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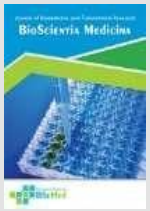

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Kawasaki Disease in a Preschooler: A Case Study on Timely Diagnosis and IVIG (Intravenous Immunoglobulin) Intervention

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A B S T R A C T

Background: Kawasaki disease (KD) is an acute, systemic vasculitis predominantly affecting young children and represents the leading cause of acquired heart disease in developed nations. Diagnostic challenges, particularly in resource-limited settings like Indonesia, contribute to underdiagnosis and delayed treatment. **Case presentation:** We report the case of a 3-year-8-month-old Indonesian male who presented with a five-day history of high-grade fever, polymorphous rash, bilateral non-purulent conjunctival injection, oropharyngeal changes (strawberry tongue, dry cracked lips), and unilateral cervical lymphadenopathy. These features fulfilled the classic diagnostic criteria for KD. Laboratory investigations revealed mild normocytic anemia and a markedly elevated erythrocyte sedimentation rate (ESR). Initial electrocardiogram showed sinus tachycardia without conduction abnormalities. Echocardiography performed during the acute phase was essential for baseline assessment and monitoring. The patient received timely administration of high-dose intravenous immunoglobulin (IVIG) (2 g/kg) and high-dose aspirin within the optimal treatment window. **Conclusion:** This case underscores the paramount importance of early clinical recognition based on established criteria and prompt initiation of IVIG therapy in mitigating the risk of CAA in children with KD. Despite successful treatment in this instance, the challenges of underdiagnosis and variable clinical presentations, including incomplete forms, persist globally, particularly in regions like Indonesia. Continued research into KD pathogenesis, improved diagnostic markers, management of IVIG resistance, and long-term cardiovascular surveillance protocols are crucial for optimizing patient outcomes.

1. Introduction

Kawasaki disease (KD), historically recognized as mucocutaneous lymph node syndrome, represents a perplexing yet critical pediatric condition. It is characterized by an acute, self-limiting systemic vasculitis. This syndrome was first meticulously described by Dr. Tomisaku Kawasaki in Japan in 1967. KD predominantly affects medium-sized arteries, demonstrating a striking predilection for the coronary arteries. This predilection renders KD the most common cause of acquired heart disease among children in many developed countries, surpassing acute rheumatic fever in prevalence. The global health significance of KD is emphasized by its potential for long-term cardiovascular sequelae. These sequelae include coronary artery aneurysms (CAA), stenosis, thrombosis, myocardial infarction, and, in rare instances, sudden cardiac death, posing risks that

extend into adulthood. Despite intensive research spanning decades, the precise etiology of KD remains elusive. The prevailing hypothesis suggests an exaggerated or dysregulated immune response. This aberrant response is thought to be triggered by one or more ubiquitous infectious agents or environmental factors acting upon genetically predisposed individuals. A variety of viral and bacterial pathogens have been investigated as potential triggers. These include coronaviruses, Epstein-Barr virus, parvovirus B19, and superantigen-producing bacteria. However, a definitive causal link has not yet been established. Genetic studies have identified several susceptibility loci, often related to immune function and vascular biology. This suggests a complex interplay between host genetics and external triggers in the pathogenesis of KD. The epidemiologic features of KD further complicate the understanding of its origins. These features include its peak incidence in young children (under 5 years), male predominance (approx. 1.5:1 ratio), a predilection for individuals of East Asian ancestry, and seasonal variations observed in some regions. Countries such as Japan, South Korea, and Taiwan report the highest incidences globally, although the disease occurs worldwide. Recent trend analyses indicate a potentially increasing incidence in some developing regions. This increase may reflect improved awareness and diagnosis, although the rates are still lower than those observed in East Asia.[1-4]

The diagnosis of KD is primarily clinical, based on a constellation of characteristic signs and symptoms. The classic criteria, established by organizations such as the American Heart Association (AHA) and echoed by Japanese and other international guidelines, require the presence of fever lasting at least five days. This fever must be accompanied by four or more of the five principal clinical features. These features include; bilateral non-exudative bulbar conjunctival injection; oropharyngeal mucosal changes (erythema, fissured lips, strawberry tongue); changes in the peripheral extremities (acute erythema/edema of hands/feet, subacute periungual desquamation); polymorphous rash (typically truncal, non-vesicular); and cervical lymphadenopathy (usually unilateral, >1.5 cm diameter). However, relying solely on these classic criteria presents significant challenges. A substantial proportion of children, particularly infants and older children, may present with 'incomplete' or 'atypical' KD. These cases are characterized by prolonged fever but fewer than four principal features. This variability complicates diagnosis, often leading to delays. The delay occurs because KD mimics various common childhood febrile illnesses. These illnesses include viral exanthems, bacterial infections (such as scarlet fever or cervical adenitis), Stevens-Johnson syndrome, and, more recently, Multisystem Inflammatory Syndrome in Children (MIS-C) associated with SARS-CoV-2. Delayed diagnosis, beyond the optimal treatment window (typically the first 10 days of fever), significantly increases the risk of developing CAA. This risk can be as high as 25% in untreated patients, compared to approximately 3-5% in those receiving timely intravenous immunoglobulin (IVIG) therapy.[5-7]

