Case Report

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Dilemma in diagnosing incomplete Kawasaki disease in a resource limited setting

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Introduction and importance: Kawasaki disease (KD) is an acute febrile systemic vasculitis that predominantly affects small to medium sized vessels and mostly occurs in children below 5 years of age. The morbidity and mortality mostly occur due to cardiac involvement.

Case presentation: The authors present a case of a 5-year-old male child from hilly region of Nepal who presented with fever for 7 days along with strawberry tongue and non-exudative conjunctivitis without rashes, extremity changes or lymphadenopathy. A suspicion of incomplete KD (IKD) was made. The notable investigation findings were increased erythrocyte sedimentation rate, C-reactive protein, leucocyte count and platelets. Echocardiography showed normal findings. Based on the clinical features and supplemental laboratory findings, a diagnosis of IKD was made. The patient improved after intravenous immunoglobulin and Aspirin.

Clinical discussion: The main learning objective that the authors get from this case is the challenges in the diagnosis of IKD in the resource limited setting like Nepal. Whether or not to start intravenous immunoglobulin is a dilemma for the physician in most of the cases of suspected IKD, due to the high cost and poor availability of intravenous immunoglobulin in this setting. Hence, the use of inflammatory markers, supplemental laboratory findings together with the few diagnostic criteria met by the patient helps in making a diagnosis and institute timely treatment with intravenous immunoglobulin and aspirin.

Conclusion: Diagnosis of KD in difficult in resource limited setting.

Keywords: diagnosis dilemma, incomplete Kawasaki disease, Kawasaki disease, resource limited setting

Introduction

Kawasaki disease (KD) is an acute febrile systemic vasculitis that predominantly affects small to medium sized vessels and mostly occurs in children below 5 years of age[1]. The bulk of morbidity and mortality in KD are caused by cardiac involvement, which results in the development of coronary artery aneurysms, myocarditis, shock, heart failure, impaired ventricular function, and ischaemic heart disease as a result of inflammatory vasculitic changes in and around the heart and arrhythmias. KD used to be referred to as mucocutaneous lymph node syndrome[1].

There are multiple possible triggers hypothesized in the causation and pathogenesis of KD. Rife *et al.*[2] in their study mentioned about various factors like genetic, post-vaccine exposure, post-infectious or immune dysregulation, as possible triggers. However, exact mechanism is still unknown.

HIGHLIGHTS

- Our study highlights the difficulty faced by the paediatrists during the diagnosis of incomplete Kawasaki disease (KD) in resource limited setting like Nepal.
- The lack of proper laboratory parameter for the incomplete KD diagnosis makes it difficult for the confirmation of the diagnosis.
- Further challenges is added due to lack of paediatric cardiologist and rheumatologist.
- Our research holds value in understanding and keeping KD as a differential diagnosis whenever a child presents with Fever not relieved by medication for more than 5 days so, that the diagnosis is not missed and life of the child is not risked.

The progression of cardiovascular involvement of KD[3] includes a spectrum of changes ranging from mild transient dilation of coronary artery which could be remodelled to normal upon treatment, to aneurysm formation leading to thrombotic occlusion, which could either recanalize later or might lead to permanent occlusion with stenosis or abnormal vascular wall remodelling.

Table 1 defines the diagnostic criteria for KD[4].

If 4 or more principal criteria are present, the diagnosis may be made on day 4 (or, rarely, even day-3) of fever.

Incomplete KD (IKD) Criteria: Fever for 5 or more days and failure to meet at least 4 of 5 diagnostic criteria for complete KD.

