


Incomplete Kawasaki Disease in an Adult South Asian Patient

Journal of Investigative Medicine High Impact Case Reports
Volume 6: 1–5
© 2018 American Federation for Medical Research
DOI: 10.1177/2324709618792028
journals.sagepub.com/home/hic


Neetu Boodoosingh, MBBS¹, Rajeev Seecheran, MBBS¹, Saleem Varachhia, MBBS¹, Narine Mack, MBBS¹, Vinay Minocha, MBBS¹, Stanley Giddings, MBBS², and Naveen Anand Seecheran, MBBS, MSc, FACC, FESC²

Abstract

Kawasaki disease is an acute multisystemic vasculitis occurring predominantly in children and rarely in adults, with sequelae of potentially life-threatening coronary artery aneurysms. “Incomplete” Kawasaki disease is a novel concept and considered a diagnosis of exclusion as it alludes to patients with fever lasting ≥ 5 days and 2 or 3 clinical criteria without another reasonable explanation for the illness. The multidisciplinary team should be vigilant for this oligosymptomatic clinical presentation, specifically within this subgroup despite age and ethnicity, and the syndrome should be considered as a differential diagnosis in challenging cases presenting as infectious or autoimmune disease.

Keywords

incomplete Kawasaki disease, incomplete Kawasaki syndrome, South Asian, adult

Introduction

Kawasaki disease (KD) is an acute multisystemic vasculitis occurring predominantly in children and rarely in adults with sequelae of potentially life-threatening coronary artery aneurysms (CAAs).^{1,2} The precise etiology is yet to be ascertained; however, epidemiologic studies have implicated infectious agents with both autoimmune and genetic mechanisms being postulated as well.³ The pathophysiology involves a complex inflammatory milieu with a predilection for small- to medium-sized arteries, especially the coronary vessels.^{4,5}

It is estimated that there are approximately 10 000 incident cases per year in Japan alone and 4000 in the United States.^{6,7} The epidemiology and characteristics of this enigmatic syndrome are virtually unknown in the largely heterogeneous Caribbean population; however, it remains the leading cause of acquired heart disease in the developed world. The most devastating complication is that of CAA, but also include other organ systems.⁸

The diagnosis is usually clinched via guidelines as there is no specific, confirmatory test available. “Incomplete” KD is a novel concept and considered a diagnosis of exclusion as it alludes to patients with fever lasting ≥ 5 days and 2 or 3 clinical criteria without another reasonable explanation for the illness.² The term “atypical” KD should be reserved for

patients who display symptoms that are not common in classical KD, such as renal impairment, acute surgical abdomen, and pleural effusion.⁸

We describe a first case report of an adult South Asian patient with incomplete features of KD, which can masquerade as a clinical distractor.

Case Report

A 29-year-old South Asian male with no significant medical history presented to the emergency department with a 14-day symptom complex of persistent, high-grade fever refractory to antibiotics and antipyretics, malaise, and anorexia with a 10-pound weight loss. There were no recent medications, ill contacts, or travel history. His vital signs

¹South West Regional Health Authority, San Fernando, Trinidad and Tobago

²University of the West Indies, St Augustine, Trinidad and Tobago

Received May 20, 2018. Revised June 15, 2018. Accepted June 24, 2018.

Corresponding Author:

Naveen Anand Seecheran, MBBS, MSc, FACC, FESC, Department of Clinical Medical Sciences, Faculty of Medical Sciences, The University of the West Indies, 2nd Floor, Building #67, Eric Williams Medical Sciences Complex, Mt Hope, Trinidad, West Indies.
Email: NSeecheran@gmail.com



