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Issue.3

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DEPARTMENT OF PAEDIATRICS, ANDHRA HOSPITALS, VIJAYAWADA
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Foreword

Greetings from the Andhra Hospitals!

For the past two decades, we are delivering excellence in terms of quality health care in the field of Paediatrics including Paediatric and Neonatal intensive care, Paediatric cardiac intensive care and other allied Paediatric sub-specialities.We take pride in introducing ECMO in pediatric specialty for the first time in the state of Andhra Pradesh. In this context, we convey our heartfelt thanks to you for your continued support and encouragement which played a pivotal role in our success.

As a token of our commitment to contribute to continuous medical education, we are introducing this monthly E-journal to showcase important clinical guidelines, recent advances in paediatric sub-specialties, interesting case reports, image quiz, OSCE scenarios etc, gathered from our patient database.

We hope this endeavor would prove to be useful to practicing paediatricians, intensivists, neonatologists and post-graduate students.

Please send your valuable feedback and suggestions to ***maramkp@gmail.com***.

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Introduction

KD is an acute self-limiting inflammatory disorder, affecting predominantly medium sized arteries, particularly coronaries; causing coronary artery aneurysms (CAA) in 15-25% of untreated patients; while 2-3% of untreated cases die as a result of coronary vasculitis[1].

KD is the commonest cause of acquired heart disease in children in developed countries and potentially important cause of long term cardiac disease in adult life with risk of thrombosis and/or stenosis of the coronary artery, which may result in coronary thrombosis and myocardial ischaemia or infarction in patients with KD related aneurysms (NHS patient safety alert stage1, 11th May 2016)[4].

Epidemiology

Incidence in UK - 8.1/10,000 children; younger than 5 years, peak incidence at 18-24 months.
Less common in patients aged less than 3 months or more than 5 years, but are at increased risk for coronary artery aneurysm (CAA) formation[1].

Clinical features and diagnosis

KD is a purely clinical diagnosis with combined criteria and absence of gold standard for diagnosis.

There is no diagnostic test for KD, thus the diagnosis rests on combination of clinical criteria and laboratory findings of raised inflammatory markers.
Fever of more than 38'C lasting at least five days without any other explanation is a mandatory criterion.

Complete KD

Fever persisting for at least 5 days without any other explanation PLUS 4 out of 5 of the following criteria:
1. Bilateral non suppurative conjunctivitis
2. Cervical lymphadenopathy, often more than 1.5 cm
3. Polymorphous rash- non specific maculopapular eruption, usually extensive with involvement of trunk and extremities, no vesicles or crusts
4. Changes in lips or oral mucosa (red cracked lips; strawberry tongue; or diffuse erythema of oral mucosa
5. Changes in extremities: Initial stage: erythema and edema of the palms and soles; Convalescent stage: peeling of skin from finger and toe tips in week 2 or 3.

Incomplete KD

10 - 40% of cases have some but not all the above features. Diagnosis of these "**Incomplete KD**'' depends on high level of suspicion in children presenting with some of the KD features and evidence of systemic inflammation (such as. elevated CRP, ESR, and or leucocytosis).

Should start presumptive treatment as KD particularly if febrile exanthematous illness persists longer than 4-5 days with no other explanation (KD may be diagnosed with fewer than 4 of the above criterions if coronary abnormalities are detected.) (Seek an expert advice in such cases).

Refractory Kawasaki disease

20% of the cases have resistance to initial course of IVIG: Persistent or recurrent fever of any magnitude between 36 hours to about 2 weeks after the start of treatment in patients with KD is generally assumed to be the result of failure to abort the disease process.

Patients who have persistent or recurrent fever more than 24 hours after completion of the initial treatment should also be assessed for intercurrent infection, and the diagnosis of KD should be reevaluated.

However, these patients should be retreated for presumed recrudescence of KD unless there is clear evidence of another explanation for fever, since numerous studies have confirmed an association between prolonged fever and development of coronary artery abnormalities. (seek an expert advice from rheumatologist and cardiologist)

- Fever within 36 hours of the start of intravenous IVIG does not warrant re-treatment, because it may represent a reaction to the medication or a slow response to therapy.

Severe disease & high risk of CAA – especially with the following features. (if in doubt, seek an expert advice and refer to pediatric cardiologists)

Already failed IVIG: Refractory KD.

Severe cases: very young <12 month, those with markers of severe inflammation ie. persistently elevated CRP despite IVIG, liver dysfunction, hypoalbuminaemia, anaemia.

Features of hemophagocystic lymphohistocytosis (HLH) or shock.

Already have on going evolving coronary and/or peripheral aneurysm with ongoing inflammation.

Kobayashi risk score more than or equal to 5 (please see appendix. table 1)

Additional features of KD

Irritability is characteristic. The desquamation may affect the genital area, a characteristic but late feature.

Other features may include: joint pain and swelling, vomiting, abdominal pain and diarrhoea, proteinuria, cough, rhinorrhoea, pneumonitis, CNS involvement with meningism and CSF pleocytosis, fits,

meatal inflammation in boys, hydrops of gall bladder, erythema and induration of BCG scars, abnormal LFT and sterile pyuria, SIADH resulting in hyponatremia.

Vascular involvement

The main sites of clinically important vascular involvement are coronary arteries. CAA occur in 15-25% of untreated cases, with additional cardiac features including ECG abnormalities, myocarditis, endocarditis, pericarditis +/- effusion, valvular incompetence, heart failure and myocardial infarction.

- Systemic arterial injury (major limb arteries, renal and other visceral vessels) occurs, but it is rarely seen in absence of CAA.

Differential diagnosis

- The presence of any of above criteria and/or the absence of fever should suggest a diagnosis other than KD.

- Of note, concurrent infections (both viral and bacterial) are common in patients with KD, found in up to 33 percent of children in one study. In any event, diagnosis of an infectious condition does not preclude a concurrent diagnosis of KD[1,5].

- Common differential diagnosis are viral exanthems (e.g. measles, adenovirus, enterovirus, echovirus, EBV, mycoplasma, CMV, parvovirus), Scarlet fever, Staphylococcal scalded skin syndrome, Stevens-Johnson syndrome, Juvenile idiopathic arthritis (JIA)(systemic onset), Toxic shock syndrome and drug hypersensitivity reactions. (Please see appendix table 2 for differentiating features)

Investigations and Laboratory findings

There is no diagnostic test for KD.

KD is invariably associated with an inflammatory process with raised ESR, CRP and white cell counts. In The absence of systemic inflammatory inflammation, KD is unlikely.

1. FBC- mild anaemia, neutrophil leucocytosis, thrombocytosis occurs towards the end of second week of illness and not helpful in early stage. Acute thrombocytopenia may be associated with poorer prognosis.
2. CRP raised >10 mg/dl. Raised ESR.
3. U&E - hyponatremia may be present.
4. LFT - Liver function may be deranged and some patients present with jaundice and elevation of serum transaminases. Hypoalbuminaemia is common.
5. Urine microscopy and culture - sterile pyuria.
6. Other - pleocytosis of cerebrospinal fluid
7. ECG - non specific ST changes, prolong PR interval if myocarditis present.
8. Echocardiogram (ECHO) - should request on diagnosis (discuss with on-call paediatric cardiology

registrar- bleep 2528).

Subsequent ECG and repeat ECHO (a minimum of 3 ECHO) should be performed in the first 6 weeks of illness and liaise with cardiology (but do not delay therapy prior to obtaining ECHO).

Early ECHO may reveal evidence of coronary vasculitis and confirm diagnosis but negative ECHO does not exclude the diagnosis.

9. Other investigations to consider exclude/confirm differential diagnoses by the attending clinician

ASOT and anti - DNAse B, throat swab, blood culture, urine culture, lumber puncture, coagulation screen, ANA, rheumatoid factor, viral serology.

Treatment

All patients need hospital admission and should be reviewed by a consultant before starting a definitive treatment.

Early recognition and treatment with IV Immunoglobulin (IVIG) and aspirin has been shown to reduce the occurrence of CAA in 80% of cases.

Treatment should not be delayed waiting for an ECHO.

Recent clinical trials and meta-analyses have demonstrated that the addition of corticosteroids to IVIG is beneficial for prevention of CAA in severe KD with high risk of IVIG resistance.

