CASE SERIES

# Kawasaki Disease: Highlighting Importance of Laboratory Criteria and Minor Atypical Features of This Enigmatic Entity- A Case Series

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## ABSTRACT

**Introduction:** Kawasaki disease (KD) is an acute febrile illness of unknown etiology that primarily affects children younger than 5 years of age. The diagnosis is predominantly clinical and at times difficult, due to the absence of any confirmatory and specific diagnostic test. Early diagnosis of this disease is of paramount importance due to long term cardiovascular complications related to coronary artery aneurysm. Literature search has revealed many atypical presentations of Kawasaki disease not fulfilling the clinical diagnostic criteria. The reason for this could be the diversity in clinical manifestations involving gastrointestinal, endocrinal, musculoskeletal and nervous system. **Case Series:** Here we describe three cases with non-classic presentation of Kawasaki disease. These three cases presented with persistent fever unresponsive to antibiotics. Two cases (case one and three) later developed perianal rash and peeling that helped in early diagnosis. In the remaining case (case two) sequential appearance of features helped in the establishment of diagnosis. It was interesting to note that all the three cases were having identical laboratory parameters, highlighting the importance of laboratory investigations in case of atypical presentation. **Conclusion:** This case series culminates the importance of keeping the possibility of atypical Kawasaki disease (KD) as one of the differentials in patients with prolonged fever not responding to antibiotics, in the absence of classical diagnostic criteria.

**Keywords:** Atypical Kawasaki disease, Non-infectious leukocytosis, Skin peeling

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## INTRODUCTION

Tomisaku Kawasaki described the first case of Kawasaki Disease (KD) in a four-year-old child in the year 1967 (1). KD is an acute vasculitis of usually small- and medium-sized arteries of unknown etiology which may cause weakening of coronary artery that may later lead to development of coronary aneurysm (2). Once considered as a rare diagnosis, presently KD is one of the leading cause of acquired heart disease in children (3). None of the laboratory tests are confirmatory for establishing this diagnosis, hence specific criteria has been laid by American Heart Association (AHA) (Table I) (4). Based on clinical presentation, KD has been classified into two groups - Classic (typical) and incomplete (atypical) (5). Atypical or incomplete KD constitutes nearly 15–20% of all KD patients, occurs primarily in children who are less than 6 months and more than 5 years of age (6). Atypical KD patients usually respond poorly to treatment and manifest long term cardiac complication like coronary artery aneurysm (7,8,9,10). The reason could be delay in diagnosis and start of specific therapy. Early diagnosis of KD with prompt treatment with intravenous immunoglobulin (IVIG) has been found to be productive in decreasing the long term cardiovascular complication if started within 10 days of fever (11). This substantiates the importance of early diagnosis and treatment especially in atypical cases.

**Table I:** As per American Heart Association (AHA) principal diagnostic criteria to diagnose KD

| Persistence of fever for more than 5 days with at least four of the 5 principal clinical findings |
|---|
| 1. Changes in extremities:<br>Acute: Erythema of palm, sole; oedema of hand, feet<br>Chronic: Periungal peeling of fingers, toes in weeks 2 and 3 |
| 2. Polymorphous exanthema |
| 3. Bilateral bulbar non exudative conjunctivitis |
| 4. Oral cavity and lips changes: Erythema, lip cracking, strawberry tongue, diffuse injection of oral and pharyngeal mucosa |
| 5. Cervical lymphadenopathy (1.5 cm in diameter), usually unilateral |

In this series, we would like to highlight the importance of detailed physical examination and associated laboratory parameters to suspect KD in early stages. We report three cases, where one had a typical presentation while other two had very atypical features causing diagnostic dilemma. The only feature which led us to

suspect atypical KD was perianal rash. This feature is not a part of major criteria but has been described as a minor criteria. Interestingly, all the three cases had similar laboratory parameters.

