ESC European Society of Cardiology

European Heart Journal - Case Reports (2023) **7**, 1–7
https://doi.org/10.1093/ehjcr/ytad245

CASE REPORT
Cardiovascular imaging

Long-term follow-up of cardiac magnetic resonance imaging in myocarditis following messenger ribonucleic acid COVID-19 vaccination: a case report

Pakaparn Kittichokechai [1]*, Panupong Seripanu [1], and Thanakorn Laksomya [2]

[1]Division of Pediatric Cardiology, Department of Pediatrics, Panyananthaphikkhu Chonprathan Medical Center, Srinakharinwirot University, 222 Tiwanon road, Bang Talat, Pak Kret District, Nonthaburi 11120, Thailand; and [2]Division of Cardiology, Department of Medicine, Panyananthaphikkhu Chonprathan Medical Center, Srinakharinwirot University, 222 Tiwanon road, Bang Talat, Pak Kret District, Nonthaburi 11120, Thailand

Received 5 October 2022; first decision 1 November 2022; accepted 11 May 2023; online publish-ahead-of-print 18 May 2023

Background Presently, the association between myocarditis and messenger ribonucleic acid (mRNA) COVID-19 vaccination is well established. From the most current data, cases of myocarditis following COVID-19 vaccination seem to be mild with fast clinical recovery. Nevertheless, the complete resolution of the inflammatory process is still unclear.

Case summary We report the case of a 13-year-old boy who developed chest pain following the second dose of the Pfizer-BioNTech COVID-19 vaccine with long-term follow-up of cardiac magnetic resonance (CMR) imaging. An electrocardiogram (ECG) revealed progressively ST-segment elevation on the 2nd day of admission with a rapid improvement within 3 hours where only mild ST-segment elevation remained. The peak level of high-sensitivity cardiac troponin T was 1546 ng/L with rapid reduction. Echocardiogram revealed depressed left ventricular septal wall motion. CMR mapping techniques showed myocardial oedema with an increase in native T1 and extracellular volume (ECV). On the other hand, T1-weighted and T2-weighted images and late gadolinium enhancement (LGE) did not detect inflammation. The patient's symptoms were relieved by oral ibuprofen. After 2 weeks, ECG and echocardiogram were unremarkable. However, the inflammation process was still present based on the CMR by mapping technique. During the 6-month follow-up, CMR returned to normal.

Discussion In our case, the subtle myocardial inflammation was diagnosed by mapping technique with only a T1-based marker according to the updated Lake Louise Criteria and the inflammation of the myocardium returned to normal within 6 months after the onset of the disease. Further follow-up and larger studies are needed to determine the complete resolution of the disease.

Keywords mRNA vaccine • Myocarditis • Long-term follow-up • Cardiac magnetic resonance • Case report

ESC Curriculum 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 2.2 Echocardiography

* Corresponding author. Tel: +66865758892, Email: pakaparn.k@gmail.com
Handling Editor: Edoardo Conte
Peer-reviewers: Duygu Kocyigit Burunkaya; Emmanouil Androulakis; Takahiro Okumura
Compliance Editor: Pllyvios Demetriades
Supplementary Material Editor: Michael Waight

Learning points

- Cardiac magnetic resonance (CMR) parametric mapping technique might be needed to diagnose subtle myocardial inflammation.
- The inflammation of the myocardium in myocarditis after messenger ribonucleic acid (mRNA) vaccination can return to normal within 6 months after the onset of the disease.
- The recommendation to avoid competitive sports for 3–6 months with the re-evaluation of ECG, echocardiogram, and CMR imaging should be considered after myocarditis.

