Age is no barrier to Kawasaki disease

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Introduction

-**Kawasaki disease (KD)** is a common childhood vasculitis, mainly affecting children between 2-5 years of age.

-Rarely been reported in **infants less than 6 months of age**.

-Infants with KD have **higher incidence of incomplete form of KD as well as coronary artery abnormalities (CAAs).**

Case Details

2-month-old girl presented with-

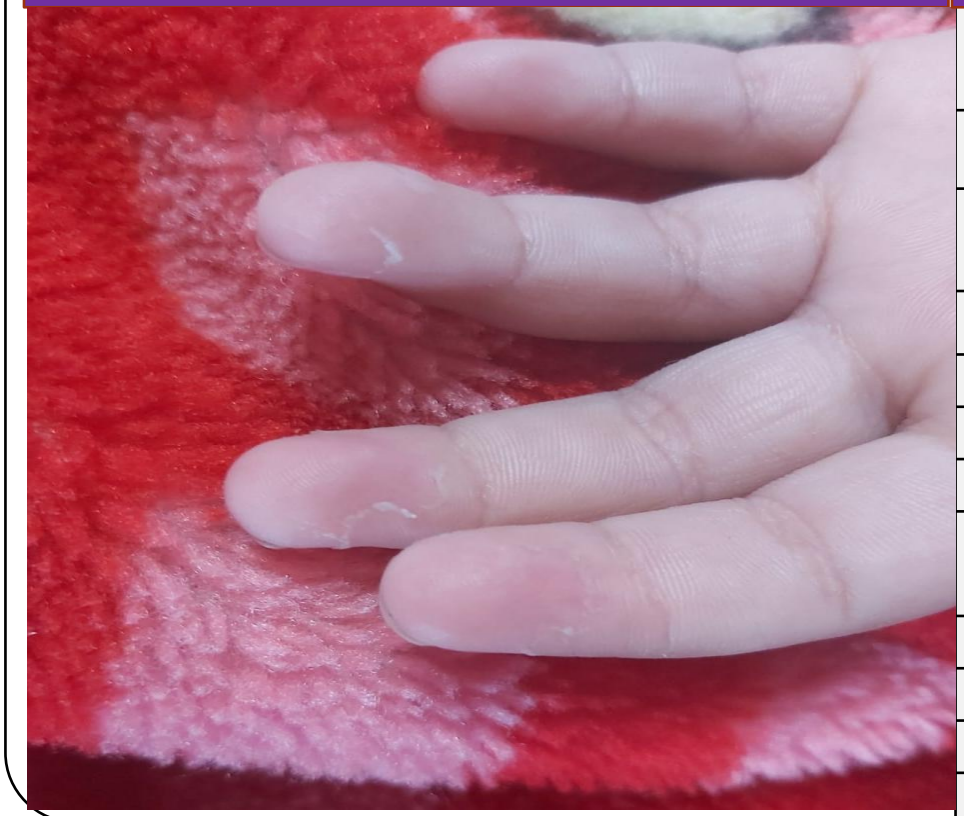
High grade fever with irritability for 7 days, managed outside as acute febrile illness.

In view of no relief and increased irritability, baby was referred to RH Bilaspur for further management.

On examination-

-Febrile
-Irritable
-Conjunctival injection
-Generalized maculopapular rash
-Bilateral cervical LAP

- On day 2 of admission, he developed bilateral periungual desquamation



Laboratory investigation	Results
Hemoglobin (g/L)	9.6
Leucocyte count (× 10^9/ L)	25.2 ($N_{82\%}L_{16\%}$)
Platelet count (× 10^9/ L)	900
ESR (mm in 1st hour)	100
CRP (mg/L)	200
RFT	Normal
LFT	Mild transminitis(1.5 times)
Na/K (Meq/L)	132/4.4
Blood culture	Sterile
Urine (R/E)	Streile PYURIA
Covid 19 RT PCR	Negative

Result

Two-dimensional echocardiography showed **giant aneurysms in proximal left anterior descending coronary artery (5 mm; 14.1z) and ecstatic left main and right coronary artery.**

- Fever with irritability - Conjunctival injection - LAP - Periungual desquamation - CAAs	-Neutrophilic leukocytosis with thrombocytosis -Raised markers of inflammation -Mild transaminitis with mild hyponatremia -Sterile cultures

Diagnosis – INCOMPLETE INFANTILE KAWASAKI DISEASE WITH GIANT CAAs

Treatment-

Intravenous infliximab (8 mg/kg), **intravenous immunoglobulin** (2 gm/kg) and **oral aspirin** (30 mg/kg/day).

Irritability and fever subsided in next 24 hours and inflammatory parameters decreased over next 7-10 days.

Discharged on subcutaneous enoxaparin (1 mg/kg 12 hourly), **low dose aspirin** (5 mg/kg/day) and was kept on follow-up

Conclusion

-**No age is barrier to KD**

-**Younger age (infancy) is a risk factor for CAAs**

and may also **pose diagnostic challenge** due to rarity of KD in children < 6 months of age

An uncommon overlap of Kawasaki disease and Henoch- Schonlein Purpura

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Introduction

- Kawasaki disease (KD) and Henoch-Schonlein purpura (HSP) are the most common childhood vasculitic disorders

- Overlap of 2 rheumatological disorders has been described but overlap of KD and HSP is extremely unusual

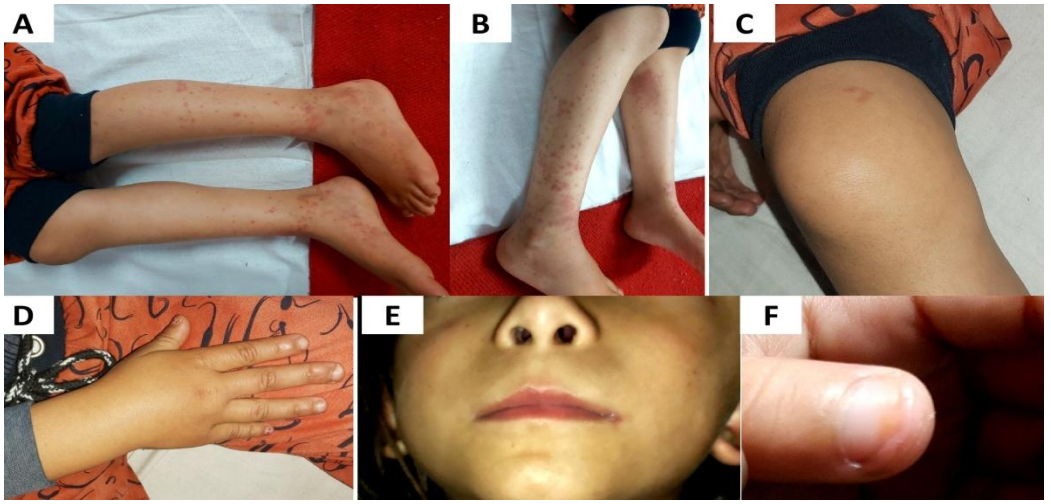
Case Details

7-year-old girl presented with –

- Fever × 10 days
- Swelling multiple joints × 5 days
- Erythematous rash on lower limbs × 5 days
- H/o redness of eyes at day 2 of fever , subsided after 3 days
- H/o strawberry tongue

Examination-

- Febrile and Irritable
- Posterior cervical LAP (2×1 cm)
- Non-pitting edema on hands and feet (D)
- Periungual desquamation (F)
- Red cracked lips (E)
- Palpable purpura on lower limbs (A and B)
- Swelling bilateral ankle, knee and wrist joints (C)

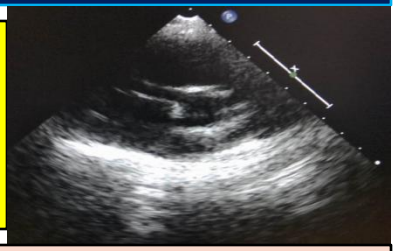


Laboratory investigation	Results
Hemoglobin (g/L)	128
Leucocyte count (× 10^9/ L)	20.4 ($N_{87\%}L_{7\%}$)
Platelet count (× 10^9/ L)	458
ESR (mm in 1st hour)	14
CRP (mg/L)	94.8
Blood urea (mg/dl)	11
Creatinine (mg/dl)	0.28
Na/K (Meq/L)	144/4.4
ASO (Todd)	> 200 <400
Urine (R/E)	Normal

Result

2-D Echo – Aneurysm RCA and LMCA (RCA 5mm, 6.5z; LMCA-5mm, 6.1z)

Skin biopsy- – leucocytoclastic vasculitis



- Fever - Conjunctival injection - Strawberry tongue - LAP - Non pitting edema of hands and feet - Periungual desquamation - CAAs	- Palpable purpura on lower limbs - Arthritis - Leucocytoclastic vasculitis

Diagnosis – Overlap of Kawasaki disease and Henoch – Schonlein purpura

Treatment- Aspirin – 50 mg/kg/day followed by 3mg/kg/day
- Intravenous immunoglobulin – 2 gm/kg
- Her fever and irritability subsided in next 24 hours and arthritis and rash in 4 days
- Discharged and kept on follow up

Conclusion

- Two or more rheumatological disorders may coexist at the same time
- An overlap of KD and HSP is extremely rare and one must always be vigilant

Kawasaki disease with concomitant chicken pox: An unusual occurrence

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Introduction

- Kawasaki disease (KD) is a common childhood vasculitis
- The etiology of KD is still unknown but various infections have been implicated as trigger for it

Case Details

A 7-year-old girl presented with

- High grade fever for 5 days
- Rash for 5 days
- Redness of eyes for 2 days

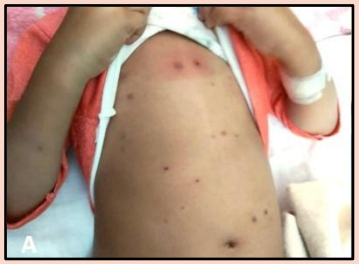
Day 1
- Erythematous papules and
- Fluid filled vesicles on abdomen

Day 2
- Vesicles progressed to the trunk, face and limbs

Day 3
- Various vesicles evolved into scabs
- Developed conjunctival injection

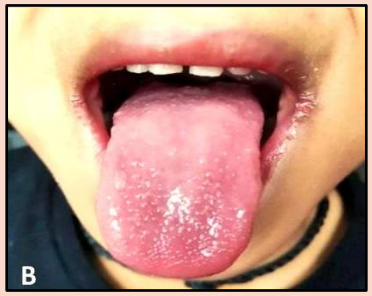
There was H/O chicken pox in one of sibling 10 days prior to her illness

On Examination



Generalized papulovesicular rash with few lesions with scabs (A)

Cracked red lips, strawberry tongue (B)



Conjunctival injection (C)

Perianal and periungual desquamation on day 3rd of admission (D)

Laboratory investigation	Results
Hemoglobin (g/L)	103
Leucocyte Count (× 10^9/ L)	15.57 (P_{92} L_6 M_2)
Platelet Count (× 10^9/ L)	114

Laboratory investigation	Results
ESR (mm in 1st hour)	19
CRP (mg/L)	168.5
Varicella Immunoglobulin M (IgM)	Positive

Result

- Fever
- Conjunctival injection
- Cracked red lips, strawberry tongue
- Perianal and periungual desquamation
- LAP

