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CONGENITAL HEART DISEASE

CASE REPORT: CLINICAL CASE

2 Rare Syndromes in 1 Patient

Determining the Cause of Sudden Cardiac Arrest

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ABSTRACT

A 19-year-old man survived sudden cardiac arrest caused by ventricular fibrillation during physical activity. The initial suspicion that this was caused by electrolyte imbalance proved to be wrong. Cardiac computed tomography revealed congenital heart disease. Coronary imaging is an essential component of the comprehensive diagnostic workup after sudden cardiac arrest. (JACC Case Rep. 2024;29:102549) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 19-year-old man collapsed during physical education class at school. Bystander cardiopulmonary resuscitation was immediately initiated by his teacher. When rescue services arrived, ventricular fibrillation was detected and treated by external defibrillation with the delivery of 1 shock. Return of spontaneous circulation was achieved; the cumulative duration of resuscitation was 20 minutes. The patient was transferred to a referral hospital in stable condition and intubated, without catecholamine support. Physical examination was unremarkable apart from basal crackles on auscultation of the lungs. Initial heart rate was 125 beats/min, and blood pressure was 105/60 mm Hg.

TAKE-HOME MESSAGES

- Thorough evaluation of every patient after sudden cardiac arrest in an interdisciplinary team is essential, including comprehensive family and personal history, provocative exercise testing, cardiac imaging, and genetic testing.
- Although coronary artery disease is rare the young, the most common causes of sports-related sudden cardiac arrest are associated with the coronary arteries. (Noninvasive) coronary angiography is therefore an essential part of the diagnostic workup.

PAST MEDICAL HISTORY

Past medical history consisted of genetically diagnosed Alport syndrome (2 heterozygous mutations: CL44A3 sc 1909 G>A and C.4981C>T). Alport syndrome is a rare genetic disorder that causes glomerulonephritis and progressive chronic kidney disease because of a defect in type IV collagen. Before admission, the patient had been evaluated closely at

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ABBREVIATION AND ACRONYMS

ALCAPA = anomalous left coronary artery from the pulmonary artery

ECG = electrocardiogram

ESC = European Society of Cardiology

ICD = implantable cardioverter-defibrillator

o.d. = once daily

the nephrologic department of our tertiary care hospital and his local nephrologist for chronic kidney disease stage 4, categorized according to the KDIGO (Kidney Disease: Improving Global Outcomes) classification and hypertension, but he had not yet required dialysis. Family history included Alport syndrome in his sister and hematuria in his mother and his maternal grandfather. There was no history of sudden cardiac arrest in the family. Medication included ramipril 10 mg once daily (o.d.), amlodipine 10 mg o.d., dapagliflozin 10 mg o.d., sodium bicarbonate 1 g 3 times a day, sevelamer 800 mg 3 times a day, and vitamin D o.d.

DIFFERENTIAL DIAGNOSIS

The initial hypothesis regarding the etiology of sudden cardiac arrest was electrolyte imbalance caused by underlying Alport syndrome. Hereditary arrhythmic syndrome appeared less likely because of the lack of past medical or family history thereof and unsuspicious baseline and continuous electrocardiogram (ECG) monitoring. Further differential diagnoses included cardiomyopathies such as hypertrophic cardiomyopathy or arrhythmogenic right ventricular cardiomyopathy. Previously undiagnosed congenital heart disease or myocarditis were taken into consideration as well. Noncardiac differential diagnoses included pulmonary embolism and aortic dissection.

INVESTIGATIONS

Initial laboratory results showed metabolic acidosis (pH 7.10) and hyperkalemia (6.4 mmol/L), which was treated with 50 mmol intravenous sodium bicarbonate. No hypoxia was evident (Table 1). Typical features of hyperkalemia were evident on the ECG: peaked T waves and unspecific QRS interval prolongation (Figure 1). N-terminal pro-B-type natriuretic peptide was 2,857 ng/L, and high-sensitivity troponin T was 29.1 pg/mL; both were interpreted as attributable to cardiopulmonary resuscitation and chronic kidney disease. The patient was directly transferred to computed tomography imaging to exclude pulmonary embolism. Before administration of the contrast agent, ventricular fibrillation occurred twice and was successfully treated with the delivery of 3 and 2 shocks, respectively, by manual external defibrillation. To stabilize the patient, he was transferred to the intensive care unit before completion of the examination and was treated with intravenous amiodarone. Native computed tomography images displayed no evidence of intracranial hemorrhage or early signs of ischemia; pneumothorax and pneumoperitoneum were excluded. Point-of-care ultrasound showed no signs of increased right ventricular load, and left ventricular function was mildly reduced without regional wall motion abnormalities.