Introduction

After the emergency use authorization for the BNT162b2 messenger ribonucleic acid (mRNA) (Pfizer-BioNTech) vaccine to adolescents by the Food and Drug Administration of the United States (US) to prevent COVID-19 infection, cases of myopericarditis have been reported to the Vaccine Adverse Event Reporting System (VAERS) primarily in adolescent males after the second dose in the US.[1] There were several case reports of confirmed myocarditis following the mRNA vaccine in the US and Israel.[2] The most current data of short-term and mid-term follow-up suggest that the complete resolution of the inflammatory process may last over 3 months.[3–5] However, long-term follow-up data are still limited.[6,7] The Centre for Disease Control and Prevention (CDC) has started active follow-up surveillance to assess cardiac outcomes at 3 to 6 months in cases of myocarditis after COVID-19 vaccination.[8] In this case report, we report a long-term follow-up case of confirmed myocarditis after the Pfizer-BioNTech COVID-19 vaccine with a focus on the dynamic changes in electrocardiography (ECG) and cardiac magnetic resonance (CMR) mapping techniques.

Timeline

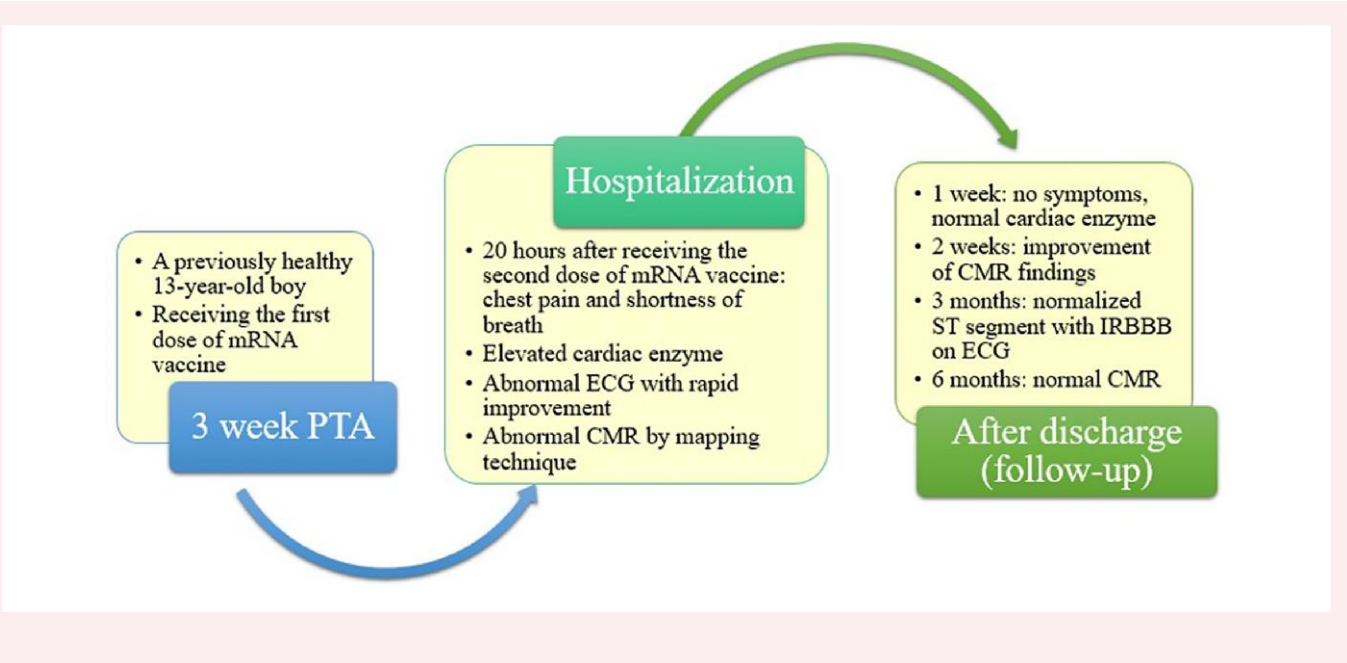
PTA, prior to admission; ECG, electrocardiogram; CMR, cardiac magnetic resonance; IRBBB, incomplete right bundle branch block.

