Kawasaki Disease: A Clinical Case Report with Dramatic Presentation

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Abstract

Kawasaki disease (KD) is an acute vasculitis of childhood that predominantly affects the coronary arteries. Also known as Kawasaki syndrome and mucocutaneous syndrome, it involves skin, mouth, lymph nodes and inflammation of blood vessels. It is an acute systemic inflammatory illness. Kawasaki disease has replaced rheumatic fever to become the commonest cause of acquired heart disease amongst children in Japan, Northern America and Europe. Although we do not have countrywide epidemiologic data for India, anecdotal reports strongly suggest that the incidence of KD is showing an upward trend over the last 20 years and it may soon replace acute rheumatic fever to become the commonest cause of acquired heart disease amongst children. Here the patient presentation with KD is presented with details to get an idea about its clinical picture.

KD is a systemic necrotising vasculitis affecting the medium and small sized arteries. It is not only the commonest vasculitic disorder of children, but also the commonest cause of acquired heart disease in children in many countries. It primarily affects infants and young children, 80-85 percent of below 4 years of age. Boys are affected more commonly than girls and there is an ethnic bias in favour of children of Asian (especially Japanese and Korean) and Afro- Caribbean extraction.

The annual incidence of KD in children of Japanese descent is about 150 per 100,000 children younger than five years. In the United States, 19 per 100,000 children younger than five years are hospitalised with KD annually. The first, and so far the only, epidemiologic study on KD from India was published in 2011. This suggested that the incidence of KD at Chandigarh is at least 4.54 /100,000 children below 15 years of age. This figure is probably an underestimate as many children with KD are being missed. In India, KD is more common among children of age of 5 years with male predominance. Periungual desquamation which is a typical of KD often appears prior to day 10 of fever in India whereas in developed regions it occurs a couple of days later. Similarly thrombocytosis is also seen earlier in India as compared to developed countries.

Causative agent: The aetiology of KD remains obscure. It is believed that KD may be triggered by a streptococcal/staphylococcal toxin which acts as a super antigen and causes widespread immune activation. Genetic susceptibility is also considerable. Evidence for this hypothesis comes from the selective expansion of T lymphocytes bearing Vb2 and Vb8 T-cell receptors which is seen in children with KD. This pattern is very similar to that which is seen in toxin mediated streptococcal infections.

Proposed infectious agents are parvovirus, Staphylococcus aureus, Epstein-Barr virus, chlamydia and mycobacteria. Reports of rickettsiae, retroviruses, house-dust mites and skin commensals (e.g. *Propionibacterium acnes*) as possible causative agents have not been confirmed. Other possible and intriguing associations include exposure to rug shampoo, mercury poisoning and residence close to a body to water. This case reports of a child doesn't seems to have genetic susceptibility, but may be exposed to causative agent/toxin. Classic (typical) Kawasaki disease is marked by fever lasting five or more days, accompanied by four out of five findings: bilateral conjunctival injection non-exudative, oral changes such as cracked and erythematous lips and strawberry tongue, cervical lymphadenopathy, extremity changes such as erythema on palm and sole desquamation, and polymorphous rash. Classic KD also can be diagnosed with three clinical features if coronary artery abnormalities are observed on echo-cardiography, the case presented here fell in this category. Incomplete (atypical) KD occurs in persons with fever lasting five or more days and with two or three of these findings. It is more common in children younger than one year.

