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Case Report

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Kawasaki disease in an infant: Diagnostic and therapeutic challenges at the University Teaching Hospital of Yaoundé, Cameroon

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Abstract

Introduction: Kawasaki disease (KD) is an acute multi-systemic vasculitis which represents the leading etiology of acquired heart disease in children in high-income countries. Its rarity in black Africans may lead to misdiagnosis, delayed management with resultant fatal coronary artery lesions. We discuss a case of KD diagnosed in an infant in Yaoundé, Cameroon. **Case presentation:** A 10-month-old male Cameroonian presented with irritability, a generalised cutaneous eruption, and a prolonged high-grade fever. Although initial diagnosis of meningitis was made, the emerging laboratory and typical clinical features suggestive of KD prompted a quick diagnostic review. His clinical condition improved on Aspirin and corticosteroids. **Conclusion:** Due to the risk of potential complications from KD and the management challenges akin to resource-limited settings, we highlight the need for a high index of suspicion by healthcare providers when faced with febrile children with mucocutaneous lesions.

Keywords: Kawasaki disease, Challenges, Aspirin, Corticosteroids, Cameroon.

INTRODUCTION

Kawasaki disease (KD) is an acute multi-systemic vasculitis of medium- and small-sized vessels [1]. Due to its predilection for coronary arteries, KD is currently the first cause of acquired heart disease in children in developed countries, while rheumatic heart disease dominates in low-income settings [1]. The aetiology of KD remains unclear, hindering efforts to identify specific diagnostic tests and targeted treatments [1].

Contrary to Europe, Asia and the United States [2], its relative rarity in Africa is in part due to diagnostic and therapeutic difficulties such as low index of suspicion, inaccessibility to echocardiography by most patients, high cost and scarcity of intravenous immunoglobulin (IVIG) [3].

Due to the absence of pathognomonic signs or specific diagnostic investigations, the diagnosis for KD is based on clinical criteria **(Table 1)**, approved by the American Heart Association [1]. KD may simulate other acute febrile conditions or its clinical features may be variably expressed as seen in Incomplete Kawasaki Disease, making the diagnosis more challenging [1,4]. However, a prompt diagnosis of KD is crucial for timely intervention aimed at preventing the development of coronary artery lesions and their sequelae [1].

We herein discuss a 10-month-old infant who fits the case definition of KD, apparently the first in the Cameroonian literature.

CASE REPORT

A previously healthy 10-month-old Cameroonian male from rural Yaoundé presented at our Paediatric unit with a four-day history of high-grade fever, incoercible cries, and a generalized itching skin rash. He had never been hospitalized in the past and had not received vaccines against measles and yellow fever at the age of nine months as recommended by the Cameroonian Expanded Programme of Immunization.

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Similarly, he had no prior contact with an ill person or recent travel. Both parents were of Haemoglobin AA genotype.

On examination, he was ill looking, fully conscious, very irritable and well nourished (weighed 10 kg). His temperature was 40°C (104°F), heart rate of 170 beats per minute and respiratory rate of 46 cycles per minute. There was a generalized non-blanching erythematous maculopapular rash, bilateral conjunctival injection without discharge, while the lips were red and cracked. He had diffused erythema of the buccal mucosa without koplik spot. He was neither pale nor icteric and had no cervical adenopathy. A warm, tender non-pitting oedema of the dorsum of the hands and feet, associated with erythema of the palms and soles of his feet were seen (**Figure 1**). The scrotum was erythematous, tender and desquamated (**Figure 2**), with perianal erythema. The anterior fontanel was opened and normotensive. There was no neurological deficit. Examinations of the heart, lungs and abdomen were normal. A provisional diagnosis of viral meningitis was made, with differentials of measles, streptococcal scarlet fever and Kawasaki disease.

