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CASE REPORT
Cardiac imaging

Case report: the role of multimodal imaging to optimize the timing of return to sports in an elite athlete with persistent COVID-19 myocardial inflammation

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Background COVID-19 has been associated with myocardial abnormalities on cardiac magnetic resonance imaging (CMR). We report a case of COVID-19 myocarditis in an elite athlete.

Case summary A male, 21-year-old elite football player had tested positive for SARS-CoV-2 on a polymerase-chain-reaction test and was referred for cardiac evaluation after experiencing palpitations after returning to sports (RTS). Biochemical evaluation demonstrated elevated N-terminal pro b-type natriuretic peptide (NT-proBNP) and high-sensitive Troponin T. Echocardiography demonstrated left ventricular function within normal ranges for athletes but with diminished basal, posterolateral, and septal strain. Cardiac magnetic resonance imaging (CMR) showed increased T1 values and late gadolinium enhancement (LGE) in the basolateral and mid-ventricular posterior segments. Focal COVID-19 myocarditis was diagnosed and the patient remained restricted from sports, in line with the 2020 ESC sports cardiology guidelines. Two months later, his electrocardiogram (ECG) showed inferoposterolateral T-wave inversion (TWI). Serial imaging studies were performed to optimize RTS timing. Cardiac magnetic resonance imaging showed persistently increased T1/T2 values and persistent LGE at 5 and 7 months. At 9 months, 18 F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)-computerized tomography (CT) demonstrated no pathologically increased cardiac FDG-uptake. Subsequent exercise ECG and Holters demonstrated no complex ventricular arrhythmias. The patient made a complete return to elite competitive sports, without any adverse events at 15 months of follow-up.

Discussion Cardiac symptoms in athletes post-COVID-19 should prompt cardiac evaluation. As COVID-19 myocarditis inflammation can persist beyond the 3–6 months of recommended sports restriction, a more personalized approach to RTS timing can be warranted. In cases with myocardial oedema without other signs of inflammation, FDG-PET-CT can be of added value to assess active myocardial inflammation.

Keywords Case report • Myocarditis • COVID-19 • Athlete's heart • Cardiac magnetic resonance imaging • FDG-PET-CT • Return to sport

ESC curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 2.3 Cardiac magnetic resonance • 8.1 Sports cardiology

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Learning points

- Exercise-related chest discomfort, palpitations, or syncope post-SARS-CoV-2 infection might indicate myocardial injury and necessitate cardiac screening.
- COVID-19-related myocardial inflammation may persist after resolution of symptoms, elevated biomarkers, and electrocardiographic changes, beyond the 3–6 months of sports abstinence recommended by the ESC Sport Cardiology guideline.
- 18 F-Fluorodeoxyglucose-positron emission tomography-computerized tomography might aid the assessment of active cardiac inflammation and can help time return-to-sports in the case of persistent myocardial oedema on CMR without other signs of inflammation.

Introduction

COVID-19 is associated with myocarditis and myocarditis-like injury in a broad spectrum of patients, including asymptomatic athletes.[1–5] In general, myocarditis accounts for up to 20% of athletes' sudden cardiac death (SCD). Exercise is an established risk factor for SCD in patients with myocarditis as it can accelerate the inflammatory response and exacerbate myocardial injury, potentially precipitating malignant ventricular arrhythmias.[6] Athletes with COVID-19-related cardiac complications may therefore be at increased risk of SCD. Determining abnormalities in athlete's electrocardiogram (ECG) and transthoracic echocardiogram (TTE) can be challenging as some findings [e.g. increased left ventricular (LV) and right ventricular (RV) end-diastolic volume, mildly reduced systolic function, and increased LV wall thickness] do not necessarily indicate pathology, but may be attributed to physiological adaptation to sports.[6–10] Exercise-related chest discomfort, palpitations, or transient loss of consciousness post-COVID-19 can indicate myocardial injury and therefore necessitates evaluation in a centre with sports cardiology expertise. Current return-to-sports (RTS) protocols are commonly based on COVID-19 severity and no evidence-based guidelines are available to assist clinicians in determining the right moment for athletes to RTS after COVID-19.[8] In general, RTS protocols advise refraining from sports for at least 10 days after symptom onset, including a minimum of 7 days with complete symptom resolution.[8–10] RTS screening and timing can however be challenging and potentially holds serious consequences when (subclinical) myocarditis is suspected, as the 2020 ESC sports cardiology guidelines recommend abstaining from moderate-to high-intensity exercise for a period of 3–6 months if myocarditis is confirmed. Cardiac magnetic resonance (CMR) imaging currently is the non-invasive gold standard in clinically suspected myocarditis and is the recommended imaging modality in RTS protocols in the presence of symptoms and findings suggestive of cardiac complications. We report a case of an elite athlete diagnosed with focal COVID-19 myocarditis with persistent inflammation in which imaging modalities were central for RTS timing.

