Case Report

Incomplete Kawasaki Disease in an Adult South Asian Patient

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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 (CAAs). “Incomplete” Kawasaki disease is a novel concept and considered a diagnosis of exclusion as it alludes to patients with fever lasting \( \geq 5 \) 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). 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. The pathophysiology involves a complex inflammatory milieu with a predilection for small- to medium-sized arteries, especially the coronary vessels. It is estimated that there are approximately 10 000 incident cases per year in Japan alone and 4000 in the United States. 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.

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 \( \geq 5 \) days and 2 or 3 clinical criteria without another reasonable explanation for the illness. 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.

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

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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 gastroprotective 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). 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. 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. 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

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.
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 × 103/µL    | 156-373 × 103/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 U/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       |
| Veneral 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          |
| Adenovirus antibodies (6,7,9,11, and 30)                    | Negative         | Positive or negative          |
| Echovirus antibodies (B1-B6)                                | <1:10            | <1:10                         |
| Coxsackie B virus antibodies (B1-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          |
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. 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.成人期Kawasaki病应被视为感染或自身免疫性疾病的一个可能诊断，即使患者不属于东亚族裔。

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. 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.

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.

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. 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.

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.

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.

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 oligosymptomatic 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.

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 erthema 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 |

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