Exploration of Cardiology

Open Exploration

Open Access Case Report

Anakinra for resistant Kawasaki disease in an infant: case report and literature review

Andriana Anagnostopoulou[1*], Nikolaos Andreou[1], Elena Tsitsami[2], Maria Tsinti[2], Nikolaos G Eleftherakis[1]

[1]Pediatric Cardiology Department, Agia Sophia Children's Hospital, GR11526 Athens, Greece
[2]First Department of Pediatrics, National and Kapodistrian University of Athens, GR11526 Athens, Greece

***Correspondence:** Andriana Anagnostopoulou, Pediatric Cardiology Department, Agia Sophia Children's Hospital, Thivon and Livadias, GR11526 Athens, Greece. Andrianouska@gmail.com
Academic Editor: Geu-Ru Hong, Yonsei University College of Medicine, Korea
Received: May 18, 2025 **Accepted:** September 3, 2025 **Published:** September 22, 2025

Cite this article: Anagnostopoulou A, Andreou N, Tsitsami E, Tsinti M, Eleftherakis NG. Anakinra for resistant Kawasaki disease in an infant: case report and literature review. Explor Cardiol. 2025;3:101271. https://doi.org/10.37349/ec.2025.101271

Abstract

Resistant Kawasaki has been associated with the aggressive development of large coronary aneurysms, despite prompt treatment. In this paper, we present an infant who presented with resistant Kawasaki. Although initially he seemed to defervesce after the initial administration of intravenous immunoglobulin, he developed a new onset of fever, requiring a repeat dose of immunoglobulin. Coronary aneurysms developed rapidly, necessitating a second dose of immunoglobulins and second-line treatments such as anakinra and infliximab. High titers of COVID-19 antibodies have been a confounding factor in the management of that child, as the alternative diagnosis of multisystem inflammatory syndrome in children (MIS-C) was considered. Finally, the clinical and laboratory values were more in keeping with MIS-C.

Keywords

Kawasaki, COVID-19, coronary arteries, anakinra, case report

Introduction

Kawasaki disease is the most common childhood vasculitis affecting the medium-sized arteries. The estimated incidence is 25 per 100,000 in North America [1]. Intravenous immunoglobulin (IVIG) and aspirin remain the mainstay of treatment, as prompt administration has decreased the incidence of the development of coronary artery aneurysms [1, 2]. However, patients unresponsive to IVIG are at higher risk of developing coronary artery aneurysms.

The second-line treatment for these patients has been studied, yet the optimal treatment has not been determined. Here, we describe a young infant with acute Kawasaki who developed large coronary aneurysms despite initial defervescence after treatment [3].

Case report

A two-month-old male infant presented to the local hospital with a two-day history of pyrexia up to 40°C, a concurrent mild diarrheal illness, and slightly decreased feeding. He had received the first dose of the routine childhood immunization of the hexavalent vaccine twenty-four hours prior to the symptoms. There was no history of viral infection.

He was born at 37 + 2 weeks of gestation with an elective cesarean secondary to a previous cesarean with a birth weight of 2,820 g. He is the third child of non-consanguineal healthy parents. Prior to the admission, he had been gaining weight appropriately.

His present weight was 5,200 g, height 54 cm, and head circumference 40 cm.

On examination, he was pyrexial with a fever of 38°C. On inspection, he had a blanching maculopapular rash, with a heart rate of 100 bpm, and blood pressure of 100/57 mmHg. The chest was clear with normal vesicular sounds, and the heart sounds were normal. The femoral arteries were palpable.

A few hours after admission, he had a new onset of pyrexia up to 39.5°C and a pulsating fontanelle. A lumbar puncture was undertaken, showing leucocytes 10/µL, RBC 4,800/µL, glucose 87 mg/dL, protein 50.6 mg/dL, negative culture, and antibiotic treatment was commenced with cefotaxime.

An extended nasopharyngeal viral panel, including SARS-CoV-2, was negative. More, cerebrospinal fluid PCR was negative for extended viral panel as well as bacterial *Neisseria meningitides*, *Streptococcus pneumonia*, *Hemophilus influenzae* type b, and *Listeria monocytogenes*.

However, two days later, four days after the onset of the fever, the patient developed strawberry tongue, cheilitis, and widespread maculopapular blanching rash over the limbs and torso. An initial echocardiogram was normal, but an abdominal echo showed edema surrounding the gallbladder. A diagnosis of incomplete Kawasaki was made. The patient was treated with IVIG 2 g/kg and high-dose aspirin 80 mg/kg/day. The fever subsided after 72 hours; however, he did develop peripheral and scrotal edema, which resolved.

Despite being afebrile, two days after the initial fever resolution, on the ninth day of illness, a new onset of fever was noted up to 38.2°C, so oral prednisolone was commenced at a dose of 2 mg/kg/day. Subsequently, desquamation of the fingers was noted.