In regions like Indonesia, the challenge of KD diagnosis is particularly pronounced. While estimates suggest thousands of new cases annually, reported numbers remain significantly lower, indicating substantial underdiagnosis. Several factors likely contribute to this gap. These include limited awareness among primary healthcare providers, the confounding overlap with highly prevalent infectious diseases, variable access to diagnostic tools like echocardiography, and potentially distinct epidemiological or clinical patterns in the region. Addressing this diagnostic gap is crucial for improving pediatric cardiovascular health outcomes in Indonesia and similar settings. The cornerstone of acute KD management is the timely administration of high-dose IVIG, typically 2 g/kg infused over 8-12 hours. This is accompanied by aspirin, initially at anti-inflammatory doses, then reduced to antiplatelet doses. IVIG acts through complex immunomodulatory mechanisms to reduce systemic inflammation. It has dramatically reduced the incidence of CAA when given within the first 10 days of illness. However, approximately 10-20% of patients exhibit IVIG resistance. Resistance is

defined by persistent or recrudescent fever 36-48 hours after completion of the initial IVIG infusion. These individuals are at a markedly higher risk for developing CAA and require second-line therapies. Second-line therapies may include a repeat dose of IVIG, corticosteroids (oral or intravenous pulse methylprednisolone), or biologic agents like infliximab (a TNF-alpha inhibitor). Predicting IVIG resistance remains challenging. Various clinical and laboratory scoring systems have been developed, primarily in Japan, but their applicability varies across different populations. This case report details the presentation, diagnosis, and successful management of a preschool-aged child with classic KD at a tertiary hospital in West Sumatra, Indonesia.[8-10] The report aims to reinforce the importance of adhering to established diagnostic criteria. It also highlights the critical window for effective IVIG intervention in preventing coronary complications. Furthermore, it contributes to increased awareness and improved management strategies for KD within the Indonesian healthcare context.

2. Case Presentation

The patient was a 3-year-8-month-old male. He presented at the Emergency Department of Dr. M. Djamil General Hospital in Padang, West Sumatra, Indonesia. His past medical history was notable for a mild COVID-19 infection approximately 1.5 years prior to this presentation. The patient had received complete immunizations, demonstrated appropriate growth and development, and maintained adequate nutrition. These factors indicate a generally healthy baseline, with the prior COVID-19 infection being the only significant antecedent medical event. The patient's age is consistent with the typical demographic affected by Kawasaki disease, which predominantly affects young children. The patient exhibited several key presenting symptoms, most notably a persistent and recurring fever. The fever had been present for five days and was described as high-grade. Initially, the fever responded to antipyretic medications, but it recurred, suggesting an underlying inflammatory process that was not being adequately controlled by symptomatic treatment. This pattern of fever, initially responsive to antipyretics but subsequently recurring, is a crucial clinical feature that often raises suspicion for Kawasaki disease and other systemic inflammatory conditions. In addition to the fever, the patient developed a rash over a period of three days. This rash progressively spreads across various anatomical regions, including the abdomen, chest, neck, arms, and legs. The rash was associated with itching, indicating a dermatological manifestation of an inflammatory or immune-mediated process. The distribution and characteristics of the rash are essential in the diagnostic evaluation, as the polymorphous rash of Kawasaki disease has a particular pattern and morphology. The patient also presented with ocular symptoms characterized by eye redness, which was bilateral. Bilateral non-purulent bulbar conjunctival injection is one of the cardinal signs of Kawasaki disease. The absence of purulent discharge is important in differentiating this condition from bacterial conjunctivitis. Oral symptoms were also prominent, including a complaint of dry mouth and difficulty swallowing. Further examination revealed a “strawberry tongue,” dry, cracked, and erythematous lips, along with diffuse pharyngeal and oral mucosal erythema. These oropharyngeal changes are classic manifestations of Kawasaki disease. The strawberry tongue, characterized by enlarged, erythematous papillae, and the fissured, erythematous lips are highly suggestive of the disease's impact on the mucous membranes. General symptoms included a significantly decreased appetite over the preceding three days. The patient also denied experiencing cough, shortness of breath, vomiting, or joint pain. The decrease in appetite is a non-specific symptom but reflects the systemic nature of the illness and its impact on the patient's overall well-being. The denial of respiratory symptoms and vomiting is important in ruling out other common pediatric conditions that might present with fever and rash. The absence of joint pain helps to differentiate Kawasaki disease from other rheumatologic conditions. The patient’s general