Timeline

Time	Events
Day 1	PCR confirmed SARS-CoV-2 infection with mild symptoms but no chest pain, shortness of breath or fever
	Restricted from sports
Day 15	Resumed training
Day 16	Palpitations during a resting phase after exercise
	Restricted from sports and referred for cardiac evaluation
Month 1	Laboratory: increased high sensitive Troponin T (hsTNT) and NT-proBNP
	ECG: decrease of T wave amplitude in lead II and aVF, and T wave inversion (TWI) in lead III
	TTE: LVEF 51% with diminished global longitudinal systolic peak strain (GLS) of 16% of the basal and posterolateral and septal segments
	CMR: epicardial basolateral to mid ventricular posterior LGE with increased T1 values and extra cellular volume
	Ambulatory ECG monitoring (8 days): solitary PVCs without complex ventricular arrhythmias
	Diagnosis: focal COVID-19 myocarditis
	Sport restriction extended in line with the ESC sports cardiology guideline
Month 2	ECG: inferolateral T-wave inversion
	Laboratory: increased hsTNT but resolution of increased NT-proBNP
Month 5	CMR: persistent LGE and locally increased T1 values
Month 6	Laboratory: resolution of hsTNT
Month 7	ECG: resolution of T-wave inversion
	CMR: persistent LGE and locally increased T1 values
Month 9	FDG-PET-CT: no increased cardiac FDG-uptake
	TTE: LVEF 56% with globally improved GLS but diminished GLS in the lateral segment
	Exercise-ECG: multifocal solitary premature ventricular complexes without malignant characteristics
	Resuming indoor-sport (low intensity and strength training with heartrate monitoring) under expert supervision
Month 10	48h Holter: 135 PVCs, no complex ventricular arrhythmias
	Increase in training volume
Month 11	48h Holter: 200 PVCs, no complex ventricular arrhythmias
Month 13	Patient made a full return to competitive sports
Month 15	CMR: persistent LGE with normalisation of T1 times
	Follow-up: no adverse events

Case presentation

A male, 21-year-old otherwise healthy elite football player was referred for cardiac evaluation after experiencing palpitations post-exercise 1 day after returning to sports; he had a positive polymerase-chain-reaction (PCR) test for SARS-CoV-2 15 days prior. During infection, he experienced mild symptoms (nasal congestion, muscle ache, and tiredness), but no chest pain, shortness of breath, or fever. He was asymptomatic after ~2 weeks, including 7 days with complete symptom resolution, and resumed training according to current (inter-)national guidelines.[8–10] He experienced palpitations during a resting period and was consecutively restricted from sports and referred for cardiac evaluation. During the initial cardiac evaluation, he had no physical complaints and his physical examination was normal. The biochemical evaluation was negative for inflammatory markers but showed elevated NT-proBNP (117 ng/L) and high-sensitive Troponin T (hsTnT) (15 ng/L). The ECG showed sinus arrhythmia at 39–48 b.p.m., an intermediate heart axis, normal conduction times,