On the 11th day of admission, 13 days after the initial pyrexia, a new echocardiogram showed dilation of the left coronary artery (LCA) with a 2.3 mm diameter (previously 1.7 mm), z score 2.9, and the left anterior descending (LAD) branch had a diameter of 2.2 mm with a z score of 3.87. The right coronary artery (RCA) measured 2.1 mm (previously 1.7 mm) with a z score of 2.9 (Dallaire and Dahdah, JASE 2011 [4]). The next day, as he continued to be pyrexial with a fever up to 37.7°C, he was transferred to our hospital (Table 1).

Table 1. Timeline.

Timeline	Intervention
Seventy-two hours before admission	1st dose of the hexavalent routine immunization
Day 1: 48 hours before admission	Pyrexia up to 40°C
Day 3: admission, pyrexia, bulging fontanelle, diffuse maculopapular rash	Lumbar puncture, cefotaxime 200 mg/kg/day for 7 days total
Day 4: rash, diagnosis of “incomplete” Kawasaki	IVIG 2 g/kg
Day 5: pyrexial	Aspirin 80 mg/kg/day, also gentamycin 7.5 mg/kg/day and omeprazole 2 mg/kg/day
Day 7: peripheral oedema, scrotal swelling	-
Day 9: relapse pyrexia 38.2°C	Prednisolone po 2 mg/kg/day
Day 10: fever subsided	Change antibiotics to ampicillin-clavulanate
Day 11: desquamation of the fingers	-
Day 13: cardiac echocardiography	Generalized dilation of the coronary arteries. LCA 2.3 mm, z score 2.9; LAD 2.2 mm, z score 3.87

Table 1. Timeline. (*continued*)

Timeline	Intervention
Day 14: new onset of pyrexia 37.7°C	Transferred to our centre. Aneurysm LCA 2.6 mm, LAD 3.4 mm, RCA 3.1 mm
Day 15	Second dose IVIG 2 g/kg, methylprednisolone 2 mg/kg, anakinra 8 mg/kg, infliximab 25 stat
Day 17: apyrexial	Commenced SC tinzaparin 1,000 IU × 1
Day 19	Decrease methylprednisolone 1.5 mg/kg, SC anakinra 4 mg/kg

IVIG: intravenous immunoglobulin; LAD: left anterior descending; LCA: left coronary artery; po: per os; RCA: right coronary artery; SC: subcutaneous; -: no data.

At our hospital, a new echocardiogram was performed. It showed good systolic function of the left ventricle, mitral and tricuspid regurgitation, and a small aneurysm of LCA 2.6 mm (z score 3.86), a medium aneurysm of the LAD 3.4 mm (z score 6.41), and RCA 3.1 mm (z score 6.94) (Figure 1A and 1B). Subsequently, a second dose of immunoglobulin was given. The oral prednisolone was changed to intravenous methylprednisolone, followed by a single dose of infliximab. More, anakinra was added 8 mg/kg as it was felt that an intensification of therapy was warranted due to the rapid appearance of medium-sized aneurysms, the persistence of a high white cell count and platelets, and high inflammatory markers. However, the coagulation screening was normal. Regarding the cardiac markers, the troponin was borderline raised (15.9 pg/mL, normal < 14 pg/mL), and the NT proBNP was raised to 220 pg/mL. Finally, the patient's young age < 6 months placed him in a higher risk category (Table 2). As per American Heart Association (AHA) guidelines, the patient was also given tinzaparin and anakinra, continued at a reduced dose of 4 mg/kg/day.

