultaneous orthogonal long-axis (115°) and short-axis (−15°) views, demonstrates the vegetation on the noncoronary cusp of the damaged trileaflet AV and an echo-free space on the anteromedial side of the aortic root at the RCA ostium, representing the origin of the CAF with a vegetation visible within it.

**Video 3:** TEE, midesophageal simultaneous orthogonal long-axis (115°) and short-axis (−15°) views with color flow Doppler, demonstrates turbulent flow at the origin of the fistula and moderate to severe AR.

**Video 4:** TEE, midesophageal long-axis (115°) view, demonstrates the CAF and the vegetation within the fistula.

**Video 5:** TEE, midesophageal long-axis (115°) view with color flow Doppler, demonstrates the CAF with continuous turbulent flow.

**Video 6:** Three-dimensional TEE, midesophageal volume-rendered short-axis view, demonstrates the fistula tract draining into the RA near the superior vena cava.

**Video 7:** Three-dimensional TEE, midesophageal volume-rendered short-axis view with color flow Doppler, demonstrates the fistula tract with continuous turbulent flow.

**Video 8:** Three-dimensional TEE, midesophageal multiplanar reconstructed orthogonal view, demonstrates the fistula tract draining into the RA near the superior vena cava and a large vegetation at the drainage site in the RA.

**Video 9:** Three-dimensional TEE, midesophageal multiplanar reconstructed orthogonal view with color flow Doppler, demonstrates the fistula tract with continuous, turbulent flow draining into the RA near the superior vena cava.

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analysis, which revealed that the lesions were composed of fibrin, platelets, inflammatory cells, and microorganisms. The patient completed a 4-week course of antibiotic therapy under the consultation of an infectious disease specialist. The postoperative course was uneventful, and follow-up TTE 1 week after the procedure demonstrated reduction in ventricular dimensions, mild left ventricular systolic dysfunction, mild to moderate secondary mitral regurgitation, mild secondary tricuspid regurgitation, and a normally functioning prosthetic AV (Table 1).

**Table 1** Transthoracic echocardiographic findings

| Parameter | Preoperative TTE | Postoperative TTE |
|---|---|---|
| LVEDVi, mL/m$^2$ | 173 | 79 |
| LVEF, % | 60 | 45 |
| RVd, mm | 40 | 33 |
| RV TDE S′, cm/s | 8 | 6 |
| LAVI, mL/m$^2$ | 80 | 37 |
| RAVI, mL/m$^2$ | 87 | 29 |

*LAVI*, Left atrial volume index; *LVEDVi*, left ventricular end-diastolic volume indexed to body surface area; *RAVI*, right atrial volume index; *RV*, right ventricular; *RVd*, right ventricular dimension at midventricle; *TDE S′*, Doppler tissue echocardiographic S′ velocity at the right ventricular tricuspid annulus.

## DISCUSSION

A CAF is a rare congenital coronary artery anomaly characterized by communication between a coronary artery and a cardiac chamber or great vessel. A CAF originating from the RCA is more common than those from the left coronary arteries, and most fistulas drain into a cardiac chamber or central vein, which are considered low-pressure structures.[1] A CAF is typically asymptomatic and is most often discovered incidentally during coronary angiography. Nevertheless, it may be associated with complications such as myocardial ischemia, congestive heart failure, IE, and aneurysm rupture.[2] IE is a rare but life-threatening complication of CAF, with a reported incidence ranging from 3% to 12% in patients with CAF.[3,4] The 1-year mortality rate in various studies has been observed to be approximately 30%.[5] Dilated unilateral fistulas draining into the heart are most commonly complicated by IE.

We report a rare case of a complicated CAF from the RCA to the RA, featuring vegetation at the fistula's origin, drainage site, and inside the fistula, as well as on the AV. This resulted in severe AR due to valve damage.

In 2016, an analysis of 25 reported cases of congenital CAF complicated by IE revealed left-sided valve involvement in five cases in which the fistula originated on the right side. Additionally, septic emboli were reported in 24% of cases.[4] Green and Crilley[6] reported a case of a 50-year-old woman with an RCA-to-RA fistula who presented with AV endocarditis and pulmonary septic emboli. Nonvalvular vegetation has also been documented at the drainage point of the fistula. Zhang *et al.*[7] described a case involving the surgical repair of a left main coronary artery–to–RA fistula with endocarditis at the fistula orifice in the RA. It is postulated that endothelial damage near the drainage site of the fistula, resulting from the high-speed jet, can create a focal vulnerable site for endocarditis.

