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LETTER TO THE EDITOR

Late presentation of multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection, Kawasaki disease, pancarditis, and great vessels arteritis

Presentación tardía de síndrome inflamatorio multisistémico pediátrico asociado a infección por SARS-CoV-2 con enfermedad de Kawasaki, pancarditis, y arteritis de grandes vasos

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To the Editor,

An 8-year-old child presented to the Emergency Department with abdominal pain, fever up to 39°C, conjunctival injection, and vomiting. He had been exposed to COVID-19 5 months before. His physical examination revealed a heart rate of 156 bpm, respiratory rate of 25 rpm, blood pressure 112/50 mmHg, oxygen saturation 94%, temperature 39°C, significant bilateral conjunctival injection, hyperemic pharynx, bilateral cervical lymphadenopathy, palpable liver, and spleen. His initial workup showed lymphopenia (0.6 $10^3/\mu L$), elevated fibrinogen (621 mg/dL), ESR of 30 mm/h, LDH of 437 U/L, CRP of 13.7 mg/dL, procalcitonin of 2.28 ng/mL, D-dimer of 2632 ng/mL, hs-cTnT of 22.5 pg/mL, NT-proBNP of 1291 pg/mL, AST of 182.6 U/L, ALT of 147 U/L, of ALP of 458 U/L, and total bilirubin of 1.78 mg/dL. SARS-CoV-2, Cikungunya, Dengue and Zika antibodies were negative. His ECG showed sinus tachycardia and an incomplete right bundle branch block. The patient was admitted to the pediatric intensive care unit and received inotropic support with an infusion of levosimendan, intravenous boluses of methylprednisolone, immunoglobulin for 3 days, systemic anticoagulation, and antibiotics. The transthoracic echocardiogram showed mildly reduced global left ventricular (LV) systolic function, LV ejection fraction (EF) of 48% with no regional wall motion abnormalities (RWMA), and mild ectasia of the left main coronary artery (LMA) (Fig. 1). A cardiovascular magnetic resonance (CMR) scan (Fig. 2) done 48 h later showed normal-sized cardiac chambers, mild global LV dysfunction with RWMA, moderate global right ventricular (RV) dysfunction with RVEF 37% and RWMA, diastolic "D" shape septum suggestive of RV volume overload with restrictive LV filling pattern, and mild pericardial effusion with a small apical thrombus in the pericardial space. Tissue characterization demonstrated myocardial edema in both ventricles and late gadolinium enhancement (LGE) with a non-ischemic pattern in both ventricles; in the left atrium, mitral, and aortic valves, the pericardium, in the dilated LMA, the aortic root, the ascending and descending aorta. The great vessels also exhibited some degree of wall thickening. CMR was compatible with pancarditis, great vessels, and