Case presentation

A previously healthy 13-year-old boy presented to an emergency department with chest pain and shortness of breath 20 h after receiving the second dose of Pfizer-BioNTech COVID-19 following the first dose 3 weeks ago. The symptoms started with fever, followed by chest pain and shortness of breath.

Initially, the patient had stable vital signs, normal oxygen saturation, and normal physical examination. However, ECG demonstrated diffuse ST-segment elevation (*Figure 1A*). C-Reactive protein (CRP) was slightly elevated (16.8 mg/L, normal range < 5 mg/L) but the erythrocyte sedimentation rate (ESR) and ferritin were normal. N-Terminal pro-brain natriuretic peptide (NT-proBNP) was normal (90 pg/mL, normal range < 125 pg/mL). High-sensitivity cardiac troponin T (hsTnT) was initially elevated (506 ng/L, normal range 0–16 ng/L) with a peak level on day 3 (*Table 1*). A nasopharyngeal polymerase chain reaction (PCR) for COVID-19 and another respiratory viral panel test were negative. Furthermore, the result for SARS-CoV-2 spike protein antibody was positive, and anti-nucleocapsid IgG was negative. Chest radiograph was normal. Echocardiogram revealed normal global cardiac function except mildly depressed left ventricular septal regional longitudinal strain (*Figure 2*) and no pericardial effusion.

First CMR imaging on admission revealed normal biventricular volumes and systolic function. Coronary artery abnormalities were excluded by coronary magnetic resonance angiography (see Supplementary material online, *Figure S1*). A conventional qualitative analysis of signal intensities on T2-weighted and late gadolinium



