A 19 Year Old With Fever, Rash, and Conjunctivitis: A Connection With the Heart

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CASE REPORT

The patient was a 19-year-old African American male who presented to the hospital with complaints of fever, diffuse maculopapular rash (chest, bilateral upper extremities, and back), bilateral conjunctivitis, and abdominal pain. His symptoms began approximately 3 weeks prior to presentation to our hospital. Over the 3-week period he developed a constellation of symptoms to include a polymorphous eruption, right facial nerve palsy, and bilateral conjunctivitis (Figure 1). Before presenting to our hospital, he had multiple evaluations that included near normal evaluation including a normal head computed tomography (CT) scan, mildly elevated liver-associated enzymes (LAEs), negative human immunodeficiency virus, and syphilis serologies.

On presentation to our facility he was febrile to 38.3°C, and his exam was notable for right facial palsy, edematous lips, and enlarged erythematous tongue with raised papilla (Figure 1). He also exhibited a mild leukocytosis, sterile pyuria, and elevated lipase and erythrocyte sedimentation rate (ESR) (Table 1). He was admitted for further evaluation and management. Infection, drug reaction, and rheumatologic process were all considered in the differential, and the various studies (laboratory tests, radiographs, electrocardiogram, and transthoracic echocardiogram [TTE]) performed to evaluate for these causes did not identify a clear etiology (Table 1). His abdominal pain, facial nerve palsy, and edematous lips and tongue improved with supportive care, and he was discharged with plans for follow-up examination.

He was readmitted 6 days later with continued temperatures to 38.0°C (despite scheduled acetaminophen) and continued nonpurulent conjunctivitis. In addition, he now also had new severe bilateral lower extremity pain, swelling of bilateral ankle and feet, and desquamation of his palms and soles with notable periungual desquamation (Figure 1). This constellation of symptoms was suggestive of Kawasaki’s disease (KD). Laboratory markers were also supportive of the diagnosis leukocytosis (13.8 × 10³/µL), normocytic anemia (11 g/dL), thrombocytosis (535 × 10³/µL), elevated markers of inflammation (ESR, 94 mm/hour and C-reactive protein, 18 mg/dL), and elevated LAEs (alanine aminotransferase, 111 U/L and aspartate aminotransferase, 62 U/L).

The second day of this admission, he developed complaints of dull substernal chest pain. A repeat TTE was performed and compared to one obtained a week prior. A new left anterior descending coronary artery dilatation and ectatic vessels were noted (Figure 2).

Given the coronary artery changes, treatment for KD was deemed necessary. The patient was given intravenously administered immunoglobulin (2 mg/kg) and high-dose aspirin (50 mg/kg per day). As is typical with pediatric patients, our patient defervesced 1 day after initiation of therapy with dramatic overall clinical improvement. After 3 days, he was subsequently transitioned to 81 mg of aspirin per day. He had continued follow-up tests with CT angiography performed 4 months later, which showed normal coronary arteries without any evidence of aneurysmal changes. At that time, aspirin was discontinued and the patient was advised to arrange follow-up visits with the cardiology department annually.

KD is a systemic vasculitis of unknown etiology that usually affects infants and children, with 76% of the cases in children in the United States occurring in individuals below the age of 5 [1]. Adult cases are far less reported, with approximately 100 cases reported in
the literature, including both complete and incomplete or atypical KD [2–4].

The diagnosis of KD, particularly in adults, can be challenging and possibly underdiagnosed because the clinical manifestations can present as a varying constellation over time and the diagnosis is hampered by the lack of a sensitive and specific test [4].

KD affects multiple organ systems, with a wide range of clinical and laboratory findings associated with the core diagnostic features [1, 5]. Our patient had many of the more typical symptoms to include: coronary artery abnormalities, diarrhea, abdominal pain, hepatic dysfunction, irritability, sterile pyuria, elevated inflammatory markers, anemia, leukocytosis, and thrombocytosis. In addition, our patient had a few atypical rare manifestations of KD such as right facial nerve palsy and pancreatitis [3, 5–7].