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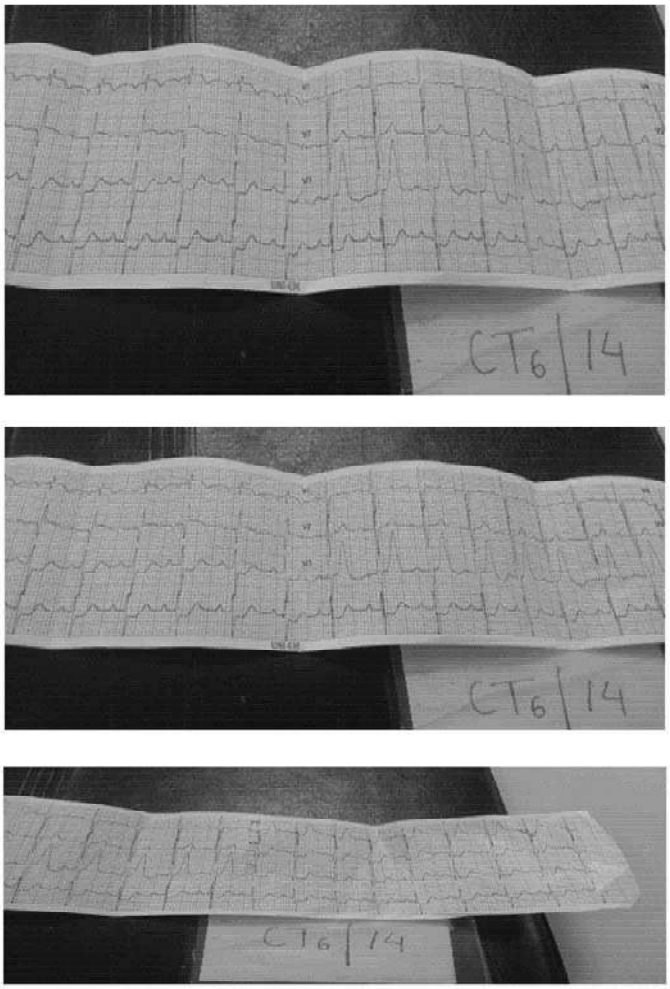


Fig 1: Emergency ECG and X-ray.

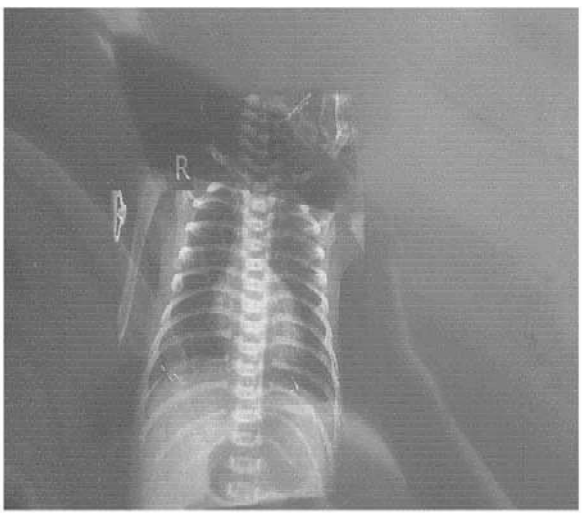


Fig 2: ECG taken- ST-T wave changes. ST depression noticed in limb leads II, III, avf and in chest lead ST depression and tall T-wave in V3-V6. Chest X-ray done; no cardiomegaly, pulmonary infiltration seen.

Pathophysiology: Theoretically, pathologic changes result from an exaggerated immune response to a pathogen with genetic susceptibility. Aberrant production of tumour necrosis factor α (TNF-α), interleukin-6, and other inflammatory cytokines purportedly promote leukocyte-endothelial cell interactions that cause endothelial damage.

Case Report

In our emergency department - a 3½ year old child presented with on and off severe irritability, agitated due to chest pain complaint lasting over 20 minutes and then subsided on its own since 20 days patient had respiratory distress also that started 5 days before admission. Immediately primary assessment done for airway, breathing and disability - everything was normal. Immediately ECG was taken, which revealed ST-T wave changes in limb leads II, III, avf and in chest lead V3-V6. Meanwhile T. Lansol JR 15 mg, T. Ecospirin 75 mg, T. Betaloc 25 mg all once daily were started. ECG repeated after 2 hours revealed tall peak T-waves; cardiac biomarker Trop-I was positive 2.54 ng/ml. Chest X-ray showed no cardiomegaly or pulmonary infiltration.

Echocardiography revealed dramatic picture of KD manifestations in aortic root site identified as coronary aneurysm with mild left ventricular (LV) dysfunction 35-45 percent. Then detailed patient history related to KD collected showed no history of cardiac problem except fever 3 months back with unknown cause. Fever duration was about one week but it extended till 4 weeks once in 3 episodes over one month. During the fever episode child care taker noticed some skin rashes around trunk, erythematic skin lesion on lips and oral mucosa and unilateral cervical lymphadenopathy. The patient went to private hospital where he was treated with antibiotics. After that there was no fever episode till 2 month but patient developed occasional chest pain. For chest pain complaint they went to one private hospital Noticing ST, T changes in ECG, some major issue was suspected and the patient was referred to AIIMS Hospital.