TABLE 1 Laboratory Data at Admission

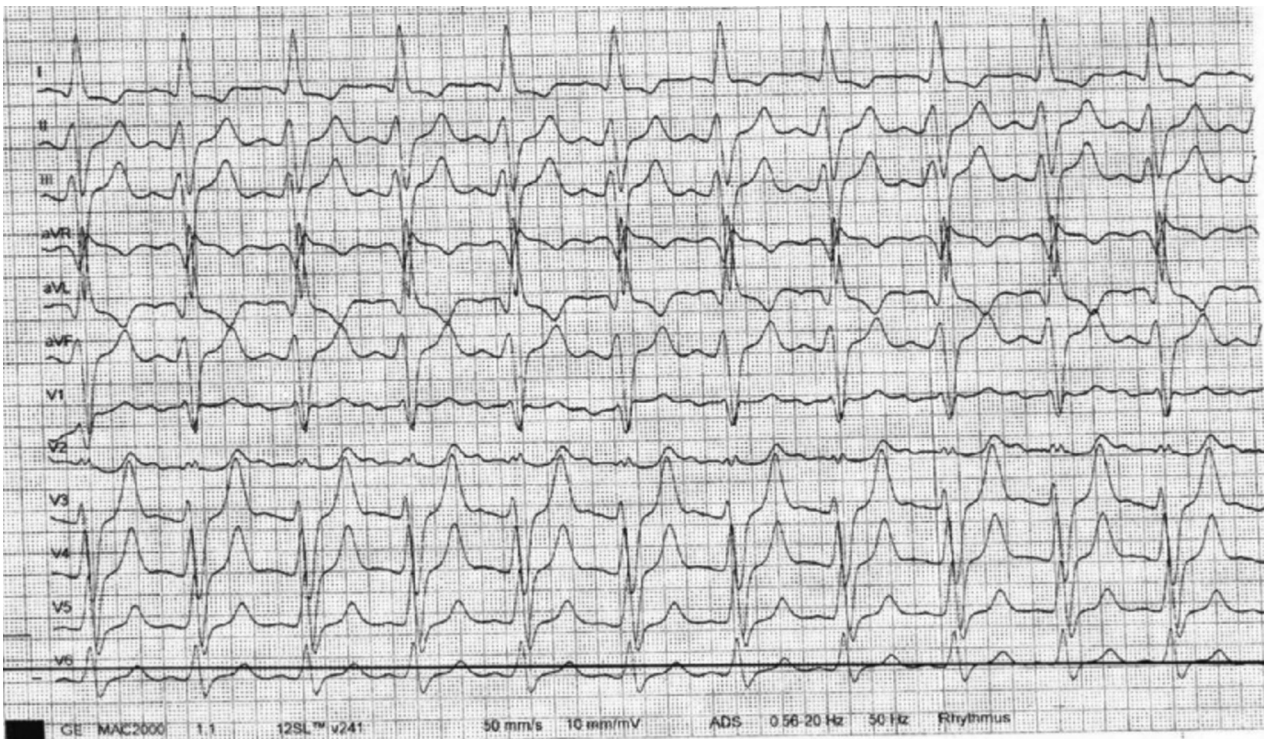
	Reference Range, Referral Hospital	At Admission
Sodium, mmol/L	135-146	142
Potassium, mmol/L	3.4-4.6	6.4
Calcium, mmol/L	2.11-2.59	2.32
Creatinine, mg/dL	0.6-1.2	4.02
Urea, mg/dL	<45	89
Glucose, mg/dL	65-100	241
Creatine kinase, U/L	<190	191
LDH, U/L	<316	419
Aspartate aminotransferase, U/L	<50	81
Alanine aminotransferase, U/L	<50	117
Alkaline phosphatase, U/L	40-130	78
γ-Glutamyl transferase, U/L	<60	17
Total bilirubin, mg/dL	<1.0	0.29
Phosphate, mmol/L	0.84-1.45	2.91
Amylase, U/L	8-53	54
Triglycerides, mg/dL	25-180	141
Albumin, g/L	37-51	37
C-reactive protein, mg/L	<5	<0.2
TSH, mU/L	0.4-4.0	7.93
Free T_3, ng/L	2.0-4.2	2.61
Free T_4, ng/L	8-18	12.41
NT-proBNP, ng/L	<125	2,857
GFR, CKD-EPI, mL/min/1.73 m^2	>60	20.2
PCT, ng/mL	<0.05	0.08
High-sensitivity troponin T, pg/mL	<14	29.1
White blood cell count, per nL	4-10	20.12
RBC, per pL	4.3-6.1	3.1
Hemoglobin, g/dL	13-17	9.5
Hematocrit, %	0.38-0.52	0.299
Platelet count, per nL	150-440	653
International normalized ratio	<1.2	1.13
Prothrombin time, s	<35	28
D-dimer, mg/L	<0.5	0.7
pH	7.37-7.45	7.10
Pco_2, mm Hg	35-45	41.1
Po_2, mm Hg	–	92
Base excess, mmol/L	-2 to +3	14.8
Lactate, mmol/L	<16	50

CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; GFR = glomerular filtration rate; LDH = lactate dehydrogenase; NT-proBNP = N-terminal pro-B-type natriuretic peptide; RBC = red blood cell; T_3 = triiodothyronine; T_4 = thyroxine; TSH = thyroid stimulating hormone.

MANAGEMENT

Following cardiac arrest, metabolic acidosis persisted, whereas hyperkalemia improved. No further ventricular arrhythmias occurred. Severe pneumonia

FIGURE 1 **Initial Electrocardiogram After Admission**



Electrocardiogram demonstrated typical features of hyperkalemia: peaked T waves and unspecific QRS interval prolongation.

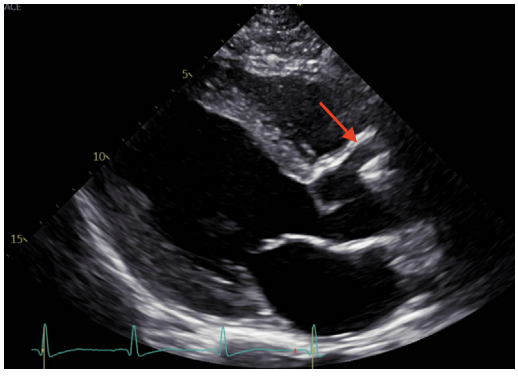
was treated with intravenous antibiotics. Because of acute-on-chronic kidney injury and persistent metabolic acidosis, hemodialysis was initiated, leading to further improvement of hyperkalemia und balanced pH. Hemodialysis withdrawal was initially unsuccessful, even though diuresis was sufficient at all times. Because of underlying Alport syndrome, the decision to implant a tunneled hemodialysis catheter was made.

Four days after admission, the patient was extubated. For further evaluation, including implantable cardioverter-defibrillator (ICD) insertion and nephrologic care, the patient was transferred to a tertiary center.

Initial diagnostic evaluation included comprehensive echocardiography, which showed normal left and right ventricular size with mildly reduced left and normal right ventricular systolic function, mild left ventricular hypertrophy, and no significant valve disease. However, the proximal part of the right coronary artery appeared prominent in the parasternal long- and short-axis views (**Figures 2 and 3**).

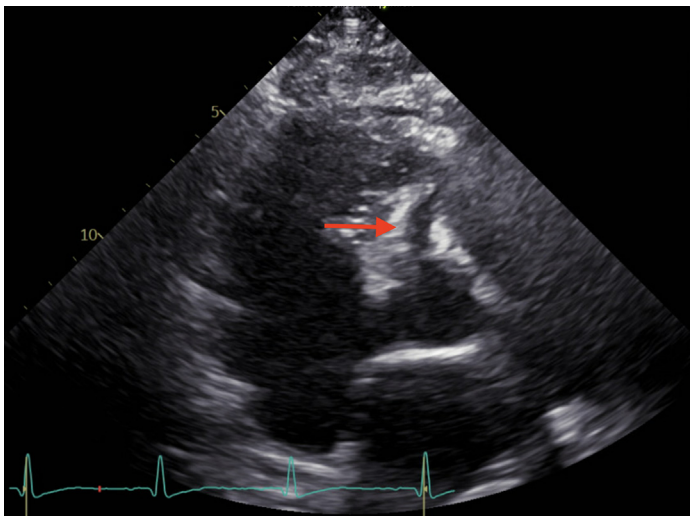
This prompted further evaluation with coronary computed tomography angiography. Anomalous left coronary artery from the pulmonary artery (ALCAPA) was revealed (**Figure 4**). The right coronary artery was dilated, with regular aortic origin and course.

