Response to: 'Correspondence on 'Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort' by Pouletty *et al* ' by Ventura *et al*

We thank Ventura *et al* for their correspondence[1] on our study on paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (MIS-TS) mimicking Kawasaki disease (KD) (Kawa-COVID-19).[2] They report a 38-year-old woman with a KD-like presentation following SARS-CoV-2 infection and highlight the need for physicians to be aware of this syndrome also in adults. We fully agree that, despite being initially described and more frequent in children, a similar presentation may occur following SARS-CoV-2 infection in adults.[3] To assess similarities and differences between paediatric and adult cases, we collected data of nine adult cases of Kawa-COVID-19 in three hospitals of the Great Paris region (six were previously reported in another case series[3]) and compared them with our paediatric Kawa-COVID-19 cohort.[2] The main characteristics of adult and paediatric patients are described in table 1.

Median (range) age of the adults was 25 (19–33) years and 55% were male. None of the adults had criteria for complete KD while 10/16 children had complete KD criteria. Adults and children shared similar characteristics including fever, gastrointestinal and neurological signs, hyponatremia, hypoalbuminaemia, lymphopaenia and biological inflammatory syndrome. Of note, differences in the presentation between adult and paediatric Kawa-COVID-19 were also observed. Respiratory features were reported in the majority of adults. Mucocutaneous manifestations were less frequent, while myocarditis, acute kidney injury and vasoplegic shock were more common in adult MIS-TS. Adults seemed in a more severe condition: six (66%) of them required intensive care unit admission, three (33%) were placed on mechanical ventilation and six (66%) required vasopressor therapy. Inflammation parameters were also more elevated in adults with significantly higher ferritin level (2124 (833–6205) g/L) and C reactive protein (CRP) (363 (278–439) mg/L). Regarding specific treatments, children received more frequently a second intravenous immunoglobulin (Ig) infusion than adults (p=0.057). All patients were in remission 3[3 4] days after treatment initiation. No patient died.

The different descriptions of this new entity (ie, multisystem inflammatory syndrome in children in the USA,[4] paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 in the UK[5] and Kawasaki-like disease or Kawa-COVID-19) reflect the uncertainty about the pathophysiology and specificities associated with SARS-CoV-2. The temporal link observed between the occurrence of COVID-19 and MIS-TS, together with positive SARS-CoV-2 serology results strongly suggest a postinfectious mechanism, which seems to occur later in age and to include more frequently myocarditis, gastrointestinal signs and inflammatory syndrome than classical KD.

In MIS-TS, the adult presentation is very similar to children, except for frequent respiratory features and uncommon mucocutaneous symptoms, without complete KD criteria. These dissimilarities should not prevent physicians to consider MIS-TS in adult patients, especially because the main difference between children and adults seems to be a higher severity of the adults' condition, with consistent myocarditis, and a higher prevalence of acute kidney injury and circulatory failure. The adult cohort seems to present higher severe prognostic factors that we identified in our initial study, with respectively higher ferritin levels (median above 1400 µg/L) and older age. Moreover, median CRP levels were higher in adults (363 mg/L) compared with children (207 mg/L): the threshold of 300 mg/mL was reported as a feature of severity by a British Delphi study.[6]

Table 1 Comparison between paediatric Kawa-COVID-19 cohort and adult Kawa-COVID cohort

Clinical and biological results	Adult Kawa-COVID (N=9)	Paediatric Kawa-COVID-19 cohort (N=16)	P value
Median age (IQR)	25 (19–33)	10 (4.7–12.5)	
Male gender	5 (55%)	8 (50%)	1.0
Comorbidities; n (%)	4	6 (37%)	1.0
Overweight	4	4	0.63
Clinical features: n (%)			
Fever	9 (100%)	16 (100%)	1.0
Skin rash	1 (11%)	13 (81%)	0.035
Hands and feet erythema/ oedema	2 (22%)	11 (68%)	0.14
Conjunctivitis	4 (44%)	15 (94%)	0.062
Dry cracked lips	1 (9%)	14 (87%)	0.024
Cervical lymphadenopathy	3 (33%)	6 (37%)	0.84
Gastrointestinal signs	8 (88%)	13 (81%)	1.0
Neurological signs	6 (66%)	9 (56%)	0.69
Respiratory symptoms	8 (88%)	2 (12%)	0.0003
KDSS	4 (44%)	7 (14%)	0.67
Complete Kawasaki disease: n (%)	0	10 (71%)	<0.0001
Biological results: median (IQR)			
CRP (mg/L)	363 (278–439)	207 (162–236)	0.0004
Platelets (g/L)	240 (128–243)	188 (164–244)	0.64
Lymphocytes (g/L)	0.6 (0.33–0.87)	1.15 (0.8–1.7)	0.023
Natremia (mmol/L)	132 (129–134)	130 (127–134)	0.91
Creatinine (µmol/L)	140 (83–439)	59 (44–124)	*
Albumin (g/L)	24 (20–25)	21 (19–23)	0.29
SGOT (UI/L)	120 (75–166)	48 (33–86)	0.012
SGPT (UI/L)	103 (69–139)	35 (33–86)	0.042
Ferritinaemia (g/L)	2124 (833–6205)	1067 (272–1709)	0.049
Troponin (ng/L)	1164 (765–2666)	58 (36–165)	0.006
BNP (pg/ml)	24 540 (2585–35 000)	4319 (2747–6493)	0.17
Echocardiography abnormalities: n (%)	9 (100%)	11 (69%)	
Myocarditis	9 (100%)	7 (44%)	0.008
Coronary dilations	1 (11%)	3 (19%)	0.63
Pericarditis	1 (11%)	4 (25%)	0.32
Treatment: n (%)			
Intravenous Ig	6 (66%)	15 (93%)	0.12
Single infusion	6 (66%)	9 (56%)	0.69
Second infusion	0	6 (37%)	0.057
Steroids	3 (33%)	3 (18%)	0.63
No anti-inflammatory treatment	3 (33%)	1 (6%)	0.12

