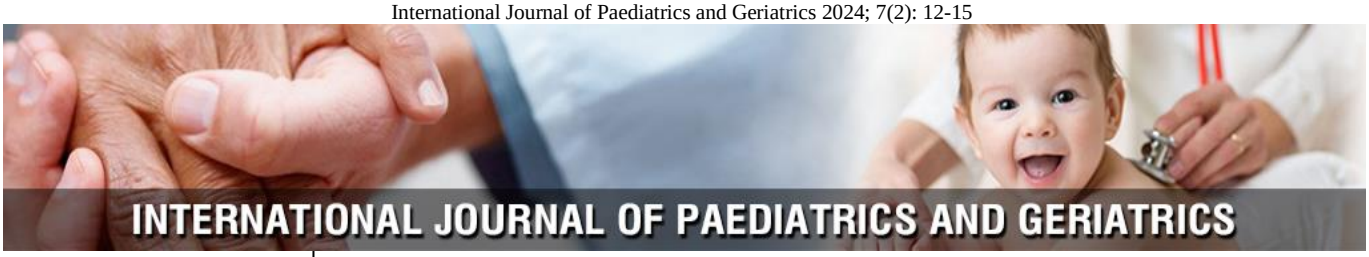

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Navigating diagnostic uncertainty: A case report on incomplete Kawasaki disease in infants

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Abstract
Incomplete Kawasaki Disease (KD) presents a diagnostic challenge due to its varied and atypical presentation. This case report describes a 7-month-old male with an incomplete form of KD, highlighting the clinical features, diagnostic process, and treatment outcomes. The patient did not initially present with all clinical features simultaneously, which, coupled with the sequential evolution of symptoms, delayed the diagnosis and treatment. Additionally, there was an initial dilemma regarding whether the symptoms were due to a drug rash, further complicating the clinical picture. Early recognition and prompt treatment with intravenous immunoglobulin (IVIG) and corticosteroids were crucial in preventing complications. This case was managed in a resource-limited peripheral hospital, highlighting the challenges and importance of early diagnosis and treatment in such settings.

Keywords: Kawasaki Disease, KD, Incomplete KD, IVIG, coronary aneurysm

Introduction

Background

Kawasaki Disease (KD) is a pediatric vasculitis that predominantly affects children under the age of five. Initially described in Japan by Dr. Tomisaku Kawasaki in 1967, it has since been recognized worldwide, with the highest incidence in East Asia, particularly Japan, Korea, and Taiwan. The etiology of KD remains unknown, though it is hypothesized to involve an infectious agent triggering an abnormal immune response in genetically predisposed individuals [1].

KD is characterized by prolonged fever and at least four of the following five principal clinical features: polymorphous rash, extremity changes (erythema of palms and soles, edema of hands and feet, and periungual desquamation), bilateral non-purulent conjunctival injection, oral mucosal changes (including injected or fissured lips, injected pharynx, or strawberry tongue), and cervical lymphadenopathy (typically unilateral and larger than 1.5 cm in diameter). Incomplete KD, where patients present with fever and fewer than four of the principal clinical criteria, poses significant diagnostic challenges, leading to potential delays in treatment and increased risk of coronary artery complications [2].

The importance of early diagnosis and treatment cannot be overstated, as delayed treatment is associated with an increased risk of coronary artery aneurysms, which can lead to long-term cardiovascular complications. High-dose intravenous immunoglobulin (IVIG) administered within the first ten days of illness significantly reduces the risk of coronary artery abnormalities. Adjunctive therapies, including corticosteroids and anti-inflammatory agents like aspirin, are also commonly used to manage inflammation and prevent thrombosis.

In resource-limited settings, managing KD poses additional challenges. Limited access to diagnostic tools and specialist care can delay diagnosis and treatment [3]. The high cost of IVIG and other necessary medications can also be a significant barrier. In such settings, a high index of suspicion, timely recognition of symptoms, and prompt initiation of treatment with available resources are crucial steps to improving outcomes [4]. Strengthening healthcare infrastructure, ensuring the availability of essential medications, and training healthcare providers in early recognition and management of KD are critical for better management in these settings [5].