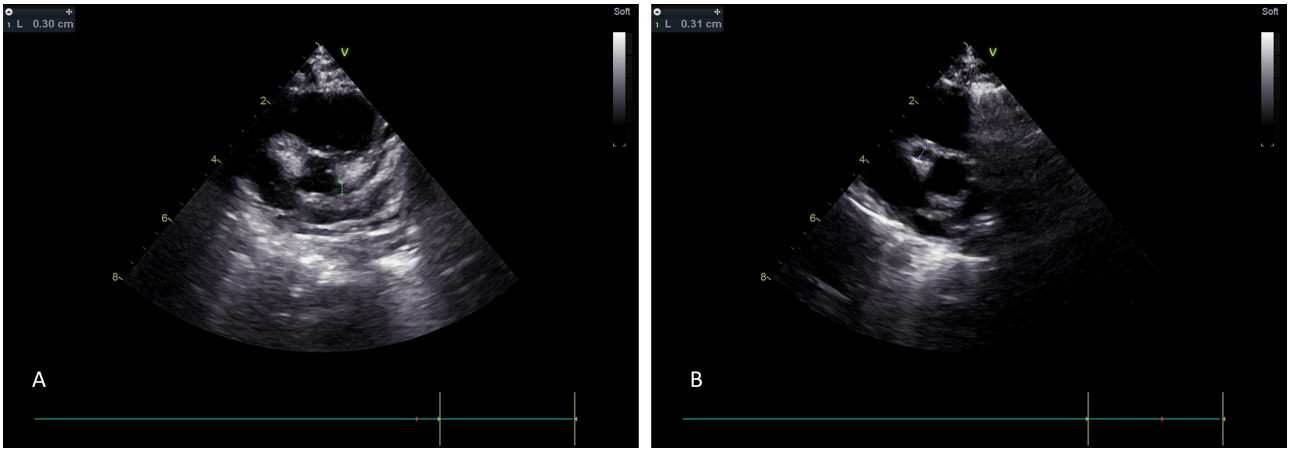

Figure 1. Echocardiogram on day 14. (**A**) Dilation of the left coronary artery and the left anterior descending branch. (**B**) Dilation of the right coronary artery.

Table 2. Laboratory results.

Laboratory parameters	Day of admission							
	14/7/2023	16/7/2023	20/7/2023	26/7/2023	31/7/2023	2/8/2023	8/8/2023	11/8/2023
White cell count (× 10^3/μL)	8,500	24,900	21,100	24,760	29,940	19,360	17,270	24,900
Polymorphs (%)	33.0	50.0	51.0	-	41.0	-	27.5	44.0
Lymphocytes (%)	28.0	34.0	26.0	52.0	43.8	-	49.8	41.0
Monocytes (%)	9.0	6.0	10.0	13.0	8.2	14.0	13.9	12.0
Eosinophils (%)	0.0	-	6.0	3.0	1.3	1.0	3.2	3.0
RABDO (%)	30	10	5	-	-	-	-	-
Hemoglobin (g/dL)	9.5	8.9	7.9	7.8	8.6	8.6	9.9	8.4
Hematocrit (%)	27.9	25.3	22.7	25.0	28.6	28.2	31.2	31.4
Mean corpuscular volume (fL)	87.7	86.0	86.5	86.1	85.9	88.6	83.5	82.6

Table 2. Laboratory results. (*continued*)

Laboratory parameters	Day of admission							
	14/7/2023	16/7/2023	20/7/2023	26/7/2023	31/7/2023	2/8/2023	8/8/2023	11/8/2023
Mean corpuscular hemoglobin (pg)	29.7	30.2	30.0	27.0	26.2	27.1	26.5	22.1
RDW (%)	12.9	13.6	14.6	-	-	-	-	-
Platelets (× 10^3/μL)	505,000	386,000	583,000	693,000	850,000	888,000	891,000	900,000
ESR (mm/h)	-	-	-	-	75	101	55	18
CRP (mg/dL)	32.00	31.70	24.60	70.60	10.70	7.57	-	28.30
Glucose (mg/dL)	163	81	85	82	102	101	110	115
Urea (mg/dL)	17	17	7	18	14	39	22	20
Creatinine (mg/dL)	0.26	-	0.22	0.23	0.23	0.25	0.25	0.27
Potassium (mmol/L)	4.4	3.8	4.7	4.9	5.6	4.8	5.3	5.0
Sodium (mmol/L)	134	134	139	136	135	134	-	135
Chloride (mmol/L)	-	104	102	100	99	98	97	100
Calcium (mmol/L)	-	-	-	9.4	10.6	10.6	10.8	10.1
SGOT (IU/L)	43	22	26	81	52	39	37	34
SGPT (IU/L)	25	14	9	52	51	35	42	30
GGT (IU/L)	-	-	-	63	140	115	88	74
Total bilirubin (mg/dL)	-	-	-	0.27	-	-	0.16	0.15
DBILI (mg/dL)	-	-	-	0.13	-	-	0.09	0.09
Fibrinogen (mg/dL)	-	-	-	-	-	-	300	332
NT proBNP (pg/mL)	-	-	-	-	-	220	-	-

CRP: C-reactive protein; DBILI: direct bilirubin; ESR: erythrocyte sedimentation rate; GGT: gamma-glutamyl transferase; RABDO: rhabdomyolysis; RDW: red cell distribution width; SGOT: serum glutamate oxaloacetate transaminase; SGPT: serum glutamate pyruvate transaminase; -: no data.

The antibodies for SARS-CoV-2 IgG2 taken on day 17 were positive at 23,847.2 AU/mL (negative < 50 AU/mL).

On day 23, a repeat echocardiogram showed mild mitral and tricuspid regurgitation, LCA 2.6 mm (z score 3.86), LAD ectasia, measuring 3.9 mm (z score 9.66), and RCA with dilation of the proximal part of 4 mm (z score 8.94). The distal part was 2.9 mm (z score 4) (Figure 2).

