Two zebras and a cardiac arrest: a case report of concomitant Brugada syndrome and an anomalous coronary artery

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Background
Discovering concomitant diagnoses results in a challenge to determine the true cause of a patient’s presentation. Evaluating this fully is vital to plan appropriate and avoid inappropriate therapy.

Case summary
A 55-year-old gentleman presents in cardiac arrest whilst watching an unusual occurrence of England dominating a Football World Cup game vs. Panama in 2018. Diagnostic coronary angiography discovered an anomalous right coronary artery from the opposite sinus (R-ACAOS), but clinical suspicion this was incidental lead to a further diagnosis of Type 1 Brugada Syndrome (BrS) following a positive Ajmaline provocation challenge. Risk stratification of these two zebras using computed tomography coronary angiography (CTCA), Cardiac magnetic resonance imaging (CMRI), Exercise Stress Echocardiography was performed and following a multi-disciplinary meeting, BrS was felt to be the primary diagnosis. The patient received a secondary prevention implantation of a cardiac defibrillator and avoided cardiac surgery.

Discussion
Diagnosing a rare condition does not necessarily mean it is the cause of a patient’s presentation and should not end the investigative process. Right coronary artery from the opposite sinus rarely causes cardiac arrest in middle age and is typically associated with peak exercise. Type 1 BrS is associated with cardiac arrest with vagal activity, perhaps such as England winning a World Cup game! Clinical correlation and risk stratification is required for suspected incidental findings.

Keywords
Brugada syndrome • Anomalous coronary artery • Cardiac arrest • Sudden cardiac death • Concomitant diagnoses • Case report

Learning points
• Finding one zebra does not mean there cannot be another, clinical correlation is required.
• Concomitant diagnoses require individual evaluation and risk stratification to establish the primary cause of a patient’s presentation, as treatments could differ significantly.
Introduction

Determining the relevance of concomitant diagnoses poses a managerial challenge. Indeed, one diagnosis could be purely incidental, misleading a clinician and result in potentially misguided patient treatment.

Brugada syndrome (BrS) is an ion channelopathy associated with malignant ventricular arrhythmia and sudden cardiac death (SCD). Typically, an arrhythmia occurs during vagotonic activity such as sleep or a large meal. Treatment of BrS is through implantation of a cardiac defibrillator (ICD).

Anomalous origination of a right coronary artery from the opposite sinus (R-ACAOS) is also associated with SCD but this is typically at peak exertion. Treatment of patients with R-ACAOS causing aborted SCD is with coronary stenting or surgery.

Our case describes a patient presenting with aborted SCD and was diagnosed with both conditions. His case demonstrates the importance of establishing accurate aetiology for aborted SCD, and how to assess incidental findings.

Case presentation

A 55-year-old man with hypertension suffered an out of hospital cardiac arrest whilst sitting watching the England vs. Panama football match during the 2018 World Cup. He had no preceding symptoms. There was no family history of SCD. His wife provided immediate cardiopulmonary resuscitation. His cardiac rhythm was ventricular fibrillation (VF) and he received two shocks before achieving spontaneous circulation. He was intubated at the scene before transfer to our centre.

Physical examination was unremarkable.

Initial investigations included a potassium of 3.1 mmol/L (3.5–5.3 mmol/L), but no other electrolyte abnormalities. This was replaced intravenously. Serial troponin I taken on admission and at 12 h measured 573 and 303 ng/L, respectively (<21 ng/L). A computed tomography (CT) Head was unremarkable. Echocardiography showed mild left ventricular hypertrophy but no regional wall motion abnormalities, pericardial effusion, or valvular pathology.

His electrocardiogram (ECG) showed sinus tachycardia, a QTc of 490 ms, and 1 mm ST depression in II, III, aVF, and V6. There was subtle ST-elevation of <0.5 mm that varied between QRS complexes in aVR (Figure 1). On a subsequent ECG, the inferolateral ST changes and QTc prolongation had resolved, however, new subtle downsloping ST-elevation of 1 mm was present in V1 (Figure 2).

Coronary angiography revealed unobstructed coronary arteries, however, an R-ACAOS was identified (Figure 3 and supplementary materials).

