Case report of an isolated myocarditis due to COVID-19 infection in a paediatric patient

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Background
Cardiovascular complications of COVID-19 have been reported in the adult population including myocarditis. However, less is known about the myocardial involvement in paediatric patients.

Case summary
A 15-year-old boy was admitted to our intensive cardiac care unit with COVID-19 and an isolated acute myocarditis, confirmed on cardiac magnetic resonance imaging. No pulmonary lesion was observed on the chest CT scan. We report here the initial presentation, medical care, and clinical course of this patient.

Discussion
In the context of the acute COVID-19 outbreak, screening for COVID-19 infection should be performed in children presenting with myocardial injury in an inflammatory context.

Keywords
Case report • Myocarditis • COVID-19 • Children

Introduction
Coronavirus disease-2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The outbreak of COVID-19 appeared in China in December 2019 and, since then, has spread worldwide at a rapid pace and has been declared a global pandemic by the World Health Organization as of 11 March 2020.1

Several cardiovascular complications of COVID-19 have been described in the adult population, and acute myocarditis appears to be relatively frequent.2 Younger patients with COVID-19 infection can present with few or no symptoms or with atypical symptoms.3 On 27 April 2020, the Paediatric Intensive Care Society launched an alert concerning an increased number of reported cases of multisystem inflammatory disease with myocardial injury in children tested positive for COVID-19.4 We report here the initial presentation, medical care, and clinical course of a paediatric patient presenting with an isolated myocarditis due to COVID-19 infection.

Learning points
• Cases of multisystem inflammatory disease with myocardial injury are increasing in children tested positive for COVID-19.
• Acute myocarditis without pulmonary lesion can be observed in COVID-19 children.
• In the context of the acute COVID-19 outbreak, screening for COVID-19 infection should be performed in patients presenting with myocardial injury in an inflammatory context.
Timeline

| Time       | Events                                                                 |
|------------|------------------------------------------------------------------------|
| 7 April    | First symptoms: persistent chest pain with mild fever (38°C)          |
| 10 April   | The patient presented to the emergency department. Despite apyrexia and absence of respiratory signs, a nasopharyngeal swab was performed. |
| 10 April   | Nasopharyngeal swab returned positive for SARS-CoV-2.                  |
| 10 April   | Chest CT scan showed no lung anomalies.                                |
| 10 April   | Blood tests revealed a slight increase in C-reactive protein level (41 mg/L, normal <6 mg/L) with normal leucocytes (6.1 x 10^9/L), and elevated cardiac troponin 6.1 μg/L (99th upper reference limit 0.045 μg/L). |
| 10 April   | Transthoracic echocardiography showed a mild diffuse hypokinesia with left ventricular ejection fraction at 50%, mild pericardial effusion around the lateral wall of the left ventricle (maximum, 5 mm) without signs of tamponade. |
| 10 April   | The patient was admitted to the cardiologic intensive care unit with a diagnosis of suspected myocarditis. |
| 10 April   | CMR showed moderate left ventricle dysfunction with LVEF of 48% and normal right ventricular function. It showed abnormal hyperintensity on T2-weighted image involving the posterolateral wall of the left ventricle, related to acute myocardial oedema. There was also late subepicardial post-gadolinium enhancement in the corresponding area. CMR fulfilled all the Lake Louise criteria and was typical of acute myocarditis |
| 10 April   | Beta-blockers and angiotensin-converting enzyme inhibitors were started. |
| 13 April   | High-sensitivity troponin I peaked at 13.1 μg/L (99th upper reference limit 0.045 μg/L). |
| 15 April   | The haemodynamics of the patient remained stable without indication for inotropic support. Patient was discharged from the hospital. |
| 10 April   | The echocardiography performed at discharge showed a preserved LVEF at 55% with normal cardiac output. |

Case presentation

A 15-year-old boy without cardiovascular risk factors or previous history of cardiovascular disease presented to the emergency department in our institution for persistent chest pain with mild fever (<38°C) for the last 3 days. The patient reported no respiratory tract signs.

The physical examination revealed blood pressure of 100/60 mmHg, heart rate of 75 b.p.m., oxygen saturation of 98% while breathing ambient air, and body temperature of 36.9°C. The electrocardiogram showed diffuse ST elevation without reciprocal changes (Figure 1).

Blood tests revealed a slight increase in C-reactive protein level (41 mg/L, normal <6 mg/L) with normal leucocytes (6.1 x 10^9/L, normal 4–10 x 10^9 cells/L) and elevated cardiac troponin 6.1 μg/L (99th upper reference limit 0.045 μg/L). N-terminal probrain natriuretic peptide (NT-proBNP 65 ng/L, normal <300 ng/L) and D-dimer (259 ng/mL, normal <500 ng/mL) remained normal.