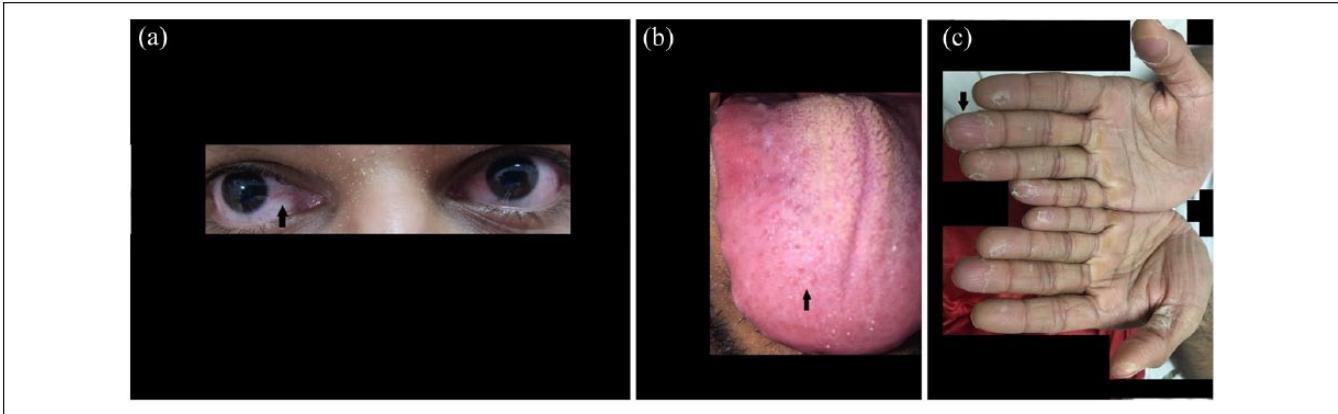


Figure 1. (a) The patient's bilateral keratoconjunctivitis with chemosis, indicated by the black arrow. (b) The patient's strawberry tongue glossitis with hyperplastic fungiform papillae, indicated by the black arrow. (c) The patient's palmar desquamation with incomplete dehiscence of the epidermis and associated ichthyosis, indicated by the black arrow.

affirmed normotensive blood pressures, a resting sinus tachycardia of 110 beats per minute, and pulse oximetry of 98% on room air with a mild pyrexia of 38.8°C. Physical examination revealed bilateral conjunctivitis with chemosis, a strawberry tongue glossitis, palmar desquamation, and ichthyosis (see Figure 1a-c, respectively). There was no evidence of lymphadenopathy or dermatologic manifestations, such as rash.

Recent pertinent laboratory investigations (see Table 1) included a leukocytosis and notable thrombocytosis, normal comprehensive metabolic panel, markedly elevated inflammatory markers of erythrocyte sedimentation rate, and C-reactive protein. An extensive infectious disease diagnostic workup indicated negative blood, urine, and stool cultures and normal tests for human immunodeficiency virus, mycobacterium tuberculosis, hepatitis B and C, influenza A and B, adenovirus, echovirus, coxsackie virus, dengue, malaria, leptospirosis, mycoplasma, legionella, Epstein-Barr virus, cytomegalovirus, and *Clostridium difficile* toxin. An in-depth immunological panel revealed no evidence of vasculitides or rheumatological disease, such as systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, polyarteritis nodosa, the polyangiitis spectrum, and cryoglobulinemia. A potential adverse drug reaction was not entertained as the patient was not administered any recent therapeutic or complementary alternative agents. Cardiovascular testing with both an electrocardiogram and echocardiogram were normal and advanced imaging with a pan-body computed tomography scan was also unremarkable. He was deemed to have an incomplete presentation of KD and was initiated on high-dose enteric-coated aspirin (Bayer HealthCare Pharmaceuticals LLC, Berlin, Germany) 325 mg every 8 hours, as well as single infusion of intravenous immunoglobulin (GammaGard, Baxter International Inc, Glenview, IL) at a dose of 2 g/kg over a 12-hour period. Subsequently, his clinical syndrome gradually resolved over the ensuing hospitalization as his pyrexia de-effervesced

along with steady improvement of his inflammatory markers. He did not receive any glucocorticoids or immunomodulating therapies. He was safely discharged after 1 week of inpatient care on low-dose aspirin monotherapy with gastro-protective proton-pump inhibitors and subsequently scheduled for a dedicated cardiac computed tomography angiogram that did not reveal any CAAs at a later outpatient clinic appointment (2 weeks from index hospitalization).

Discussion

The diagnosis of classic KD is usually verified via guidelines as there is no specific, confirmatory test available (Table 2).⁸⁻¹⁰ Adult incomplete KD was clinically diagnosed based on the absence of overt infection, persistence, and recrudescence of high-grade fever despite empirical antibiotics and antipyretics, and the presence of conjunctivitis, glossitis, and palmar desquamation.^{9,11} A recent French study evaluated 9 patients who fulfilled criteria for incomplete disease. The median time to diagnosis was 13 days, which coincided with our patient's time to presentation and the main symptoms were fever (100%), exanthema (98%), changes in the extremities (91%), conjunctivitis (77%), oral cavity changes (89%), cervical adenitis (55%), and cardiac abnormalities (45%) of which fever, changes in the extremities, conjunctivitis, and oral cavity changes featured as clinical signs in our patient. Overall, 35% of the patients showed large-vessel vasculitis: coronary vasculitis (26%) and coronary aneurysm (19%), neither of which were replicated in our patient.^{11,12} Another large, international-based registry of non-East Asian incomplete KD patients reported statistically significant increases in the occurrence of conjunctivitis, mucosal changes, and extremity alteration, which paralleled our observations.¹²

To our knowledge, this is the first reported case of an adult South Asian male in the Caribbean presenting with incomplete KD. Apart from his age, our patient was also of

Table 1. Comprehensive Laboratory Testing Including the Infectious and Immunologic Panels.