Investigations

First, emergency primary assessment was done for Airway - open, stable SPO_2 maintained at room air, child respiratory rate was 30/min-mild distress but no extra respiratory effort seen. Auscultation revealed bilateral air entry with no added crebs. Next circulation status assessed - no tachycardia, heart rate was

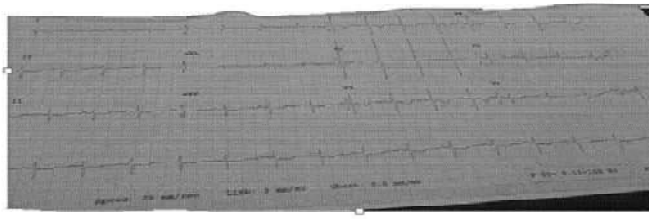


Fig 3: ECG changes reveal ST depression (decreased as compare to previous), T-wave inversion seen.

Table 1: Routine and specific Blood investigations for Kawasaki disease

Blood Haemogram	Values	Other Test	Values	
Hb	10.8 gm	CRP	0.95 mg/dl	
TLC	8700 cu mm	Serum ferritin	47.5	
DIC	N42L44Mo8	Ionised calcium	4.26 mg/dl	
ESR	16 mm/hr			
PLT	2.6 lakh			
Sugar	66 mg/dl	PT	14.6	36.7 sec
Urea	24 mg/dl	INR	1.29	3.377
Creatinine	0.3 mg/dl	aPTT	36 sec	
Uric acid	3.9 mg/dl			
Sodium	142 meq/l			
Potassium	4.8 meq/l			
SGOT	82 IU			
SGPT	29 IU			
Total protein	6.7 gm/dl	DIC profile	Normal PT, APTT, TT, Fibrinogen	
Albumin/globulin	4.1 gm/dl		Raised D-Dimer	
Total serum bilirubin	0.2 mg/dl			

86/min. Not a hypotensive patient, BP was 90/60 mmHg. Apical pulse and peripheral pulses were normal and skin was warm. Disability assessment showed that patient was conscious with good motor activity. Immediately ECG and chest X-ray were done. ECG repeated after 2 hours showed abnormal tall peak t waves (Fig 1-3).

Trop-I was positive 2.54 ng/ml. Echocardiogram reveal RWMA (+), hypokinesia of RCA territory, global hypokinesia (+), moderate LV function, EF 35-40 percent, mild MR, No AS/AR/MS, No co-arctation of aorta. Dilated LMCA was around 4.5 mm (turbulence +), dilated RCA ostium 5mm, post-ostial aneurysm (+) 8 mm. Overall echo impression Kawasaki disease/ moderate LV dysfunction / coronary aneurysm (+). Remaining all valves were normal.

General appearance of the child in the ward showed that the child was very active and condition was generally stable and was taking orally well. Cardiac monitor showed vitals as stable. Occasionally child had 2 episodes of fever, about 100.4°F. Blood pressure usually maintained around 90/60 mmHg. No tachycardia; urinary output was also adequate. No other abnormalities were noted on inspection, ausculatation, percussion and palpation. No skin rashes, erythematic lesions seen (although it was present during fever episode 3 months before).

CT Angiography showed aneurysmally dilated RCA with thrombosis and occlusion. Ectasia of LMCA and LAD with presence of thrombus in mid LAD. LCX also showed multiple areas of dilatation and narrowing. Resting global myocardial perfusion deficit.

Only after admission patient had left mass over gluteal region it was mobile, child used to have pain when it pressed firmly. USG of the mass revealed overall well defined hetero-echoic lesion measuring 2.6* 2.1 cm in left gluteal region in subcutaneous plaque with few cystic area at its superior aspect. No internal vascularity seen. Need clinical co-pathological co-relation.

There is need for continuous follow-up, regular ECHO, ECG monitoring. Increase in Chest pain frequency, fever episodes are signs needing other modality treatments like stenting, CABG, and cardiac transplant.

This case report child may come across the stage of myocarditis and coronary arteritis which develops into coronary artery aneurysms later (multiple aneurysm and thrombosis).