1) IV Gammaglobulin: 2g/kg single infusion over 10 hours is the optimal dose. Most effective if given at D 5-7 or within 10 days of onset. It may be beneficial in late presenting cases even given after 10 days have elapsed if signs of inflammation persists. (IVIG form (available on INSITE) must be completed and emailed to immunoglobulins.mailbox@uhl-tr.nhs.uk)

2) **Aspirin: Anti-inflammatory dose of 30-50 mg/kg/D in 4 divided doses** is recommended during the acute phase of the illness. The dose should be reduced to anti-platelet dose of 3-5 mg/kg/D in single dose once fever and inflammation have subsided.

Aspirin should be continued for minimum of 6 weeks but should be continued longer if CAA persists. For those on low dose aspirin, we also recommend avoiding the concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs) as these interfere with the anti-platelet effect of low dose aspirin.

3) **Corticosteroids are recommended as part of primary treatment** in severe KD/ cases of high risk of IVIG resistance as described above (seek an expert advice from cardiology and or rheumatology if in doubt). There are two suggested steroids regimen and treating clinician can determine the suitable regimen for an individual patient.

Methyl-prednisolone 0.8 mg/kg BD IV for 7 days or until CRP normalize; then convert to prednisolone 2mg/kg/day PO and wean off over the next 2-3 weeks.

(OR)

Methyl-prednisolone 10-30 mg/kg IV once a day for 3 days followed by prednisolone 2mg/kg/day PO until D7 or until CRP normalize, then wean over next 2-3 weeks.

4) Consider gastro- protection with ranitidine/ omeprazole/ lansoprazole while on high dose aspirin and or steroid.

5) Fluid balance should be closely monitored.

6) If no disease effervescence occurs within 48 hours or disease recrudescence within 2 weeks, **second dose of IVIG** is recommended to be given at the same time as commencing steroids if they have not already been commenced for severe KD. (Seek expert advice to consider if in doubt)

7) **Role of anti-tumor necrosis factor (anti- TNF)**- infliximab or etanercept should be considered in patients with IVIG resistant KD with the expert advice from Cardiology and Rheumatology.

8) Management of KD in convalescence phase

If CAA persists, anti- platelet therapy in the form of aspirin should be continued at 3-5 mg/kg/dose OD long term until CAA resolves (Duration as per advice by cardiology team).

Clopidogrel could be considered as an alternative anti-platelet.

In the presence of giant CAA (>8 mm), warfarin is recommended in addition to aspirin. Heparin should be administered initially for 48 hours and stopped only when warfarin has been commenced and INR stable between 2-3.

In small children less than one year with giant aneurysms Warfarin absorption and metabolism is erratic making INR control extremely difficult LMWH is recommended with Clopidogrel or aspirin , target factor Xa is around 1.0[1]

In acute giant aneurysms with Z score above 10; the 2017 AHA guideline recommendation is for triple therapy in the form of dual antiplatelet and warfarin or LMWH[1]

Follow up

All patients should be followed up by general paediatrics (SE of steroids if received should be vigilant - hypertension, behavioral changes, secondary infections, hyperglycaemia and bone necrosis).

Regular follow up by paediatric cardiology team will be needed, and tailored according to the degree of coronary involvement, recommendations regarding anti-platelet and anticoagulant therapy, physical activity, follow-up assessment, and the appropriate diagnostic procedures to evaluate cardiac disease are classified according to risk strata.

Immunisations with all vaccinations should be deferred for at least 3 months following an episode of KD treated with IVIG.

Varicella Zoster immunization should be considered for patients who require long term aspirin for persistent CAA.

Cross sectional imaging is increasingly considered especially in severe disease within first 3-6 months of first diagnosis then tailored according to involvement

NOTE: Etiology, pathogenesis, genetics, long term cardiology complications and long term investigations and management of cardiac complications are out of the scope of this guideline, however reference number 5 the AHA guidelines 2017 in 72 pages has covered all aspects of the acute and chronic disease in a very comprehensive which makes it an essential and highly recommended for both Paediatric and adult clinicians dealing with the disease.

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Appendix

Table 1- Kobayashi scoring system for predicting IVIG resistance

1) Table 2- Differential diagnosis of Kawasaki disease
2) Table 3- Recommended clinical guideline for the management of Kawasaki disease in the UK
3) Recommendation for prevention of thrombosis during the acute illness AHA 2017 guidelines
4) Recommended Coronary artery views and position of measurements (ASE 2010 paediatric Echo Guidelines).
5) Table 4- Kawasaki disease: Audit check list: please complete the form
6) Immunoglobulin request form- available from In site
7) Parents information leaflets- www.chfed.org.uk/info (please download, print out and give to parents)

Table 1- Kobayashi scoring system for predicting IVIG resistance

8) Na< or equal to 132 (2 points)
9) Illness < or equal to 4 days (2 points)
10) ALT > or equal to 100 U/L (1 point)
11) Platelets < or equal to 300* 109 /L (1 point)
12) CRP > or equal to 10 mg/dl (1 point)
13) Age < or equal to 12 months (1 point)
14) > or equal to 80% neutrophils (2 points)

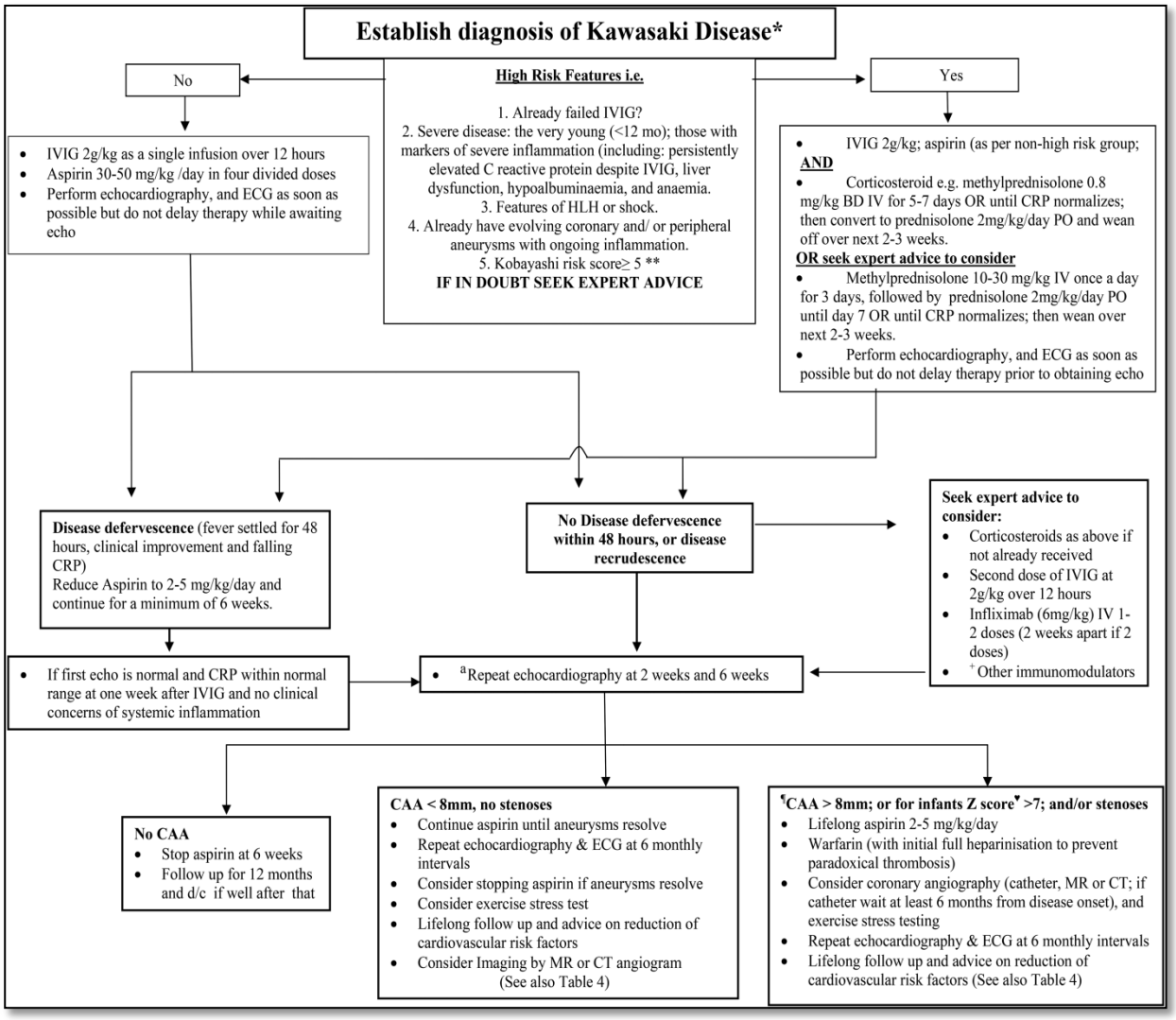
High risk > or equal to 5 points.