## CASE SERIES

### Case 1

A 2 year old girl child was brought with complaints of fever for 5 days. On examination, child was having mild erythema over the periurethral area (Fig. 1a), rest of the examination was normal. Laboratory investigation showed hemoglobin 9.8 gm/dl, total leucocyte count 22900/mm3 with 82% polymorphs, platelet count 3.6 lakh/mcl, ESR 89 mm/hour and CRP 83 mg/l. Urine routine was suggestive of pyuria (20-25 pus cells/hpf). A provisional diagnosis of urinary tract infection was considered. The urine culture and blood culture were ordered. The child was started on empirical IV antibiotics along with other symptomatic measures.

After 3 days of hospital admission, fever spikes persisted and child became more irritable. The erythema over the periurethral area had progressed over the perianal area along with some excoriation and mild peeling at the periphery (Fig. 1b). There was no history of loose stools or diaper use. Blood culture and urine culture were sterile after 72 hours of incubation. In view of persisting fever spikes without evidence of infection along with a rash over the perianal area and repeat laboratory investigations showing persistent leukocytosis (TLC 22400/mm3 with 80% polymorphs), raised platelet count of 10.1 lakh/mcl and persistently high ESR (105mm/hour) and CRP (82.9 mg/L), possibility of Atypical Kawasaki disease was considered. ECHO was done and found to be normal. The child was started on IVIG 2gm/kg together with aspirin (30 mg/kg/day) on day 9 of illness. The child became afebrile after 24 hours of IVIG. Once the child was afebrile for 48 hours, she was discharged on small dose aspirin (5mg/kg/day). After 2 days of IVIG infusion peeling of skin was noted over the palm and periungal area that further supported the diagnosis of KD. On follow up at 6 weeks, the child was asymptomatic and there was no evidence of Beau's lines on nails. The repeat blood investigations were normal (ESR – 10/hr, Hemoglobin – 11.2/mg/dl, Platelet count – 3.8 lakh/mcL, TLC – 12,600/mm3). Repeat ECG and ECHO were also normal, following which aspirin was stopped. The child is on follow up since past one year and is currently doing well without any symptoms.