Coronary angiography is considered the reference standard for diagnosing CAF, as it can identify the fistula's origin, course, and termination, as well as assess the hemodynamics of the fistula by quantifying the shunt.[8] Although CCT is a valuable noninvasive modality for diagnosing CAF and evaluating its detailed anatomic characteristics before surgery,[9] TEE, particularly with 3D modality and multiplanar reconstruction, can also accurately identify a CAF and its origin, course, and drainage site with high-quality views.[2,10] Furthermore, TEE has been shown to have high sensitivity in diagnosing vegetation and endocarditis.

In our case, the patient had partially treated acute endocarditis during the first 5 months of symptoms, resulting in negative blood cultures. However, the clinical and supportive laboratory findings

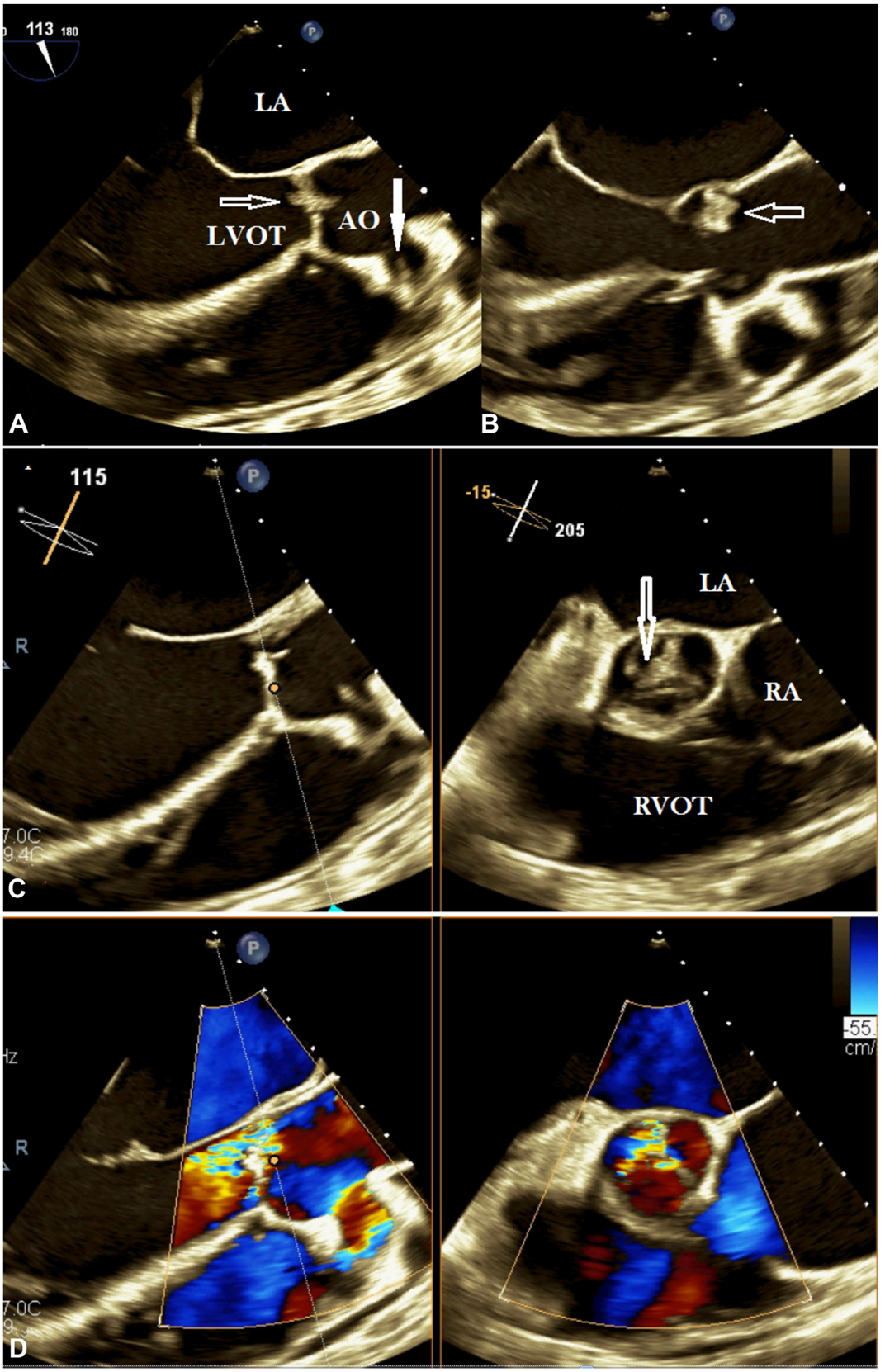


Figure 1 TEE, midesophageal long-axis (113°) diastolic **(A)** and systolic **(B)** views and simultaneous orthogonal long-axis (115°) and short-axis (−15°) diastolic views without **(C,D)** and with **(E,F)** color flow Doppler, demonstrates