and no pathological Q waves (see Supplementary material online, *Figure S1*), but demonstrated a decrease of T wave amplitude in lead II and aVF, and T-wave inversion (TWI) in lead III (*Figure 1A*). Transthoracic echocardiogram demonstrated LV ejection fraction (EF) within normal limits for athletes (51%) (see Supplementary material online, *Video S1*) with diminished global longitudinal strain (GLS) (16%) of the basal, posterolateral, and septal segments (*Figure 2A*). Right ventricular dimensions and function were normal. Due to the complaints and subtle biomarker-, ECG-, and strain abnormalities, a CMR was performed. CMR demonstrated ventricular dimensions and functions within normal limits for male athletes (LVEDV/BSA 143 mL/m^2; LVEF 53%; RVEDV/BSA 151 mL/m^2; RVEF 50%).[11] Cardiac magnetic resonance imaging also showed late gadolinium enhancement (LGE) in the basolateral and mid-ventricular posterior segments with increased T1 times (1232 ± 101 ms) (*Figure 3*). The estimated affected area of LGE was 9% of the total LV mass. The patient was diagnosed with focal COVID-19 myocarditis. Continuous ambulatory ECG monitoring for 8 consecutive days demonstrated solitary premature ventricular contractions (PVCs) without complex ventricular arrhythmias. The sports restriction was extended, in line with the 2020 ESC sports cardiology guidelines.[6,12] The national multidisciplinary sports cardiology team found no indication for medical treatment. Frequent re-evaluations subsequently took place, consisting of careful evaluation of signs and symptoms, inflammatory- and cardiac biomarkers, ECG, and CMRs. NT-proBNP gradually normalized within 2 months, while hsTNT remained elevated at 2 months (16 ng/L) and 3 months (17 ng/L), but normalized at 6 months (8 ng/L). Subsequent ECG 2 months after infection showed inferoposterolateral TWI (*Figure 1B*), which normalized within 7 months. A repeat CMR 5 and 7 months after infection demonstrated ongoing inflammation with increased T1 and T2 times and persistent LGE (*Figure 3*). Nine months after infection, an 18 F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)-computerized tomography (CT) was performed to assess the presence of active myocardial inflammation. The FDG-PET-CT showed successful myocardial suppression without increased pathologic cardiac FDG-uptake (see Supplementary material online, *Video S2*). Repeated TTE demonstrated a normal LVEF (56%) (see Supplementary material online, *Video S3*) with improved GLS (*Figure 2B*). Subsequent cardiopulmonary exercise testing showed a VO_2 max of 45 mL/min/kg at maximal load (HR 193/min; 3.8 W/kg). There were only six sporadic non-repetitive, multifocal solitary PVCs, with both 'common'- (left bundle branch block inferior axis morphology, S/R transition beyond V3) and 'uncommon' morphology (right bundle branch block superior axis morphology and wide QRS) (*Figure 4*).[13] Premature ventricular contraction frequency declined with increasing exercise intensity. There were no (bi-directional) couplets, triplets, or (non-sustained) ventricular tachycardias. As the patient was asymptomatic, had normal biomarkers and LV function and no signs of inflammation, graduated RTS was recommended, starting with indoor low-intensity endurance and strength training, with heart rate monitoring and expert supervision.[6] 48 h-Holter registration, including a training session, showed a heart rate between 39 and 118 b.p.m. with a total of 135 solitary multifocal PVCs (<0.1%; Lown grade 2) without complex arrhythmias. A 48 h-Holter registration after an increase in training volume 1 month later showed no complex arrhythmias and no significant increases in ventricular ectopy (<0.12%; Lown grade 2). Thirteen months after symptom onset, the patient made a full return to elite competitive sports. A repeat CMR 15 months after infection showed persistent, unchanged LGE without increased T1 times. The athlete continues to compete at an elite level and no adverse events have taken place during the ongoing follow-up (15 months).