KD

- Generalized papulovesicular rash with few lesions with scabs
- H/O chicken pox in sibling
- Varicella Immunoglobulin M (IgM)- Positive

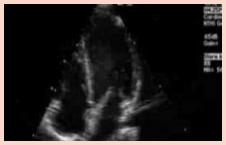
Varicella

Diagnosis – Kawasaki disease with concomitant chicken pox

Treatment

- Intravenous immunoglobulin : 2 gm/kg
- Aspirin : 4 mg/kg/day

✓ Her fever subsided in next 24 hours.
✓ 2D Echo was normal
✓ Discharged and kept on follow up



Conclusion

- KD triggered by varicella infection has been reported earlier but concomitant chicken pox and KD has rarely been reported
- The etiology of KD is still elusive but concomitant occurrence of various infections can help in elucidating it

ATYPICAL KAWASAKI DISEASE

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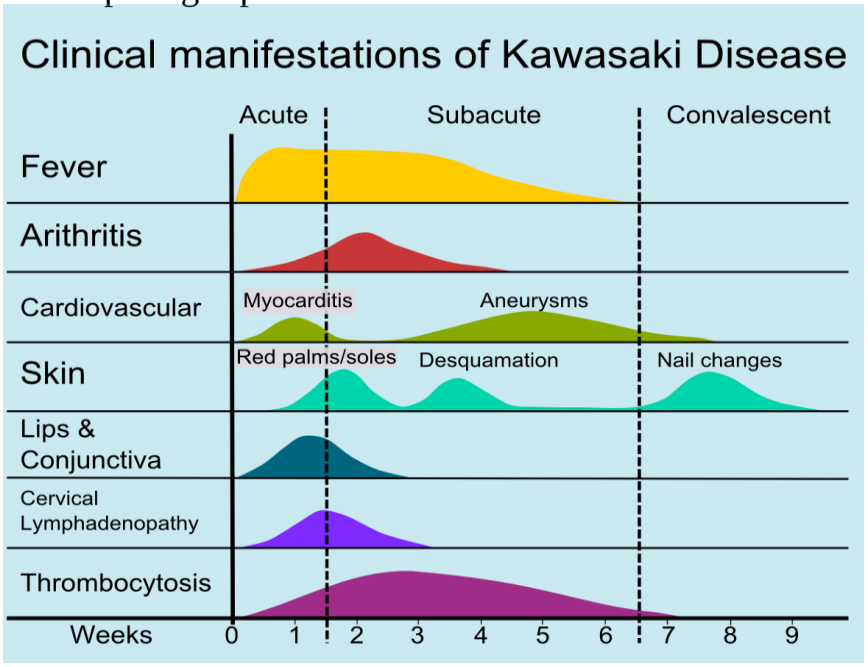
Introduction:

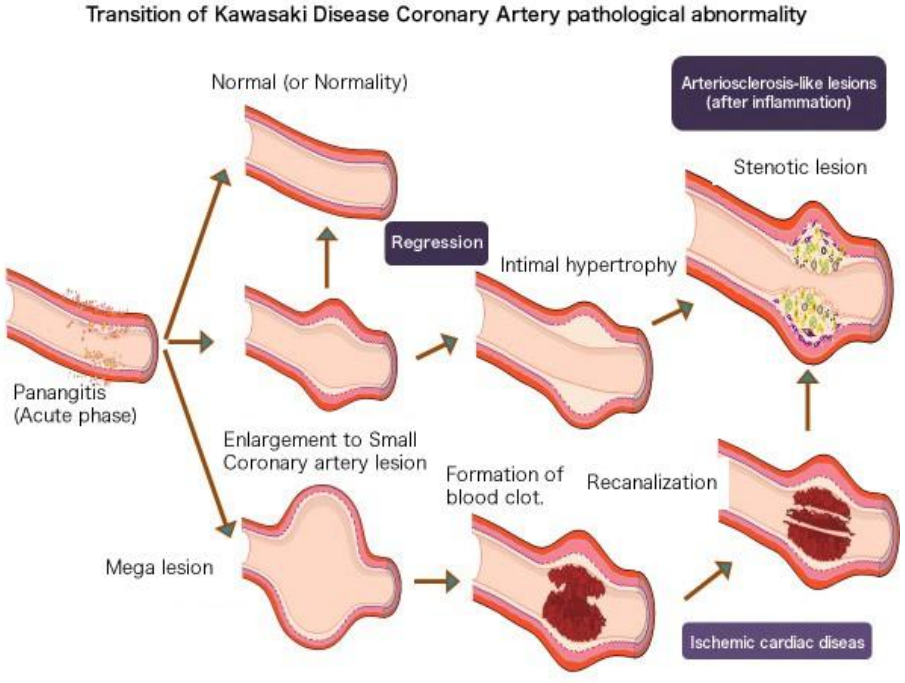
Kawasaki disease is an acute systemic vasculitis and is the most common cause of acquired heart disease in children in the developed world. The disease is believed to result from a genetically susceptible individual's exposure to an environmental trigger. Incidence is rising worldwide, and varies widely across countries and within different ethnic groups. It has surpassed rheumatic heart disease as the leading cause of acquired cardiovascular disease in children in the developed world.

Atypical Kawasaki disease usually affects infants and toddlers and, due to delayed diagnosis and treatment, is strongly associated with an increased risk of permanent heart damage. Among the possible clinical presentations of atypical KD, isolated lung involvement is considered a very uncommon feature and most cases reported in literature involve children in the first year of life.

CASE REPORT:

3.5 year old male child was admitted with complaints of high grade fever since 10 days associated with a generalized erythematous rash and paradoxical crying. Examination revealed fissured lips, perianal excoriation and oedema over hands and feet with decreased right sided air entry. Radiography showed right middle and lower lobe consolidation with hemogram showing neutrophilic leucocytosis for which IV antibiotics(Ceftriaxone and Cloxacillin) and further oral Azithromycin was given. Cultures remaining sterile and child not responding to therapy, he was further worked up, USG chest showed right sided consolidation with no synpneumonic effusion , lab parameters showed elevated Pro-BNP, CRP and ESR, hyponatremia and hypoalbuminemia. 2D ECHO showed coronary artery dilatation (LAD , Z score 3.7).With a working diagnosis of Atypical Kawasaki disease, he was given IVIG @2g/kg and started on high dose Aspirin @80mg/kg/day. Fever and symptoms subsequently abated, the patient was discharged after 8-days hospitalization on Aspirin on tapering aspirin dose.





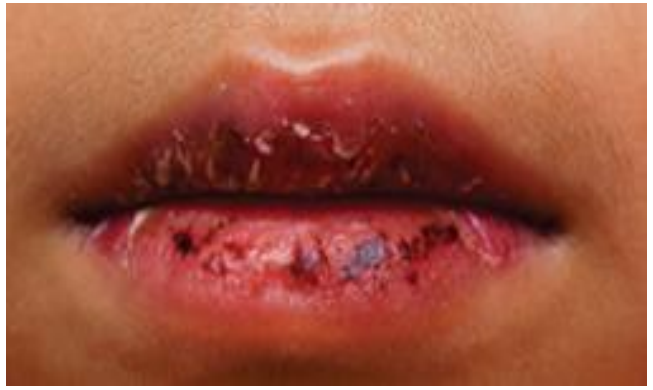
AHA Criteria for Kawasaki Disease

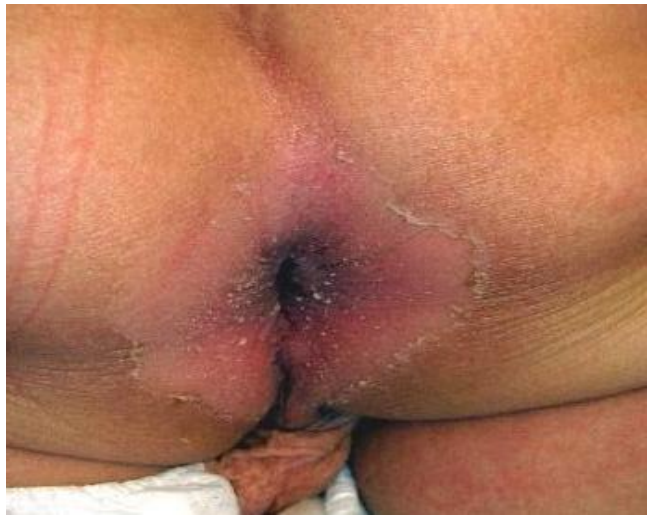
Fever persisting for ≥ 5 days

+ ≥ 4/5 of the following:

- ✓ Changes in the extremeties(edema/ erythema) or perineal area(erythema/peeling)
- ✓ Polymorphous exanthem
- ✓ Changes in lips or oral cavity(injection of oral and pharyngeal mucosa(injection of oral and pharyngeal mucosa, fissured lips, strawberry tongue)
- Bilateral conjunctival injection, non-exudative
- Cervical lymphadenopathy (frequently unilateral, ≥ 1.5 cm)

According to the diagnostic criteria of atypical Kawasaki disease established by the AHA, children ≥6 months of age with incomplete presentation might have unexplained fever for ≥5 days associated with 2 or 3 of the principal clinical features (compatible with 3 or 4 principal symptoms of the Japanese criteria) in the acute phase. The AHA recommended a diagnostic algorithm of incomplete Kawasaki disease which comprises of 6 supplemental laboratory and echocardiographic criteria(refer table). More than 3 laboratory criteria support the diagnosis of Atypical Kawasaki disease





(A)
Serum albumin ≤3.0 g/dL
Anemia for age
Elevation of alanine aminotransferase
Platlets after 7 days ≥450,000/mm^3
WBC ≥15,000/mm^3
Urine WBC≥10/HPF
(B)
Z score of LAD or RCA≥2.5
Coronary arteries meet Japanese Ministry of Health criteria for aneurysm[26]
Internal lumen diameter:
>3 mm in children <5 years old, or
>4 mm in children >5 years old
Of a segment measures ≥1.5 times that of an adjacent segment
Clearly irregular coronary lumen
Other 6 suggestive features (if ≥3 features, positive)
Perivascular brightness of coronary arteries
Lack of tapering of coronary arteries
Decreased LV function
Mitral regurgitation
Pericardial effusion
Z score in LAD or RCA of 2 to 2.5

Conclusion:

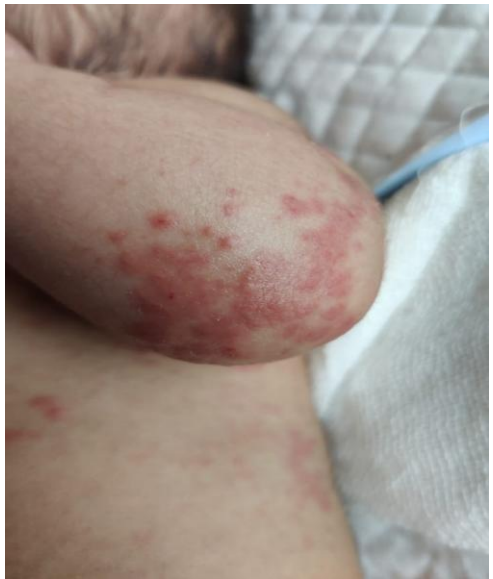
A high index of suspicion is required in children with refractory pneumonia, fever and persistently high inflammatory markers. Pediatricians should consider atypical Kawasaki disease as a possible alternative diagnosis, because early clinical suspicion and prompt treatment with IVIG and aspirin dramatically abate the high risk of permanent coronary damage. Increasing awareness about this condition is of utmost importance as it continues to be a challenge.