*No statistical analysis was possible due to different standards between children and adults.

BNP, brain natriuretic peptide; CRP, C reactive protein; Ig, immunoglobulin; KDSS, Kawasaki disease shock syndrome; SGOT, Serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase.

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This discrepancy might be explained by a recruitment bias of our adult cases, but also by under-recognition of mild forms in adults, which may be confounded with ongoing SARS-CoV-2 infection. Moreover, this could lead to delayed diagnosis, and therefore delayed treatment. This latency might partially explain an increased severity in adults. Given the potential life-threatening injury and the current active pandemic of SARS-CoV-2, clinicians should be alert and look for signs of MIS-TS, including myocarditis features in adults. Diagnosing these forms as early as possible may optimise clinical management and outcome. Ig infusions and corticosteroids with proven benefits in KD[7] may have a potential effect in this novel entity. Further studies are warranted to determine the risk factors associated with MIS-TS, its relevant pathogenesis, the benefit of IVIg and/or corticosteroids, and long-term outcome.

Juliette Chommeloux,[1] Marie Pouletty,[2] Naim Ouldali,[2,3] Mathieu Kerneis,[4] Alexis Mathian,[5] Raphaele Mestiri,[6] Julien Rohmer,[7] Guillaume Hekimian,[1] Isabelle Melki ,[2,8] Great Paris Region (GPR) Kawa-COVID-19 consortium

[1]Sorbonne Université, Institut de Cardiométabolisme et Nutrition (ICAN), Service de Médecine Intensive Réanimation, Hôpital Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France
[2]General Paediatrics, Infectious Disease and Internal Medicine Department, Reference Center for Rheumatic, AutoImmune and Systemic Diseases in Children (RAISE), Hôpital Robert Debre, AP-HP, Paris, France
[3]UMR 1123, ECEVE, INSERM, Paris, France
[4]Sorbonne Université, ACTION Study Group, INSERM UMRS1166, ICAN—Institute of CardioMetabolism and Nutrition, Institut de Cardiologie, Hôpital Pitié-Salpêtrière (AP-HP), Paris, France
[5]Sorbonne Université, Assistance Publique–Hôpitaux de Paris, Groupement Hospitalier Pitié–Salpêtrière, French National Referral Center for Systemic Lupus Erythematosus, Antiphospholipid Antibody Syndrome and Other Autoimmune Disorders, Service de Médecine Interne 2, Institut E3M, Inserm UMRS, Centre d'Immunologie et des Maladies Infectieuses (CIMI-Paris), Paris, France
[6]Internal Medicine Service, Bégin Military Teaching Hospital, Saint-Mandé, France 7 Service de Médecine Interne, Hôpital Foch, Suresnes, France
[7]Service de Médecine Interne, Hôpital Foch, Suresnes, France
[8]Laboratory of Neurogenetics and Neuroinflammation, Imagine Institute, Paris, France

Correspondence to Dr Isabelle Melki,

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Collaborators Great Paris Region (GPR) Kawa-COVID-19 consortium: Charlotte Borocco, MD, Marion Caseris MD, Romain Basmaci MD, PhD, Noémie Lachaume MD, Philippe Bensaid MD, Samia Pichard MD, Hanane Kouider MD, Guillaume Morelle MD, Irina Craiu MD, Corinne Pondarre MD, PhD, Arielle Maroni MD, Mehdi Oualha MD, PhD, Zahir Amoura MD, MSc, Julien Haroche MD, PhD, Fanny Bajolle MD, PhD, Stéphane Bonacorsi MD, PhD, Guislaine Carcelain MD, PhD, Isabelle Kone-Paut MD, Karim Aacha MD, Brigitte Bader-Meunier MD, Albert Faye, MD, PhD, Ulrich Meinzer, MD, PhD, Caroline Galeotti MD, PhD Johanna Lokmer, MD, Cherine Benzouid, MD, Constance Beyler, MD, Anna Deho, MD, Glory Dingulu, MD, Laurent Gilardin, MD, Clément Dubost, MD.

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ORCID iD
Isabelle Melki http://orcid.org/0000-0002-8057-333X

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