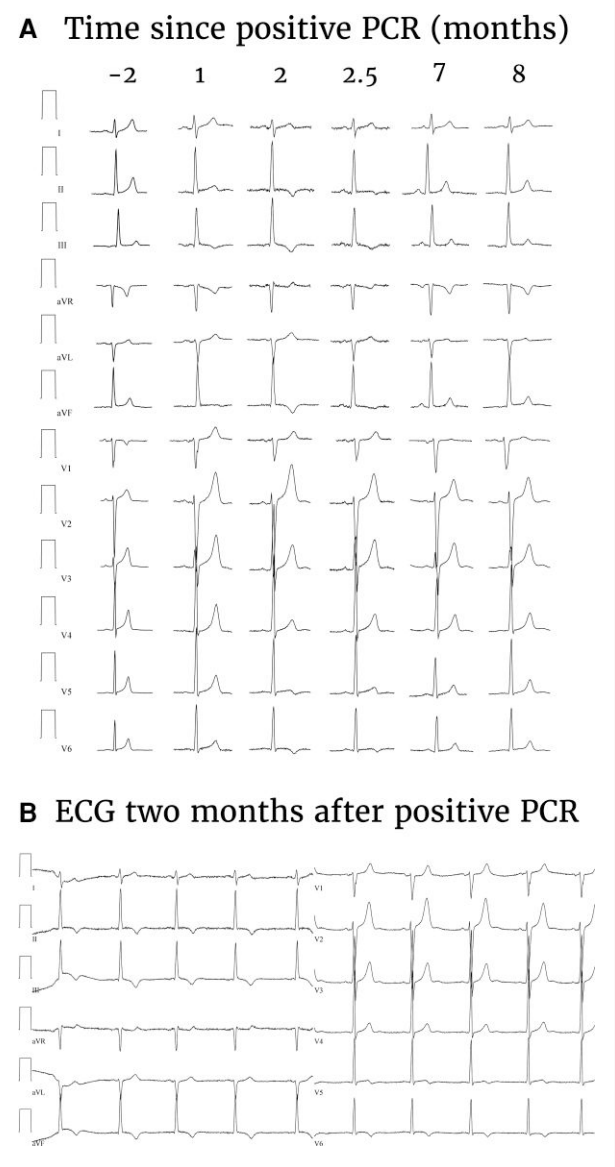

Figure 1 Electrocardiographic findings. (*A*) Temporal view of electrocardiographic changes following focal COVID-19 myocarditis over time. (*B*) Electrocardiogram 2 months after positive polymerase-chain-reaction test.

Discussion

Imaging modalities are central in timing RTS and guiding clinical decision-making in (COVID-19) myocarditis. Although CMR is highly sensitive to myocardial oedema, as is reflected by increased tissue-dependent transverse magnetization relaxation times, it cannot reliably detect or phenotype immune cells within the heart.[14,15] 18 F-fluorodeoxyglucose-PET-CT has been proposed as a tool to quantify active myocardial inflammation in myocarditis and was decisive in timing the optimal moment for RTS in our case. Although FDG-PET-CT generally demonstrates adequate agreement with CMR findings in patients with myocarditis, studies on integrated assessment of myocarditis in athletes are warranted.[15]

Conclusion

Our case demonstrates that COVID-19 myocarditis inflammation can persist beyond the 3–6 months of ESC-recommended sports restriction. Even after the resolution of symptoms and normalization of biomarkers and ECG, myocardial inflammation can be present, and RTS