Because of systematic suspicion of COVID-19 in patients with unexplained fever, a PCR was performed on a nasopharyngeal swab and resulted positive for SARS-CoV-2. A multiplex real-time PCR was also performed and resulted negative, allowing the exclusion of viral co-infections. Chest CT scan showed no lung anomalies (Supplementary material online). There were no other family members tested positive for SARS-CoV-2.

Transthoracic echocardiography showed a mild diffuse hypokinesia with left ventricular ejection fraction (LVEF) at 50%, preserved cardiac output, normal right ventricular function, no significant valvular disease, and normal pulmonary pressure without lower venous dilatation. There was a mild pericardial effusion around the lateral wall of the left ventricle (maximum, 5 mm) without signs of tamponade (Supplementary material online).

The patient was admitted to the cardiologic intensive care unit with a diagnosis of suspected myocarditis. Given the echocardiography changes and elevated markers of myocardial injury in a low cardiovascular risk patient, emergent cardiac magnetic resonance (CMR) imaging was performed on the day of admission.

CMR showed moderate left ventricular dysfunction with LVEF of 48% and normal right ventricular function. Tissue characterization based on T2-weighted and late gadolinium enhancement sequences revealed interstitial oedema and myocardial damage involving the subepicardial layer in the posterolateral wall of the left ventricle. First-pass perfusion was normal. There was a mild pericardial effusion with an enhancement of the pericardium adjacent to the posterolateral segment. Diagnosis of acute myocarditis was thus confirmed based on the classic Lake Louise criteria² (Figure 2; Supplementary material online).

According to the reliable CMR findings, typical of acute myocarditis, no subsequent coronary angiography and no endomyocardial biopsy were done.

The haemodynamics of the patient remained stable without indication for inotropic support. He remained afebrile and the biological inflammatory syndrome gradually decreased. No ventricular arrhythmia was observed during his hospitalization. High-sensitivity troponin I peaked at 13.1 μg/L (99th upper reference limit 0.045 μg/L) on day 3. The patient was treated with beta-blockers (bisoprolol 2.5 mg daily) and angiotensin-converting enzyme inhibitors (ramipril 2.5 mg daily).

Due to this favourable clinical course, no specific treatment of COVID-19 was introduced.

The patient was discharged from hospital on day 5 with a CMR scheduled control at 6 months. The echocardiography performed at...
discharge showed a preserved LVEF at 55% with normal cardiac output.

**Discussion**

Herein, we describe a 15-year-old boy without a history of cardiovascular disease admitted to the hospital with COVID-19 and an acute myocarditis. While the spectrum of clinical manifestation is highly related to the inflammation process of the respiratory tract, this case provides evidence of isolated cardiac involvement in a teenager at low cardiovascular risk without respiratory symptoms and a normal chest CT scan. There are several salient points from this case report.

First, although children are less likely than older adults to become severely ill, there are subpopulations of at-risk children including those with an underlying pulmonary pathology or immunocompromising conditions. Nevertheless, no risk factor was found in our patient, including the absence of family history of cardiomyopathies. Recently, an alert was launched concerning an increased number of reported cases of multisystem inflammatory disease with myocardial injury in children tested positive for COVID-19.4

Secondly, infection with viral pathogens, such as influenza and parvovirus B-19, has been widely described as the most common infectious cause of acute myocarditis.6 However, less is known about the cardiac involvement as a complication of SARS-CoV-2 infection. The attributable risk for severe disease from COVID-19 in children is challenging to discern. Previous studies have revealed that children in whom coronaviruses are detected from the respiratory tract can have viral co-infections in up to two-thirds of cases.7 In order to exclude viral co-infections, a multiplex real-time PCR was performed and resulted negative.

Thirdly, determination of the presence of myocardial injury in the COVID-19 population should be performed in all symptomatic patient. Shi et al.8 reported the importance of myocardial injury in COVID-19 mortality in 416 patients hospitalized with COVID-19, of whom 57 died. Approximately 20% of patients had cardiac injury defined as high-sensitivity troponin I greater than the 99% percentile upper reference limit. Unlike our patient, patients with elevated cardiac troponin in that study were older, had more comorbidities, and had higher levels of leucocytes, NT-proBNP, C-reactive protein, and procalcitonin, but lower lymphocyte counts. Patients with cardiac injury had a higher incidence of acute respiratory distress syndrome (ARDS) (58.5% vs. 14.7%; P < 0.001) and a higher mortality rate (51.2% vs. 4.5%; P < 0.001) than those without cardiac injury. In multivariable adjusted models, cardiac injury and ARDS were significantly and independently associated with mortality, with hazard ratios of 4.26 and 7.89, respectively.