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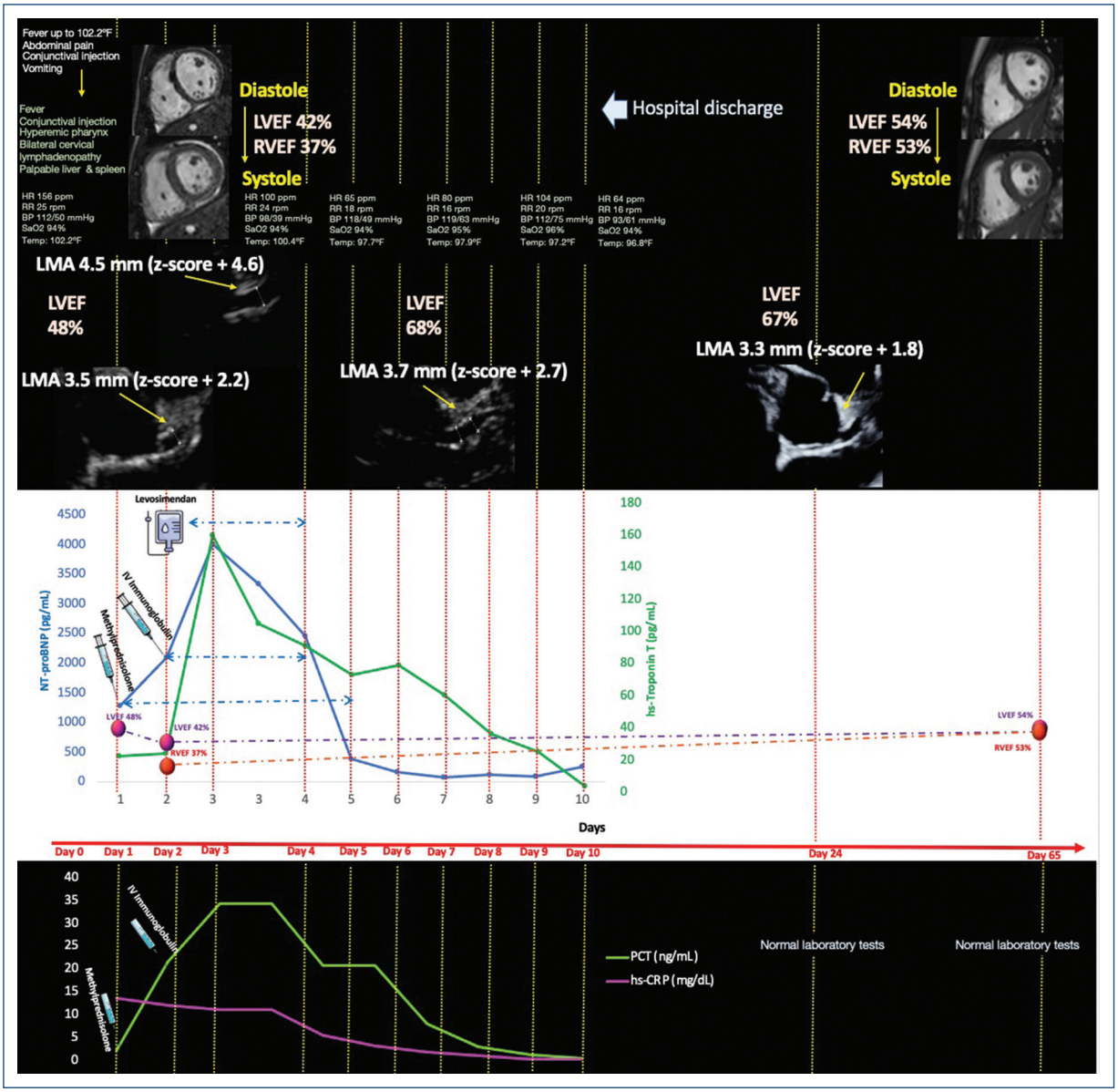

Figure 1. Timeline of the clinical course of the disease and its follow-up. This image represents a timeline of clinical signs and symptoms, vital signs, inflammation, cardiac dysfunction and damage laboratory tests, echocardiographic measurements of LVEF% and left main coronary artery size, and cardiac magnetic resonance measurements of left and right ventricular ejection fraction with the corresponding images of end-diastolic and end-systolic short-axis frames. The moment when the methylprednisolone, IV immunoglobulin, and levosimendan were administered. A red arrow in the middle of the image represents the timeline of the patient's evolution from the development of the first clinical manifestations through day 65 when the control CMR was performed. The days are marked in red next to the arrow, from day 0 to day 10 during his hospitalization until discharge from the hospital, then the days 24 and 65 of follow-up. Across the entire image (in red where the background is white and in yellow where it is black), the thin dashed lines mark and divide the days described in the timeline. According to the timeframe within the dashed lines, all clinical events, laboratory tests, and imaging findings are located in the corresponding moment. IV: intravenous; LVEF%: left ventricular ejection fraction; RVEF%: right ventricular ejection fraction; LMA: left main coronary artery; hs-Troponin T: high-sensitive Troponin T; PCT: procalcitonin; hs-CRP: high-sensitive C-reactive protein; CMR: cardiovascular magnetic resonance.

coronary arteritis. He recovered and was discharged home after 14 days to continue his medical treatment on oral therapy with aspirin and prednisone while remaining in close follow-up, regardless of his return to his city of residence, San Salvador, El Salvador, where a control CMR scan was done 6-weeks later, showing