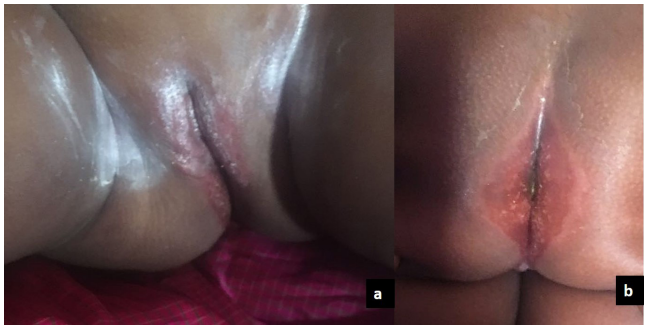


**Figure 1: (a) Initial presentation periurethral erythema, (b) later developed perianal rash with peeling of skin.**

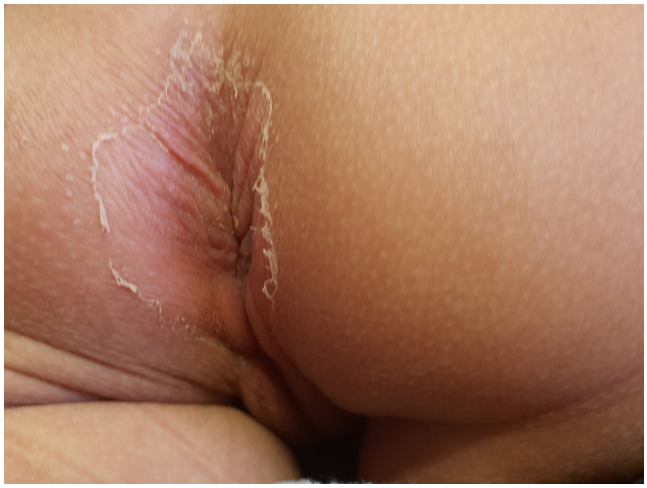

**Figure 2: Perianal rash with peeling at the periphery**

### Case 2

A two and half year old boy was brought with complaints of fever and swelling over left side of neck since 3 days. On examination, the child was having enlarged left cervical lymph nodes, largest measuring 4 cm x 3 cm associated with mild tenderness, rest of the examination was normal. Laboratory investigations showed hemoglobin 9.2 gm/dl, total leucocyte count 29800/mm3 with 81% polymorphs, platelet count 3.84 lakh/mcl, ESR 92 mm/hr and CRP 88 mg/l. A diagnosis of cervical lymphadenitis was made and the child was started on IV antibiotics after sending blood and urine cultures.

After 24 hours of hospital admission, fever spikes still persisted. The child also developed bilateral conjunctival congestion. Following day, child was found to have mild edema over the feet, cracked lips and redness of the tongue. A provisional diagnosis of KD was considered. ECHO was done and was normal. Blood culture and urine culture were sterile after 72 hours of incubation. Repeat laboratory investigation revealed hemoglobin 8.1 gm/dl, total leucocyte count 44400/mm3 with 80% polymorphs, platelet count 5.1 lakh/mcl, ESR 102 mm/hour and CRP 217 mg/l. Urine routine was suggestive of pyuria (30-35 pus cells/hpf). With the above examination findings and laboratory parameters, diagnosis of typical Kawasaki disease was considered. The child was started on IVIG, 2gm/kg and aspirin (30 mg/kg/day) on day 6 of illness. The child became afebrile after 16 hours of IVIG. Once the child remained afebrile for 48 hours, child was discharged on small dose aspirin (5mg/kg/day) for 6 weeks. On follow up after 1 week of discharge, child was having no symptoms and cervical lymph node was 1x 1cm in size. On lab investigation, hemoglobin was 10.7 gm/dl, total leucocyte count 13500 mm3 with

30% polymorphs, platelet count 6.83 lakh/mcl, ESR 35 mm/hour and CRP 1 mg/l. Repeat ECHO and ECG were normal at 6 weeks follow up, following which aspirin was stopped. At 6 weeks follow up, the examination was normal with no evidence of nail ridges or Beau's lines on nails.

**Case 3**

A 3 years old girl was brought with complaints of fever since 4 days. On examination, child was febrile with no clinical focus of infection. Laboratory investigation revealed hemoglobin 9.8 gm/dl, total leucocyte count 22500/mm3 with 70% polymorphs, platelet count 4.82 lakh/mcl, ESR 32mm/hour and CRP 39 mg/l. Urine routine was suggestive of pyuria (8-10 pus cells/hpf). A provisional diagnosis of urinary tract infection was considered. The child was started on empirical IV antibiotics along with other symptomatic measures after sending blood and urine cultures.

After 3 days of hospital admission, fever spikes still persisted and the child developed some perianal erythema and excoriation (Fig. 2). There was no history of loose stools or diaper use. Blood and urine cultures were sterile after 72 hours of incubation. In view of persisting fever spikes without evidence of any infection and development of perianal rash, possibility of atypical Kawasaki disease was considered. ECHO was done and found to be normal. The child was started on IVIG, 2gm/kg together with aspirin (30 mg/kg/day) on day 7 of illness. The child became afebrile after 24 hours of IVIG. Once the child remained afebrile for 48 hours, we noted some peeling of skin over palm and periungual area along with some peeling over the perianal rash which further supported our diagnosis. The child was discharged on a small dose aspirin (5mg/kg/day) for 6 weeks. On follow up at 6 weeks post discharge, blood investigations (ESR – 10, Hemoglobin – 11.2 gm/dl, Platelet count – 3.8 lakh/mcl, TLC – 12,600/mm3) were normal. Repeat ECG and ECHO were also normal following which aspirin was stopped. Examination was normal at 6 weeks follow up including no evidence of Beau's lines on nails.