the vegetation (*open arrow*) on the noncoronary cusp of the damaged trileaflet AV and an echo-free space on the anteromedial side of the aortic root at the RCA ostium, representing the origin of the CAF (*solid arrow*), with a vegetation visible within it; moderate to severe AR is also seen. *AO*, Aorta; *LA*, left atrium; *LVOT*, left ventricular outflow tract; *RVOT*, right ventricular outflow tract.

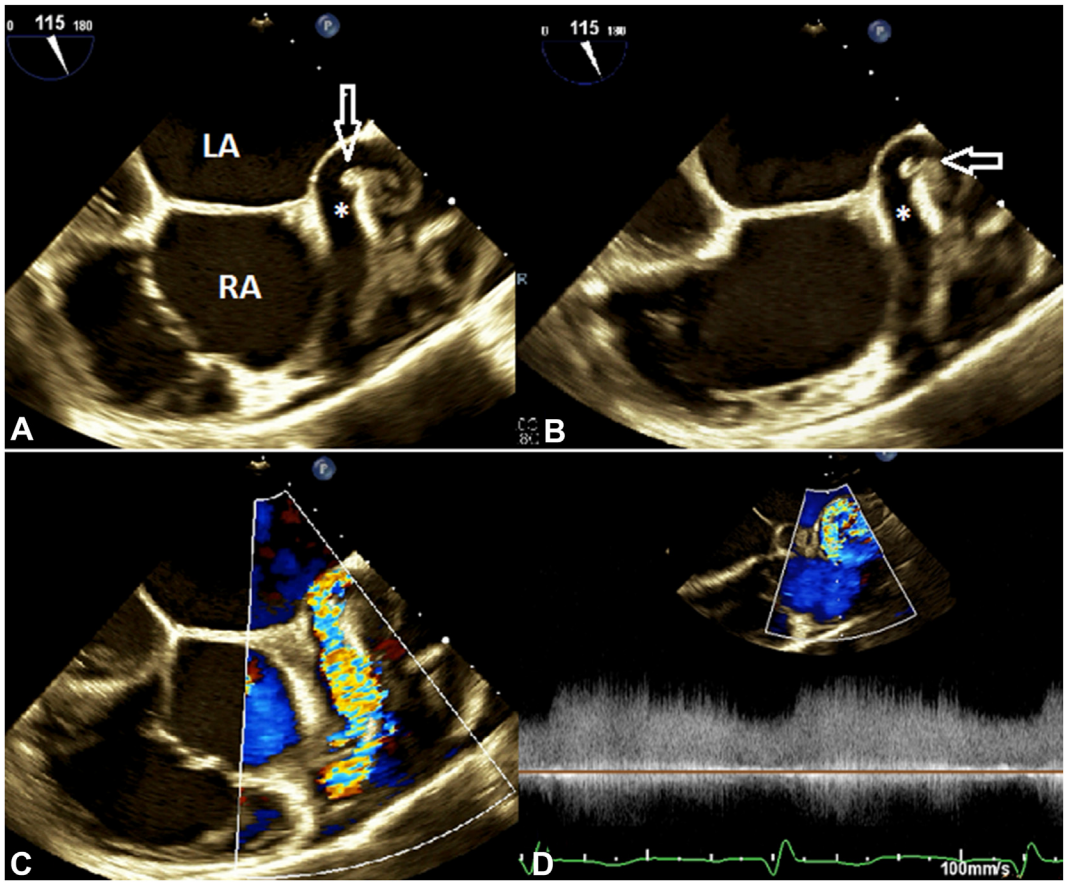


Figure 2 TEE, midesophageal long-axis (115°) systolic **(A)** and diastolic **(B)** views without **(A,B)** and with **(C,D)** color flow Doppler, including pulsed-wave spectral display **(D)**, demonstrates the CAF (*asterisk*), the vegetation within the CAF (*arrow*), and turbulent, continuous flow within the CAF.

ultimately led to the discovery of a CAF with multiple vegetations on TEE and CCT, resulting in a confirmed diagnosis of subacute IE. The information obtained through TEE analysis was corroborated by CCT, which precisely matched the surgical observations. The histologic analysis of the vegetations further confirmed the diagnosis of endocarditis.