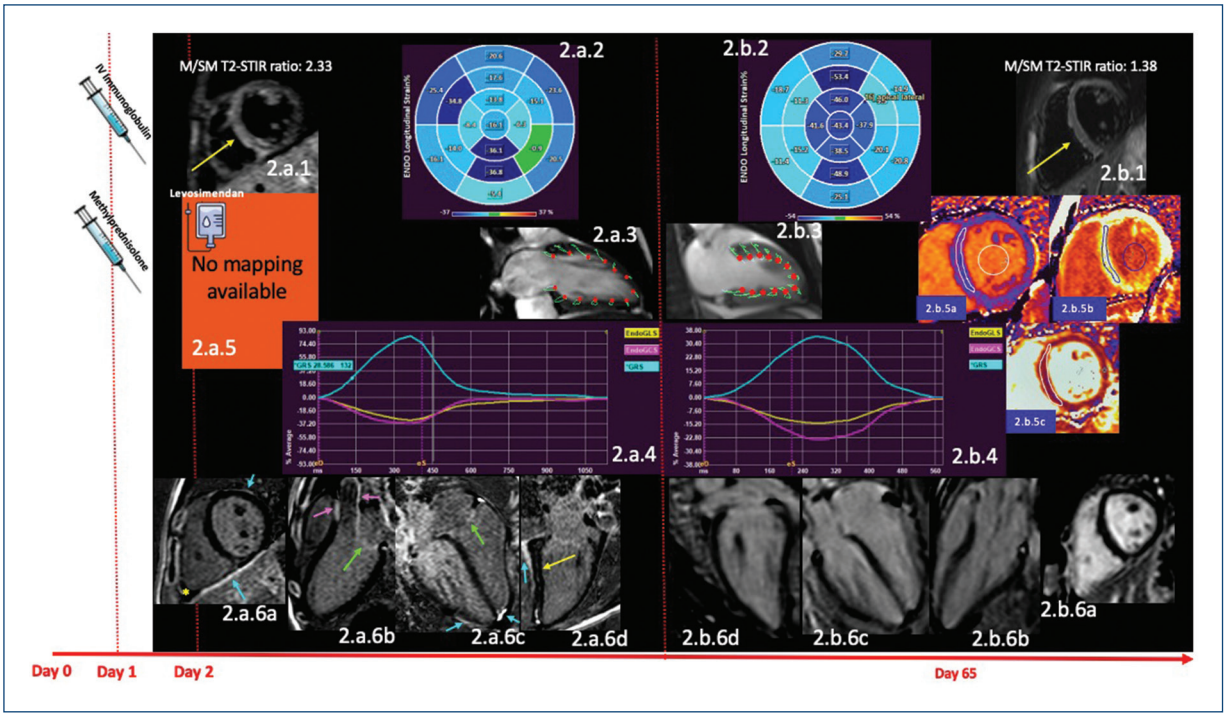

Figure 2. Side-by-side sequences and slice locations comparison of the two CMR studies. Comparison of the first CMR (2.a) study performed on day 1 of hospitalization and the follow-up CMR (2.b). 2.a.1 shows a T2-weighted STIR sequence in short-axis view of the mid ventricle where the yellow arrow highlights the areas of increased signal intensity in the interventricular septum and a myocardium/skeletal muscle ratio of 2.33 corresponding to myocardial edema, that on its corresponding follow-up image (2.b.1) shows normal signal intensity with normal myocardium/skeletal muscle ratio suggesting the absence of myocardial edema. Image 2.a.2, 3, and 4 corresponds to the functional and strain analysis showing the regional wall motion abnormalities and the reduced LV global function with a global strain of 29.20%, which on its corresponding follow-up images (2.b.2,3 and 4) shows a normal LV global function with a global strain of 46.49%. Images 2.a.5. corresponds to the mapping techniques, which were not available for the first CMR study. The corresponding images 2.b.5a, b, and c shows the mapping analysis, figure 2.b.5a shows the native T1 of 1071 msec (normal for the 1.5 Tesla magnet used), figure 2.b.5b shows the post-gadolinium map, the extracellular volume obtained was 26% which is normal, figure 2.b.5c shows the T2 mapping with a native T2 value of 48 msec (normal for the 1.5 Tesla magnet used). At the bottom of the figure, images 2a.6 and 2b.6 show the late gadolinium-enhanced T1-weighted inversion-recovery with phase-sensitive reconstruction algorithm sequences, 2.a.6a is the short-axis view at mid ventricle, 2.a.6b, is the 3-chambers view, 2.a.6c is the 4-chambers view, and the 2.a.6d is the two-chamber view of the first CMR to the left side of the figure, which shows linear intramural and patchy enhancement areas in different locations in the myocardium, as is marked by the yellow arrow in image 2.a.6d, as well as enhancement of the valves (green arrows) and ascending aorta in image 2.a.6b (pink arrows), and the enhancement of the pericardium (blue arrows) with mild pericardial effusion (yellow asterisk). To the right side of figure, the corresponding images and locations of the second study at day 65 of follow-up (images 2.b.6a, 2b.6b, 2.b.6c, and 2.b.6d) that show no myocardial, valvular, aortic, or pericardial enhancement and no pericardial effusion. M/SM: myocardium/skeletal muscle; T2-STIR: t2-weighted with Short Tau Inversion Recovery; LV: left ventricular.