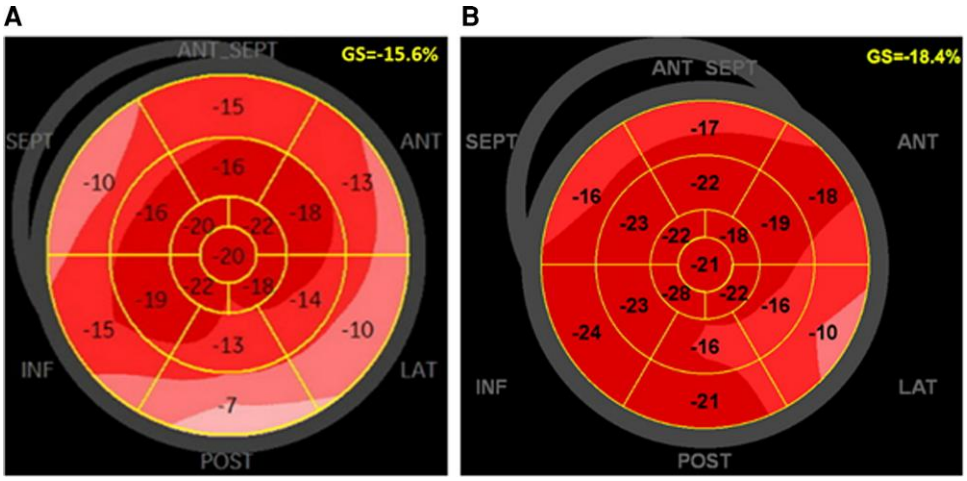

Figure 2 Global longitudinal strain as calculated by transthoracic echocardiogram demonstrating: (*A*) diminished global longitudinal strain of the basal and posterolateral and septal segments 1 month after positive polymerase-chain-reaction; (*B*) partially recovered global longitudinal strain 9 months after positive polymerase-chain-reaction with persistently diminished global longitudinal strain in the lateral segment.

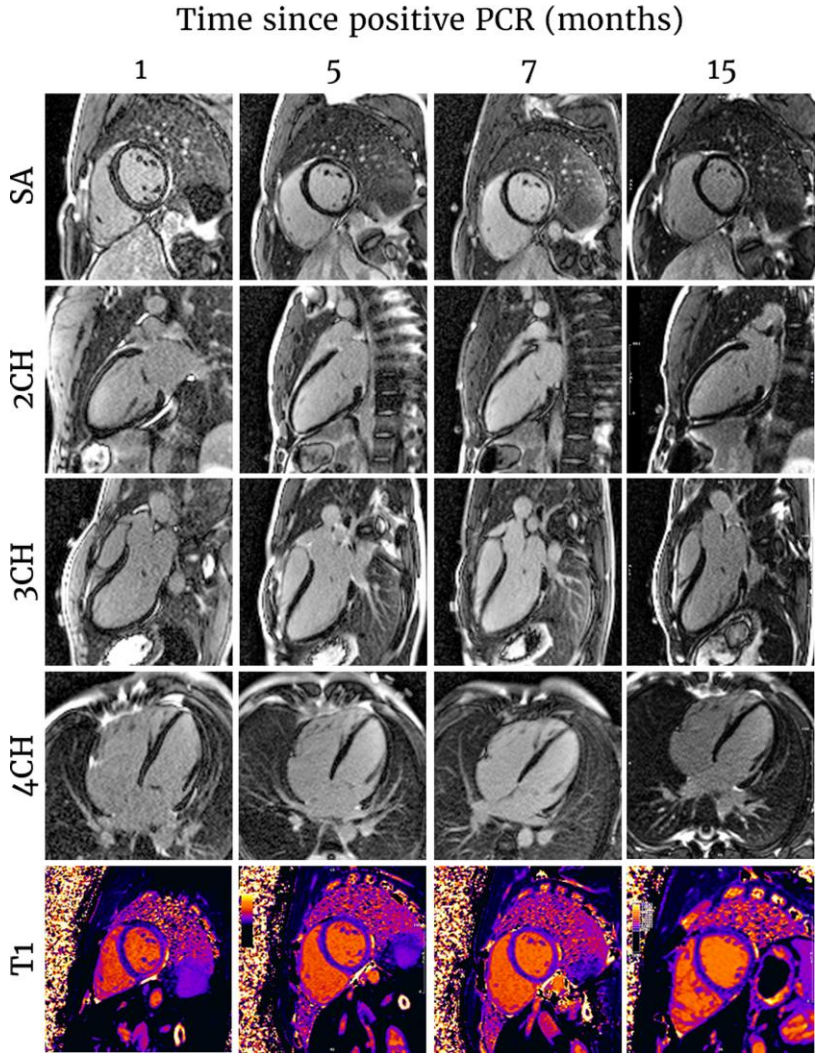

Figure 3 Cardiovascular magnetic resonance imaging demonstrating persistent late gadolinium enhancement in the basolateral and mid-ventricular posterior segments over time with temporarily increased T1 times.