Table 2- Differential diagnosis of Kawasaki disease

	Kawasaki disease	Toxic shock syndrome	Streptococcal scarlet fever	Steven-Johnson syndrome	Systemic onset Juvenile Idiopathic Arthritis)
Age (years)	Usually <5	Usually >10	Usually 2-8	All ages	2-5
Fever (days)	Persistent	Usually <10	Variable, usually <10	Prolonged	Prolonged
Eyes	Non-exudative conjunctivitis, limbal sparing, anterior uveitis	Conjunctivitis	Normal	Exudative conjunctivitis, keratitis	Normal
Oral mucosa	Diffuse erythema,strawberry tongue	Erythematous	Pharyngitis, strawberry tongue	Erythema, ulceration, pseudomembrane formation	Normal
Peripheral extremities	Erythema of palms and soles, indurative edema, periungual desquammation	Swelling of hands and feet	Flaky desquammation	Normal	Arthritis
Rash	Erythematous, polymorphous; targeted or purpuric in 20%	Erytheroderma	Papular erythroderma Pastia's lines, circumora; pallor	Target lesions	Transient, salmon pink
Cervical lymph nodes	Non purulent swelling	Normal	Painful swelling	Normal	Diffuse adenopathy
Other	Arthritis	Mental status changes, coagulopathy, shock	Throat culture positive for group A Streptococcus	Arthralgia, associated herpesvirus infection (30-75%)	Arthritis, pericarditis
Characteristic lab results	Systemic inflammation, anaemia, transaminitis	Thrombocytopenia	Positive throat swab culture	Associated herpesvirus infection	Systemic inflammation, anaemia

Table 3-Recommended clinical guideline for the management of Kawasaki disease in the UK[1] Eleftheriou D, et al. 2016.

Please also see AHA 2017 guidelines that recommend use of Dual antiplatelet, LMWH and triple therapy**,** Appendix 4**:** Recommendation for prevention of thrombosis during the acute illness AHA 2017 guidelines Which we followed in fulminant cases with giant aneurysms in infants.



*Treatment can be commenced before 5 days of fever if sepsis excluded; treatment should also be given if the presentation is > 10 days from fever onset if there are signs of persistent inflammation; **Kobayashi risk score ≥5 points Refer to paediatric cardiologist; Other specific interventions such as positron emission tomography (PET) scanning, addition of calcium channel blocker therapy, and coronary angioplasty at discretion of paediatric cardiologist. + Other immunomodulators may include ciclosporin. ♥ For infants, Z score for internal coronary artery diameter >7 based on Montreal normative data: http://parameterz.blogspot.co.uk/2010/11/montreal-coronary-artery-z-scores.html.

Appendix 4: Recommendation for prevention of thrombosis during the acute illness AHA 2017 guidelines:

Low dose Aspirin 3-5mg/kg/does should be given to patients without evidence3 of coronary artery changes until 4-6 weeks after the illness (Class I; Level of evidence C)

For Patients with rapidly expanding coronary artery aneurysms (CAA) or a maximum Z of ≥10, systemic anticoagulation with low molecular weight heparin (LMWH) or warfarin INR target 2.0-3.0 in addit5ion to low does aspirin (Class IIa; level of evidence B) .

For patients at increased risk of thrombosis for example, with large or giant aneurysms (≥8 or Z score ≥10) and a recent history of coronary artery thrombosis, "triple therapy with aspirin and a second antiplatelet agent and anticoagulation with warfarin or LMWH may be considered (Class IIb; level of evidence C).

Ibuprofen and other non-steroidal inflammatory drugs with known or potential involvement of cyclooxygenase pathway may be harmful in patients taking Aspirin for its antiplatelet effects (Class III; level of evidence B)

Appendix 5: Recommended Coronary artery views and position of measurements (ASE 2010 paediatric Echo Guidelines, Page 486 . Figure 16, please notice:

Measurements are inner to inner, 1mm distal to the CA orifice.

Measure at maximum filling in diastole, dual view (2D, and colour), low Niquest.

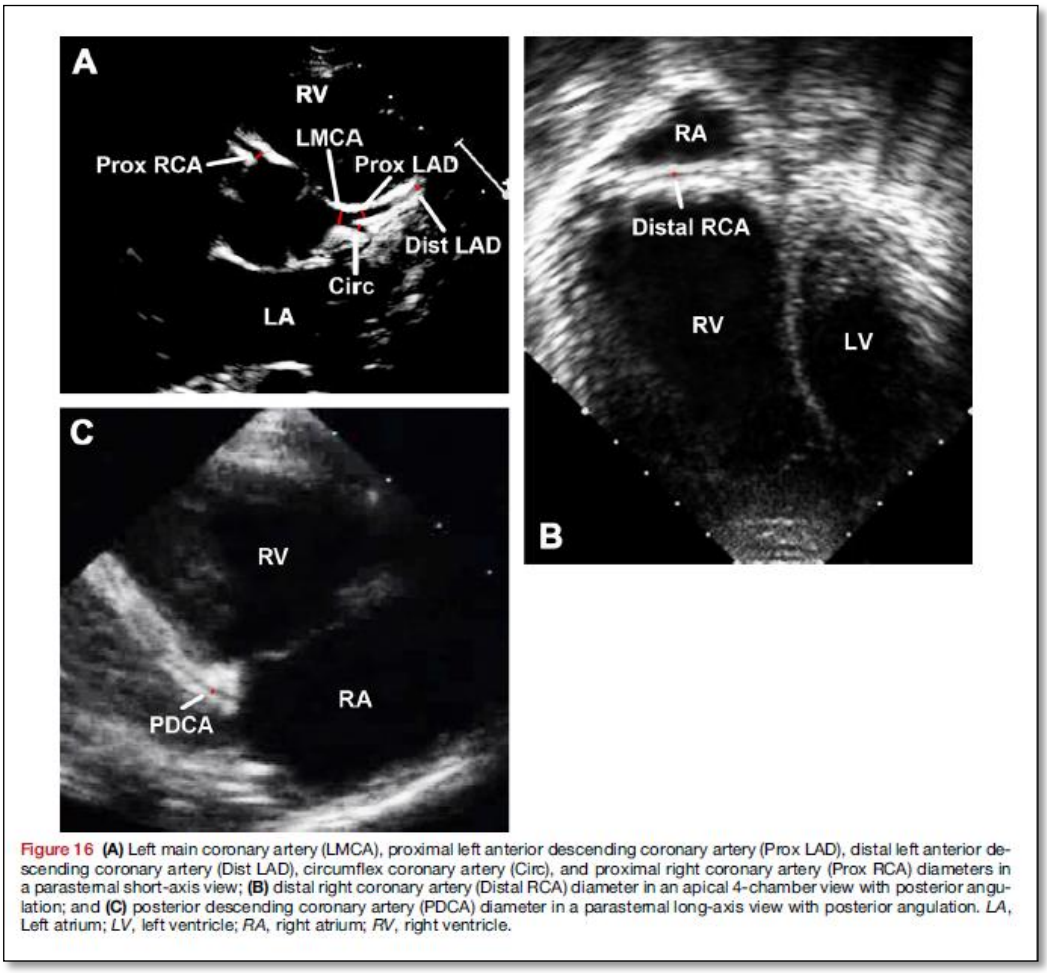


Figure 16 **(A)** Left main coronary artery (LMCA), proximal left anterior descending coronary artery (Prox LAD), distal left anterior descending coronary artery (Dist LAD), circumflex coronary artery (Circ), and proximal right coronary artery (Prox RCA) diameters in a parasternal short-axis view; **(B)** distal right coronary artery (Distal RCA) diameter in an apical 4-chamber view with posterior angulation; and **(C)** posterior descending coronary artery (PDCA) diameter in a parasternal long-axis view with posterior angulation. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

AN UNCOMMON PRESENTATION OF A CHILD WITH DILATED CARDIOMYOPATHY WITH HYPERTENSION DUE TO ACCESSORY RENAL ARTERIES: CASE REPORT

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CASE:

A 4-year -old fit and well female child presented with a 4-day-history of breathlessness, which was not associated with fever, cough and any other symptoms. On examination, she had respiratory distress (RR-35/min, SCR+) with bilateral fine crepitations, but had normal saturations in room air. She had a HR-110/min, BP-125/78(>95th percentile), normal pulse volumes and she was afebrile. Physical examination was otherwise unremarkable. Her chest-x-ray showed cardiomegaly and plethoric lung fields, hence a Pediatric Cardiologist consultation was taken. Bedside 2d-Echo revealed severe dilated cardiomyopathy with left ventricular dysfunction, with an EF of 15%. Laboratory investigation at presentation showed hypokalaemia (potassium 2.6 mmol/L) and metabolic alkalosis. Renal function, liver function, thyroid function, fasting blood glucose and lipid profile were within normal limits.