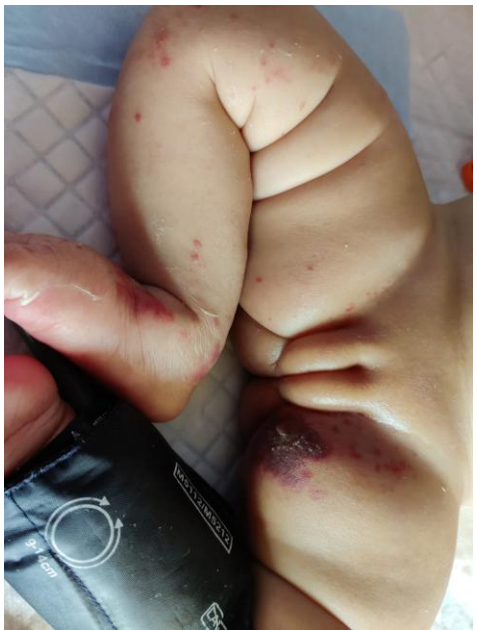
Bibliography: AHA Journal Vol. 135 Issue 17, Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association

Neonatal MIS-C – Harnessing the cytokine storm

Day 1 to Day 25

- Term baby girl, fever from day 8 with rashes - treated as late onset sepsis
- She received immunoglobulin along with broad spectrum antibiotics for thrombocytopenia following which there was a transient improvement.
- She was transferred to us on day 25 following recurrence of fever along with a generalised maculopapular rash with central necrotic patch.





Day 25 to day 30

- She was Covid positive by RT-PCR, had anaemia, thrombocytopenia, hypoalbuminemia with generalised edema and diarrhoea with cardiogenic shock.
- Needed invasive ventilation. Echocardiography revealed ejection fraction of 40% and mild pericardial effusion.
- She developed seizures, pulmonary haemorrhage and cardiac arrest but could be resuscitated. She also developed acute kidney injury
- NT-Pro BNP 33000gm/L, D-dimer 16500 µg/L, Ferritin 16000 ng/ml, CRP 78.5 mg/L.
- Methylprednisolone 2mg/kg/day, IVIg 2g/kg and Enoxaparin was started with a diagnosis of Multisystem Inflammatory Syndrome associated with COV-19 (MISC).
- Responded and extubated within 5 days ,normalised ECHO.
- Steroid stopped after total 5 days as baby developed hypertension

Day 35 to day 50

- 5 days after extubation she again developed respiratory distress and had to be reventilated.
- Echocardiography showed moderate LV dysfunction with generalised LV wall hypokinesia and there was re elevation of CRP, ferritin and NT-proBNP.
- Inj.Methyl-prednisolone was restarted and given for 5 days followed by tapering dose of oral prednisolone on which she was finally discharged on day 50.

What This Case Adds?

Though mild myocarditis with neonatal COVID is reported, MIS-C in a newborn with refractory myocarditis successfully managed with IVIg and steroids is unique. Dermatological manifestation as a presentation of neonatal Covid-19 has also not been previously reported.

KAWASAKI DISEASE IN COVID PANDEMIC ERA

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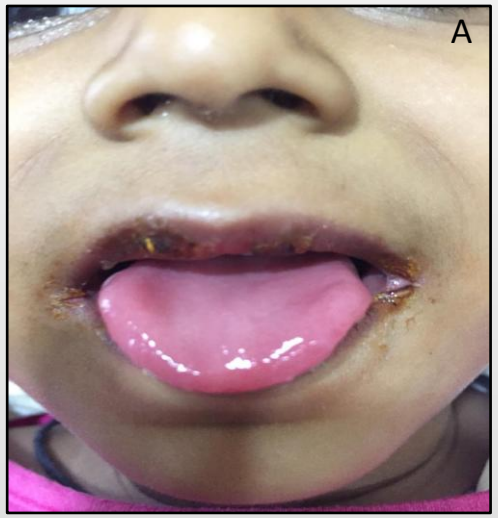
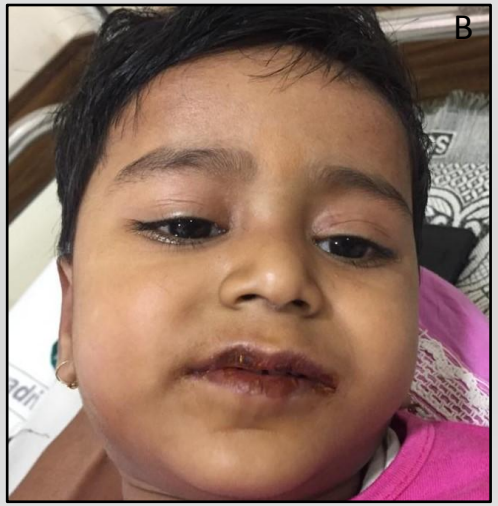
INTRODUCTION:

Kawasaki disease is an inflammation of medium vessel usually seen in pediatric population under 5 years of age. The usual peak onset is from 18 to 24 months with long term complications such as coronary artery dilatation.[1] Several reports have emerged in 2020, a inflammatory syndrome similar to Kawasaki disease during the COVID-19 pandemic, challenging previous observations that children have mostly milder form of disease.[2] Currently two guidelines are used worldwide for the diagnosis of complete Kawasaki that is AHA (American heart association) and JMH (Japanese Ministry for health). As per the current guidelines IVIg @2gm/kg and also oral aspirin are used for the treatment of Kawasaki disease. Despite timely initiation of treatment KD children have increased risk of developing coronary artery aneurysm[3] and also risk of developing IVIg resistance.[4]

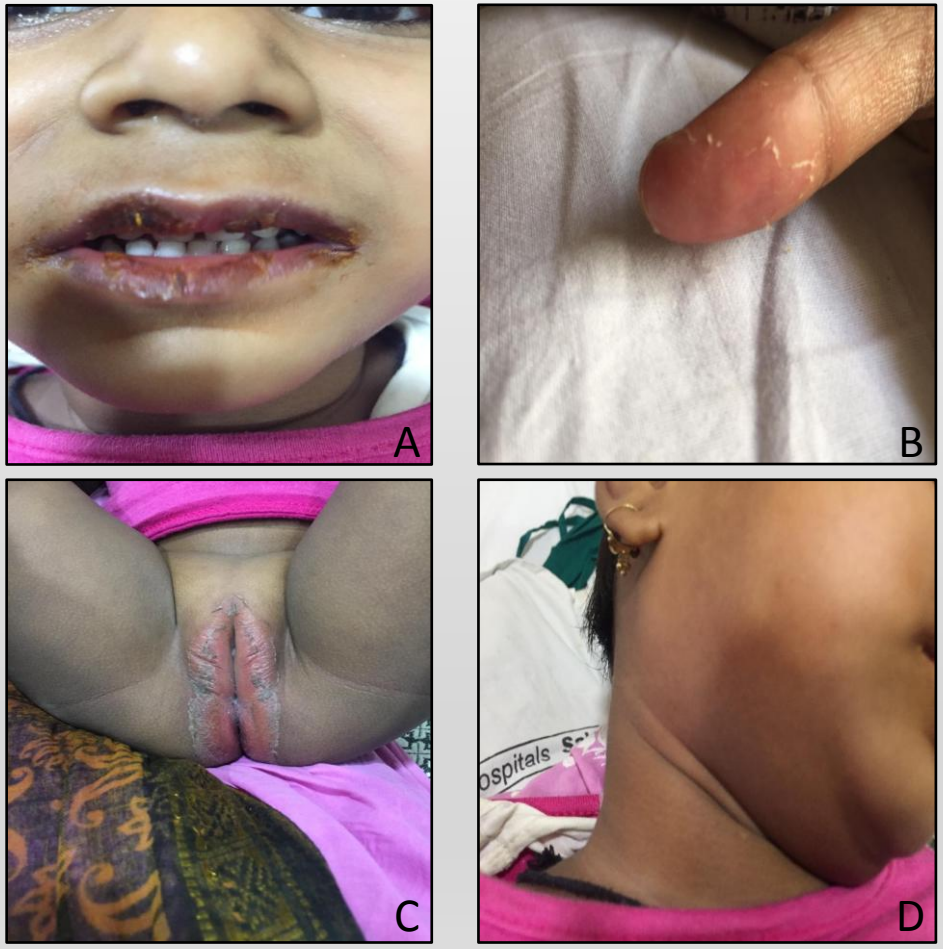




Images **A & B**: Clinical features of KD

American heart association (2017 guidelines)	Japanese ministry of health (2014 guidelines)
Classic KD is diagnosed with fever persisting for least 5 days and at least 4 of the following	Five of the following six criteria
• Erythema, lips cracking, strawberry tongue, diffuse injection of oral and pharyngeal mucosae	• Fever persisting ≥ 5 days
• Erythema of palms, periungual peeling of fingers and toes, Polymorphous exanthema	• Bilateral conjunctival congestion
• Bilateral bulbar non exudative conjunctival congestion	• Changes of lips and oral cavity
• Cervical lymphadenopathy (> 1.5 cm diameter), usually unilateral	• Polymorphous exanthema
• Exclusion of other diseases with similar findings (e.g., scarlet fever)	• Changes of peripheral extremities
	• Acute non-purulent cervical lymphadenopathy

CASE STUDY: 2 years old female child was presented to us with complaints of moderate to high grade fever spikes for 9 days along with maculopapular, erythematous rash which appeared first over bilateral limbs and gradually progressed to bilateral upper limbs. Later she also developed Peri-anal and perigenital excoriation with fissured lips and strawberry tongue. On Day 6 of illness mother also noticed redness of both eyes with no discharge which subsided with unilateral preauricular lymphadenopathy. CRP, ESR and D-dimer levels were elevated. COVID rt-PCR documented was negative. She received IVIG @2gm/kg and was started on oral high dose Aspirin. She responded well to the above line of management and gradually fever spikes and rash subsided. 2D Echo done showed no coronary abnormalities.



Images: **A**- Cracked lips, **B**- Periungual peeling, **C**- Perigenital excoriation, **D**- cervical lymphadenopathy

CONCLUSION:

The above description typically suggests a classic case of Kawasaki disease but with the advancement of laboratorial tools the major question arise that why there is a lack of clinical trials on inflammatory markers and association with KD. Why there is a association of coronary artery with the cytokinins storm? More work remains to be done, especially in long-term follow-up of pediatric COVID-19 survivors.

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2. Kam KQ, Ong JS, Lee JH. Kawasaki disease in the COVID-19 era: a distinct clinical phenotype?. The Lancet Child & Adolescent Health. 2020 Sep 1;4(9):642-3.
3. Campbell AJ, Burns JC. Adjunctive therapies for Kawasaki disease. Journal of Infection. 2016 Jul 5;72:S1-5.
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Atypical Kawasaki disease with Dengue co-infection – A diagnostic dilemma.