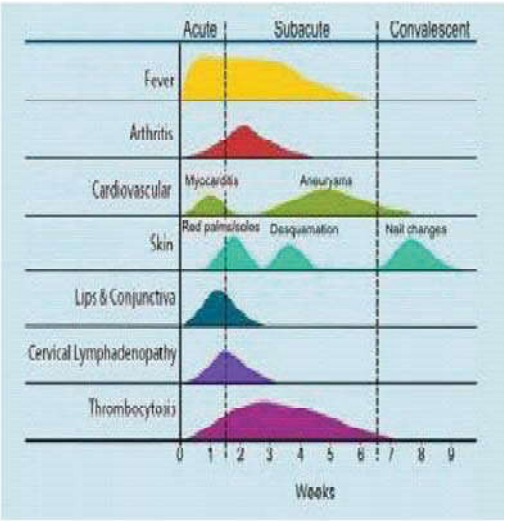
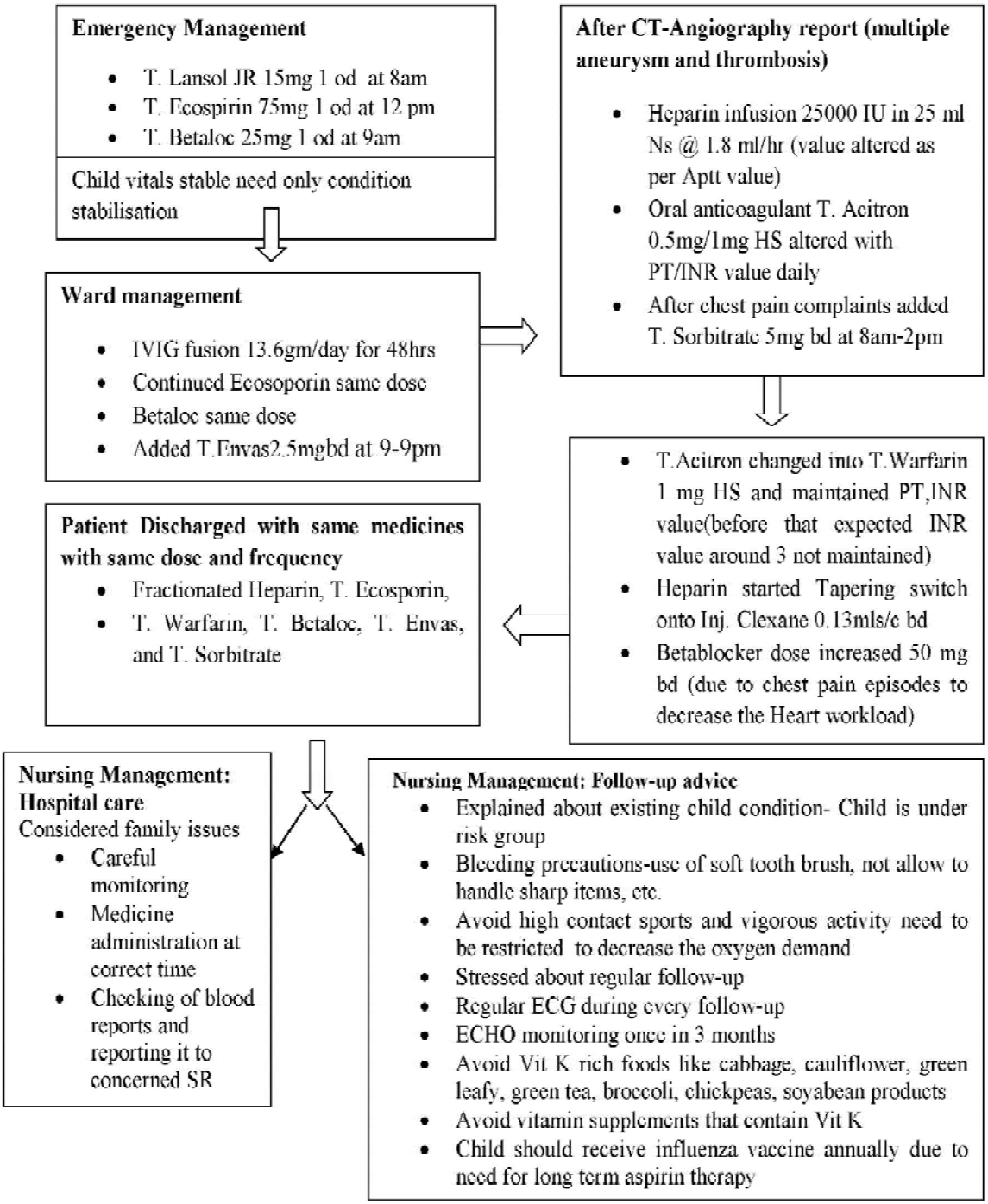


Fig 4: Clinical manifestations of Kawasaki disease.

