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CASE REPORT
Congenital heart disease

Coronary artery ectasia in a child after arterial switch operation for transposition of the great arteries and suspected multisystem inflammatory syndrome in children associated with COVID-19: a case report

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Background Multisystem inflammatory syndrome in children (MIS-C) with features resembling Kawasaki disease has been reported in association with coronavirus disease 2019 (COVID-19).

Case summary We report the rare case of a 22 months old boy with a history of operated simple transposition of the great arteries (TGA), who developed features of MIS-C likely to be associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection and involving the coronary arteries. Cardiovascular magnetic resonance imaging and cardiac catheterization showed long-distance ectasia of both coronary arteries after their origins and an origin stenosis of the right coronary artery with a perfusion defect. The patient was treated with oral anticoagulation together with antiplatelet therapy and remains under careful monitoring.

Discussion This rare case demonstrates that also patients with TGA after the arterial switch operation (ASO) can develop coronary artery dilatation in association with MIS-C. The most interesting finding in this patient was that the origins of the reimplanted coronary arteries were not dilated. We speculate that scar tissue formation in the area of coronary artery transfer after ASO has prevented proximal coronary artery dilation.

Keywords Case report • COVID-19 • Multisystem inflammatory syndrome in children • Transposition of the great arteries • Coronary vessel anomaly • Cardiac magnetic resonance

Learning points

- Coronary artery dilatation in association with multisystem inflammatory syndrome in children can also affect patients with transferred coronary arteries after the arterial switch operation (ASO).
- We speculate that the origins of the reimplanted coronary arteries after the ASO are not able to dilate due to scar tissue formation and that this poses an additional risk for coronary distortion resulting in myocardial ischaemia and infarction.

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Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a severe pandemic, with more than 1 000 000 deaths worldwide. Compared to adults, children appear to be less affected and develop milder disease.[1] However, cases of multisystem inflammatory syndrome in children (MIS-C) with features resembling Kawasaki disease (KD) have been reported. In these patients, increased incidence of cardiovascular involvement was described, with coronary artery aneurysms being a main complication.[2]

Timeline

3 days of age	Arterial switch operation
19 months of age	Episode of high fever together with a cough
22 months of age	Hospital admission persistent high fever, skin rash, conjunctivitis, red and cracked lips, and inflammation of hands and feet
11 days after symptom onset	Serological assay detected specific severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin G antibodies
18 days after symptom onset	Treatment with intravenous immunoglobulins, acetylsalicylic acid in therapeutic doses and prednisolone were initially administered
26/27 days after symptom onset	Follow-up echocardiography suggested coronary artery dilatation
28 days after symptom onset	Treatment with infliximab
7 and 13 weeks after symptom onset	Discharge in good condition
	Re-admission to paediatric cardiology department for further investigations
	Cardiovascular magnetic resonance (CMR) scan showing coronary ectasia and high suspicion of right coronary artery (RCA) stenosis
	Cardiac catheterization confirming RCA stenosis
	Patient was started on anticoagulation in addition to antiplatelet medication
	Follow-up CMR and brain magnetic resonance imaging
	Further dilatation of the coronary arteries 7 weeks after symptom onset
	Stable coronary artery size 13 weeks after symptom onset

Case presentation

We present a 22-month-old boy with transposition of the great arteries (TGA) who underwent the arterial switch operation (ASO) in our paediatric cardiology department at the age of 3 days with excellent surgical result. Cardiac catheterization performed at the age of 13 months showed normal coronary arteries and good biventricular function.

The patient presented to our partner hospital with persistent high fever in association with skin rash, conjunctivitis, red and cracked lips, and inflammation of hands and feet. An episode of vomiting and diarrhoea was also reported. The patient appeared weary, but no focal neurological deficit was detected. He and his first-degree relatives had an episode of high fever together with a cough three months before admission. A SARS-CoV2 reverse transcription polymerase chain reaction (RT-PCR) assay in nasopharyngeal secretions of the patient at the time of admission showed negative results, whereas a serological assay detected specific SARS-CoV-2 immunoglobulin G (IgG) antibodies. Brain natriuretic peptide and troponin levels were elevated (N-terminal pro-B-type natriuretic peptide: 9450 ng/L, normal range <320 ng/L; troponin T: 6252 ng/L, normal range <14 ng/L).