Case report: A 7 years old female child presented with history of fever , rash ,vomiting and pain abdomen since 6days(Figure 1), with serologically confirmed dengue fever showed expected improvement initially only to develop high grade fever spikes(Figure 2) with oral ulcers and mucositis (Figure 3) which also subsided in 36 hours without specific treatment. Secondary bacterial infection, macrophage activation syndrome, Kawasaki disease and COVID-19 co-infection/MISC were considered and child was evaluated for the same(Table 1). Criteria for incomplete KD were met once during the course of illness but in view of clinical improvement, parents did not consent for IVIg infusion. Close follow-up revealed increasing right coronary artery dilation(medium size anuerysm) 7 days later and IVIg was given. At 4weeks follow up, size of the coronary anuerysm has remained unchanged.

Figure 3 showing crusted lips.

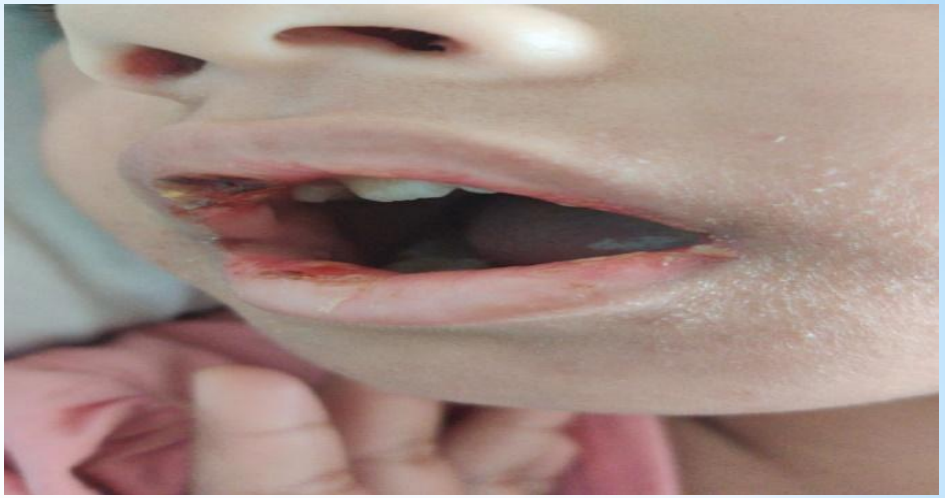

Figure 1 showing clinical features:

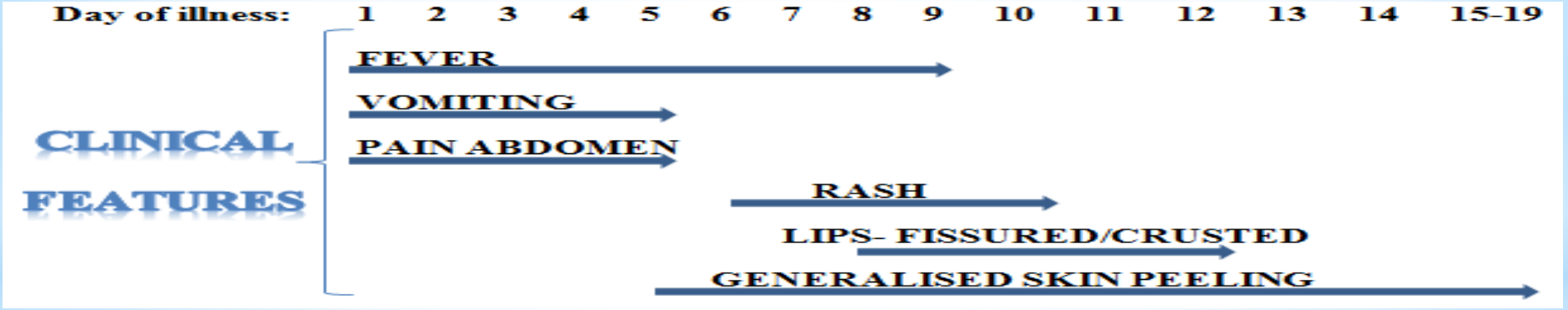

Figure 2 showing fever trends:

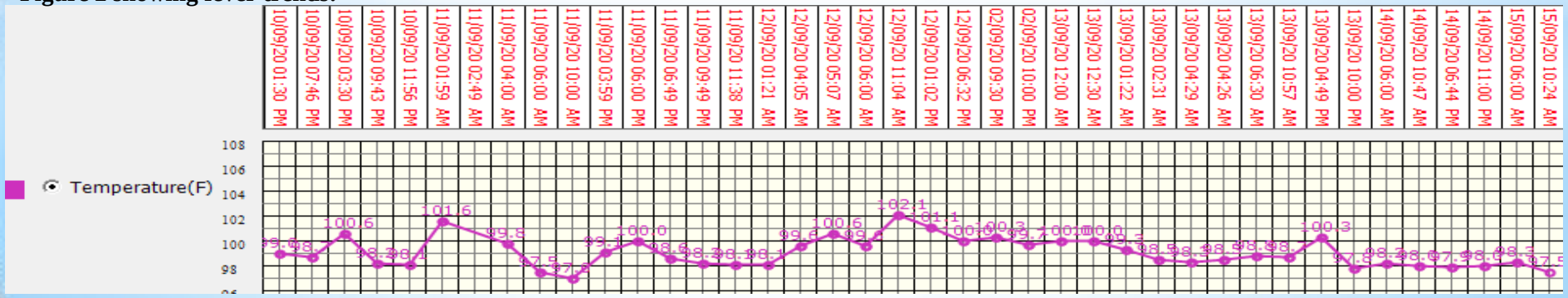

Table 1 showing investigation trends:

Day of illness	6	7	8	9	10	14	18	21
Hemoglobin (g/dl)	11.9	11.8	11.8	11	11	11	11.2	11.4
PCV(%)	34.5	35	35	33.2	33.2	33.1	33.4	33.2
WBC (cells/cumm)	3500 (N-57%)	4200 (N-62%)	7700 (N-79%)	11300 (N-77%)	9000 (N-63%)	16200 (N-65%)	17400 (N-80%)	16900 (N-79%)
Platelet (Lakhs)	1.08	1.07	1.22	1.49	2.30	4.95	5.43	4.58
Dengue	NS1 positive		NS1 and IgM positive					
Urine routine	normal		10-12 WBCs					
ESR (mm)			20	20	22	31	28	
D-dimer (ng/ml)			885			375	291	220
Fibrinogen (g/L)						2	2	2.3
Albumin (g/dl)	3.3			2.1	2.6	3.6	3.6	3.1
CRP (mg/dl)			<0.1	3.93	1.67	<0.1	<0.1	<0.1
SGOT (IU/L)	60		49	28	30	30		
SGPT (IU/L)	34		23	29	29	31		
NT PROBNP (mg/ml)					1780	226	76	
2D ECHO			Normal		Dilated RCA(z scores-2.4)	Dilated RCA(z scores-2.4)	Dilated RCA(z scores-5)	Dilated RCA(z scores-5)
COVID		RT PCR-Negative			Antibody-Negative			

Urine and blood culture - negative

Key message

- The diagnosis of KD with dengue co-infection is challenging as clinical features of both the diseases overlap
- We wish to emphasise the very short duration of acute phase of KD, atypical and incomplete presentation, higher age, generalised skin peeling and absence of periungal desquamation in our case
- Close follow up with frequent serial 2D ECHO is essential in suspected cases of Atypical KD

References:

1.Surjit Singh, Mani P.Singh, Sandesh et al. Dengue triggered Kawasaki disease- A report of 2 cases. J Clinical Rheumatology.2018;24:401-404.

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Setting the stage for genetic biomarkers of KD:

First study on miRNA profile of children with Kawasaki Disease from India

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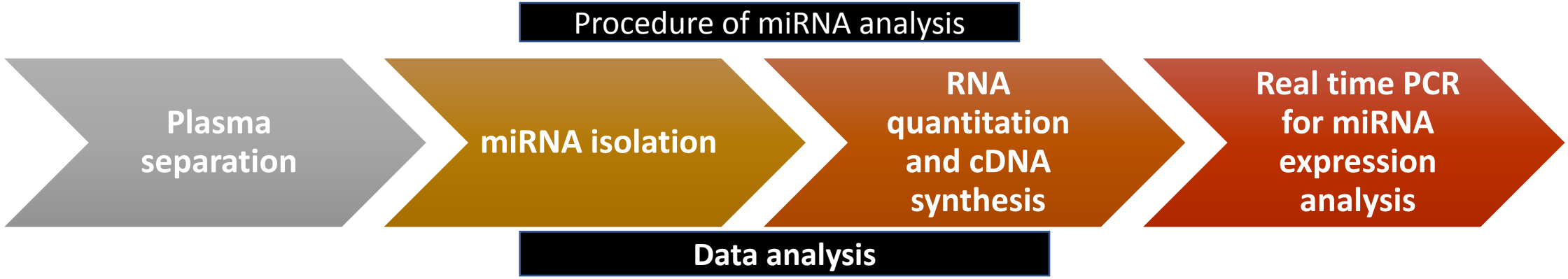
INTRODUCTION:

- MicroRNAs : class of short (18-25 nucleotide long), non-coding, endogenous RNA molecules
- Regulate the gene expression by binding to mRNAs via complementary sequences
- In KD, differential expression of miRNAs has been studied for diagnosis and predicting severity and response to therapy.
- MiR-145, modulates TGF-β signaling in the arterial wall and has high expression in acute KD subjects and lower in the convalescent phase and higher in patients with coronary artery abnormalities (CAAs) in studies from Japan and USA
- mRNA-320a interacts with bone morphogenetic protein receptor 1A (BMPR1A), and intracellular signaling via BMPR1A may correlate with TNF-α expression. miRNA 320 a and b have been shown to be upregulated in acute stages of KD
- miR-499 expression elevated in patients with viral myocarditis and co-relate with severity of viral myocarditis.