Clinical features: The clinical presentation of KD varies over time, with the clinical course conventionally divided into 3 stages: acute, subacute, and convalescent (Figs 4-6). Some authors add a fourth, chronic, phase.

Stage 1: Acute febrile stage: The acute stage begins with an abrupt onset of fever and lasts approximately 7-14 days. The fever is typically high-spiking ranging from 102-104°F (39-40°C) or higher. This fever is not responsive to antibiotics or antipyretics and can persist for up to 3-4 weeks if untreated. Other signs and symptoms of this phase may include irritability; non-exudative bilateral conjunctivitis (90%); anterior uveitis (70%); perianal erythema (70%); erythema and oedema on the hands and feet; the latter impedes ambulation; strawberry tongue and lip fissures; hepatic, renal, and GI dysfunction; myocarditis and pericarditis; lymphadenopathy (75%),

Treatment



generally a single, enlarged, non-suppurative cervical node measuring atleast 1.5 cm.

Administration of immunoglobulin (IVIG) and aspirin at this stage, the fever typically remits within 48 hours. The muco-cutaneous changes and lymphadenopathy are most evident during the acute phase. Erythema and oedema of the hands and feet may be the last finding to develop. The diagnosis should be made in this phase.

***Stage 2*:** The subacute stage begins when the fevers have abated, and it continues until week 4-6. The hallmarks of this stage are desquamation of the digits, thrombocytosis (the platelet count may exceed 1 million/iL). Persistence of fever beyond 2-3 weeks may be an indication of recrudescent KD. If fever persists, the outcome is less favourable because of a greater risk of cardiac complications.

Stage 3: Convalescent phase: The convalescent phase is marked by complete resolution of clinical signs of the illness, usually within 3 months of presentation. This stage begins with the return to baseline of the acute phase reactants (eg, erythrocyte sedimentation rate, C-reactive protein) and other laboratory abnormalities. During this stage, most of the clinical findings resolve; however, deep transverse grooves across the nails (Beau lines) may become apparent 1-2 months after the onset of fever. Cardiac abnormalities may still be apparent. Smaller coronary artery aneurysms tend to resolve on their own (60% of cases), but larger aneurysms may expand, and myocardial infarction and ischaemia may occur.

Chronic phase: This stage is of clinical importance only in patients who have developed cardiac complications. An aneurysm formed in childhood may rupture in adulthood. In some cases of aneurysms rupturing in adult life revealed febrile childhood illnesses of unknown aetiology. This case report child need

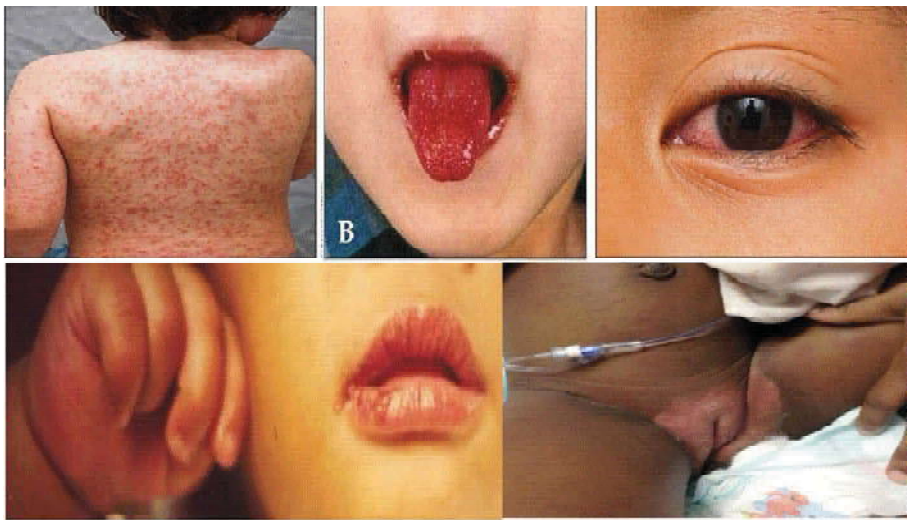


Fig 5: Kawasaki disease - Acute phase clinical features.

continuous follow-up because of the risk of aneurysm rupture and myocardial infarction in later life.