FIGURE 2 **Echocardiography After Transferal to Our Tertiary Care Center**



Parasternal long-axis view demonstrates prominent origin of the right coronary artery (red arrow).

FIGURE 3 Parasternal Short-Axis View at the Aortic Valve Level



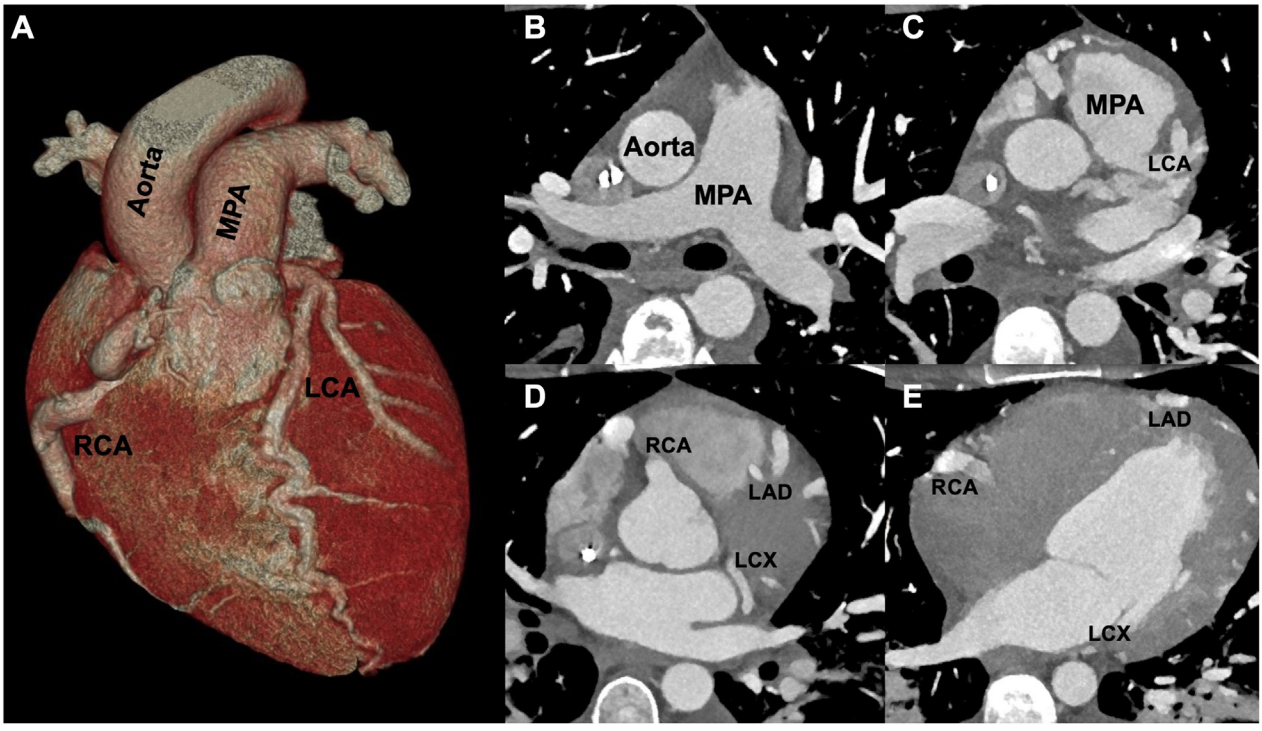
Prominent origin of the right coronary artery is visible (red arrow).

European Society of Cardiology (ESC) guidelines for the management of adult congenital heart disease recommend surgical correction in patients with ALCAPA.[1] Dual coronary system repair, including coronary button transfer, is preferred. In our patient, however, the anomalous left coronary artery originated from the nonfacing sinus of the pulmonary artery, making direct coronary artery grafting an inappropriate choice.[2] Therefore, a corrective operation with the modified Takeuchi technique was performed: an aortopulmonary window was established, and a transpulmonary tunnel was created with a pericardial patch, redirecting the left coronary artery to a neo-ostium in the aorta.

OUTCOME AND FOLLOW-UP

In the first hours after the operation, recurrent nonsustained ventricular tachycardia occurred, which was treated with intravenous amiodarone. The further postoperative course was uneventful: recurrent ventricular extrasystoles were treated with a

FIGURE 4 Coronary Computed Tomography Angiography of Anomalous Left Coronary Artery From the Pulmonary Artery With RCA Origin From the Aorta and LCA Origin From the Main Pulmonary Artery



The (A) 3-demensional reconstruction and (B to E) axial views from cranial to caudal. LAD = left anterior descending artery; LCA = left coronary artery; LCX = left circumflex artery MPA = main pulmonary artery; RCA = right coronary artery.