Small, asymptomatic fistulas typically do not require intervention, and close monitoring with regular follow-up through echocardiography or angiography is generally recommended. Still, symptomatic and larger fistulas with an increased risk for complications should be closed.[11] Although transcatheter closure has emerged as the preferred treatment option, it is not suitable for patients with large CAFs, significant aneurysmal dilatation, or multiple openings. In these cases, surgical intervention should be considered.[11] According to the 2023 European Society of Cardiology guidelines for the management of endocarditis, urgent surgery within 3 to 5 days should be considered in cases with a vegetation size of ≥10 mm and other indications for surgery, such as significant valvular dysfunction.[12] Our patient, who presented with a complicated giant fistula associated with endocarditis and severe AR, successfully underwent AV replacement and fistula repair after a short course of antibiotic therapy and subsequently completed a 4-week course of antibiotic therapy as part of the postoperative care. The European guidelines recommend antibiotic prophylaxis for patients at high risk for IE who are undergoing at-risk dental procedures, including dental extractions, oral surgery procedures, and procedures involving manipulation of the gingival or periapical region of the teeth.[12] The existing literature indicates that patients with CAF are at risk for developing IE, which can be life threatening.[2-4,6-8] Therefore, antibiotic prophylaxis is recommended for all patients with congenital CAFs.

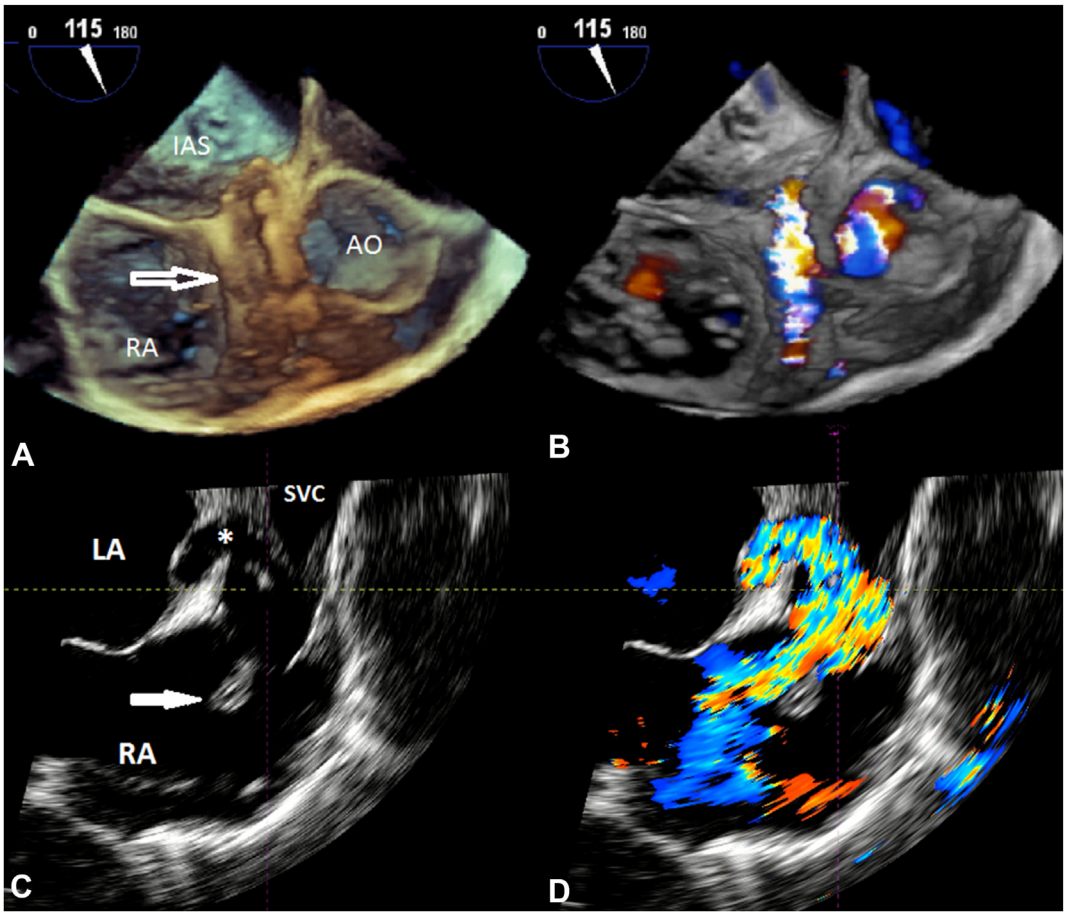


Figure 3 Three-dimensional TEE, midesophageal volume-rendered short-axis views without **(A)** and with **(B)** color flow Doppler and multiplanar reconstructed orthogonal views without **(C)** and with **(D)** color flow Doppler, demonstrates the fistula tract (*open arrow*) draining into the RA near the superior vena cava (SVC; *asterisk*) and a large vegetation (*closed arrow*) at the drainage site in the RA. *AO*, Aorta; *IAS*, interatrial septum; *LA*, left atrium.