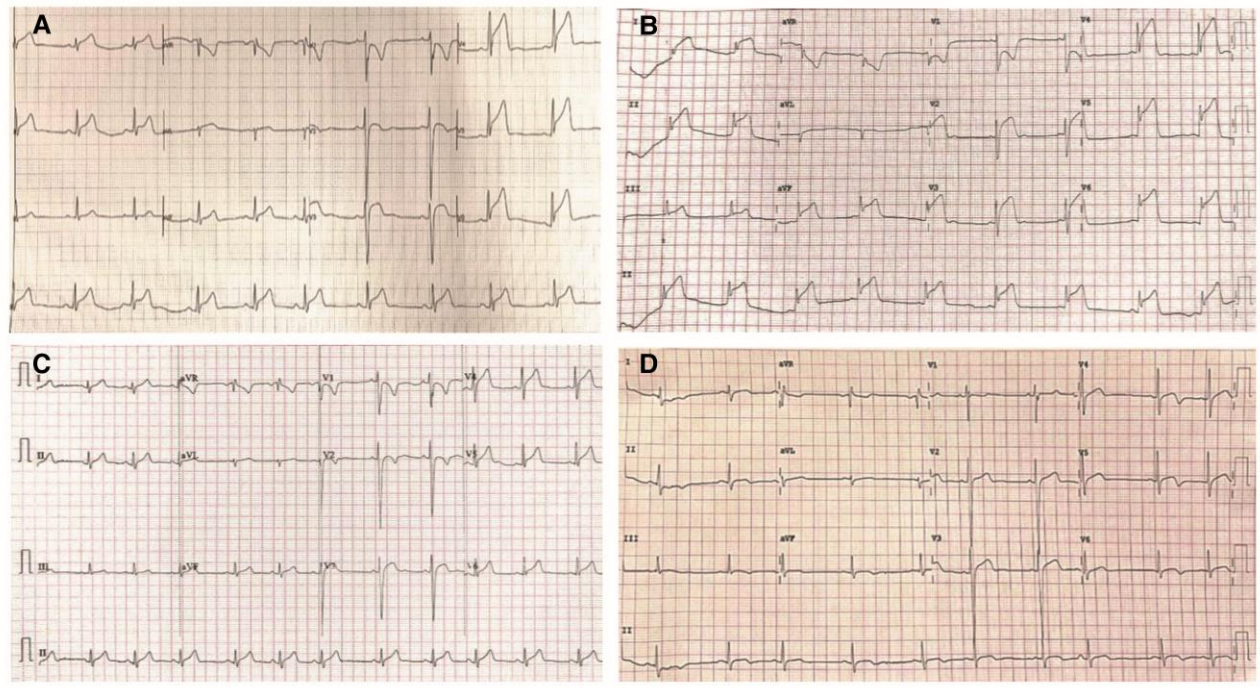


Figure 1 Electrocardiogram (ECG). (*A*) ECG on day 1 shows diffuse ST elevation in lead I, II, aVL, aVF, and V_2–V_6 with ST depression in lead V_1. (*B*) ECG on day 2 shows progressive ST elevation. (*C*) ECG on day 2 after 3 h shows significant improvement in ST-segment elevation. (*D*) ECG after 1-week follow-up shows ST elevation in lead V_2–V_5, the biphasic T waves in lead I, II, III, aVL, and V_4–V_6 with incomplete right bundle branch block.

enhancement (LGE) images did not show oedematous change or myocardial necrosis (*Figure 3*). On the other hand, a quantitative analysis of myocardial tissue showed an increase in all segments of the native T1 by mapping technique (*Figure 4*), and extracellular volume (ECV) (1031 ± 23.7 ms and 0.32, respectively) (*Table 1*). The native T1 value was highest at the inferolateral and anterior segments (1092 ± 41.8 and 1039 ± 74.8 ms, respectively), which indicated myocardial oedema and fibrosis. CMR imaging was performed on a 1.5-T MR unit (Ingenia Philips Medical Systems, Best, The Netherlands) using a body and phased array coils. Myocardial T1 mapping was assessed by the modified Look-Locker inversion recovery (MOLLI) sequence.

The patient required only an oxygen cannula for respiratory support during this admission. On day 2 of admission, he developed severe chest pain but stable vital signs. ECG showed progression of ST elevation (*Figure 1B*), hsTnT elevated to 1405 ng/L. However, his symptom was relieved by oral ibuprofen 400 mg once daily without any other medications and ECG was significantly improved within 3 h (*Figure 1C*). He was discharged on day 5. After a 1-week follow-up, he had no symptoms, normal troponin T level, mild ST elevation, and incomplete right bundle branch block (RBBB) on ECG (*Figure 1D*). He did not receive any medications at the follow-up.

Subsequently, the patient's clinical condition and ECG were assessed at week 2, month 3, and month 6. The echocardiogram and CMR were done at week 2 and month 6 until CMR returned to normal (*Figure 3* and *Table 1*). After the normalization of CMR, the last follow-up schedule was at month 12 to ensure that there is no additional change in clinical and ECG including advising any concerns about the booster vaccine before discharging the patient from our clinic.

Discussion

We reported a case of a 13-year-old boy with confirmed myocarditis following the CDC Working Case Definitions with 2018 Lake Louise criteria (LLC) for CMR[10,11] after receiving the 2nd dose of the Pfizer-BioNTech COVID-19 vaccine with the long-term follow-up.

Possible mechanisms for myocarditis after mRNA-based vaccination include a nonspecific innate inflammatory response or a molecular mimicry mechanism between viral spike protein and cardiac protein.[12] Nevertheless, the long-term effect of post-mRNA vaccine myocarditis is unclear.

Our case report showed the long-term follow-up and striking dynamic change of ECG and CMR. After the resolution of symptoms and normalized cardiac enzyme, we found an incomplete RBBB on the ECG that might be residual inflammation of the myocardium at the conduction system, compatible with mildly depressed left ventricular septal regional longitudinal strain. However, long-term follow-up of ECG at 3 months and 6 months still showed incomplete RBBB, while the result of CMR showed improvement in inflammation and returned to normal at 6 months. Therefore, the RBBB on ECG might be a pre-existing condition.

We emphasized long-term follow-up on CMR to explain the course and recovery pattern of COVID-19 vaccine–induced myocarditis. Shiyovich *et al.*[6] performed a follow-up on CMR at a median time of 212 days (IQR: 105–274 days) in seven patients with a relatively older age compared to our study's population. The results showed complete resolution of LGE in one patient and some improvement of LGE in the remaining patients.