The overall prevalence of KD was found to be 0.10% Interval (0.07–0.13%) among 11 416 patients under the age of 5 years admitted in paediatric ward in Nepal[5]. At diagnosis, the median

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Table 1

Diagnostic criteria for Kawasaki disease

Diagnostic criteria:
Fever for 5 or more days, 4 or more diagnostic criteria are met, and absence of viral or bacterial causes for symptoms. The 5 key criteria are as follows:
Rash: maculopapular, diffuse erythroderma, or erythema multiforme–like
Oral changes: erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa
Conjunctivitis: bilateral bulbar conjunctival injection without exudate
Extremity changes: erythema and oedema of hands and feet in acute phase and/or periungual desquamation in subacute phase
Cervical lymphadenopathy (1.5 cm or more in diameter); typically, unilateral

NS1, Nonstructural protein 1.

age was 10.5 months. The four symptoms that were most frequently seen were fever, rash, and oral abnormalities[5].

KD is primarily a self-limiting monophasic disease whose outcome depends on the swift diagnosis and administration of Intravenous Immunoglobulin (IVIG), within 10 days of symptoms onset which additionally helps in preventing organ dysfunction and shortening the duration of inflammation[1]. The major complications of the disease includes (but not limiting to): KD shock syndrome[6], myocardial infarction[7], non-coronary vascular involvement[8], macrophage activation syndrome[9].

Case presentation

History and examination

A 5-year-old male from hilly region of Nepal presented to a tertiary hospital with a high-grade fever for 7 days(103°F) accompanied byredness of eyes (Fig. 1), strawberry-coloured tongue, myalgia, anorexia. He had no history of rash, erythema of palms and soles, skin desquamation, any sick contacts, urinary urgency, frequency or burning micturition; shortness of breath, cough and chest pain; altered consciousness, focal neurological deficits and recent travel. Fever was not responding to oral paracetamol. On examination, at initial presentation, he was febrile and appeared unwell. Vitals were: pulse rate: 102 beats per minute, respiratory rate: 30 cycles per minute, capillary refill time was less than 3 s, temperature: 102°F. On general examination there was no pallor, icterus, cyanosis, clubbing, lymphadenopathy, oedema and dehydration. Tongue was erythematous giving a strawberry like appearance. Non-exudative Conjunctivitis was present. Throat and pharynx were normal. Chest examination had normal vesicular breath sounds bilaterally. Cardiovascular examination revealed normal heart sounds without murmur. Abdominal and neurological examinations were well within normal limits (Figure 2).

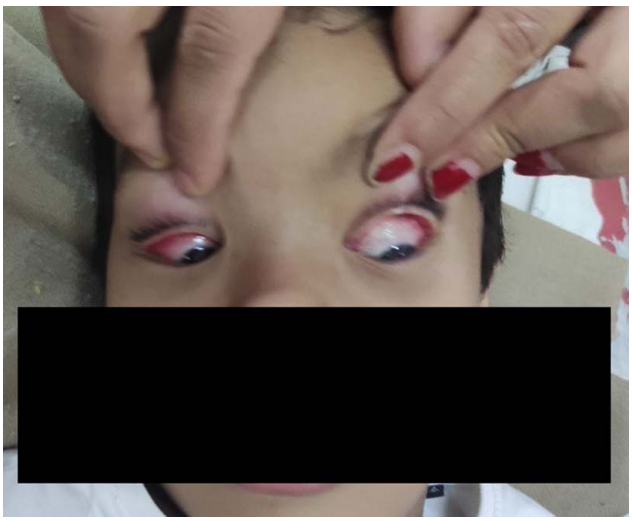

Figure 1. Non-exudative conjunctivitis.

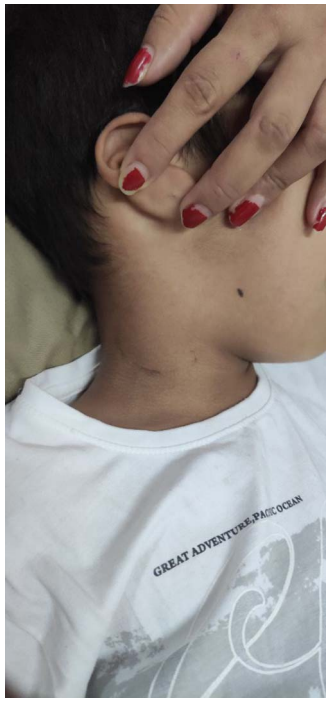

Figure 2. No cervical lymphadenopathy.