Objectives: To assess miRNA profile in patients with Kawasaki disease in comparison with febrile controls using microRNA-145-5p, miRNA-320a and miRNA-499

Method:

Study Design: Longitudinal cohort study
Study setting: Pediatric Allergy and Immunology Unit, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh.
Study period: January 2019 to June 2020
Inclusion criteria: Patients fulfilling the AHA 2017 criteria for the diagnosis of KD considered eligible for inclusion **Exclusion criteria:** Children with a proven infectious etiology for the febrile illness, inability to obtain consent.
Sample size: 20 children with a diagnosis of KD were recruited for the study; blood collected during the acute phase was analyzed.
Control group: Twenty age matched febrile (non KD illness) controls recruited from the pediatric outpatient clinic

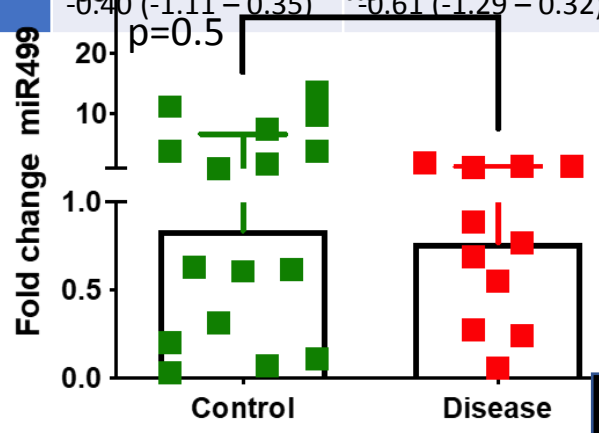


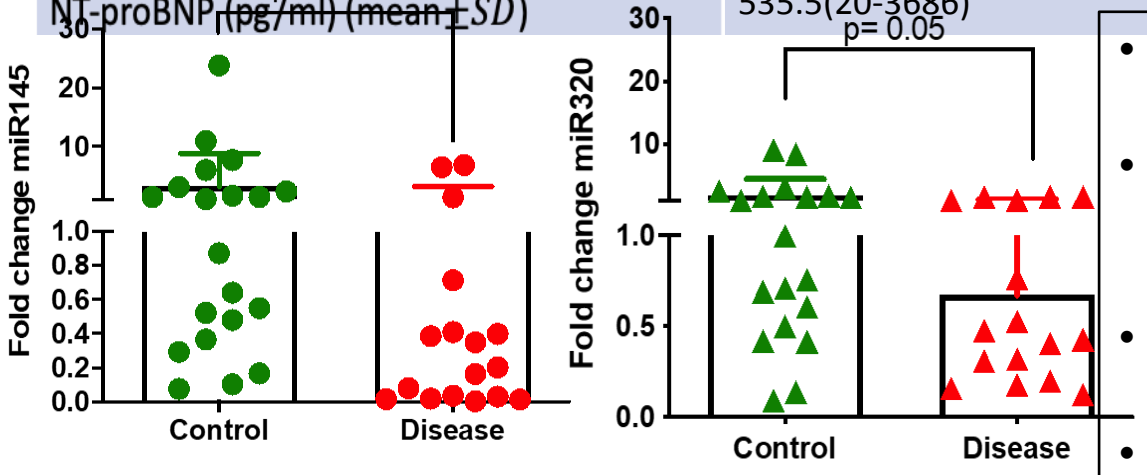
Cycle number, at which the amplification plot crossed the threshold, was calculated (CT). ΔCt was calculated by subtracting the Ct values of the endogenous control (endogenous control for this array was U6 snRNA) from the Ct values of the miRNA of interest. ΔΔCt was then calculated by subtracting ΔCt of the control from ΔCt of disease. miRNA RT PCR Data analyzed using graph pad Prism software version 16.0.

RESULTS

Parameter	Results in our cohort
No. of patients with CAAs ; N(%)	2 (10%)
Mean age of patients with KD	5.05 years
Sex ratio	4(20%) females and 16(80%) males
Thrombocytes (x 10^9 cells/L) (mean$\pm SD$)	485.6 (225.97)
ESR (mm in the first hour) (mean$\pm SD$)	47.58(22.62)
CRP (mg/L) (mean$\pm SD$)	40.11 (56.27)
Serum sodium (mEq/L) (mean$\pm SD$)	134.78(4.8)
Serum albumin (g/dl)(mean$\pm SD$)	3.24 (1.1)
NT-proBNP (pg/ml) (mean$\pm SD$)	535.5(20-3686)

	Acute phase (n=20) Median (IQR)	Convalescent phase (n=20) Median (IQR)	p value
LMCA	0.35 (-0.5 – 1.45)	-0.045 (-0.40 – 0.75)	0.001
LAD	0.15 (-0.73 – 0.80)	-0.05 (-1.03 – 0.53)	0.022
LCx	-1.08 (-1.8 – -0.07)	-1.25 (-1.78 – -0.69)	0.758
RCA	-0.40 (-1.11 – 0.35)	-0.61 (-1.29 – 0.32)	0.114





CONCLUSION

- First study in the Indian population to explore the miRNA profile in patients with KD.
- Significantly decreased expression of miR-145 and miR-320-a and no significant difference in expression of miR-499 in patients with KD in comparison to febrile controls.
- This may be due to different genetic characteristic of Indian population
- Further studies needed to establish these as potential biomarkers for diagnosis and prediction of complication in KD

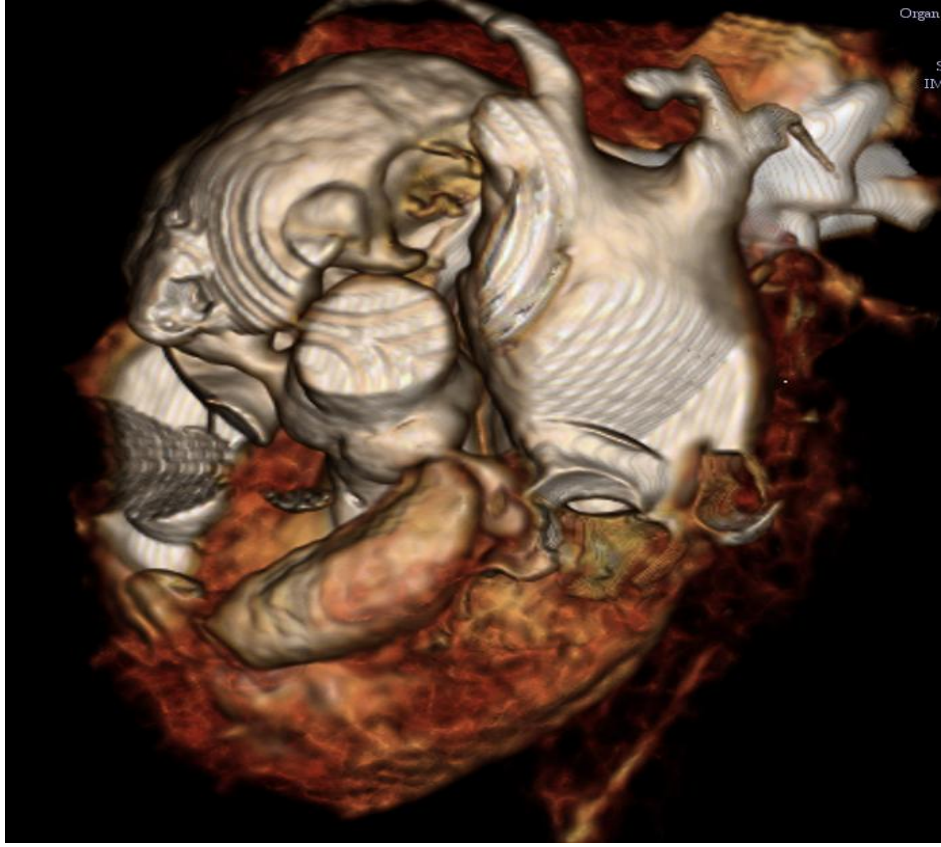
MIDTERM OUTCOMES OF KAWASAKI DISEASE WITH GIANT CORONARY ANEURYSMS IN THE INDIAN SETTING

Department of Pediatric Cardiology

Amrita Institute of Medical Sciences, Cochin

Introduction

- Tertiary cardiac care centre
- Retrospective study - January 2015 and December 2019
- 31 diagnosed Kawasaki children
- 24 (77.4%) with coronary artery abnormalities
- Of which , 11 (35.5%) with Giant Coronary Aneurysms

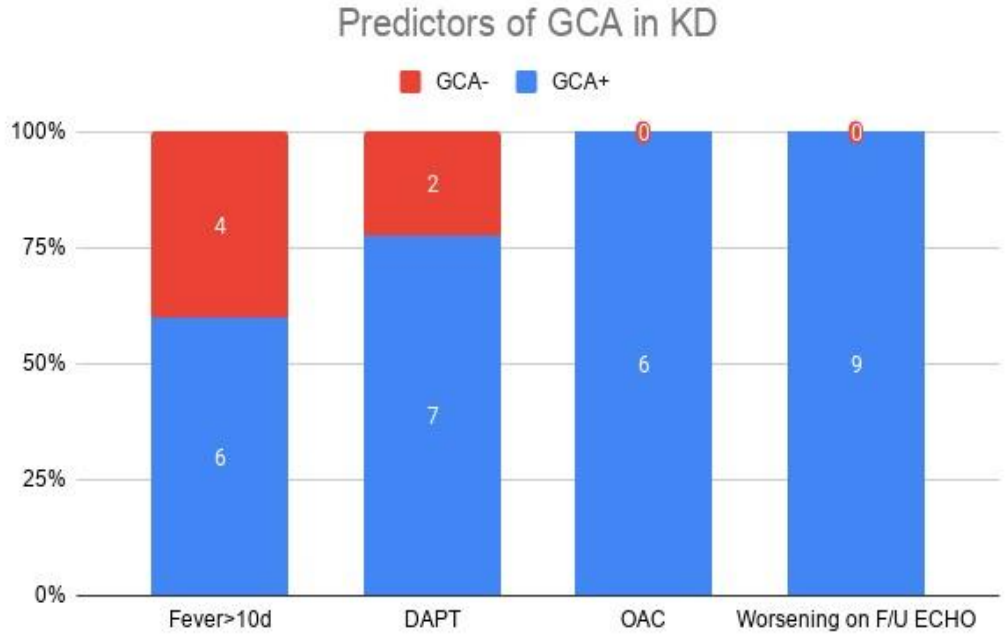


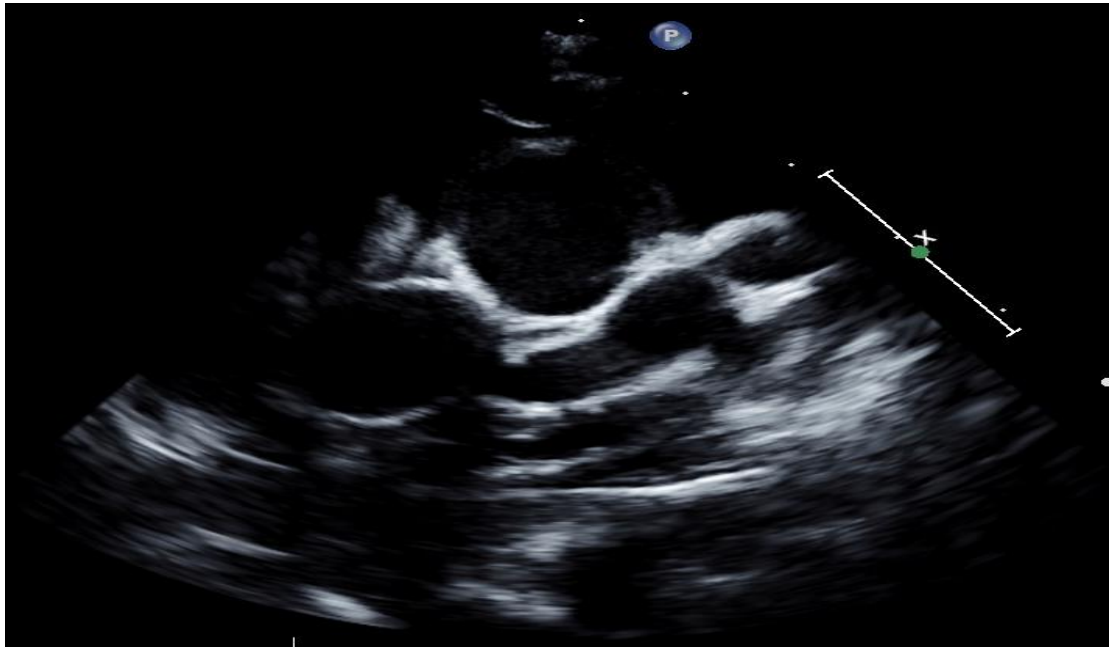
CTA showing LAD GCA

- Median age of 27 months (2-110 months)
- 21 (67.7%) were male.
- 6 patients - incomplete Kawasaki disease.
- 16 children (51.6%) diagnosed > 10 days of fever
- All except one received IVIG, however IVIG resistance noted in 5 (16.6%) patients