Table 1 Laboratory and imaging findings of the patient at presentation and follow-up

Time from admission date	Admission day					2 weeks	3 months	6 months
Cardiac enzyme								
hsTnT (ng/L)	**Day1**	**Day2**	**Day3**	**Day4**	**Day5**	5	-	-
(normal < 16)	506	1405	1546	1136	538			
Electrocardiogram								
ECG findings	ST elevation in I, II, aVL, aVF, and V_2–V_6 with ST depression in V_1					ST elevation in V_2–V_4, biphasic T waves in I, II, III, aVL, and V_4–V_6 with incomplete RBBB	No ST elevation with incomplete RBBB	No ST elevation with incomplete RBBB
Echocardiography								
LVEF (%) regional wall motion changes	61 depressed left ventricular septal regional longitudinal strain					63 normal	—	64 normal
CMR imaging								
T2 weighted and T1 weighted with LGE images	No myocardial oedema or necrosis					No myocardial oedema or necrosis	—	No myocardial oedema or necrosis
Native T1 (ms)	1031 ± 23.7					1060 ± 21.3		997 ± 33.8
Native T2 (ms)	54.1 ± 2.96					49.8 ± 2.61		45.3 ± 2.66
ECV (%)	32.3					26.1		24.2

CMR data are reported as mean ± SD (range); cutoff value for the quantitative parameter of CMR[9]: T1 native > 1000 ms, T2 native > 55.9 ms, and ECV fraction > 28.8%. The normal values at our centre: T1 native = 998 ± 23.9 ms, T2 native = 54.6 ± 8.64 ms, and ECV = 25.4 ± 4%. hsTnT, high sensitivity cardiac troponin T; ECG, electrocardiogram; RBBB, right bundle branch block; LVEF, left ventricular ejection fraction; CMR, cardiac magnetic resonance; LGE, late gadolinium enhancement; ms, milliseconds; ECV, extracellular volume; -, not applicable.