On investigations

His initial investigations are listed in Table 2.

Diagnosis and treatment

There was a difficulty in making a confident diagnosis of IKD as the patient met only two out of the five criteria. Also, there was a dilemma in using or not using IVIG in this patient, given the fact that that it is expensive and easily not available. The risks associated with not using IVIG were also weighed. Considering a raised C-reactive protein and erythrocyte sedimentation rate value, along with leukocytosis, thrombocytosis and hypoproteinemia in conjunction with fever of 7 days duration and presence of strawberry tongue and non-exudative conjunctivitis, a diagnosis of IKD was made and a decision of starting IVIG and aspirin therapy was done. Serum immunoglobulin G level was not tested in the patient because of unavailability and cost factor. It should be noted that these laboratory findings were not considered as diagnostic criteria. They rather supported our diagnosis. Hence, it was diagnosed as IKD.

The treatment was started on second day with IVIG at dose of 2 g/kg in infusion over 10–12 h and aspirin at a dose of 80 mg/kg/

Table 2

Investigations done

Investigations	Results	Normal values
Haemoglobin	11.0 g/dl	Male: 13.5–16.5 and female: 12–16 g/dl
Total leucocyte count (TLC)	15 920 cells/mm^3	4500–11 000/mm^3
Erythrocyte sedimentation rate (ESR)	38 mm/h	Male: 0–15 mm/h and female: 0–20 mm/h
Platelets	510 000/mm^3	150 000–400 000/mm^3
Alanine transaminase (ALT)	61.0 U/l	8–20 U/l
Aspartate transaminase (AST)	52.0 U/l	25–125 U/l
Alkaline phosphatase (ALP)	156 U/l	20–70 U/l
Total bilirubin	0.37 mg/dl	(0.1–1.0 mg/dl)
Conjugated bilirubin	0.07 mg/dl	0.0–0.3 md/dl
Albumin	3 g/dl	3.5–5.5 g/dl
Blood film	Normal	
Creatinine	0.34 mg/dl	0.6–1.2 mg/dl
Urine-microscopy, culture and sensitivity	Culture sterile after 24 h of aerobic incubation at 37°C	
Dengue serology: NS1, IgM, IgG	Negative	
Troponin-I	Negative	
Echocardiography	Normal	
C-reactive protein (CRP)	96 mg/l	8–10 mg/dl
COVID-19 PCR	Negative	

Note: The Normal lab value of the respective hospital has been used.
It should be noted that dengue serology was done because the patient was from Dengue Endemic region.
IgG, immunoglobulin G, IgM, immunoglobulin M; NS1,Nonstructural protein 1; PCR, polymerase chain reaction.

day along with oral paracetamol. IV antibiotic Ceftriaxone was given 1 g IV in two divided doses for 7 days. Paracetamol was given for decreasing fever.

Outcomes

On day-3 after the medication, fever subsided and vitals were improved.

Discussion and conclusions

This child of IKD primarily presents with fever, strawberry tongue and conjunctivitis, along with raised inflammatory markers, anaemia, leukocytosis, thrombocytosis, hypoalbuminemia and mildly raised liver enzymes, with normal initial echocardiogram, contrary to the usual cardiac findings contemplated in literatures[1]. The most important complication of KD arises as a result of coronary artery involvement, which leads to cardiac arrythmia, aneurysm, ischaemic heart disease, and sudden death[5]. However, the clinical course of KD is highly variable and there exists no pathognomonic clinical or laboratory findings to help diagnose KD.