appearance was notable for being conscious and alert but also mildly distressed and irritable. He exhibited mild dehydration, as evidenced by dry mucous membranes. The patient's level of consciousness and alertness is important to document, as it provides information about the severity of the illness and its impact on the central nervous system. Irritability is a common feature in febrile children, particularly those with inflammatory conditions. The finding of dry mucous membranes indicates dehydration, which is often associated with fever, decreased oral intake, and increased insensible losses. Vital signs at the initial presentation revealed a blood pressure of 95/59 mmHg. This blood pressure reading is within the normal range for a child of this age, although close monitoring is warranted in the context of systemic illness. The patient exhibited tachycardia, with a pulse rate of 130 beats per minute. Tachycardia is a common response to fever, dehydration, and systemic inflammation. The respiratory rate was elevated at 38 breaths per minute, indicating tachypnea. Tachypnea can be a compensatory mechanism for fever or reflect underlying respiratory distress, although in this case, the lungs were clear to auscultation. The patient's temperature was 38°C, confirming the presence of fever. The oxygen saturation was 100% on room air, which is reassuring and suggests that the patient was not experiencing significant respiratory compromise. A detailed examination of the eyes revealed bilateral, non-purulent bulbar conjunctival injection with limbic sparing. Bilateral conjunctival injection is a key diagnostic criterion for Kawasaki disease. The description of "non-purulent" is crucial, as it helps to differentiate this condition from bacterial conjunctivitis. The mention of "limbic sparing" refers to the absence of injection around the limbus, the border between the cornea and the sclera, which is a characteristic feature of Kawasaki disease. The oropharyngeal examination revealed the presence of a “strawberry tongue,” dry, cracked, and erythematous lips, and diffuse pharyngeal and oral mucosal erythema. The strawberry tongue, characterized by enlarged and prominent papillae, is a pathognomonic finding in Kawasaki disease. Dry, cracked, and erythematous lips are also typical findings. The diffuse erythema of the pharyngeal and oral mucosa indicates widespread inflammation of the upper aerodigestive tract. Lymph node examination revealed right cervical lymphadenopathy. The lymph node was palpable, fixed, tender, and measured 2x2x1 cm. The lymphadenopathy was unilateral. Cervical lymphadenopathy, particularly when unilateral and greater than 1.5 cm in diameter, is another diagnostic criterion for Kawasaki disease. The characteristics of the lymph node, including its size, tenderness, and fixation, are important in the clinical assessment. The skin examination demonstrated a polymorphous, maculopapular erythematous rash on the trunk and extremities. The rash was described as non-vesicular. The polymorphous nature of the rash in Kawasaki disease means that it can take on various appearances. The maculopapular nature indicates that it consists of both flat, discolored areas (macules) and raised bumps (papules). The involvement of the trunk and extremities is typical for Kawasaki disease. The fact that the rash was non-vesicular helps to differentiate it from vesicular rashes seen in conditions like chickenpox. Examination of the extremities revealed mild erythema of the palms and soles noted initially. There was no significant edema initially. Erythema of the palms and soles is another characteristic feature of Kawasaki disease. Edema of the extremities can also occur, but in this case, it was not initially present. A cardiovascular examination revealed tachycardia. The heart rhythm was regular, and the first and second heart sounds (S1 and S2) were normal. There were no murmurs auscultated. The tachycardia observed on physical examination correlates with the tachycardia noted in the vital signs. The regular rhythm and normal heart sounds are reassuring, although further cardiac evaluation, such as an electrocardiogram and echocardiogram, is essential in Kawasaki disease. The absence of murmurs does not rule out cardiac involvement, as coronary artery abnormalities can develop later in the course of the disease. A respiratory examination