She was treated with iv Furosemide infusion, Milrinone infusion and other supportive measures. Further work up revealed secondary hyperaldosteronism with elevated plasma aldosterone 980 pmol/L (Reference range 102–858) and direct plasma renin 104mIU/L (Reference range 4.2–59.7). There was no evidence of renal artery stenosis on renal Doppler study. Renal CT angiography and CECT abdomen showed bilateral normal renal arteries and presence of bilateral accessory renal arteries superior to the main renal arteries and, small right kidney with possible upper and lower polar infarcts and a compensatory increased left kidney. Renal angiography had no evidence of stenosis in the main or the accessory arteries bilaterally.

In view of the absence of demonstrable stenosis for intervention, the patient was put on medical therapy. Her blood pressure was subsequently controlled with diuretics, Carvedilol and Enalapril.Gradually,her breathlessness had subsided and her EF was slowly improved to 45% by D-7of admission.She was eventually discharged on digoxin, carvedilol, furosemide, enalapril and other supplements.

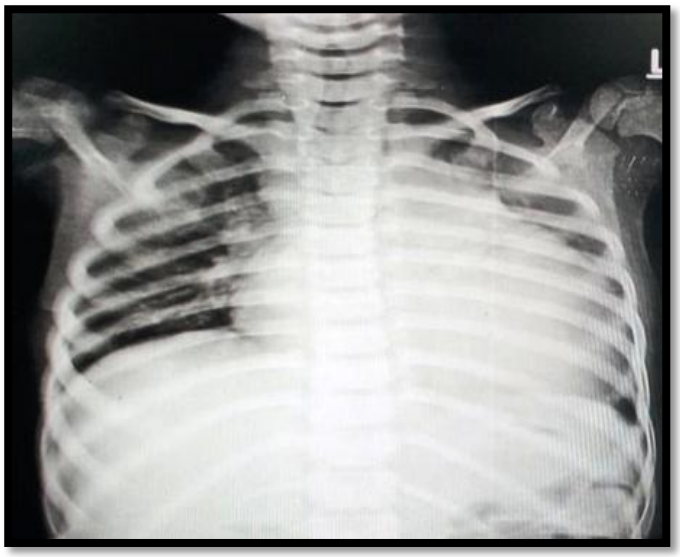


Fig 1: Chest-X-ray showing cardiomegaly and plethoric lung fields

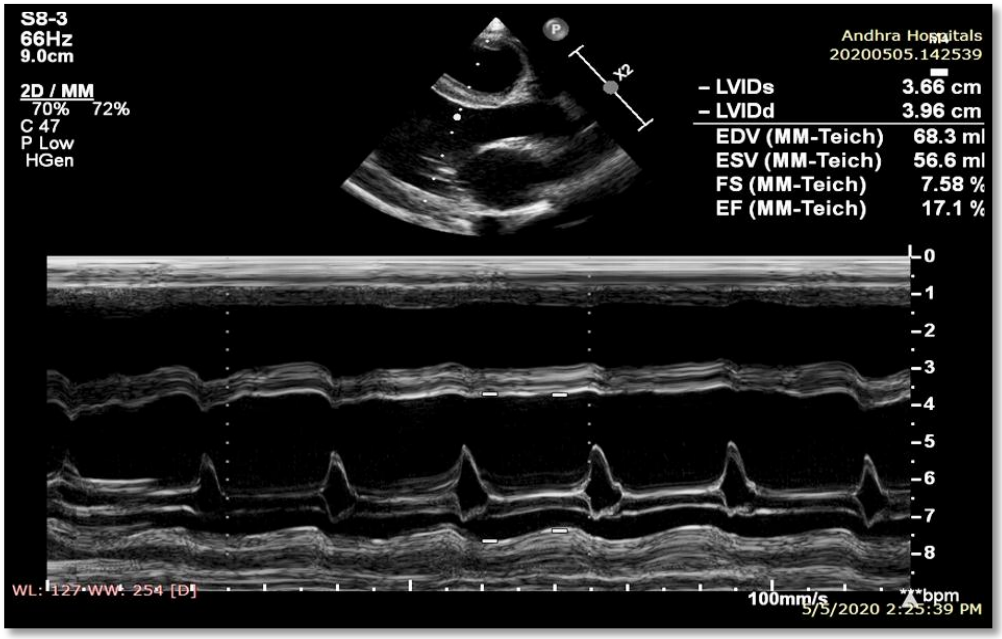


Figure -2

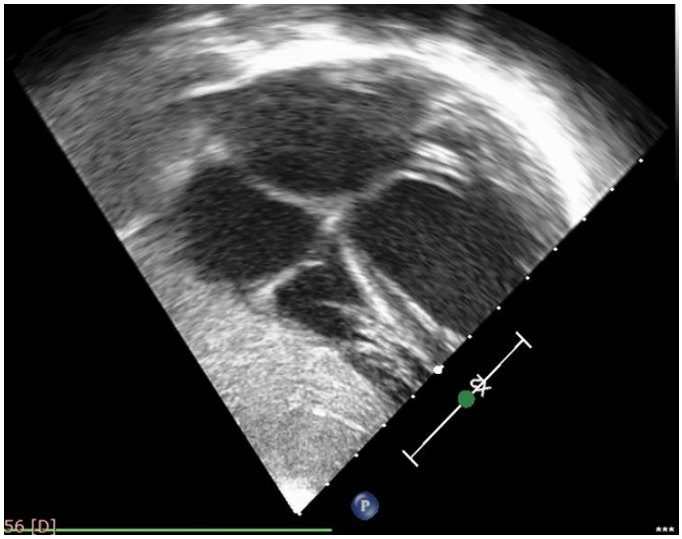
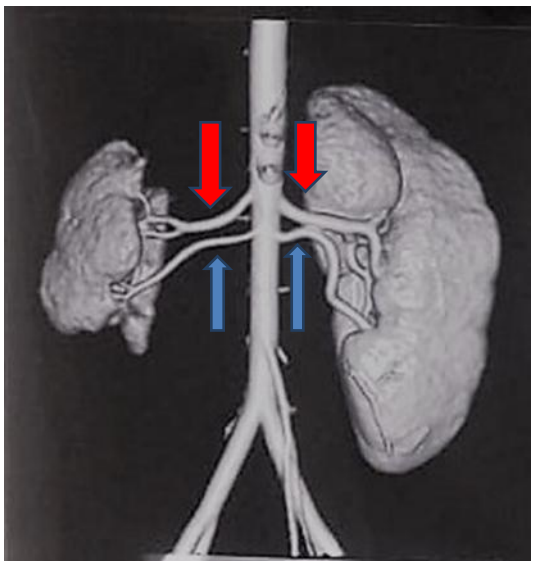


Figure -3

Figure 2 & 3 : 2D ECHO suggestive of severe dilated left atrium and left ventricle with severe left ventricular dysfunction (EF-15%).



Renal CT angiography revealing two accessory renal arteries with no obvious stenosis

Red colored arrows→ accessory renal arteries,

Blue colored arrows→ main renal arteries).

Renal veins are normal.

DISCUSSION:

This child had an unusual presentation of dilated cardiomyopathy and hypertension secondary to accessory renal arteries.

Accessory renal arteries are common and may be present in 20–60% of population. These are extra arteries that supply the renal hilum and are also known as supernumerary renal arteries. Its association to reno-vascular hypertension had been described as early as 1951 with several studies showing increased presence of multiple renal arteries in hypertensive versus normotensive patients. Györi hypothesized that accessory renal artery can lead to hypertension due to under perfusion of the kidney as a result of longer and narrow caliber which raises its resistance or predisposes it to stenosis. The resultant renal ischemia leads to activation of renin-angiotensin system and secondary hypertension. Glodny demonstrated increased renin activities in patients with multiple renal arteries compared to those with single renal artery. On the contrary, there are studies which found no association of accessory renal arteries to hypertension. This is not surprising given the marked variation in anatomy, size and hemodynamic contribution of each accessory artery to the renal vasculature as well as differences in the method of assessment and population studied. Convincing evidence of accessory renal arteries causing renin dependent renovascular hypertension has rarely been reported in the literature.