Case Report

A 7-month-old male infant presented with a history of fever and rash for one day. The fever,

initially intermittent, became continuous despite administration of paracetamol (PCM) and mefenamic acid. A maculopapular rash developed, predominantly over the perineum and face. The infant had no known comorbidities, was thriving well, and was immunized for age.

Examination at Admission

- **General:** Irritable, temperature of 102°F, heart rate (HR) 140/min, respiratory rate (RR) 52/min, capillary refill time (CRT) 2 seconds, oxygen saturation (SpO_2) 98% preductal, 97% postductal, blood pressure (BP) 98/46 mmHg (right upper limb), 102/56 mmHg (right lower limb).
- **Physical Findings:** Pallor (++), icterus (+), generalized maculopapular rashes, tachycardia without murmur, clear chest, hepatomegaly (liver 3.5 cm below right costal margin), irritable without focal deficits.

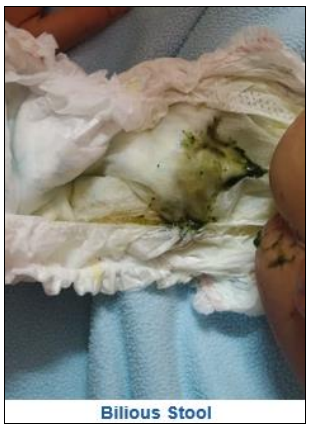
Hospital Course

Initial treatment targeted acute febrile illness with possible adverse drug reaction to mefenamic acid. Despite treatment, the fever persisted, and the rash subsided transiently with oral cetirizine. Hepatitis features were noted, including elevated total serum bilirubin and liver enzymes. By day three, the infant developed congestion of oral mucosa, fissuring of lips, strawberry tongue, and bilateral conjunctival congestion with perilimbal sparing, raising suspicion of KD.

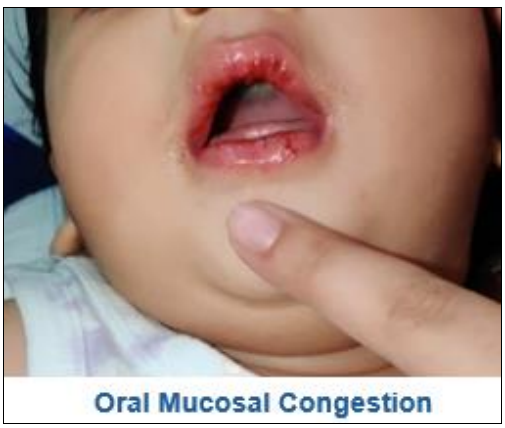
Treatment included test doses of ceftriaxone and co-amoxiclav, which caused recurrence of rash, hence could not be started. Oral azithromycin was initiated empirically, along with IV fluids, PCM, cetirizine and ranitidine. The fever remained unresponsive to PCM, and symptoms included oral ulcers, green stool, irritability, and poor appetite.

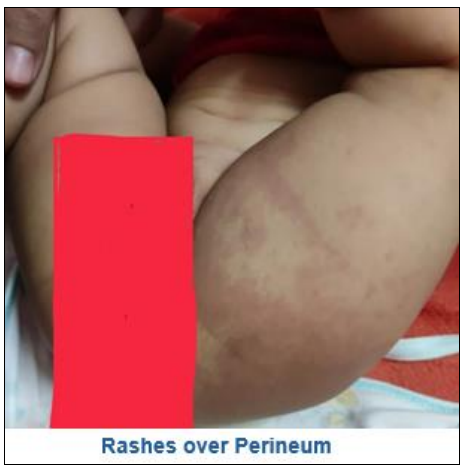
Laboratory investigations revealed increasing total leukocyte count (TLC) with neutrophil predominance, hepatic derangement with unconjugated hyperbilirubinemia, transaminitis, elevated alkaline phosphatase (ALP) levels, and borderline prothrombin time-international normalized ratio (PT-INR). Elevated inflammatory markers included serum ferritin, quantitative C-reactive protein (CRP), procalcitonin (PCT), and N-terminal pro b-type natriuretic peptide (NT-pro BNP).