revealed that the lungs were clear to auscultation bilaterally. This finding suggests that the patient did not have significant primary respiratory involvement despite the presence of tachypnea. Clear lung sounds help to rule out conditions such as pneumonia or bronchitis. A complete blood count revealed a hemoglobin level of 10.8 g/dL, indicating mild anemia. The white blood cell count (WBC) was 8,700/mm³, which is within the normal range. The platelet count was 306,000/mm³, also within the normal range initially. The mild anemia observed in this patient is a common finding in Kawasaki disease, reflecting the systemic inflammatory process. While the WBC was within the normal range, it's important to note that leukocytosis (elevated WBC) can be seen in Kawasaki disease, particularly in the acute phase. The platelet count, although normal initially, typically becomes elevated later in the course of the disease (thrombocytosis), usually after the first week. Inflammatory markers showed a markedly elevated erythrocyte sedimentation rate (ESR) of 110 mm/h. The ESR is a non-specific marker of inflammation but is often significantly elevated in Kawasaki disease, reflecting the intense systemic inflammatory response. Biochemistry results showed normal renal function, with urea and creatinine levels within the normal range. Liver function tests, including ALT, AST, and bilirubin, were also within the normal range. Normal renal and liver function tests are important in ruling out other conditions that might present with similar symptoms. While liver enzyme elevations can occur in Kawasaki disease, they are not a primary diagnostic criterion. The urinalysis was normal, with no signs of infection. A normal urinalysis helps to rule out urinary tract infections or other renal involvement. Sterile pyuria (white blood cells in the urine without bacteria) can sometimes be seen in Kawasaki disease, but it was not reported in this case. The electrocardiogram (ECG) showed sinus tachycardia with a rate of approximately 160 beats per minute. The axis and intervals were normal, and there were no conduction abnormalities or signs of ischemia. The sinus tachycardia observed on the ECG correlates with the tachycardia noted in the vital signs and cardiovascular examination. While the ECG was normal in terms of axis, intervals, and conduction, it's crucial to remember that ECG changes can evolve over time in Kawasaki disease, particularly if there is coronary artery involvement. An echocardiogram was performed, and a baseline study was planned. Details of the baseline study were not provided in the source text, but subsequent follow-up echocardiograms were planned. Echocardiography is a critical investigation in Kawasaki disease. It is used to assess coronary artery size and function, as well as overall cardiac function. Baseline echocardiography is essential to establish a baseline for comparison with subsequent studies, as coronary artery abnormalities can develop during the course of the disease. Serial echocardiograms are necessary to monitor for the development of coronary artery aneurysms or other cardiac complications. The working diagnosis for this patient was classic Kawasaki disease. This diagnosis was based on the fulfillment of the diagnostic criteria, which include the presence of fever for at least five days along with at least four of the five principal clinical signs. In this case, the patient exhibited prolonged fever, bilateral non-exudative conjunctival injection, oropharyngeal changes (strawberry tongue, dry cracked lips, and diffuse erythema), polymorphous rash, and cervical lymphadenopathy. The constellation of these clinical findings, along with the laboratory evidence of inflammation (elevated ESR), strongly supports the diagnosis of classic Kawasaki disease. The prompt recognition of these clinical features is crucial for the timely initiation of appropriate treatment to prevent the development of coronary artery aneurysms, the most serious complication of Kawasaki disease (Table 1).

The acute hospitalization phase of this patient's care was critical, focusing on the initial management of his symptoms, the administration of specific Kawasaki disease (KD) therapy, and the commencement of essential monitoring and investigations. This phase occurred during the patient's admission, which began on day 5 of his illness. The patient's initial management during acute

hospitalization involved the administration of intravenous (IV) fluids and antipyretics. The primary goals of this initial management were to provide symptomatic relief and address any hydration issues. The use of IV fluids was crucial in addressing the patient's mild dehydration, as noted during the physical examination. Dehydration can be a common complication of febrile illnesses, and ensuring adequate hydration is a fundamental aspect of supportive care. Antipyretics were administered to manage the patient's high-grade fever. While antipyretics provide symptomatic relief, it is important to recognize that they do not address the underlying inflammatory process of Kawasaki disease. The fact that the fever initially responded to antipyretics but later recurred highlights the importance of specific KD therapy. The outcome of the initial management was that symptomatic relief and hydration were addressed, setting the stage for more definitive treatment of the underlying Kawasaki disease. The cornerstone of treatment for Kawasaki disease involves the administration of specific therapies aimed at modulating the immune response and preventing coronary artery complications. In this patient, the specific KD therapy consisted of intravenous immunoglobulin (IVIG) and high-dose aspirin. The patient received IVIG therapy on day 5 of his illness. The administration of IVIG is a critical intervention in Kawasaki disease, as it has been shown to significantly reduce the incidence of coronary artery aneurysms (CAA), the most serious complication of the disease. The dose of IVIG administered was 2 g/kg of body weight. This is the standard high-dose regimen used in the treatment of KD. The IVIG was given as a single infusion. The patient demonstrated a good clinical response to IVIG therapy, and there was no evidence of IVIG resistance. The reduction of fever and improvement in the patient's overall clinical condition were specifically mentioned as positive outcomes of the IVIG treatment. IVIG's mechanism of action is complex and involves various immunomodulatory effects, including the neutralization of potential triggers, suppression of cytokine production, and modulation of immune cell function. The absence of IVIG resistance is a favorable prognostic indicator, as IVIG resistance is associated with a higher risk of developing CAA and necessitates further treatment strategies. In addition to IVIG, the patient received aspirin therapy. High-dose aspirin was started on day 5 of the illness. The specific dose of aspirin was not stated in the table, but it was assumed to be the standard high dose used in the acute phase of Kawasaki disease. High-dose aspirin is used for its anti-inflammatory and anti-thrombotic effects. The anti-inflammatory effect is particularly important in the acute phase of KD, where there is intense systemic inflammation. The patient tolerated the high-dose aspirin well, and no adverse effects were noted during hospitalization. This is important, as aspirin can have potential side effects, including gastrointestinal irritation and, rarely, Reye's syndrome in children. The intended outcome of high-dose aspirin therapy was to achieve both anti-inflammatory and anti-thrombotic effects, addressing the key pathophysiological processes in Kawasaki disease. During the acute hospitalization phase, close monitoring of the patient's clinical course was essential. This involved frequent assessment of vital signs, fluid balance, and overall clinical status. Monitoring is critical to detect any changes in the patient's condition, identify potential complications, and evaluate the response to treatment. A baseline echocardiogram was planned and performed during the admission. Echocardiography plays a vital role in the management of Kawasaki disease. It is used to assess the coronary arteries and cardiac function. The baseline echocardiogram is crucial for establishing a baseline for comparison with subsequent studies. This allows clinicians to monitor for the development of coronary artery abnormalities, such as aneurysms or ectasia, which are the most serious cardiovascular complications of KD. The outcome of this investigation was to assess the baseline coronary arteries and cardiac function. During the acute hospitalization phase, a referral was arranged for a pediatric cardiologist. The involvement of a specialist in