There is no specific diagnostic test, although laboratory and echocardiographic findings e.g., elevated erythrocyte sedimentation rate and C-reactive protein level, hyponatremia, hypoalbuminemia, coronary aneurysms may help in evaluating suspected cases and differentiating Kawasaki disease from other conditions.

Paediatric conditions which can mimic clinical features of KD include viral exanthems (especially measles), drug reactions, Stevens-Johnson Syndrome, systemic onset juvenile rheumatoid arthritis, scarlet fever and toxic shock syndrome.

Acute stage diagnosis and early treatment is necessary to reduce the development of coronary aneurysm abnormalities. Acute management should be initiated within 10 days of fever onset/after 10 days of fever still should be treated of having persistent fever, aneurysms, or inflammation, including an elevated ESR or CRP level. Single dose of IVIG (2 g per kg) administered as a single infusion over 8 to 12 hours. Either high-dose aspirin (80 to 100 mg/kg/day, divided into four doses)/ low-dose aspirin (3 to 5 mg per kg per day, given as a single dose) should be continued until six to eight weeks after disease onset if there are no coronary artery abnormalities.

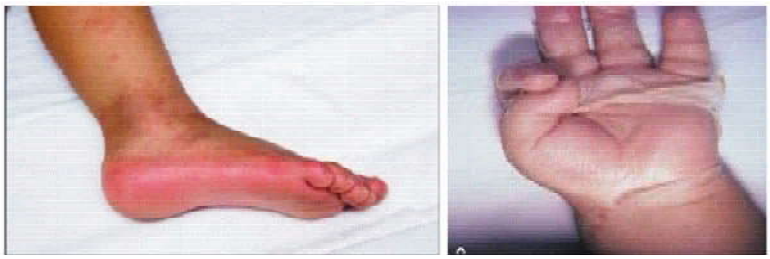


Fig 6. Stage 2 Clinical features.

If coronary aneurysms develops, aspirin may need to be continued indefinitely. IVIG suppresses the formation of coronary aneurysms, improves myocardial perfusion and reverses lymphocyte activation. The mechanism of action is through down regulation of cytokine production, blockage of Fc receptors and suppression of antibody function through the anti-idiotypic pathway.

IVIG Adverse effects: Despite its advantages, IVIG is an expensive and potentially toxic intervention. Significant haemolysis requiring transfusion can occur within 5 to 10 days of infusion due to isoagglutinins in the IVIG products. The risk of haemolysis is dose-related and is particularly increased in patients who receive more than one dose of IVIG. Children with non-type O blood are also at increased of developing significant haemolysis following IVIG therapy.

Treatment of refractory disease: Approximately 10 percent of patients have refractory disease that does not respond to initial therapy (i.e., fever persists or recurs 36 hours after initial IVIG dose). These patients usually receive a second infusion of IVIG at 2 gm per kg. The AHA guideline states that the relative roles of repeated use of IVIG and other adjunctive therapies (e.g., corticosteroids, TNF-α antagonists, plasma exchange, cyclophosphamide) are uncertain. Long-term risk of coronary disease is a result of intimal thickening and stenosis in segments adjacent to giant aneurysms and in areas of resolved smaller aneurysms. Patients without aneurysms or stenosis tend not to have late complications, although evidence of long-term atherosclerotic risk is mixed (Table 2).

The case report child belonged to risk IV level management.

Other treatment modalities: If the patient not responding or symptoms are worsening like chest pain frequency increase then immediate need for other treatment modalities like coronary artery stenting/ PTCA,CABG or cardiac transplant.