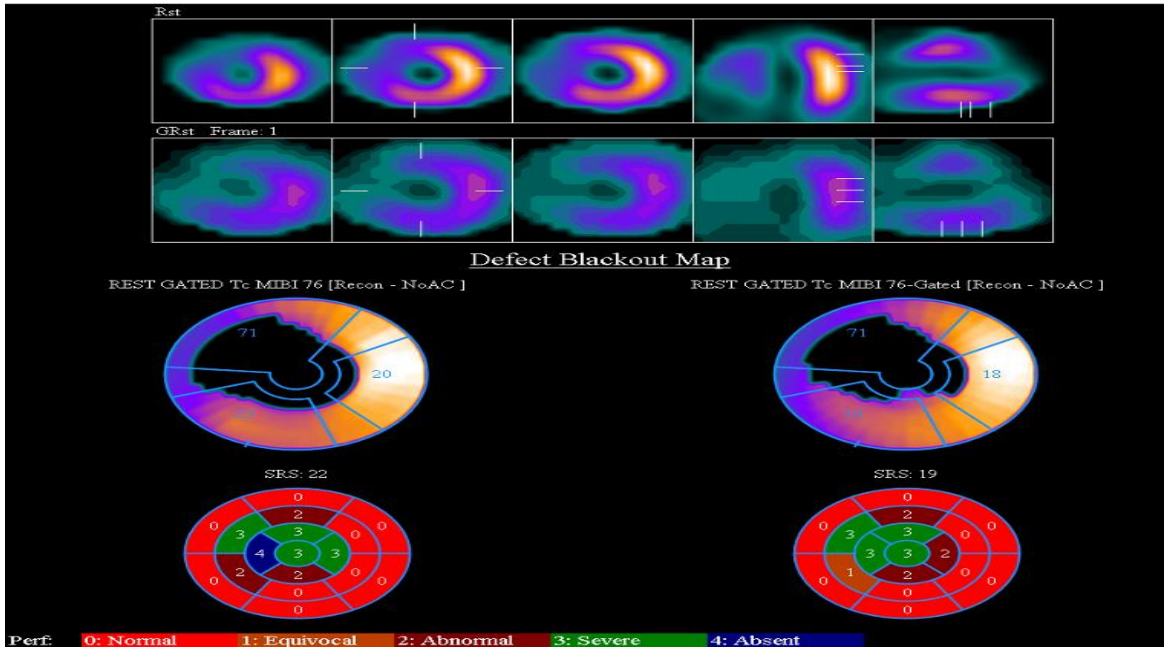
GIANT CORONARY ANEURYSM

- 11 (35.5%) patients – 90.9% males
- More likely to be diagnosed after 10 days of fever (p=0.01).
- Dual antiplatelet therapy (DAPT)(p-0.003)
- Oral anticoagulant (OAC) – Warfarin (p-0.001)
- Follow up ECHO showed significant worsening (p-0.001)





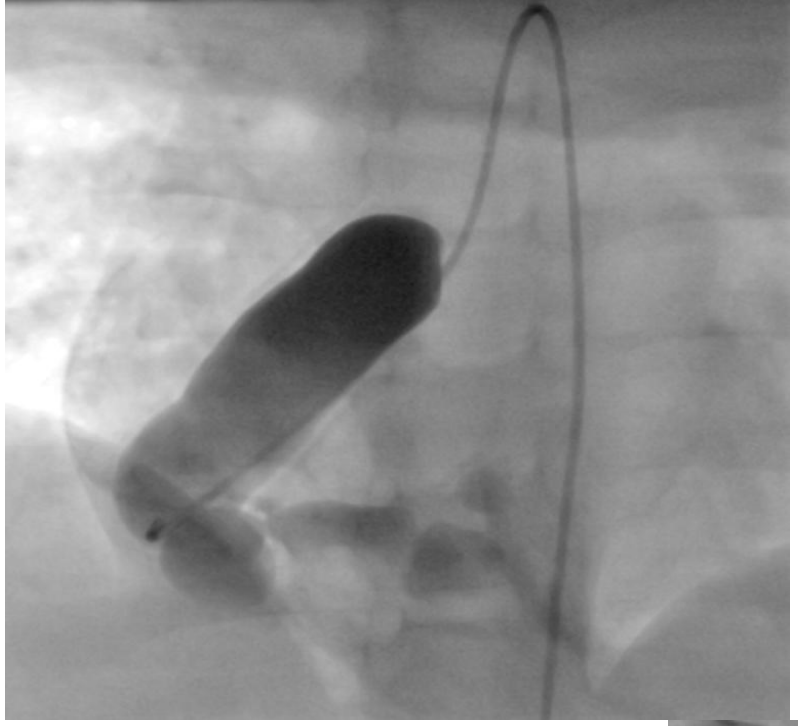
ECHO – LAD GCA

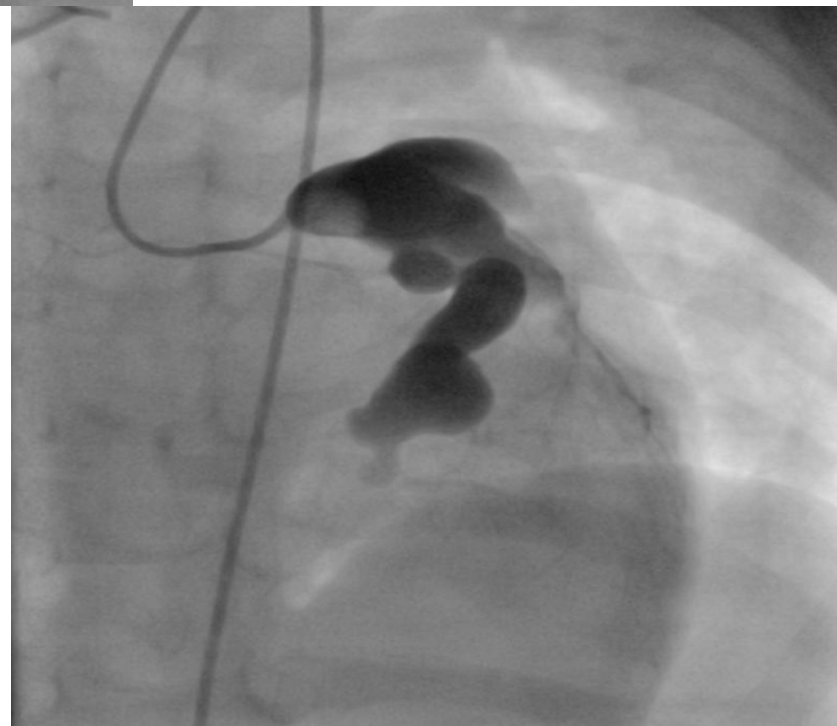


MIBG-Large LAD infarct

GCA

- LAD involvement in 8 patients (72.7%)
- MIBI scans done in 7 GCA patients showed ischemic changes predominantly in LAD territory
- On a median follow up of 35 months, 2 children had a MACE
- One child developed an aneurysm of the LV apex secondary to infarction involving the LAD
- Another child presented with recurrent myocardial infarction 30 days after discharge from the hospital and underwent CABG
- Both the children remained clinically well at the last follow up.





CAG showing giant aneurysms of RCA (above) and LAD (below

A preliminary observational study on predicting treatment intensification in Pediatric Multisystem Inflammatory Syndrome (PIMS)based on CRP, NT-proBNP and initial echocardiography

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INTRODUCTION

With the emergence of COVID 19 pandemic, there has been a rise in an elusive entity named as Pediatric Multisystem Inflammatory Syndrome temporally associated with COVID 19.

Being quite in the nascent stage, a consensus guideline is yet to be achieved on the treatment protocol.

Presently we are using intravenous immunoglobulin 2g/kg as initial therapy, methyl prednisolone is being added in patients with inadequate clinical / biochemical response.

CRP (C reactive protein) and N-terminal brain natriuretic peptides(NT-proBNP) are 2 commonly used markers in KD as well as PIMS.

We have attempted to observe the predictive values of these two parameters along with the initial ECHO report in determining the need for treatment intensification in these patients.

METHODS & MATERIAL

We performed a retrospective analysis of data of PIMS patients admitted from July 2020 till mid September 2020.

Out of the patients admitted with PIMS, those patients were included in the study who had data on the initial CRP, NT proBNP values and the initial echocardiography report

The patients were divided into two groups, one who needed both IVIG and methyl prednisolone and the other group who responded to IVIG alone; data of the corresponding CRP, NT pro-BNP and initial echocardiograph reports were tabulated.

A logistic regression model was implemented to find out the dependence of methylprednisolone on CRP, NTproBNP levels and Echocardiography findings (EF levels) and an attempt was made to predict steroid requirement from these 3 factors.

The computation was done using the Statsmodels library in Python.

A separate T-test was run to compare mean values of CRP levels in patients requiring only IVIG and patients requiring both IVIG and Methyl Prednisolone.

The same test was run for NTproBNP levels in both groups of patients.

RESULTS

The study had 19 patients of PIMS with data available on their CRP, NTproBNP and initial echocardiography report. 9 of them responded to IVIG alone (Table 2), while the other 10 required IVIG and methylprednisolone (Table 1)

The coefficients for CRP, NTproBNP and EF levels did not show any significant difference from 0 (p value>0.05), meaning that they have no significant dependence on Steroid requirement criteria, or the log odds (probability) of methylprednisolone requirement does not change significantly on changes in any of those 3 variables.

A separate T-test was run to compare mean values of CRP levels in patients requiring only IVIG and patients requiring both IVIG and methylprednisolone. There was no significant difference in the mean levels of CRP in both types of patients. The same test was run for NTproBNP levels in both groups of patients, and there was no significant difference in the levels here either.

Table 1: CRP, NT pro-BNP and echo findings of Patients requiring both IVIG and Methyl Prednisolone (N=10)

SN of patients	CRP	NT Pro BNP	Echocardiography
1.	362	37307	48% EF
2.	120	5105	45% EF
3.	295	2840	LAD +3.35z
4.	146	11553	Normal
5.	200	1446	Normal
6.	302	4567	40% EF
7.	152	23499	Myocarditis, decreased EF
8.	13	328	RCA +4.8 Z. LAD +3 z
9.	372	16079	+40% EF
10.	108	20030	Dilated LA LV, EF 47%

Table 2: CRP NT proBNP and echocardiography values of patient who responded to IVIG(N=9)

SN of patients	CRP	NT proBNP	Echocardiography
1.	104	1098	Normal
2.	111	262	Normal
3.	216	179	Normal
4.	318	2917	normal
5.	362	13343	47% EF+ LMCA +2 Z
6.	178	5340	Normal
7.	55	27541	Normal
8.	100	4131	Normal
9.	109	109	LMCA +3.4z

CONCLUSION

With the present data, it was not possible to statistically predict the requirement of steroids along with the use of IVIg based on initial CRP, NT-pro BNP and initial echocardiography values.

Limitation : inadequate number of patients.

A large scale study may help us to formulate the predictive values of these markers in treatment intensification of PIMS patients.