pediatric cardiology is essential in the management of Kawasaki disease, given the potential for significant cardiac complications. The pediatric cardiologist provides expertise in the diagnosis, management, and long-term follow-up of KD patients, particularly those with coronary artery involvement. The outcome of this referral was that specialist input was obtained, ensuring comprehensive and specialized care for the patient. The post-discharge follow-up phase is crucial for the long-term management of Kawasaki disease. It involves ongoing monitoring for potential complications, adjusting medications, and providing necessary vaccinations. The patient was planned to receive aspirin (ASA) at a low dose post-discharge. The specific dose was not stated, but it was assumed to be the standard low dose used in the subacute and convalescent phases of Kawasaki disease. Low-dose aspirin is intended for its antiplatelet effect. Thrombocytosis, an elevation in platelet count, typically occurs in the subacute phase of KD, increasing the risk of thrombosis. Low-dose aspirin helps to prevent blood clot formation and reduces the risk of coronary artery thrombosis, particularly in patients with coronary artery abnormalities. The planned duration of low-dose aspirin therapy was for 6-8 weeks or longer. The continuation of aspirin therapy is dependent on the findings of follow-up evaluations. If coronary artery abnormalities persist, aspirin therapy may be continued for a longer duration, or even indefinitely. Serial echocardiograms were planned post-discharge. These serial echocardiograms are essential to monitor for the development or progression of coronary artery abnormalities over time. Coronary artery aneurysms can develop or change in size even after the acute phase of the illness, making ongoing monitoring critical. The frequency of echocardiograms is determined by the initial findings and the patient's risk stratification. The importance of close follow-up was emphasized, highlighting the need for vigilance in detecting and managing potential cardiac complications. In addition to cardiology follow-up, general clinical follow-up was also planned post-discharge. This involves ongoing assessment of the patient's overall health and well-being. It includes monitoring for any signs or symptoms that might indicate complications or the need for further intervention. Specific vaccination guidance was provided post-IVIG. Live vaccines, such as MMR (measles, mumps, and rubella) and varicella (chickenpox), should be deferred after IVIG administration. IVIG can interfere with the effectiveness of live vaccines, so it is recommended to delay their administration for several months after IVIG treatment. This is a standard recommendation in the management of patients who have received IVIG (Table 2).

3. Discussion

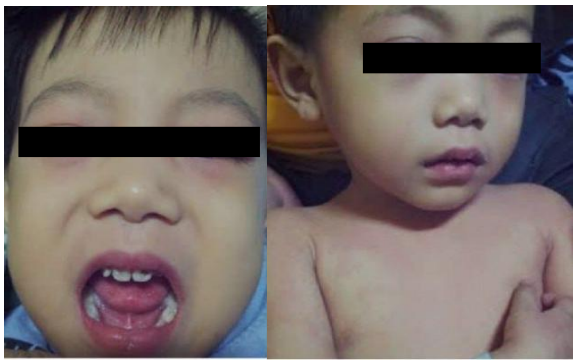
While the precise etiology of KD remains an area of active investigation, the prevailing understanding centers on the concept of a systemic vasculitis driven by a dysregulated immune response. The pathogenesis is believed to involve an unidentified trigger, potentially of infectious origin, initiating a complex inflammatory cascade within genetically susceptible hosts. This cascade involves the activation of various components of the innate and adaptive immune systems, including neutrophils, monocytes/macrophages, lymphocytes (both T and B cells), and mast cells. A critical role is played by a variety of pro-inflammatory cytokines and chemokines, such as Tumor Necrosis Factor-alpha (TNF-α), Interleukin-1 beta (IL-1β), IL-6, IL-8, and Interferon-gamma (IFN-γ), which contribute to endothelial activation, vascular inflammation, and subsequent tissue damage. The inflammatory process in KD exhibits a predilection for medium-sized arteries, with a particular tropism for the coronary arteries. Histopathological studies of affected vessels in the acute phase of KD reveal necrotizing arteritis, characterized by the infiltration of neutrophils into the vessel wall.