Following admission, blood and cerebrospinal fluid (CSF) samples were collected. He was then placed on parenteral ceftriaxone (100mg/kg/24h), paracetamol (15mg/kg/6h), dexamethasone (0.15mg/kg/6h) and oral cetirizine (2.5mg/24h). At 24 hours of hospitalization, initial CSF analysis showed normal cytology and biochemistry with no germ or soluble antigen isolated. The complete blood count (CBC) showed; white blood cell (WBC) count 16,400/mm^3 with neutrophilia (12,300/mm^3 or 75%); haemoglobin 10.1g/dl; haematocrit 29.5%; platelet count of 320,000/mm^3. Other laboratory analyses showed raised C-reactive proteins (CRP) at 48mg/l, erythrocyte sedimentation rate (ESR) at 63mm 1^{st} hour and 104 mm 2^{nd} hour, aspartate transaminases 80.79 IU/L and alanine transaminases 92.85 IU/L. Together with the clinical features were suggestive of KD, ruling out meningitis and measles. He was started on high dose Acetylsalicylic acid (100mg/kg/24h in 4 divided doses), ranitidine 1mg/kg/8h and antibiotherapy was continued while waiting for results of CSF and blood culture. Echocardiography and IVIG could not be done and started respectively, due to non-availability in our hospital and financial constraints of the parents.

On the third day of hospitalization (one week following onset of fever), he was afebrile. Conjunctivitis and pruritus disappeared, while the rash began to regress. The initial CSF culture was sterile; dexamethasone was stopped and ceftriaxone was reduced to 50mg/kg/24h while awaiting blood culture results. By the eighth hospital day (12^{th} day since the start of illness), he had remained apyretic for 5 days, with partial regression of oedema of the feet and hands, complete regression of the exanthema (**Figure 3**) and the start of periungual desquamation of the toes. The initial blood culture was sterile and the repeat CRP negative; Ceftriaxone was discontinued and low dose acetylsalicylic acid (5mg/kg/24h) initiated.

The outcome at 13 days of hospitalization (18 days following onset of fever), was remarkable for polyarthralgia, recrudescence of fever (temperature of 38.8°C) and oedema of the dorsum of his feet and hands. Repeat blood tests showed normal WBC 11,200/mm^3, haemoglobin 8.9 g/dl, thrombocytosis 690,000/mm^3, elevated CRP 55.8mg/l, ESR 64mm at 1^{st} hour and negative rheumatoid factor. We concluded on refractory Kawasaki disease. Acetylsalicylic acid was stopped, corticosteroids (oral prednisolone 2mg/kg/24h) were initiated and apyrexia was achieved the following day. The 18^{th} hospitalisation day (23 days following onset of fever), was notable for a good general state with no complaint. The dose of prednisolone was tapered to 1mg/kg/24h. Day 21 of hospitalisation was marked by complete clinical improvement with desquamation of the soles of the feet and absence of oedema of the extremities (**Figure 4**). Another laboratory panel showed negative CRP, ESR at 28mm at 1^{st} min and a platelet count of 430,000/mm^3 and corticosteroids which had reached minimum doses were discontinued. The infant was discharged home and parents were counselled on the importance of doing the cardiac ultrasound scan. The infant wasn't brought back to the hospital for follow-up visits but was reported by the parents to be in good health from our phone call inquiries at one week, one month, 3 months and 6 months following discharge.

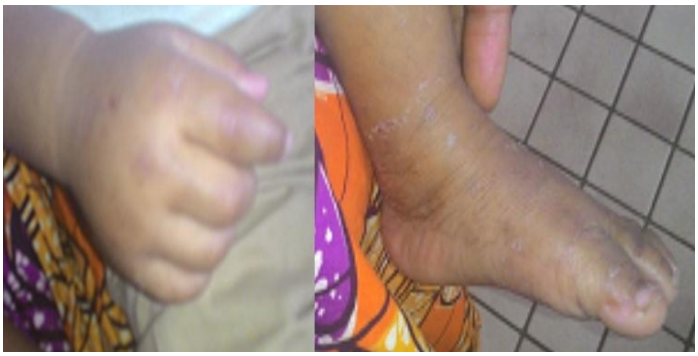

Figure 1: Changes in extremities seen in Kawasaki disease: oedema of the right hand and left foot