Tests Performed	Result	Reference Range
Complete blood count, comprehensive metabolic panel		
White cell count	16.1 × 10 ⁹ /L	4.5-11.0 × 10 ⁹ /L
Hemoglobin	12.9 g/dL	14.0-17.5 g/dL
Platelet count	606 × 10 ³ /μL	156-373 × 10 ³ /μL
Serum potassium	4.1 μmol/L	3.5-5.1 μmol/L
Serum sodium	136 μmol/L	135-145 μmol/L
Serum creatinine	0.7 mg/dL	0.5-1.2 mg/dL
Blood urea nitrogen	10 mg/dL	3-20 mg/dL
Fasting blood sugar	80 mg/dL	60-120 mg/dL
Alanine aminotransferase	90 IU/L	20-60 IU/L
Aspartate aminotransferase	35 IU/L	5-40 IU/L
Total bilirubin	0.9 mg/dL	0.2-1.2 mg/dL
Alkaline phosphatase	120 U/L	40-129 IU/L
Albumin	3.4 g/dL	3.5-5.5 g/dL
Albumin-corrected calcium	9.6 mg/dL	9.6-11.2 mg/dL
Infectious diseases panel		
Erythrocyte sedimentation rate	60 mm/h	0-22 mm/h
C-reactive protein	90 mg/dL	0.0-1.0 mg/dL
Blood cultures	Negative	Positive or negative
Urine culture	Negative	Positive or negative
Stool culture	Negative	Positive or negative
Stool ova, cyst, and parasites	Negative	Positive or negative
Human immunodeficiency virus enzyme-linked immunosorbent assay	Nonreactive	Nonreactive or reactive
Venereal disease research laboratory test	Nonreactive	Nonreactive or reactive
QuantiFERON-TB GOLD (Cellestis Limited, Carnegie, Victoria, Australia)	Negative	Positive or negative
Hepatitis B surface antigen	Negative	Positive or negative
Hepatitis C immunoglobulin M (IgM) antibodies	Negative	Positive or negative
Hepatitis C Immunoglobulin G (IgG) antibodies	Negative	Positive or negative
Influenza A and B nasal swabs	Negative	Positive or negative
Adenoplus (Quidel Corporation, San Diego, CA)	Negative	Positive or negative
Echovirus antibodies (6,7,9,11, and 30)	< 1:10	< 1:10
Coxsackie B virus antibodies (BI-B6)	< 1:10	< 1:10
Dengue IgM antibodies	Negative	Positive or negative
Dengue IgG antibodies	Negative	Positive or negative
Malaria thick and thin smears	Negative	Positive or negative
Leptospirosis IgM antibodies	Negative	Positive or negative
Mycoplasma IgM antibodies	Negative	Positive or negative
Mycoplasma IgG antibodies	Negative	Positive or negative
Urine Legionella antigen	Negative	Positive or negative
Heterophile antibody test	Negative	Positive or negative
Epstein-Barr virus IgM antibodies	Negative	Positive or negative
Epstein-Barr virus IgG antibodies	Negative	Positive or negative
Cytomegalovirus IgM antibodies	Negative	Positive or negative
Cytomegalovirus IgG antibodies	Negative	Positive or negative
Stool clostridium difficile toxin A/B	Negative	Positive or negative
Antistreptolysin O Titer	90 IU/mL	0-200 IU/mL
Immunologic and rheumatologic panel		
Antinuclear factor	Negative	Positive or negative
Anti-double stranded deoxyribonucleic acid antibodies	<30.0 U/mL	<30.0 U/mL (negative)
C3	190 mg/dL	83-193 mg/dL
C4	43 mg/dL	15-75 mg/dL
Anti-cyclic citrullinated peptide antibodies	<20.0 U/mL	<20.0 U/mL (negative)
Rheumatoid factor	Negative	Positive or negative
Extractable nuclear antigen panel including anti-RNP, -Ro, -La, -SCL-70, -Jo1, and -centromere	All negative	Positive or negative
Perinuclear anti-neutrophil cytoplasmic antibodies	5.42 U/mL	< 10.0 U/mL (negative)
Cytoplasmic anti-neutrophil cytoplasmic antibodies	3.73 U/mL	< 10.0 U/mL (negative)
Cryoglobulin blood test	Negative	Positive or negative