CLASSIC KAWASAKI DISEASE : A CASE REPORT

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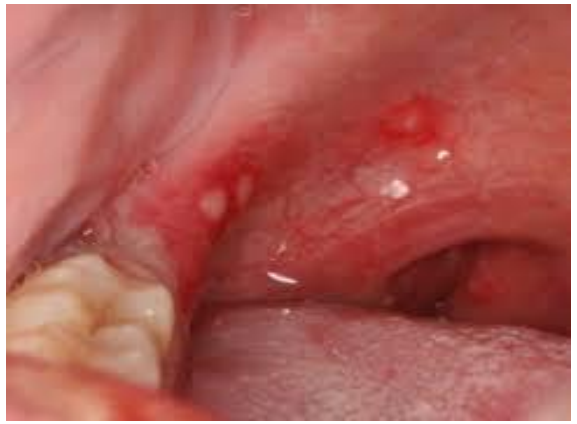
Introduction:

Kawasaki disease is an acute systemic vasculitis and is the most common cause of acquired heart disease in children in the developed world. The disease is believed to result from a genetically susceptible individual's exposure to an environmental trigger. Incidence is rising worldwide, and varies widely across countries and within different ethnic groups. It has surpassed rheumatic heart disease as the leading cause of acquired cardiovascular disease in children in the developed world.



CASE REPORT:

4.5 year old male child presented with complaints of high grade fever responding to symptomatic treatment associated with a generalized maculopapular erythematous rash over neck, wrists, back and arms since 6 days. Examination revealed stomatits, glossitis with fissured lips, perianal excoriation, right cervical lymphadenopathy, hepatomegaly and oedema over hands and feet. Not responding to antibiotics, he was further worked up, lab parameters showed elevated CRP and ESR, hyponatremia and hypoalbuminemia. Zoonosis was ruled out with negative ricketssial, leptospiral and brucellosis workup. 2D ECHO showed coronary artery dilatation (Z score LAD 4.31, RCA 3.55).With a working diagnosis of Classic Kawasaki disease, he was given IVIG @2g/kg and started on high dose Aspirin @80mg/kg/day. Fever and symptoms subsequently resolved, and the patient was discharged after a 10 day hospital stay.

CRITERIA FOR CLASSIC KAWASAKI DISEASE

Fever persisting at least 5 days† and the presence of at least 4 of the following 5 principal features:

1.Changes in extremities: Acute: Erythema and edema of hands and feet Convalescent: Membranous desquamation of fingertips

2.Polymorphous exanthema

3.Bilateral, painless bulbar conjunctival injection without exudate

4.Changes in lips and oral cavity: Erythema and cracking of lips, strawberry tongue, diffuse injection of oral and pharyngeal mucosae

5.Cervical lymphadenopathy (≥1.5 cm in diameter), usually unilateral

Conclusion:

Given its severe morbidity and potential mortality, Kawasaki disease should be considered as a potential diagnosis in cases of prolonged paediatric fever. Early clinical suspicion and prompt treatment with IVIG and aspirin dramatically abate the high risk of permanent coronary damage. Increasing awareness about this condition is of utmost importance and it continues to be a challenge for pediatricians to this day.

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HYPERINFLAMMATORY SYNDROME IN CHILDREN IN COVID ERA

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Department of Paediatrics,
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INTRODUCTION

Hyper-inflammatory syndromes are life-threatening disorders caused by overwhelming host immune response often resulting from defects in negative feedback mechanisms. These include Classical Kawasaki disease (KD),Incomplete KD, KD shock syndrome, toxic shock syndrome (TSS), macrophage activation syndromes (MAS) and multisystem inflammatory syndrome in children (MIS-C).

OBJECTIVE

We are describing a case series of 10 patients with hyper-inflammatory Syndrome highlighting clinical presentations, laboratory profiles with management and outcome during this COVID-19 pandemic to raise awareness among paediatricians.

METHODOLOGY

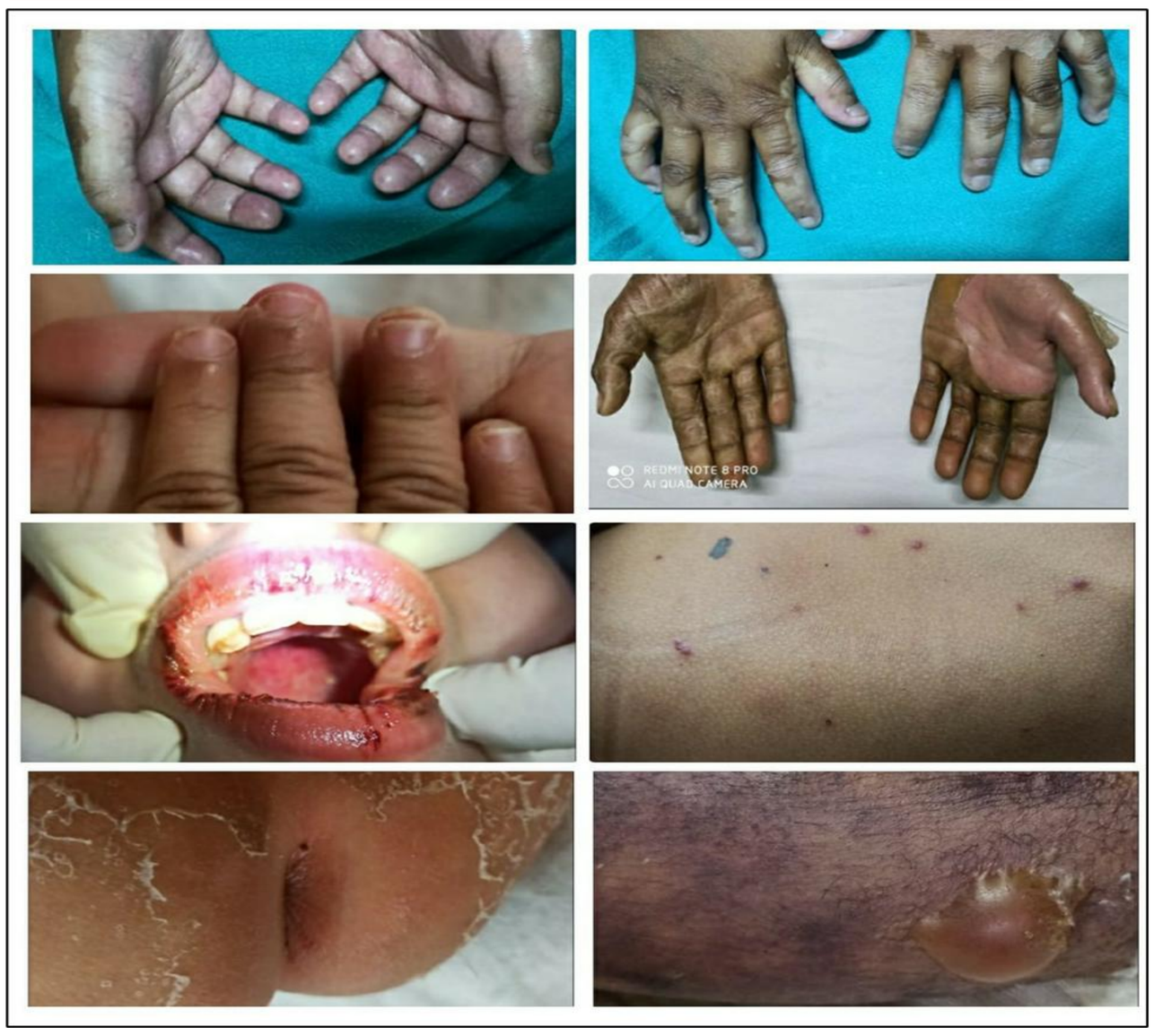
Criteria for inclusion in the study were based on the case definitions given by AHA,WHO, Ravelli and Kenegaye et al. For patients who met criteria, we collected demographic data; past medical history; clinical symptoms; physical examination findings; and results of imaging ,cardiac and laboratory testing performed at presentation and throughout the hospital admission. We also collected data of complications, outcome, and length of hospital stay.

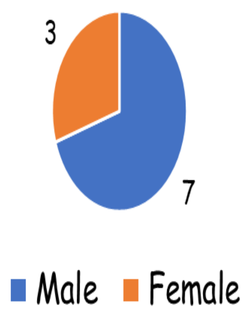
Table I- Clinical Profile of Children With Hyperinflammatory Syndrome

Characteristics*	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
PICU indication	shock	RF/S	RF/S	RF/S	RF/S	RF/S	RF/S	RF/S	Shock	RF/S
Mucocutaneous manifestations	+	-	+	-	+	+	+	-	-	+
MODS	+	+	+	+	+	+	+	+	+	+
ARDS$^{\Delta}$	-	+	+	+	-	-	+	+	-	-
Pneumonia	+	+	+	-	-	+	+	+	+	+
Circulatory shock										
Cardiogenic/ Septic	+/-	-/+	-/+	-/+	-/+	-/+	-/+	-/+	-/+	-/+
Vasoactive drugs	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No
Blood components	+	+	+	-	+	+	+	+	+	+
Medicines										
Corticosteroids	+	-	-	+	+	-	+	-	-	+
IgIV single dose 2g / kg	-	-	-	-	+	+	+	-	-	-
Mechanical ventilation	-	+	+	+	+	+	+	+	-	+

*RF: respiratory failure; MODS:Multiple organ dysfunction syndrome ; ARDS:Acute respiratory distress syndrome

RESULTS





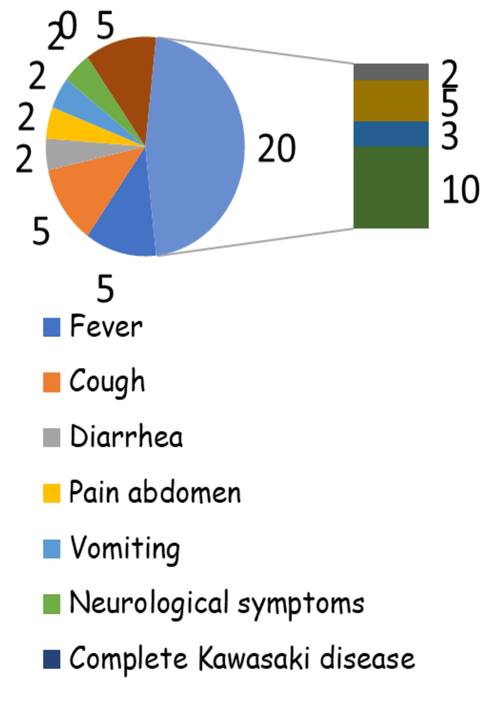
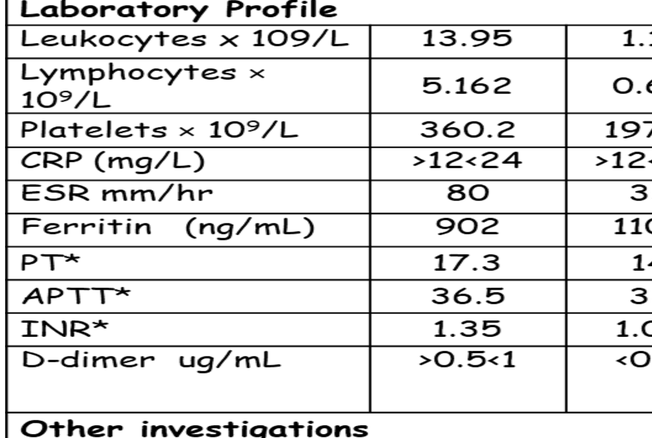