The overall initial clinical presentation was consistent with the diagnosis of KD. According to the statement from the American Heart Association,[3] intravenous immunoglobulins, acetylsalicylic acid in therapeutic doses and prednisolone were initially administered.

Echocardiography was performed shortly after admission and did not demonstrate coronary artery changes. A follow-up echocardiography performed 11 days after the onset of symptoms showed dilatation of both coronary arteries. Ventricular function was preserved. Due to clinical deterioration and coronary dilatation, the patient was transferred to the intensive care unit and was treated with infliximab and steroids. This was followed by a clinical improvement. The patient was scheduled for further investigations in our paediatric cardiology department.

An electrocardiogram at the time of admission in our department was normal. Detailed assessment of the coronary arteries by echocardiography was difficult (*Figure 1*) and therefore cardiovascular magnetic resonance imaging (MRI) was performed. This showed ectasia of both coronary arteries after its origin (*Figure 2*). The right coronary artery (RCA) had a maximum diameter of 8 × 9 mm but its origin could not be adequately displayed. All branches of the left coronary artery (LCA) were significantly dilated with a maximum diameter of the left anterior descending artery (LAD) of 4 × 7 mm. Perfusion MRI at rest showed a perfusion defect in the RCA territory (*Figure 2*). Stress perfusion was not performed due to safety reasons because rest perfusion already suggested significant ischaemia. Biventricular systolic function was normal (left ventricular ejection fraction 63% and right ventricular ejection fraction 61%). Late enhancement imaging did not demonstrate any myocardial fibrosis (*Figure 2*) and there was no evidence of myocardial inflammation on T2-weighted images.

After multidisciplinary team discussion, the indication for cardiac catheterization was made, considering both, the difficulty to visualize the RCA origin and the perfusion defect. Cardiac catheterization confirmed the likely diagnosis of a proximal RCA stenosis (*Figure 3*).

Anticoagulation therapy with dicoumarol in addition to acetylsalicylic acid was started and a betablocker therapy was initiated. The patient was discharged in stable conditions. In retrospect MIS-C associated with COVID-19 was thought to be the most likely diagnosis for the overall clinical presentation.

Due to the difficulty to assess the coronary arteries on echocardiography, follow-up MRI scans were performed 7 and 13 weeks after disease onset. These investigations demonstrated a further dilatation of the coronary arteries compared to the first cardiac MRI (maximal

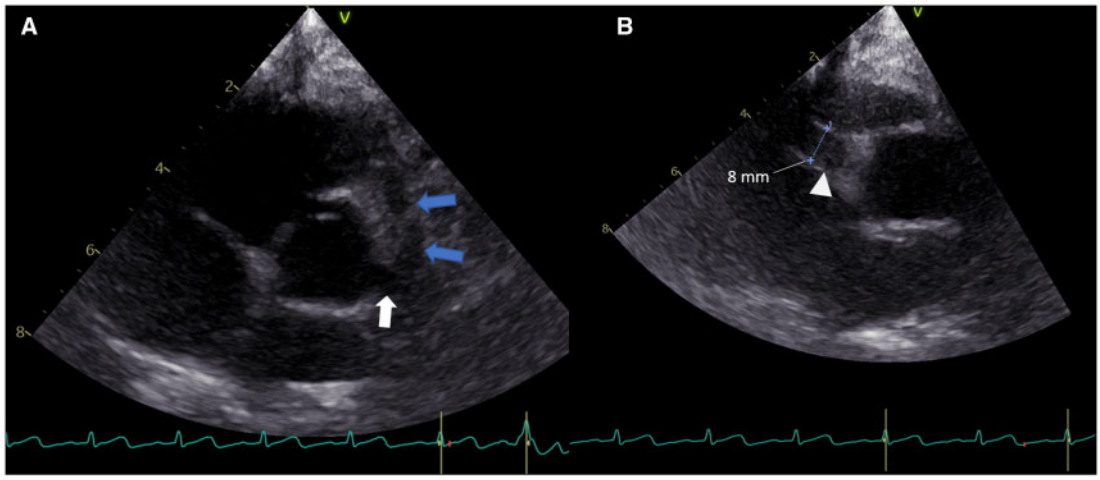

Figure 1 Echocardiogram from the parasternal short-axis view. (*A*) Dilated origin of the left coronary artery (white arrow) and the left anterior descending artery (blue arrows). (*B*) Dilated right coronary artery.