Table 1. Summary of patient's clinical findings.

Category	Finding	Details
Demographics & history	Age	3 years and 8 months
	Gender	Male
	Presentation Location	Emergency Department, Dr. M. Djamil General Hospital, Padang, West Sumatra, Indonesia
	Past Medical History	Mild COVID-19 approx. 1.5 years prior; Complete immunizations; Appropriate growth & development; Adequate nutrition
Presenting symptoms	Fever	5-day history; High-grade, initially responsive to antipyretics but recurred
	Rash	Developed over 3 days prior; Progressively spread to abdomen, chest, neck, arms, legs; Associated with itching
	Ocular Symptoms	Eye redness (bilateral)
	Oral Symptoms	Dry mouth; Difficulty swallowing
	General Symptoms	Significantly decreased appetite over 3 days; Denied cough, shortness of breath, vomiting, joint pain
Physical examination (Figure 1)	General Appearance	Conscious, alert, mildly distressed/irritable; Mildly dehydrated (dry mucous membranes)
	Vital Signs (Initial)	BP: 95/59 mmHg; Pulse: 130 bpm (tachycardia); Resp Rate: 38/min (tachypnea); Temp: 38°C; SpO_2: 100% (room air)
	Eyes	Bilateral, non-purulent bulbar conjunctival injection, limbic sparing
	Oropharynx	"Strawberry tongue"; Dry, cracked, erythematous lips; Diffuse pharyngeal/oral mucosal erythema
	Lymph Nodes	Right cervical lymphadenopathy: palpable, fixed, tender, 2x2x1 cm; Unilateral
	Skin	Polymorphous, maculopapular erythematous rash on trunk and extremities; Non-vesicular
	Extremities	Mild erythema of palms/soles noted initially; No significant edema initially
	Cardiovascular	Tachycardia; Regular rhythm; Normal S1/S2; No murmurs
	Respiratory	Lungs clear to auscultation bilaterally
Laboratory findings	Complete Blood Count	Hemoglobin: 10.8 g/dL (mild anemia); WBC: 8,700/mm^3 (normal); Platelets: 306,000/mm^3 (normal initially)
	Inflammatory Markers	ESR: 110 mm/h (markedly elevated)
	Biochemistry	Renal function (urea, creatinine): Normal; Liver function (ALT, AST, bilirubin): Normal
	Urinalysis	Normal, no signs of infection
Investigations	Electrocardiogram (ECG)	Sinus tachycardia (rate ~160 bpm); Normal axis, intervals; No conduction abnormalities or signs of ischemia
	Echocardiogram	Baseline study planned/performed (details not provided in source text); Subsequent follow-up echocardiograms planned
Diagnosis	Working Diagnosis	Classic Kawasaki disease (fulfilled criteria: fever + 5 principal signs)

Table 2. Patient treatment and follow-up.

Phase	Intervention/ Monitoring	Details/Parameters	Duration/Timing	Outcome/Results
Acute hospitalization	**Initial Management**	IV Fluids, Antipyretics	Admission (Day 5 illness)	Symptomatic relief, hydration addressed
	Specific KD Therapy	**IV Immunoglobulin (IVIG)**	Day 5 illness	Good clinical response indicated; No IVIG resistance noted
		Dose: 2 g/kg body weight	Single infusion	Reduction of fever and improvement in clinical condition mentioned
		Aspirin (ASA) - High Dose	Started Day 5 illness	Tolerated well; No adverse effects noted during hospitalization
		Dose: (Specific dose not stated, standard high dose assumed)	Acute phase	Anti-inflammatory & anti-thrombotic effect intended
	Monitoring	Clinical course	During admission	Closely monitored
	Investigations	**Baseline Echocardiogram**	Planned/Performed during admission	To assess baseline coronary arteries and cardiac function
	Referral	Pediatric Cardiologist	Arranged	Specialist input obtained
Post-discharge follow-up	**Medication**	**Aspirin (ASA) - Low Dose**	Planned post-discharge	Intended for antiplatelet effect during subacute phase
		Dose: (Specific dose not stated, standard low dose assumed)	Planned for 6-8 weeks+	Continuation dependent on follow-up findings
	Cardiology Follow-up	**Serial Echocardiograms**	Planned post-discharge	Essential to monitor for coronary artery abnormalities over time
		Clinical Follow-up	Planned post-discharge	Importance of close follow-up emphasized
	Vaccination Guidance	Defer live vaccines (MMR, Varicella)	Post-IVIG	Standard recommendation



Figures 1. Eye redness; strawberry tongue; red rash in neck, chest, and arms.