Fourthly, patients presenting with myocardial injury may be susceptible to proarrhythmic effects of COVID-19-related issues such as fever, stress, electrolyte disturbances, and use of antiviral drugs. Our patient did not present with any ventricular arrhythmia during his hospitalization. Moreover, immune injury observed in COVID-19 patients may be the main cause of myocardial injury. A study showed that after SARS-CoV infection, interferon-related cytokine storms may be involved in the immunopathology of SARS patients.9 Cytokine storms may lead to increased vascular wall permeability and myocardial oedema.10 However, in view of the patient’s rapid recovery, low increase of C-reactive protein,

Figure 1 Electrocardiogram recorded at admission showed diffuse ST elevation without reciprocal changes.

Isolated COVID-19 myocarditis in a paediatric patient
and the early presentation of the acute myocarditis, myocardial injury was considered to be transient damage from viral infection rather than from the cytokine storm. In addition, the clinical outcome of the patient was favourable, without use of corticosteroids, antiviral drugs, or chloroquine.

Conclusion

We report here the case of a paediatric patient presenting with an isolated acute myocarditis as the sole manifestation of COVID-19 infection and without pulmonary lesion.

In the context of an acute COVID-19 outbreak, screening for COVID-19 infection should be performed in children presenting with myocardial injury in an inflammatory context.

Figure 2 CMR confirming the diagnosis of myocarditis. Black blood T2-weighted with fat saturation image (A) and post-gadolinium SSFP image (B) in short-axis view showed diffuse myocardial signal hyperintensity involving the posterolateral basal wall of the left ventricle, suggesting interstitial oedema. Myocardial damage was confirmed on the late gadolinium enhancement involving the subepicardial layer of the myocardium (C and D). Pericardial enhancement (D) and pericardial effusion were seen around the laterobasal wall of the left ventricle (Supplementary material online, Video S1), suggesting pericardial oedema.

Lead author biography

Dr Quentin Fischer is a 31-year-old interventional cardiologist working in Bichat Hospital, Paris, France.
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 submission and publication of this case report including images and associated text has been obtained from the patient and his parents in line with COPE guidance.

Conflict of interest: none declared.

References

1. World Health Organization. WHO Director-General’s opening remarks at the media briefing on COVID-19. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-mission-briefing-on-covid-19 (12 March 2020).
2. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Bondi-Zoccai G, Brown TS, Der Ngohghossan C, Zidar DA, Haythe J, Brodie D, Beckman JA, Kirtane AJ, Stone GW, Krumholz HM, Parikh SA. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. J Am Coll Cardiol 2020;75:2352–2371.
3. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S. Epidemiology of COVID-19 among children in China. Pediatrics 2020;145.e20200702.
4. Paediatric Intensive Care Society Statement: Increased number of reported cases of novel presentation of multisystem inflammatory disease. https://picsociety.uk/wp-content/uploads/2020/04/PICS-statement-re-novel-KD-C19-presentation-v2-27042020.pdf
5. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, White JA, Abdel-Aty H, Gutberlet M, Prasad S, Aletras A, Lassiy JP, Paterson I, Filipchuk NG, Kumar A, Pauschinger M, Liu P. International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis. Cardiovascular magnetic resonance in myocarditis: a JACC White Paper. J Am Coll Cardiol 2009;53:1475–1487.
6. Fang G, Luo H, Qiu Y, Yang D, McManus B. Myocarditis. Circ Res 2016;118:496–514.
7. Heimdal I, Moe N, Kroksstad S, Christensen A, Skanke LH, Nordba SA, Dallner H. Human coronavirus in hospitalized children with respiratory tract infections: a 9-year population-based study from Norway. J Infect Dis 2019;219:1198–1206.
8. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, Huang H, Yang B, Huang C. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020;doi: 10.1001/jamacardio.2020.0950
9. Huang KJ, Su IJ, Theron M, Wu YC, Lai SK, Liu CC, Lee H-Y. An interferon-gamma-related cytokine storm in SARS patients. J Med Virol 2005;75:185–194.
10. Sawamura A, Okumura T, Ito M, Otsuki M, Ohie N, Amano T, Murohara T; CHANGE PUMP Investigators. Prognostic value of electrocardiography in patients with fulminant myocarditis supported by percutaneous venoarterial extracorporeal membrane oxygenation—analysis from the CHANGE PUMP Study. Circ J 2018;82:2089–2095.