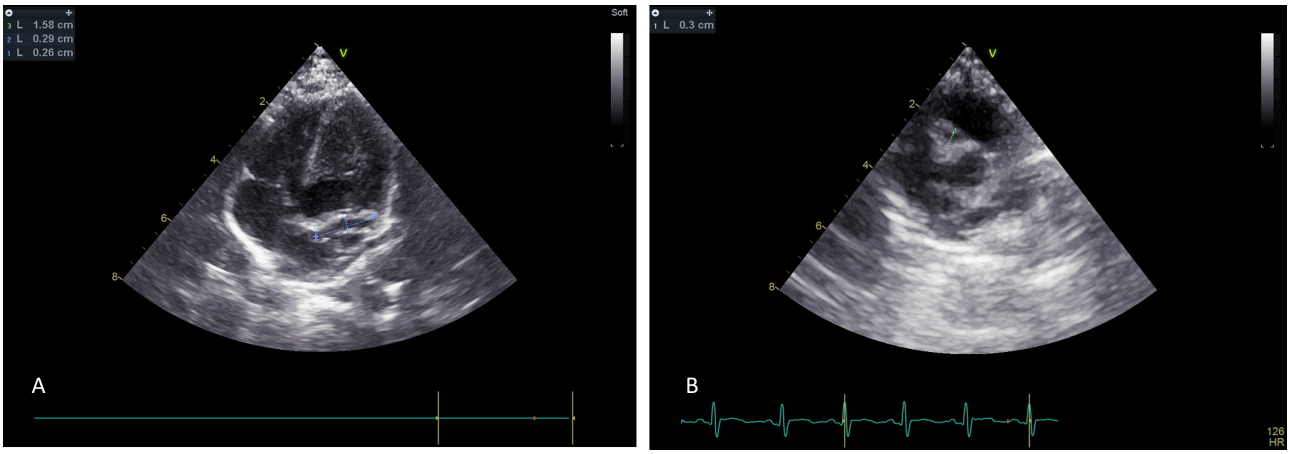

Figure 2. Echocardiogram on day 23. (**A**) Dilation of the left coronary artery and left anterior descending branch. (**B**) Remaining right coronary artery dilation.

He continued to be stable until discharge and follow-up.

One year later, the repeat echocardiogram showed improvement of the aneurysms with the LCA measuring 1.72 mm (z score 1.07) and the RCA measuring 1 mm (z score 0.53) (Figure 3).

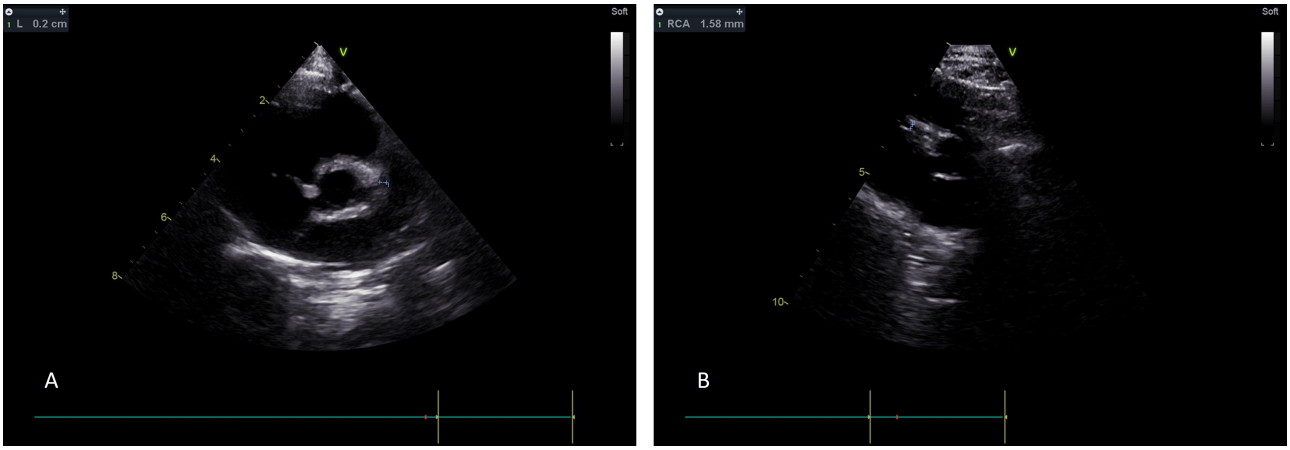

Figure 3. Echocardiogram one year later showing full resolution of the aneurysms. (**A**) The LCA aneurysm has fully resolved. (**B**) Similarly, the RCA now has a normal diameter. LCA: left coronary artery; RCA: right coronary artery.

Discussion

Kawasaki disease and multisystem inflammatory syndrome in children (MIS-C) appear to share some of the host immunological responses to a viral infection and subsequently clinical patterns. However, they also diverge in epidemiology, clinical presentation, and laboratory characteristics [5, 6].

Initial observations mentioned the decreased incidence of thrombocytosis in MIS-C [7, 8]. MIS-C patients typically have lower lymphocyte, platelet, and albumin levels but higher C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, D-dimers, and cardiac markers than patients with Kawasaki disease [9].