Various imaging methods have been used to further assess patients with renovascular hypertension. The detection of accessory renal artery is better with the use of CT angiography or gadolinium enhanced MRA compared to Doppler ultrasound .To further evaluate the hemodynamic significance of a stenotic

vessel, renal vein renin sampling as well as radionuclide imaging such as captopril renogram have been used though its role in accessory renal artery have only been reported in a few case reports. Treatment included medical therapy, or stenting in the presence of stenosis or fibromuscular dysplasia and nephrectomy in patient who failed medical therapy.

More recently, the finding of accessory renal arteries was highlighted in cases of treatment resistant hypertension undergoing sympathetic renal denervation. Studies have found higher rates of nonresponses or less pronounced blood pressure reduction in those with accessory renal arteries compared to those with bilateral single renal arteries, especially if the accessory arteries were not treated, again supporting the possibility of their contributing role in hypertension. Newer technologies that are able to target accessory arteries for more complete renal denervation may offer another treatment option for patients with resistant hypertension

DCM is primarily diagnosed using echocardiography or, more recently, cardiac magnetic resonance (MR) imaging in symptomatic patients (e.g., unexplained heart failure) or via screening studies in children who have a familial history of DCM, an inborn error of metabolism, a neuromuscular disorder or a malformation syndrome associated with DCM. Some children with acute myocarditis may also progress to chronic DCM. Systolic dysfunction and progressive LV dilation are the hallmarks of DCM. Severity of LV dilation at the time of listing for heart transplant is associated with the risk of death. Echocardiography is the primary source of information for diagnosing and monitoring the disease; for example, measures of systolic versus diastolic diameter (fractional shortening) or volume (ejection fraction) are routinely collected to monitor LV systolic function.

DCM is characterized by changes at molecular, cellular and interstitial levels following apoptosis, death of cardiomyocytes or collagen deposition, which can have long-term manifestations, such as dilatation of the LV, fibrosis, thinning of the interventricular septum and posterior wall of the LV, and a change in shape such that the LV tends to become more round with decreased contractility. These changes are described as ‘remodeling’ of the heart. Historically, the goal of medical treatment has been the improvement of symptoms. Over the last two decades, the goal of treatment has not been limited to treating the symptoms, but has focused on reversing this remodeling process that is linked to the progression of heart failure. Follow-up of patients with heart failure secondary to DCM focuses on the assessment of symptoms and response to medical treatment, assessment of functional capacity and imaging study (echocardiogram and

MRI) to assess the status of the remodeling process. Similar to adult patients, the role of biomarkers such as N-terminal pro-brain natriuretic peptide is gaining a more significant role in children and appears to be helpful in assessing and monitoring heart failure patients.

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PEDIATRIC INFLAMMATORY MULTISYSTEM SYNDROME TEMPORALLY ASSOCIATED WITH SARS-COV-2 (PIMS-TS)

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Key Messages

- PIMS-TS is characterized by a multi-systemic inflammation secondary to a presumed post-infectious abnormal immune response to COVID -19 infection
- Shares many clinic-pathological features of Kawasaki Disease but more common in older children
- SARS Co V-2 PCR result may be positive or negative
- Treatment is mainly supportive, IV IG,high dose Aspirin, steroids depending on clinical presentation

INTRODUCTION:

Since its first appearance in Wuhan, a city in the Hubei province of China, Novel corona virus (COVID-19) induced disease has rapidly spread globally, assuming a pandemic nature by March 2020. In February 2020, the World Health Organization (WHO) designated the disease COVID-19, which stands for coronavirus disease 2019 . The virus that causes COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); previously, it was referred to as 2019-nCoV.

In children, COVID-19 is usually mild. Most children are asymptomatic or exhibit mild symptoms. However, in the last 3 months a small number of children have been identified who develop a significant systemic inflammatory response which may differ from adults. In April of 2020, reports emerged from the UK of a presentation in children similar to incomplete Kawasaki disease (KD) or toxic shock syndrome .Since then, there have been increasing reports of similarly affected children in other parts of the world]. The syndrome has been termed multisystem inflammatory syndrome in children (MIS-C; also referred to as pediatric multisystem inflammatory syndrome [PMIS], pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 [PIMS-TS], pediatric hyper inflammatory syndrome, or pediatric hyperinflammatory shock.

EPIDEMIOLOGY

While the incidence of MIS-C is unknown, it appears to be a rare complication of COVID-19 in children. Though the initial reports are from UK, similar cases were reported from across the globe including US, Canada and Europe.

Many children with MIS-C meet criteria for complete or incomplete Kawasaki disease (KD). However, the epidemiology differs from that of classic KD. Most MIS-C cases have occurred in older children and adolescents who were previously healthy, with predilection for black and Hispanic children and less commonly in children of Ascian decent. However, by contrast, classic KD typically affects

infants and young children and has a higher incidence in East Asia and in children of Asian descent. MIS-C also differs from that of acute COVID-19 illness in children, which tends to be most severe in infants <1 year of age and in children with underlying health problems. The average age was 9 to 11 years (range 1 to 17 years).The most commonly reported comorbidities were obesity and asthma.

There seems to be a lag of several weeks between the peak of COVID-19 cases within communities to the peak of MIS-C cases. This 3 to 4 week lag coincides with the timing of acquired immunity suggesting that MIS-C may indicate a post-infectious complication of the virus rather than cute infection.

PATHOPHYSIOLOGY

The pathophysiology of MIS-C is poorly understood. It has been suggested that the syndrome results from an abnormal immune response to the virus, with some similarities to Kawasaki disease (KD), macrophage activation syndrome (MAS), and cytokine release syndrome. The mechanisms by which SARS-CoV-2 triggers the abnormal immune response are unknown. A postinfectious process is speculated, based on the timing of the rise of these cases relative to the peak of COVID-19 cases in communities, as discussed above.

Many affected children have negative polymerase chain reaction (PCR) testing for SARS-CoV-2 but have positive serology that further supports the hypothesis that MIS-C is related to immune dysregulation occurring after acute infection has passed. However, some children do have positive PCR testing, while few were negative for both PCR and serology. Infection with COVID-19 triggers the formation of antibodies to viral surface epitopes. Virus neutralization is a direct function of the stochiometric concentration and affinity of the antibodies. It is speculated that low titer non-neutralizing antibodies may exaggerate virus induced immune responses instead, thereby increasing the risk of severe illness in affected individuals . It is hypothesized that antibody dependent enhancement (ADE) responses have been implicated in COVID-19 induced immune injury.Although, evidence base for this pathway is demonstrated for coronaviruses, the exact role in PIMS-TS is only speculative .

PRESENTING SYMPTOMS

Box 1. Clinical features

All Persistent fever >38.5ºC	**Some** • Abdominal pain • Confusion • Conjunctivitis • Cough • Diarrhea • Headache • Lymphadenopathy • Mucus membrane changes • Neck swelling • Rash • Respiratory symptoms • Sore throat • Swollen hands and feet • Syncope • Vomiting
Most Oxygen requirement Hypotension	

The median duration of fever is four days and gastrointestinal symptoms mimicking acute appendicitis arecommon and some children have been noted to have terminal ileitis on abdominal imaging and/or colitis on colonoscopy. Children may present with 3-4 days of fever, then went onto develop vasodilatory/distributive shock which is often resistant to volume resuscitation, needing inotrope administration.Lung involvement was uncommon in most cases, though many children required supplemental oxygen or positive pressure ventilation for cardiovascular stabilization. Respiratory symptoms (tachypnea, labored breathing), when present, were most often due to severe shock. Cough was uncommon.

CLINICAL FINDINGS

- Shock – 50 to 80 percent
- Criteria met for complete Kawasaki disease (KD) (table 2) – 22 to 64 percent
- Myocardial dysfunction (by echocardiogram or elevated troponin) – 51 to 100 percent
- Acute respiratory failure requiring noninvasive or invasive ventilation – 43 to 52 percent
- Acute kidney injury (most cases were mild) – 22 to 70 percent
- Serositis (small pleural, pericardial, and ascitic effusions) – 24 to 57 percent
- Acute hepatic failure – 21 percent

There appears to be a wide sprectrum of disease severity of MIS-C.The initial reported case series represent more severe end of the spectrum with, higher incidence of shock,myocarditis and respiratory failure while in the milder variety of MIC-s, the incidence of shock,LV dysfunction, respiratory failure and AKI appear to be less.