β-blocker. Echocardiography showed persistent mildly reduced left ventricular systolic function. Coronary-pulmonary artery fistula and aortic valve insufficiency, which are common complications of Takeuchi corrective operation, were excluded.[2]

Postoperatively, diuresis was stimulated with furosemide infusions. Hemodialysis was performed only once thereafter; withdrawal was successful. The patient was discharged with antihypertensive and heart failure medications and low-dose acetylsalicylic acid. The patient did not undergo implantation of a cardioverter-defibrillator.

At the 5-month follow-up, the patient was asymptomatic and reported no inadequate dyspnea or angina. Echocardiography showed no significant change. Renal function was still severely impaired, with glomerular filtration rate 17 mL/min/1.73 m^2 (chronic kidney disease stage G4 according to the KDIGO classification), no hyperkalemia had occurred. Preemptive evaluation for renal transplantation is currently being conducted.

DISCUSSION

Sudden cardiac arrest is rare in the young. This case reinforces the importance of considering a broad range of possible etiologies when sudden cardiac arrest occurs. The initially suspected etiology of sudden cardiac arrest was attributed to Alport syndrome, a rare genetic syndrome. Thorough investigation, however, revealed a second rare disease: ALCAPA. Both syndromes are uncommon as a sole manifestation—to the best of our knowledge, this is the first report of one patient presenting with both syndromes combined.

Inherited cardiac disease is a main cause of sudden cardiac arrest, including cardiomyopathies and primary electrical disorders. Thorough evaluation of every patient after sudden cardiac arrest in an interdisciplinary team is essential, although this process may be complex and sometimes inconclusive. Up to 40% of sudden cardiac arrest cases in the young show apparently normal hearts.[3] Thus, comprehensive family and personal history, ECG monitoring, and provocative exercise testing may all be crucial parts of the evaluation.[4] Advances in technology allow for genetic testing as a potentially valuable and specific tool for clinical investigation.[5] Also, this case emphasizes the significance of noninvasive multimodality imaging. Comprehensive echocardiography, cardiac magnetic resonance imaging, and computed tomography coronary angiography comprise valuable tools in the diagnostic pathway and are crucial to identifying the etiology of sudden cardiac arrest.

One point that must be addressed in this context is the decision of whether and when to perform coronary angiography on a survivor of sudden cardiac arrest. Several randomized trials have found no significant benefit for immediate coronary angiography for patients with sudden cardiac arrest without ST-segment elevations.[6] In the context of electrolyte imbalance in this patient, the decision not to perform coronary angiography appears reasonable. However, hyperkalemia was only moderately severe, which makes it unlikely as the cause of ventricular fibrillation in the patient.[7] In survivors of sudden cardiac arrest without a clear underlying cause, coronary artery imaging is recommended.[8] Although coronary artery disease is rare in young patients, the most common causes of sports-related sudden cardiac arrest are still associated with the coronary arteries, such as coronary artery disease or anomalies.[9] Mechanisms of myocardial ischemia for patients with coronary artery anomalies during exercise may include compression of coronary arteries during peak exercise. Ischemic changes in ECG may not be apparent after the event because ischemia abates once exercise is over; diagnosis may therefore be missed. Moreover, in electrically unstable patients after sudden cardiac arrest with suspicion of ongoing myocardial ischemia, the ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death recommend invasive coronary angiography.[8] Whether an earlier invasive coronary angiography may have led to a faster diagnosis and a change of clinical management in this case remains to be discussed. However, in this patient, computed tomography coronary angiography was the optimal diagnostic choice to evaluate the coronary arteries: the pretest probability for coronary artery disease was very low. Additionally, computed tomography coronary angiography is the current gold standard for the assessment of coronary artery anomalies.[10]

Finally, according to ESC guidelines, ICD insertion is recommended in patients who have survived sudden cardiac arrest in the absence of reversible causes.[8] Coronary anomaly was considered a reversible cause; the decision against inserting an ICD was made by an interdisciplinary heart team.

CONCLUSIONS

This case reinforces the importance of considering a broad range of differential diagnoses, even rare ones, when sudden cardiac arrest occurs in a young person. Coronary imaging is an essential component of diagnostic evaluation.

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