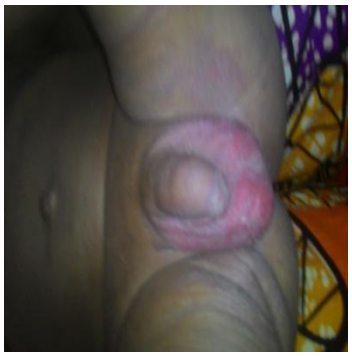

Figure 2: Erythematous maculopapular rash of Kawasaki disease

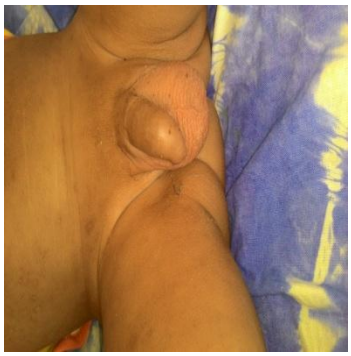

Figure 3: Complete regression of the exanthema of Kawasaki disease

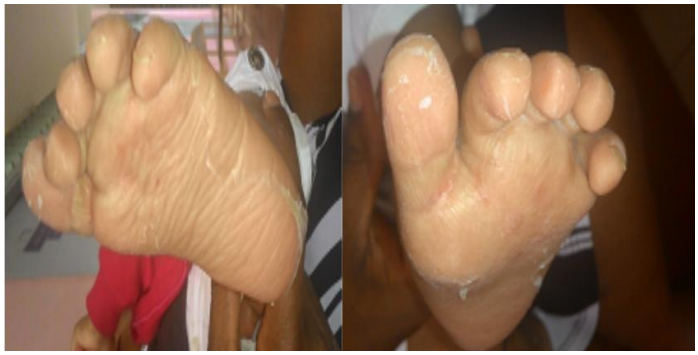

Figure 4: Desquamative changes of the feet during convalescence commenced periungual

DISCUSSION

Our case fulfilled five out of the six criteria for the diagnosis of KD as suggested by guidelines, **Table 1** [1]. Cervical lymphadenopathy was absent, however, is reported to be the least common feature [1]. Initially, the diagnosis of KD was uncertain, owing to the scarcity of this disease in our setting. Our differential diagnoses included a range of mainly infectious diseases not confirmed by laboratory investigations. This prompted a quick diagnostic review, focusing on clinical and laboratory features thereby advocating for KD.

Since the first report of KD about five decades ago by Tomasaku Kawasaki, KD is currently endemic in the United States and Europe, and epidemic in Asia [1,2], with the highest worldwide annual incidence of 218.6 per 100,000 children younger than 5 years in Japan [2]. In Africa,

sporadic cases have been described in Sudan [5], Ghana [6], Nigeria [7], Congo [3] and Egypt [4]. This paucity of reports and lack of a population-based study on KD in Africa may reflect the rarity of the disease in the continent, though under-diagnosis also seems likely. In 80% of cases, KD is a disease of childhood affecting more male children (ratio of 1.3–1.6), usually under 5 years with a peak incidence between 6 to 11 months as seen in our male patient of 10 months [2]. However, we note a few reports of KD in atypical age groups; a 2-week-old-newborn, the youngest age in the literature [8] and in adults [9].

Coronary artery involvement represents the most life threatening sequel of KD and thus determines the prognosis of KD [1]. This may manifest as coronary artery aneurysms, myocardial infarction, or sudden death in 5% of treated patients compared to 25-30% of untreated patients [1]. Predictive factors for coronary artery lesions include platelet count < 350,000/mm^3, albuminaemia < 3.5g/dl, age ≤ 12 months, leucocytosis > 12,000/mm^3, haematocrit < 35% and male gender have been described [1]. Our patient had all but one of the factors, thus a high-risk infant. However, limited availability of echocardiography in resource-challenged settings contributes significantly to diagnostic and management difficulties. Mouko *et al*. in Congo, described similar diagnostic challenges [3]. Due to the absence of the echocardiographic exam, the infant had regular cardiopulmonary examinations which otherwise remained normal through hospitalisation.