At this stage, the primary diagnosis was unclear and further investigation was required to delineate contributing factors. The differential diagnosis included a primary arrhythmia from long QT syndrome, BrS, hypertrophic cardiomyopathy, or an inferior myocardial infarction associated with a malignant course of the R-ACAOS.

Cardiac magnetic resonance imaging (CMRI) revealed borderline left ventricular hypertrophy, normal systolic function, and no scar on late gadolinium enhancement. The findings were consistent with hypertensive heart disease rather than hypertrophic cardiomyopathy or myocardial infarction.

A CT coronary angiogram confirmed the course of the R-ACAOS leaving the left sinus acutely with an intramural path before travelling between the aorta and pulmonary artery (Figure 4). Consequently, a functional test with exercise stress echocardiography was performed and completed with no symptoms, ECG changes, arrhythmia, or regional wall motion abnormalities. QT analysis was also normal.

Ajmaline testing occurred the following day and revealed classic downsloping ST-elevation in V1, V2, high V1, and high V2, consistent with type 1 BrS (Figure 5).

Extensive discussion at the joint cardiology/cardiac surgery multidisciplinary meeting took place. There was clear indication for an ICD reflecting the diagnosis of BrS. However, the significance of the R-ACAOS was debated. Ultimately, with the cardiac arrest occurring at rest, no evidence of myocardial infarction on CMRI, nor evidence of inducible ischaemia or arrhythmia on functional testing, the R-ACAOS was felt to be incidental, and its correction unnecessary.

Our case was discharged the day after successful ICD implantation. At follow-up at 3, 12, and 24 months, he was asymptomatic and

Timeline

| Date  | Events |
|-------|--------|
| Day 0 | Out of hospital cardiac arrest |
|       | Bedside transthoracic echocardiography reveals mild left ventricular hypertrophy |
|       | Diagnostic coronary angiography reveals unobstructed coronary arteries but a right coronary artery from the opposite sinus (R-ACAOS) |
|       | Admitted to intensive care |
| Day 4 | Extubated and good neurological recovery obtained |
| Day 6 | Discharged to cardiology ward |
| Day 9 | Cardiac magnetic resonance imaging shows normal left ventricular systolic function and no scar on late gadolinium enhancement |
| Day 12 | Computed tomography Coronary Angiography shows R-ACAOS leaving the left sinus acutely, travelling a malignant path between the aorta and pulmonary artery with an intramural component to the proximal vessel |
| Day 15 | Exercise Stress Echocardiography is completed with no symptoms, no electrocardiogram (ECG) changes, no arrhythmia, and no regional wall motion abnormalities. |
| Day 16 | Due to suspicious ECG and unclear cause of cardiac arrest, ajmaline testing undertaken revealing Type 1 Brugada syndrome (BrS) |
| Day 19 | Discussed at multi-disciplinary meeting, decided BrS primary cause of cardiac arrest |
|       | Successful implantable defibrillator procedure |

A. Bates et al.
received no device therapies. Aside from minor memory loss he has excellent neurological function, has returned to work and regained his driving licence.

Genetic screening for 17 genes associated with BrS returned negative.

**Discussion**

BrS is a rare ion channelopathy with a global prevalence of 1/2000.1 Diagnosing the condition is challenging as classic ECG changes of J-point and ST-elevation in right-sided precordial leads are often concealed. These changes can be affected by heart rate, body temperature, medications, glucose-induced insulin secretion, and ECG lead placement.3–7 Therefore, there is often variability between ECG tracings particularly in acutely unwell patients. This provides a diagnostic clue and emphasizes the importance of serial ECGs in patients with aborted SCD. Confirmation of the diagnosis is completed with provocation testing using a Class 1 sodium channel blocker such as ajmaline or flecainide. An additional diagnostic clue to the diagnosis is aborted SCD at rest. Studies have shown a circadian rhythm of VF episodes in BrS.
patients, particularly focused during sleep. The mechanism underlying this derives from the increased vagal tone during sleep, a resultant increase in premature ventricular ectopy from the right ventricular outflow tract which trigger polymorphic ventricular tachycardia and deterioration to VF.