Moreover, there are differences in epidemiology and clinical presentation of these two conditions. Both conditions have a predilection for boys. Kawasaki disease is more prevalent in Asians, whereas MIS-C is more frequent in Hispanic/African children [10].

Although both conditions may result in coronary aneurysms, they are more frequent in Kawasaki disease than in MIS-C. On the contrary, cardiac dysfunction such as ventricular dilation and need for vasopressors and intensive care admission are more likely to be associated with MIS-C. That is confirmed in laboratory indices such as high levels of NT proBNP and troponin levels [9, 10]. Moreover, multiorgan dysfunction is more likely in MIS-C. Pulmonary dysfunction is usually absent in Kawasaki but is frequently present in MIS-C [11]. Gastrointestinal complaints are more persistent in MIS-C [11–13].

Both conditions are characterized by increased CRP and ESR. However, increased white cell count, thrombocytosis, and eosinophilia are often observed in Kawasaki disease. In MIS-C, however, bone marrow suppression results in leucopenia and thrombocytopenia. Fibrinogen and ferritin levels are also elevated [11–13].

Due to the high titers of SARS-CoV-2 antibodies and the absence of any other virus, the diagnosis of MIS-C associated with SARS-CoV-2 and hyperinflammation in pediatric COVID-19 was considered. Although fever was present, apart from the skin changes, there was no other notable multisystem involvement that would contradict the definitions of MIS-C set by the Centers for Disease Control, Royal College of Pediatric and Child Health, and the World Health Organization, respectively [14–17]. Moreover, the age of the patient is more in keeping with Kawasaki disease rather than MIS-C. He did not fulfill the criteria for neonatal MIS [18]. The mucocutaneous symptoms of the baby were reminiscent of the classically described Kawasaki disease [19–21]. Finally, our patient showed a white cell count and high lymphocyte counts. There was thrombocytosis. Although the inflammatory markers were raised, the cardiac function markers were not significantly raised. Also, the fibrinogen was normal (Table 2). Resistance to immunoglobulins is associated with the development of coronary aneurysms. Therefore, adjunct therapies are being evaluated [22]. Interleukin 1 (IL-1) receptor blockade has proven to be beneficial in preventing myocardial dysfunction [23].

That is not unprecedented, given the pivotal role that IL-1α plays in the proinflammatory cycle of many tissues [24]. IL-1 blockade has been used in polygenic autoinflammatory disorders such as systemic juvenile idiopathic arthritis, adult-onset Still's disease, idiopathic recurrent pericarditis, Behcet syndrome, and gout [25]. Anakinra, an IL-1α receptor antagonist, has been used as a second-line therapy in giant coronary artery aneurysms in Kawasaki disease [26]. Anakinra has been used as an off-label therapy for the treatment of IVIG-resistant Kawasaki disease in doses of 1–9 mg/kg/day [27]. Similarly, other studies report dosing schedules from 1–8 mg/kg/day [28]. There is less information about neonatal dosing. However, off-label anakinra has been used in neonates with Kawasaki disease from 1 to 6–9 mg/kg/day [29].

Indeed, anakinra has been used in IVIG-resistant Kawasaki to promote apyrexia and prevent the appearance of coronary aneurysms [30]. More relevant, anakinra has been used as a second-line treatment in the case of infants with resistant Kawasaki and giant aneurysms. The result was improvement and stability, but not complete resolution [31, 32]. In older infants, however, with resistant Kawasaki and medium to giant aneurysms treated with anakinra, there was complete resolution of the aneurysms [33–35]. Recurrent Kawasaki has been successfully treated with adjunctive anakinra, with full resolution of medium-sized aneurysms [36]. Treatment with anakinra has also resulted in the resolution of medium-sized aneurysms in older children as well [37, 38]. In a case series of 11 children with ages from 4 months to 9 years, all patients exhibited improvement with variable regression of the coronary aneurysms, with one exception, who died from complications of coronary artery rupture [39]. A trial of anakinra in refractory Kawasaki has shown some improvement in the dilation of coronary arteries and improvement of fever [40] (Table 3).

Future and existing trials will help clarify the potential role of prompt treatment to prevent coronary aneurysm formation.

Table 3. Literature review.