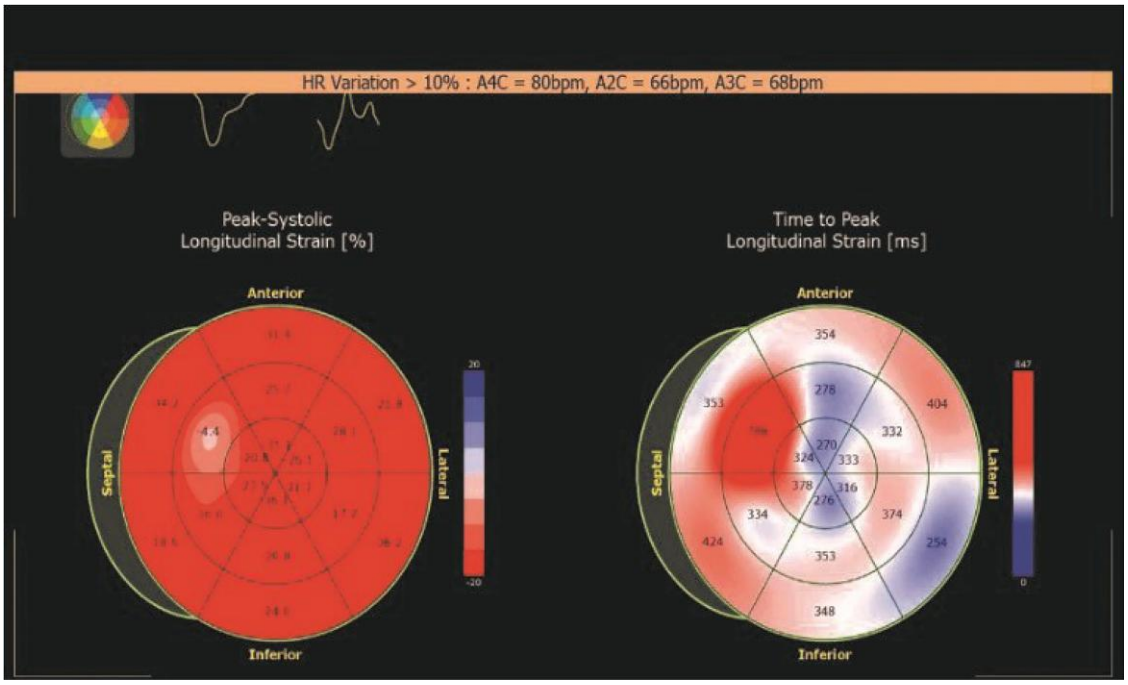


Figure 2 Strain imaging echocardiography: regional longitudinal strain shows mildly depressed left ventricular function at anteroseptal and inferoseptal area.

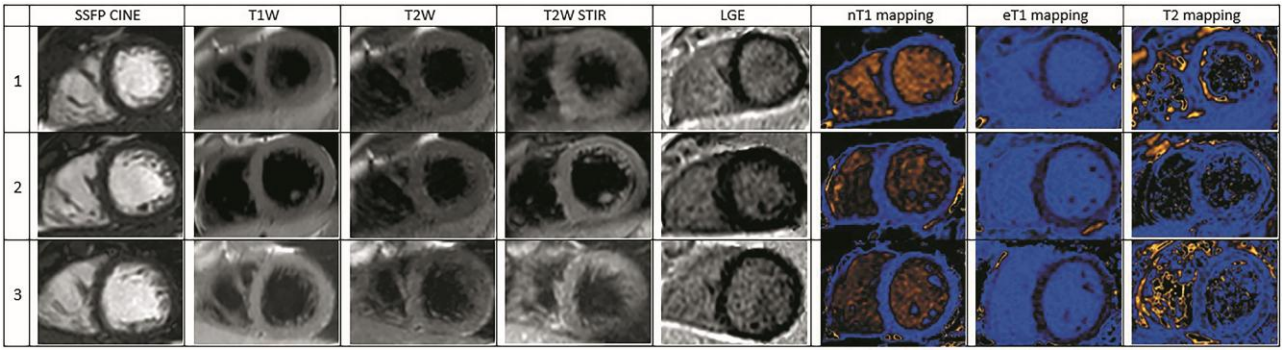


Figure 3 Serial cardiac magnetic resonance (CMR) imaging performed on admission day (1), 2 weeks (2), and 6 months (3). The figure shows steady-state free precession imaging (SSFP CINE), T1-weighted imaging (T1W), T2-weighted imaging (T2W), T2-weighted short-tau inversion recovery imaging (T2W STIR), late gadolinium enhancement imaging (LGE), native T1 mapping (nT1 mapping), enhanced T1 mapping (eT1 mapping), and T2 mapping.

In our study, we skipped CMR at 3 months and chose the 6-month follow-up to reduce unnecessary exposure to contrast and ensured that there was a higher chance that the myocardium would return to normal. In our case report, we recognized that the inflammation of the myocardium can return to normal within 6 months after the onset of the disease.

Unlike the previous studies,[3–7] we found that the myocardial oedema was detected using T1 mapping and ECV without evidence of positive LGE. Thus, myocarditis can be diagnosed based only on T1-based criteria relying on the updated LLC,[10] though with less specificity. Therefore, to confirm the diagnosis, we suggest performing the T1-mapping in cases of suspected myocarditis with negative results of T2-weighted image and LGE.