full recovery of the heart and great vessels damage. A timeline that graphically describes all of the above is shown in figure 1. A side-by-side sequences and slice locations comparison of the two CMR studies is shown in figure 2, demonstrating all components of the heart and vessels disease and its full resolution after proper treatment and follow-up period.

Some case series have been published in Europe and the USA[1], showing that cardiac involvement is frequent where 75% of cases present LV dysfunction (LVEF < 50%), 80% require the use of inotropic agents and mechanical ventilation, and all have total recovery at discharge[2]. The authors recommended a CMR study in case of LV dysfunction, persistent elevation of BNP, and/or troponin at 4-6 months[3]. Coronary aneurysms or ectasia are reported in 6-25% of cases, with some cases of giant coronary arteries and progression after discharge[4].

Blondiaux et al.[5] described specific CMR findings of MIS-C, where the main abnormalities were observed in the T1 native value (> 1100 ms), the T2 relaxation time of 50 ms, and the hyperintense signal in the myocardium in T2-STIR-weighted sequences, with the infraspinatus muscle-myocardium ratio > 2.0 suggesting of myocardial edema (findings that are consistent with to those found in our case). Interestingly, the absence of LGE[5] is contrary to our findings since we identified several areas of LGE with non-ischemic patterns suggestive of myocarditis and pericardial enhancement consistent, with inflammatory pericarditis, as shown in figure 2.

Puntman and Cols[6] showed that 78% of patients infected with SARS-CoV-2 had cardiovascular involvement detected by CMR irrespective of the preexisting conditions, the severity, and the overall course of the disease. Furthermore, they found that myocardial inflammation was the most prevalent abnormality with abnormal T1 and T2 values in mapping sequences.

Our case illustrates that physicians should have a high grade of suspicion of the possibility of the presence of MIS-C when a child has a previous history of contact or clinically documented infection with SARS-CoV2, regardless of the time of infection, since a late presentation with a lapse time of even 5 months and different clinical manifestations are possible. These children can have a disastrous course if not correctly studied, diagnosed, treated, and followed. It is crucial to have adequate confirmation of the complete resolution of the cardiovascular involvement to avoid long-term sequelae. CMR plays a key role in the diagnosis, treatment guidance, follow-up, and prognosis of MIS-C and should be done whenever feasible.

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Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

1. Jiang L, Tang K, Levin M, Irfan O, Morris SK, Wilson K, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. Lancet Infect Dis. 2020;20:e276-88.
2. Rowley A. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nat Rev Immunol. 2020;20:453-4.
3. Sperotto F, Friedman KG, Son MB, VanderPluym CJ, Newburger JW, Dionne A. Cardiac manifestations in SARS-CoV-2-associated multisystem inflammatory syndrome in children: a comprehensive review and proposed clinical approach. Eur J Pediatr. 2021;180:307-22.
4. Carter MJ, Shankar-Hari M, Tibby SM. Paediatric inflammatory multisystem syndrome temporally-associated with SARS-CoV-2 infection: an overview. Intensive Care Med. 2021;47:90-3.
5. Blondiaux E, Parisot P, Redheuil A, Tzaroukian L, Levy Y, Sileo C, et al. Cardiac MRI in children with multisystem inflammatory syndrome associated with COVID-19. Radiology. 2020;297:E283-8.
6. Puntman VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from Coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5:1265-73.