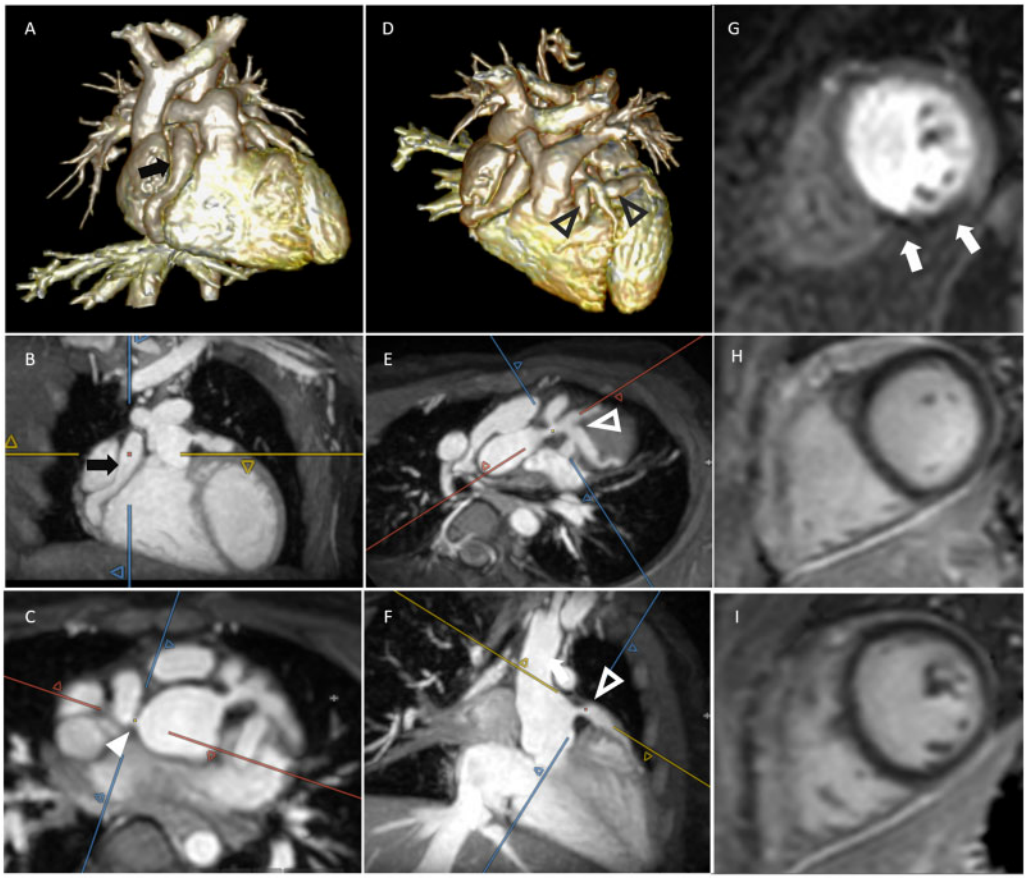

Figure 2 The left panel of electrocardiogram-gated mDixon angiography images (*A–C*) demonstrate the origin and course of the right coronary artery (black arrows). There was high suspicion of an origin stenosis of the right coronary artery due to distortion (navigation crosshair in image *C* and white arrowhead). The middle panel (*D–F*) illustrates the dilated left coronary artery and its branches (open arrowheads). The upper image of the right panel (*G*) shows a first pass perfusion image at rest with a perfusion defect in the right coronary artery territory (white arrows). The lower images of the right panel demonstrate late enhancement images at basal (*H*) and midventricular (*I*) level with no hyperenhancement seen.