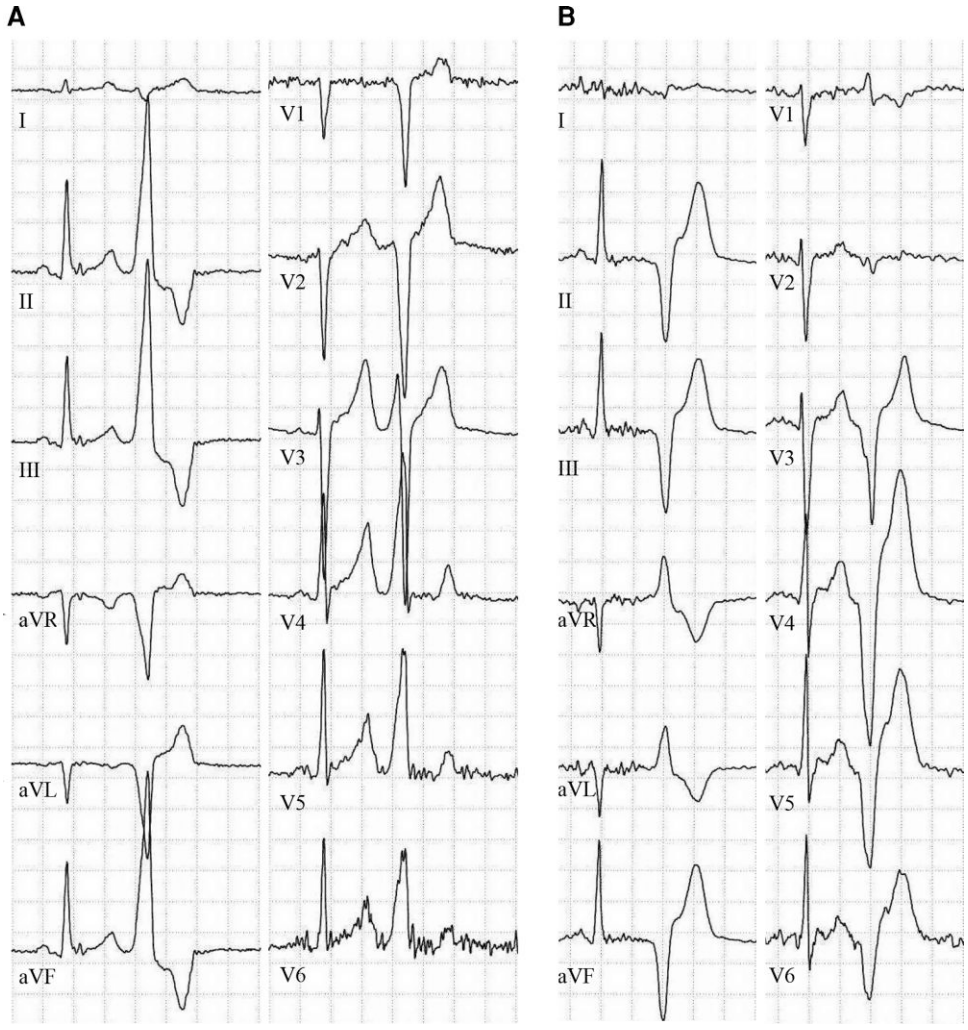

Figure 4 Exercise-electrocardiogram demonstrating solitary multifocal premature ventricular contractions during rest and exercise. (*A*) A 'common' type premature ventricular contraction with left bundle branch block inferior axis morphology, S/R transition beyond V3. (*B*) An 'uncommon' type premature ventricular contraction with right bundle branch block superior axis morphology and wide QRS.

timing can warrant a more personalized approach. Additional imaging techniques, such as FDG-PET-CT, can be of value to phenotype inflammation when CMR demonstrates persistent myocardial oedema with LGE. More data on the long-term prognosis of COVID-19 myocarditis in athletes is urgently needed to assist RTS and follow-up.

Lead author biography

Joelle J.N. Daems is a current PhD candidate at the department of sport cardiology at the Amsterdam University Medical Centre. He completed his medical degree at the Utrecht University Medical Centre and has done a residency in cardiology at the Meander Medical Center in Amersfoort, the St Antonius Hospital in Nieuwegein and at the Amsterdam University Medical Centre.

Supplementary material

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

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

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