Table 2. Criteria for Diagnosis of Kawasaki Disease.⁸⁻¹⁰

Fever ≥ 5 days and ≥ 4 days of the following:

- Rash: diffuse maculopapular eruption, diffuse erythroderma, or erythema multiforme-like rash
- Conjunctivitis: bilateral bulbar conjunctival injection without exudate
- Cervical lymphadenopathy: usually unilateral, ≥ 1.5 cm lymph node, anterior cervical triangle
- Extremity changes: erythema and edema of the hands and feet in acute phase, desquamation of the fingers and toes usually begin in the periungual region in subacute phase
- Oral changes: erythema and cracking of lips, strawberry tongue with erythema, and prominent fungiform papillae, diffuse erythema of the oropharyngeal mucosa

South Asian ethnicity; and currently, there exists a paucity of literature with regard to this subgroup. In many developing countries, including India, the majority of patients with KD continue to remain undiagnosed likely attributed to lack of awareness among clinicians.¹³ Adult-onset KD should be considered as a differential diagnosis in challenging cases presenting as infectious or autoimmune disease even if the patient is not of East Asian lineage.¹³⁻¹⁵

The key therapeutic strategy for KD is to prevent the formation of CAAs and symptom alleviation. Inpatient supportive management and administration of intravenous immunoglobulin (IVIG) is considered to be the mainstay of treatment.¹⁶⁻¹⁸ Currently, there are several risk scores for IVIG resistance that could identify patients at high-risk for nonresponse to IVIG treatment, which in turn is highly associated with the development of CAAs.¹⁹⁻²¹

American Heart Association (AHA) guidelines recommend a second dose of IVIG, methylprednisolone, a longer tapering course of prednisolone or prednisone plus IVIG, cyclosporine, immunomodulatory monoclonal antibody therapy, cytotoxic agents, or plasma exchange for patients resistant to IVIG.^{10,18,22}

Aspirin has been the conventional, standard therapy for its antiplatelet effects, initially a high-dose regimen for a variable period, followed by a lower dose for a protracted period in patients with small CAAs, whereas dipyridamole is indicated in patients with larger CAAs.²³ It is recommended by the AHA guidelines that these patients should be treated with low-dose aspirin until aneurysms are documented to have regressed. Clopidogrel has also been used in cases of aspirin hypersensitivity.⁴

As of 2017, the AHA and the Japanese Circulation Society guidelines specify that KD patients require vigilant follow-up with noninvasive imaging and cardiac stress testing and to detect progressive stenosis, thrombosis, and luminal occlusion that may lead to myocardial ischemia and infarction.^{10,24,25}

The literature is not replete with describing this subpopulation of incomplete KD with regard to age and ethnicity and this case emphasizes its rarity, but also underscores the absolute necessity for specific guidelines in this patient panel.²

Conclusion

In summary, we describe the first case report of incomplete KD in an adult South Asian patient based in the Caribbean.

The multidisciplinary team should be vigilant for this oligo-symptomatic clinical presentation, specifically within this subpopulation despite age and ethnicity, and the syndrome should be considered as a differential diagnosis in challenging cases presenting as infectious or autoimmune disease.

Author Contributions

NB, RS, SV, NM, VM, SG, and NAS all contributed equally in writing the manuscript. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

The patient provided written informed consent to have the details of his case published.

References

1. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children [in Japanese]. *Arerugi*. 1967;16:178-222.
2. Gomard-Menesson E, Landron C, Dauphin C, et al. Kawasaki disease in adults: report of 10 cases. *Medicine (Baltimore)*. 2010;89:149-158. doi:10.1097/md.0b013e3181df193c.
3. Yanagawa H, Nakamura Y, Yashiro M, et al. Results of the nationwide epidemiologic survey of Kawasaki disease in 1995 and 1996 in Japan. *Pediatrics*. 1998;102:E65.
4. Rowley AH, Shulman ST. Pathogenesis and management of Kawasaki disease. *Expert Rev Anti Infect Ther*. 2010;8:197-203. doi:10.1586/eri.09.109.
5. Mitani Y. Functional and structural alterations of coronary arteries late after Kawasaki disease and the risk of acute coronary syndrome in adults. In: Saji BT, Newburger JW, Burns JC,