Based on our results and the recommendation to avoid competitive sports for 3–6 months after myocarditis[13] and multisystem inflammatory syndrome in children (MIS-C),[14] we suggest re-evaluation with

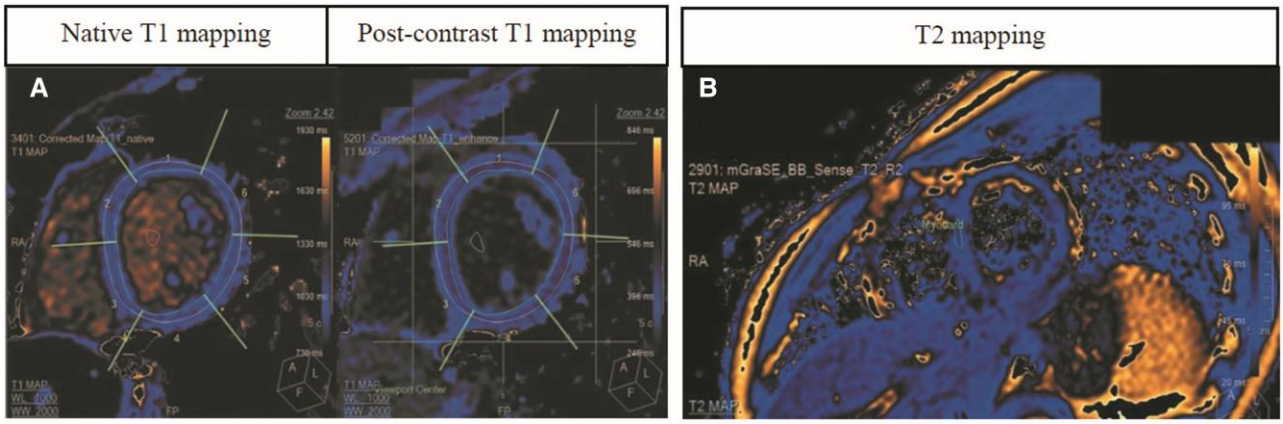


Figure 4 (*A*) Native T1 mapping and postcontrast images showing a region of interest (ROI) draw in the six basal segments with increased T1 native in all segments (1031 ± 23.7 ms) and postcontrast T1 mapping (469 ± 20.3 ms), and (*B*) T2 mapping image with value (54.1 ± 2.96 ms). Data are reported as mean ± SD (range). Cutoff value[9]: T1 native > 1000 ms, T2 native > 55.9 ms. The normal values at our centre: native T1 mapping = 998 ± 23.9 ms, enhanced T1 mapping = 420 ± 9 ms, T2 mapping = 54.6 ± 8.64 ms. ms, milliseconds. Cardiac magnetic resonance (CMR) acquisition protocol included balanced steady-state free precession cine-MR (SSFP cine MR) images. Oedema CMR was performed by black–blood T2-weighted short tau inversion recovery (STIR) and T2 mapping. A dose of 0.2 mmol/kg Gadobutrol (Gd-DO3A-butrol, Gadovist; Bayer Healthcare, Leverkusen, Germany) was injected with a rate of 2.5 mL/s.

ECG, echocardiogram, exercise test, and CMR with the quantitative analysis in those with abnormalities on the baseline before a resumption of sports to confirm that there is no subtle myocardial inflammation.

In terms of a booster vaccine in the patient, the patient's perspective is also concerned about a booster vaccine during follow-up. Our suggestion relies on the current US Centre for Disease Control advice on vaccine boosters in postvaccination myocarditis.[15] Since the patient has no risk of severe acute COVID-19, a booster vaccine should be avoided until additional safety data are available.

Based on the current data, the benefits of vaccination still outweigh the risk. However, our single case represents only mild clinical severity. Therefore, further studies with larger numbers of cases and various severities for long-term follow-up data are required.

Lead author biography

Pakaparn Kittichokechai is a paediatric cardiologist in the Department of Paediatrics, Panyananthaphikkhu Chonprathan Medical Centre, Srinakharinwirot University, Nonthaburi, Thailand—initial date submitted: Oct 05, 2022; date of final disposition set: 11 May 2023; date of revision being submitted: 05 May 2023.