General Nursing management

It includes monitoring temperature frequently; Cardiac monitoring - frequently check ECG changes, Heart rate, sp02; Assess extremities for oedema, redness and desquamation; Examine eyes for conjunctivitis(non-exudative); Monitor mucous membrane changes for inflammation-give soft foods and liquids neither too hot nor too cold; Monitor intake and

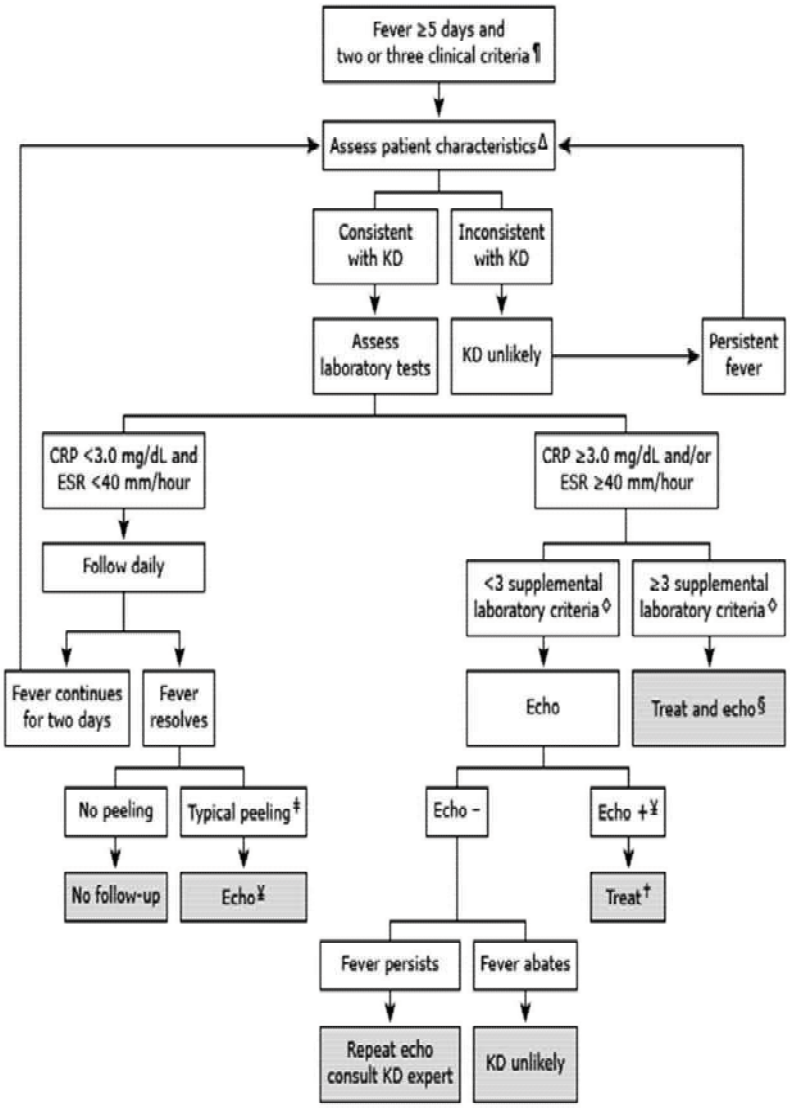


Fig 7: General diagnosis algorithm for Kawasaki disease

output chart and weigh child daily; Facilitate passive range of motion exercises to facilitate joint movement; Administer IVIG with hypersensitivity precautions and administer aspirin; Assess the signs and symptoms of adverse effects of IVIG- haemolysis; Administer other medications as per prescribed- if aneurysm is present anticoagulants to be added. If myocardial ischaemia/infarction occurs then need to administer beta-blocker, ACE inhibitor, nitrates.

Parent education/instructions may be explained about regular follow-up care and its importance; persisting signs and symptoms after acute illness treatment: Irritability lasting for 2 months after the onset of symptoms; peeling of hands and feet may occur; Joint pain persist for several weeks. They may be advised to record the temperature because fever is expected until the child is afebrile for several days and notify the physician if it exceeds 101°F.

Child whoever taking long term aspirin should know about the toxicity like tinnitus, headache, vertigo and bruising. Tell the parents avoiding aspirin or aspirin containing product when child has been exposed to chickenpox or flu (to prevent Reyes syndrome). Children on long-term aspirin therapy should receive annual influenza vaccination.

Other measures: Explain about signs and symtoms of (a) bleeding such as epistaxis, haemoptysis, haematemesis, haematuria, malena and bruises on the body, (b) cardiac complications such as chest pain, tightness, cool and pale extremities, abdominal pain, nausea and vomiting, irritability, restlessness and uncontrollable cry. Tell the parents child should avoid contact sports for bleeding precautions. Avoid administration of measles, mumps and rubella/MMR or varicella vaccine to the child for 11 months after IVLG administration. Antacids not to be given along with anticoagulant; Ibuprofen should be avoided. Atherosclerosis risk factor counselling and reproductive counseling for women of childbearing age should be provided.