- Takahashi M, eds. *Kawasaki Disease. Current Understanding of the Mechanism and Evidence-Based Treatment*. Tokyo, Japan: Springer; 2016:421-425. doi:10.1007/978-4-431-56039-5_44.
6. Nakamura Y, Yashiro M, Uehara R, Oki I, Kayaba K, Yanagawa H. Increasing incidence of Kawasaki disease in Japan: nationwide survey. *Pediatr Int*. 2008;50:287-290. doi:10.1111/j.1442-200X.2008.02572.x.
 7. Holman RC, Curns AT, Belay ED, Steiner CA, Schonberger LB. Kawasaki syndrome hospitalizations in the United States, 1997 and 2000. *Pediatrics*. 2003;112(3 pt 1):495-501.
 8. Sánchez-Manubens J, Bou R, Anton J. Diagnosis and classification of Kawasaki disease. *J Autoimmun*. 2014;48-49:113-117. doi:10.1016/j.jaut.2014.01.010.
 9. Wolff AE, Hansen KE, Zakowski L. Acute Kawasaki disease: not just for kids. *J Gen Intern Med*. 2007;22:681-684. doi:10.1007/s11606-006-0100-5.
 10. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation*. 2017;135:e927-e999. doi:10.1161/CIR.0000000000000484.
 11. Sève P, Stankovic K, Smail A, Durand DV, Marchand G, Broussolle C. Adult Kawasaki disease: report of two cases and literature review. *Semin Arthritis Rheum*. 2005;34:785-792. doi:10.1016/j.semarthrit.2005.01.012.
 12. Falcini F, Ozen S, Magni-Manzoni S, et al. Discrimination between incomplete and atypical Kawasaki syndrome versus other febrile diseases in childhood: results from an international registry-based study. *Clin Exp Rheumatol*. 2012;30:799-804.
 13. Inokuchi R, Kurata H, Harada M, et al. Coronary artery aneurysms after adult-onset Kawasaki disease. *Circulation*. 2013;127:1636-1637. doi:10.1161/CIRCULATIONAHA.112.130153.
 14. Shulman ST. Early steroid therapy reduces Kawasaki disease coronary complications. *J Pediatr*. 2017;182:401-404. doi:10.1016/j.jpeds.2016.12.065.
 15. Kontopoulou T, Kontopoulos DG, Vaidakis E, Mousoulis GP. Adult Kawasaki disease in a European patient: a case report and review of the literature. *J Med Case Rep*. 2015;9:75. doi:10.1186/s13256-015-0516-9.
 16. Newburger JW, Takahashi M, Beiser AS, et al. A single intravenous infusion of gamma globulin as compared with four infusions in the treatment of acute Kawasaki syndrome. *N Engl J Med*. 1991;324:1633-1639. doi:10.1056/nejm199106063242305.
 17. Newburger JW, Takahashi M, Burns JC, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. *N Engl J Med*. 1986;315:341-347. doi:10.1056/nejm198608073150601.
 18. Saji BT, Newburger JW, Burns JC, Takahashi M, eds. *Kawasaki Disease: Current Understanding of the Mechanism and Evidence-Based Treatment*. New York, NY: Springer; 2016:552. <https://market.android.com/details?id=book-HZPqDAAAQBAJ>.
 19. Wallace CA, French JW, Kahn SJ, Sherry DD. Initial intravenous gammaglobulin treatment failure in Kawasaki disease. *Pediatrics*. 2000;105:E78.
 20. Hashino K, Ishii M, Iemura M, Akagi T, Kato H. Re-treatment for immune globulin-resistant Kawasaki disease: a comparative study of additional immune globulin and steroid pulse therapy. *Pediatr Int*. 2001;43:211-217. doi:10.1046/j.1442-200x.2001.01373.x.
 21. Han JW. Factors predicting resistance to intravenous immunoglobulin and coronary complications in Kawasaki disease: IVIG resistance in Kawasaki disease. *Korean Circ J*. 2018;48:86-88. doi:10.4070/kcj.2017.0376.
 22. Chen S, Dong Y, Kiuchi MG, et al. Coronary artery complication in Kawasaki disease and the importance of early intervention: a systematic review and meta-analysis. *JAMA Pediatr*. 2016;170:1156-1163. doi:10.1001/jamapediatrics.2016.2055.
 23. Baumer JH, Love SJL, Gupta A, Haines LC, Maconochie I, Dua JS. Salicylate for the treatment of Kawasaki disease in children. *Cochrane Database Syst Rev*. 2006;(4):CD004175. doi:10.1002/14651858.CD004175.pub2.
 24. Denby KJ, Clark DE, Markham LW. Management of Kawasaki disease in adults. *Heart*. 2017;103:1760-1769. doi:10.1136/heartjnl-2017-311774.
 25. Gersony WM. The adult after Kawasaki disease the risks for late coronary events. *J Am Coll Cardiol*. 2009;54:1921-1923. doi:10.1016/j.jacc.2009.06.057.