LABORATORY FINDINGS

Box 2. Laboratory Features

All
- Abnormal fibrinogen
- High CRP
- High D-dimers
- High Ferritin
- Hypoalbuminaemia
- Lymphopenia

Most
- Neutrophilia
- Elevated pro-BNP

Some
- Acute kidney injury
- Anaemia
- Coagulopathy
- High IL-10
- High IL-6
- Proteinuria
- Raised CK
- Raised LDH
- Raised triglycerides
- Raised troponin
- Thrombocytopenia
- Transaminitis
- Normal neutrophils in some cases

Laboratory markers of inflammation appear to correlate with severity of illness. children who developed shock had higher CRP, lower lymphocyte counts, and lower serum albumin compared with children withoutshock . Elevated cardiac markers (Troponin-T or Pro BNP) are common in children with shock.

- **Echocardiography** – Echocardiographic findings may include depressed LV function (30% -60%) and coronary artery (CA) abnormalities 14-50%(including dilation or aneurysm), mitral valve regurgitation, and pericardial effusion The frequency of cardiac involvement in MIS-C is uncertain and the risk of cardiac involvement appear less in milder cases.
- **Chest radiograph** – Many patients had normal chest radiographs. Abnormal findings included small pleural effusions, patchy consolidations, focal consolidation, and atelectasis.
- **Computed tomography (CT) of chest** – Chest CT (when obtained) generally had findings similar to those on chest radiograph. A few patients had nodular ground-glass opacification.
- **Abdominal imaging** – Findings on abdominal ultrasound or CT included free fluid, ascites, and bowel and mesenteric inflammation including terminal ileitis, mesenteric adenopathy/adenitis, and pericholecystic edema .

CASE DEFINITION

The criteria used for case definition vary slightly between different health agencies . For example, the Centers for Disease Control and Prevention (CDC) case definition requires that the child have severe symptoms requiring hospitalization, whereas the World Health Organization (WHO) case does not.

CDC case definition

Centers for Disease Controland Prevention (UnitedStates)[9]
An individual aged <21 y presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, kidney, respiratory, hematologic, gastrointestinal, dermatologic, or neurological)
Fever > 38.0° C for ≥ 24 h or report of subjective fever lasting ≥ 24h
Laboratory evidence including, but not limited to, ≥1 of the following: an elevated CRP level, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase, or IL-6; elevated neutrophils; reduced lymphocytes; and low albumin
AND No alternative plausible diagnoses
AND Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 wk prior to the onset of symptoms
Additional comments Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

WHO case definition

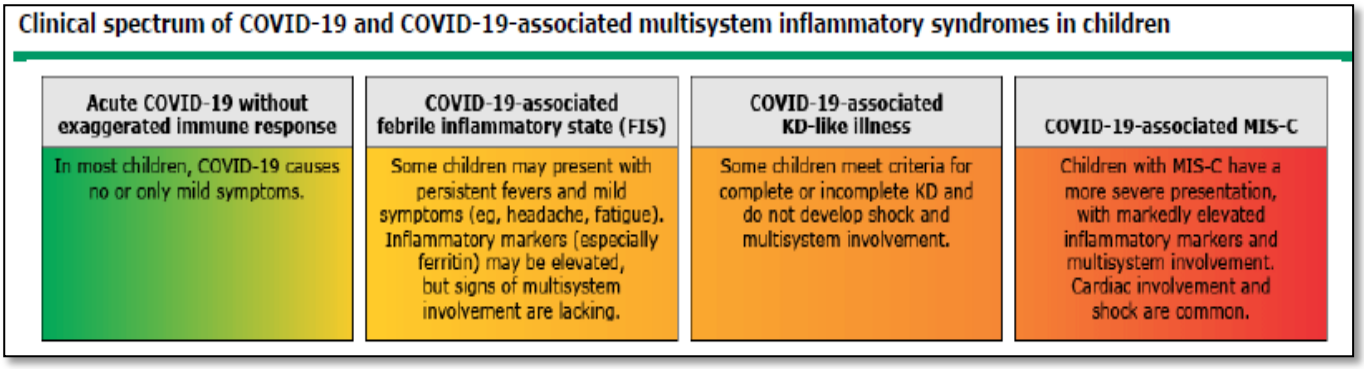
World Health Organization[8]
Children and adolescents 0-19 y of age with fever >3 d AND 2 of the following: 1.Rash or bilateral non purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet) 2.Hypotension or shock 3.Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP) 4.Evidence of coagulopathy (by PT, APTT, elevated D-dimers) 5.Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)
AND Elevated markers of inflammation such as ESR, CRP, or procalcitonin.
AND No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.
AND Evidence of COVID-19 (RT-PCR, antigen test, or serology positive), or likely contact with patients with COVID-19 Consider this syndrome in children with features of typical or atypical Kawasaki disease or toxic shock syndrome

RCPCH case definition

Royal College of Paediatrics and Child Health (United Kingdom)[7]
A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP, and lymphopenia) and evidence of single or multi organ dysfunction (shock, cardiac, respiratory, kidney, gastrointestinal, or neurological disorder) with additional features (see listed in eAppendix in Supplement 2). This may include children fulfilling full or partial criteria for Kawasaki disease[a] Exclusion of any other microbial with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice) SARS-CoV-2 PCR test results may be positive or negative

Spectrum of disease

As more is learned about COVID-19 and MIS-C in children, it is becoming apparent that the spectrum of disease ranges from mild to severe our understanding of the full spectrum, including subphenotypes, is evolving.



EVALUATION

Patients with suspected MIS-C should have laboratory studies performed to assess for evidence of inflammation as well as cardiac, renal, and hepatic involvement. Testing should also include polymerase chain reaction (PCR) and/or serology for SARS-CoV-2. In addition, patients should be assessed for other infectious or noninfectious conditions that may have a similar presentation. The American College of Rheumatology (ACR) MIS-C and COVID-19 Related Hyperinflammation Task Force has published preliminary diagnostic guidelines that are consistent with our approach outlined below .

Laboratory testing — The initial laboratory evaluation of a child with suspected MIS-C depends on the presentation.

Moderate to severe – For children with moderate to severe symptoms, the following are suggested

- Complete blood cell count with differential
- C-reactive protein and erythrocyte sedimentation rate (optional: procalcitonin)
- Ferritin level
- Liver function tests and lactate dehydrogenase
- Serum electrolytes and renal function tests
- Urinalysis
- Coagulation studies (prothrombin time/international normalized ratio, activated partial thromboplastin time, D-dimer, fibrinogen, antithrombin- 3)
- Troponin
- Brain natriuretic peptide (BNP), or NT-pro-BNP
- Cytokine panel (if available)

Inflammatory markers (C-reactive protein, erythrocyte sedimentation rate, procalcitonin, ferritin) are measured at the time of admission and then serially to monitor progression.

- **Well-appearing** – For patients presenting with fever for ≥3 days and who are well-appearing with only mild symptoms suggestive of MIS-C, it is reasonable to perform a more limited evaluation

initially. For example, it may be reasonable to start with a complete blood count and C-reactive protein and then obtain additional testing only if these are abnormal.

Testing for SARS-CoV-2 — All patients should be tested for COVID-19, including both serology and RT-PCR on a nasopharyngeal swab.

Testing for other pathogens — Testing for other viral and bacterial pathogens includes

- Blood culture
- Urine culture
- Throat culture
- Stool culture
- Nasopharyngeal aspirate or throat swab for respiratory viral panel (EBV,CMV,Enterovirus,Adeno virus)

This testing is appropriate for children with moderate to severe MIS-C (ie, children who require hospitalization). However, an extensive infectious work-up is generally not necessary in well-appearing children presenting with mild symptoms. In such patients, microbiologic testing should be done as clinically indicated according to the age of the child and his/her specific symptoms (eg, throat culture if the child has sore throat, respiratory viral panel if there are respiratory symptoms). Testing should follow the same general approach as is used for fever evaluation more broadly.

Cardiac testing — In addition to troponin and BNP/NT-pro-BNP levels, the cardiac evaluation of a patient with suspected MIS-C includes a 12-lead electrocardiogram (ECG) and echocardiography. Echocardiography is also recommended for children with documented SARS-CoV-2 who do not meet all criteria for MIS-C but who have either shock or features consistent with incomplete or complete Kawasaki disease (KD).