Prevention: Development of coronary artery abnormalities is the hallmark of KD and accounts for most of the morbidity and mortality associated with the disease. Prompt recognition of the disease and early initiation of treatment with intravenous immunoglobulin (IVIG) and aspirin results in significant reduction in the occurrence of coronary artery aneurysm. So KD should be considered in the differential diagnosis of all febrile illnesses in young children where the fever persists for more than 5-7 days. One needs to refrain from misusing antimicrobials empirically.

Complications: Complications include coronary artery (CA) aneurysms, depressed myocardial contractility and heart failure, myocardial infarction, arrhythmias, and peripheral arterial occlusion. Coronary artery aneurysm may predispose to premature atherosclerosis. Non-cardiac complications are generally uncommon.

Prognosis: Prognosis is based upon the severity of CA involvement as a risk marker for myocardial infarction. If the symptoms are recognised early, kids with KD can fully recover within a few days. Children without cardiovascular abnormalities detected in the acute and subacute phase appear to be clinically asymptomatic 10 to 21 years later, however, the long-term effect on cardiovascular health is unknown.

Patients with giant aneurysms (maximum diameter ≥ 8 mm) are at the greatest risk for myocardial

Table 2: Risk stratification and long-term management in patients with Kawasaki disease

Risk level		Pharmacological therapy	Physical activity	Follow-up and diagnostic testing	Invasive imaging
I	No coronary artery changes at any stage of illness	None beyond 1st 6–8 weeks	No restrictions beyond 1st 6–8 weeks	Cardiovascular risk assessment, counselling at 5-y intervals	None recommended
II	Transient coronary artery ectasia disappears within 1st 6–8 weeks	None beyond 1st 6–8 weeks	No restrictions beyond 1st 6–8 weeks	Cardiovascular risk assessment, counselling at 3- to 5-y intervals	None recommended
III	1 small–medium coronary artery aneurysm/major coronary artery	Low-dose aspirin (3–5 mg/kg aspirin/d), at least until regression documented	For patients < 11 y old, no restriction beyond 1st 6–8 weeks; patients 11–20 y old, physical activity guided by biennial stress test, evaluation of myocardial perfusion scan; contact or high-impact sports discouraged in patients taking antiplatelet agents	Annual cardiology follow-up with echocardiogram + ECG, combined with cardiovascular risk assessment, counselling; biennial stress test/evaluation of myocardial perfusion scan	Angiography, if non-invasive test suggests ischemia
IV	≥ 1 large or giant coronary artery aneurysm, or multiple or complex aneurysms in same coronary artery, without obstruction	Long-term antiplatelet therapy and warfarin (target INR 2.0–2.5) or low-molecular-weight heparin (target: antifactor Xa level 0.5–1.0 U/ml) should be combined in giant aneurysms	Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations guided by stress test/evaluation of myocardial perfusion scan outcome	Biannual follow-up with echocardiogram + ECG; annual stress test/evaluation of myocardial perfusion scan	1st angiography at 6–12 month or sooner if clinically indicated; repeated angiography if non-invasive test, clinical, or laboratory findings suggest ischemia; elective repeat angiography under some circumstances
V	Coronary artery obstruction	Long-term low-dose aspirin; warfarin or low-molecular-weight heparin if giant aneurysm persists; consider use of β-blockers to reduce myocardial O2 consumption	Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations guided by stress test/myocardial perfusion scan outcome	Biannual follow-up with echocardiogram + ECG; annual stress test/evaluation of myocardial perfusion scan	Angiography recommended to address therapeutic options

infarction resulting from CA occlusion. In this condition the prognosis is unexpected.

Conclusion

In India KD is commonly being diagnosed in many parts of the country. In several regions (North East, Uttar Pradesh, Uttarakhand, Madhya Pradesh, Chhattisgarh, Bihar, Jharkhand, Haryana, Jammu & Kashmir) where the condition is not being diagnosed as required. We need information and education campaigns for both the health care professionals and the lay public to increase the awareness about this condition.

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