The diagnosis of KD in this case was made using the American Heart Association criteria[5]. In the presence of at least 5 days of fever, if there are at least four of the five principal criteria (cervical adenopathy, bilateral non-purulent conjunctivitis, oropharyngeal mucosal changes, polymorphous rash, erythema of the palms or soles, and oedema of the hands or feet). IKD is a dangerous diagnostic dilemma, as children present with prolonged fever and do not meet all of the clinical criteria for complete KD diagnosis; since the patient meets two out of five principal criteria he is diagnosed as having IKD.

There have been various studies and case reports in the past describing the varied manifestations of IKD. Pratap *et al.*[10] described KD in an adult with predominant hepatic involvement which is rare. Hu C *et al.*[11] reported KD in a 4 years old boy with predominant gastrointestinal symptoms with signs of gastrointestinal haemorrhage on Endoscopy. In another report by Liu *et al.*[12], they described KD in a 2 years girl child with predominant respiratory symptoms diagnosed with KD shock syndrome who was treated with extracorporeal membrane oxygenation and eventually recovered completely. KD in a 7-years-old girl with predominant respiratory symptoms with provisional diagnosis of pneumonia with pleural effusion not responding to antibiotics was mentioned by Arslanoglu *et al.*[13]. Osman *et al.*[14] reported KD in a 7 months fully vaccinated Asian-boy with non-bilious, non-projectile vomiting with passage of bloody mucoid stool diagnosed with intussusception which was manually reduced on laparotomy. Similarly, another case report by Lin *et al.*[15] mentioned KD in a 5 months old boy with fever and symptoms of KD shock syndrome and hepatosplenomegaly with decreased red blood cells and platelets giving the diagnosis of macrophage activation syndrome, which was managed by emergency shock therapy and methyl prednisolone.

IKD diagnosis is often late and confusing which often worsens the prognosis of the child. Li T *et al.*[16] mentions the difficulty of diagnosis of IKD due to its occurrence with other infections and rheumatic diseases. Hence, any child presenting with unexplained fever for longer duration clinician should be vigilant for possibility with KD or IKD.

Miller *et al.*[17] described a case of 4-year boy presented with skin changes of lips and oral cavity, generalized rash, oedema of hands and feet and peeling of skin of periungual areas of fingers as well as of groyne and perianal area, who was diagnosed with IKD after investigations and cardiologist consultation. As explained in the literature the diagnosis was challenging without the help from cardiologist consultation. Idris *et al.*[18] reported a case of 4-month female with fever for less than 4 days and not following the latest American Heart Association guideline for IKD but was diagnosed as IKD after cardiologist consultation and echocardiogram which revealed coronary artery aneurysm. As mentioned in the literature even with resources available, the diagnosis was delayed by 10 days giving evidence to its challenging diagnosis. Pilania *et al.*[19] emphasized about the difficulty in diagnosis of KD in older child. The authors further added that delay in diagnosis is associated with higher risk of coronary abnormalities. Also, the absence of a confirmatory laboratory marker creates further difficulties in diagnosis of KD. The findings of Pilania and colleagues are similar to that of Vervoort *et al.*[20].

Moreover, the diagnosis becomes tricky in resource limited setting like Nepal where the cost factor of IVIG and limited availability makes the decision making challenging and time consuming. The problem is added further in our setting due to lack of paediatric rheumatologist and paediatric cardiologist in our setting. Among the dilemma in diagnosis and dilemma in cost, the former is the first priority to be addressed.

Methods

The work has been reported in line with the SCARE criteria[21].

Ethics approval and consent to participate

Not applicable for case reports.

Consent for publication

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Author contribution

M.B.: analyzed and interpreted the data, conceptualization, investigations, visualization, supervision, writing—review and editing. A.B.: data curation, writing—original draft, writing—review and editing. D.K.: data curation, writing—original draft, writing—review and editing. K.B.: data curation, writing—original draft, writing— review and editing. A.S.: data curation, writing—original draft, writing—review and editing. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no competing interests.

Guarantor

All the authors are guarantor.

Availability of data and materials

Not applicable.

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