Reference number	Study	Year	Study type	Number of patients	Sex	Age	Condition	Reason	Treatment	Outcome	Follow up	Max z score
[30]	Sánchez-Manubens et al.	2017	Case report	1	Female	3 years	KD	Resistant	2 doses IVIG + glucocorticosteroids + aspirin + anakinra 2 mg/kg OD for 14 days	No CAA	16 weeks	No CAA
[31]	Shafferman et al.	2014	Case report	1	Female	11 weeks	KD + MAS	Aneurysms	3 doses IVIG + aspirin + glucocorticosteroids + infliximab Anakinra 3 mg/kg BD for 3 days, then 3 mg/kg TID	Mild dilation RCA	8 months	11 (giant)
[32]	Walser et al.	2020	Case report	1	Male	3 months	KD resistant	Resistant + aneurysms	2 doses IVIG + aspirin + etanercept + anakinra 6–8 mg/kg/day	Improvement	2 years	11 (giant)
[33]	Lind-Holst et al.	2019	Case report	1	Male	12 weeks	KD + MAS	Aneurysms	2 doses IVIG + aspirin + anakinra 10 mg/kg/day	CAA stable	19 months	12.68 (giant)
[34]	Gambacorta et al.	2020	Case report	1	Male	9 months	KD + MAS	Resistant + aneurysms	2 doses IVIG + clopidogrel	Normalization of CAA	1 year	11.49 (giant)
[35]	Barbara et al.	2021	Case report	1	Male	12 months	KD + *Salmonella* so	Resistant + aneurysms	2 doses IVIG + aspirin + anakinra 8 mg/kg/day	Normalization of CAA	19 days	3.27 (small)
[36]	Guillaume et al.	2018	Case report	1	Male	18 months	KD	Resistant + aneurysms	2 doses IVIG + glucocorticosteroids + aspirin + anakinra 6 mg/kg/day	Improvement	7 months	9.94 (large)
[37]	Bossi et al.	2022	Case report	1	Male	2 months	Recurrent KD	Aneurysms	IVIG + corticosteroids + aspirin + anakinra 2 mg/kg/day	Normalization of CAA	2 years	4.89 (medium)
[38]	Blonz et al.	2020	Case report	1	Female	16 years	KD	Resistant + aneurysms	IVIG + heparin + anakinra 100 mg SC	Improvement	6 months	Aneurysmal dilation 9 mm
[39]	Kone-Paut et al.	2018	Retrospective case series	11	8 male, 3 female	4 months–9 years	KD resistant	Resistant IVIG	IVIG + corticosteroids + aspirin + anakinra 2–6 mg/kg/day	1 died, 10 improved	Variable	Variable
[40]	Kone-Paut et al.	2020	Prospective open-label study	16	14 male, 2 female	3 months–83 months	KD resistant	Resistant	Variable	Improvement	45 days	Variable

BD: bis die; CAA: coronary artery abnormalities; IVIG: intravenous immunoglobulin; KD: Kawasaki disease; MAS: macrophage activation syndrome; OD: once daily; RCA: right coronary artery; SC: subcutaneous; so: status post; TID: three times daily.

Abbreviations

CRP: C-reactive protein

ESR: erythrocyte sedimentation rate

IL-1: interleukin 1

IVIG: intravenous immunoglobulin

LAD: left anterior descending

LCA: left coronary artery

MIS-C: multisystem inflammatory syndrome in children

RCA: right coronary artery

Declarations

Author contributions

AA and NA: Conceptualization, Investigation, Writing—original draft, Writing—review & editing. ET: Resources, Supervision. MT: Resources, Writing—review & editing. NGE: Validation, Writing—review & editing, Supervision. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

The study was approved by the Ethics Committee of Agia Sofia Children's Hospital Reference Number 5893/2022, and complies with the Declaration of Helsinki.

Consent to participate

Informed consent to participate in the study was obtained from the participant's guardians.

Consent to publication

Informed consent to publication was obtained from relevant participant guardians.

Availability of data and materials

The data of this manuscript could be available from the corresponding authors upon reasonable request.

Funding

Not applicable.