In children with MIS-C, baseline ECGs may be nonspecific, though arrhythmia and heart block have been described . Findings on initial echocardiography may include CA dilation, left ventricular (LV) systolic dysfunction, and pericardial effusion. The CA abnormalities can progress to aneurysm, including giant coronary aneurysms

The echocardiographic evaluation should include:

- Quantitative assessment of LV size and systolic function (LV end-diastolic volume, ejection fraction)
- Qualitative assessment of right ventricular systolic function
- CA abnormalities (dilation or aneurysm)
- Assessment of valvar function
- Evaluation for the presence and size of pericardial effusion
- Evaluation for intracardiac thrombosis and/or pulmonary artery thrombosis, particularly apical thrombus in severe LV dysfunction

DIFFERENTIAL DIAGNOSIS

In children presenting with signs and symptoms consistent with MIS-C, the differential diagnosis is broad and includes other infectious and inflammatory conditions:

1.Bacterial sepsis – Bacterial sepsis is an important consideration in children presenting with fever, shock, and elevated inflammatory markers. All children with suspected moderate to severe MIS-C should have blood cultures sent, and empiric antibiotics should be administered pending culture results.

- **2. Kawasaki disease (KD)** – Some children along the MIS-C spectrum meet criteria for complete or incomplete KD . However, there appear to be some key differences:
  - MIS-C appears to affect older children and adolescents, whereas classic KD typically affects infants and young children
  - Gastrointestinal symptoms (particularly abdominal pain) are very common in MIS-C; whereas these symptoms are less prominent in classic KD
  - Myocardial dysfunction and shock occur more commonly in MIS-C compared with classic KD
  - Inflammatory markers (especially ferritin and D-dimer) tend to be more elevated in MIS-C compared with KD [10]

Ultimately, the designation of MIS-C versus KD is based on SARS-CoV-2 testing. Patients with positive SARS-CoV-2 testing (or with an exposure to an individual with COVID-19) who also fulfill full or partial criteria for KD should be considered to have MIS-C and should receive standard treatments for KD.

- **3.Toxic shock syndrome** – Staphylococcal and streptococcal toxic shock syndromes share many similarities with MIS-C . Microbiologic tests (ie, SARS-CoV-2 testing, bacterial cultures) are necessary to make the distinction.

- **4. Appendicitis** – As discussed above, many children with MIS-C present with fever associated with abdominal pain and vomiting. This can mimic the presentation of acute appendicitis. Abdominal imaging may be necessary to make the distinction.

- **5. Other viral infections** – Other viral pathogens that may manifest with multisystem involvement and/or myocarditis include Epstein-Barr virus, cytomegalovirus, adenovirus, and enteroviruses. These viruses rarely cause severe multisystem disease in immunocompetent children. Serology and polymerase chain reaction (PCR) testing can distinguish these from COVID-19-related MIS-C.

- **6. Hemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS)** – HLH and MAS are aggressive and life-threatening conditions that have some features in common with MIS-C. HLH/MAS are syndromes of excessive immune activation that can occur in previously healthy children (often triggered by an infection) and in children with underlying rheumatologic conditions. Most children with HLH/MAS are acutely ill with multiorgan involvement, cytopenias, liver function

abnormalities, and neurologic symptoms. Cardiac and gastrointestinal involvement are less common, and neurologic symptoms are more prominent. The diagnosis of MAS/HLH requires specialized immunologic testing,

- **7.Systemic lupus erythematosus (SLE)** – SLE can present with fulminant multisystem illness. Such patients generally have considerable kidney and central nervous system involvement, which are not common features of MIS-C. In addition, though patients with SLE may present acutely with fulminant illness, most report feeling fatigued and unwell for an extended period of time prior to the onset of severe symptoms. This is not the case with MIS-C, in which most children are completely well prior to acute onset of febrile illness.

- **8. Vasculitis** – Other vasculitides can present with fevers, rash, and elevated inflammatory markers. Rashes seen in COVID-19-associated illness can have an appearance that can mimics vasculitis (eg, pernio [chilblain]-like lesions of acral surfaces, sometimes referred to as "COVID toes", but they are not vasculitic.

MANAGEMENT

The level of care is determined by the severity of illness. Children with moderate to severe signs and symptoms should be admitted to the hospital .Admission to a pediatric intensive care unit is appropriate for children with hemodynamic instability (shock, arrhythmia), significant respiratory compromise, or other potentially life-threatening complications.It may be reasonable to manage select patients with mild symptoms in the outpatient setting. However, given the uncertainty regarding the risk of progression from mild to severe, hospital admission is advised for patients who have markedly elevated inflammatory markers so that levels can be monitored until trending down.

For children who are managed in the outpatient setting, it is critical to provide instructions for when to seek care and to ensure appropriate follow-up. Most children should have follow-up within 48 hours if persistently febrile. Follow-up should include clinical assessment and repeat laboratory testing.

Multidisciplinary care — By definition, MIS-C is a multisystem disease, and care for affected children requires coordination of many different specialties. This may include:

- Pediatric infectious disease specialists
- Pediatric rheumatologists
- Pediatric cardiologists
- Pediatric intensivists
- Pediatric hematologists

Antimicrobial therapy

Antibiotic therapy — MIS-C can present with signs and symptoms that mimic those of septic shock and toxic shock syndrome. Thus, patients presenting with severe multisystem involvement, particularly those with shock, should receive prompt empiric broad-spectrum antibiotic therapy pending culture results. Choice of antibiotics is decided by local unit protocols, guided by antibiotic sensitivity patterns. Antibiotics should be discontinued once bacterial infection has been excluded if the child's clinical status has stabilized.

Antiviral therapy — The role of SARS-CoV-2 antiviral therapies (eg, Remdesivir) in the management of MIS-C is uncertain. Many patients are polymerase chain reaction (PCR)-negative for SARS-CoV-2, and MIS-C likely represents a postinfectious complication rather than active infection . However, some children do have positive PCR testing and may have active infection. Thus, antiviral therapy may have potential to impact the disease process in some, but not all, patients. Use of antiviral agents is generally limited to children with severe MIS-C manifestations.

Additional therapy based on presentation — Additional therapy depends on the clinical presentation. These presentations can overlap, and it may be appropriate to provide interventions from more than one category. For example, patients presenting with Kawasaki disease (KD) with associated distributive shock should receive treatment for KD (ie intravenous immune globulin [IVIG 2 grams/kg] and Aspirin (30-50 mg/kg/day followed by 5mg/kg/day) and appropriate hemodynamic support (ie, volume expansion and epinephrine).

Shock — Children presenting with shock should be resuscitated according to standard protocols. In the available case series, most children with MIS-C presented with vasodilatory shock that was refractory to volume expansion. Epinephrine or norepinephrine are the preferred vasoactive agents for the management of fluid-refractory shock in children; epinephrine is preferred when there is evidence of ventricular dysfunction. In children presenting with severe ventricular dysfunction, the addition of milrinone may be helpful.

Myocardial dysfunction — During the acute inflammatory phase of illness, children with myocardial dysfunction may present with arrhythmias and hemodynamic compromise. Serial echocardiographic assessment of cardiac function and monitoring of brain natriuretic peptide (BNP) and troponin levels can help guide therapy. Management focuses on supportive care to maintain hemodynamic stability and ensure adequate systemic perfusion. IVIG is often used in severe cases when the clinical picture is consistent with myocarditis, though conclusive evidence of benefit is lacking. Continuous cardiac monitoring is essential so that arrhythmias are promptly detected and treated. Patients with significant ventricular dysfunction are treated with intravenous diuretics and inotropic agents, such as milrinone, dopamine, and dobutamine. In cases of fulminant disease, mechanical hemodynamic support may be necessary in the form of extracorporeal membrane oxygenation (ECMO) or a ventricular assist device.