Cardiovascular sequelae are of greatest concern in KD. Up to 20% of pediatric cases and 5% of adult cases progress to coronary aneurysmal disease [8]. Several risk scores for predicting aneurysms have been reported in the literature; however, their applicability in adults is not known [9]. Cardiac imaging should be performed in all patients with KD. Subsequent follow-up examination and management are stratified based on the severity and progression of the coronary changes ranging from no long-term antiplatelet therapy with 5-year follow up to long-term antiplatelet therapy and 6- to 12-month reevaluation. In general, for individuals with transient ectasia (ie, lasting 6–8 weeks), such as our patient, antiplatelet therapy for 6–8 weeks, cardiovascular risk assessment, and counseling at 3- to 5-year intervals are recommended [1], whereas those with ≥1 large coronary aneurysm should undergo long-term antiplatelet therapy and 6-month follow-up examination.

| Test              | Week 3–Admission | Week 4–Readmission | Week 12–Follow up |
|-------------------|------------------|--------------------|-------------------|
| WBC (×10³/µL)    | 11.8             | 13.8               | 5.1               |
| Hemoglobin (g/dL)| 12               | 11                 | 11.2              |
| Platelets (×10³/µL)| 374             | 535                | 369               |
| AST/ALT(U/L)     | 24 of 50         | 64 of 111          | 17 of 25          |
| ESR (mm/h)       | 64               | 94                 | –                 |
| CRP (mg/dL)      | –                | 18                 | 5.3               |
| Lipase (U/L)     | 1031             | 26                 | –                 |
| Ferritin (ng/mL)| 521              | 693                | –                 |
| Infectious work up* | –            | IgG positive (mycoplasma and mumps) | – |
| Rheumatology work up* | –            | Negative (mycoplasma and mumps) | – |

Abbreviations: ALT, alanine aminotransferase; ANCA, antineutrophil cytoplasmic antibodies; AST, aspartate aminotransferase; CRP, C-reactive protein; DS, double-stranded; ELISA, enzyme-linked immunosorbent assay; ENA, extractable nuclear antigens; ESR, erythrocyte sedimentation rate; HIV, human immunodeficiency virus; Ig, immunoglobulin; Lab, laboratory; PCR, polymerase chain reaction; WBC, white blood cells.

*HIV ELISA and viral load; rapid plasma reagin; blood, urine, and throat bacterial cultures; respiratory viral culture (adenovirus, respiratory syncytial virus, influenza, and parainfluenza); influenza PCR; enterovirus stool culture; lyme ELISA; cytomegalovirus IgM and IgG; Epstein-Barr virus IgM and IgG; herpes simplex virus IgM and IgG; chlamydia/chronicgia NAAT (urine, pharyngeal, and rectal); parvovirus IgM and IgG.

*Antinuclear antibody; ENA antibodies (Smith, SSA, SSB, Jo-1, SCL-70); DNA DS antibody; ANCA (proteinase 3 antibody and myeloperoxidase antibody).

Figure 1. Physical exam findings are as follows: (A) conjunctival injection; (B) edematous lip and tongue, raised papilla; (C) erythematous papular rash; (D) edematous feet with bilateral desquamation, close up in right lower inset.

Figure 2. Transthoracic echocardiogram illustration: aortic valve (AoV); 1. left anterior descending artery (LAD) dilated 4.55 mm; 2. normal left circumflex; 3. left main coronary artery (LMCA) dilated 5.76 mm. Echobrightness around left LMCA and LAD.
In conclusion, KD can be difficult to diagnose in the adult population, but it should be considered in patients with persistent fever, systemic inflammation, multisystem findings suggestive of a vasculitis, and otherwise negative work up. Some of the more common clinical finding in adult cases of KD include adenopathy, hepatitis, and arthralgias [8]. Some studies in the work up may need to be repeated if clinical presentation changes, such as repeat TTE as in our patient who developed coronary changes over time. The etiology of KD remains unclear. Although underlying infectious etiologies and triggers have been postulated, they remain highly controversial at this time [10].

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