Publisher's note

References

1. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al.; American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Surgery and Anesthesia; and Council on Epidemiology and Prevention. Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association. Circulation. 2017;135:e927–99. [DOI] [PubMed]
2. Jone P, Tremoulet A, Choueiter N, Dominguez SR, Harahsheh AS, Mitani Y, et al.; American Heart Association Rheumatic Fever, Endocarditi, and Kawasaki Disease Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Radiology and Intervention; and Council on Clinical Cardiology. Update on Diagnosis and Management of Kawasaki Disease: A Scientific Statement From the American Heart Association. Circulation. 2024;150:e481–500. [DOI] [PubMed]
3. Liu Y, Lin M, Wang J, Wu M. State-of-the-art acute phase management of Kawasaki disease after 2017 scientific statement from the American Heart Association. Pediatr Neonatol. 2018;59:543–52. [DOI] [PubMed]
4. Dallaire F, Dahdah N. New equations and a critical appraisal of coronary artery Z scores in healthy children. J Am Soc Echocardiogr. 2011;24:60–74. [DOI] [PubMed]
5. Ghosh P, Katkar GD, Shimizu C, Kim J, Khandelwal S, Tremoulet AH, et al.; Pediatric Emergency Medicine Kawasaki Disease Research Group; Bocchini J, Das S, Burns JC, Sahoo D. An Artificial Intelligence-guided signature reveals the shared host immune response in MIS-C and Kawasaki disease. Nat Commun. 2022;13:2687. [DOI] [PubMed] [PMC]
6. Rivas MN, Arditi M. Kawasaki Disease and Multisystem Inflammatory Syndrome in Children: Common Inflammatory Pathways of Two Distinct Diseases. Rheum Dis Clin North Am. 2023;49:647–59. [DOI] [PubMed] [PMC]
7. Yeo WS, Ng QX. Distinguishing between typical Kawasaki disease and multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2. Med Hypotheses. 2020;144:110263. [DOI] [PubMed] [PMC]
8. Lee J, Kim BJ, Cho K, Rhim JW, Lee S, Jeong DC. Similarities and Differences between Multisystem Inflammatory Syndrome in Children (MIS-C) and Kawasaki Disease Shock Syndrome. Children (Basel). 2023;10:1527. [DOI] [PubMed] [PMC]
9. Ulu K, Çağlayan Ş, Coşkuner T, Vazgeçer EO, Öner T, Sözeri B. Differentiating Kawasaki Disease and Multisystem Inflammatory Syndrome in Children Using Blood Composite Scores: Insights into Clinical Outcomes and Predictive Indices. Pediatr Cardiol. 2025;46:1390–9. [DOI] [PubMed] [PMC]
10. Wessels PA, Bingler MA. A comparison of Kawasaki Disease and multisystem inflammatory syndrome in children. Prog Pediatr Cardiol. 2022;65:101516. [DOI] [PubMed] [PMC]
11. Zhang Q, Xu B, Du J. Similarities and differences between multiple inflammatory syndrome in children associated with COVID-19 and Kawasaki disease: clinical presentations, diagnosis, and treatment. World J Pediatr. 2021;17:335–40. [DOI] [PubMed] [PMC]
12. Lee M, Liu Y, Tsai C, Hsu J, Wu J. Similarities and Differences Between COVID-19-Related Multisystem Inflammatory Syndrome in Children and Kawasaki Disease. Front Pediatr. 2021;9:640118. [DOI] [PubMed] [PMC]
13. Tong T, Yao X, Lin Z, Tao Y, Xu J, Xu X, et al. Similarities and differences between MIS-C and KD: a systematic review and meta-analysis. Pediatr Rheumatol Online J. 2022;20:112. [DOI] [PubMed] [PMC]

14. Melgar M, Lee EH, Miller AD, Lim S, Brown CM, Yousaf AR, et al. Council of State and Territorial Epidemiologists/CDC Surveillance Case Definition for Multisystem Inflammatory Syndrome in Children Associated with SARS-CoV-2 Infection—United States. MMWR Recomm Rep. 2022;71:1–14. [DOI] [PubMed] [PMC]
15. Guidance: Paediatric multisystem inffammatory syndrome temporally associated with COVID-19 [Internet]. [cited 2025 Jul 23]. Available from: https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf
16. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 [Internet]. [cited 2025 Jul 23]. Available from: https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19
17. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 2. Arthritis Rheumatol. 2021;73:e13–29. [DOI] [PubMed] [PMC]
18. Molloy EJ, Nakra N, Gale C, Dimitriades VR, Lakshminrusimha S. Multisystem inflammatory syndrome in children (MIS-C) and neonates (MIS-N) associated with COVID-19: optimizing definition and management. Pediatr Res. 2023;93:1499–508. [DOI] [PubMed] [PMC]
19. Marzano AV, Cassano N, Moltrasio C, Verdoni L, Genovese G, Vena GA. Multisystem Inflammatory Syndrome in Children Associated with COVID-19: A Review with an Emphasis on Mucocutaneous and Kawasaki Disease-Like Findings. Dermatology. 2022;238:35–43. [DOI] [PubMed] [PMC]
20. Jiang L, Tang K, Irfan O, Li X, Zhang E, Bhutta Z. Epidemiology, Clinical Features, and Outcomes of Multisystem Inflammatory Syndrome in Children (MIS-C) and Adolescents-a Live Systematic Review and Meta-analysis. Curr Pediatr Rep. 2022;10:19–30. [DOI] [PubMed] [PMC]
21. Giryes S, McGonagle D. Immune and non-immune mechanisms that determine vasculitis and coronary artery aneurysm topography in Kawasaki disease and MIS-C. Autoimmun Rev. 2023;22:103240. [DOI] [PubMed]
22. Tremoulet AH. Adjunctive therapies in Kawasaki disease. Int J Rheum Dis. 2018;21:76–9. [DOI] [PubMed] [PMC]
23. Gorelik M, Lee Y, Abe M, Andrews T, Davis L, Patterson J, et al. IL-1 receptor antagonist, anakinra, prevents myocardial dysfunction in a mouse model of Kawasaki disease vasculitis and myocarditis. Clin Exp Immunol. 2019;198:101–10. [DOI] [PubMed] [PMC]
24. Cavalli G, Colafrancesco S, Emmi G, Imazio M, Lopalco G, Maggio MC, et al. Interleukin 1α: a comprehensive review on the role of IL-1α in the pathogenesis and treatment of autoimmune and inflammatory diseases. Autoimmun Rev. 2021;20:102763. [DOI] [PubMed]
25. Malcova H, Milota T, Strizova Z, Cebecauerova D, Striz I, Sediva A, et al. Interleukin-1 Blockade in Polygenic Autoinflammatory Disorders: Where Are We now? Front Pharmacol. 2021;11:619273. [DOI] [PubMed] [PMC]
26. Campbell AJ, Burns JC. Adjunctive therapies for Kawasaki disease. J Infect. 2016;72:S1–5. [DOI] [PubMed]
27. Maniscalco V, Abu-Rumeileh S, Mastrolia MV, Marrani E, Maccora I, Pagnini I, et al. The off-label use of anakinra in pediatric systemic autoinflammatory diseases. Ther Adv Musculoskelet Dis. 2020;12:1759720X20959575. [DOI] [PubMed] [PMC]
28. Ferrara G, Giani T, Caparello MC, Farella C, Gamalero L, Cimaz R. Anakinra for Treatment-Resistant Kawasaki Disease: Evidence from a Literature Review. Paediatr Drugs. 2020;22:645–52. [DOI] [PubMed] [PMC]
29. Rose DUD, Campi F, Maddaloni C, Ronci S, Caoci S, Savarese I, et al. Off-Label Use of Anakinra in Inflammatory Conditions in Neonates and Infants Up to 3 Months of Age: A Case Series and a Review of the Literature. Paediatr Drugs. 2025;27:293–305. [DOI] [PubMed] [PMC]