Right coronary artery from the opposite sinus has a prevalence of 0.1–0.9% depending on definition. If symptomatic, patients can present with angina, dyspnoea, palpitations, presyncope, or SCD at peak exertion.

Based on autopsy reports from young athletes who suffered SCD, it is theorized that patients with R-ACAOS are at higher risk of SCD if the coronary artery has a slit-like ostium, arises from the aorta acutely, runs intramurally, and travels between the aorta and pulmonary artery. These factors are believed to increase exertional ischaemia due to increased myocardial demand, dynamic compression of the intramural R-ACAOS or coronary ostium, and decreased diastolic coronary perfusion. However, these findings are based on small numbers and overall incidence of SCD in young athletes aged 15–35 with R-ACAOS over a 20-year period is estimated at 0.2%.

Current AHA/ACC guidelines recommend treatment of symptomatic patients or those with positive ischaemia testing with coronary surgery. Expert consensus guidelines also recommend surgery but also comment catheter-based intervention can be considered for those deemed high surgical risk.

In asymptomatic young individuals with an incidental finding of R-ACAOS, the management is challenging. The clinician must decide between intervention or run the small risk but huge consequence of SCD. Furthermore, there is no evidence available that intervention eliminates SCD risk. For middle-aged patients (56 ± 11 years), major adverse cardiac events are similar to those with conventional coronary anatomy.

Our patient did not have exertional aborted SCD, which lead us to suspect his R-ACAOS was incidental. However, its presence raised concern and required assessment for potential future cardiac events. Thorough investigative process was imperative to determine

Figure 3 Invasive coronary angiography using an AL1 diagnostic coronary catheter from (A) posteroanterior caudal and (B) right anterior oblique windows. An aberrant right coronary artery arising from the left coronary sinus is shown. The origin of the left coronary artery can also be seen adjacent to the right coronary artery from the opposite sinus.

Figure 4 Multiplane reconstruction (A) and (B) a maximum intensity projection of computerized tomography coronary angiogram. The right coronary artery can be seen arising acutely from the left coronary sinus (R-ACAOS) next to the left main stem (LMS).
the cause of the cardiac arrest as treatment options differed significantly.

There was a paucity of evidence his R-ACAOS was responsible. In his case, the intramural segment of the R-ACAOS was minimal and his coronaries arteries were unobstructed on diagnostic angiography and CTCA. Also, there was no evidence of infarction on cardiac MRI, nor inducible ischaemia with functional testing.

Consequently, it was clear BrS had precipitated the cardiac arrest, the R-ACAOS was incidental and cardiac surgery unnecessary. He was educated to avoid the precipitants of ventricular arrhythmia with BrS, particularly fever, alcohol binges, and dehydration. He was also notified of www.brugadadrugs.org, a website with extensive information of medications safe to take and those to avoid in BrS. Regarding his R-ACAOS no

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**Figure 5** Electrocardiograms (A) pre-ajmaline testing and (B) following 100 mg of ajmaline. Classic down-sloping ST-elevation is seen in HV1, HV2, V1, and V2 following the infusion. HV1 and HV2 are High V1/V2 and placed in the right and left 3rd parasternal intercostal spaces, respectively.
specific exercise limitation was set but he was advised not to undertake extreme exercise.

**Conclusion**

Finding one rare diagnosis does not mean there cannot be another, clinical correlation is required. Concomitant diagnoses and incidental findings require individual evaluation and risk stratification as treatments could differ significantly.

**Lead author biography**

Dr Alexander Bates, MA MB BChir, is a Cardiology Specialist Registrar and Electrophysiology Research Fellow at University Hospital Southampton, UK. He graduated from University of Cambridge in 2011 and has undergone postgraduate training in Gloucestershire Hospitals, UK, University Hospitals Plymouth, UK, and Palmerston North Hospital, New Zealand. He began specialist cardiology training in 2017 in the Wessex Deanery. His research interests are of 3D electroanatomical mapping and ablation of complex arrhythmia.

**Supplementary material**

Supplementary material is available at European Heart Journal - Case Reports online.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent:** The authors confirm that written consent for the submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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