## CONCLUSION

A CAF is an uncommon anomaly, and IE is a rare but potentially fatal complication associated with CAF that can involve both valvular and nonvalvular vegetations. TEE, particularly with 3D modality, is crucial to the diagnostic process by identifying CAF, its characteristics, and potential complications, such as endocarditis. Early, accurate diagnosis and appropriate treatment are essential in reducing the mortality rate associated with this condition.

## ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

## CONSENT STATEMENT

Complete written informed consent was obtained from the patient (or appropriate parent, guardian, or power of attorney) for the publication of this study and accompanying images.

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## DISCLOSURE STATEMENT

The authors report no conflict of interest.

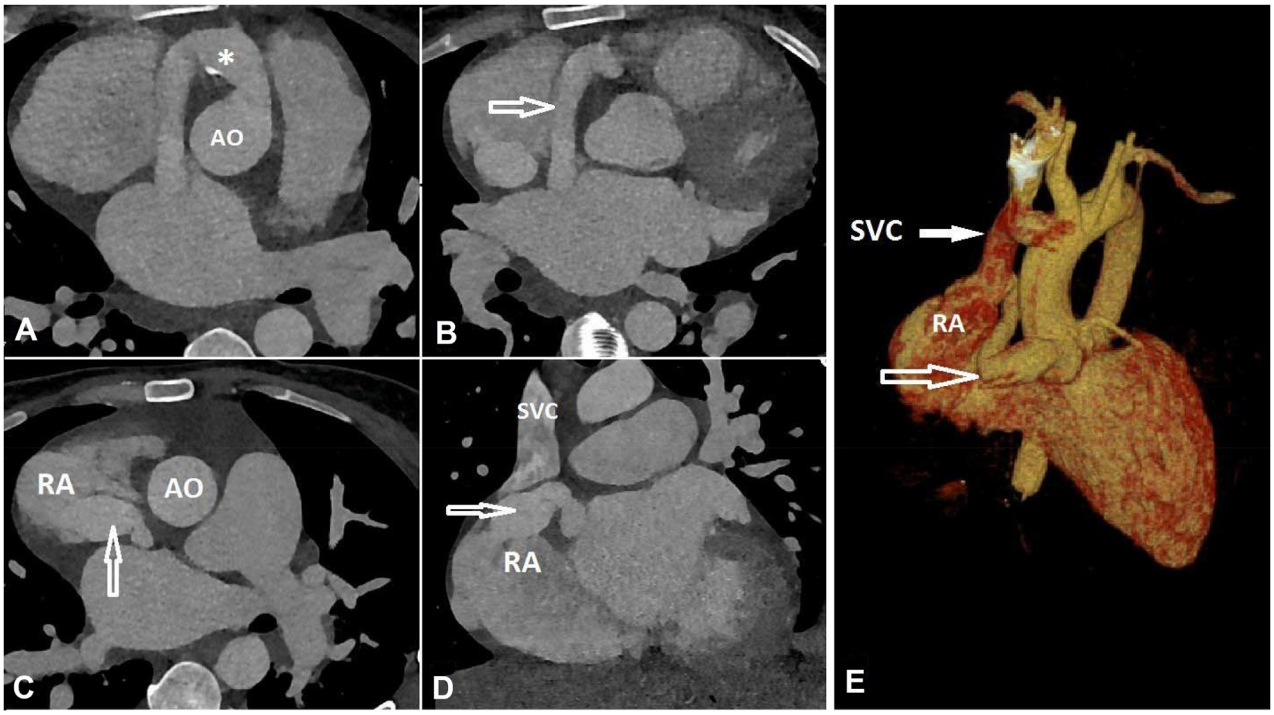


Figure 4 CCT, multiplanar reconstruction inferior-superior axial **(A–C)**, coronal **(D)**, and volume-rendered whole-heart **(E)** displays, demonstrates the origin of a tortuous and aneurysmal fistula (*open arrows*) from the proximal RCA (*asterisk*) coursing near the interatrial septum with the distal part of the fistula draining into the RA at the cavoatrial junction with the superior vena cava (SVC; *closed arrow*). *AO*, Aorta.

## SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2025.01.002.

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