Adjunctive immune-modifying therapies — The benefits and risks of adjunctive therapies (glucocorticoids, interleukin-1 [IL-1] inhibitors [eg, anakinra, canakinumab], IL-6 inhibitors [eg,

tocilizumab], convalescent plasma from recovered COVID-19 patients) are uncertain. Consultation with pediatric infectious disease and rheumatology specialists is advised. Decisions about the use of adjunctive therapies should be made on a case-by-case basis, according to disease severity and markers of inflammation or active SARS-CoV-2 infection. Glucocorticoids are appropriate for patients with features of KD who have persistent fever after IVIG or CA dilation/aneurysm . In addition, glucocorticoids (pulse intravenous methylprednisolone 10 mg/kg/day for 3 days followed by oral prednisolone in a gradual tapering regimen) can be considered for patients with cytokine release syndrome (CRS; also called cytokine storm, which is characterized by persistent fever, markedly elevated inflammatory markers [eg, C-reactive protein, D-dimer, ferritin] and elevated proinflammatory cytokines [eg, IL-6]). tocilizumab (8 mg/kg), Infliximab (5mg/kg) are alternative options for treatment of CRS in patients who cannot receive glucocorticoids and those who are refractory to glucocorticoids. Such decisions should be made under the direction of a pediatric rheumatologist and should occur in the context of a clinical trial whenever possible.

OUTCOME & FUTURE DIRECTIONS

The prognosis of MIS-C is uncertain, given that it is a new clinical entity and our understanding of the disease is still evolving. Though MIS-C has many similarities to Kawasaki disease (KD) and toxic shock syndrome, it is clear that the disease course in MIS-C can be more severe, with many children requiring intensive care interventions. Most children survive, but there have been several deaths reported. Understanding the mechanisms of the exaggerated immune response in MIS-C is an area of active investigation and more research is needed for potential role of other therapies like IL-1, IL-6 and Anti-TNF blockage in MIS-C.

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IMAGE QUIZ

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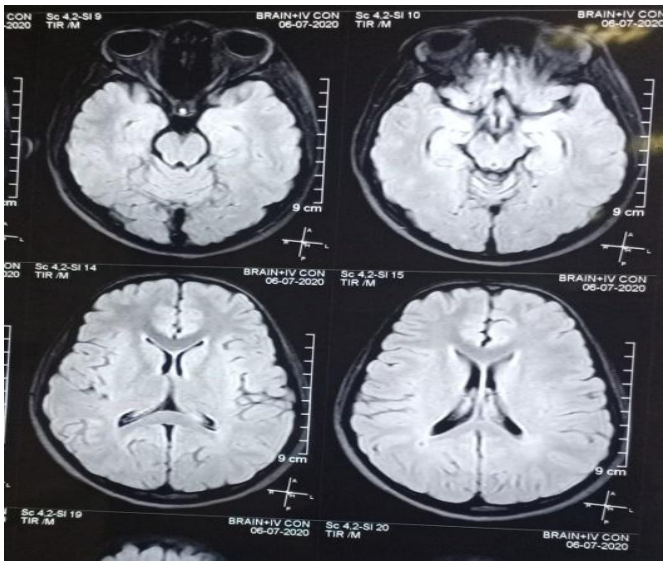
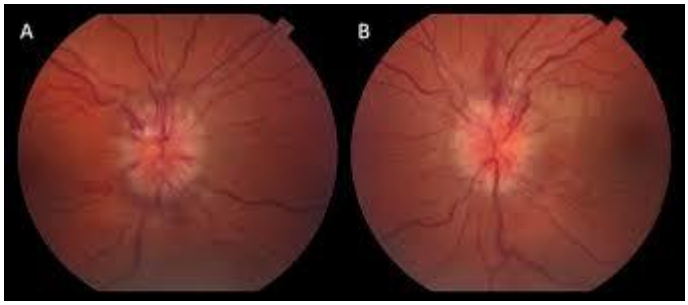
DNB (Ped) Resident

A 13 years old female was admitted with front-ooccipital headache since 20 days, acute onset, gradually progressive and associated with non bilious, projectile vomiting's since 20 days (5 to 6 episodes per day) and, 2 episodes of loss of consciousness for 5 minutes with spontaneous recovery. Child has h/o menorrhagia for the past 1 month, which was suspected to be PID, and treated with tranexamic acid and doxycycline for 5 days in a out-side hospital. There was no H/o fever, cough, breathlessness, or loose stools. On examination, child was hemodynamically stable with a HR 80 b/m, BP – 110/80 (77) mm Hg, RR – 18 breath/ min. On investigation, Hb – 7.8, WCC -12500, platelets – 312000, CRP –Ve, normal electrolytes, USG abdomen → Normal, and normal Renal, Liver function. Child was started on analgesics & PPI but headache has not subsided. Fundus examination showed B/L papilloedema, and MRI brain was normal. A lumbar puncture demonstrated high opening pressure and a normal CSF analysis .





1. What is your diagnosis?
2. How do you treat it?

ANSWERS :

1. **IDIOPATHIC INTRACRANIAL HYPERTENSION**
2. Child was started on Acetazolamide with Topiramate. I unit PRBC transfusion given with discharge & advised regular ophthalmology & neurologist review.

Idiopathic Intra-cranial Hypertension

Definition:

- IIH is characterized by increased intracranial pressure (Pressure around the brain) without a detectable cause.
- Normal CSF pressure in children 2 to 5 years – 10 mm of Hg.
- Adult level of CSF pressure is reached by 8 years of age.
- Currently the 90th percentile of CSF pressure on lumber puncture has been reported to be 22 mm of Hg in children 1 to 18 years without a significant age after.

Etiology:

Primary IIH: Will not have identifiable cause: A large proportion of children referred to the pediatrician with possible or probable IIH after a through history, examination and careful investigation will have secondary intracranial hypotension.

Secondary IIH:

Infection: acute sinusitis, otitis media, mastoidites tonsillitis, measles VZV.

- Nutritional disorders: Hypervitaminosis, vitamin A intoxication, Vitamin D dependent rickets.
- Hematological: Iron deficiency anemia, wiskott aldrich syndrome, aplastic anemia, sickle cell disease, fanconi anemia
- Drugs: Tetracycline, salfonamide, nalidixic acid fluoroquinolones, nitrofurantoin, phenytoin, amiodarone, corticosteroids, withdral ocp
- Renal disorder: Nephrotic syndrome, chronic renal insufficiency.
- Endocrine causes: PCOD, hypoparathyroidism, ADH, hypothyroidism

Clinical features:

- Chronic (weeks to months) progressive frontal headache may worsen with postural changes associated with vomitings
- Transient visual obscuration lasting seconds and diplopia (secondary to 6th nerve damage) also occurs pulsatile tinnitus.
- Papilloedema with an enlarged blind spot is the most consistent sign.

Investigations:

- All children should undergo cranial MRI brain, which may show papilloedema (or) enlargement of optic nerve sheath/ pituitary fossa.
- MR venography is essential, both to exclude a venous thrombosis and to identify the tapering of lateral sinuses that commonly seen in intracranial HTN.

- Measurement of CSF pressure, electronic transducer which will give a computer aided record with wave from analysis both on openly and steady state for 20 min
- When lumbar puncture done in general anaesthesia, it is important to record a normal end tidal postal pressure of CO2 (ET – CO2)

Diagnostic criteria for TIH

Diagnosis of IIH is definite If patient satisfies full criteria from A to E

A . Papilloedema

B. Normal neurologist exams except 6th nerve palsy.

C. Neuroimaging – Normal brain parenchyma without evidence of hydrocephalus, mass structural lesion, with no abnormal meningeal enhancement.

D. Normal CSF composition.

E. Elevated lumbar puncture opening pressure (> 250 mm of Hg) in adult > 280 mm of Hg in children – A properly performed LP.

Diagnosis of IIH without papilloedema

- In absence of papilloedema, a diagnosis of IIH can be made if B-E are satisfied, patient had unilateral/bilateral abducent nerse palsy
- In the absence of papilloedema or sixth nerve palsy a diagnosis of IIH can be suggested but not made if B – E are satisfied. Atleast 3 of the following are present on Neuroimaging.
    1. Empty sella
    2. flattening of posterior aspect of the globe
    3. Distension to the penoptic subarchnoid space with or without tortous optic nerve.
    4. Transvers venous sinus stenosis

Management:

- There are no randomized control trials to guide the treatment of IIH.
- Secondary IH should be treated.
- Acetazolamide (10 – 30 mg / 24 hrs probably an effective regimen
- Corticosteroid used only in severe IIH, risk of losing visual function and awaiting surgical intervention for venticuloperitoneal shunt or lumboperitoneal shunt
- Optic nerve sheath fenestration may also be attempted in refractory situation of IIH

Complications- optic atrophy and visual impairment

Follow Up:

Serial monitoring of visual function (visual acuity, color vision, visual field)

Optical coheerance tomogratphy for papilloedema changes.