A single dose of IVIG (2 g/kg) and methylprednisolone (1 mg/kg every 6 hours) was administered. Fever subsided after the first dose. By day five, the infant exhibited scrotal skin desquamation, and follow-up showed thrombocytosis. Antiplatelet therapy with aspirin (5 mg/kg/day) was started. Follow-up inflammatory markers and NT-pro BNP levels normalized. Cultures were negative for any growth, and antibiotics were discontinued after six days. After 4 weeks child reported with periungual desquamation. Repeat 2D Cardiac Echo was normal at 6 weeks and after 3 months. Child was advised to delay MMR vaccine, Varicella vaccine, Live Hepatitis A vaccine and other live for 11 months.


Bilious Stool


Periungual Peeling


Oral Mucosal Congestion


Rashes over Perineum


Non purulent conjunctivitis

Fig 1: Clinical features observed in the case

Discussion

Incomplete Kawasaki Disease (KD) presents a significant diagnostic challenge due to its varied and often atypical clinical presentation. This case highlights the need for a high index of suspicion in children presenting with prolonged fever and rash, even when the full clinical criteria are not met. The clinical progression of the patient described here underscores the importance of thorough and ongoing clinical evaluation to detect evolving symptoms indicative of KD.

The pathophysiology of KD is believed to involve an exaggerated immune response to an unidentified trigger, likely an infectious agent. Genetic factors, including specific HLA class II alleles, are associated with increased susceptibility to KD and its complications. The resulting inflammatory cascade leads to widespread endothelial damage and vasculitis, particularly affecting the coronary arteries [6, 7].

The timely administration of intravenous immunoglobulin (IVIG) has been shown to modulate the immune response and significantly reduce the risk of coronary artery aneurysms. Research has demonstrated that IVIG treatment within the first ten days of illness decreased the incidence of coronary artery abnormalities from 25% to 4% [8]. Another study corroborated these findings, noting that high-dose IVIG administered in the acute phase of KD leads to a fivefold reduction in the prevalence of coronary aneurysms [9]. Additionally, the use of corticosteroids, as seen in this case, can further reduce inflammation and improve outcomes, especially in patients at high risk for IVIG resistance or with severe inflammation. Monitoring inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and N-terminal pro b-type natriuretic peptide (NT-pro BNP) is crucial for assessing disease activity and therapeutic response [10].

A multidisciplinary approach, involving pediatricians, cardiologists, and infectious disease specialists, is essential in managing the complex and evolving presentation of KD. This approach is especially critical in resource-limited settings, where access to diagnostic tools and specialist care is limited, and the cost of IVIG and other necessary medications can be prohibitive. A Cochrane review (2022) emphasized that in such settings, maintaining a high index of suspicion, recognizing symptoms promptly, and initiating treatment with available resources are crucial steps to improving outcomes [11].

Long-term follow-up is vital for patients with KD, particularly those with coronary artery involvement, to monitor for potential late-onset cardiovascular complications. Regular follow-up using echocardiography and other relevant investigations is necessary to detect and manage any evolving cardiovascular issues effectively. Studies have shown that monitoring inflammatory markers and cardiac function through echocardiography aids significantly in the early detection and management of coronary artery abnormalities [12].

Ongoing research into the etiology and pathogenesis of KD, as well as advancements in diagnostic and therapeutic strategies, will be critical in improving outcomes for affected children. Studies focusing on identifying specific biomarkers and genetic predispositions may aid in earlier diagnosis and personalized treatment approaches, ultimately reducing the burden of coronary artery complications and improving the long-term health of patients with KD [13].

Conclusion

The case of incomplete KD presented here illustrates the diagnostic and therapeutic challenges associated with this condition. Early recognition and prompt treatment with IVIG and corticosteroids are paramount to preventing serious complications, including coronary artery aneurysms. This case emphasizes the need for heightened clinical suspicion and a proactive approach in managing young children with prolonged fever and rash, even in the absence of classic KD criteria. Ongoing research into the etiology and pathogenesis of KD, as well as advancements in

diagnostic and therapeutic strategies, will be critical in improving outcomes for affected children.

Furthermore, continued education and awareness among healthcare providers about the varied presentations of KD, including incomplete forms, are essential to ensure timely and appropriate management. Future studies focusing on the identification of specific biomarkers and genetic predispositions may aid in earlier diagnosis and personalized treatment approaches, ultimately reducing the burden of coronary artery complications and improving the long-term health of patients with KD [14].

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