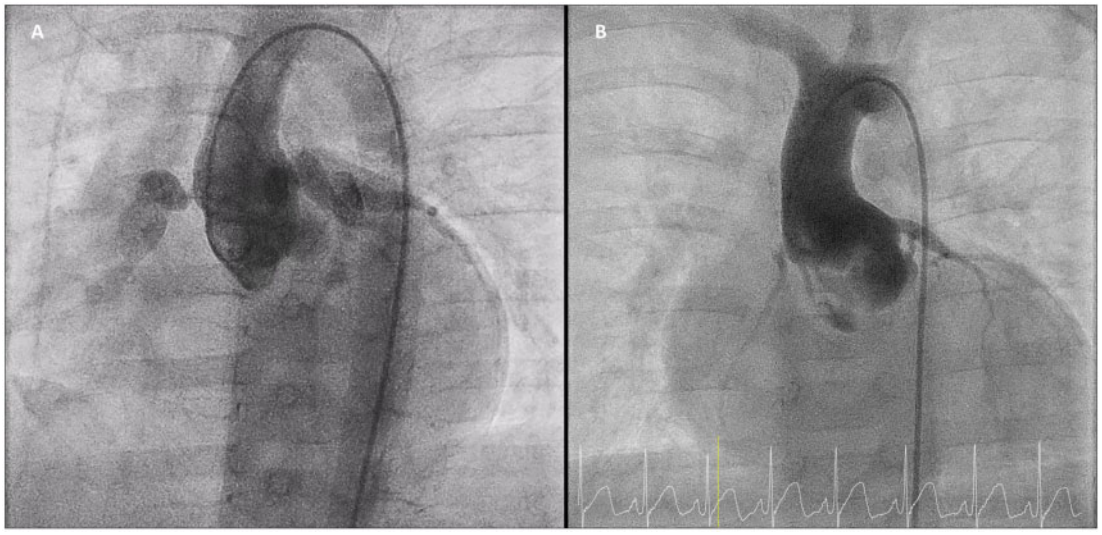

Figure 3 Cardiac catheterization at the time of the current admission (*A*) and 1 year before (*B*).

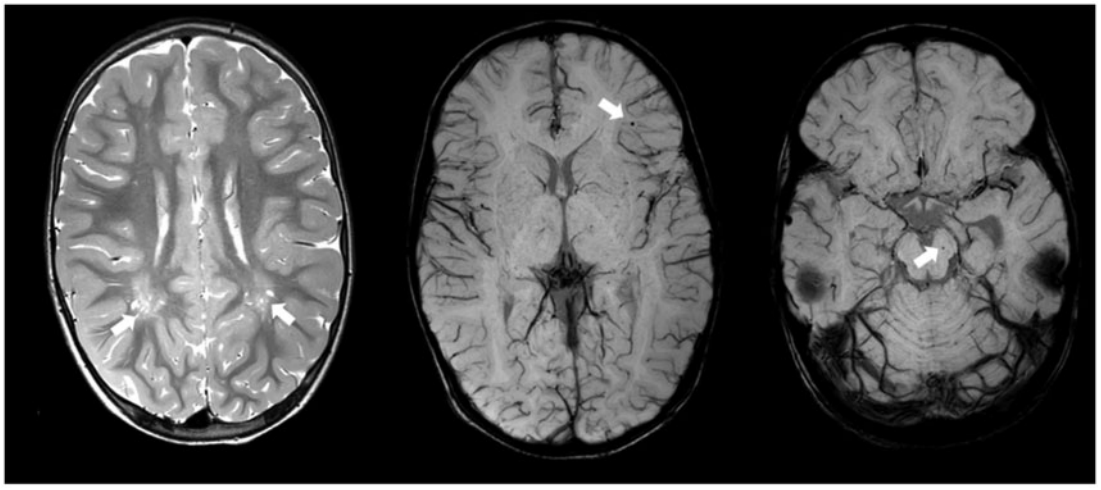

Figure 4 Periventricular leukoencephalopathy and enlarged perivascular spaces on axial T2-weighted images (left, white arrows), as well as microbleeds on susceptibility weighted images (middle and right, white arrows) compatible with residuals after cardiosurgery.