Table II-INVESTIGATION PROFILE OF CHILDREN WITH HYPERINFLAMMATORY SYNDROME

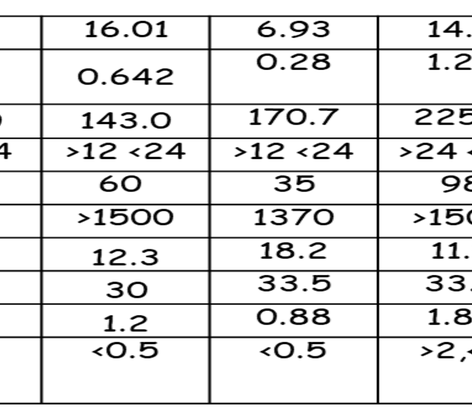
Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Reference range
Laboratory Profile											
Leukocytes x 109/L	13.95	1.11	16.01	6.93	14.2	9.60	9.273	20.51	4.96	7.40	4.0--10.0
Lymphocytes x 10^9/L	5.162	0.66	0.642	0.28	1.28	1.54	0.463	2.87	0.46	1.99	1.5—4.0
Platelets x 10^9/L	360.2	197.0	143.0	170.7	225.0	71.0	453.0	127.5	103.0	120.0	150--450
CRP (mg/L)	>12<24	>12<24	>12 <24	>12 <24	>24 <48	>6<12	>24<48	>12<24	>12<24	>6<12	<6
ESR mm/hr	80	35	60	35	98	35	35	40	25	35	
Ferritin (ng/mL)	902	1100	>1500	1370	>1500	>2000	1440	1200	159	>2000	7-140ng/ml
PT*	17.3	14	12.3	18.2	11.9	25	16.6	16	15	13.3	10--14"
APTT*	36.5	32	30	33.5	33.5	42	40	38	30.2	29.2	24--40"
INR*	1.35	1.08	1.2	0.88	1.88	1.2	1.46	1.6	1.4	1.05	0.8--1
D-dimer ug/mL	>0.5<1	<0.5	<0.5	<0.5	>2,<4	<0.5	<0.5	<0.5	<0.5	<0.5	<250ng/ml or <0.5ug/ml
Other investigations											
X ray	PE	ND	BFI	BFI	N	BFI	N	BFI	N	N	
ECG	M	N	N	N	N	N	N	N	N	N	
ECHO	N	N	N	N	N	N	AR	N	N	N	
NCV	B/L CPN AN*	ND	ND	ND	ND	ND	AMSAN*	ND	ND	ND	

*CRP: C-reactive protein; PT: prothrombin time; APPT: activated partial thromboplastin time; N: NORMAL; ND: NOT DONE; ECG: electrocardiogram; ECHO: echocardiograph;B/L CPN AN: Bilateral common peroneal axonal neuropathy; AMSAN: Acute motor sensory axonal neuropathy

TREATMENT



OUTCOME



CONCLUSION

The importance of suspecting hyper inflammatory disease in febrile children with mucocutaneous symptoms and multi organ involvement during this pandemic cannot be overemphasized. These patients can deteriorate very rapidly. Hence, Early recognition and prompt treatment are essential for better outcome.

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KAWASAKI DISEASE CAMOUFLAGING AS INTESTINAL PSEUDO-OBSTRUCTION

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Background

- Kawasaki Disease (KD) is a disorder characterized by vasculitis of medium sized arteries predominantly affecting coronary arteries(1).
- 20–25% of untreated KD cases develop coronary artery abnormalities (CAA).
- <5% cases even after treatment with intravenous immune globulin (IVIG) can develop CAA.
- The spectrum of clinical presentation of KD is diverse ; Intestinal pseudo obstruction as seen in our patient is one of the uncommon presentations in KD

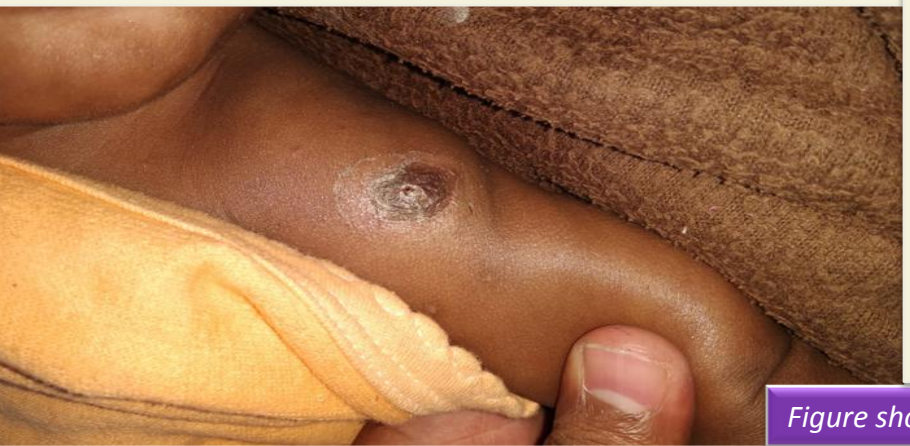


Figure showing BCG-it is that developed on day 3 of illness

Case report

Initial Presentation as clinical sepsis:

- A 3-month-old previously healthy female infant presented with fever, bilious vomiting for 2 days and abdominal distension for 1 day.
- The child was a term born with birth weight of 2.9 kg.
- She is developmentally normal with immunized up to age.

- On examination, she was febrile (101^0 F) with otherwise stable vitals.
- Abdomen examination revealed distended abdomen with decreased bowel sounds.
- There was a progression in distension after admission.
- The differential diagnosis considered were acute intestinal obstruction secondary to sepsis , surgical causes of obstruction

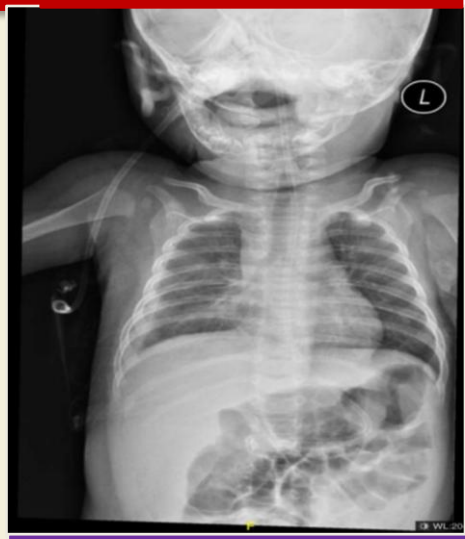
Further course in hospital

- Investigations revealed normocytic anemia(7.9g/dL), leucocytosis(27x10^9/L), thrombocytosis(604x10^9/L), elevated C-Reactive Protein(4.8mg/dL) and erythrocyte sedimentation rate(100mm/1st hour); sterile pyuria(300 WBC/HPF), hypoalbuminemia(2.8g/dL) and normal serum potassium (4.9 mEq/L) .
- Blood and urine cultures were sterile.
- Xray abdomen revealed dilated bowel loops loops with multiple air fluid levels.Ultrasonogram (USG) Abdomen ruled out any evidence of malrotation.

Suspicion of Kawasaki Disease:

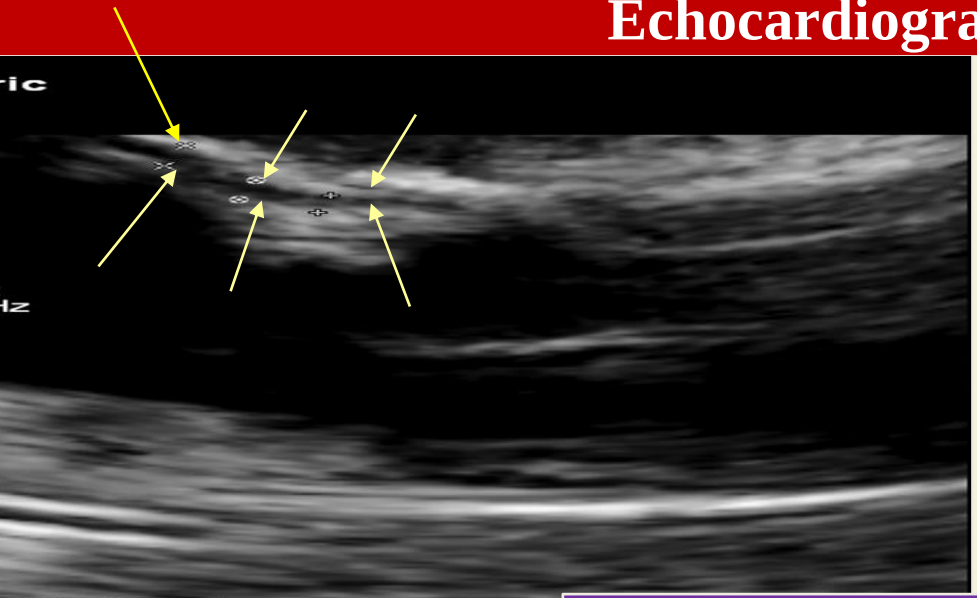
- As surgical causes were ruled out, a provisional diagnosis of septicemia with intestinal pseudo-obstruction (IPO) was considered and hence empirical antibiotics were administered.
- BCG-itis was noted on day 3 of illness, incited us to suspect KD and hence Echocardiography was done that revealed small aneurysms

X-ray



Xray of the infant showing dilated bowel loops multiple air fluid levels

Echocardiogram



Day 4 Echocardiography

LMCA : 2.5 mm (3.08 Z) – small aneurysm
LAD : 1.7 mm (2.37 Z) – dilation
LCX : 1.4 mm (1.61 Z) – normal
RCA : 1.4 mm (0.93 Z) – normal
RCM : 1.6 mm (2.23 Z) – dilation
RCAD : 1.7 mm(3.002Z) – small aneurysm

Figure : Arrows in picture demonstrating uniform dilatation of coronary artery

Resistant Kawasaki Disease

- She was treated with intravenous immunoglobulin (IVIG) 2g/kg and aspirin (60mg/kg/day).
- Fever persisted even after 36 hours of IVIG; Hence resistant KD was diagnosed
- IVIG was re-administered,following which defervescence occurred.
- Echocardiogram on day 14 and day 60 after illness revealed no residual coronary artery abnormalities (CAA).
- Aspirin was stopped at 6th week of illness .

Pathogenesis

- **Why Pseudo-obstruction in incomplete KD?**

Vasculitis and thrombosis in small subserosal arteries of the intestines causes Ischemia of the myenteric plexus thus causing reduction of bowel movements and hence the features of intestinal obstruction(4).

Conclusion

- Our case highlights the point that KD can present as acute intestinal pseudo-obstruction.
- BCG-itis appears usually by 1-4 days & is seen in up to 50% of cases (2,3). It is an early & important marker of KD.
- Thrombocytosis and CAA which usually occur after 7 days of fever (5). But it can appear within the first week as well, as in our case by day 3 & 4 of illness, respectively.
- The axiom ‘a young infant with fever persisting for > 7 days without focus should be investigated for KD (1), may not be entirely valid as it could lead to delayed diagnosis, thereby impeding our goal of preventing CAA.

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