## DISCUSSION

Kawasaki disease (KD) is a rare vasculitis of the small vessels seen predominantly in children less than 5 years (12,13). In patients with KD, coronary artery involvement is the leading cause of morbidity and mortality. Coronary artery vasculitis causes dilatation or aneurysm of the arteries that may cause myocardial infarction (14). This vasculitis is usually self-limiting but due to long term cardiovascular complications, early diagnosis and specific treatment is of paramount importance (15).

Diagnosis of KD is usually clinical and at times may pose difficulties. The reason behind this is the absence of any confirmatory diagnostic test. It is difficult to fulfill the diagnostic criteria in many cases due to diverse clinical manifestations involving gastrointestinal, endocrinal, musculo-skeletal and nervous system. In few cases sequential appearance of manifestations make the early diagnosis difficult. If clinical features are not fulfilling the diagnostic criteria, diagnosis can only be thought off by high index of clinical suspicion.

Two of our cases were not fulfilling the diagnostic criteria for typical KD where high index of clinical suspicion helped us to render the correct diagnosis. Importantly, all cases had in common high leucocyte counts, high CRP, high ESR, platelets counts higher than normal and sterile pyuria (Table II). Fever was also persistent in all. Thus in all three cases laboratory pointers were highly suggestive which had helped us in establishing the diagnosis. In case 1 and case 3, children presented with a possible urinary tract infection. As they did not improve after the course of antibiotics and the rash over the perianal region could not be explained by other differentials, possibility of KD was considered. Other differential diagnosis of perianal rash like perianal infectious dermatitis, psoriasis, inflammatory bowel disease, atopic dermatitis and candidiasis were ruled out as there was no history of diarrhea or diaper use, no rash at other parts of the body, clinical morphology of the rash (i.e. peeling of skin at the periphery of rash), presence of systemic features and no history of similar rash in the past. The presence of the perianal rash in both the cases helped us in making early diagnosis of KD. Perianal rash has been described as one of the other significant clinical findings by AHA and may even appear before the skin peeling elsewhere. Similar finding of perianal peeling was reported by Vignesh P et al in a 10-month old child emphasizing perineal desquamation as an important key clinical feature which may get overlooked (16). Case 2 was diagnosed typical KD after the sequential appearance of manifestations and thus had met with the diagnostic criteria. Based on our observations in these three cases, we conclude that in all febrile cases without any clinical focus of infection, with predominantly high

**Table II:** Clinical characteristics and laboratory investigations in all three cases

| | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| **Fever > 5 days** | + | + | + |
| **Perianal rash** | + | _ | + |
| **Skin peeling** | + | + | + |
| **Cervical Lymphadenopathy** | _ | + | _ |
| **Oral mucosa and tongue** | _ | + | _ |
| **Conjunctivitis** | _ | + | _ |
| **Leukocytosis** | + | + | + |
| **Thrombocytosis** | + | + | + |
| **High CRP** | + | + | + |
| **High ESR** | + | + | + |
| **Sterile Pyuria** | + | + | + |
| **Blood and Urine Culture** | Sterile | Sterile | Sterile |
| **ECHO** | Normal | Normal | Normal |

leukocytosis and high CRP, KD should be kept as one of the differentials. Clinicians must have high index of suspicion for this disease due to the possible uncommon and atypical presentations of these cases. Early starting of specific IVIG treatment is protective and prevents cardiovascular complications. This also emphasizes the importance of early diagnosis and recognizing atypical presentations as well. The only clinical feature in our two cases besides fever was perianal rash, thus highlighting the importance of complete physical examination of all the febrile children.

## CONCLUSION

This case series culminates the importance of keeping the possibility of atypical KD as one of the differentials in patients with prolonged fever not responding to antibiotics, in the absence of classical diagnostic criteria. Clinicians should be made aware about atypical manifestations of this disease to facilitate early diagnosis as early specific treatment prevents the long term cardiac morbidity in children. As the diagnosis of KD is based on certain criteria, clinicians should correlate both physical examination findings and laboratory parameters so that early diagnosis can be made and prompt treatment can be instituted to prevent later complications.

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