This infiltration leads to edema and damage to the internal elastic lamina and smooth muscle cells, structural changes that predispose the vessel to dilatation and aneurysm formation. Aneurysm formation typically occurs during the subacute phase of the illness, which spans weeks 2-4, and is also characterized by thrombocytosis and persistent inflammation involving lymphocytes and plasma cells. Over the longer term, the proliferation of myofibroblasts can contribute to intimal thickening, potentially leading to stenosis in the affected vessels. Even in patients who do not develop overt aneurysms, the resolution phase may be characterized by persistent vascular dysfunction and an increased risk

of long-term cardiovascular events.[11,12]

In the presented case, the patient exhibited classic KD, meeting the criteria of fever plus ≥4 of the 5 principal clinical features. However, the diagnosis of KD is not always straightforward and can be complicated by the existence of incomplete KD. Incomplete KD, where patients present with prolonged fever but only 2 or 3 of the principal clinical criteria, poses a significant diagnostic challenge, particularly in infants younger than 6 months or in older children. To aid in the diagnosis of incomplete KD, the AHA has developed algorithms that incorporate supportive laboratory findings and echocardiographic findings. Supportive laboratory findings that may be present in incomplete KD include elevated CRP (≥3 mg/dL) and/or ESR (≥40 mm/h), plus ≥3 of the following anemia, high platelet count after day 7, albumin ≤3.0 g/dL, elevated ALT, high WBC (≥15,000/mm^3), and sterile pyuria. Echocardiography is not only crucial for diagnosing incomplete KD (in cases where coronary abnormalities are present) but also for baseline assessment and follow-up in all patients with KD. Echocardiographic findings that support the diagnosis of KD can include coronary artery Z-scores ≥2.5, overt aneurysms, or other suggestive features such as decreased left ventricular function, mitral regurgitation, or pericardial effusion. In this particular case, the timely diagnosis of classic KD on day 5 allowed for the prompt initiation of appropriate therapy within the critical treatment window. However, it is important to acknowledge that underdiagnosis of KD is a significant problem, and recognizing both classic and incomplete forms of the disease requires a high degree of clinical vigilance. The differential diagnosis of KD is broad and includes a variety of infectious and non-infectious conditions. These include viral infections (such as adenovirus, enterovirus, and measles), bacterial infections (such as scarlet fever, staphylococcal scalded skin syndrome, and cervical adenitis), drug reactions, Stevens-Johnson syndrome, and systemic-onset juvenile idiopathic arthritis. In recent years, the emergence of Multisystem Inflammatory Syndrome in Children (MIS-C) post-SARS-CoV-2 infection has added another layer of complexity to the differential diagnosis, as MIS-C shares overlapping features with KD, including fever, rash, conjunctivitis, and cardiac involvement. However, key differences often exist between KD and MIS-C, such as age distribution, the prominence of gastrointestinal symptoms, the severity of cardiac dysfunction, and specific inflammatory markers.[13,14]

The current standard of care for acute KD involves the administration of high-dose IVIG (2 g/kg) as a single infusion, ideally within the first 10 days of illness onset, in conjunction with aspirin therapy. IVIG exerts its therapeutic effects through a variety of complex immunomodulatory mechanisms. These mechanisms include the neutralization of potential antigens or toxins, the suppression of pro-inflammatory cytokine production, the modulation of T-cell and B-cell function, and the blockade of Fc receptors on phagocytes. The efficacy of IVIG in reducing the rate of CAA development is well-established, decreasing the rate from approximately 25% in untreated patients to approximately 3-5% in those treated promptly. This underscores the critical importance of timely administration of IVIG in KD. Aspirin is another key component of the treatment regimen. It is typically used initially at high (anti-inflammatory) doses (e.g., 80-100 mg/kg/day) until the patient has been afebrile for 48-72 hours. After this, the dose is reduced to low (antiplatelet) doses (3-5 mg/kg/day) and is generally continued for at least 6-8 weeks, or longer if coronary abnormalities persist. While the anti-inflammatory benefit of high-dose aspirin is a subject of some debate, its antiplatelet effect is important, particularly during the subacute phase of KD when thrombocytosis occurs. In the presented case, the patient received IVIG and aspirin according to standard protocols. A significant challenge in the management of KD is the occurrence of IVIG resistance, which is observed in 10-20% of patients. IVIG resistance is typically defined as the persistence or recrudescence of fever ≥36 hours after the completion of the initial IVIG infusion. Patients