Evidence from pooled Randomized Controlled Trials (RCT) recommend a combination of IVIG and high dose Acetyl Salicylic Acid (ASA) as standard first-line treatment for KD [1]. This is effective and safe in reducing the inflammatory syndrome and the incidence of coronary artery disease [1]. Refractory KD is defined as the persistence or recrudescence of fever more than 36 hours after completion of the initial IVIG infusion [1]. IVIG was not incorporated in the management of our infant due its high cost and non-availability in our hospital; a significant therapeutic challenge similarly reported in other African series [3, 6, 7]. We were compelled to treat our patient with only ASA, which may explain the initial 'treatment failure'. Nonetheless, there was a favourable response to corticosteroids, as supported by results from a recent meta-analysis of RCTs [10]. The observed therapeutic responses to ASA and corticosteroids as well as consistent laboratory findings (**Table 2**) favoured the diagnosis of KD in the index case. Yet, follow-up cardiac ultrasounds till adulthood are needed to rule a latent coronary lesion.

Table 1: Case definition of Kawasaki disease by the American Heart Association Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease

CASE DEFINITION OF KAWASAKI DISEASE	
Fever ≥ five days duration plus the presence of at least 4 out of 5 Principal features	
Principal Features	**Bilateral non-exudative conjunctivitis**
	Oral and lip involvement: - erythema and cracking of lips - strawberry tongue - diffuse erythema of oral and pharyngeal mucosae
	Changes in extremities: - Acute phase: erythema and oedema of hands and feet - Subacute: membranous desquamation of fingers and toes, starting peri-ungually.
	Polymorphous rash: - macular rash - maculopapular rash - urticarial or morbilliform rash
	Cervical lymphadenopathy (≥1.5 cm in diameter), usually unilateral

PMC full text: Pediatrics 2004;114(6):1708–33
available at http://circ.ahajournals.org/content/110/17/2747/T1.expansion.html

Table 2: Laboratory findings of Kawasaki disease approved by American Heart Association Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease

Laboratory findings of Kawasaki disease
Leukocytosis with neutrophilia and immature forms
Elevated erythrocyte sedimentation rate
Elevated C-reactive protein
Anaemia
Abnormal plasma lipids
Hypoalbuminemia
Hyponatremia
Thrombocytosis after week 1
Sterile pyuria
Elevated serum transaminases
Elevated serum gamma glutamyl transpeptidase
Pleocytosis of cerebrospinal fluid
Leukocytosis in synovial fluid

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CONCLUSION

We have reported the first case of KD in Cameroon. Although limited resources precluded proper investigation including echocardiography and treatment with IVIG in our patient, we have shown that ASA and corticosteroids could yield favourable outcomes. This would need to be further explored in large multi-centre clinical trials in our setting. Health care personnel should have a high index of clinical suspicion for KD as a potential differential diagnosis in febrile Cameroonian children with mucocutaneous lesions. The benefits of reducing the fatal consequences of its complications cannot be overemphasised in a setting already faced with increasing cardiovascular disease burden.

Consent

Written informed consent was obtained from the parents of the patient for publication of this case report and accompanying images.

Abbreviations

ASA: Acetylsalicylic acid
CRP: C-reactive protein
CSF: Cerebrospinal fluid analysis
ESR: Erythrocyte sedimentation rate
IVIG: Intravenous immunoglobulin
KD: Kawasaki disease
RCT: Randomized Controlled Trials

Competing interests

The authors declare that they have no competing interests.

Authors' contribution

JNT contributed to the management of the patient, acquisition of data and wrote the initial manuscript. LNA contributed in data acquisition and manuscript revision. FM contributed to the management of the patient and provided critically revisions of the manuscript. All authors read and approved the final manuscript.

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