RCA diameter 11 mm and LAD diameter 8 mm) with a stable perfusion defect, preserved biventricular systolic function and no evidence of myocardial fibrosis. No further dilatation of the coronary arteries between the two follow-up MRI scans was seen. Two brain MRIs performed in conjunction with cardiac MRI demonstrated stable mild periventricular leukoencephalopathy, enlarged perivascular spaces and some cerebral microbleeds compatible with residuals from heart surgery with heart–lung machine (*Figure 4*). No acute or recent inflammatory changes were detected.

The follow-up plan includes frequent cardiac examinations every 3 months either in our outpatient department or by a local paediatric cardiologist. Furthermore, the patient continues with long-term thromboprophylaxis as suggested in the AHA Scientific statement[3] including both low-dose aspirin and oral anticoagulation with dicoumarol. In addition, assessment for inducible myocardial ischaemia will be performed every 6–12 months or if the patient has symptoms.[3]

Discussion

The cause of KD is unknown, with the most accepted pathogenetic hypothesis being an aberrant response of the immune system to unidentified pathogens in genetically predisposed subjects.[4] Over the past 20 years, it has been proposed that viruses of the coronavirus

family are involved in the pathogenesis of KD.[5] In a small series from Bergamo, a 30-fold increase in the incidence of KD during the COVID-19 outbreak was reported, with most patients showing a positive antibody test for SARS-CoV-2 and a negative RT-PCR test when presenting with symptoms and signs of KD.[2] Other groups in the UK also reported hospital admissions of children with fever and multisystem inflammation associated with SARS-CoV2.[6] Our patient developed symptoms consistent with a SARS-CoV2 infection three months before the admission with KD. RT-PCR for SARS-CoV2 performed at the time of admission showed negative results, whereas SARS-CoV-2 IgG antibodies were detected.

The delay between onset of KD and an acute SARS-CoV2 infection reported here and in the report from Bergamo suggest a host immune response trigged by the infection with the coronavirus.

Coronary artery dilatation has been reported in up to 24% of patients with SARS-CoV-2 associated MIS-C. Most cases, however, described only mild coronary artery dilation.[7] To our knowledge, this is the first case with suspected MIS-C showing a long-distance ectasia of both coronary arteries in a patient with TGA after ASO. In our patient, MRI provided detailed information on the coronary artery anatomy, myocardial perfusion and myocardial viability and helped to diagnose RCA stenosis which was confirmed by cardiac catheterization. It is of interest, that the RCA stenosis was caused by a distorted and not a dilated RCA origin and that the proximal LCA was also not enlarged. We speculate that scar tissue formation in the area of coronary artery transfer after ASO has prevented proximal coronary artery dilation. Cerebral imaging could not demonstrate any changes previously described in children with COVID-19.[8] Our patient exhibited only mild and unspecific neurological symptoms at the time presentation, and we cannot exclude that imaging signs of an acute SARS-CoV2 infection had already resolved.

Conclusion

In patients presenting with KD during the pandemic, a more severe disease course was described with resistance to intravenous immunoglobulins and need of adjunctive steroids to treat the cytokine storm.[9,10] The same was true for our patient who required intensive care treatment, administration of infliximab and steroids in addition to intravenous immunoglobulins.

Lead author biography

Dr Mohamed Sobh is a fellow in congenital cardiovascular magnetic resonance imaging (MRI) in the Department of Congenital Heart Disease and Paediatric Cardiology at the University Hospital Schleswig-Holstein, Campus Kiel. He has finished the Egyptian Board in paediatrics and paediatric cardiology. Currently, he focuses on clinical cardiovascular MRI imaging as well as on a research MRI project about the right ventricular function in patients with hypoplastic left heart syndrome.

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's next of kin in line with COPE guidance.

Conflict of interest: None declared.

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