30. Sánchez-Manubens J, Gelman A, Franch N, Teodoro S, Palacios JR, Rudi N, et al. A child with resistant Kawasaki disease successfully treated with anakinra: a case report. BMC Pediatr. 2017;17:102. [DOI] [PubMed] [PMC]
31. Shafferman A, Birmingham JD, Cron RQ. High dose Anakinra for treatment of severe neonatal Kawasaki disease: a case report. Pediatr Rheumatol Online J. 2014;12:26. [DOI] [PubMed] [PMC]
32. Walser M, Hermann M, Hufnagel M, Haas NA, Fischer M, Dalla-Pozza R, et al. Anakinra And Etanercept Combination Treatment in a Child With Severe, Nonresponsive Kawasaki Disease. Pediatr Infect Dis J. 2020;39:e310–3. [DOI] [PubMed]
33. Lind-Holst M, Hartling UB, Christensen AE. High-dose anakinra as treatment for macrophage activation syndrome caused by refractory Kawasaki disease in an infant. BMJ Case Rep. 2019;12: e229708. [DOI] [PubMed] [PMC]
34. Gambacorta A, Buonsenso D, Rosa GD, Lazzareschi I, Gatto A, Brancato F, et al. Resolution of Giant Coronary Aneurisms in a Child With Refractory Kawasaki Disease Treated With Anakinra. Front Pediatr. 2020;8:195. [DOI] [PubMed] [PMC]
35. Barbara Z, Ellenwood SP, Loe ED, Choi J, Ryan K, Joseph N. Kawasaki Disease Complicated by *Salmonella oranienburg* Coinfection. Case Rep Pediatr. 2021;2021:5584514. [DOI] [PubMed] [PMC]
36. Guillaume M, Reumaux H, Dubos F. Usefulness and safety of anakinra in refractory Kawasaki disease complicated by coronary artery aneurysm. Cardiol Young. 2018;28:739–42. [DOI] [PubMed]
37. Bossi G, Codazzi AC, Vinci F, Clerici E, Regalbuto C, Crapanzano C, et al. Efficacy of Anakinra on Multiple Coronary Arteries Aneurysms in an Infant with Recurrent Kawasaki Disease, Complicated by Macrophage Activation Syndrome. Children (Basel). 2022;9:672. [DOI] [PubMed] [PMC]
38. Blonz G, Lacroix S, Benbrik N, Warin-Fresse K, Masseau A, Trewick D, et al. Severe Late-Onset Kawasaki Disease Successfully Treated With Anakinra. J Clin Rheumatol. 2020;26:e42–3. [DOI] [PubMed]
39. Kone-Paut I, Cimaz R, Herberg J, Bates O, Carbasse A, Saulnier JP, et al. The use of interleukin 1 receptor antagonist (anakinra) in Kawasaki disease: A retrospective cases series. Autoimmun Rev. 2018;17:768–74. [DOI] [PubMed]
40. Kone-Paut I, Tellier S, Belot A, Brochard K, Guitton C, Marie I, et al. Phase II Open Label Study of Anakinra in Intravenous Immunoglobulin-Resistant Kawasaki Disease. Arthritis Rheumatol. 2020;73: 151–61. [DOI] [PubMed]