Supplementary material

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

Acknowledgements

The authors would like to acknowledge the paediatricians and emergency physicians at Panyananthaphikkhu Chonprathan Medical Centre for taking care of the patient. We would like to thank Professor Anant Khositseth for the comprehensive language review and editing of this manuscript and Dr. Kitchawan Hengkrawi for the data on COVID-19 mRNA vaccines. The study has been approved by the Committee on Human Rights Related Research Involving Human Subjects, Panyananthaphikkhu Chonprathan Medical Center, Srinakharinwirot University (EC 018/64).

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 has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: There is no source of financial grants and other funding.

Data availability

The data underlying this article are available in the article and in its online supplementary material.

References

1. Oster ME, Shay DK, Su JR, Gee J, Creech CB, Broder KR, *et al.* Myocarditis cases reported after mRNA-based COVID-19 vaccination in the US from December 2020 to August 2021. *JAMA* 2022;**327**:331–340.
2. Bozkurt B, Kamat I, Hotez PJ. Myocarditis with COVID-19 mRNA vaccines. *Circulation* 2021;**144**:471–484.
3. Hadley SM, Prakash A, Baker AL, de Ferranti SD, Newburger JW, Friedman KG, *et al.* Follow-up cardiac magnetic resonance in children with vaccine-associated myocarditis. *Eur J Pediatr* 2022;**181**:2879–2883.
4. Ahmed T, Chishti E, Sinner GJ, Duncan MS, Leung SW, Ramachandran P. A report on short-term follow-up cardiac imaging and clinical outcomes of myocarditis after coronavirus disease 2019 vaccination. *J Cardiovasc Med* 2022;**23**:691–693.

5. Imran AFMA, Park WJ, Sood M. Partially resolving myocardial fibrosis five months following the mRNA COVID-19 vaccine: an MRI based case report. *Int J Clin Cardiol* 2022; **9**:253.
6. Shiyovich A, Plakht Y, Witberg G, Aviv Y, Shafir G, Kornowski R, *et al.* Myocarditis following COVID-19 vaccination. *JACC Cardiovasc Imaging* 2022;**15**:2006–2007.
7. Amir G, Rotstein A, Razon Y, Beyersdorf GB, Barak–Corren Y, Godfrey ME, *et al.* CMR imaging 6 months after myocarditis associated with the BNT162b2 mRNA COVID-19 vaccine. *Pediatr Cardiol* 2022;**43**:1522–1529.
8. US Centers for Disease Control and Prevention. Investigating long-term effects of myocarditis. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myo-outcomes.html. (26 August 2022).
9. Luetkens JA, Homsi R, Sprinkart AM, Doerner J, Dabir D, Kuetting DL, *et al.* Incremental value of quantitative CMR including parametric mapping for the diagnosis of acute myocarditis. *Eur Heart J Cardiovasc Imaging* 2016;**17**:154–161.
10. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, *et al.* Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. *J Am Coll Cardiol* 2018;**72**:3158–3176.
11. Luetkens JA, Faron A, Isaak A, Dabir D, Kuetting D, Feisst A, *et al.* Comparison of original and 2018 Lake Louise criteria for diagnosis of acute myocarditis: results of a validation cohort. *Radiol Cardiothorac Imaging* 2019;**1**:e190010.
12. Segal Y, Shoenfeld Y. Vaccine-induced autoimmunity: the role of molecular mimicry and immune crossreaction. *Cell Mol Immunol* 2018;**15**:586–594.
13. Pelliccia A, Solberg EE, Papadakis M, Adami PE, Biffi A, Caselli S, *et al.* Recommendations for participation in competitive and leisure time sport in athletes with cardiomyopathies, myocarditis, and pericarditis: position statement of the sport cardiology section of the European Association of Preventive Cardiology (EAPC). *Eur Heart J* 2019;**40**:19–33.
14. American Academy of Pediatrics. COVID-19 Interim Guidance: Return to Sports and Physical Activity. https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/covid-19-interim-guidance-return-to-sports/ (18 January 2023).
15. US Centers for Disease Control and prevention. Interim Clinical Considerations for Use of COVID-19 Vaccines. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#myocarditis-pericarditis. (7 November 2022).