who exhibit IVIG resistance are at a substantially higher risk of developing CAA. Predicting which patients will develop IVIG resistance remains a significant clinical challenge. However, several risk factors have been identified in some studies, including younger age, delayed diagnosis, higher inflammatory markers (such as CRP and neutrophil count), lower albumin levels, lower serum sodium levels, and the presence of baseline coronary abnormalities. Various scoring systems have been developed, primarily in Japan, to predict IVIG resistance (e.g., the Kobayashi, Egami, and Sano scores), but their predictive power is often limited and may vary across different populations. The management of IVIG resistance involves the use of second-line therapies. Options for second-line treatment include a second dose of IVIG (2 g/kg), systemic corticosteroids (e.g., pulse methylprednisolone 30 mg/kg/day for 1-3 days, or oral prednisone 2 mg/kg/day), or TNF-α inhibitors such as infliximab (5-10 mg/kg as a single dose). Some studies have suggested that infliximab may be particularly beneficial, potentially even as part of intensified primary therapy for patients at high risk of IVIG resistance, although the optimal strategies for managing IVIG resistance are still evolving. In the case presented, the patient appeared to respond to the initial IVIG treatment, as suggested by the text, although specific data on the resolution of fever is not provided.[15,16]

Long-term follow-up is essential for all patients with KD, and the intensity and duration of follow-up are guided by the degree of coronary artery involvement as assessed by serial echocardiography. Patients who do not have any coronary artery changes typically have an excellent prognosis. In these patients, aspirin therapy may be discontinued after 6-8 weeks if inflammatory markers have normalized and echocardiograms remain normal. A follow-up cardiology review is often recommended at specific intervals (e.g., 2 weeks, 6-8 weeks, 6 months, 1 year), and then perhaps every 3-5 years or based on individual risk stratification. Patients with coronary artery abnormalities require more intensive and prolonged management. Those with transient ectasia or small, persistent aneurysms (Z-score < 5) are usually continued on low-dose aspirin indefinitely or until resolution is documented. Patients with medium aneurysms (Z-score 5 to <10, or absolute dimension <8mm) often warrant long-term aspirin therapy, and additional antiplatelet agents (e.g., clopidogrel) or anticoagulation may be considered depending on the morphology of the aneurysms and the presence of other risk factors. Giant aneurysms (Z-score ≥10 or absolute dimension ≥8mm) carry the highest risk of thrombosis and stenosis, which can lead to myocardial infarction or sudden death. Management of giant aneurysms typically involves long-term low-dose aspirin in combination with anticoagulation (e.g., warfarin or low-molecular-weight heparin). These patients require lifelong, specialized cardiology follow-up, often including advanced imaging techniques (such as CT angiography, MR angiography, and stress testing) to monitor for stenosis and assess the risk of ischemia. Catheter-based or surgical revascularization procedures (e.g., coronary artery bypass grafting) may be necessary in cases of significant stenosis or thrombosis. Given the potential for long-term endothelial dysfunction, even in the absence of aneurysms, promoting cardiovascular health (through diet, exercise, and avoidance of smoking) is recommended for all survivors of KD. In the presented case, follow-up echocardiograms were planned to monitor for any late-developing coronary changes.[17,18]

The successful outcome in this case underscores the effectiveness of standard KD treatment protocols when the diagnosis is made in a timely manner. However, the documented rates of underdiagnosis in Indonesia pose a significant public health concern. Improving KD outcomes at the national level requires a multifaceted approach. This includes enhancing physician awareness and education regarding both classic and incomplete KD presentations, improving access to timely echocardiography, potentially developing regionally-adapted diagnostic or risk-stratification tools, and ensuring the availability and

affordability of IVIG therapy. Further epidemiological studies within Indonesia are needed to better characterize the local incidence, triggers, and clinical spectrum of KD.[19,20]

4. Conclusion

In conclusion, this case report highlights the successful management of classic Kawasaki disease (KD) in a preschool-aged child through timely diagnosis and adherence to established treatment protocols. The prompt recognition of the characteristic clinical features, including prolonged fever, bilateral non-exudative conjunctival injection, oropharyngeal changes, polymorphous rash, and cervical lymphadenopathy, was crucial in facilitating early initiation of intravenous immunoglobulin (IVIG) and aspirin therapy. This case underscores the critical role of early clinical recognition and timely IVIG administration in mitigating the risk of coronary artery aneurysms (CAA), the most serious complication associated with KD. Despite the positive outcome in this instance, the challenges of underdiagnosis and the existence of incomplete KD, which can complicate timely recognition and treatment, remain significant, particularly in resource-limited settings. The case also highlights the importance of continuous monitoring for potential cardiac complications through serial echocardiograms and the need for long-term follow-up to optimize patient outcomes. Addressing the issue of underdiagnosis requires a multi-faceted approach, including enhanced awareness and education among healthcare providers, improved access to diagnostic tools like echocardiography, and the development of regionally-adapted diagnostic and risk-stratification tools. Furthermore, continued research into the pathogenesis of KD, improved diagnostic markers, strategies for managing IVIG resistance, and the establishment of effective long-term cardiovascular surveillance protocols are essential for further improving the outcomes for children affected by this potentially serious condition.

5. References

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